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Des Jarlais, Don C.; Sypsa, Vana; Feelemyer, Jonathan; Abagiu, Adrian O.; Arendt, Vic; Broz, Dita; Chemtob, Daniel; Seguin-Devaux, Carole; Duwve, Joan M.; Fitzgerald, Margaret; Goldberg, David J.; Hatzakis, Angelos; Jipa, Raluca E.; Katchman, Eugene; Keenan, Eamon; Khan, Ibrahim; Konrad, Stephanie; McAuley, Andrew; Skinner, Stuart; Wiessing, Lucas

Published in: The Lancet HIV

DOI:

10.1016/S2352-3018(20)30082-5

Publication date: 2020

Document Version Author accepted manuscript

Link to publication in ResearchOnline

Citation for published version (Harvard):
Des Jarlais, DC, Sypsa, V, Feelemyer, J, Abagiu, AO, Arendt, V, Broz, D, Chemtob, D, Seguin-Devaux, C, Duwve, JM, Fitzgerald, M, Goldberg, DJ, Hatzakis, A, Jipa, RE, Katchman, E, Keenan, E, Khan, I, Konrad, S, McAuley, A, Skinner, S & Wiessing, L 2020, 'HIV outbreaks among people who inject drugs in Europe, North America and Israel', *The Lancet HIV*, vol. 7, no. 6, pp. E434-E442. https://doi.org/10.1016/S2352-3018(20)30082-5

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Download date: 24. Apr. 2022

A Comparative Analysis of Recent HIV Outbreaks among People Who Inject Drugs in Europe, North America and Israel

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Abstract

During 2011-2016, HIV outbreaks occurred among people who inject drugs (PWID) in Athens, Greece; Bucharest, Romania; Dublin, Ireland; Glasgow, Scotland; Luxembourg; southeastern Saskatchewan, Canada; Scott County, Indiana, United States; and Tel Aviv, Israel. Factors common to several many of these outbreaks included: community economic problems, homelessness, and changes in drug injection patterns. The outbreaks differed in size (from under 100 to over 1000 newly reported HIV cases among PWID) and in the extent to which combined prevention had been implemented prior, during and after the outbreaks. Countries need to ensure high coverage of HIV prevention services; coverage higher than current UNAIDS recommendation may be needed in areas in which short acting drugs are injected. In addition, monitoring of PWID with special attention for changing drug use patterns, risk behaviors and vulnerable subgroups, such as homeless PWID, needs to be in place to prevent or rapidly detect and contain new HIV outbreaks.

Funding: This work was supported through grant R01DA003574, from the US National Institute on Drug Abuse.

Keywords: People who inject drugs (PWID), HIV, Outbreaks, Harm Reduction, Opioid substitution treatment (OST), Needle and syringe programmes (NSP)

Introduction

Three generations of HIV epidemics among people who inject drugs (PWID) can be identified. The first occurred in the late 1970s to early 1980s, before there was awareness of HIV/AIDS among PWID as a global public health problem. Examples include New York (peak seroprevalence in the early 1980s of 55-60%), Amsterdam (peak seroprevalence in 1986-87 of 34%), and Edinburgh (peak seroprevalence in the mid-1980s of 65%).

The second generation of outbreaks occurred during the late 1980s through the 1990s after development of the antibody test had been developed and after it was known that HIV outbreaks and HIV transmission among PWID could be controlled through large-scale syringe access programs and through developing trusting relationships between PWID and local public health authorities. Locations experiencing HIV epidemics among PWID during this period include France (1993), Italy (1994), Portugal (1995), Spain (1994), and Vancouver, Canada (1997) as well as Ireland, the Netherlands and Finland (before 2001) and Eastern Europe 6.7

By 2000, however, the practice of "combined prevention and care for HIV among PWID" as well as the concept of "monitoring intervention coverage" had been fully developed. Combined prevention and care emphasizes simultaneous, high coverage implementation of needle and syringe programs (NSP), opioid substitution treatment (OST), and antiretroviral treatment (ART) for HIV infection, within a "harm reduction" framework. The combined prevention approach has been successful in preventing outbreaks in many areas and has also been used effectively to interrupt transmission of HIV in high prevalence epidemics among PWID. Policy of the programs of HIV in high prevalence epidemics among PWID.

Despite the many successes of combined prevention and the large evidence base for preventing HIV transmission among PWID, we are now in a third generation of HIV outbreaks among PWID in high-income countries (examples include Estonia, Finland, Iceland, Lithuania and

In this report we present a review of eight outbreaks of HIV that were confined to PWID and their sexual partners in Europe, North America and Israel between 2011-2016. For the purposes of this paper, we used a World Health Organization (WHO) definition of an outbreak: "A disease outbreak is the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season".

Search strategy and selection criteria for identifying HIV outbreaks:

A research group of public health professionals working on outbreaks of HIV among PWID in the WHO European region and North America was formed by the European Monitoring Center for Drugs and Drug Addiction (EMCDDA) to conduct a review of recent HIV outbreaks in high income settings.¹⁹ Contacts were established with North-American HIV surveillance organizations (CDC in US and Health Canada) leading to identification of additional outbreaks. Data and related information about HIV outbreaks reported in conferences and in scientific journals were collected from experts in each of the HIV outbreak locations (see references (20-42) for publications documenting HIV outbreaks for each location) [Panel 1]. Case histories of the individual outbreaks were first prepared by researchers who had investigated the outbreaks. A standardized template [Appendix, Figure 2] was then developed for structured comparisons of the outbreaks. The template included the following variables for each outbreak: dates, size, prior conditions, potential precipitating factors, vulnerable subgroups of PWID, and public health responses for the outbreaks. The researchers from each location were asked to compile information for better understanding the outbreaks. Data were compiled from publications, conference presentations, unpublished reports, and local expert opinion. A mixed quantitative/qualitative synthesis was developed through successive rounds of data analyses and

interpretation among members of the group. Data were aggregated into three tables, detailing the outbreak with respect to 1) methods used to identify the outbreaks; 2) interventions to contain the outbreaks, and 3) HIV outbreak case details for each location.

Descriptions of HIV outbreaks and methodology in identifying outbreaks in different locations

Between 2011-2016, HIV outbreaks occurred among PWID in *Athens*, Greece; ²⁰⁻²⁸, *Bucharest*, *Romania*, ²⁷⁻³¹ *Dublin*, *Ireland*; ^{32,33} *Glasgow*, *Scotland*; ^{34,35} *Luxembourg*; ^{36,37} *Saskatchewan*, *Canada*, ^{38,39} *Scott County*, *Indiana*, *United States*; ^{40,41} *and Tel Aviv*, *Israel*. ⁴²
All sites (8/8) reported having HIV case reporting in place, which in most cases was the key system detecting the outbreak [Table 1]. All sites except one (Southeastern Saskatchewan) had an estimate of the PWID population available, showing a very large range in estimated population sizes (range 500 – 20·000 (in the country)). Contact tracing was performed in 6 of the 8 sites (not in Athens and Luxembourg). In 2 of the 8 sites a cohort study was set up to follow trends in incidence and identify risk factors (Athens and Tel Aviv). ²² In 6 of the 8 sites a cross-sectional study was set up to examine risk factors for HIV seropositive status (not in Bucharest and Tel Aviv). Both qualitative interviews with various stakeholders and phylogenetic analyses of HIV cases were performed in all 8 of the sites. Among the outbreaks, all of them occurred in high-income countries except for the outbreak in Romania (a high middle-income country).

Interventions that were used to contain HIV outbreaks

All of the sites implemented multiple interventions, with almost all sites implementing or increasing coverage of standard "combined prevention" of NSP, OST, and ART [Table 2]. As described in the publications from the sites and case histories [Appendix, pg. 1-4], there was considerable variation in the time needed to implement the various interventions and in the

current level of coverage of the interventions. Implementation of the interventions often occurred over years; for example, there was important community resistance and hostility to implementing interventions in Scott County.

Details of the individual outbreaks

Rates of newly reported cases pre-outbreak ranged from less than 1 case to 20 cases per year, increasing to 16-525 cases during the peak year(s) of the outbreaks, then decreasing to 2-108 cases per year at the end of 2018 [Table 3]. Seven of the 8 sites expanded testing for high-risk populations or PWID, which most likely resulted in a more pronounced peak of cases detected [Table 2]. While there were great similarities in the methods used to assess the outbreaks [Table 1] and in the interventions implemented to contain the outbreaks [Table 2], there was wide variation in the current status of the outbreaks [Table 3]. In some outbreaks (Tel Aviv, Luxembourg), the current rate of new cases is back at or close to the pre-outbreak level, while in others (Athens, Bucharest, Glasgow) the current rate of new cases in 2018 was still higher than the pre-outbreak rate.

Further information collected included an estimate of the level of combined prevention coverage (OST, NSP, ART) at the time of the outbreak, community economic problems associated with the outbreak, changes in drug use patterns and information on highly vulnerable groups [Table 3].

Sizes of the different HIV outbreaks:

The size of the different outbreaks is a critical epidemiological characteristic that requires some consideration. Larger outbreaks clearly involve greater burdens of disease, greater possibilities of ongoing injecting drug use and sexual transmission, greater need for resources for controlling the

outbreak, and, to the extent that HIV seropositive PWID may travel to other areas, a greater likelihood of new HIV transmissions in those areas.

Precise quantification of the size of these outbreaks is difficult for at several reasons. First, HIV testing and surveillance was limited in many sites prior to the outbreaks, so that the pre-outbreak rates were likely to have been underestimated. Second, a number of outbreaks have not "ended" in terms of the rates of new diagnoses returning to pre-outbreak levels in many of the sites.

Third, the number of identified cases also depended on the level of testing implemented in each site. Despite these difficulties, we consider four outbreaks—Athens, Bucharest, Glasgow, and Scott County—to have been "large," with at least 150 new HIV diagnoses above "pre-outbreak" rates. In none of these large outbreaks has the rate of new HIV diagnoses returned to the pre-outbreak level [Table 3].

In three of the large outbreaks, Athens, Bucharest, Glasgow, the estimated size of the local PWID population was relatively large, 5.000 or more. In Scott County, however, the estimated local PWID population was moderate—500 to 600. A large local PWID population increases the likelihood of a large outbreak but is not a necessary condition. Note also that the Tel Aviv outbreak was not large, even though the estimated PWID population (20.000) for the entire country was certainly quite large.

Common factors among the outbreaks

Four common factors can be distinguished among the outbreaks [Table 3]:

1) Limited prevention at the time of the outbreak, with low or declining service provision across most, but not all, sites [Table 3].

In Scott County there was no OST, no ART and syringe exchange was non-existent and illegal.

In Bucharest, HIV prevention services had been based on international (Global Fund) funding

which was interrupted. In Athens, the coverage of harm reduction programs was very low with an estimated coverage of around 16 syringes per PWID per year (in 2010), and had a OST coverage of around 21% with a seven-year waiting list.²³ In Tel Aviv service provision was high but declined pre-outbreak. Community economic problems also led to reductions in HIV prevention services prior to the outbreak in Dublin. Saskatchewan had medium coverage for prevention services for PWID in the outbreak area; however, these services were concentrated in urban centers and indigenous PWID who lived on reservations likely did not access these services at the same rate as PWID who lived in the urban centers.

2) Homelessness

There was a distinct concentration of new HIV infections among homeless PWID in 6 of the 8 outbreaks (except in Bucharest and Scott County). Additionally, homelessness was identified as a risk factor for being HIV positive and for HIV seroconversion during the outbreak in Athens. ^{22,24,25} In Glasgow, the City Centre contained many homeless PWID, a large proportion of whom (~60%) had a history of frequent (greater than 5 times) incarceration, and whose situation may have been negatively impacted due to austerity budgets. ⁴³

3) Community economic problems

Seven of the eight outbreaks were preceded by severe economic problems in the community, while in Luxembourg, although there were no generalised economic problems the economic situation of PWID deteriorated pre-outbreak. It is likely that these economic problems contributed to increased homelessness and other social problems among PWID as well as to decreasing levels of combined prevention. Three of the largest outbreak sites also experienced severe economic difficulties: Athens (and all of Greece) had experienced a severe recession, leading to large reductions in public health services.⁴⁴ The recession in Greece coincided with

economic problems in other Mediterranean and Middle Eastern countries, and with migration of PWID from those countries to Greece. Some of these migrant PWID were HIV seropositive and started HIV transmission chains in Athens in addition to the transmission chains among native Greek PWID.⁴⁴ Migrant PWID also constituted a vulnerable group, likely with low access to services due to their often illegal status, and subsequent analyses have shown that the majority of infections among them occurred postmigration.⁴⁵ Similar findings have been reported from Catalonia, Spain.⁴⁶

In Bucharest, most of the PWID who were infected with HIV were young men living in the suburbs with low socioeconomic status, and who had histories of incarceration. Scott County is an economically depressed area and was among the poorest counties in the state of Indiana in terms of both economic and health indicators. In Glasgow, austerity policies have potentially impacted the numbers of individuals experiencing homelessness and the services available to support them. ⁴³

4) Change in injection patterns

A third common factor was changes in drug injecting patterns, which occurred in 6 outbreaks. Where such changes occurred, they were in the direction of drugs with shorter effect duration, leading to more frequent injection, and much greater need for sterile injecting equipment. In Bucharest, short-acting new psychoactive substances ("bath salts") were injected. In Scott County, the change was from non-injecting use to injection of oxymorphone, prepared from dissolved prescription tablets. The large volumes of drug solution from the dissolved tablets often led to multiple injections within a single injecting episode.⁴¹

The factors associated with the Glasgow outbreak were the introduction of cocaine injection and homeless PWID as a highly vulnerable group with high (~60%) levels of frequent

incarceration.³⁴ Cocaine injection creates special problems for HIV prevention among PWID. OST is specific to opioid use disorders and would not be expected to have a major effect on cocaine injecting. Even the newly WHO recommended standard of 300 syringes/PWID/year⁴⁷ may not be adequate to prevent HIV transmission associated with cocaine injection. Because of the short duration of the effect of injected cocaine, persons may inject cocaine 10 to 20 in a day.^{48,49} Users often work together to purchase drugs, and then divide the drugs and inject together. If multiple injections occur in a group setting, it will be difficult to have sufficient supplies of sterile syringes to avoid sharing. Group injection of cocaine thus provides many opportunities for sharing, particularly if members confuse which syringe belongs to whom or if a syringe should become clogged/jammed [Panel 2].⁵⁰

The HIV prevention services prior to the Glasgow outbreak deserve additional comment. Glasgow had implemented HIV prevention for PWID in the 1980s and had a low rate of new HIV diagnoses prior to the outbreak [Panel 2].^{34,51} The outbreak in Glasgow has multiple similarities to the large HIV outbreak in Vancouver, Canada, in which increased cocaine injection was also followed by a great increase in HIV incidence.^{52,53}

PWID: In all of the sites, the rates of newly diagnosed cases of HIV among PWID were low prior to the outbreak. We have previously used the term "complacency" as a description of the attitude towards HIV prevention in several of the sites prior to the outbreaks, ⁵⁴ based on the mostly low or declining investments in and coverage of harm reduction (mainly OST and NSP), in what had always been low HIV prevalence settings. Scott County may be the clearest example of this complacency. Prior to the outbreak, Scott County had experienced an epidemic of opioid analgesic use that had transition from non-injecting to injecting use. Despite the transition to

injecting use, not only were there essentially no HIV prevention services for PWID; there were no NSPs, and NSPs were illegal. Athens, where HIV prevention programs existed at only a minimal level prior to the outbreak, is another example of complacency.

The budget reductions for HIV prevention services that occurred in some sites (Bucharest and Dublin) can be seen as a variant of complacency. There is a typical cycle in public health where funding for prevention efforts is reduced because there does not seem to be a current problem, only to see greatly increased numbers of cases after prevention efforts are reduced (see the case example of tuberculosis in the US).⁵⁵

We would also add that a complacency attitude can exist among frontline service workers and among PWID themselves as well as among public health officials and funding decision-makers. Prior to the outbreak, new cases of HIV among PWID were so rare in Glasgow (approximately 10 new cases/year in an estimated PWID population of approximately 9.000) that HIV prevention was no longer salient for the staff of drug service agencies nor for PWID. While complacency was common across these outbreak sites, it may not have been a factor in all sites. In Tel Aviv, OST was being expanded prior to the outbreak. The outbreak in Luxembourg also occurred without a reduction in HIV prevention services.

Lessons Learned II: Community economic problems and vulnerability to substance use and HIV risk: As noted above, community economic problems served as a rationale for reductions in HIV prevention services in many outbreak locations. There are other ways in which economic problems may have contributed to the outbreaks, such as in-migration of HIV seropositive PWID (Athens), increased unemployment, and increased homelessness (an individual-level risk factor for becoming HIV infected in 6 of the 8 outbreaks).^{5,46}

We were not able to collect information on the causal pathways for HIV transmission among homeless PWID in the outbreak sites. Previous studies of homeless PWID attending syringe exchange programs in various locations found higher rates of injecting risk behavior among homeless compared to stably housed PWID. 46,56-59 There are multiple ways in which homelessness may contribute to HIV transmission: homeless PWID may not have places to store sterile injection equipment, they may associate with large numbers of other homeless PWID and thus have many different injecting partners in short periods of time, and they are likely to have pressing competing priorities—obtaining food and shelter—in addition to safer injecting. 60-63 These findings suggest that combined HIV prevention measures for PWID may have to be broadened to focus on services for homelessness and other highly vulnerable groups of PWID. We would recommend that efforts to reduce homelessness among PWID be done within a "harm reduction/housing first" framework, in which people do not need to cease drug use before receiving services.

Lessons Learned III: The importance of changes in patterns of drug use: Changes in patterns of drug use occurred in 6 of the outbreak sites. In Scott County, the change was from non-injecting to injecting use of opioid analgesics. The other site changes were in the direction of shorter acting drugs (cocaine, "novel psycho-active substances") that generated higher frequencies of injection, so that previous supplies of sterile injecting equipment were probably no longer sufficient to control HIV transmission. Note that an earlier outbreak of HIV transmission occurred among PWID in Vancouver, Canada, occurred in association with a large increase in cocaine injection. ⁵² OST, which is a mainstay of HIV prevention among persons who inject opioids may have little utility for reducing injection of cocaine and other stimulant drugs. ⁴⁶

Lessons Learned IV: Need for a pro-active approach: In contrast to an attitude of complacency, we propose the need for a "pro-active" attitude towards continuation of low HIV incidence. A proactive attitude would include ongoing monitoring of levels of intervention coverage and quality (OST, NSP, ART), 8,65,66 of the social/economic environment of drug use, 67 of changes in patterns of drug use, and of changes in injecting and sexual risk behavior. 68 Monitoring a local drug use situation should include regular bio-behavioral surveys in addition to standard HIV and viral hepatitis case surveillance (apart from their own public health relevance, increases in viral hepatitis may act as an 'early warning sign' of increases in injecting risk prior to an HIV outbreak). Monitoring should also include regular evaluation (e.g. in stakeholder meetings at both local and national level) of 'soft' information from drug users, outreach workers, drug services, police and other 'front line' workers.

Monitoring particularly vulnerable subgroups such as homeless PWID or migrants and PWID not in contact with services is also of vital importance as these are the subpopulations likely to be affected first in the case of an outbreak. Community-based programs implementing chain-referral recruitment (e.g. Respondent-Driven Sampling) – such as the ARISTOTLE program in Athens ^{22,24,25} – or repeated cross-sectional studies as in Glasgow are suitable to identify these hard-to-reach subpopulations. Key factors to be monitored would include drugs being injected, particularly how often drugs were injected, risk behaviors, including sharing and injecting in group settings, ability to obtain and store adequate supplies of sterile injection equipment and sexual risks, e.g. sex work by homeless PWID. Rapid oral HIV testing might be used to detect new infections. The key concept in a proactive attitude is to expect and be prepared for changes in the local drug use situation. Another important element of a proactive attitude to monitoring PWID is continually addressing stigmatization of PWID and community resistance to providing

services to PWID, for example by meaningfully involving PWID representatives and community representatives in the planning and coordination of the monitoring system.

Finally, a pro-active attitude should also include contingency planning for rapidly containing any outbreak that is detected.

Need for further research

To our knowledge, this is the first comparative analysis of recent outbreaks of HIV infection among PWID in North America, Europe and Israel. This study included a modest number of outbreaks and most of the data were necessarily collected retrospectively. Despite these limitations, we identified a number of factors that occurred in many of the outbreaks: inadequate prevention programming prior to the outbreak, community economic problems, including homeless PWID as a highly vulnerable group, and changes in patterns of drug use. We have not yet identified causal pathways that would permit us to classify various factors as necessary or sufficient causes of an outbreak. There have been a number of additional recent HIV outbreaks among PWID, e.g., Lowell and Lawrence, Massachusetts, ⁶⁹ Seattle WA, ⁷⁰ West Virginia, ⁷¹ and Taiwan ⁷² that have occurred since this research project began. Such newer outbreaks need to be included in future analyses. It will also be critical to include comparisons with areas that have varying degrees of HIV prevention services, homelessness among PWID, and changes in patterns of drug use but have not experienced outbreaks in order to identify causal pathways for outbreaks.

Three particular questions of interest are: 1) what are the conditions that generate stable low HIV prevalence and very low HIV incidence in PWID populations? 2) What types of perturbations in a stable low prevalence/very low HIV incidence situation could generate outbreaks? The data presented here suggest inadequate HIV prevention services and/or reductions in HIV prevention

services, increases in homelessness, and changes in drug injection patterns all might facilitate outbreaks. And, 3) how can incipient HIV outbreaks within PWID populations be quickly identified and contained, particularly outbreaks due to changes in patterns of drug injection? Answering these questions will require a larger sample of outbreaks (which unfortunately is likely to be available soon), as well as analyses of sites where outbreaks have not occurred. Finally, this review suggests a need for re-examining the present technical guidelines for HIV prevention and care for PWID, particularly for situations in which cocaine or other short-acting drugs are being injected. Even a standard of one syringe/PWID/day (~300 syringes/year) may not be sufficient for short-acting drugs. Recommendations for OST may not be meaningful in situations where stimulant drugs are being injected. Specific guidelines for highly vulnerable sub-populations such as homeless PWID may be needed. That a large outbreak occurred in Glasgow, with its long history of effective HIV prevention, indicates the need for adapting HIV prevention guidelines to the current "outbreak era" that includes a wide variety of injected drugs and vulnerable subgroups such as homeless PWID.

Conclusions

Despite the success of combined prevention and care for HIV among PWID in many sites in North American and Europe, 73 multiple outbreaks of HIV among PWID have occurred over the last decade. While there is important variation among these outbreaks, common factors in many of the outbreaks have included inadequate or disrupted prevention services, community economic problems, changes in the patterns of drugs injected, and homeless PWID as a highly vulnerable subgroup. Long-term successful maintenance of low rates of new HIV infections among PWID needs to be based on: a pro-active attitude, high coverage of combined prevention programs (particularly for highly vulnerable sub-populations), continuous monitoring for

changes in the local drug use situation, and prior planning for addressing an outbreak.

Author contributions:

LW and VS conceived and assembled an EMCDDA working group to compare HIV outbreaks among people who use drugs in Europe. DDJ and DB assembled HIV outbreaks from North America. DDJ and JF wrote the different versions of the manuscript and LW and JF handled data management. AOA, VA, DB, DC, C S-D, JMD, MF, DJG, AH, DI, REJ, Eugene K, Eamon K, IK, SK, AM, VS, SS and LW all contributed data and important information for the particular HIV outbreaks included in the report. All co-authors were involved in revising the manuscript and all co-authors have approved the final manuscript for submission to the Lancet HIV.

Conflict of Interest:

Dr. Stuart Skinner reports grants and personal fees from Merck Canada, grants and personal fees from ViiV Healthcare, grants from Abbvie, grants and personal fees from Gilead Sciences, outside the submitted work. Dr Vana Sypsa reports grants and personal fees and non-financial support from Gilead Sciences, grants, and personal fees and non-financial support from Abbvie, outside the submitted work. Dr. Angelos Hatzakis reports grants from AbbVIE, GILEAD, and MSD, outside their submitted work. Dr. Joan Duwve reports grants from AbbVIE, Gilead, outside the submitted work.

Role of funding sources:

This work was supported through grant R01DA003574 from the US National Institute on Drug Abuse The funding agency had no role in the design, conduct, data analysis or report preparation for the study

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Panel 1 Search strategy details:

- We searched the literature and news reports for documentation of HIV outbreaks that occurred in among PWID in North America or the WHO European region (which includes Israel).
- Data for this review were identified through searches of MEDLINE, PUBMED, and Web of Science, as well as from references from relevant articles using the search terms "HIV," "Disease Outbreaks," and "Substance Abuse, Intravenous" or "Injection Drug Use."
- Articles that were published from 2009 to November 2019 were included.
- The unit of analysis was each outbreak site.
- A standardized template for data collection was developed for structured comparisons of the outbreaks. The first/initial template included the following variables for each outbreak: dates, size, prior conditions, potential precipitating factors, vulnerable subgroups of PWID, and public health responses for the outbreaks. The template was used to generate case histories for each outbreak.
- The template was refined and additional data collected through multiple rounds of data collection and analysis by the group members. The tables in the paper served as the final templates.

- Dates:
 - 2015-2019 (outbreak ongoing)
- Size:
- Over 160 new HIV cases among PWID (compared to typically 10 new diagnoses per year). HIV prevalence among PWID increased from 0.1% to 4.8% in Glasgow and from 1.1% to 10.8% in Glasgow city center during the outbreak.
- Almost all HIV cases were subtype C and had E138A and V179E mutations in the RT region that led to NNRTI resistance.
- Prior conditions/precipitating factors:
 - Transmission networks among a population who inject psychoactive drugs within Glasgow city center, with increased cocaine injecting (reaching up to 77% of PWID in 2017-2018).
- Highly vulnerable subgroups:
 - Homeless PWID, (approximately 45% of newly identified HIV seropositive PWID were homeless), with high levels of incarceration/involvement in the criminal justice system.
- Public Health Response/Current situation:
 - Education of the at-risk population and addiction services staff to increase awareness of the risks of HIV.
 - Increasing capacity of needle and syringe programs (e.g., greater evening availability), improving the frequency of HIV testing and its accessibility, and proactively supporting the early treatment of those newly diagnosed so as to reduce the risk of onward transmission.