



**HIV among people who inject drugs in Central and Eastern Europe and Central Asia: A systematic review with implications for policy**

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8 **HIV among people who inject drugs in Central and Eastern Europe and Central**  
9 **Asia:**  
10 **A systematic review with implications for policy**

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**ABSTRACT**

*Background and objectives:* HIV among people who inject drugs (PWID) is a major public health concern in Eastern and Central Europe and Central Asia. HIV transmission in this group is growing and over 27,000 HIV cases were diagnosed among PWID in 2010 alone. The objective of the systematic review was to examine risk factors associated with HIV prevalence among people who inject drugs (PWID) in Central and Eastern Europe and to describe the response to HIV in this population.

*Design:* A systematic review of peer-reviewed and grey literature addressing HIV prevalence and risk factors for HIV prevalence among PWID and a synthesis of key resources describing the response to HIV in this population. We used a comprehensive search strategy across multiple electronic databases to collect original research papers addressing HIV prevalence and risk factors among PWID since 2005. We summarised the extent of key harm reduction interventions and described the policy environments in which they are implemented by synthesising data from key sources.

*Studies reviewed:* Of the 5,644 research papers identified from electronic databases and 40 documents collected from our grey literature search, 70 documents provided unique estimates of HIV and 14 provided multivariate risk factors for HIV among PWID.

*Results:* HIV prevalence varies widely, with generally low or medium (<5%) prevalence in the Centre and high (>10%) prevalence in the East. We found evidence for a number of structural factors associated with HIV including gender, socio-economic position and contact with law enforcement agencies.

*Conclusions:* The HIV epidemic among PWID in the region is varied, with the greatest burden generally in the East. Data suggests that the current response to HIV among PWID is insufficient, and hindered by multiple environmental barriers including restricted access to services and unsupportive policy or social environments.

## ARTICLE SUMMARY

### *Article focus*

- A systematic review to identify and synthesise prevalence estimates and risk factors for HIV among PWID in Central and Eastern Europe and Central Asia.
- A summary of key data to describe the response to HIV among PWID in Central and Eastern Europe and Central Asia, including a brief characterisation of the policy environments.

### *Key messages*

- The review highlights that the HIV epidemic among PWID in the region varies from country to country, with Eastern European countries generally the worst affected. Prevalence is extremely high among PWID in many countries with some studies suggesting more than one in two PWID are infected with the virus in parts of Estonia, Russia and Ukraine.
- Despite few studies explicitly examining environmental factors, our review found that gender, socio-economic position and contact with law enforcement agencies to be associated with HIV prevalence. The complex interplay between the environment and individual behaviour of PWID is not fully understood and further emphasis on understanding the social epidemiology of HIV in this group is needed.
- An integrated package of needle exchange programmes (NSP), opiate substitution therapy (OST) and antiretroviral therapy (ART) is core to an effective response to HIV in this group. The coverage of such interventions in the region varies from low to non-existent and must be improved. Further resources coupled with improvement in the policy environments are key to reducing HIV transmission in this group.

### *Strengths and limitations of this study*

#### *Strengths*

- This review is the most comprehensive synthesis of HIV prevalence and risk factors among PWID in Central and Eastern Europe and Central Asia to date and is complemented by a clear synopsis of the state of the national policy environments and responses to HIV for people who inject drugs.

#### *Limitations*

- The quality of the review relies upon quality of the original articles, which are variable. The samples included are often selective as many studies recruited participants from specialist services or via drug user networks. Multivariate analyses are adjusted for a variety of factors, rendering direct comparisons between point-estimates difficult.
- The service coverage data is not measured in a standard fashion across the region, and is from different years. The quality of data varies hugely by country, thus undermining the comparisons we can make about coverage.
- The policy index is crude and is developed with binary indicators that cannot account for important nuances influencing inter-and intra-country environments.

## INTRODUCTION

The HIV epidemics of Europe are diverse but in all European countries HIV disproportionately affects populations that are socially marginalised and people whose behaviour is socially stigmatised or illegal. The epidemics in the East, which are predominantly associated with injecting drug use, are among the fastest growing in the world.[1] Over two thirds of all HIV diagnoses to date in Europe fall in the East, and over 70% of these emanate from Russia.[2 3] Over 27,000 new cases of HIV were attributed to injecting drug use in Central and Eastern Europe in 2010.[2 3] Almost all of these (99.6%) were made in the East of the region. Accounting for differences in absolute population size, between 2006 and 2010, 89 new HIV diagnoses associated with injecting drug use have been made on average each year in the East per million people. This contrasts with the Centre region where the rate is 100 times less at 0.8 per million.

Because of low access to and uptake of HIV testing and counselling – especially among the marginalised and stigmatised populations most at risk of HIV infection and transmission – not all HIV cases in Europe are diagnosed and reported. Estimates suggest that reported cases probably represent just over half of all people living with HIV in Europe. It is estimated that just over 2.3 million people were living with HIV in Europe in 2010, 840 000 in the West and 1.5 million in the East.[4]

There are an estimated 3.1 million people who inject drugs (PWID) in Central and Eastern Europe and Central Asia, of whom one million are estimated to be HIV infected.[5] In Russia alone, there are an estimated 1.8 million PWID, of whom around 700,000 are thought to be HIV infected.[5] Estimates of the prevalence of HIV among PWID in Central and Eastern Europe vary widely, from zero in some Central European countries where injecting drug use is less widespread, to over 20% in some countries in the East, including Estonia, Moldova, Russia, and Ukraine.[5 6]

HIV and other blood-borne infections contribute significantly to the excess morbidity and mortality experienced by PWID in Europe and elsewhere.[7 8] HIV has the potential to spread rapidly via the sharing of needles and syringes between PWID as well as via unprotected sex between PWID and their injecting and non-injecting partners.

### *The social contexts of HIV epidemics*

A growing body of work substantiates relationships between health harms related to drug use and social-material factors that shape vulnerability to HIV.[9-16] The heuristic of the HIV 'risk environment' envisages HIV risk as the product of reciprocal relationships between micro and macro level influences in the physical, social, economic, and policy environments which contextualise individual and community actions in relation to risk.[9-15] This interaction has been described as a reciprocal process whereby individual actions are constrained as well as enabled by their environments and in turn shape as well as reproduce those contexts.[17] Qualitative work among PWID in Russia, for example, has illustrated how reduced capacity for HIV risk reduction in the micro environment is shaped by street-level policing practices which are in turn contextualised by broader structural policies of criminalisation and cultural practices of marginalisation which taken together produce a collectively internalised fear and sense of constrained agency among PWID.[17 18]

Recent reviews have thus called for a shift towards social epidemiological approaches.[9-15] These investigate how the distribution of HIV in populations is in part shaped by 'social factors', that is, forces that extend beyond 'proximal' individual-level factors and their biological mediators. This simultaneously demands a shift from binary models of 'cause and effect' to 'multi-level' models, which enable HIV risk to be understood as an effect of multiple contributing factors, at once interacting together, including potentially in 'non-linear' and 'indirect' ways.[19] Delineating causal pathways to inform structural interventions is thus a daunting yet critical challenge. Recent evidence reviews suggest that currently the epidemiology of HIV among PWID rarely explicitly embraces the study of social determinants.[20]

The social and economic transitions transforming the Central and Eastern European region in the past twenty years have been abrupt, dramatic, and long lasting. In many countries of the region, economic uncertainty has combined with weakening social capital, an embryonic and fragile civil society, a poorly resourced and overly vertically-

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3 structured health system, and public policies tackling drug use that have emphasised law enforcement and security  
4 at the expense of public health.[16 21] Social and economic transformations following the dramatic political  
5 change in Eastern European countries have played a role in shaping transitions in problematic substance use as  
6 well as vulnerability to HIV.[21-26] The opening-up of international and trade borders, for instance, has facilitated  
7 population mixing as well as the development of heroin trafficking routes from Afghanistan to the West, also  
8 linked to the diffusion of heroin use.[27] There was evidence of explosive HIV outbreaks linked to injecting drug  
9 use in the former Soviet region by the mid 1990s, especially in Russia, Ukraine, and Moldova.[21]

### 11 *Enabling policy environments for HIV prevention*

12 Recognising HIV epidemics as features of their social and structural contexts emphasises the potentially pivotal  
13 role of social and structural interventions in creating environments which are enabling, rather than constraining, of  
14 evidence-based HIV prevention.[28-30] Key dimensions of 'enabling' policy environments conducive to effective  
15 HIV prevention for PWID include, but are not restricted to: the meaningful engagement of key stakeholders  
16 (including PWID) in policy formation and programming; a coordinated multi-sectoral national HIV prevention  
17 strategy emphasising an evidence-based public health and rights-oriented approach; the generation of research  
18 and surveillance on HIV epidemic spread and response; and the development and scale-up of a package of  
19 evidence-based interventions, including the removal of structural obstacles limiting their implementation.[31-33]  
20 This has led to calls to de-emphasise the criminalisation of PWID by developing policies emphasising public health  
21 above law enforcement dominated approaches, and for the rapid scaling-up of harm reduction interventions  
22 including syringe exchange, opioid substitution treatment (OST), and antiretroviral HIV treatment (ART), as well as  
23 community action and social support interventions.[31 32 34-36]

### 26 *Review scope*

27 We aim to systematically review epidemiological research investigating the burden of HIV, and associated risk  
28 factors, among PWID in Central and Eastern Europe. We seek to identify the extent to which such epidemiological  
29 research captures measures of the HIV risk environment by delineating HIV risk factors identified at the levels of  
30 the individual and environment. We situate this epidemiological work by synthesising current evidence reviews of  
31 the extent and availability of HIV prevention targeting PWID in the region and by developing a simple index of  
32 'enabling' policy environment at the country level.

## 36 **METHODS**

37  
38 We reviewed data from the 30 Eastern and Central European countries in WHO defined Europe, including 15 from  
39 Eastern Europe (Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic  
40 of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan), "the East", and 15 from  
41 Central Europe (Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Hungary, Macedonia  
42 (FYR), Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia, and Turkey), "the Centre".

### 45 *Search strategy and selection criteria*

46 We systematically searched Medline, Embase, Global Health, Social Science Citation Index, Popline, and CINAHL for  
47 studies published from 2005 to October 20, 2011. To identify articles we combine four broad search themes with  
48 the Boolean operator "AND". The first theme, HIV, combined the Medical Subject Headings (MESH) terms "HIV" or  
49 "HIV infections" with the free word search for "HIV", "human immunodeficiency virus" with "OR". The second  
50 theme, prevalence, incidence and risk factors, included the MESH terms "prevalence", "incidence", "risk", "factor  
51 analysis", "statistical", "regression analysis", "risk factors", "risk-taking", and "epidemiology" with the free words  
52 "prevalen\*", "incidence", "risk\*", "correlat\*", "determinant\*", "vulnerab\*", "regression", "risk", "(enhanc\*adj3)  
53 transmission", "multivar\*", "(route\*adj3 transmission)", "(factor\*adj3 transmission)", "social norm\*", "network",  
54 "socio-demographic", "socio-economic", "lifestyle", and "epidemiol\*" with "OR". The third theme, geographic  
55 coverage, included the names of the countries in the region, as well as the free word terms "Europe\*" and "Central  
56 Asia\*" combined with "OR". The fourth theme, PWID, combined the MESH terms "substance abuse",  
57 "intravenous", "needle sharing" and "heroin dependence" with the free word terms "IDU\*", "inject\*",  
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3 “intravenous”, “heroin”, “addict\*”, “opiate\*”, “narco\*”, “psychotropic\*”, “psychoactive\*”, “drug depend#n\*”,  
4 “(recreation\*adj3 drug\*)”, “harm reduction”, “syringe\*”, “methadone”, “opioid\*”, “syringe\*”, “(needle\*adj3  
5 shar\*)”, and “(illegal\*adj3 drug\*)” combined with “OR”.

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8 Additionally, we systematically searched websites of research institutes, service providers, and donor organisations  
9 working with PWID across the region including recent reports from countries reporting to the United Nations  
10 General Assembly Special Session on HIV/AIDS (UNGASS). We searched the website of the European Monitoring  
11 Centre for Drugs and Drug Addition (EMCDDA) for data and sources reported from member and neighbouring  
12 countries. Conference abstracts from the International Conference on the Reduction of Drug Related Harm (2005-  
13 2011) and the International AIDS Conference (2006, 2008, 2010) were also searched. Our review conformed to the  
14 PRISMA checklist for systematic reviews.[37]

### 15 16 *Study selection and eligibility criteria*

17 All abstracts were reviewed. Studies were excluded if they were: a) published before 2005; b) fell outside the  
18 defined geographic region; c) did not focus on HIV among PWID; d) did not sample PWID; or e) did not focus on  
19 bio-confirmed HIV prevalence or incidence, or injecting or sexual risk practices. Papers were also excluded if they  
20 contained no primary data, although the references were searched to gather primary studies not identified by the  
21 search. Papers not fitting the inclusion criteria were set aside to aid interpretation of the systematic review  
22 findings. Figure 1 summarises the papers searched and retained in the review.

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24 We assessed the quality of the studies reporting HIV prevalence estimates using a scoring system that graded the  
25 papers on: wide geographic coverage; most recent study; population sampled; and recruitment setting. We  
26 allocated up to three points each for most recent studies, population sampled, country coverage, and for the range  
27 of settings sampled, and deducted one point for drug treatment only samples due to the potential for bias.[38]

### 28 29 30 *Data extraction*

31 The results of the multivariate studies meeting our inclusion criteria were extracted as presented, regardless of the  
32 strength of association. Comparable factors were collected and examined using forest plots showing the effect  
33 estimates and 95% confidence intervals (95%CI). We classified the results of the multivariate studies as ‘individual-  
34 level’ factors or ‘environmental-level’ factors based on the proximity of the risk of the factor in terms of HIV  
35 transmission. Individual-level risk characteristics or activities included injecting and sexual risks, such as sharing  
36 needles or unprotected sex, that shape an individual’s HIV risk through direct biological mechanisms.  
37 Environmental-level factors are those which have no direct biological means of influencing HIV risk, however, their  
38 presence or absence has been identified as an independent factor in the risk faced by an individual, indicating their  
39 role in shaping a ‘risk environment’.

### 40 41 42 *Coverage of HIV prevention interventions*

43 In addition to the systematic review, data summarising the coverage of HIV prevention interventions was drawn  
44 primarily from recently published reviews [39] and previously published country level data[40]. These data are  
45 collected from a variety of sources, including UNGASS, WHO, and systematic reviews of scientific literature[39], as  
46 well as from routine national reports.[40]

### 47 48 *Policy environment index*

49 We generated a simple index of ‘enabling’ policy environment. Our interpretation of an enabling policy  
50 environment drew upon guidelines generated by WHO [41], UNAIDS,[42] international non-government  
51 organisations (NGOs),[43] and peer-reviewed papers in this field.[20 30 32 44] As outlined in Box 1, the core items  
52 of the index included indicators, at the country level, of: coordinated national strategy to HIV prevention and drug  
53 use (indicated by evidence of explicit inclusion of ‘harm reduction’ in national-level strategy, and monitoring and  
54 evaluating HIV epidemics); meaningful engagement of stakeholders in HIV prevention policy formation and  
55 programming (indicated by evidence of a national organisation of drug users); and evidence-based HIV prevention  
56 intervention approaches (indicated by presence of OST and NSP, presence of OST and NSP in prison settings, and  
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evidence of de-emphasising criminalisation through the use of administrative penalties for drug use possession for personal use).

#### [BOX 1]

Indicator data were obtained from a combination of sources, including: global reports of harm reduction policy and coverage;<sup>[45]</sup> country profiles collated and updated by the EMCDDA;<sup>[46]</sup> our systematic review of research studies (see above and Figure 1); and the International Network of People who Use Drugs<sup>[47]</sup>. The index was constructed by allocating equal weight to each of the six items and aggregating a score for each country, with higher scores indicating a more 'enabling' environment conducive to evidence-based public health approaches.

## RESULTS

### [FIGURE 1]

#### *HIV incidence*

Only three papers reviewed reported HIV incidence among PWID in this region. Two in Tallinn, Estonia, reported an HIV incidence rate of 31/100 person years (PY) in 2004, decreasing to 9/100 PY in 2009 among people injecting for less than three years.<sup>[48 49]</sup> The other from St Petersburg, Russia, reported a rate of 4.5/100 PY.<sup>[50]</sup>

#### *HIV prevalence*

Estimates of HIV prevalence among PWID vary widely throughout the region. A total of 79 sources reported HIV prevalence estimates (some multiple), of which 67 reported unique HIV prevalence estimates among PWID in the region; 44 from Eastern Europe and Central Asia<sup>[6 50-89]</sup> and 21 from Central Europe<sup>[90-110]</sup> and two that contained data from both regions.<sup>[40 111]</sup>

### [FIGURE 2]

Multiple estimates exist for many countries (Figure 2), and where this was the case we applied the scoring system described above (see Methods) to select the estimate that appeared to be most representative at the country-level. Using these estimates, we have categorised country HIV epidemics among PWID as: "low" (up to 1%); "medium" (2% - 5%); "high" (5% - 20%); and "very high" (greater than 20%).

No country in the East can be considered to have a 'low level' of HIV among PWID, and only Kazakhstan, Georgia and Lithuania have 'medium level' epidemics, according to the studies examined here. Of the remaining 11 countries with data (no data exists for Turkmenistan), three have prevalence estimates of over 20% (Moldova, Russia, and Ukraine) and Estonia has a prevalence of over 50%. In the Centre only Poland and Bulgaria appear to have 'high level' epidemics and neither of these exceed 10% prevalence. Several countries (Albania, Croatia, Cyprus, Hungary, Macedonia, and Slovenia) report 0% HIV prevalence among PWID. However, there is less data from this region and sample sizes are generally smaller so the estimates may be less robust than those from the East.

#### *Demographic profile*

Generally, three times as many men as women inject drugs, although male predominance reached as high as 95% in some studies from the Caucuses.<sup>[51 55 56 63 65 86 112]</sup> The mean age of PWID participating in studies was mid-twenties, although many studies restrict recruitment to PWID aged 18 or over. The proportion of PWID reporting having regular income was generally low.

#### *Pattern of injecting drug use*

Heroin is the drug of choice among PWID in Europe, although there are sub-regional differences. In Moldova<sup>[113]</sup>, Ukraine<sup>[74]</sup> and Russia<sup>[53]</sup>, the injection of home-produced opioids such as 'hanka' or 'shirka'(a liquid poppy extract) is reported alongside heroin injection. In Estonia the use of the synthetic opiate, fentanyl ('China White',



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'White Persian' or 'Afghan'), has become common alongside amphetamine injection.[72 114] In Central Europe, heroin is reported as the main drug injected, although studies also report between 30% and 51% injecting amphetamines as their main drug[101 115 116], and the Czech Republic reports the highest prevalence of methamphetamine use in Europe.[117-119] The frequency of injection varies widely throughout the region.

### Contact with criminal justice systems

The data reviewed from Eastern Europe and the former Soviet Union suggests that between half and three-quarters of PWID have experienced arrest. A study among 600 PWID in Odessa, Ukraine found that police beatings were common, with nearly 50% reporting at least one such experience.[20 120] Studies in other regions also suggest relatively high rates of police arrest (42% - 76% ever having been arrested).[18 27 108 121] In Estonia and Lithuania, an estimated 58%-70% of PWID had been in prison at least once.[75] In Georgia and Russia, this figure was between 6% and 37%,[18 53 65 66 80 122 123]In Central Europe, between 18% and 50% of respondents report previously having been in prison[94 108]

### Individual-level risk factors for HIV

No studies examined risk factors linked to HIV in the Centre, and so we summarise the findings of the multivariate HIV risk factor analyses from 14 papers identified by our review in the East[50 52-54 58 66 73 74 89 114 122 124-126], although two[66 73] present new analyses of data already published in other papers also presented here.[124 126] The forest plots summarised in Figures 4 and 5 synthesise the effects of particular individual and environmental risk factors on HIV. Although studies measure similar associations, it is important to note that each may have carried out analyses in a unique fashion, adjusting for different confounding variables.

### [TABLE 1]

As shown by the individual risk factor estimates presented in Figure 3, many studies investigated the link between HIV and *injecting with a used or shared needle*. Although the effect sizes tend towards increased HIV risk, most results are inconclusive, "social-desirability" bias possibly influencing self-reported responses. Injecting with the used needle of a sex partner was found in Volgograd[53] and Tallinn[114] to clearly increase an individual's odds of HIV. More definitively, injecting with a needle previously used by someone known to have HIV or hepatitis C is shown in most studies to be clearly positively correlated.[74 126] *Daily injecting* is also found to be positively associated. Many reviewed studies also associate *longer injecting careers* with greater odds of having HIV[126]. Although a Russian study found no difference in an individual's odds of HIV according to the primary drug they inject[127], studies in Estonia found that primary injectors of an opiate (fentanyl) had between three and four and a half times greater odds of HIV than individuals who primarily inject amphetamines.[114 128]

### [FIGURE 3]

Regarding exploration of HIV and associated *sexual risk*, most multivariate analyses explored the associations between exchanging sex for drugs or money, the number of sexual partners, and unprotected vaginal or anal sex, as risk factors. Although several strong univariate associations were found, these tended not to hold in the multivariate models (Figure 3). This could be because sample sizes were insufficient or because much sexual risk behaviour is determined by other individual or environmental factors such as gender, socio-economic status or injecting behaviour.

### Environmental-level risk factors for HIV

Although most studies presented show adjusted odds ratios identifying female *gender* as a risk factor for HIV (Figure 4), the confidence intervals generally straddle one and are inconclusive.

Multiple studies link HIV to the *socio-economic status* of PWID, though economic status is defined through different measures, including level of education, employment (regular or not) and income (regular or not, legal or not) (Figure 4). Of these measures, only an individual's employment status showed a consistent association with HIV, with unemployed individuals or those having a main source of income that was not work, showing greater

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3 odds of HIV than others.[54 58 89 122] An Estonian multi-level study included neighbourhood level data in its  
4 analyses and found neighbourhood level effects of unemployment (10% increment in unemployment AOR 5.95,  
5 95%CI 2.47-14.31) and habitat change since 1989 (10% change AOR 1.89, 95%CI 1.09-3.26) to be both associated  
6 with HIV prevalence(results not presented).  
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9 Several studies have examined *contact with law enforcement agencies* as an environmental factor linked with the  
10 odds of being HIV infected, although the results produced by the systematic review have large confidence intervals  
11 and are largely inconclusive.[53 66 114 126] The review reveals that contact between police and PWID in the  
12 region is highly commonplace and no studies examined the frequency or duration of contact.  
13

14 In addition to the universally relevant factors highlighted above, some studies analysed the relationship between  
15 HIV and determinants that are particular to local context (results not shown). For example, a study in Tajikistan  
16 found that respondents identifying as Tajik (AOR 7.06,  $p < 0.001$ ) or other ethnicity (AOR 6.05,  $p < 0.001$ ) as opposed  
17 to Russian were at higher risk of testing positive for HIV.[73] A study in Uzbekistan similarly found respondents of  
18 Uzbek ethnicity to have higher odds of HIV than their Russian counterparts (AOR 1.20, 95%CI 0.80-1.80).[54]  
19 However, a study in Estonia found that ethnic Estonians had a reduced odds of HIV compared with those of  
20 Russian or other backgrounds (AOR 0.63, 95%CI 0.28-1.25).[114] An association between HIV among PWID and  
21 being of a minority ethnicity that cannot otherwise be explained by needle sharing has been noted elsewhere, and  
22 linked to material as well as other social inequalities, including access to support services.[129 130] In parts of  
23 Eastern Europe where PWID are often required to register as such to obtain drug treatment or are forced to  
24 through contact with police, this can lead to increased social marginalisation as well as reducing their ability to gain  
25 employment or even to drive a car.[131] In Moscow and Tallinn ever having been registered as a PWID at drug  
26 treatment was found to be associated with more than double the odds of HIV (AOR 2.4, 95%CI 1.3-4.7; AOR 2.4,  
27 95%CI 1.5-3.8)[53][114]. Conversely, a study in Togliatti in Russia conducted among 96 new (<three years)  
28 injectors found having been in drug treatment in the past as negatively associated with risk of HIV (AOR 0.4, 95%CI  
29 0.1-1.0).[132]  
30

#### 31 [FIGURE 4]

##### 32 *HIV prevention coverage*

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34 Coverage – the proportion of the population at risk reached by an intervention, ideally with sufficient intensity to  
35 have probable impact – emerges as a critical determinant of HIV prevention effectiveness.[32 133-135] Our review  
36 did not focus on collating primary data but sought to synthesise coverage estimates relevant to the Central and  
37 Eastern European and Central Asian region from key recently published reviews regarding NSPs, OST, and ART.[39  
38 40] These data are contained in Figure 5. They indicate that NSPs were available in all countries of the region,  
39 except Turkey, though intervention coverage varies widely. For instance, whereas 50% of PWID in Hungary in 2007  
40 had access to NSPs, with each receiving around 135 clean needles a year (135 per PWID based on country-level  
41 estimates of PWID), in Russia only 7% of PWID had such access to NSPs, with each receiving 56 needles each a year  
42 (four per PWID based on country-level estimates of PWID). These estimates do not include pharmacy-based  
43 provision, which is a primary source in some countries in this region, including Russia.[136] Figure 5 also shows  
44 that four of the 30 countries in this region reporting evidence of injecting drug use did not provide OST: Russia,  
45 Uzbekistan, Turkmenistan, and Turkey. Coverage of OST is generally low, with Slovenia showing the greatest  
46 coverage.  
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#### 49 [FIGURE 5]

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51 Comparing the proportion of HIV cases caused by injecting drug use with the corresponding proportion of people  
52 receiving antiretroviral therapy who inject drugs, in 2002, 71% of the reported people living with HIV acquired HIV  
53 infection through injecting drug use, whereas only 20% of those receiving antiretroviral therapy were people who  
54 injected drugs. In 2005 and 2006, among 21 and 23 countries with available data, people who injected drugs  
55 represented 77% of reported cases and 26% of antiretroviral therapy recipients, a proportion that declined to 22%  
56 in 2010 among 19 reporting countries. Although no trends can be statistically ascertained due to incomparable  
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3 samples (notably missing data from the Russian Federation in 2002 and 2010), these data suggest that most of the  
4 people who acquire infection in reporting countries are people who inject drugs and that, despite this, their  
5 treatment needs remain considerably underserved.[4]  
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8 We found no data relating to the impact or coverage of structural level interventions on HIV among PWID,  
9 although recent legislative changes in Moldova and the Czech Republic have de-emphasised the criminalisation of  
10 small amounts of drugs possession.

### 11 *Enabling policy environments*

12 Figure 6 shows the results of the policy index developed (see Methods) to describe the distribution of enabling  
13 policy environments throughout Central and Eastern Europe. Darker shading represents seemingly more  
14 supportive policy environments for HIV prevention and lighter shading seemingly less supportive environments.  
15

### 16 **[FIGURE 6]**

17  
18 Of the 30 countries in the region, 25 explicitly and supportively mentioned harm reduction in their national  
19 strategies, and 27 have undertaken at least one sero-prevalence and one behavioural study among PWID in the  
20 last ten years. In 26 countries, OST and NSP are available generally, but available in prison in only three countries.  
21 Five countries have national organisations of drug users, and five countries use administrative rather than criminal  
22 penalties for people found possessing small quantities of drugs for personal use.  
23

24  
25 Based on the index, the countries with the most supportive policy environments are Moldova and Romania. The  
26 countries with the least supportive environments are Turkmenistan and Turkey. Turkmenistan does not show any  
27 of the features of a supportive environment according to our index, although Turkey has conducted at least one  
28 sero-prevalence and one behavioural study among PWID in the last ten years. In Russia, where the majority share  
29 of HIV infections among PWID in the region are located, the national strategy refers to harm reduction as a threat  
30 to efforts to reduce the demand for drugs, with NSPs and OST specifically mentioned as problematic for federal  
31 level support.[137] OST is unavailable in Russia, and NSPs are limited in number, with none available to prisoners,  
32 and there is a focus on criminal rather than administrative penalties for drugs possession. However, there is some  
33 evidence of drug user activism and organisation.[47]  
34

35  
36 Russia and Ukraine both feature among the countries experiencing high HIV prevalence among PWID, and like  
37 Russia, criminal punishment rather than administrative sanctions for drug use and possession is the norm in  
38 Ukraine. While Ukraine has a relatively high number of NSPs alongside increasing availability of OST, it does not  
39 provide harm reduction services in prisons. Moldova and Estonia also feature among the high HIV prevalent  
40 countries but both appear as to present relatively supportive environments for PWID. However, to our knowledge,  
41 neither has an active national drug user organisation and neither NSP or OST in prison settings.  
42

## 43 **DISCUSSION**

### 44 *HIV epidemic contexts*

45  
46 All but one country (Turkmenistan) in Central and Eastern Europe and Central Asia has generated survey-based  
47 estimates of HIV prevalence among PWID. Our review of these studies shows that HIV prevalence among PWID is  
48 highest in the Eastern European countries of Estonia, Russia, Moldova, and Ukraine (over 20% in each), and lowest  
49 in the Central European countries of Albania, Croatia, Cyprus, Hungary, Macedonia (FYR), and Slovenia (0% in  
50 each). We identified only three HIV incidence studies among PWID in the region, showing incidence of 9/100  
51 person years in Estonia in 2009[49] and 4.5/100 person years in Russia[50]. Accepting that country estimates of  
52 HIV prevalence inevitably only reflect the characteristics of the particular samples from which they are drawn,  
53 these estimates taken together reiterate that the burden of HIV linked to injecting drug use falls in the East, and  
54 especially Russia, where over half of all HIV cases among PWID in the region are located.  
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3 Multivariate analyses of HIV risk factors among PWID underscore injecting with a used needle/syringe, frequent  
4 injecting, and injecting opiates as opposed to amphetamines as proximal factors associated with increased risk of  
5 HIV. We acknowledge that the findings of the multivariate studies we synthesise in the review may not be directly  
6 comparable, as they have been derived from studies using different regression techniques and adjusting for  
7 different confounding factors. While most of the epidemiological studies we reviewed did not embrace, by design,  
8 the exploration of environmental risk factors – as is the case with HIV epidemiological studies globally[20] – a  
9 number of important factors in the HIV risk environment can be identified. These included increased HIV risk  
10 among *women*, an association we interpret to have indirect, rather than biological, causative roots through  
11 pathways involving multiple linked socio-economic differences related to gender. Although most studies showed  
12 women at greater risk of HIV than men, the confidence intervals presented include the null value, preventing us  
13 from drawing conclusions on the effect of gender on HIV risk. The lack of conclusive evidence could be due to the  
14 small number of women often recruited in to research, as well as genuine variability in the consequences of female  
15 gender in different settings. Qualitative data from Ukraine suggests that female PWID are at increased risk of  
16 psychological, physical (including sexual) and economic violence from their male partners, constraining capacity to  
17 negotiate safer sex, safer injecting practices, and access to helping services, in consequence elevating their HIV  
18 risk.[138]  
19

20  
21 Additionally, *socio-economic status* – whether measured by income or employment – emerged as important,  
22 although only employment status appeared conclusively associated with HIV risk. The direction and pathways  
23 income and employment effects have on HIV risk may vary locally. The ways in which HIV links to wealth and  
24 poverty is shaped by social context, and in some settings injecting has diffused among those whose economic  
25 status may be comparable to the wider local population.[53 139]  
26

27  
28 Lastly, we note contact with *criminal justice agencies*, including experience of incarceration, as an important risk  
29 factor,[53 66 114 126] although the studies systematically reviewed here were inconclusive in this regard. Studies  
30 evidencing the adverse effects of the legal environment on HIV risk among PWID suggest a relationship between  
31 street-based policing practices, including extra-judicial ones such as police violence, and increased HIV  
32 vulnerability, including through reduced capacity for risk avoidance as a consequence of safety short-cuts and  
33 rushed injections borne out of a fear of detection or arrest.[18 27 120 140-142] While evidence internationally  
34 links prison and a history of incarceration to elevated odds of HIV among PWID[143 144], only three countries in  
35 the region (Moldova, Romania, and Kyrgyzstan) provide harm reduction services to prisoners.  
36

37  
38 Whilst the epidemiological studies we reviewed provide some pointers to the role of HIV risk environments, they  
39 are self-evidently limited in their capacity to capture how HIV is an effect of social context. This highlights the  
40 urgency to develop specifically tailored social epidemiological approaches, which build into their designs from the  
41 outset measures of micro and macro risk environment. It also highlights the importance of mixed-methods  
42 approaches, especially those combining qualitative with epidemiological data[145]. For example, by linking HIV  
43 epidemiology to data on shifting drug trafficking routes it has been possible to plot the macro physical distribution  
44 of HIV.[146] In the region of Central and Eastern Europe, the potentially HIV risk productive role of transit routes  
45 for heroin originating from Afghanistan through Central Asian countries along the “Northern Route” to Russia and  
46 beyond provides a similar example. In 2009, UNODC estimated that 25% of all Afghan heroin (95 metric tons) was  
47 transported along this route, with the majority travelling through Tajikistan, to Osh in Kyrgyzstan, and then on to  
48 Kazakhstan, before arriving in Russia.[147] The effects of this trafficking route appear to have HIV impacts with  
49 Kulyab, in Tajikistan, a major hub for Afghan opiate trafficking, reporting the highest HIV prevalence among PWID  
50 in Tajikistan at 34.5% in 2009 compared with the national average of 17.3%.[148] Jalal-Abad reported the highest  
51 HIV prevalence among PWID in Kyrgyzstan at 14% in 2007[149] compared with a national average of 7.7%.[84] In  
52 Kazakhstan, there is substantial overlap between the sites with the largest number of diagnosed HIV infections,  
53 largest number of registered drug users and highest number of heroin seizures.[150]  
54

55  
56 Future epidemiological studies of HIV among PWID need to better systematically develop measures of HIV risk  
57 environment and how these combine to increase or reduce HIV risk.[20] Because epidemiological studies of PWID  
58 tend to focus on the proximal determinants of risk behaviour and HIV transmission, there is a need to shift towards  
59 capturing distal factors and how these interplay to produce pathways of risk. [147 151] [147, 151] [147 151]<sup>147, 151</sup>  
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3 147, 151 148, 152 (Rhodes 2009; United Nations Office on Drugs and Crime (UNODC) 2010) (Rhodes 2009; United  
4 Nations Office on Drugs and Crime (UNODC) 2010) (Rhodes 2009; United Nations Office on Drugs and Crime  
5 (UNODC) 2010) 148, 152 148, 152 148, 152 148, 152 148, 152 149, 153 148, 152 148, 152 146, 150 138, 142 150, 154150, 154 Principal among these,  
6 according to our review, should be gender, social-economic status, and the effects of criminalisation.  
7

### 8 *Towards enabling policy environments*

9  
10 It is well established that HIV prevention targeting PWID requires a 'combination intervention' approach tailored  
11 to local setting, including a balance of: needle and syringe distribution programmes (NSPs); opioid substitution  
12 treatment (OST); antiretroviral HIV treatment (ART); peer education and outreach; HIV testing and counselling  
13 services; and the promotion of public policies and other structural changes conducive to public health approaches.  
14 [20 32 33 152-154] Evidence for the effectiveness of these interventions is well established.[32 152 155 156] The  
15 extent of HIV prevention intervention coverage, however, varies throughout the region, and is largely  
16 inadequate[39 40]. Many of the countries with the lowest levels of harm reduction service provision are also those  
17 with the highest HIV prevalence and the largest per-capita number of new diagnoses. The unavailability of OST in  
18 Russia in particular means that the majority of PWID in the region do not have access to an integral component of  
19 evidence-based HIV prevention.  
20

21 Structural interventions seek to remove environmental barriers to HIV prevention while enabling environmental  
22 conditions which protect against vulnerability to HIV. While the relationships between HIV-related policies and  
23 their impacts upon micro-level HIV risk practices are clearly not straight forward, the policy environment is a clear  
24 object of structural intervention and change. Our review identified no evidence specifically relating to the impact  
25 or coverage of structural level interventions on HIV among PWID, although recent legislative changes in Moldova  
26 and the Czech Republic have de-emphasised the criminalisation of small amounts of drug possession, and evidence  
27 elsewhere in Europe links such initiatives with reduced HIV risk and increased access to helping services[157].  
28

29  
30 In the absence of social epidemiological data generated from systematic review, we developed a crude index of  
31 'enabling policy environment' based on indicators of: national-level policy endorsing of harm reduction  
32 approaches; research of HIV prevalence and risk behaviour among PWID; drug user community organisation;  
33 availability of OST and NSPs; availability of OST and NSPs in prison settings; and application of administrative rather  
34 than criminal penalties for drug use and possession (see Box 1). Such an index seeks to include quantifiable  
35 indicators of the practical application of 'healthy policy', at least as far as such data is comparatively available. We  
36 acknowledge the limits of this exercise, but argue for the need for future epidemiological research to better  
37 monitor indicators of enabling and risk environment alongside proximal risk factors for HIV, especially those  
38 pertaining to community involvement and partnership in policy formation, availability of HIV prevention in criminal  
39 justice settings, and shifts towards de-emphasising the criminalisation of drug use through providing treatment or  
40 care as an alternative to arrest or imprisonment.  
41

42 Applying our index of enabling policy environment highlighted large discrepancies throughout the region. Of the  
43 countries with a seemingly unsupportive environment for HIV prevention among PWID, Turkmenistan may present  
44 a particular concern, for it is located between countries of high HIV prevalence, situated on a heroin trafficking  
45 route, and appears to lack a baseline of epidemiological evidence. Other countries – including Russia, Uzbekistan  
46 and Azerbaijan – appear to present weak policy environments for HIV prevention, compounding potential risk  
47 linked to low level HIV prevention coverage. The lack of systematic monitoring of policy environment indicators in  
48 the region, and the neglected attention paid to monitoring the effect of structural-level factors on micro risk  
49 relationships in epidemiological research, hampers an understanding of how European HIV epidemic contexts may  
50 differ markedly regarding HIV prevention need and potential. The development of structural HIV prevention  
51 interventions as part of a combination intervention approach clearly requires evidence of how environmental-level  
52 factors impact upon HIV risk.  
53

54  
55 The importance of reducing vulnerability to HIV/AIDS, by understanding and removing structural barriers, is  
56 increasingly recognised in European HIV policy, for example as one of the four strategic directions of the European  
57 Action Plan for HIV/AIDS 2012-2015, which proposes actions to: address laws and regulations that present  
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obstacles to effective HIV prevention, treatment care and support; strengthen the enforcement of protective laws and regulations; strengthen civil society involvement in the HIV response and ensure gender and age equity in access to HIV and related health services.

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**AUTHORS CONTRIBUTIONS**

Tim Rhodes, Lucy Platt and Vivian Hope developed the methodology for the systematic review.  
Tim Rhodes, Lucy Platt, Vivian Hope, Alisher Latypov and Emma Jolley reviewed the collected literature.  
Emma Jolley extracted the data and conducted the data analysis.  
Tim Rhodes and Emma Jolley interpreted the data and drafted the manuscript.  
All authors reviewed the manuscript and commented on the data and interpretation.  
All authors gave approval for the manuscript to be submitted.

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3 **CONFLICTS OF INTEREST**  
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5 None declared.  
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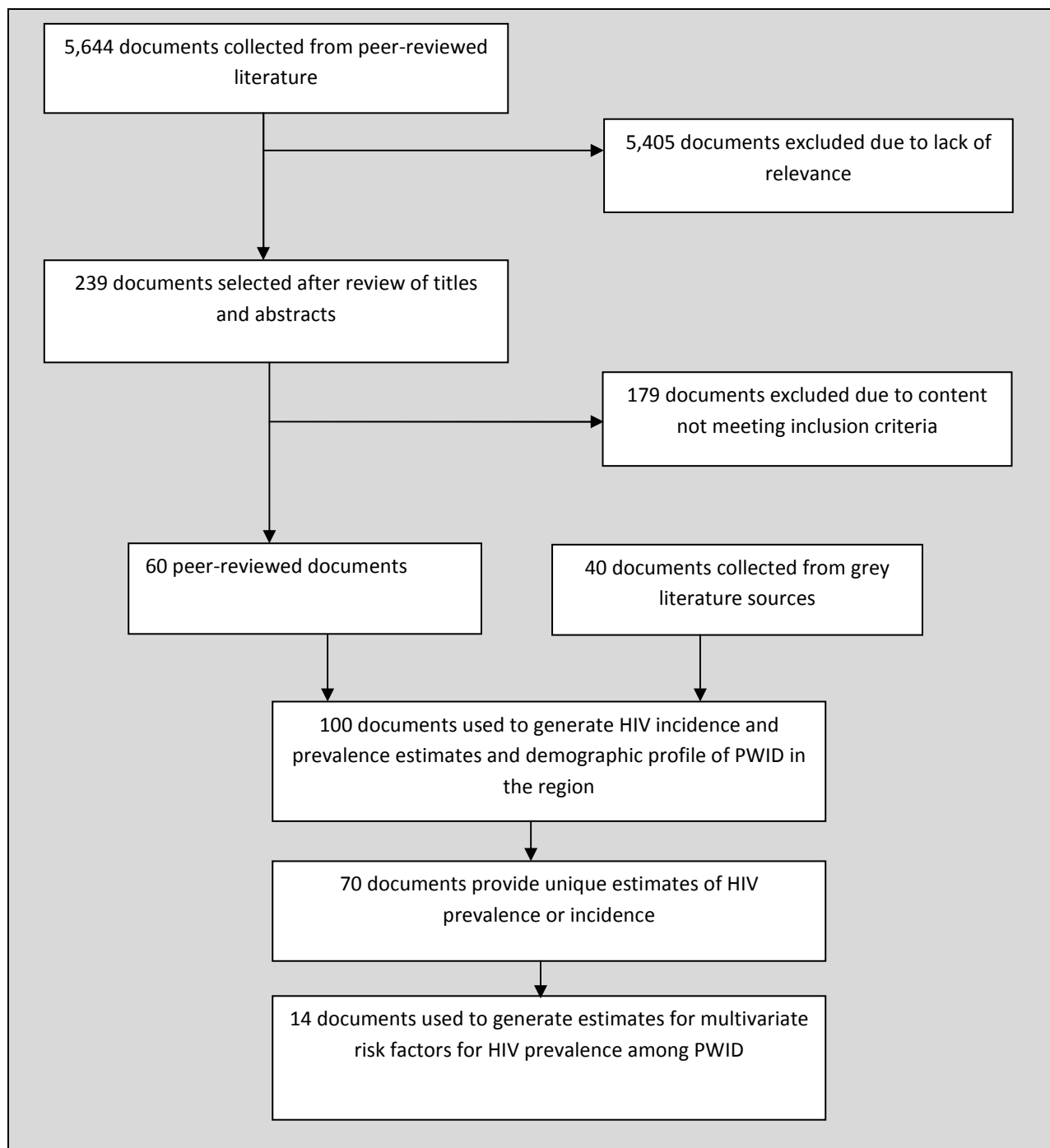


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Figure 1: Flowchart of study selection



**Box 1: A simple index of enabling policy environment****MEANINGFUL ENGAGEMENT OF STAKEHOLDERS**

1. The meaningful involvement of PWID in policies affecting their health and welfare and in related HIV prevention programming is accepted as an important indicator of 'health policy' formation.[42 158] While assessing 'meaningful involvement' is complex, we adopt a simple indicator: the ***presence of a national organisation of drug users***.

**COORDINATED NATIONAL STRATEGY TO HIV PREVENTION AND DRUG USE**

2. Explicit and supportive reference to 'harm reduction' in national policy documents can mark a commitment to evidence-based interventions as part of HIV prevention responses targeting PWID. International agencies advocate institutional and national-level endorsement of harm reduction as a feature of national strategy.[33 159] We adopt ***evidence of explicit supportive reference to harm reduction in national strategy*** as an indicator of enabling policy environment.

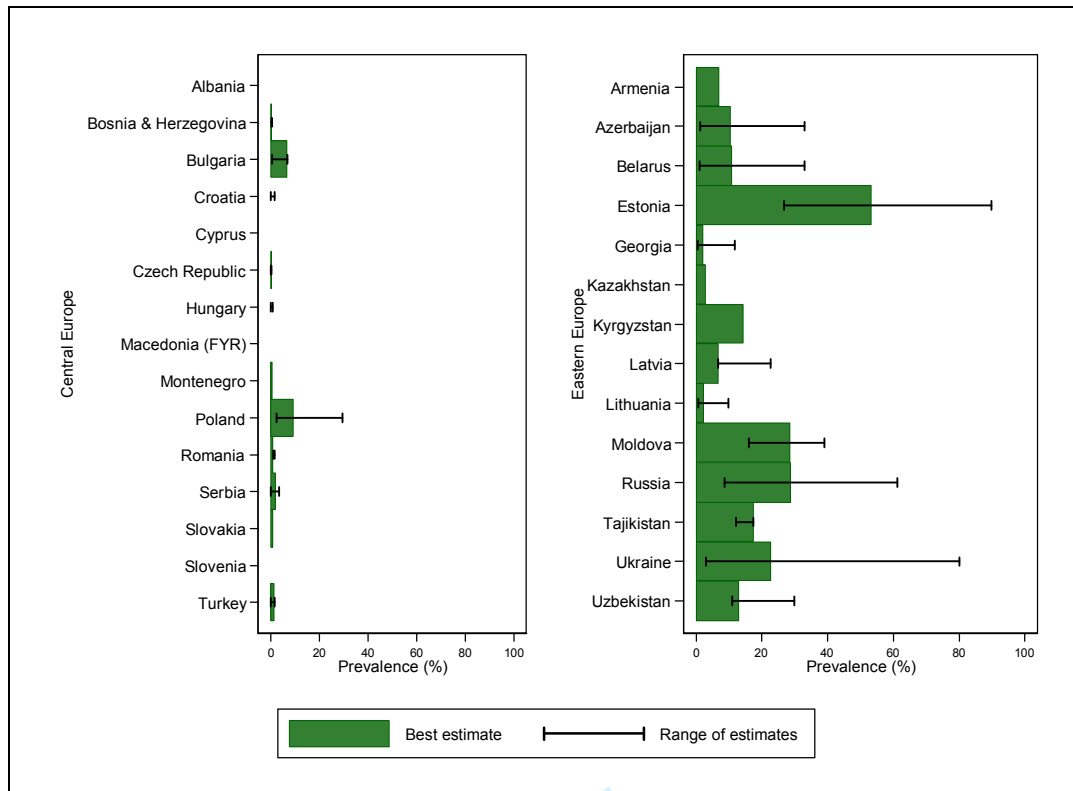
3. Monitoring and evaluating the state of the epidemic and response is an important element of building evidence-based responses.[40 160] Targeted sero-prevalence and behavioural surveillance is recommended in concentrated HIV epidemics.[161] We adopt as an indicator of enabling policy ***evidence of at least one HIV sero-prevalence and one behavioural study among PWID since 2000***.

**IMPLEMENTATION OF PUBLIC HEALTH ORIENTED APPROACHES TO REDUCING HARM**

4. Drug control policies which seek to distinguish drug users from drug traders and traffickers, and which de-emphasise the criminalisation of drug users, can give priority to public health oriented approaches to reducing drug-related harm. We adopt the ***application of administrative rather than criminal penalties for drug use and possession of quantities for personal use*** as an indicator of an enabling policy environment.

5. We adopt ***the legal availability of OST and NSP*** in a country as an indicator of enabling policy environment. These are core components of the recommended nine combination HIV prevention interventions for PWID[33]. Many countries have adopted at least some recommended measures, but often the components missing are OST and NSPs. The effectiveness of both in improving the health of PWID is well established[32 155 162], especially for OST[163-168] [169]. OST also facilitates access to and augments the effects of other interventions, such ART[32 152].

6. ***The availability of OST and NSPs in prison*** can show a country's willingness to address the needs of even the most marginalised of its citizens, as well as demonstrating noteworthy scale of the programmes. Because of existing laws concerning drug use and possession, PWID in many countries account for disproportionately high rates of incarceration[143]. Prisons may act as a risk environment for HIV transmission linked to drug injecting. International guidelines[170] recommend continuity of services between prison and communities and some countries have developed successful partnerships between penal systems and HIV services, including in the European region.[171]



**Figure 2** The range of HIV prevalence estimates for countries in the Central and Eastern European region, along with the estimate judged “best” highlighted in green.

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
Platt et al, 2006[114]	Estonia, Tallinn	350 PWID who injected in past four weeks recruited by respondent-driven sampling (RDS)	Primary injection of opioid or amphetamine in past four weeks*; Duration of injecting career; Shared needle in past four weeks; Shared equipment in past four weeks; Injected with a used needle of a sex partner in past four weeks*; Number of sexual partners in past year	Age; Gender; Main source of income in past four weeks; Ethnicity; Ever registered in drug treatment*; Ever been in prison; Ever attended needle exchange
Abel-Ollo et al, 2009[72]	Estonia, Tallinn and Kohtla-Järve	<p>450 PWID (350 from Tallinn and 100 from Kohtla-Järve) who injected in past four weeks recruited by respondent-driven sampling (RDS). For analysis the participants were categorised as HIV-, HIV+ aware of their status and HIV+ unaware of their status, according to self-reported status at the time of testing.</p> <p>The data from Tallinn is also analysed above.</p>	<p><b>Analysis of risk factors for HIV among participants aware of their status (ref HIV- participants):</b>            Sharing used needles/ syringes in past four weeks*; Unprotected sex in past four weeks; Sharing water*; PWID as sex partner in past year*; Sharing injection equipment with sexual partner in past year*; Having two or more sex partners in past year; Unprotected intercourse in past year; Ever sharing needles with HIV+ person*.</p> <p><b>Analysis of risk factors for HIV among participants unaware of their status (ref HIV- participants):</b>            Sharing used needles/ syringes in past four weeks; Unprotected sex in past four weeks; Sharing water; PWID as sex partner in past year; Sharing injection equipment with sexual partner in past year;</p>	

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Having two or more sex partners in past year*; Unprotected intercourse in past year*; Ever sharing needles with HIV+ person.	
Uusküla et al, 2010[89]	Estonia, Tallinn	350 PWID, aged 18+, who injected in past two months recruited by RDS	Earlier age of initiation to injecting*; Primary injection of opioid or amphetamine*; Receptive sharing in past six months*	Ever attended syringe exchange*; Main source of income other than work*; Unemployment at habitat level*; Residential change at habitat level*
Platt et al, 2005[126]	Russia, Togliatti	268 male PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks*; Injected with used needle in past four weeks; Ever injected homemade drugs; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+*; Unprotected anal or vaginal sex with a regular partner in past four weeks; Unprotected anal or vaginal sex with a casual partner in past four weeks*; Ever had an STI	Ever been in prison; Ever been in drug treatment; Ever been arrested;
	Russia, Togliatti	89 female non-sex worker PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks; Injected with used needle in past four weeks*; Ever injected homemade drugs; Injected with used needle from someone known to be HIV+; Injected with used needle	Ever been in prison; Ever been in drug treatment; Ever been arrested



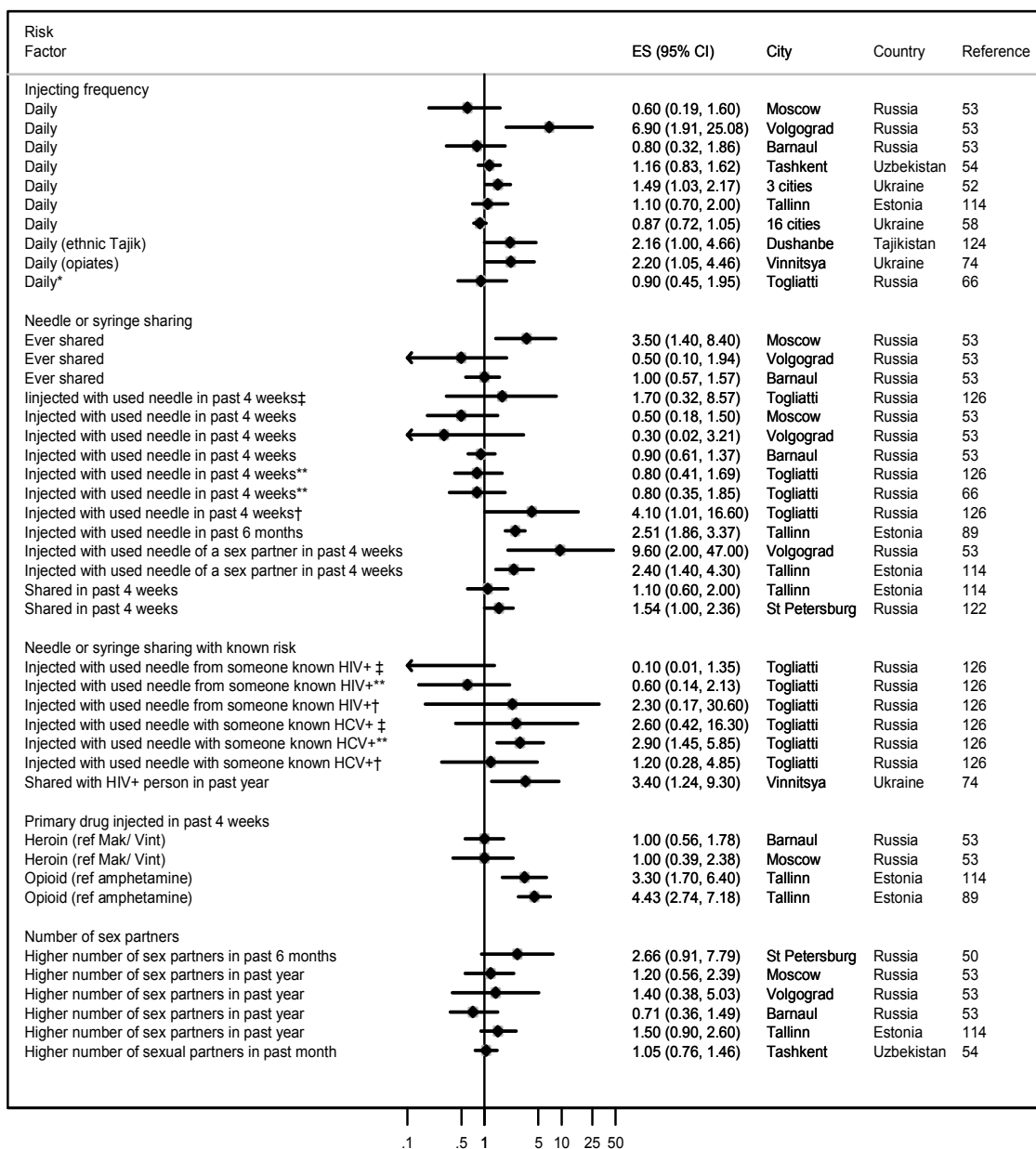
Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			from someone known to be HCV+; Unprotected anal or vaginal sex with a regular partner in past four weeks; Ever had an STI	
	Russia, Togliatti	66 female sex worker PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks; Injected with used needle in past four weeks; Ever injected homemade drugs*; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+; Unprotected anal or vaginal sex with a regular partner in past four weeks; Ever had an STI	Ever been in prison; Ever been in drug treatment; Ever been arrested;
Platt et al, 2008[66]	Russia, Togliatti	230 PWID (134 in 2001 from the study above, and 96 from 2004) who reported injecting for three years or less and injected in past four weeks were recruited by outreach workers in 2001 and through RDS in 2004	Duration of injecting career*; Frequency of injection; Ever injected homemade drugs; Injected with used needles in past four weeks; Used a previously used filter; Frontloading in past four weeks*; Injected with a prefilled syringe; Frequency of reusing the same needle; Ever exchanged sex for money, drugs or goods*; History of STIs	Year of study*; Gender; Age; District of residence; Education; Main source of income in past four weeks; History of prison; Police arrest in past year; Ever in drug treatment*; Main source of needles in past four weeks; Ever been tested for HIV
Kozlov et al, 2006[50]  *outcome is HIV incidence at 12 month follow up to	Russia, St Petersburg	520 sero-negative PWID enrolled in cohort study who injected at least three times / week in past month or reused another's injecting equipment at least three times in past three months	Frequency of injecting psychostimulants*; Number of sex partners in past six months; Selling sex for money or goods in past six months	

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
enrolment				
Niccolai et al, 2010 [122]	Russia, St Petersburg	387 ever injectors were enrolled through RDS	Unsafe injection in past 30 days*; Has STI*;	Unemployed*
Rhodes et al, 2006 [53]	Russia, Moscow	455 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Last day injected, number of times injected*; Frequency of injection; Main drug injected in past four weeks; Injected with used needle in past four weeks; Shared paraphernalia in past four weeks; Ever injected with used needles*; Number of sex partners in past year; History of STI*	Gender; Age; Education; Main source of income in past four weeks; Ever been in prison*; Ever registered as a drug user*
	Russia, Volgograd	517 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Frequency of injection*; Ever injected homemade drugs; Injected with used needle in past four weeks; Shared paraphernalia in past three weeks; Ever injected with used needles; Injected with needle previously used by sex partner in past 12 months*; Number of sex partners in past year; History of STI	Gender; Age; Education; Main source of income in past four weeks*; Ever registered as a drug user
	Russia, Barnaul	501 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Last day injected, number of times injected*; Frequency of injection; Main drug injected in past four weeks; Ever injected homemade drugs; Injected with used needle in past four weeks; Shared paraphernalia in past four weeks*; Filled syringe from working syringe in past four weeks;	Gender; Age; Education; Main source of income in past four weeks; Ever been in prison; Ever registered as a drug user

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Ever injected with used needles; Number of sex partners in past year; History of STI	
Beyrer et al, 2009[73]	Tajikistan, Dushanbe	419 PWID who injected in past month aged 17 or over recruited through snowball technique	Daily injection in past six months*	Ethnicity*  Model adjusted for gender
Stachowiak et al, 2006[124]	Tajikistan, Dushanbe	207 ethnic Tajik PWID (subsample of above) aged 17 or over recruited through snowball technique	Injecting at least daily for past six months*; Less than three years since initiation of injection; Injects 'alone'*; Injected with used needle in past six months	Reports narcotics 'very easy' to obtain*; Ever experienced drug treatment*
Booth et al, 2006[52]	Ukraine, Kiev, Odessa, Makeevka/ Donetsk	778 PWID aged 18+ who injected in past 30 days and were unaware of their HIV status recruited through outreach workers	Injected sedative/ opiate mix in past 30 days*; Daily injection in past 30 days*; Sex in past 30 days*; Sex with HIV+ or unknown status partner in past 30 days*	Age*; Gender*; City of origin*
Robbins et al, 2010[125]	Ukraine, Odessa, Kiev, Donetsk	313 youth aged 15-24 who live part or full time on the street and reported ever injecting recruited by time-location sampling	Last sex unprotected*; Ever diagnosed with STI*  Model adjusted for gender, age, education, work for pay, orphan status, spending nights outside of residence $\geq 2$ nights/ week for past few months/ no place to live, city of residence	
Dumchev et al, 2009[74]	Ukraine, Vinnitsya	268 PWID aged 18+ who report at least three injections in past 30 days and have lived in Vinnitsya for past year, recruited through snowball sampling	Shared needles with HIV+ person in past year*; Inject opiates daily*	HIV knowledge score*
Taran et al, 2011[58]	Ukraine, 16 cities	3,487 PWID aged 16+ who injected in past 30 days and were recruited through RDS	Type of drug injected in past month; Duration of injecting career*; Injecting frequency in past month; Used alcohol with drugs in past month*; Shared needle at last	Gender*; Marital status; Occupation*; Education*

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			injection*; Frequency of sharing paraphernalia in past month*; Sexual contact in past year;	
Sanchez et al, 2006[54]	Uzbekistan, Tashkent	701 self-identified PWID aged 18+available for two weeks after enrolment by outreach workers	Age at first drug use; First illicit drug of use*; Duration of injecting career; Current heroin use; Injecting frequency; Poppy-straw use; Group drug use; Sharing needles; Own syringe; Blood transfusion; STI history; Hepatitis history*; TB history; STI symptoms; Sell sex for drugs; Condom use*; Number of sexual partners in past month	Age; Gender; Nationality; Marital status; Employment status*; Education status; Needle exchange programme; AIDS knowledge; protection for AIDS; Donated blood for money*; for money*; for money*

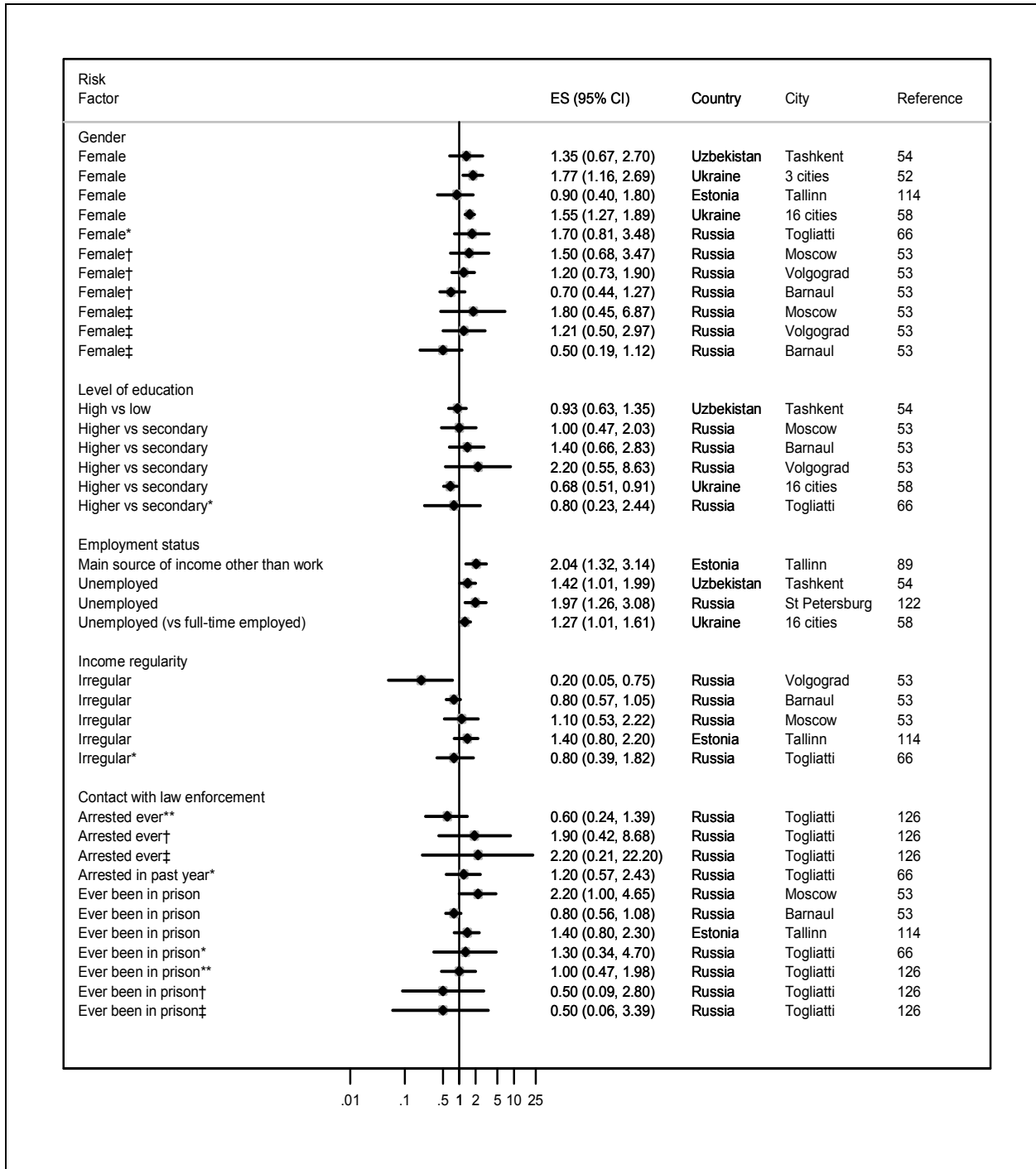
**Table 1:** Summary of studies presenting multivariate analyses of risk factors for HIV among PWID in Central and Eastern Europe and Central Asia\* P-value reported  $\leq 0.05$



\* new PWID (≤3 years); \*\*male PWID; †female (non-SW) PWID; ‡female (SW) PWID

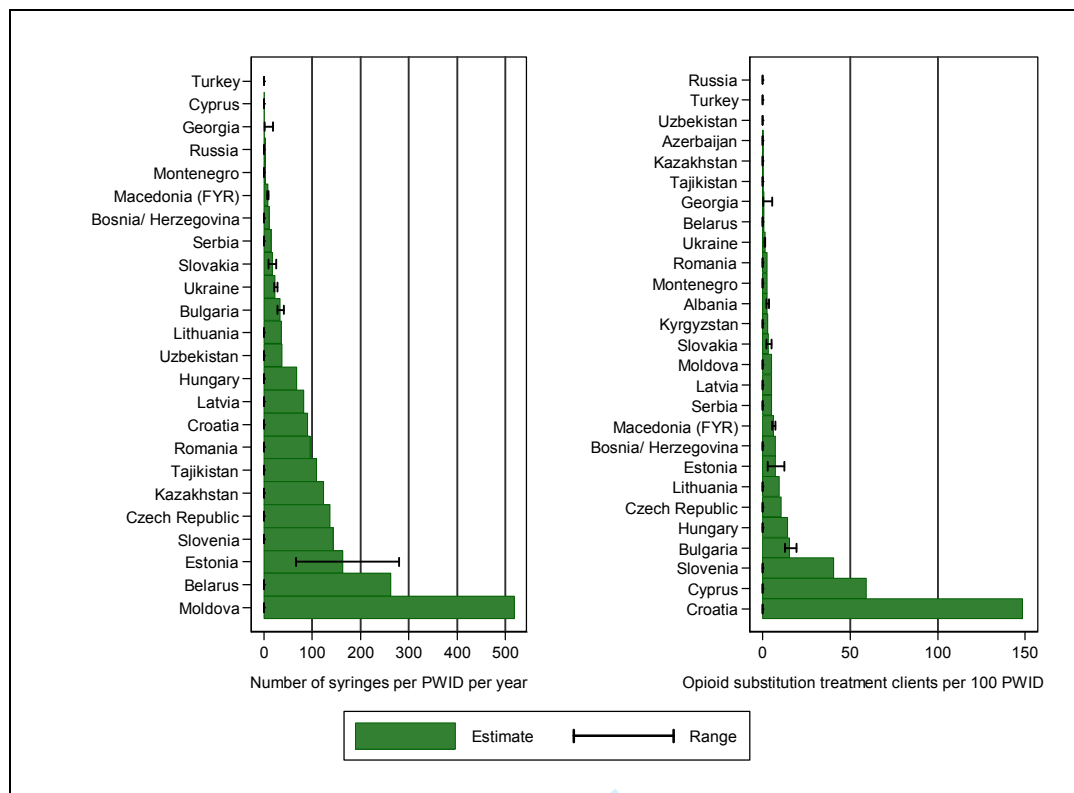
Figure 3 Adjusted effect estimates of individual level risk factors present in multivariate studies of PWID

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\* new PWID (≤3 years); \*\*male PWID; †female (non-SW) PWID; ‡female (SW) PWID

Figure 4 Adjusted effect estimates of environmental level risk factors present in multivariate studies of PWID



**Figure 5** Estimated numbers of syringes distributed per PWID per year and estimated number of OST clients per 100 PWID in the latest year for which data is available.[39 40]

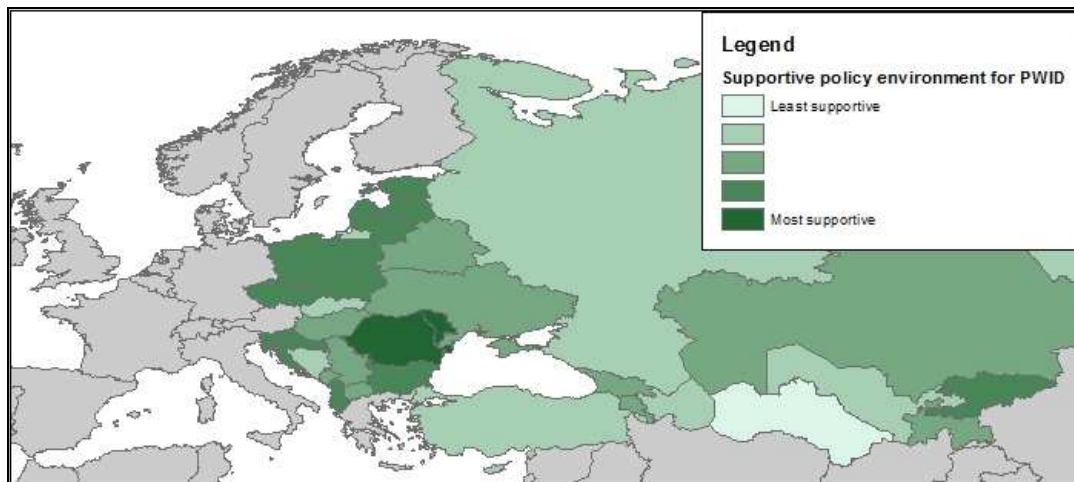


Figure 6 Map showing the supportiveness of the policy environments for HIV among PWID in Europe.[39 45-47]





# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4/5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5/6
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5/6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ for each meta-analysis).	N/A



# PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8/9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8/9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8/9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10/11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10/11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10/11/12
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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**HIV among people who inject drugs in Central and Eastern Europe and Central Asia: A systematic review with implications for policy**

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2012-001465.R1
Article Type:	Research
Date Submitted by the Author:	20-Aug-2012
Complete List of Authors:	Jolley, Emma; London School of Hygiene & Tropical Medicine, Dept of Social and Environmental Health Research Rhodes, Tim; London School of Hygiene & Tropical Medicine, Dept of Social and Environmental Health Research Platt, Lucy; London School of Hygiene & Tropical Medicine, Dept of Social and Environmental Health Research Hope, Vivian; London School of Hygiene & Tropical Medicine, Dept of Social and Environmental Health Research; Health Protection Agency, Centre for Infections Latypov, Alisher; Eurasian Harm Reduction Network, ; Columbia University, Global Health Research Center of Central Asia Donoghoe, Martin; World Health Organization Regional Office, Division of Communicable Diseases, Health Security and Environment Wilson, David; The World Bank, Global HIV/ AIDS Programme
<b>Primary Subject Heading</b>:	Infectious diseases
Secondary Subject Heading:	Public health, Epidemiology, HIV/AIDS
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Substance misuse < PSYCHIATRY

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Manuscripts

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8 **HIV among people who inject drugs in Central and Eastern Europe and Central**  
9 **Asia:**  
10 **A systematic review with implications for policy**

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13 Emma Jolley<sup>1</sup>, Tim Rhodes<sup>1</sup>, Lucy Platt<sup>1</sup>, Vivian Hope<sup>1,2</sup>, Alisher Latypov<sup>3,4</sup>,  
14 Martin Donoghoe<sup>5</sup>, David Wilson<sup>6</sup>  
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**ABSTRACT**

*Background and objectives:* HIV among people who inject drugs (PWID) is a major public health concern in Eastern and Central Europe and Central Asia. HIV transmission in this group is growing and over 27,000 HIV cases were diagnosed among PWID in 2010 alone. The objective of this systematic review was to examine risk factors associated with HIV prevalence among PWID in Central and Eastern Europe and Central Asia and to describe the response to HIV in this population and the policy environments in which they live.

*Design:* A systematic review of peer-reviewed and grey literature addressing HIV prevalence and risk factors for HIV prevalence among PWID and a synthesis of key resources describing the response to HIV in this population. We used a comprehensive search strategy across multiple electronic databases to collect original research papers addressing HIV prevalence and risk factors among PWID since 2005. We summarised the extent of key harm reduction interventions, and using a simple index of 'enabling' environment described the policy environments in which they are implemented.

*Studies reviewed:* Of the 5,644 research papers identified from electronic databases and 40 documents collected from our grey literature search, 70 documents provided unique estimates of HIV and 14 provided multivariate risk factors for HIV among PWID.

*Results:* HIV prevalence varies widely, with generally low or medium (<5%) prevalence in Central Europe and high (>10%) prevalence in Eastern Europe. We found evidence for a number of structural factors associated with HIV including gender, socio-economic position and contact with law enforcement agencies.

*Conclusions:* The HIV epidemic among PWID in the region is varied, with the greatest burden generally in Eastern Europe. Data suggests that the current response to HIV among PWID is insufficient, and hindered by multiple environmental barriers including restricted access to services and unsupportive policy or social environments.

## ARTICLE SUMMARY

### *Article focus*

- A systematic review to identify and synthesise prevalence estimates and risk factors for HIV among PWID in Central and Eastern Europe and Central Asia.
- A summary of key data to describe the response to HIV among PWID in Central and Eastern Europe and Central Asia, including a brief characterisation of the policy environments.

### *Key messages*

- The review highlights that the HIV epidemic among PWID in the region varies from country to country, with Eastern European countries generally the worst affected. Prevalence is extremely high among PWID in many countries with some studies suggesting more than one in two PWID are infected with the virus in parts of Estonia, Russia and Ukraine.
- Despite few studies explicitly examining environmental factors, our review found that gender, socio-economic position and contact with law enforcement agencies to be associated with HIV prevalence. The complex interplay between the environment and individual behaviour of PWID is not fully understood and further emphasis on understanding the social epidemiology of HIV in this group is needed.
- An integrated package of needle exchange programmes (NSP), opiate substitution therapy (OST) and antiretroviral therapy (ART) is core to an effective response to HIV in this group. The coverage of such interventions in the region varies from low to non-existent and must be improved. Further resources coupled with improvement in the policy environments are key to reducing HIV transmission in this group.

### *Strengths and limitations of this study*

#### *Strengths*

- This review is the most comprehensive synthesis of HIV prevalence and risk factors among PWID in Central and Eastern Europe and Central Asia to date and is complemented by a clear synopsis of the state of the national policy environments and responses to HIV for people who inject drugs.

#### *Limitations*

- The quality of the review relies upon quality of the original articles, which are variable. The samples included are often selective as many studies recruited participants from specialist services or via drug user networks. Multivariate analyses are adjusted for a variety of factors, rendering direct comparisons between point-estimates difficult.
- The service coverage data is not measured in a standard fashion across the region, and is from different years. The quality of data varies hugely by country, thus undermining the comparisons we can make about coverage.
- We use a crude index of 'policy environment' which is developed from binary indicators that cannot account for important nuances influencing inter- and intra-country environments.

## INTRODUCTION

The HIV epidemics of Europe are diverse but in all European countries HIV disproportionately affects populations that are socially marginalised and people whose behaviour is socially stigmatised or illegal. The epidemics in Eastern Europe and Central Asia, which are predominantly associated with injecting drug use, are among the fastest growing in the world.[1] Over two thirds of all HIV diagnoses to date in Europe fall in Eastern Europe and Central Asia, and over 70% of these emanate from Russia.[2 3] Over 27,000, or over 30% of new cases of HIV were attributed to injecting drug use in Central and Eastern Europe and Central Asia in 2010.[2 3] Almost all of these (99.6%) were made in Eastern Europe and Central Asia. Accounting for differences in absolute population size, between 2006 and 2010, 89 new HIV diagnoses associated with injecting drug use have been made on average each year in the East per million people. This contrasts with Central Europe where the rate is 100 times less at 0.8 per million.[2]

Because of low access to and uptake of HIV testing and counselling – especially among the marginalised and stigmatised populations most at risk of HIV infection and transmission – not all HIV cases in Europe are diagnosed and reported.[4] Estimates suggest that reported cases probably represent just over half of all people living with HIV in Europe.[4] It is estimated that just over 2.3 million people were living with HIV in Europe in 2010, 840 000 in Western Europe and 1.5 million in Eastern Europe.[4]

There are an estimated 3.1 million people who inject drugs (PWID) in Central and Eastern Europe and Central Asia, of whom one million are estimated to be HIV infected.[5] In Russia alone, there are an estimated 1.8 million PWID, of whom around 700,000 are thought to be HIV infected.[5] Estimates of the prevalence of HIV among PWID in Central and Eastern Europe and Central Asia vary widely, from zero in some Central European countries where injecting drug use is less widespread, to over 20% in some countries in Eastern Europe and Central Asia, including Estonia, Moldova, Russia, and Ukraine.[5 6]

HIV and other blood-borne infections contribute significantly to the excess morbidity and mortality experienced by PWID in Europe and elsewhere.[7 8] HIV has the potential to spread rapidly via the sharing of needles and syringes between PWID as well as via unprotected sex between PWID and their injecting and non-injecting partners.

### *The social contexts of HIV epidemics*

A growing body of work substantiates relationships between health harms related to drug use and social-material factors that shape vulnerability to HIV.[9-16] The heuristic of the HIV ‘risk environment’ envisages HIV risk as the product of reciprocal relationships between micro and macro level influences in the physical, social, economic, and policy environments which contextualise individual and community actions in relation to risk.[9-15] This interaction has been described as a reciprocal process whereby individual actions are constrained as well as enabled by their environments and in turn shape as well as reproduce those contexts.[17] Qualitative work among PWID in Russia, for example, has illustrated how reduced capacity for HIV risk reduction in the micro environment is shaped by street-level policing practices which are in turn contextualised by broader structural policies of criminalisation and cultural practices of marginalisation which taken together produce a collectively internalised fear and sense of constrained agency among PWID.[17 18]

Recent reviews have thus called for a shift towards social epidemiological approaches.[9-15] These investigate how the distribution of HIV in populations is in part shaped by ‘social factors’, that is, forces that extend beyond ‘proximal’ individual-level factors and their biological mediators. This simultaneously demands a shift from binary models of ‘cause and effect’ to ‘multi-level’ models, which enable HIV risk to be understood as an effect of multiple contributing factors, at once interacting together, including potentially in ‘non-linear’ and ‘indirect’ ways.[19] Delineating causal pathways to inform structural interventions is thus a daunting yet critical challenge. Recent evidence reviews suggest that currently the epidemiology of HIV among PWID rarely explicitly embraces the study of social determinants.[20]

1  
2  
3 The social and economic transitions transforming the Central and Eastern European and Central Asian region in the  
4 past twenty years have been abrupt, dramatic, and long lasting. In many countries of the region, economic  
5 uncertainty has combined with weakening social capital, an embryonic and fragile civil society, a poorly resourced  
6 and overly vertically-structured health system, and public policies tackling drug use that have emphasised law  
7 enforcement and security at the expense of public health.[16 21] Social and economic transformations following  
8 the dramatic political change in Eastern European and Central Asian countries have played a role in shaping  
9 transitions in problematic substance use as well as vulnerability to HIV.[21-26] The opening-up of international and  
10 trade borders, for instance, has facilitated population mixing as well as the development of heroin trafficking  
11 routes from Afghanistan to the West, also linked to the diffusion of heroin use.[27] There was evidence of  
12 explosive HIV outbreaks linked to injecting drug use in the former Soviet region by the mid 1990s, especially in  
13 Russia, Ukraine, and Moldova.[21]  
14

### 15 16 *Enabling policy environments for HIV prevention*

17 Recognising HIV epidemics as features of their social and structural contexts emphasises the potentially pivotal  
18 role of social and structural interventions in creating environments which are enabling, rather than constraining, of  
19 evidence-based HIV prevention.[28-30] Key dimensions of 'enabling' policy environments conducive to effective  
20 HIV prevention for PWID include, but are not restricted to: the meaningful engagement of key stakeholders  
21 (including PWID) in policy formation and programming; a coordinated multi-sectoral national HIV prevention  
22 strategy emphasising an evidence-based public health and rights-oriented approach; the generation of research  
23 and surveillance on HIV epidemic spread and response; and the development and scale-up of a package of  
24 evidence-based interventions, including the removal of structural obstacles limiting their implementation.[31-33]  
25 This has led to calls to de-emphasise the criminalisation of PWID by developing policies emphasising public health  
26 above law enforcement dominated approaches, and for the rapid scaling-up of harm reduction interventions  
27 including syringe exchange, opioid substitution treatment (OST), and antiretroviral HIV treatment (ART), as well as  
28 community action and social support interventions.[31 32 34-36]  
29

### 30 31 *Review scope*

32 We aim to systematically review epidemiological research investigating the burden of HIV, and associated risk  
33 factors, among PWID in Central and Eastern Europe and Central Asia. We seek to identify the extent to which such  
34 epidemiological research captures measures of the HIV risk environment by delineating HIV risk factors identified  
35 at the levels of the individual and environment. We situate this epidemiological work by synthesising current  
36 evidence reviews of the extent and availability of HIV prevention targeting PWID in the region and by developing a  
37 simple index of 'enabling' policy environment at the country level.  
38  
39

## 40 41 **METHODS**

42 We reviewed data from the 30 Eastern and Central European and Central Asian countries in WHO defined Europe,  
43 including 15 from Eastern Europe and Central Asia (Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan,  
44 Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and  
45 Uzbekistan), 'the East', and 15 from Central Europe (Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus,  
46 Czech Republic, Hungary, Macedonia (FYR), Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia, and Turkey),  
47 'the Centre'.  
48

### 49 50 *Search strategy and selection criteria*

51 We systematically searched Medline, Embase, Global Health, Social Science Citation Index, Popline, and CINAHL for  
52 studies published from 2005 to October 20, 2011. To identify articles we combine four broad search themes with  
53 the Boolean operator "AND". The first theme, HIV, combined the Medical Subject Headings (MESH) terms "HIV" or  
54 "HIV infections" with the free word search for "HIV", "human immunodeficiency virus" with "OR". The second  
55 theme, prevalence, incidence and risk factors, included the MESH terms "prevalence", "incidence", "risk", "factor  
56 analysis", "statistical", "regression analysis", "risk factors", "risk-taking", and "epidemiology" with the free words  
57 "prevalen\*", "incidence", "risk\*", "correlat\*", "determinant\*", "vulnerab\*", "regression", "risk", "(enhanc\*adj3)  
58  
59  
60



transmission", "multivar\*", "(route\*adj3 transmission)", "(factor\*adj3 transmission)", "social norm\*", "network", "socio-demographic", "socio-economic", "lifestyle", and "epidemiol\*" with "OR". The third theme, geographic coverage, included the names of the countries in the region, as well as the free word terms "Europe\*" and "Central Asia\*" combined with "OR". The fourth theme, PWID, combined the MESH terms "substance abuse", "intravenous", "needle sharing" and "heroin dependence" with the free word terms "IDU\*", "inject\*", "intravenous", "heroin", "addict\*", "opiate\*", "narco\*", "psychotropic\*", "psychoactive\*", "drug depend#n\*", "(recreation\*adj3 drug\*)", "harm reduction", "syringe\*", "methadone", "opioid\*", "syringe\*", "(needle\*adj3 shar\*)", and "(illegal\*adj3 drug\*)" combined with "OR".

Additionally, we systematically searched websites of research institutes, service providers, and donor organisations working with PWID across the region including recent reports from countries reporting to the United Nations General Assembly Special Session on HIV/AIDS (UNGASS). We searched the website of the European Monitoring Centre for Drugs and Drug Addition (EMCDDA) for data and sources reported from member and neighbouring countries. Conference abstracts from the International Conference on the Reduction of Drug Related Harm (2005-2011) and the International AIDS Conference (2006, 2008, 2010) were also searched. Our review conformed to the PRISMA checklist for systematic reviews.[37]

### *Study selection and eligibility criteria*

All abstracts were reviewed. Studies were excluded if they were: a) published before 2005; b) fell outside the defined geographic region; c) did not focus on HIV among PWID; d) did not sample PWID; or e) did not focus on bio-confirmed HIV prevalence or incidence, or injecting or sexual risk practices. Papers were also excluded if they reported a sample size less than 50, had unclear sampling methods, or they contained no primary data, although the references were searched to gather primary studies not identified by the search. Papers not fitting the inclusion criteria were set aside to aid interpretation of the systematic review findings. Figure 1 summarises the papers searched and retained in the review. Following full-text review 100 peer-reviewed and grey literature documents were identified as meeting our criteria, of which 70 reported an incidence or prevalence measure, and 30 demographic or risk factor data only. Of the 70 documents reporting prevalence or incidence data, 14 included the results of a multivariate analysis.

### **[FIGURE 1]**

Two authors (EJ and LP) independently assessed the quality of the studies reporting HIV prevalence estimates using a scoring system that graded the papers on: wide geographic coverage; most recent study; population sampled; and recruitment setting. We allocated up to three points each for most recent studies, population sampled, country coverage, and for the range of settings sampled, and deducted one point for drug treatment only samples due to the potential for bias.[38]

### *Data extraction*

The results of the multivariate studies meeting our inclusion criteria were extracted as presented, regardless of the strength of association. Comparable factors were collected and examined using forest plots showing the effect estimates and 95% confidence intervals (95%CI). We classified the results of the multivariate studies as 'individual-level' factors or 'environmental-level' factors based on the proximity of the risk of the factor in terms of HIV transmission. Individual-level risk characteristics or activities included injecting and sexual risks, such as sharing needles or unprotected sex, that shape an individual's HIV risk through direct biological mechanisms. Environmental-level factors are those which have no direct biological means of influencing HIV risk, however, their presence or absence has been identified as an independent factor in the risk faced by an individual, indicating their role in shaping a 'risk environment'.

### *Coverage of HIV prevention interventions*

In addition to the systematic review, data summarising the coverage of HIV prevention interventions was drawn primarily from recently published reviews [39] and previously published country level data[40]. These data are

1  
2  
3 collected from a variety of sources, including UNGASS, WHO, and systematic reviews of scientific literature[39], as  
4 well as from routine national reports.[40]  
5

### 6 *Policy environment index*

7 We generated a simple index of 'enabling' policy environment. Our interpretation of an enabling policy  
8 environment drew upon guidelines generated by WHO [41], UNAIDS,[42] international non-government  
9 organisations (NGOs),[43] and peer-reviewed papers in this field.[20 30 32 44] As outlined in Box 1, the core items  
10 of the index included indicators, at the country level, of: coordinated national strategy to HIV prevention and drug  
11 use (indicated by evidence of explicit inclusion of 'harm reduction' in national-level strategy, and monitoring and  
12 evaluating HIV epidemics); meaningful engagement of stakeholders in HIV prevention policy formation and  
13 programming (indicated by evidence of a national organisation of drug users); and evidence-based HIV prevention  
14 intervention approaches (indicated by presence of OST and NSP, presence of OST and NSP in prison settings, and  
15 evidence of de-emphasising criminalisation through the use of administrative penalties for drug use possession for  
16 personal use).  
17

### 18 **[BOX 1]**

19  
20 Indicator data were obtained from a combination of sources, including: global reports of harm reduction policy and  
21 coverage;[45] country profiles collated and updated by the EMCDDA;[46] our systematic review of research studies  
22 (see above and Figure 1); and the International Network of People who Use Drugs[47]. The index was constructed  
23 by allocating equal weight to each of the six items and aggregating a score for each country, with higher scores  
24 indicating a more 'enabling' environment conducive to evidence-based public health approaches.  
25  
26

## 27 **RESULTS**

### 28 *HIV incidence*

29 Only three papers reviewed reported HIV incidence among PWID in this region. Two in Tallinn, Estonia, reported  
30 an HIV incidence rate of 31/100 person years (PY) in 2004, decreasing to 9/100 PY in 2009 among people injecting  
31 for less than three years.[48 49] The other from St Petersburg, Russia, reported a rate of 4.5/100 PY.[50]  
32

### 33 *HIV prevalence*

34 Estimates of HIV prevalence among PWID vary widely throughout the region. A total of 79 sources reported HIV  
35 prevalence estimates (some multiple), of which 67 reported unique HIV prevalence estimates among PWID in the  
36 region; 44 from Eastern Europe and Central Asia[6 50-89] and 21 from Central Europe[90-110] and two that  
37 contained data from both regions.[40 111]  
38

### 39 **[FIGURE 2]**

40 Multiple estimates exist for many countries (Figure 2), and where this was the case we applied the scoring system  
41 described above (see Methods) to select the estimate that appeared to be most representative at the country-  
42 level. Using these estimates, we have categorised country HIV epidemics among PWID as: "low" (up to 1%);  
43 "medium" (2% - 5%); "high" (5% - 20%); and "very high" (greater than 20%).  
44

45 No country in the East can be considered to have a 'low level' of HIV among PWID, and only Kazakhstan, Georgia  
46 and Lithuania have 'medium level' epidemics, according to the studies examined here. Of the remaining 11  
47 countries with data (no data exists for Turkmenistan), three have prevalence estimates of over 20% (Moldova,  
48 Russia, and Ukraine) and Estonia has a prevalence of over 50%. In the Centre only Poland and Bulgaria appear to  
49 have 'high level' epidemics and neither of these exceed 10% prevalence. Several countries (Albania, Croatia,  
50 Cyprus, Hungary, Macedonia, and Slovenia) report 0% HIV prevalence among PWID. However, there is less data  
51 from this region and sample sizes are generally smaller so the estimates may be less robust than those from the  
52 East.  
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### Demographic profile

Generally, three times as many men as women inject drugs, although male predominance reached as high as 95% in some studies from the Caucasus.[51 55 56 63 65 86 112] The mean age of PWID participating in studies was mid-twenties, although many studies restrict recruitment to PWID aged 18 or over. The proportion of PWID reporting having regular income was generally low.

### Pattern of injecting drug use

Heroin is the drug of choice among PWID in Europe, although there are sub-regional differences. In Moldova[113], Ukraine[74] and Russia[53], the injection of home-produced opioids such as 'hanka' or 'shirka'(a liquid poppy extract) is reported alongside heroin injection. In Estonia the use of the synthetic opiate, fentanyl ('China White', 'White Persian' or 'Afghan'), has become common alongside amphetamine injection.[72 114] In Central Europe, heroin is reported as the main drug injected, although studies also report between 30% and 51% injecting amphetamines as their main drug[101 115 116], and the Czech Republic reports the highest prevalence of methamphetamine use in Europe.[117-119] The frequency of injection varies widely throughout the region.

### Contact with criminal justice systems

The data reviewed from Eastern Europe and Central Asia suggests that between half and three-quarters of PWID have experienced arrest. A study among 600 PWID in Odessa, Ukraine found that police beatings were common, with nearly 50% reporting at least one such experience.[20 120] Studies in other regions also suggest relatively high rates of police arrest (42% - 76% ever having been arrested).[18 27 108 121] In Estonia and Lithuania, an estimated 58%-70% of PWID had been in prison at least once.[75] In Georgia and Russia, this figure was between 6% and 37%.[18 53 65 66 80 122 123] In Central Europe, between 18% and 50% of respondents report previously having been in prison[94 108]

### Individual-level risk factors for HIV

No studies examined risk factors linked to HIV in the Centre, and so we summarise the findings of the multivariate HIV risk factor analyses from 14 papers identified by our review in the East[50 52-54 58 66 73 74 89 114 122 124-126], although two[66 73] present new analyses of data already published in other papers also presented here.[124 126] Table 1 summarises the key characteristics of the 14 papers as well as the factors explored in the multivariate analysis. The forest plots summarised in Figures 3 and 4 synthesise the effects of particular individual and environmental risk factors on HIV. Although studies measure similar associations, it is important to note that each may have carried out analyses in a unique fashion, adjusting for different confounding variables.

#### [TABLE 1]

As shown by the individual risk factor estimates presented in Figure 3, many studies investigated the link between HIV and *injecting with a used or shared needle*. Although the effect sizes tend towards increased HIV risk, most results are inconclusive, "social-desirability" bias possibly influencing self-reported responses. Injecting with the used needle of a sex partner was found in Volgograd[53] and Tallinn[114] to clearly increase an individual's odds of HIV. More definitively, injecting with a needle previously used by someone known to have HIV or hepatitis C is shown in most studies to be clearly positively correlated.[74 126] *Daily injecting* is also found to be positively associated. Many reviewed studies also associate *longer injecting careers* with greater odds of having HIV[126]. Although a Russian study found no difference in an individual's odds of HIV according to the primary drug they inject[127], studies in Estonia found that primary injectors of an opiate (fentanyl) had between three and four and a half times greater odds of HIV than individuals who primarily inject amphetamines.[114 128]

#### [FIGURE 3]

Regarding exploration of HIV and associated *sexual risk* including sex work (SW), most multivariate analyses explored the associations between exchanging sex for drugs or money, the number of sexual partners, and unprotected vaginal or anal sex, as risk factors. Although several strong univariate associations were found, these

1  
2  
3 tended not to hold in the multivariate models (Figure 3). This could be because sample sizes were insufficient or  
4 because much sexual risk behaviour is determined by other individual or environmental factors such as gender,  
5 socio-economic status or injecting behaviour.  
6

#### 7 *Environmental-level risk factors for HIV*

8 Although most studies presented show adjusted odds ratios identifying female *gender* as a risk factor for HIV  
9 (Figure 4), the confidence intervals generally straddle one and are inconclusive.  
10

#### 11 **[FIGURE 4]**

12  
13 Multiple studies link HIV to the *socio-economic status* of PWID, though economic status is defined through  
14 different measures, including level of education, employment (regular or not) and income (regular or not, legal or  
15 not) (Figure 4). Of these measures, only an individual's employment status showed a consistent association with  
16 HIV, with unemployed individuals or those having a main source of income that was not work, showing greater  
17 odds of HIV than others.[54 58 89 122] An Estonian multi-level study included neighbourhood level data in its  
18 analyses and found neighbourhood level effects of unemployment (10% increment in unemployment AOR 5.95,  
19 95%CI 2.47-14.31) and habitat change since 1989 (10% change AOR 1.89, 95%CI 1.09-3.26) to be both associated  
20 with HIV prevalence (results not presented).  
21

22  
23 Several studies have examined *contact with law enforcement agencies* as an environmental factor linked with the  
24 odds of being HIV infected, although the results produced by the systematic review have large confidence intervals  
25 and are largely inconclusive.[53 66 114 126] The review reveals that contact between police and PWID in the  
26 region is highly commonplace and no studies examined the frequency or duration of contact.  
27

28  
29 In addition to the universally relevant factors highlighted above, some studies analysed the relationship between  
30 HIV and determinants that are particular to local context (results not shown). For example, a study in Tajikistan  
31 found that respondents identifying as Tajik (AOR 7.06,  $p < 0.001$ ) or other ethnicity (AOR 6.05,  $p < 0.001$ ) as opposed  
32 to Russian were at higher risk of testing positive for HIV.[73] A study in Uzbekistan similarly found respondents of  
33 Uzbek ethnicity to have higher odds of HIV than their Russian counterparts (AOR 1.20, 95%CI 0.80-1.80).[54]  
34 However, a study in Estonia found that ethnic Estonians had a reduced odds of HIV compared with those of  
35 Russian or other backgrounds (AOR 0.63, 95%CI 0.28-1.25).[114] In Moscow and Tallinn ever having been  
36 registered as a PWID at drug treatment was found to be associated with more than double the odds of HIV (AOR  
37 2.4, 95%CI 1.3-4.7; AOR 2.4, 95%CI 1.5-3.8)[53][114]. Conversely, a study in Togliatti in Russia conducted among  
38 96 new (<three years) injectors found having been in drug treatment in the past as negatively associated with risk  
39 of HIV (AOR 0.4, 95%CI 0.1-1.0).[129]  
40

#### 41 *HIV prevention coverage*

42  
43 Coverage – the proportion of the population at risk reached by an intervention, ideally with sufficient intensity to  
44 have probable impact – emerges as a critical determinant of HIV prevention effectiveness.[32 130-132] Our review  
45 did not focus on collating primary data but sought to synthesise coverage estimates relevant to the Central and  
46 Eastern European and Central Asian region from key recently published reviews regarding NSPs, OST, and ART.[39  
47 40] These data are contained in Figure 5. They indicate that NSPs were available in all countries of the region,  
48 except Turkey, though intervention coverage varies widely. For instance, whereas 50% of PWID in Hungary in 2007  
49 had access to NSPs, with each receiving around 135 clean needles a year (135 per PWID based on country-level  
50 estimates of PWID), in Russia only 7% of PWID had such access to NSPs, with each receiving 56 needles each a year  
51 (four per PWID based on country-level estimates of PWID). These estimates do not include pharmacy-based  
52 provision, which is a primary source in some countries in this region, including Russia.[133] Figure 5 also shows  
53 that four of the 30 countries in this region reporting evidence of injecting drug use did not provide OST: Russia,  
54 Uzbekistan, Turkmenistan, and Turkey. Coverage of OST is generally low, with Slovenia showing the greatest  
55 coverage.  
56  
57  
58  
59  
60

**[FIGURE 5]**

Comparing the proportion of HIV cases caused by injecting drug use with the corresponding proportion of people receiving antiretroviral therapy who inject drugs, in 2002, 71% of the reported people living with HIV acquired HIV infection through injecting drug use, whereas only 20% of those receiving antiretroviral therapy were people who injected drugs. In 2005 and 2006, among 21 and 23 countries with available data, people who injected drugs represented 77% of reported cases and 26% of antiretroviral therapy recipients, a proportion that declined to 22% in 2010 among 19 reporting countries. Although no trends can be statistically ascertained due to incomparable samples (notably missing data from the Russian Federation in 2002 and 2010), these data suggest that most of the people who acquire infection in reporting countries are people who inject drugs and that, despite this, their treatment needs remain considerably underserved.[4]

We found no data relating to the impact or coverage of structural level interventions on HIV among PWID, although recent legislative changes in Moldova and the Czech Republic have de-emphasised the criminalisation of small amounts of drugs possession.

*Enabling policy environments*

Figure 6 shows the results of the policy index developed (see Methods) to describe the distribution of enabling policy environments throughout Central and Eastern Europe and Central Asia. Darker shading represents seemingly more supportive policy environments for HIV prevention and lighter shading seemingly less supportive environments.

**[FIGURE 6]**

Of the 30 countries in the region, 25 explicitly and supportively mentioned harm reduction in their national strategies, and 27 have undertaken at least one sero-prevalence and one behavioural study among PWID in the last ten years. In 26 countries, OST and NSP are available generally, but available in prison in only three countries. Five countries have national organisations of drug users, and five countries use administrative rather than criminal penalties for people found possessing small quantities of drugs for personal use.

Based on the index, the countries with the most supportive policy environments are Moldova and Romania. The countries with the least supportive environments are Turkmenistan and Turkey. Turkmenistan does not show any of the features of a supportive environment according to our index, although Turkey has conducted at least one sero-prevalence and one behavioural study among PWID in the last ten years. In Russia, where the majority share of HIV infections among PWID in the region are located, the national strategy refers to harm reduction as a threat to efforts to reduce the demand for drugs, with NSPs and OST specifically mentioned as problematic for federal level support.[134] OST is unavailable in Russia, and NSPs are limited in number, with none available to prisoners, and there is a focus on criminal rather than administrative penalties for drugs possession. However, there is some evidence of drug user activism and organisation.[47]

Russia and Ukraine both feature among the countries experiencing high HIV prevalence among PWID, and like Russia, criminal punishment rather than administrative sanctions for drug use and possession is the norm in Ukraine. While Ukraine has a relatively high number of NSPs alongside increasing availability of OST, it does not provide harm reduction services in prisons. Moldova and Estonia also feature among the high HIV prevalent countries but both appear as to present relatively supportive environments for PWID. However, to our knowledge, neither has an active national drug user organisation and neither NSP or OST in prison settings.

**DISCUSSION***HIV epidemic contexts*

1  
2  
3 All but one country (Turkmenistan) in Central and Eastern Europe and Central Asia has generated survey-based  
4 estimates of HIV prevalence among PWID. Our review of these studies shows that HIV prevalence among PWID is  
5 highest in the Eastern European countries of Estonia, Russia, Moldova, and Ukraine (over 20% in each), and lowest  
6 in the Central European countries of Albania, Croatia, Cyprus, Hungary, Macedonia (FYR), and Slovenia (0% in  
7 each). We identified only three HIV incidence studies among PWID in the region, showing incidence of 9/100  
8 person years in Estonia in 2009[49] and 4.5/100 person years in Russia[50]. Accepting that country estimates of  
9 HIV prevalence inevitably only reflect the characteristics of the particular samples from which they are drawn,  
10 these estimates taken together reiterate that the burden of HIV linked to injecting drug use falls in the East, and  
11 especially Russia, where over half of all HIV cases among PWID in the region are located.  
12

13  
14 Multivariate analyses of HIV risk factors among PWID underscore injecting with a used needle/syringe, frequent  
15 injecting, and injecting opiates as opposed to amphetamines as proximal factors associated with increased risk of  
16 HIV. We acknowledge that the findings of the multivariate studies we synthesise in the review may not be directly  
17 comparable, as they have been derived from studies using different regression techniques and adjusting for  
18 different confounding factors. While most of the epidemiological studies we reviewed did not embrace, by design,  
19 the exploration of environmental risk factors – as is the case with HIV epidemiological studies globally[20] – a  
20 number of important factors in the HIV risk environment can be identified. These included increased HIV risk  
21 among *women*, an association we interpret to have indirect, rather than biological, causative roots through  
22 pathways involving multiple linked socio-economic differences related to gender. Although most studies showed  
23 women at greater risk of HIV than men, the confidence intervals presented include the null value, preventing us  
24 from drawing conclusions on the effect of gender on HIV risk. The lack of conclusive evidence could be due to the  
25 small number of women often recruited in to research, as well as genuine variability in the consequences of female  
26 gender in different settings. Qualitative data from Ukraine suggests that female PWID are at increased risk of  
27 psychological, physical (including sexual) and economic violence from their male partners, constraining capacity to  
28 negotiate safer sex, safer injecting practices, and access to helping services, in consequence elevating their HIV  
29 risk.[135]  
30

31 Additionally, *socio-economic status* – whether measured by income or employment – emerged as important,  
32 although only employment status appeared conclusively associated with HIV risk. The direction and pathways  
33 income and employment effects have on HIV risk may vary locally. The ways in which HIV links to wealth and  
34 poverty is shaped by social context, and in some settings injecting has diffused among those whose economic  
35 status may be comparable to the wider local population.[53 136]  
36

37  
38 Lastly, we note contact with *criminal justice agencies*, including experience of incarceration, as an important risk  
39 factor,[53 66 114 126] although the studies systematically reviewed here were inconclusive in this regard. Studies  
40 evidencing the adverse effects of the legal environment on HIV risk among PWID suggest a relationship between  
41 street-based policing practices, including extra-judicial ones such as police violence, and increased HIV  
42 vulnerability, including through reduced capacity for risk avoidance as a consequence of safety short-cuts and  
43 rushed injections borne out of a fear of detection or arrest.[18 27 120 137-139] While evidence internationally  
44 links prison and a history of incarceration to elevated odds of HIV among PWID[140 141], only three countries in  
45 the region (Moldova, Romania, and Kyrgyzstan) provide harm reduction services to prisoners. An association  
46 between HIV among PWID and being of a minority ethnicity that cannot otherwise be explained by needle sharing  
47 has been noted elsewhere, and linked to material as well as other social inequalities, including access to support  
48 services.[142 143] In parts of Eastern Europe and Central Asia where PWID are often required to register as such to  
49 obtain drug treatment or are forced to through contact with police, this can lead to increased social  
50 marginalisation as well as reducing their ability to gain employment or even to drive a car.[144]  
51

52 Whilst the epidemiological studies we reviewed provide some pointers to the role of HIV risk environments, they  
53 are self-evidently limited in their capacity to capture how HIV is an effect of social context. This highlights the  
54 urgency to develop specifically tailored social epidemiological approaches, which build into their designs from the  
55 outset measures of micro and macro risk environment. It also highlights the importance of mixed-methods  
56 approaches, especially those combining qualitative with epidemiological data[145]. For example, by linking HIV  
57 epidemiology to data on shifting drug trafficking routes it has been possible to plot the macro physical distribution  
58  
59  
60

1  
2  
3 of HIV.[146] In the region of Central and Eastern Europe and Central Asia, the potentially HIV risk productive role of  
4 transit routes for heroin originating from Afghanistan through Central Asian countries along the “Northern Route”  
5 to Russia and beyond provides a similar example. In 2009, UNODC estimated that 25% of all Afghan heroin (95  
6 metric tons) was transported along this route, with the majority travelling through Tajikistan, to Osh in Kyrgyzstan,  
7 and then on to Kazakhstan, before arriving in Russia.[147] The effects of this trafficking route appear to have HIV  
8 impacts with Kulyab, in Tajikistan, a major hub for Afghan opiate trafficking, reporting the highest HIV prevalence  
9 among PWID in Tajikistan at 34.5% in 2009 compared with the national average of 17.3%.[148] Jalal-Abad reported  
10 the highest HIV prevalence among PWID in Kyrgyzstan at 14% in 2007[149] compared with a national average of  
11 7.7%.[84] In Kazakhstan, there is substantial overlap between the sites with the largest number of diagnosed HIV  
12 infections, largest number of registered drug users and highest number of heroin seizures.[150]  
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14  
15 Future epidemiological studies of HIV among PWID need to better systematically develop measures of HIV risk  
16 environment and how these combine to increase or reduce HIV risk.[20] Because epidemiological studies of PWID  
17 tend to focus on the proximal determinants of risk behaviour and HIV transmission, there is a need to shift towards  
18 capturing distal factors and how these interplay to produce pathways of risk.[19 20 28 151] Principal among these,  
19 according to our review, should be gender, social-economic status, and the effects of criminalisation.  
20

21 In addition to the limitations discussed above, the study is subject to several potential biases including missing key  
22 documents, especially those not published in the English language. Individual studies may tend to publish what are  
23 considered ‘interesting’ results, leading to potential publication bias towards analyses reporting significant results.  
24 This can lead a systematic review such as ours to overstate the effect of several factors. As some elements of this  
25 review were undertaken by the same authors, this may reduce protection against human error and preservation of  
26 independence between the stages of the review.  
27

### 28 *Towards enabling policy environments*

29 It is well established that HIV prevention targeting PWID requires a ‘combination intervention’ approach tailored  
30 to local setting, including a balance of: needle and syringe distribution programmes (NSPs); opioid substitution  
31 treatment (OST); antiretroviral HIV treatment (ART); peer education and outreach; HIV testing and counselling  
32 services; and the promotion of public policies and other structural changes conducive to public health approaches.  
33 [20 32 33 152-154] Evidence for the effectiveness of these interventions is well established.[32 152 155 156] The  
34 extent of HIV prevention intervention coverage, however, varies throughout the region, and is largely  
35 inadequate[39 40]. Many of the countries with the lowest levels of harm reduction service provision are also those  
36 with the highest HIV prevalence and the largest per-capita number of new diagnoses. The unavailability of OST in  
37 Russia in particular means that the majority of PWID in the region do not have access to an integral component of  
38 evidence-based HIV prevention.  
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40  
41 Structural interventions seek to remove environmental barriers to HIV prevention while enabling environmental  
42 conditions which protect against vulnerability to HIV. While the relationships between HIV-related policies and  
43 their impacts upon micro-level HIV risk practices are clearly not straight forward, the policy environment is a clear  
44 object of structural intervention and change. Our review identified no evidence specifically relating to the impact  
45 or coverage of structural level interventions on HIV among PWID, although recent legislative changes in Moldova  
46 and the Czech Republic have de-emphasised the criminalisation of small amounts of drug possession, and evidence  
47 elsewhere in Europe links such initiatives with reduced HIV risk and increased access to helping services[157].  
48

49 In the absence of social epidemiological data generated from systematic review, we developed a crude index of  
50 ‘enabling policy environment’ based on indicators of: national-level policy endorsing of harm reduction  
51 approaches; research of HIV prevalence and risk behaviour among PWID; drug user community organisation;  
52 availability of OST and NSPs; availability of OST and NSPs in prison settings; and application of administrative rather  
53 than criminal penalties for drug use and possession (see Box 1). Such an index seeks to include quantifiable  
54 indicators of the practical application of ‘healthy policy’, at least as far as such data is comparatively available. We  
55 acknowledge the limits of this exercise, but argue for the need for future epidemiological research to better  
56 monitor indicators of enabling and risk environment alongside proximal risk factors for HIV, especially those  
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3 pertaining to community involvement and partnership in policy formation, availability of HIV prevention in criminal  
4 justice settings, and shifts towards de-emphasising the criminalisation of drug use through providing treatment or  
5 care as an alternative to arrest or imprisonment.  
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7  
8 Applying our index of enabling policy environment highlighted large discrepancies throughout the region. Of the  
9 countries with a seemingly unsupportive environment for HIV prevention among PWID, Turkmenistan may present  
10 a particular concern, for it is located between countries of high HIV prevalence, situated on a heroin trafficking  
11 route, and appears to lack a baseline of epidemiological evidence. Other countries – including Russia, Uzbekistan  
12 and Azerbaijan – appear to present weak policy environments for HIV prevention, compounding potential risk  
13 linked to low level HIV prevention coverage. The lack of systematic monitoring of policy environment indicators in  
14 the region, and the neglected attention paid to monitoring the effect of structural-level factors on micro risk  
15 relationships in epidemiological research, hampers an understanding of how European HIV epidemic contexts may  
16 differ markedly regarding HIV prevention need and potential. The development of structural HIV prevention  
17 interventions as part of a combination intervention approach clearly requires evidence of how environmental-level  
18 factors impact upon HIV risk.  
19

20 The importance of reducing vulnerability to HIV/AIDS, by understanding and removing structural barriers, is  
21 increasingly recognised in European HIV policy, for example as one of the four strategic directions of the European  
22 Action Plan for HIV/AIDS 2012-2015, which proposes actions to: address laws and regulations that present  
23 obstacles to effective HIV prevention, treatment care and support; strengthen the enforcement of protective laws  
24 and regulations; strengthen civil society involvement in the HIV response and ensure gender and age equity in  
25 access to HIV and related health services.  
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**AUTHORS CONTRIBUTIONS**

Tim Rhodes, Lucy Platt and Vivian Hope developed the methodology for the systematic review.

Tim Rhodes, Lucy Platt, Vivian Hope, Alisher Latypov and Emma Jolley reviewed the collected literature.

Emma Jolley and Vivian Hope extracted the data.

Emma Jolley conducted the data analysis.

Tim Rhodes and Emma Jolley interpreted the data and drafted the manuscript.

All authors reviewed the manuscript and commented on the data and interpretation.

All authors gave approval for the manuscript to be submitted.

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3 **CONFLICTS OF INTEREST**  
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5 None declared.  
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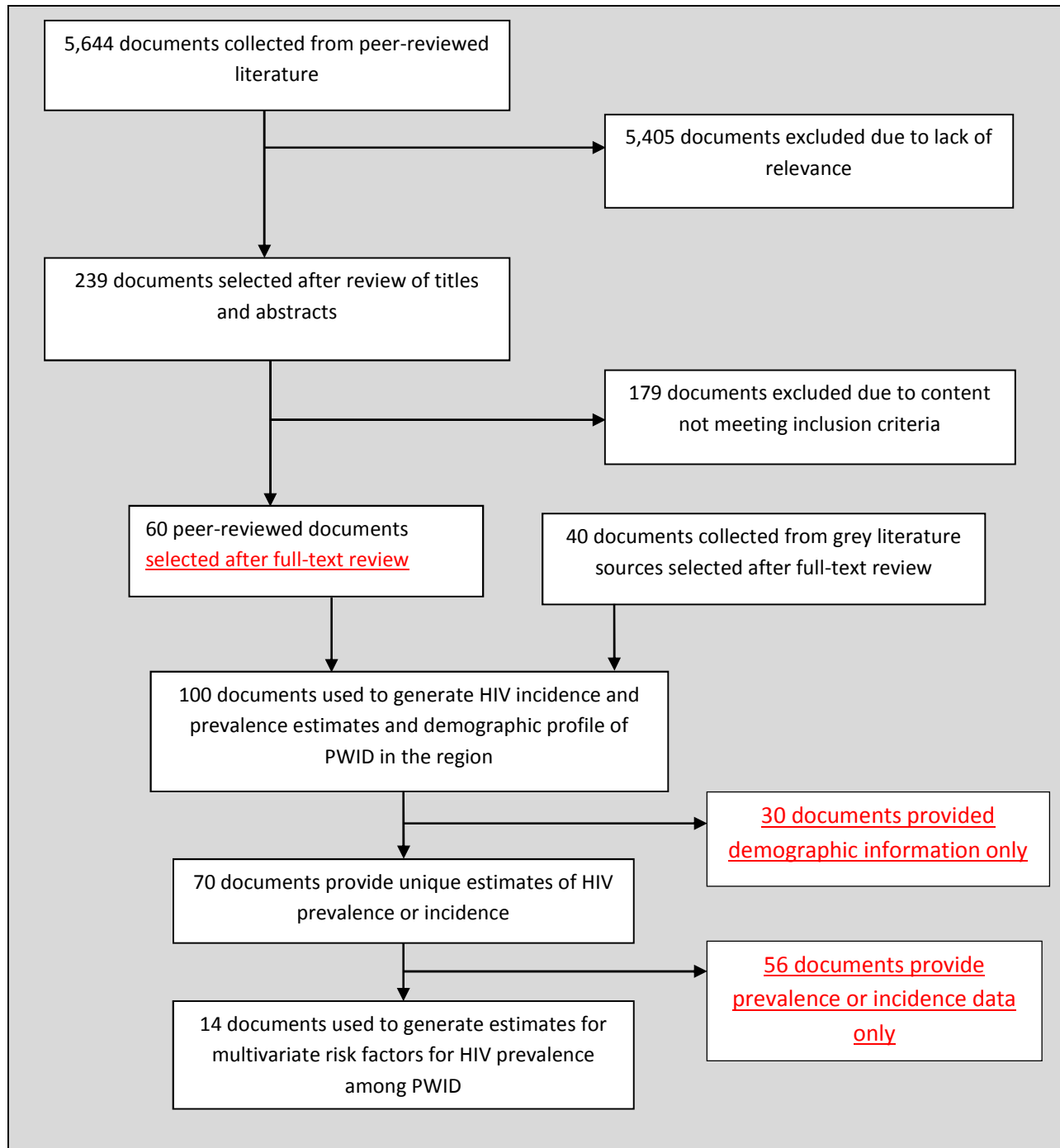
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Figure 1: Flowchart of study selection



**Box 1: A simple index of enabling policy environment****MEANINGFUL ENGAGEMENT OF STAKEHOLDERS**

1. The meaningful involvement of PWID in policies affecting their health and welfare and in related HIV prevention programming is accepted as an important indicator of 'health policy' formation.[42 158] While assessing 'meaningful involvement' is complex, we adopt a simple indicator: the **presence of a national organisation of drug users**.

**COORDINATED NATIONAL STRATEGY TO HIV PREVENTION AND DRUG USE**

2. Explicit and supportive reference to 'harm reduction' in national policy documents can mark a commitment to evidence-based interventions as part of HIV prevention responses targeting PWID. International agencies advocate institutional and national-level endorsement of harm reduction as a feature of national strategy.[33 159] We adopt **evidence of explicit supportive reference to harm reduction in national strategy** as an indicator of enabling policy environment.

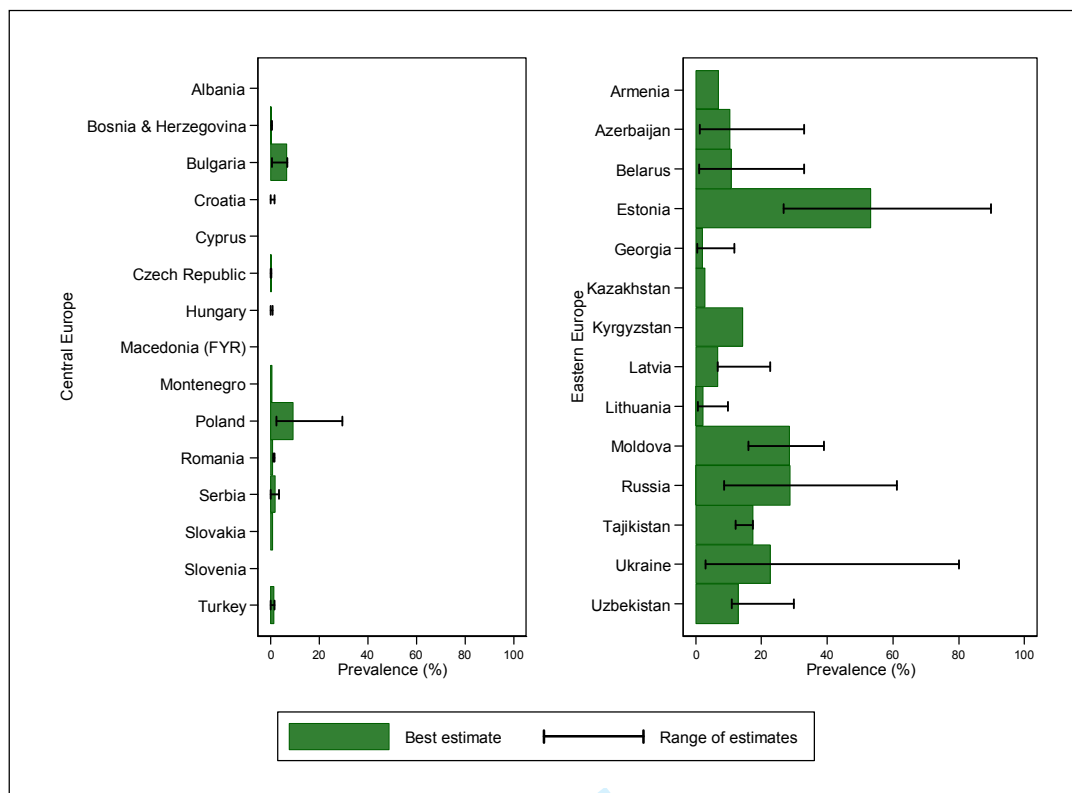
3. Monitoring and evaluating the state of the epidemic and response is an important element of building evidence-based responses.[40 160] Targeted sero-prevalence and behavioural surveillance is recommended in concentrated HIV epidemics.[161] We adopt as an indicator of enabling policy **evidence of at least one HIV sero-prevalence and one behavioural study among PWID since 2000**.

**IMPLEMENTATION OF PUBLIC HEALTH ORIENTED APPROACHES TO REDUCING HARM**

4. Drug control policies which seek to distinguish drug users from drug traders and traffickers, and which de-emphasise the criminalisation of drug users, can give priority to public health oriented approaches to reducing drug-related harm. We adopt the **application of administrative rather than criminal penalties for drug use and possession of quantities for personal use** as an indicator of an enabling policy environment.

5. We adopt **the legal availability of OST and NSP** in a country as an indicator of enabling policy environment. These are core components of the recommended nine combination HIV prevention interventions for PWID[33]. Many countries have adopted at least some recommended measures, but often the components missing are OST and NSPs. The effectiveness of both in improving the health of PWID is well established[32 155 162], especially for OST[163-168] [169]. OST also facilitates access to and augments the effects of other interventions, such ART[32 152].

6. **The availability of OST and NSPs in prison** can show a country's willingness to address the needs of even the most marginalised of its citizens, as well as demonstrating noteworthy scale of the programmes. Because of existing laws concerning drug use and possession, PWID in many countries account for disproportionately high rates of incarceration[140]. Prisons may act as a risk environment for HIV transmission linked to drug injecting. International guidelines[170] recommend continuity of services between prison and communities and some countries have developed successful partnerships between penal systems and HIV services, including in the European region.[171]



**Figure 2** The range of HIV prevalence estimates for countries in the Central and Eastern European region, along with the estimate judged “best” highlighted in green.

Review only

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
Platt et al, 2006[114]	Estonia, Tallinn	350 PWID who injected in past four weeks recruited by respondent-driven sampling (RDS)	Primary injection of opioid or amphetamine in past four weeks*; Duration of injecting career; Shared needle in past four weeks; Shared equipment in past four weeks; Injected with a used needle of a sex partner in past four weeks*; Number of sexual partners in past year	Age; Gender; Main source of income in past four weeks; Ethnicity; Ever registered in drug treatment*; Ever been in prison; Ever attended needle exchange
Abel-Ollo et al, 2009[72]	Estonia, Tallinn and Kohtla-Järve	<p>450 PWID (350 from Tallinn and 100 from Kohtla-Järve) who injected in past four weeks recruited by respondent-driven sampling (RDS). For analysis the participants were categorised as HIV-, HIV+ aware of their status and HIV+ unaware of their status, according to self-reported status at the time of testing.</p> <p>The data from Tallinn is also analysed above.</p>	<p><b>Analysis of risk factors for HIV among participants aware of their status (ref HIV- participants):</b>            Sharing used needles/ syringes in past four weeks*; Unprotected sex in past four weeks; Sharing water*; PWID as sex partner in past year*; Sharing injection equipment with sexual partner in past year*; Having two or more sex partners in past year; Unprotected intercourse in past year; Ever sharing needles with HIV+ person*.</p> <p><b>Analysis of risk factors for HIV among participants unaware of their status (ref HIV- participants):</b>            Sharing used needles/ syringes in past four weeks; Unprotected sex in past four weeks; Sharing water; PWID as sex partner in past year; Sharing injection equipment with sexual partner in past year; Having two or more sex partners in past year*;</p>	



Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Unprotected intercourse in past year*; Ever sharing needles with HIV+ person.	
Uusküla et al, 2010[89]	Estonia, Tallinn	350 PWID, aged 18+, who injected in past two months recruited by RDS	Earlier age of initiation to injecting*; Primary injection of opioid or amphetamine*; Receptive sharing in past six months*	Ever attended syringe exchange*; Main source of income other than work*; Unemployment at habitat level*; Residential change at habitat level*
Platt et al, 2005[126]	Russia, Togliatti	268 male PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks*; Injected with used needle in past four weeks; Ever injected homemade drugs; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+*; Unprotected anal or vaginal sex with a regular partner in past four weeks; Unprotected anal or vaginal sex with a casual partner in past four weeks*; Ever had an STI	Ever been in prison; Ever been in drug treatment; Ever been arrested;
	Russia, Togliatti	89 female non-sex worker PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks; Injected with used needle in past four weeks*; Ever injected homemade drugs; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+;	Ever been in prison; Ever been in drug treatment; Ever been arrested

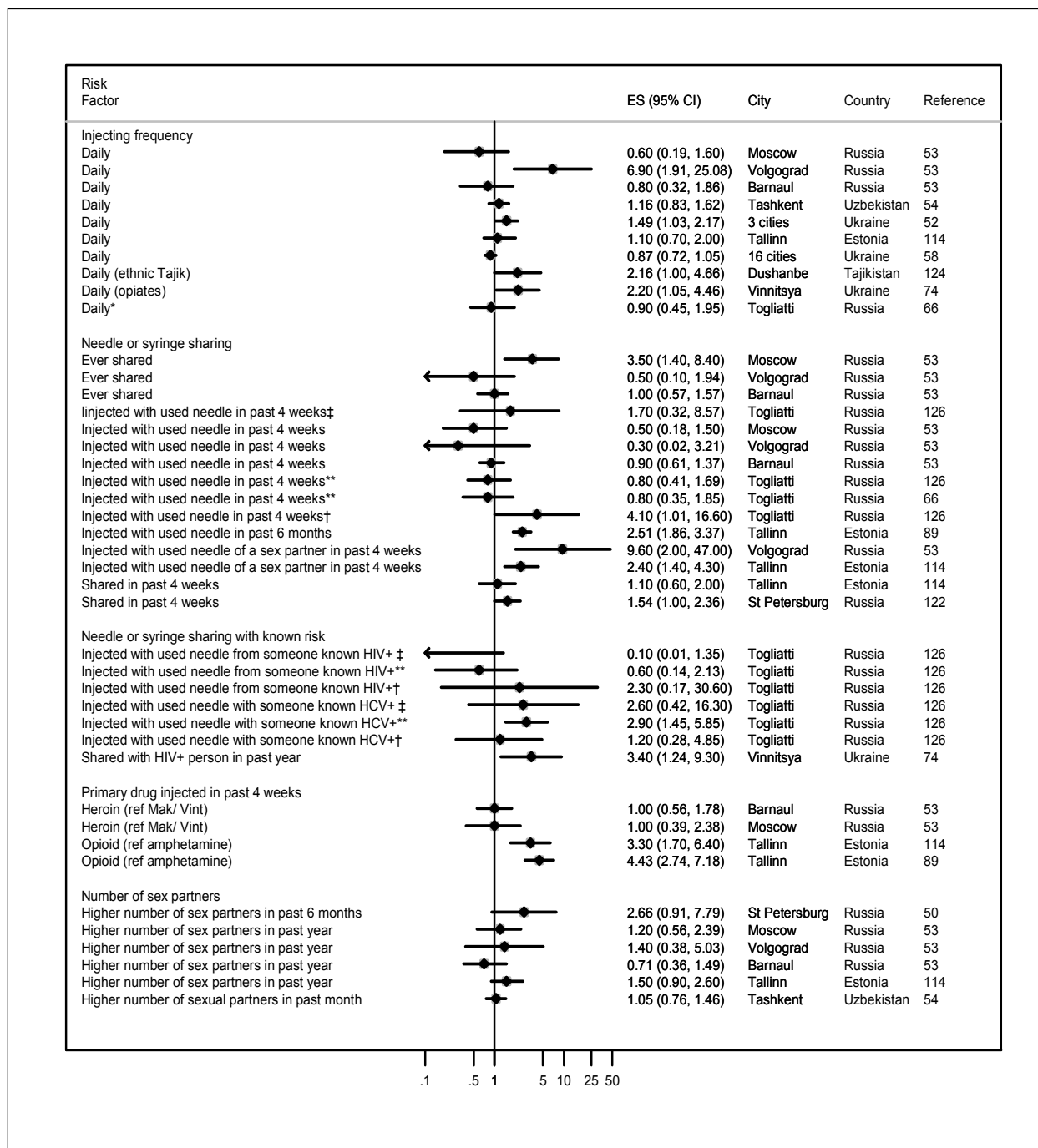
Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Unprotected anal or vaginal sex with a regular partner in past four weeks; Ever had an STI	
	Russia, Togliatti	66 female sex worker PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks; Injected with used needle in past four weeks; Ever injected homemade drugs*; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+; Unprotected anal or vaginal sex with a regular partner in past four weeks; Ever had an STI	Ever been in prison; Ever been in drug treatment; Ever been arrested;
Platt et al, 2008[66]	Russia, Togliatti	230 PWID (134 in 2001 from the study above, and 96 from 2004) who reported injecting for three years or less and injected in past four weeks were recruited by outreach workers in 2001 and through RDS in 2004	Duration of injecting career*; Frequency of injection; Ever injected homemade drugs; Injected with used needles in past four weeks; Used a previously used filter; Frontloading in past four weeks*; Injected with a prefilled syringe; Frequency of reusing the same needle; Ever exchanged sex for money, drugs or goods*; History of STIs	Year of study*; Gender; Age; District of residence; Education; Main source of income in past four weeks; History of prison; Police arrest in past year; Ever in drug treatment*; Main source of needles in past four weeks; Ever been tested for HIV
Kozlov et al, 2006[50]  *outcome is HIV incidence at 12 month follow up to enrolment	Russia, St Petersburg	520 sero-negative PWID enrolled in cohort study who injected at least three times / week in past month or reused another's injecting equipment at least three times in past three months	Frequency of injecting psychostimulants*; Number of sex partners in past six months; Selling sex for money or goods in past six months	
Niccolai et al,	Russia, St	387 ever injectors were	Unsafe injection in past 30	Unemployed*

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
2010 [122]	Petersburg	enrolled through RDS	days*; Has STI*;	
Rhodes et al, 2006 [53]	Russia, Moscow	455 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Last day injected, number of times injected*; Frequency of injection; Main drug injected in past four weeks; Injected with used needle in past four weeks; Shared paraphernalia in past four weeks; Ever injected with used needles*; Number of sex partners in past year; History of STI*	Gender; Age; Education; Main source of income in past four weeks; Ever been in prison*; Ever registered as a drug user*
	Russia, Volgograd	517 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Frequency of injection*; Ever injected homemade drugs; Injected with used needle in past four weeks; Shared paraphernalia in past three weeks; Ever injected with used needles; Injected with needle previously used by sex partner in past 12 months*; Number of sex partners in past year; History of STI	Gender; Age; Education; Main source of income in past four weeks*; Ever registered as a drug user
	Russia, Barnaul	501 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Last day injected, number of times injected*; Frequency of injection; Main drug injected in past four weeks; Ever injected homemade drugs; Injected with used needle in past four weeks; Shared paraphernalia in past four weeks*; Filled syringe from working syringe in past four weeks; Ever injected with used needles;	Gender; Age; Education; Main source of income in past four weeks; Ever been in prison; Ever registered as a drug user

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Number of sex partners in past year; History of STI	
Beyrer et al, 2009[73]	Tajikistan, Dushanbe	419 PWID who injected in past month aged 17 or over recruited through snowball technique	Daily injection in past six months*	Ethnicity*  Model adjusted for gender
Stachowiak et al, 2006[124]	Tajikistan, Dushanbe	207 ethnic Tajik PWID (subsample of above) aged 17 or over recruited through snowball technique	Injecting at least daily for past six months*; Less than three years since initiation of injection; Injects 'alone'*; Injected with used needle in past six months	Reports narcotics 'very easy' to obtain*; Ever experienced drug treatment*
Booth et al, 2006[52]	Ukraine, Kiev, Odessa, Makeevka/ Donetsk	778 PWID aged 18+ who injected in past 30 days and were unaware of their HIV status recruited through outreach workers	Injected sedative/ opiate mix in past 30 days*; Daily injection in past 30 days*; Sex in past 30 days*; Sex with HIV+ or unknown status partner in past 30 days*	Age*; Gender*; City of origin*
Robbins et al, 2010[125]	Ukraine, Odessa, Kiev, Donetsk	313 youth aged 15-24 who live part or full time on the street and reported ever injecting recruited by time-location sampling	Last sex unprotected*; Ever diagnosed with STI*  Model adjusted for gender, age, education, work for pay, orphan status, spending nights outside of residence $\geq 2$ nights/ week for past few months/ no place to live, city of residence	
Dumchev et al, 2009[74]	Ukraine, Vinnitsya	268 PWID aged 18+ who report at least three injections in past 30 days and have lived in Vinnitsya for past year, recruited through snowball sampling	Shared needles with HIV+ person in past year*; Inject opiates daily*	HIV knowledge score*
Taran et al, 2011[58]	Ukraine, 16 cities	3,487 PWID aged 16+ who injected in past 30 days and were recruited through RDS	Type of drug injected in past month; Duration of injecting career*; Injecting frequency in past month; Used alcohol with drugs in past month*; Shared needle at last injection*; Frequency of sharing	Gender*; Marital status; Occupation*; Education*

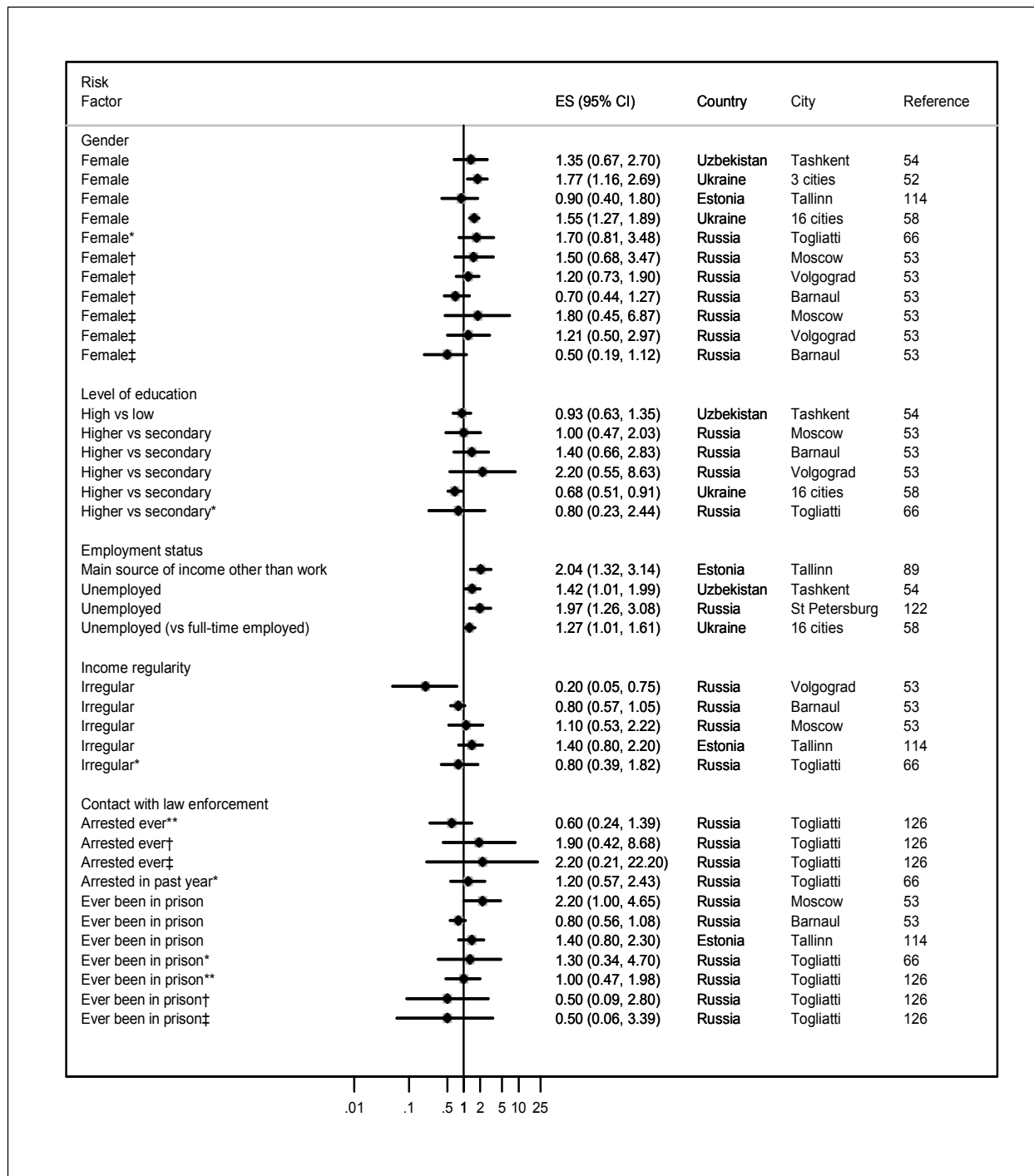
Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			paraphernalia in past month*; Sexual contact in past year;	
Sanchez et al, 2006[54]	Uzbekistan, Tashkent	701 self-identified PWID aged 18+available for two weeks after enrolment by outreach workers	Age at first drug use; First illicit drug of use*; Duration of injecting career; Current heroin use; Injecting frequency; Poppy-straw use; Group drug use; Sharing needles; Own syringe; Blood transfusion; STI history; Hepatitis history*; TB history; STI symptoms; Sell sex for drugs; Condom use*; Number of sexual partners in past month	Age; Gender; Nationality; Marital status; Employment status*; Education status; Needle exchange programme; AIDS knowledge; protection for AIDS; Donated blood for money*;

**Table 1:** Summary of studies presenting multivariate analyses of risk factors for HIV among PWID in Central and Eastern Europe and Central Asia\* P-value reported  $\leq 0.05$



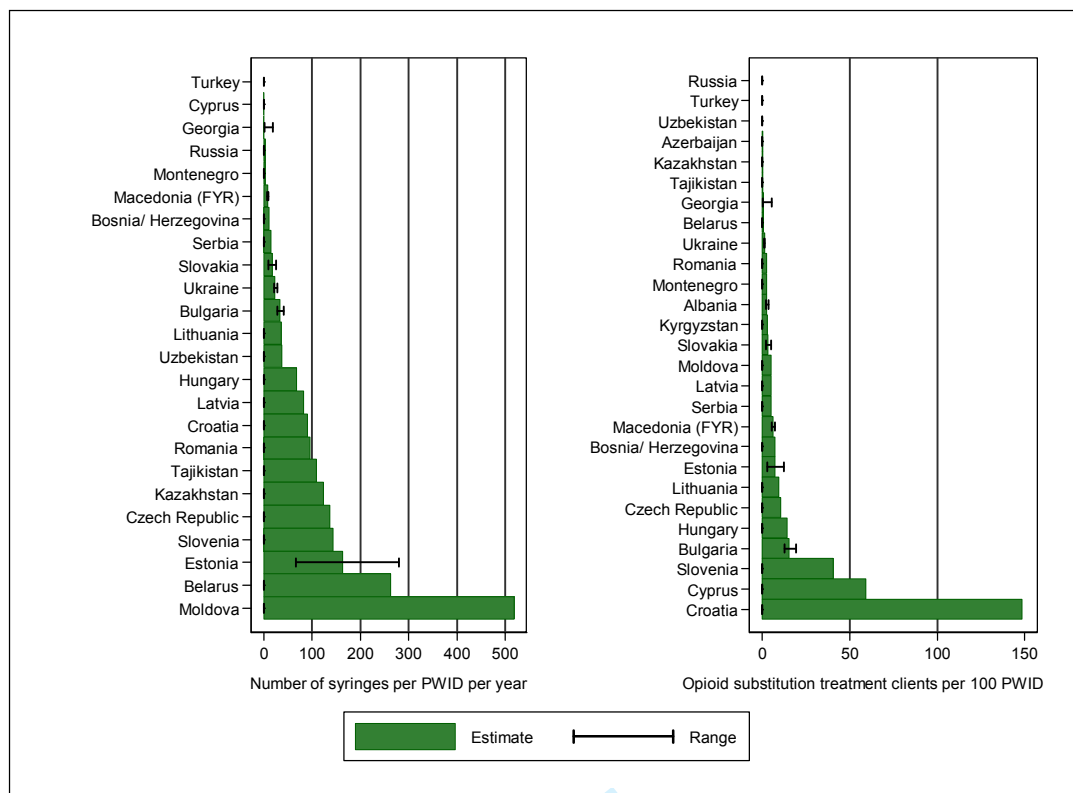
\* new PWID ( $\leq 3$  years); \*\*male PWID; †female (non-SW) PWID; ‡female (SW) PWID

Figure 3 Adjusted effect estimates of individual level risk factors present in multivariate studies of PWID



\* new PWID (≤3 years); \*\*male PWID; †female (non-SW) PWID; ‡female (SW) PWID

Figure 4 Adjusted effect estimates of environmental level risk factors present in multivariate studies of PWID



**Figure 5** Estimated numbers of syringes distributed per PWID per year and estimated number of OST clients per 100 PWID in the latest year for which data is available.[39 40]

Review only



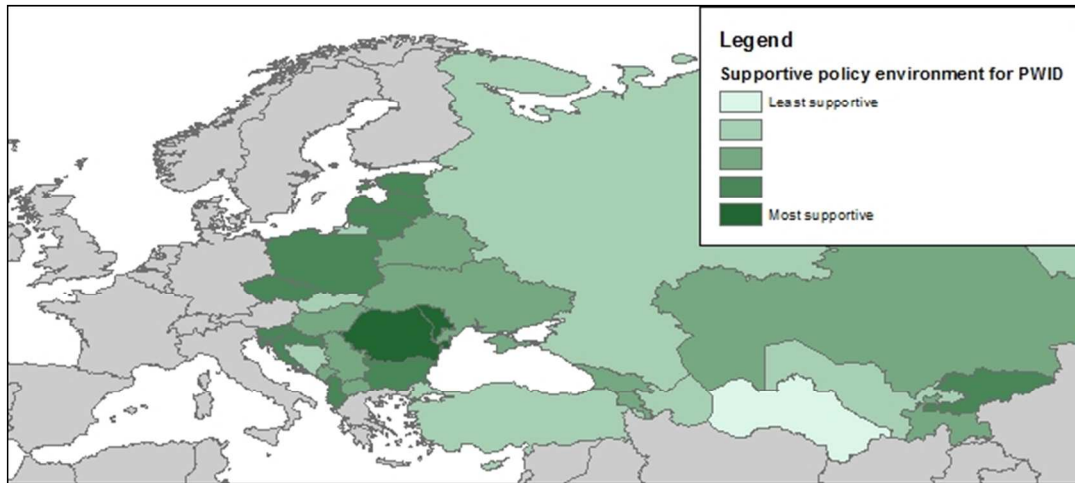


Figure 6 Map showing the supportiveness of the policy environments for HIV among PWID in Europe.[39 45-47]

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8 **HIV among people who inject drugs in Central and Eastern Europe and Central**  
9 **Asia:**  
10 **A systematic review with implications for policy**

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12  
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## ABSTRACT

*Background and objectives:* HIV among people who inject drugs (PWID) is a major public health concern in Eastern and Central Europe and Central Asia. HIV transmission in this group is growing and over 27,000 HIV cases were diagnosed among PWID in 2010 alone. The objective of this systematic review was to examine risk factors associated with HIV prevalence among ~~people who inject drugs (PWID)-PWID~~ in Central and Eastern Europe ~~and Central Asia and Central Asia~~ and to describe the response to HIV in this population ~~and the policy environments in which they live and the policy environments in which they live.~~

*Design:* A systematic review of peer-reviewed and grey literature addressing HIV prevalence and risk factors for HIV prevalence among PWID and a synthesis of key resources describing the response to HIV in this population. We used a comprehensive search strategy across multiple electronic databases to collect original research papers addressing HIV prevalence and risk factors among PWID since 2005. We summarised the extent of key harm reduction interventions, and ~~using a simple index of 'enabling' policy-environment~~ described the policy environments in which they are implemented ~~by synthesising data from key sources.~~

*Studies reviewed:* Of the 5,644 research papers identified from electronic databases and 40 documents collected from our grey literature search, 70 documents provided unique estimates of HIV and 14 provided multivariate risk factors for HIV among PWID.

*Results:* HIV prevalence varies widely, with generally low or medium (<5%) prevalence in ~~Central Europe~~ ~~Central Europe~~ and high (>10%) prevalence in ~~Eastern Europe~~ ~~Eastern Europe~~. We found evidence for a number of structural factors associated with HIV including gender, socio-economic position and contact with law enforcement agencies.

*Conclusions:* The HIV epidemic among PWID in the region is varied, with the greatest burden generally in ~~the~~ ~~East~~ ~~Eastern Europe~~. Data suggests that the current response to HIV among PWID is insufficient, and hindered by multiple environmental barriers including restricted access to services and unsupportive policy or social environments.

## ARTICLE SUMMARY

### *Article focus*

- A systematic review to identify and synthesise prevalence estimates and risk factors for HIV among PWID in Central and Eastern Europe and Central Asia.
- A summary of key data to describe the response to HIV among PWID in Central and Eastern Europe and Central Asia, including a brief characterisation of the policy environments.

### *Key messages*

- The review highlights that the HIV epidemic among PWID in the region varies from country to country, with Eastern European countries generally the worst affected. Prevalence is extremely high among PWID in many countries with some studies suggesting more than one in two PWID are infected with the virus in parts of Estonia, Russia and Ukraine.
- Despite few studies explicitly examining environmental factors, our review found that gender, socio-economic position and contact with law enforcement agencies to be associated with HIV prevalence. The complex interplay between the environment and individual behaviour of PWID is not fully understood and further emphasis on understanding the social epidemiology of HIV in this group is needed.
- An integrated package of needle exchange programmes (NSP), opiate substitution therapy (OST) and antiretroviral therapy (ART) is core to an effective response to HIV in this group. The coverage of such interventions in the region varies from low to non-existent and must be improved. Further resources coupled with improvement in the policy environments are key to reducing HIV transmission in this group.

### *Strengths and limitations of this study*

#### *Strengths*

- This review is the most comprehensive synthesis of HIV prevalence and risk factors among PWID in Central and Eastern Europe and Central Asia to date and is complemented by a clear synopsis of the state of the national policy environments and responses to HIV for people who inject drugs.

#### *Limitations*

- The quality of the review relies upon quality of the original articles, which are variable. The samples included are often selective as many studies recruited participants from specialist services or via drug user networks. Multivariate analyses are adjusted for a variety of factors, rendering direct comparisons between point-estimates difficult.
- The service coverage data is not measured in a standard fashion across the region, and is from different years. The quality of data varies hugely by country, thus undermining the comparisons we can make about coverage.
- ~~The We use a crude policy~~ index of 'policy environment' is crude and which is is developed ~~with from~~ binary indicators that cannot account for important nuances influencing inter- and intra-country environments.

## INTRODUCTION

The HIV epidemics of Europe are diverse but in all European countries HIV disproportionately affects populations that are socially marginalised and people whose behaviour is socially stigmatised or illegal. The epidemics in [Eastern Europe and Central Asia](#)~~the East~~, which are predominantly associated with injecting drug use, are among the fastest growing in the world.[1] Over two thirds of all HIV diagnoses to date in Europe fall in [Eastern Europe and Central Asia](#)~~the East~~, and over 70% of these emanate from Russia.[2 3] Over 27,000, or over 30% of new cases of HIV were attributed to injecting drug use in Central and Eastern Europe [and Central Asia](#) in 2010.[2 3] Almost all of these (99.6%) were made in ~~the East of the region~~[Eastern Europe and Central Asia](#). Accounting for differences in absolute population size, between 2006 and 2010, 89 new HIV diagnoses associated with injecting drug use have been made on average each year in the East per million people. This contrasts with ~~the Centre region~~[Central Europe](#) where the rate is 100 times less at 0.8 per million.[2]

Because of low access to and uptake of HIV testing and counselling – especially among the marginalised and stigmatised populations most at risk of HIV infection and transmission – not all HIV cases in Europe are diagnosed and reported.[4] Estimates suggest that reported cases probably represent just over half of all people living with HIV in Europe.[4] It is estimated that just over 2.3 million people were living with HIV in Europe in 2010, 840 000 in ~~the West~~[Western Europe](#) and 1.5 million in [Eastern Europe](#)~~the East~~. [4]

There are an estimated 3.1 million people who inject drugs (PWID) in Central and Eastern Europe and Central Asia, of whom one million are estimated to be HIV infected.[5] In Russia alone, there are an estimated 1.8 million PWID, of whom around 700,000 are thought be HIV infected.[5] Estimates of the prevalence of HIV among PWID in Central and Eastern Europe [and Central Asia](#) vary widely, from zero in some Central European countries where injecting drug use is less widespread, to over 20% in some countries in [Eastern Europe and Central Asia](#)~~the East~~, including Estonia, Moldova, Russia, and Ukraine.[5 6]

HIV and other blood-borne infections contribute significantly to the excess morbidity and mortality experienced by PWID in Europe and elsewhere.[7 8] HIV has the potential to spread rapidly via the sharing of needles and syringes between PWID as well as via unprotected sex between PWID and their injecting and non-injecting partners.

### *The social contexts of HIV epidemics*

A growing body of work substantiates relationships between health harms related to drug use and social-material factors that shape vulnerability to HIV.[9-16] The heuristic of the HIV ‘risk environment’ envisages HIV risk as the product of reciprocal relationships between micro and macro level influences in the physical, social, economic, and policy environments which contextualise individual and community actions in relation to risk.[9-15] This interaction has been described as a reciprocal process whereby individual actions are constrained as well as enabled by their environments and in turn shape as well as reproduce those contexts.[17] Qualitative work among PWID in Russia, for example, has illustrated how reduced capacity for HIV risk reduction in the micro environment is shaped by street-level policing practices which are in turn contextualised by broader structural policies of criminalisation and cultural practices of marginalisation which taken together produce a collectively internalised fear and sense of constrained agency among PWID.[17 18]

Recent reviews have thus called for a shift towards social epidemiological approaches.[9-15] These investigate how the distribution of HIV in populations is in part shaped by ‘social factors’, that is, forces that extend beyond ‘proximal’ individual-level factors and their biological mediators. This simultaneously demands a shift from binary models of ‘cause and effect’ to ‘multi-level’ models, which enable HIV risk to be understood as an effect of multiple contributing factors, at once interacting together, including potentially in ‘non-linear’ and ‘indirect’ ways.[19] Delineating causal pathways to inform structural interventions is thus a daunting yet critical challenge. Recent evidence reviews suggest that currently the epidemiology of HIV among PWID rarely explicitly embraces the study of social determinants.[20]

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3 | The social and economic transitions transforming the Central and Eastern European [and Central Asian](#) region in the  
4 past twenty years have been abrupt, dramatic, and long lasting. In many countries of the region, economic  
5 uncertainty has combined with weakening social capital, an embryonic and fragile civil society, a poorly resourced  
6 and overly vertically-structured health system, and public policies tackling drug use that have emphasised law  
7 enforcement and security at the expense of public health.[16 21] Social and economic transformations following  
8 the dramatic political change in Eastern European [and Central Asian](#) countries have played a role in shaping  
9 transitions in problematic substance use as well as vulnerability to HIV.[21-26] The opening-up of international and  
10 trade borders, for instance, has facilitated population mixing as well as the development of heroin trafficking  
11 routes from Afghanistan to the West, also linked to the diffusion of heroin use.[27] There was evidence of  
12 explosive HIV outbreaks linked to injecting drug use in the former Soviet region by the mid 1990s, especially in  
13 Russia, Ukraine, and Moldova.[21]  
14

### 15 16 *Enabling policy environments for HIV prevention*

17 Recognising HIV epidemics as features of their social and structural contexts emphasises the potentially pivotal  
18 role of social and structural interventions in creating environments which are enabling, rather than constraining, of  
19 evidence-based HIV prevention.[28-30] Key dimensions of 'enabling' policy environments conducive to effective  
20 HIV prevention for PWID include, but are not restricted to: the meaningful engagement of key stakeholders  
21 (including PWID) in policy formation and programming; a coordinated multi-sectoral national HIV prevention  
22 strategy emphasising an evidence-based public health and rights-oriented approach; the generation of research  
23 and surveillance on HIV epidemic spread and response; and the development and scale-up of a package of  
24 evidence-based interventions, including the removal of structural obstacles limiting their implementation.[31-33]  
25 This has led to calls to de-emphasise the criminalisation of PWID by developing policies emphasising public health  
26 above law enforcement dominated approaches, and for the rapid scaling-up of harm reduction interventions  
27 including syringe exchange, opioid substitution treatment (OST), and antiretroviral HIV treatment (ART), as well as  
28 community action and social support interventions.[31 32 34-36]  
29

### 30 31 *Review scope*

32 We aim to systematically review epidemiological research investigating the burden of HIV, and associated risk  
33 factors, among PWID in Central and Eastern Europe [and Central Asia](#). We seek to identify the extent to which such  
34 epidemiological research captures measures of the HIV risk environment by delineating HIV risk factors identified  
35 at the levels of the individual and environment. We situate this epidemiological work by synthesising current  
36 evidence reviews of the extent and availability of HIV prevention targeting PWID in the region and by developing a  
37 simple index of 'enabling' policy environment at the country level.  
38  
39

## 40 41 **METHODS**

42 | We reviewed data from the 30 Eastern and Central European [and Central Asian](#) countries in WHO defined Europe,  
43 including 15 from Eastern Europe [and Central Asia](#) (Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan,  
44 Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and  
45 Uzbekistan), 'the East', and 15 from Central Europe (Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus,  
46 Czech Republic, Hungary, Macedonia (FYR), Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia, and Turkey),  
47 'the Centre'.  
48

### 49 50 *Search strategy and selection criteria*

51 We systematically searched Medline, Embase, Global Health, Social Science Citation Index, Popline, and CINAHL for  
52 studies published from 2005 to October 20, 2011. To identify articles we combine four broad search themes with  
53 the Boolean operator "AND". The first theme, HIV, combined the Medical Subject Headings (MESH) terms "HIV" or  
54 "HIV infections" with the free word search for "HIV", "human immunodeficiency virus" with "OR". The second  
55 theme, prevalence, incidence and risk factors, included the MESH terms "prevalence", "incidence", "risk", "factor  
56 analysis", "statistical", "regression analysis", "risk factors", "risk-taking", and "epidemiology" with the free words  
57 "prevalen\*", "incidence", "risk\*", "correlat\*", "determinant\*", "vulnerab\*", "regression", "risk", "(enhanc\*adj3)  
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transmission", "multivar\*", "(route\*adj3 transmission)", "(factor\*adj3 transmission)", "social norm\*", "network", "socio-demographic", "socio-economic", "lifestyle", and "epidemiol\*" with "OR". The third theme, geographic coverage, included the names of the countries in the region, as well as the free word terms "Europe\*" and "Central Asia\*" combined with "OR". The fourth theme, PWID, combined the MESH terms "substance abuse", "intravenous", "needle sharing" and "heroin dependence" with the free word terms "IDU\*", "inject\*", "intravenous", "heroin", "addict\*", "opiate\*", "narco\*", "psychotropic\*", "psychoactive\*", "drug depend#n\*", "(recreation\*adj3 drug\*)", "harm reduction", "syringe\*", "methadone", "opioid\*", "syringe\*", "(needle\*adj3 shar\*)", and "(illegal\*adj3 drug\*)" combined with "OR".

Additionally, we systematically searched websites of research institutes, service providers, and donor organisations working with PWID across the region including recent reports from countries reporting to the United Nations General Assembly Special Session on HIV/AIDS (UNGASS). We searched the website of the European Monitoring Centre for Drugs and Drug Addition (EMCDDA) for data and sources reported from member and neighbouring countries. Conference abstracts from the International Conference on the Reduction of Drug Related Harm (2005-2011) and the International AIDS Conference (2006, 2008, 2010) were also searched. Our review conformed to the PRISMA checklist for systematic reviews.[37]

### *Study selection and eligibility criteria*

All abstracts were reviewed. Studies were excluded if they were: a) published before 2005; b) fell outside the defined geographic region; c) did not focus on HIV among PWID; d) did not sample PWID; or e) did not focus on bio-confirmed HIV prevalence or incidence, or injecting or sexual risk practices. Papers were also excluded if [they reported a sample size less than 50, had unclear sampling methods, or](#) they contained no primary data, although the references were searched to gather primary studies not identified by the search. Papers not fitting the inclusion criteria were set aside to aid interpretation of the systematic review findings. Figure 1 summarises the papers searched and retained in the review. [Following full-text review 100 peer-reviewed and grey literature documents were identified as meeting our criteria, of which 70 reported an incidence or prevalence measure, and 30 demographic or risk factor data only. Of the 70 documents reporting prevalence or incidence data, 14 included the results of a multivariate analysis.](#)

### **[FIGURE 1]**

[We Two authors \(EJ and LP\) independently](#) assessed the quality of the studies reporting HIV prevalence estimates using a scoring system that graded the papers on: wide geographic coverage; most recent study; population sampled; and recruitment setting. We allocated up to three points each for most recent studies, population sampled, country coverage, and for the range of settings sampled, and deducted one point for drug treatment only samples due to the potential for bias.[38]

### *Data extraction*

The results of the multivariate studies meeting our inclusion criteria were extracted as presented, regardless of the strength of association. Comparable factors were collected and examined using forest plots showing the effect estimates and 95% confidence intervals (95%CI). We classified the results of the multivariate studies as 'individual-level' factors or 'environmental-level' factors based on the proximity of the risk of the factor in terms of HIV transmission. Individual-level risk characteristics or activities included injecting and sexual risks, such as sharing needles or unprotected sex, that shape an individual's HIV risk through direct biological mechanisms. Environmental-level factors are those which have no direct biological means of influencing HIV risk, however, their presence or absence has been identified as an independent factor in the risk faced by an individual, indicating their role in shaping a 'risk environment'.

### *Coverage of HIV prevention interventions*

In addition to the systematic review, data summarising the coverage of HIV prevention interventions was drawn primarily from recently published reviews [39] and previously published country level data[40]. These data are

collected from a variety of sources, including UNGASS, WHO, and systematic reviews of scientific literature[39], as well as from routine national reports.[40]

### *Policy environment index*

We generated a simple index of 'enabling' policy environment. Our interpretation of an enabling policy environment drew upon guidelines generated by WHO [41], UNAIDS,[42] international non-government organisations (NGOs),[43] and peer-reviewed papers in this field.[20 30 32 44] As outlined in Box 1, the core items of the index included indicators, at the country level, of: coordinated national strategy to HIV prevention and drug use (indicated by evidence of explicit inclusion of 'harm reduction' in national-level strategy, and monitoring and evaluating HIV epidemics); meaningful engagement of stakeholders in HIV prevention policy formation and programming (indicated by evidence of a national organisation of drug users); and evidence-based HIV prevention intervention approaches (indicated by presence of OST and NSP, presence of OST and NSP in prison settings, and evidence of de-emphasising criminalisation through the use of administrative penalties for drug use possession for personal use).

### **[BOX 1]**

Indicator data were obtained from a combination of sources, including: global reports of harm reduction policy and coverage;[45] country profiles collated and updated by the EMCDDA;[46] our systematic review of research studies (see above and Figure 1); and the International Network of People who Use Drugs[47]. The index was constructed by allocating equal weight to each of the six items and aggregating a score for each country, with higher scores indicating a more 'enabling' environment conducive to evidence-based public health approaches.

## **RESULTS**

### **[FIGURE 1]**

#### *HIV incidence*

Only three papers reviewed reported HIV incidence among PWID in this region. Two in Tallinn, Estonia, reported an HIV incidence rate of 31/100 person years (PY) in 2004, decreasing to 9/100 PY in 2009 among people injecting for less than three years.[48 49] The other from St Petersburg, Russia, reported a rate of 4.5/100 PY.[50]

#### *HIV prevalence*

Estimates of HIV prevalence among PWID vary widely throughout the region. A total of 79 sources reported HIV prevalence estimates (some multiple), of which 67 reported unique HIV prevalence estimates among PWID in the region; 44 from Eastern Europe and Central Asia[6 50-89] and 21 from Central Europe[90-110] and two that contained data from both regions.[40 111]

### **[FIGURE 2]**

Multiple estimates exist for many countries (Figure 2), and where this was the case we applied the scoring system described above (see Methods) to select the estimate that appeared to be most representative at the country-level. Using these estimates, we have categorised country HIV epidemics among PWID as: "low" (up to 1%); "medium" (2% - 5%); "high" (5% - 20%); and "very high" (greater than 20%).

No country in the East can be considered to have a 'low level' of HIV among PWID, and only Kazakhstan, Georgia and Lithuania have 'medium level' epidemics, according to the studies examined here. Of the remaining 11 countries with data (no data exists for Turkmenistan), three have prevalence estimates of over 20% (Moldova, Russia, and Ukraine) and Estonia has a prevalence of over 50%. In the Centre only Poland and Bulgaria appear to have 'high level' epidemics and neither of these exceed 10% prevalence. Several countries (Albania, Croatia, Cyprus, Hungary, Macedonia, and Slovenia) report 0% HIV prevalence among PWID. However, there is less data



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2  
3 from this region and sample sizes are generally smaller so the estimates may be less robust than those from the  
4 East.  
5

### 6 7 *Demographic profile*

8 Generally, three times as many men as women inject drugs, although male predominance reached as high as 95%  
9 in some studies from the Caucasus.[51 55 56 63 65 86 112] The mean age of PWID participating in studies was mid-  
10 twenties, although many studies restrict recruitment to PWID aged 18 or over. The proportion of PWID reporting  
11 having regular income was generally low.  
12

### 13 *Pattern of injecting drug use*

14 Heroin is the drug of choice among PWID in Europe, although there are sub-regional differences. In Moldova[113],  
15 Ukraine[74] and Russia[53], the injection of home-produced opioids such as 'hanka' or 'shirka'(a liquid poppy  
16 extract) is reported alongside heroin injection. In Estonia the use of the synthetic opiate, fentanyl ('China White',  
17 'White Persian' or 'Afghan'), has become common alongside amphetamine injection.[72 114] In Central Europe,  
18 heroin is reported as the main drug injected, although studies also report between 30% and 51% injecting  
19 amphetamines as their main drug[101 115 116], and the Czech Republic reports the highest prevalence of  
20 methamphetamine use in Europe.[117-119] The frequency of injection varies widely throughout the region.  
21

### 22 *Contact with criminal justice systems*

23 The data reviewed from Eastern Europe and [the former Soviet Union](#)[Central Asia](#) suggests that between half and  
24 three-quarters of PWID have experienced arrest. A study among 600 PWID in Odessa, Ukraine found that police  
25 beatings were common, with nearly 50% reporting at least one such experience.[20 120] Studies in other regions  
26 also suggest relatively high rates of police arrest (42% - 76% ever having been arrested).[18 27 108 121] In Estonia  
27 and Lithuania, an estimated 58%-70% of PWID had been in prison at least once.[75] In Georgia and Russia, this  
28 figure was between 6% and 37%.[18 53 65 66 80 122 123] In Central Europe, between 18% and 50% of respondents  
29 report previously having been in prison[94 108]  
30

### 31 *Individual-level risk factors for HIV*

32 No studies examined risk factors linked to HIV in the Centre, and so we summarise the findings of the multivariate  
33 HIV risk factor analyses from 14 papers identified by our review in the East[50 52-54 58 66 73 74 89 114 122 124-  
34 126], although two[66 73] present new analyses of data already published in other papers also presented  
35 here.[124 126] [Table 1 summarises the key characteristics of the 14 papers as well as the factors explored in the](#)  
36 [multivariate analysis](#). The forest plots summarised in Figures [4-3](#) and [5-4](#) synthesise the effects of particular  
37 individual and environmental risk factors on HIV. Although studies measure similar associations, it is important to  
38 note that each may have carried out analyses in a unique fashion, adjusting for different confounding variables.  
39  
40

### 41 [TABLE 1]

42  
43 As shown by the individual risk factor estimates presented in Figure 3, many studies investigated the link between  
44 HIV and *injecting with a used or shared needle*. Although the effect sizes tend towards increased HIV risk, most  
45 results are inconclusive, "social-desirability" bias possibly influencing self-reported responses. Injecting with the  
46 used needle of a sex partner was found in Volgograd[53] and Tallinn[114] to clearly increase an individual's odds of  
47 HIV. More definitively, injecting with a needle previously used by someone known to have HIV or hepatitis C is  
48 shown in most studies to be clearly positively correlated.[74 126] *Daily injecting* is also found to be positively  
49 associated. Many reviewed studies also associate *longer injecting careers* with greater odds of having HIV[126].  
50 Although a Russian study found no difference in an individual's odds of HIV according to the primary drug they  
51 inject[127], studies in Estonia found that primary injectors of an opiate (fentanyl) had between three and four and  
52 a half times greater odds of HIV than individuals who primarily inject amphetamines.[114 128]  
53  
54

### 55 [FIGURE 3]

Regarding exploration of HIV and associated *sexual risk including sex work (SW)*, most multivariate analyses explored the associations between exchanging sex for drugs or money, the number of sexual partners, and unprotected vaginal or anal sex, as risk factors. Although several strong univariate associations were found, these tended not to hold in the multivariate models (Figure 3). This could be because sample sizes were insufficient or because much sexual risk behaviour is determined by other individual or environmental factors such as gender, socio-economic status or injecting behaviour.

#### *Environmental-level risk factors for HIV*

Although most studies presented show adjusted odds ratios identifying female *gender* as a risk factor for HIV (Figure 4), the confidence intervals generally straddle one and are inconclusive.

#### **[FIGURE 4]**

Multiple studies link HIV to the *socio-economic status* of PWID, though economic status is defined through different measures, including level of education, employment (regular or not) and income (regular or not, legal or not) (Figure 4). Of these measures, only an individual's employment status showed a consistent association with HIV, with unemployed individuals or those having a main source of income that was not work, showing greater odds of HIV than others.[54 58 89 122] An Estonian multi-level study included neighbourhood level data in its analyses and found neighbourhood level effects of unemployment (10% increment in unemployment AOR 5.95, 95%CI 2.47-14.31) and habitat change since 1989 (10% change AOR 1.89, 95%CI 1.09-3.26) to be both associated with HIV prevalence (results not presented).

Several studies have examined *contact with law enforcement agencies* as an environmental factor linked with the odds of being HIV infected, although the results produced by the systematic review have large confidence intervals and are largely inconclusive.[53 66 114 126] The review reveals that contact between police and PWID in the region is highly commonplace and no studies examined the frequency or duration of contact.

In addition to the universally relevant factors highlighted above, some studies analysed the relationship between HIV and determinants that are particular to local context (results not shown). For example, a study in Tajikistan found that respondents identifying as Tajik (AOR 7.06,  $p < 0.001$ ) or other ethnicity (AOR 6.05,  $p < 0.001$ ) as opposed to Russian were at higher risk of testing positive for HIV.[73] A study in Uzbekistan similarly found respondents of Uzbek ethnicity to have higher odds of HIV than their Russian counterparts (AOR 1.20, 95%CI 0.80-1.80).[54] However, a study in Estonia found that ethnic Estonians had a reduced odds of HIV compared with those of Russian or other backgrounds (AOR 0.63, 95%CI 0.28-1.25).[114] ~~An association between HIV among PWID and being of a minority ethnicity that cannot otherwise be explained by needle sharing has been noted elsewhere, and linked to material as well as other social inequalities, including access to support services.[129-130] In parts of Eastern Europe where PWID are often required to register as such to obtain drug treatment or are forced to through contact with police, this can lead to increased social marginalisation as well as reducing their ability to gain employment or even to drive a car.[131]~~ In Moscow and Tallinn ever having been registered as a PWID at drug treatment was found to be associated with more than double the odds of HIV (AOR 2.4, 95%CI 1.3-4.7; AOR 2.4, 95%CI 1.5-3.8)[53][114]. Conversely, a study in Togliatti in Russia conducted among 96 new (<three years) injectors found having been in drug treatment in the past as negatively associated with risk of HIV (AOR 0.4, 95%CI 0.1-1.0).[129]

#### **[FIGURE 4]**

#### *HIV prevention coverage*

Coverage – the proportion of the population at risk reached by an intervention, ideally with sufficient intensity to have probable impact – emerges as a critical determinant of HIV prevention effectiveness.[32 130-132] Our review did not focus on collating primary data but sought to synthesise coverage estimates relevant to the Central and Eastern European and Central Asian region from key recently published reviews regarding NSPs, OST, and ART.[39 40] These data are contained in Figure 5. They indicate that NSPs were available in all countries of the region,

1  
2  
3 except Turkey, though intervention coverage varies widely. For instance, whereas 50% of PWID in Hungary in 2007  
4 had access to NSPs, with each receiving around 135 clean needles a year (135 per PWID based on country-level  
5 estimates of PWID), in Russia only 7% of PWID had such access to NSPs, with each receiving 56 needles each a year  
6 (four per PWID based on country-level estimates of PWID). These estimates do not include pharmacy-based  
7 provision, which is a primary source in some countries in this region, including Russia.[133] Figure 5 also shows  
8 that four of the 30 countries in this region reporting evidence of injecting drug use did not provide OST: Russia,  
9 Uzbekistan, Turkmenistan, and Turkey. Coverage of OST is generally low, with Slovenia showing the greatest  
10 coverage.  
11

### 12 [FIGURE 5]

13  
14 Comparing the proportion of HIV cases caused by injecting drug use with the corresponding proportion of people  
15 receiving antiretroviral therapy who inject drugs, in 2002, 71% of the reported people living with HIV acquired HIV  
16 infection through injecting drug use, whereas only 20% of those receiving antiretroviral therapy were people who  
17 injected drugs. In 2005 and 2006, among 21 and 23 countries with available data, people who injected drugs  
18 represented 77% of reported cases and 26% of antiretroviral therapy recipients, a proportion that declined to 22%  
19 in 2010 among 19 reporting countries. Although no trends can be statistically ascertained due to incomparable  
20 samples (notably missing data from the Russian Federation in 2002 and 2010), these data suggest that most of the  
21 people who acquire infection in reporting countries are people who inject drugs and that, despite this, their  
22 treatment needs remain considerably underserved.[4]  
23  
24

25 We found no data relating to the impact or coverage of structural level interventions on HIV among PWID,  
26 although recent legislative changes in Moldova and the Czech Republic have de-emphasised the criminalisation of  
27 small amounts of drugs possession.  
28

### 29 *Enabling policy environments*

30 Figure 6 shows the results of the policy index developed (see Methods) to describe the distribution of enabling  
31 policy environments throughout Central and Eastern Europe and Central Asia. Darker shading represents  
32 seemingly more supportive policy environments for HIV prevention and lighter shading seemingly less supportive  
33 environments.  
34

### 35 [FIGURE 6]

36  
37 Of the 30 countries in the region, 25 explicitly and supportively mentioned harm reduction in their national  
38 strategies, and 27 have undertaken at least one sero-prevalence and one behavioural study among PWID in the  
39 last ten years. In 26 countries, OST and NSP are available generally, but available in prison in only three countries.  
40 Five countries have national organisations of drug users, and five countries use administrative rather than criminal  
41 penalties for people found possessing small quantities of drugs for personal use.  
42  
43

44 Based on the index, the countries with the most supportive policy environments are Moldova and Romania. The  
45 countries with the least supportive environments are Turkmenistan and Turkey. Turkmenistan does not show any  
46 of the features of a supportive environment according to our index, although Turkey has conducted at least one  
47 sero-prevalence and one behavioural study among PWID in the last ten years. In Russia, where the majority share  
48 of HIV infections among PWID in the region are located, the national strategy refers to harm reduction as a threat  
49 to efforts to reduce the demand for drugs, with NSPs and OST specifically mentioned as problematic for federal  
50 level support.[134] OST is unavailable in Russia, and NSPs are limited in number, with none available to prisoners,  
51 and there is a focus on criminal rather than administrative penalties for drugs possession. However, there is some  
52 evidence of drug user activism and organisation.[47]  
53  
54

55 Russia and Ukraine both feature among the countries experiencing high HIV prevalence among PWID, and like  
56 Russia, criminal punishment rather than administrative sanctions for drug use and possession is the norm in  
57 Ukraine. While Ukraine has a relatively high number of NSPs alongside increasing availability of OST, it does not  
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3 provide harm reduction services in prisons. Moldova and Estonia also feature among the high HIV prevalent  
4 countries but both appear as to present relatively supportive environments for PWID. However, to our knowledge,  
5 neither has an active national drug user organisation and neither NSP or OST in prison settings.  
6  
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## 8 9 DISCUSSION

### 10 11 *HIV epidemic contexts*

12 All but one country (Turkmenistan) in Central and Eastern Europe and Central Asia has generated survey-based  
13 estimates of HIV prevalence among PWID. Our review of these studies shows that HIV prevalence among PWID is  
14 highest in the Eastern European countries of Estonia, Russia, Moldova, and Ukraine (over 20% in each), and lowest  
15 in the Central European countries of Albania, Croatia, Cyprus, Hungary, Macedonia (FYR), and Slovenia (0% in  
16 each). We identified only three HIV incidence studies among PWID in the region, showing incidence of 9/100  
17 person years in Estonia in 2009[49] and 4.5/100 person years in Russia[50]. Accepting that country estimates of  
18 HIV prevalence inevitably only reflect the characteristics of the particular samples from which they are drawn,  
19 these estimates taken together reiterate that the burden of HIV linked to injecting drug use falls in the East, and  
20 especially Russia, where over half of all HIV cases among PWID in the region are located.  
21

22 Multivariate analyses of HIV risk factors among PWID underscore injecting with a used needle/syringe, frequent  
23 injecting, and injecting opiates as opposed to amphetamines as proximal factors associated with increased risk of  
24 HIV. We acknowledge that the findings of the multivariate studies we synthesise in the review may not be directly  
25 comparable, as they have been derived from studies using different regression techniques and adjusting for  
26 different confounding factors. While most of the epidemiological studies we reviewed did not embrace, by design,  
27 the exploration of environmental risk factors – as is the case with HIV epidemiological studies globally[20] – a  
28 number of important factors in the HIV risk environment can be identified. These included increased HIV risk  
29 among *women*, an association we interpret to have indirect, rather than biological, causative roots through  
30 pathways involving multiple linked socio-economic differences related to gender. Although most studies showed  
31 women at greater risk of HIV than men, the confidence intervals presented include the null value, preventing us  
32 from drawing conclusions on the effect of gender on HIV risk. The lack of conclusive evidence could be due to the  
33 small number of women often recruited in to research, as well as genuine variability in the consequences of female  
34 gender in different settings. Qualitative data from Ukraine suggests that female PWID are at increased risk of  
35 psychological, physical (including sexual) and economic violence from their male partners, constraining capacity to  
36 negotiate safer sex, safer injecting practices, and access to helping services, in consequence elevating their HIV  
37 risk.[135]  
38

39 Additionally, *socio-economic status* – whether measured by income or employment – emerged as important,  
40 although only employment status appeared conclusively associated with HIV risk. The direction and pathways  
41 income and employment effects have on HIV risk may vary locally. The ways in which HIV links to wealth and  
42 poverty is shaped by social context, and in some settings injecting has diffused among those whose economic  
43 status may be comparable to the wider local population.[53 136]  
44

45  
46 Lastly, we note contact with *criminal justice agencies*, including experience of incarceration, as an important risk  
47 factor,[53 66 114 126] although the studies systematically reviewed here were inconclusive in this regard. Studies  
48 evidencing the adverse effects of the legal environment on HIV risk among PWID suggest a relationship between  
49 street-based policing practices, including extra-judicial ones such as police violence, and increased HIV  
50 vulnerability, including through reduced capacity for risk avoidance as a consequence of safety short-cuts and  
51 rushed injections borne out of a fear of detection or arrest.[18 27 120 137-139] While evidence internationally  
52 links prison and a history of incarceration to elevated odds of HIV among PWID[140 141], only three countries in  
53 the region (Moldova, Romania, and Kyrgyzstan) provide harm reduction services to prisoners. [An association  
54 between HIV among PWID and being of a minority ethnicity that cannot otherwise be explained by needle sharing  
55 has been noted elsewhere, and linked to material as well as other social inequalities, including access to support  
56 services.\[142 143\] In parts of Eastern Europe and Central Asia where PWID are often required to register as such to](#)  
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[obtain drug treatment or are forced to through contact with police, this can lead to increased social marginalisation as well as reducing their ability to gain employment or even to drive a car.](#)[144]

Whilst the epidemiological studies we reviewed provide some pointers to the role of HIV risk environments, they are self-evidently limited in their capacity to capture how HIV is an effect of social context. This highlights the urgency to develop specifically tailored social epidemiological approaches, which build into their designs from the outset measures of micro and macro risk environment. It also highlights the importance of mixed-methods approaches, especially those combining qualitative with epidemiological data[145]. For example, by linking HIV epidemiology to data on shifting drug trafficking routes it has been possible to plot the macro physical distribution of HIV.[146] In the region of Central and Eastern Europe [and Central Asia](#), the potentially HIV risk productive role of transit routes for heroin originating from Afghanistan through Central Asian countries along the “Northern Route” to Russia and beyond provides a similar example. In 2009, UNODC estimated that 25% of all Afghan heroin (95 metric tons) was transported along this route, with the majority travelling through Tajikistan, to Osh in Kyrgyzstan, and then on to Kazakhstan, before arriving in Russia.[147] The effects of this trafficking route appear to have HIV impacts with Kulyab, in Tajikistan, a major hub for Afghan opiate trafficking, reporting the highest HIV prevalence among PWID in Tajikistan at 34·5% in 2009 compared with the national average of 17·3%.[148] Jalal-Abad reported the highest HIV prevalence among PWID in Kyrgyzstan at 14% in 2007[149] compared with a national average of 7·7%.[84] In Kazakhstan, there is substantial overlap between the sites with the largest number of diagnosed HIV infections, largest number of registered drug users and highest number of heroin seizures.[150]

Future epidemiological studies of HIV among PWID need to better systematically develop measures of HIV risk environment and how these combine to increase or reduce HIV risk.[20] Because epidemiological studies of PWID tend to focus on the proximal determinants of risk behaviour and HIV transmission, there is a need to shift towards capturing distal factors and how these interplay to produce pathways of risk.[19 20 28 151] Principal among these, according to our review, should be gender, social-economic status, and the effects of criminalisation.

[In addition to the limitations discussed above, the study is subject to several potential biases including missing key documents, especially those not published in the English language. Individual studies are likely to may only tend to publish what can be considered to be ‘interesting’ results, leading to potential a publication bias towards analyses that reporting significant results. This ,which can lead a systematic review such as ours -to overstate the effect of several factors. Further,As some several elements of this study review were undertaken by the same aAuthorss, this may reduce protection against human error and preservation of removing independence between the stages of the review and possibly increasing the likelihood of human error.](#)

### *Towards enabling policy environments*

It is well established that HIV prevention targeting PWID requires a ‘combination intervention’ approach tailored to local setting, including a balance of: needle and syringe distribution programmes (NSPs); opioid substitution treatment (OST); antiretroviral HIV treatment (ART); peer education and outreach; HIV testing and counselling services; and the promotion of public policies and other structural changes conducive to public health approaches. [20 32 33 152-154] Evidence for the effectiveness of these interventions is well established.[32 152 155 156] The extent of HIV prevention intervention coverage, however, varies throughout the region, and is largely inadequate[39 40]. Many of the countries with the lowest levels of harm reduction service provision are also those with the highest HIV prevalence and the largest per-capita number of new diagnoses. The unavailability of OST in Russia in particular means that the majority of PWID in the region do not have access to an integral component of evidence-based HIV prevention.

Structural interventions seek to remove environmental barriers to HIV prevention while enabling environmental conditions which protect against vulnerability to HIV. While the relationships between HIV-related policies and their impacts upon micro-level HIV risk practices are clearly not straight forward, the policy environment is a clear object of structural intervention and change. Our review identified no evidence specifically relating to the impact or coverage of structural level interventions on HIV among PWID, although recent legislative changes in Moldova

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3 and the Czech Republic have de-emphasised the criminalisation of small amounts of drug possession, and evidence  
4 elsewhere in Europe links such initiatives with reduced HIV risk and increased access to helping services[157].  
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6  
7 In the absence of social epidemiological data generated from systematic review, we developed a crude index of  
8 'enabling policy environment' based on indicators of: national-level policy endorsing of harm reduction  
9 approaches; research of HIV prevalence and risk behaviour among PWID; drug user community organisation;  
10 availability of OST and NSPs; availability of OST and NSPs in prison settings; and application of administrative rather  
11 than criminal penalties for drug use and possession (see Box 1). Such an index seeks to include quantifiable  
12 indicators of the practical application of 'healthy policy', at least as far as such data is comparatively available. We  
13 acknowledge the limits of this exercise, but argue for the need for future epidemiological research to better  
14 monitor indicators of enabling and risk environment alongside proximal risk factors for HIV, especially those  
15 pertaining to community involvement and partnership in policy formation, availability of HIV prevention in criminal  
16 justice settings, and shifts towards de-emphasising the criminalisation of drug use through providing treatment or  
17 care as an alternative to arrest or imprisonment.  
18

19 Applying our index of enabling policy environment highlighted large discrepancies throughout the region. Of the  
20 countries with a seemingly unsupportive environment for HIV prevention among PWID, Turkmenistan may present  
21 a particular concern, for it is located between countries of high HIV prevalence, situated on a heroin trafficking  
22 route, and appears to lack a baseline of epidemiological evidence. Other countries – including Russia, Uzbekistan  
23 and Azerbaijan – appear to present weak policy environments for HIV prevention, compounding potential risk  
24 linked to low level HIV prevention coverage. The lack of systematic monitoring of policy environment indicators in  
25 the region, and the neglected attention paid to monitoring the effect of structural-level factors on micro risk  
26 relationships in epidemiological research, hampers an understanding of how European HIV epidemic contexts may  
27 differ markedly regarding HIV prevention need and potential. The development of structural HIV prevention  
28 interventions as part of a combination intervention approach clearly requires evidence of how environmental-level  
29 factors impact upon HIV risk.  
30

31 The importance of reducing vulnerability to HIV/AIDS, by understanding and removing structural barriers, is  
32 increasingly recognised in European HIV policy, for example as one of the four strategic directions of the European  
33 Action Plan for HIV/AIDS 2012-2015, which proposes actions to: address laws and regulations that present  
34 obstacles to effective HIV prevention, treatment care and support; strengthen the enforcement of protective laws  
35 and regulations; strengthen civil society involvement in the HIV response and ensure gender and age equity in  
36 access to HIV and related health services.  
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**AUTHORS CONTRIBUTIONS**

Tim Rhodes, Lucy Platt and Vivian Hope developed the methodology for the systematic review.

Tim Rhodes, Lucy Platt, Vivian Hope, Alisher Latypov and Emma Jolley reviewed the collected literature.

Emma Jolley [and Vivian Hope](#) extracted the data.

[Emma Jolley](#) ~~and~~ conducted the data analysis.

Tim Rhodes and Emma Jolley interpreted the data and drafted the manuscript.

All authors reviewed the manuscript and commented on the data and interpretation.

All authors gave approval for the manuscript to be submitted.

For peer review only



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3 **CONFLICTS OF INTEREST**  
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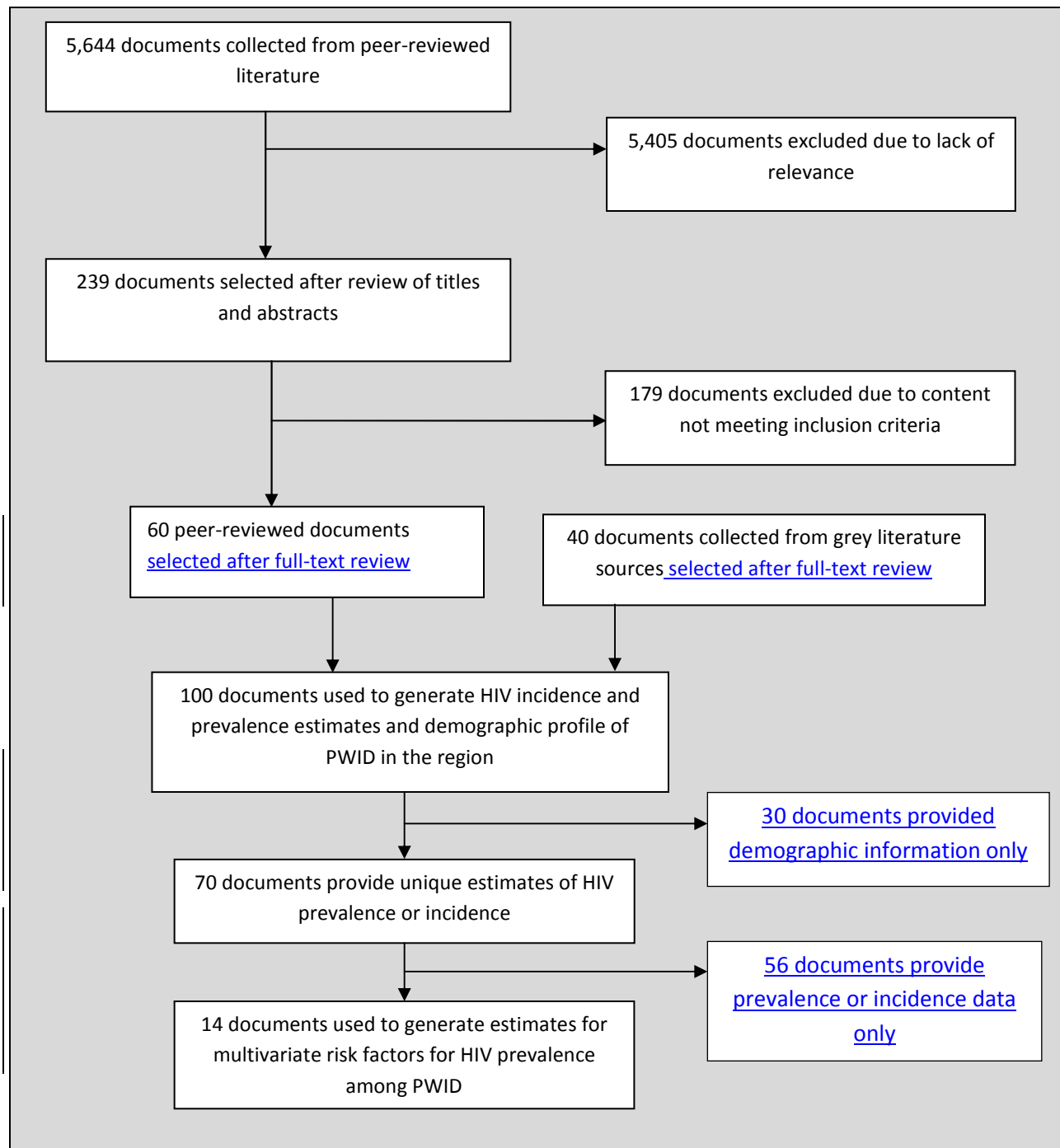
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Figure 1: Flowchart of study selection



**Box 1: A simple index of enabling policy environment****MEANINGFUL ENGAGEMENT OF STAKEHOLDERS**

1. The meaningful involvement of PWID in policies affecting their health and welfare and in related HIV prevention programming is accepted as an important indicator of 'health policy' formation.[42 158] While assessing 'meaningful involvement' is complex, we adopt a simple indicator: the ***presence of a national organisation of drug users***.

**COORDINATED NATIONAL STRATEGY TO HIV PREVENTION AND DRUG USE**

2. Explicit and supportive reference to 'harm reduction' in national policy documents can mark a commitment to evidence-based interventions as part of HIV prevention responses targeting PWID. International agencies advocate institutional and national-level endorsement of harm reduction as a feature of national strategy.[33 159] We adopt ***evidence of explicit supportive reference to harm reduction in national strategy*** as an indicator of enabling policy environment.

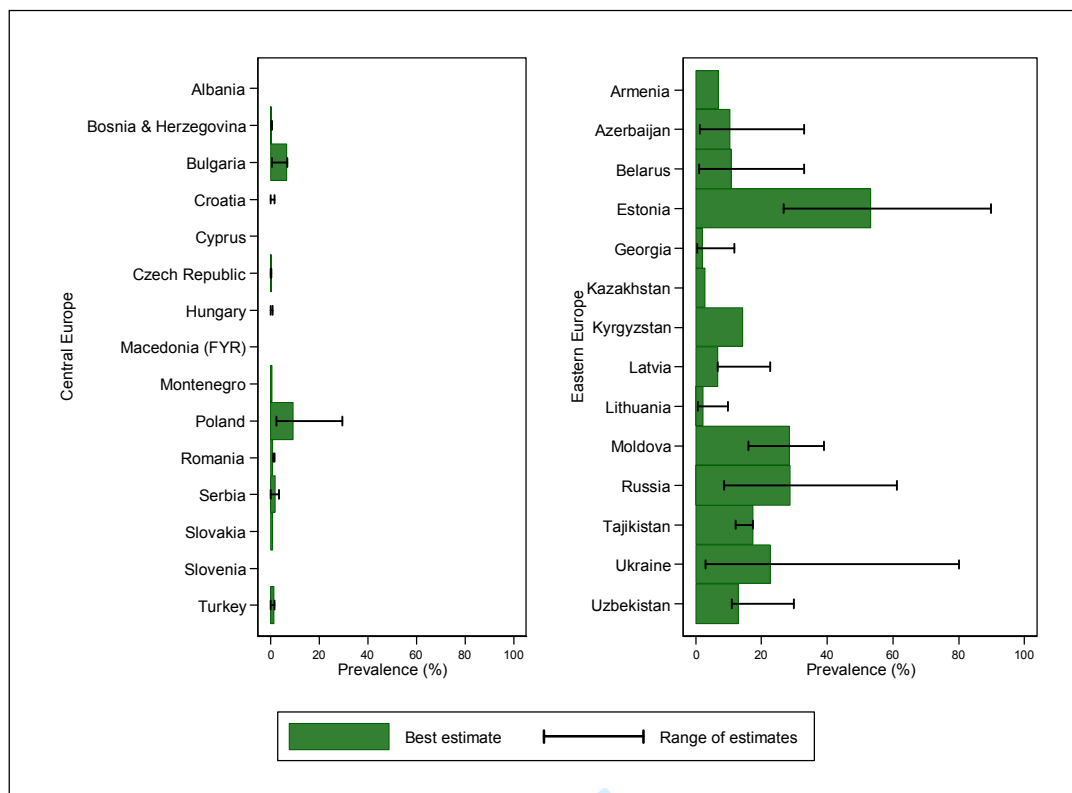
3. Monitoring and evaluating the state of the epidemic and response is an important element of building evidence-based responses.[40 160] Targeted sero-prevalence and behavioural surveillance is recommended in concentrated HIV epidemics.[161] We adopt as an indicator of enabling policy ***evidence of at least one HIV sero-prevalence and one behavioural study among PWID since 2000***.

**IMPLEMENTATION OF PUBLIC HEALTH ORIENTED APPROACHES TO REDUCING HARM**

4. Drug control policies which seek to distinguish drug users from drug traders and traffickers, and which de-emphasise the criminalisation of drug users, can give priority to public health oriented approaches to reducing drug-related harm. We adopt the ***application of administrative rather than criminal penalties for drug use and possession of quantities for personal use*** as an indicator of an enabling policy environment.

5. We adopt ***the legal availability of OST and NSP*** in a country as an indicator of enabling policy environment. These are core components of the recommended nine combination HIV prevention interventions for PWID[33]. Many countries have adopted at least some recommended measures, but often the components missing are OST and NSPs. The effectiveness of both in improving the health of PWID is well established[32 155 162], especially for OST[163-168] [169]. OST also facilitates access to and augments the effects of other interventions, such ART[32 152].

6. ***The availability of OST and NSPs in prison*** can show a country's willingness to address the needs of even the most marginalised of its citizens, as well as demonstrating noteworthy scale of the programmes. Because of existing laws concerning drug use and possession, PWID in many countries account for disproportionately high rates of incarceration[140]. Prisons may act as a risk environment for HIV transmission linked to drug injecting. International guidelines[170] recommend continuity of services between prison and communities and some countries have developed successful partnerships between penal systems and HIV services, including in the European region.[171]



**Figure 2** The range of HIV prevalence estimates for countries in the Central and Eastern European region, along with the estimate judged “best” highlighted in green.

Review only

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
Platt et al, 2006[114]	Estonia, Tallinn	350 PWID who injected in past four weeks recruited by respondent-driven sampling (RDS)	Primary injection of opioid or amphetamine in past four weeks*; Duration of injecting career; Shared needle in past four weeks; Shared equipment in past four weeks; Injected with a used needle of a sex partner in past four weeks*; Number of sexual partners in past year	Age; Gender; Main source of income in past four weeks; Ethnicity; Ever registered in drug treatment*; Ever been in prison; Ever attended needle exchange
Abel-Ollo et al, 2009[72]	Estonia, Tallinn and Kohtla-Järve	450 PWID (350 from Tallinn and 100 from Kohtla-Järve) who injected in past four weeks recruited by respondent-driven sampling (RDS). For analysis the participants were categorised as HIV-, HIV+ aware of their status and HIV+ unaware of their status, according to self-reported status at the time of testing.  The data from Tallinn is also analysed above.	<b>Analysis of risk factors for HIV among participants aware of their status (ref HIV- participants):</b> Sharing used needles/ syringes in past four weeks*; Unprotected sex in past four weeks; Sharing water*; PWID as sex partner in past year*; Sharing injection equipment with sexual partner in past year*; Having two or more sex partners in past year; Unprotected intercourse in past year; Ever sharing needles with HIV+ person*.  <b>Analysis of risk factors for HIV among participants unaware of their status (ref HIV- participants):</b> Sharing used needles/ syringes in past four weeks; Unprotected sex in past four weeks; Sharing water; PWID as sex partner in past year; Sharing injection equipment with sexual partner in past year; Having two or more sex partners in past year*;	

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Unprotected intercourse in past year*; Ever sharing needles with HIV+ person.	
Uusküla et al, 2010[89]	Estonia, Tallinn	350 PWID, aged 18+, who injected in past two months recruited by RDS	Earlier age of initiation to injecting*; Primary injection of opioid or amphetamine*; Receptive sharing in past six months*	Ever attended syringe exchange*; Main source of income other than work*; Unemployment at habitat level*; Residential change at habitat level*
Platt et al, 2005[126]	Russia, Togliatti	268 male PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks*; Injected with used needle in past four weeks; Ever injected homemade drugs; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+*; Unprotected anal or vaginal sex with a regular partner in past four weeks; Unprotected anal or vaginal sex with a casual partner in past four weeks*; Ever had an STI	Ever been in prison; Ever been in drug treatment; Ever been arrested;
	Russia, Togliatti	89 female non-sex worker PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks; Injected with used needle in past four weeks*; Ever injected homemade drugs; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+;	Ever been in prison; Ever been in drug treatment; Ever been arrested

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Unprotected anal or vaginal sex with a regular partner in past four weeks; Ever had an STI	
	Russia, Togliatti	66 female sex worker PWID who injected in past four weeks recruited in 2001 by outreach workers	Duration of injection; Injected with used paraphernalia in past four weeks; Injected with used needle in past four weeks; Ever injected homemade drugs*; Injected with used needle from someone known to be HIV+; Injected with used needle from someone known to be HCV+; Unprotected anal or vaginal sex with a regular partner in past four weeks; Ever had an STI	Ever been in prison; Ever been in drug treatment; Ever been arrested;
Platt et al, 2008[66]	Russia, Togliatti	230 PWID (134 in 2001 from the study above, and 96 from 2004) who reported injecting for three years or less and injected in past four weeks were recruited by outreach workers in 2001 and through RDS in 2004	Duration of injecting career*; Frequency of injection; Ever injected homemade drugs; Injected with used needles in past four weeks; Used a previously used filter; Frontloading in past four weeks*; Injected with a prefilled syringe; Frequency of reusing the same needle; Ever exchanged sex for money, drugs or goods*; History of STIs	Year of study*; Gender; Age; District of residence; Education; Main source of income in past four weeks; History of prison; Police arrest in past year; Ever in drug treatment*; Main source of needles in past four weeks; Ever been tested for HIV
Kozlov et al, 2006[50]  *outcome is HIV incidence at 12 month follow up to enrolment	Russia, St Petersburg	520 sero-negative PWID enrolled in cohort study who injected at least three times / week in past month or reused another's injecting equipment at least three times in past three months	Frequency of injecting psychostimulants*; Number of sex partners in past six months; Selling sex for money or goods in past six months	
Niccolai et al,	Russia, St	387 ever injectors were	Unsafe injection in past 30	Unemployed*



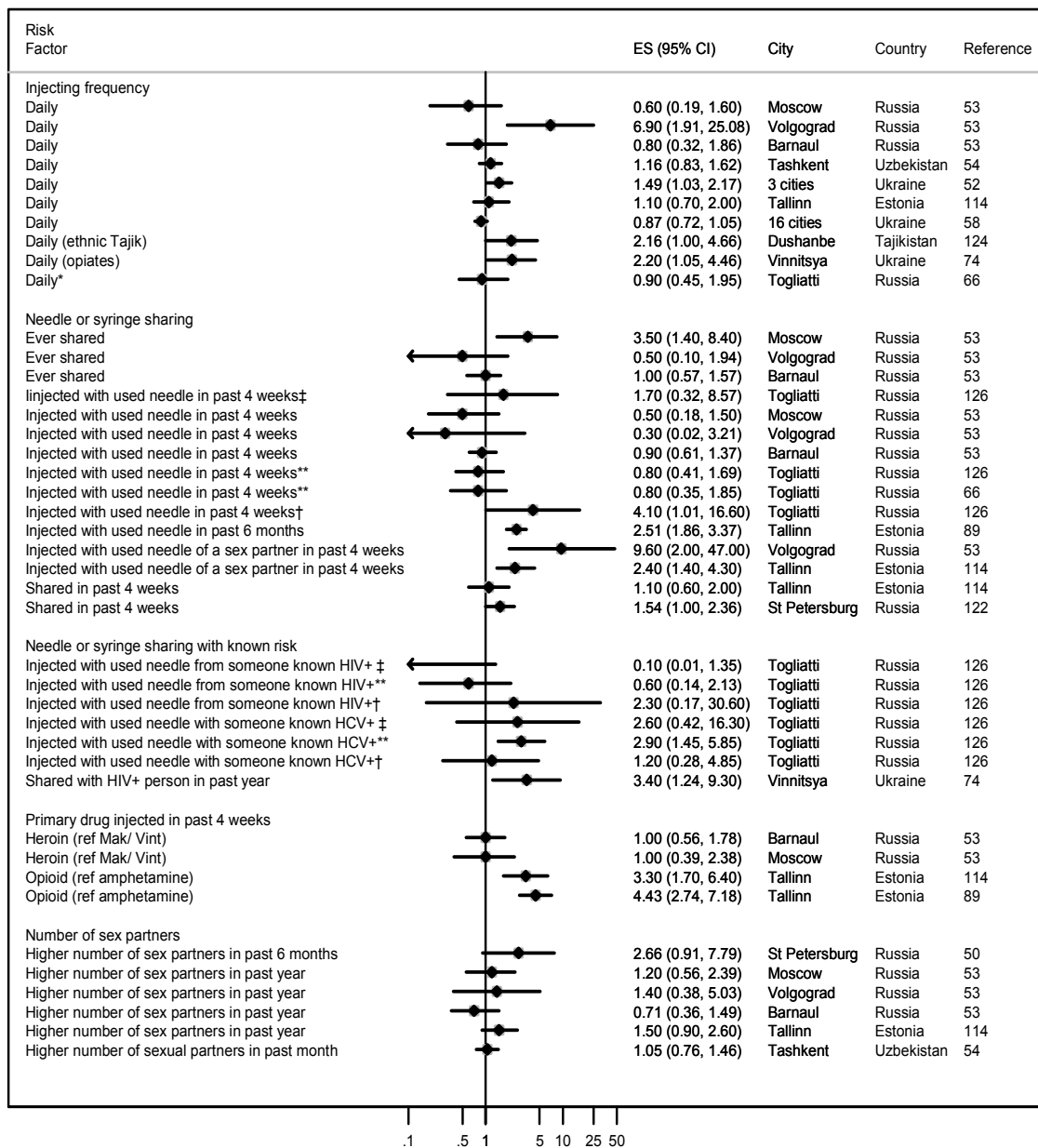
Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
2010 [122]	Petersburg	enrolled through RDS	days*; Has STI*;	
Rhodes et al, 2006 [53]	Russia, Moscow	455 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Last day injected, number of times injected*; Frequency of injection; Main drug injected in past four weeks; Injected with used needle in past four weeks; Shared paraphernalia in past four weeks; Ever injected with used needles*; Number of sex partners in past year; History of STI*	Gender; Age; Education; Main source of income in past four weeks; Ever been in prison*; Ever registered as a drug user*
	Russia, Volgograd	517 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Frequency of injection*; Ever injected homemade drugs; Injected with used needle in past four weeks; Shared paraphernalia in past three weeks; Ever injected with used needles; Injected with needle previously used by sex partner in past 12 months*; Number of sex partners in past year; History of STI	Gender; Age; Education; Main source of income in past four weeks*; Ever registered as a drug user
	Russia, Barnaul	501 PWID who injected in past four weeks recruited by outreach workers	Duration of injecting career; Last day injected, number of times injected*; Frequency of injection; Main drug injected in past four weeks; Ever injected homemade drugs; Injected with used needle in past four weeks; Shared paraphernalia in past four weeks*; Filled syringe from working syringe in past four weeks; Ever injected with used needles;	Gender; Age; Education; Main source of income in past four weeks; Ever been in prison; Ever registered as a drug user

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			Number of sex partners in past year; History of STI	
Beyrer et al, 2009[73]	Tajikistan, Dushanbe	419 PWID who injected in past month aged 17 or over recruited through snowball technique	Daily injection in past six months*	Ethnicity*  Model adjusted for gender
Stachowiak et al, 2006[124]	Tajikistan, Dushanbe	207 ethnic Tajik PWID (subsample of above) aged 17 or over recruited through snowball technique	Injecting at least daily for past six months*; Less than three years since initiation of injection; Injects 'alone'*; Injected with used needle in past six months	Reports narcotics 'very easy' to obtain*; Ever experienced drug treatment*
Booth et al, 2006[52]	Ukraine, Kiev, Odessa, Makeevka/ Donetsk	778 PWID aged 18+ who injected in past 30 days and were unaware of their HIV status recruited through outreach workers	Injected sedative/ opiate mix in past 30 days*; Daily injection in past 30 days*; Sex in past 30 days*; Sex with HIV+ or unknown status partner in past 30 days*	Age*; Gender*; City of origin*
Robbins et al, 2010[125]	Ukraine, Odessa, Kiev, Donetsk	313 youth aged 15-24 who live part or full time on the street and reported ever injecting recruited by time-location sampling	Last sex unprotected*; Ever diagnosed with STI*  Model adjusted for gender, age, education, work for pay, orphan status, spending nights outside of residence $\geq 2$ nights/ week for past few months/ no place to live, city of residence	
Dumchev et al, 2009[74]	Ukraine, Vinnitsya	268 PWID aged 18+ who report at least three injections in past 30 days and have lived in Vinnitsya for past year, recruited through snowball sampling	Shared needles with HIV+ person in past year*; Inject opiates daily*	HIV knowledge score*
Taran et al, 2011[58]	Ukraine, 16 cities	3,487 PWID aged 16+ who injected in past 30 days and were recruited through RDS	Type of drug injected in past month; Duration of injecting career*; Injecting frequency in past month; Used alcohol with drugs in past month*; Shared needle at last injection*; Frequency of sharing	Gender*; Marital status; Occupation*; Education*

Study, year	Location	Sample	Individual-level risk factors	Environmental-level risk factors
			paraphernalia in past month*; Sexual contact in past year;	
Sanchez et al, 2006[54]	Uzbekistan, Tashkent	701 self-identified PWID aged 18+available for two weeks after enrolment by outreach workers	Age at first drug use; First illicit drug of use*; Duration of injecting career; Current heroin use; Injecting frequency; Poppy-straw use; Group drug use; Sharing needles; Own syringe; Blood transfusion; STI history; Hepatitis history*; TB history; STI symptoms; Sell sex for drugs; Condom use*; Number of sexual partners in past month	Age; Gender; Nationality; Marital status; Employment status*; Education status; Needle exchange programme; AIDS knowledge; protection for AIDS; Donated blood for money*;

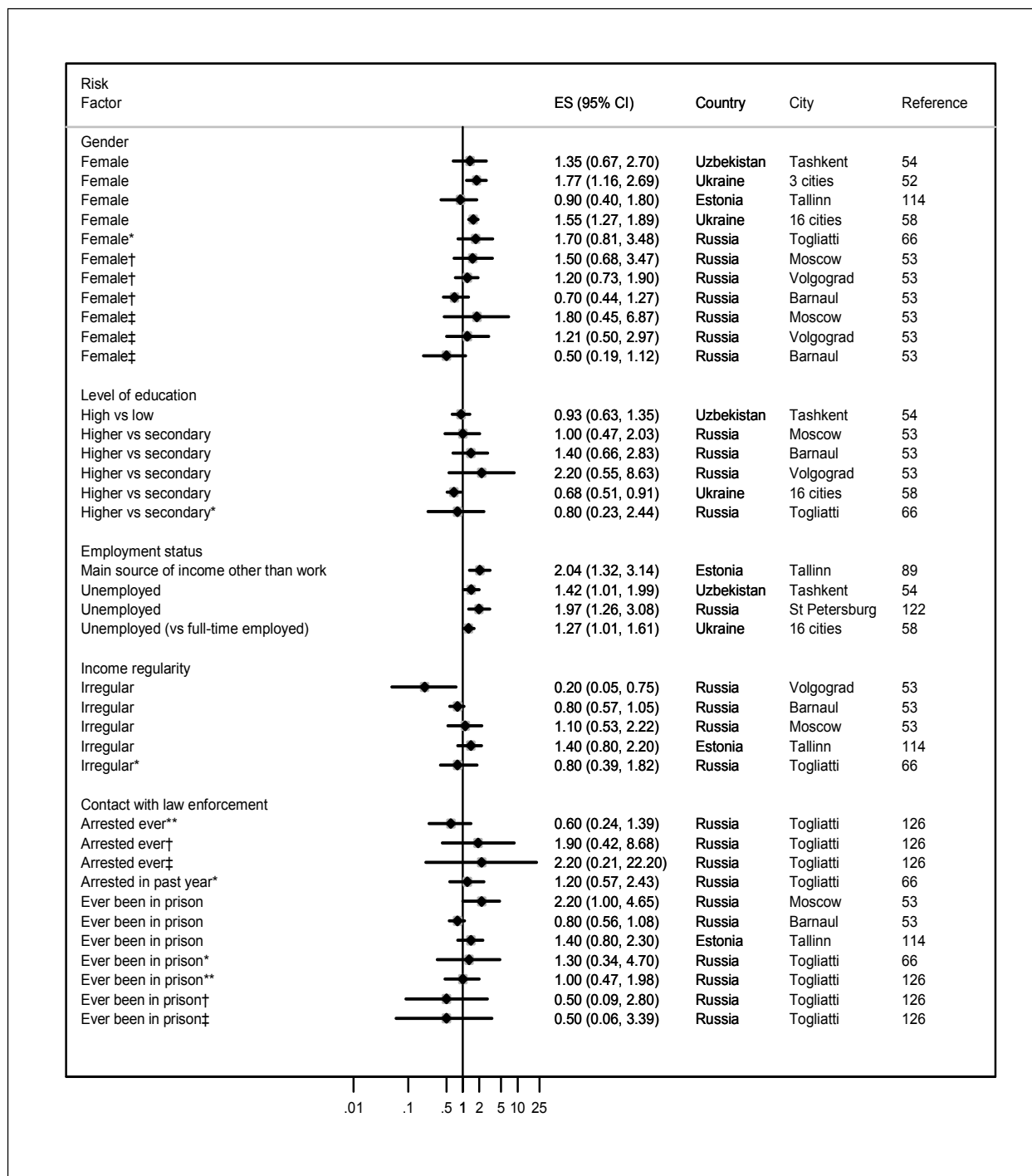
**Table 1:** Summary of studies presenting multivariate analyses of risk factors for HIV among PWID in Central and Eastern Europe and Central Asia\* P-value reported  $\leq 0.05$

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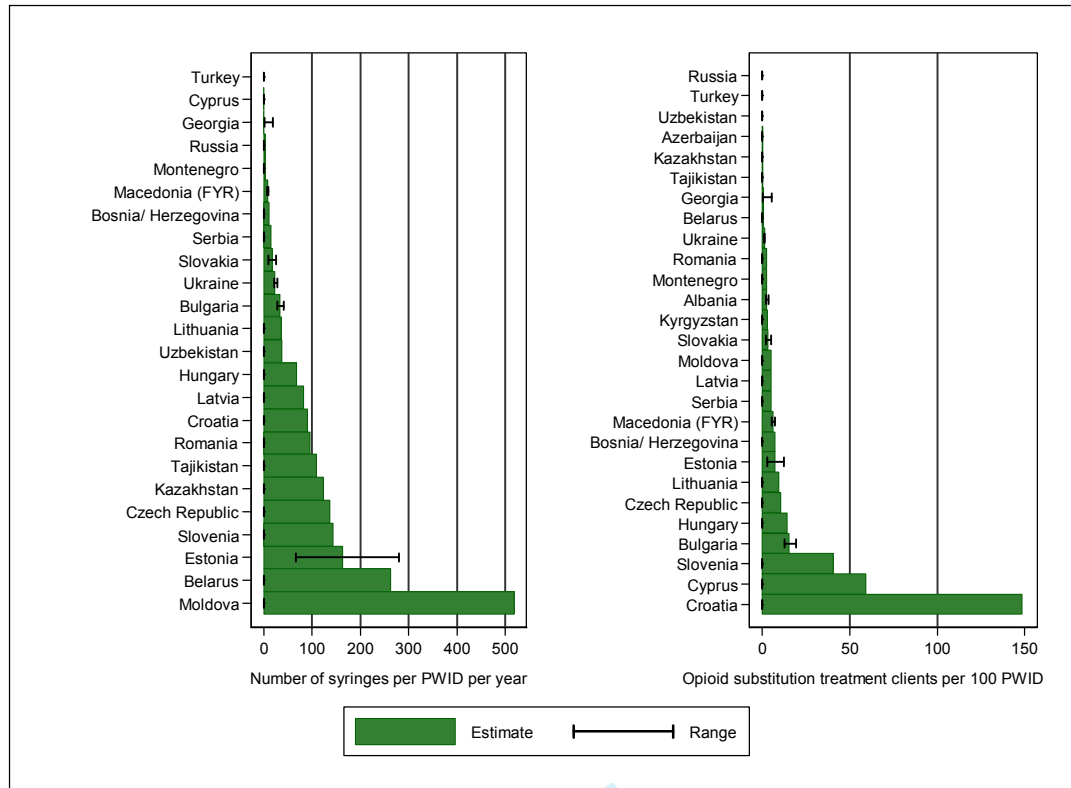
\* new PWID (≤3 years); \*\*male PWID; †female (non-SW) PWID; ‡female (SW) PWID

Figure 3 Adjusted effect estimates of individual level risk factors present in multivariate studies of PWID



\* new PWID (≤3 years); \*\*male PWID; †female (non-SW) PWID; ‡female (SW) PWID

Figure 4 Adjusted effect estimates of environmental level risk factors present in multivariate studies of PWID



**Figure 5** Estimated numbers of syringes distributed per PWID per year and estimated number of OST clients per 100 PWID in the latest year for which data is available.[39 40]

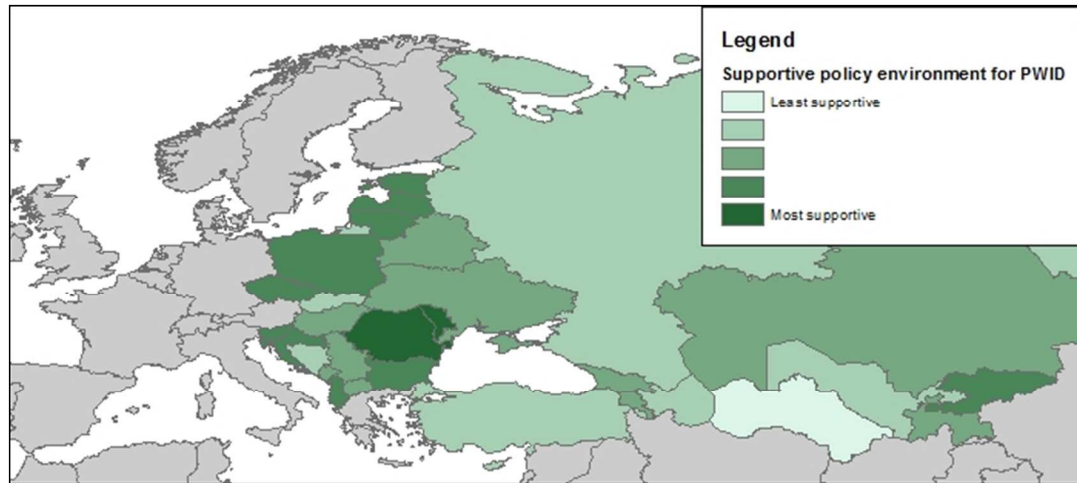


Figure 6 Map showing the supportiveness of the policy environments for HIV among PWID in Europe.[39 45-47]



# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4/5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5/6
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5/6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ for each meta-analysis).	N/A





# PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8/9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8/9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8/9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10/11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10/11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10/11/12
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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