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Global systematic review and ecological analysis of HIV in people who inject drugs: National population sizes and factors associated with HIV prevalence

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Abstract

Background: People who inject drugs (PWID) are at elevated risk of HIV infection. Data on population sizes of PWID living with HIV are needed to inform the implementation of prevention, treatment and care programs. We estimated national population sizes of people who recently (past 12 months) injected drugs living with HIV and evaluated ecological associations with HIV prevalence in PWID.

Methods: We used national data on the prevalence of injecting drug use and of HIV among PWID, derived from systematic reviews, to estimate national population sizes of PWID living with HIV. Uncertainty was estimated using Monte Carlo simulation with 100,000 draws. We extracted data on sample characteristics from studies of HIV prevalence among PWID, and identified national indicators that have been observed or hypothesised to be associated with HIV prevalence in PWID. We used linear regression to evaluate associations between these variables and HIV prevalence in PWID.

Results: Four countries comprised 55% of the estimated global population of PWID living with HIV: Russia (572,500; 95% uncertainty interval (UI) 235,500-1,036,500); Brazil (462,000; 95% UI 283,500-674,500); China (316,500; 95% UI 171,500-493,500), and the United States (195,500; 95% UI 80,000-343,000). Greater anti-HCV prevalence and national income inequality were associated with greater HIV prevalence in PWID.

Conclusion: The countries with the largest populations of PWID living with HIV will need to dramatically scale up prevention, treatment and care interventions to prevent further increases in population size. The association between anti-HCV prevalence and HIV prevalence among PWID corroborates findings that settings with increasing HCV should implement effective interventions to prevent HIV outbreaks. The association between income inequality and HIV among PWID reinforces the need to implement structural interventions alongside targeted individual-level strategies.

Keywords: HIV; people who inject drugs; population size; hepatitis C virus; income inequality

An estimated 15.6 million (95% uncertainty interval (UI): 10.2-23.7 million) people globally have recently (in the past 12 months) injected drugs. Just under one in five people who recently injected drugs (18%, or 2.8 million people) are living with HIV infection.[1] Although there are effective interventions to prevent HIV among PWID, including needle and syringe programs (NSP) and opioid substitution therapy (OST),[2,3] these are infrequently implemented at sufficient scale,[4] and PWID living with HIV may experience considerable barriers to accessing antiretroviral treatment.[5] As such, incident HIV infections continue to occur among PWID. In the last decade, HIV outbreaks among PWID have been reported in multiple settings including Athens,[6] Glasgow,[7] rural United States,[8] and Bucharest.[9]

We estimated national HIV prevalence among people who have recently injected drugs for 108 countries, identifying wide variation within and between regions.[1] Such data provide a baseline to assess progress towards the Sustainable Development Goal of ending the AIDS epidemic by 2030.[10] Additional data are needed, however, to understand the relative numbers of people who have recently injected drugs living with HIV across countries. Awareness of the population size of people who have recently injected drugs living with HIV is critical for planning and monitoring prevention, treatment, and care services, and for modelling future HIV burden.

Although much attention is given to individual-level risk behaviours (e.g. receptive needle sharing) for HIV infection, these behaviours are shaped by the risk environment in which injecting drug use occurs.[11,12] The influence of the risk environment on HIV prevalence among PWID has been widely studied, including associations with law enforcement indicators[13] and access to needle and syringe programs.[14] Cross-national ecological studies have examined associations between HIV infection in PWID and environmental factors such as hepatitis C prevalence,[15] time since implementation of harm reduction measures,[16] and income inequality.[17] Although there are limitations to ecological studies, chiefly the inability to infer that observed relationships persist at the individual level,[18] they do provide insights into social determinants of health that may be targeted to improve population

health outcomes. The collation of global data on HIV infection among PWID to produce population estimates also provided an opportunity to examine associations between a wide range of micro- and macro-environmental factors and HIV prevalence in PWID. The aims of this study were to:

1. Estimate national population sizes of people who recently injected drugs living with HIV infection; and
2. Evaluate associations between risk environment variables and the prevalence of HIV infection in people who recently injected drugs.

Methods

As this study includes population health estimates derived from a systematic review, reporting is in compliance with the PRISMA guidelines and GATHER statement.[19] PWID were defined as people who have recently (in the past 12 months) injected illicit drugs or extra-medical pharmaceuticals.

Population size estimates of PWID living with HIV

This analysis uses data from systematic reviews on the prevalence of injecting drug use and HIV prevalence among PWID. The review protocols were registered with PROSPERO (record numbers CRD42016052858 and CRD42016052853) and full methods are published elsewhere.[1] The study flow diagram is shown in supplementary figure 1. We searched peer-reviewed literature databases (Medline, Embase and PsycINFO) and reports from government, intergovernmental and non-government organisations to identify estimates of the prevalence of injecting drug use or HIV prevalence (serologically confirmed) among samples of PWID. There were no language restrictions, but searches were restricted to works published since 2008. Searches were conducted in June 2017.

Eligible data were selected using pre-specified decision rules, including grading of the quality of study methods (see supplementary materials). Estimates of the prevalence of injecting drug use that were obtained using multi-parameter evidence synthesis, indirect prevalence estimation methods, or network scale-up methods were considered the highest quality methods. Multi-site seroprevalence studies were the highest quality method for estimating HIV prevalence in PWID. If the method used to estimate the prevalence of injecting drug use or HIV prevalence among PWID was not provided, the estimate was automatically excluded. Estimates of HIV prevalence based on self-reported HIV status or registration data were also excluded. Where multiple estimates were available for a country, those with a more highly rated method, and/or more recent data, were included in analyses. Multiple estimates for a country were pooled using random effects meta-analysis. This produced national estimates of the prevalence of injecting drug use, and HIV

prevalence among PWID.[1] Studies included in the population size estimates are shown in supplementary table 1.

To estimate population sizes of PWID living with HIV, we first multiplied the prevalence of injecting drug use by the prevalence of HIV among PWID. We then multiplied this product by the national population size aged 15-64 years[20] to obtain the number of PWID living with HIV. Uncertainty intervals (UIs) were estimated using Monte Carlo simulation taking 100,000 draws. A binomial distribution was used because our parameters of interest were proportions. Estimated sample sizes associated with the proportions for simulation input were derived based on the 95% confidence intervals (CIs) and standard errors of proportion estimates in each country. The simulated UIs incorporated the uncertainty of the estimates of the prevalence of injecting drug use and of the estimates of HIV prevalence among PWID.

Ecological analysis of variables associated with HIV prevalence in PWID

We modelled across studies to examine risk environment variables associated with HIV prevalence in people who have recently injected drugs. Studies were excluded if the study inclusion criteria restricted the sample by age (other than restricting the sample to adults), sex, or use of specific drugs. For each included study, we extracted data for a pre-defined set of demographic characteristics and behaviours of the sample. These were: the proportion of each study sample that was female; the mean or median age of the sample; the proportion of the sample with hepatitis C virus antibody (anti-HCV; included only serologically confirmed anti-HCV); the mean or median duration of injecting drug use within the sample; the proportion of the sample reporting lifetime or recent homelessness or unstable housing, incarceration, sex work, injecting risk behaviours, and sexual risk behaviours; the proportion of each sample reporting opioids or stimulants as their main drug injected; and the year that data collection for the study was completed.

We further identified national indicators of health, development and inequality that have been observed or hypothesised to be associated with HIV infection. These included national HIV

prevalence in the general population;[21] estimated national prevalence of injecting drug use;[1] country income level (low/middle or high; low- and middle-income countries were combined due to sparse data from low-income countries);[22] income inequality, as measured by the Gini coefficient (with a higher coefficient indicating greater income inequality);[23] the Gender Inequality Index;[24] the Human Development Index (incorporating life expectancy, education and national income);[25] national incarceration rates;[26] and national coverage of NSP (number of needles distributed per PWID annually) and OST (number of OST recipients per 100 PWID).[4] National indicator data are shown in supplementary table 2.

Generalized linear models were used for the analysis, clustering by country, with the study as the unit of analysis and study-level HIV prevalence in PWID as the outcome variable. We had planned to examine associations between HIV prevalence and all the study-level variables described above but elected not to build models for variables that were available for 25% or fewer of HIV prevalence estimates in the database. These variables were lifetime or recent homelessness, incarceration, or sex work; and opioids or stimulants as the main drug injected. We elected to use an unweighted analysis of world regions to accurately represent the availability of data and not penalise regions with more, often higher quality, studies. Where a single study presented multiple estimates (e.g. for several cities within a country), all estimates were included separately in models, with adjustment for within country data-points dependency in the analyses. Residuals and linear predicted values were checked for each analysis.

We plotted linear regression lines on scatter plots depicting HIV prevalence against each explanatory variable; for variables where the model fit was improved after adding the quadratic term (described below), we also plotted polynomial lines for trend models of degree two. We presented the R-squares for the linear trend models and polynomial trend models based on the data-points plotted. All plots use transformed values to concord with values shown in results tables.

The outcome variable (HIV prevalence in PWID) was a proportion, and thus logit transformation was performed by the formula ln (y / (1 - y)). In the same fashion, exposure variables that were proportions were logit transformed. An unadjusted linear model for each exposure variable on the logit transformed outcome was fitted first; henceforth 'linear' models refer to the linear relationship on HIV prevalence on a logit transformed scale. Then, to assess if trends were non-linear, a quadratic term was tested by adding the squared exposure variable. Likelihood ratio analyses with chi-square tests (type III) were used to evaluate if adding the quadratic term provided a significantly better model; if yes, the results for the second model with quadratic term were presented. An exposure by region interaction term was entered to test for regional differences in exposures to HIV prevalence in PWID.

General population HIV prevalence was assumed *a priori* to be an important influence on prevalence in PWID; hence, adjusted models included the general population HIV prevalence entered as an additional exposure variable. A p-value of <0.003 was used for significance to account for the number of exposure variables examined. Analyses were undertaken using SAS 9.4.

Results

National population sizes of current PWID living with HIV

Sufficient data to estimate national population sizes of PWID living with HIV were available for 78 of 179 (44%) countries where evidence of injecting drug use has been identified (Table 1). National population sizes of PWID living with HIV are presented in Table 2. Thirty-two countries (40%) have estimated populations of fewer than 1,000 PWID living with HIV; an additional 23 countries (29%) have fewer than 10,000 PWID living with HIV. Countries with the largest national populations of PWID living with HIV are Russia (572,500; 95% uncertainty interval (UI) 235,500-1,036,500), Brazil (462,000; 95% UI 283,500-674,500), China (316,500; 95% UI 171,500-493,500), and the United States (195,500; 95% UI 80,000-343,000). Together, these countries comprise more than half (55%) of the estimated global population of PWID living with HIV (Figure 1).

Ecological analysis of variables associated with HIV prevalence in PWID

The database included 626 estimates of HIV prevalence among PWID in 93 countries (52% of countries with evidence of injecting drug use). These are summarised in Table 3, with study-level HIV prevalence data provided in supplementary Table 3. Plots of HIV prevalence among PWID by exposure variables are presented in Figures 2 and 3. For study-level variables, a higher percentage of women in the study sample, higher anti-HCV prevalence, and older studies (as indicated by less recent year of data collection) were associated with higher HIV prevalence among PWID (Figure 2). The scatter plot suggested that anti-HCV prevalence was typically higher than HIV prevalence in any given study. Supplementary table 4 provides detail to aid interpretation of the logit transformed scatter plots.

Among the country-level variables tested, higher national prevalence of injecting drug use, higher gender inequality, lower Human Development Index, higher incarceration rate, and lower NSP coverage were associated with higher HIV prevalence among PWID (Figure 3). A quadratic trend indicated lower HIV prevalence amongst PWID as coverage of OST increased, with a reversal of this

association at the higher end of the OST coverage scale, which was driven by a small number of data-points from South Asian and Western European countries. HIV prevalence among PWID also had quadratic associations with general population HIV prevalence, and income inequality. The PWID HIV prevalence increased as the general population HIV prevalence and as income inequality increased; this association was not observed at higher values of both variables, where only a small number of data-points were available. A box plot suggested higher HIV prevalence in low- and middle-income countries as compared to high-income countries (Figure 3).

Statistical associations between PWID HIV prevalence and the tested variables are presented in Table 4. Addition of the squared exposure variables improved the fit for the models that examined age of sample, population HIV prevalence, income inequality, and NSP and OST coverage. Models with regional interaction terms did not improve the model fit, and therefore interactions terms were not included in the final models. Unadjusted analyses showed that higher anti-HCV prevalence in PWID, general population HIV prevalence, Gender Inequality Index, and lower Human Development Index were all associated with higher HIV prevalence in current PWID. In models adjusted for general population HIV prevalence, the statistically significant positive linear association between study-level anti-HCV prevalence and PWID HIV prevalence remained. There was a quadratic association between income inequality and PWID HIV prevalence after adjusting for general population HIV prevalence. The trend suggested increasing PWID HIV prevalence with increasing income inequality up to moderately high levels of income inequality, which was not observed thereafter, driven by the few data-points with high income inequality but low HIV prevalence among PWID in the Latin America region (Figure 3).

Discussion

National estimates of the number of PWID living with HIV were calculated for 78 of 179 countries where injecting drug use is known to occur. Four countries accounted for more than half of the estimated global population of PWID living with HIV: Russia, Brazil, China, and the United States. In ecological analyses, after adjusting for general population HIV prevalence, higher study-level anti-HCV prevalence and country-level income inequality were associated with higher HIV prevalence in PWID.

Implications

Previous work has highlighted the potential to use HCV prevalence to estimate HIV epidemic potential in PWID,[15,27] and increasing HCV prevalence pre-dated a large HIV outbreak in rural PWID in the United States.[28] The findings presented here provide further support for the contention that settings experiencing HCV outbreaks in PWID must take steps to prevent HIV (as well as prevent further HCV infection), including scaling up of harm reduction measures as described above. This is of particular importance in areas where HIV prevalence is still low among PWID, but HCV is high and harm reduction coverage is very poor, such as in the Middle East and North Africa,[1] and in areas that are seeing rapid increases in the prevalence of injecting drug use and associated HCV infections, such as in many parts of the United States.[29,30]

The ecological association between income inequality and HIV prevalence in PWID has previously been demonstrated at the national level for European Economic Area countries,[17] in US metropolitan areas,[31] and in communities in Vietnam.[32] Our finding suggests that national income inequality is an important factor in the HIV epidemic in PWID globally. These findings highlight the importance of higher-level contextual factors in potentially influencing HIV prevalence among PWID, and the concomitant need to address these through structural interventions and policies. Although the causal pathway between income inequality and HIV infection in PWID is unclear, community-level analyses in Vietnam show that income inequality interacts with individual-level income such

that PWID with the lowest personal incomes in areas with the greatest income inequality are most at risk of HIV infection.[32] Efforts to reduce income inequality and economic deprivation at the structural level while improving the personal economic circumstances of PWID (through increased access to employment or social security benefits, for example) may therefore work to reduce HIV prevalence in this key population.

Numerous studies and meta-analyses have identified reductions in HIV prevalence and incidence associated with greater coverage of NSP[33,34] and OST.[2,3,33] A cross-national ecological analysis using time since introduction of NSP and OST in European nations reported that nations with each of these interventions for a greater number of years had lower HIV incidence in PWID than nations with more recent implementation.[16] A statistical association between HIV prevalence and current NSP or OST coverage was not observed in our ecological analysis, which is likely due to limitations of the analysis rather than a true lack of association. Critically, NSP and OST coverage estimates employed in the analysis were for the most recent year available, while the study-level HIV prevalence data related to all years from 1995 onwards, with most data being collected from 2005 onwards. Outlier observations had a clear impact on the modelled relationship between OST coverage and study-level HIV prevalence.

Limitations

Although there are 197 countries where injecting drug use occurs,[1] we were only able to estimate the national population size of PWID living with HIV for 78 countries. Data estimating the prevalence of injecting drug use and the prevalence of HIV among PWID are scarce or even non-existent for many countries. Countries with data may be those with more visible or accessible populations of PWID, which may be related to unmeasured factors such as drug law enforcement. When data are available, it is often uncertain.[1] Highlighting the uncertainty in these data points, we note that the estimated number of PWID living with HIV infection in Pakistan is greater than the UNAIDS estimate of the number of people living with HIV in that country.[35] There are considerable disparities in

population size estimates of PWID in Brazil[1,36,37] due to differences in data sources and decision rules around inclusion of estimates in a given exercise.[38] There is an enormous need for a greater quantity of, and better quality, epidemiological data on both injecting drug use and HIV infection among PWID. This is particularly so, but not exclusively, in countries where injecting drug use is an emerging behaviour (e.g. in parts of sub-Saharan Africa) and may not previously have been relevant for HIV prevention programming.[1]

There are important caveats to bear in mind when interpreting the findings of the ecological analysis. Several associations that have been repeatedly observed at the individual level (e.g. positive correlations between HIV prevalence and age or duration of injecting drug use) were not apparent in this analysis. This demonstrates a key limitation of using study-level average indicators to assess relationships across studies: an association observed within multiple studies may not be the same as the association across studies.[18]

Most data points included in the ecological analysis were from studies conducted in Eastern and Western Europe, with very little data from Central Asia, Latin America, or Caribbean nations. We did not observe any regional differences in the predictors of HIV in people who have recently injected drugs. However, we do not have strong evidence as to whether this was due to a lack of regional variation, or a lack of data in some regions. Additionally, our analysis did not consider the sample size of studies; we explored the option of weighting by sample sizes but several very large studies would have dominated the results, masking associations with country-level exposure variables. An increase in data availability from diverse world regions would permit better examination of regional differences in predictors of HIV in people who have recently injected drugs.

We were unable to test two key indicators that may influence HIV prevalence among PWID: the criminal justice environment, and coverage of ART among PWID living with HIV. Criminalisation of drug use appears to be associated with HIV prevalence among PWID,[13] but we were unable to identify a national index measuring drug use criminalisation to allow for inclusion of this variable in

the study. We were also unable to include study-level recent or lifetime incarceration as a predictor variable in our models due to lack of data. We modelled national incarceration rate against HIV prevalence in PWID but did not identify any trend. ART coverage could not be included due to a lack of data.[4] We did not use general population ART coverage data as PWID frequently experience significant barriers to accessing treatment for HIV infection,[39] and general population data are therefore unlikely to reflect coverage in PWID.

Conclusion

We estimate that 55% of the world's estimated population of PWID living with HIV can be found in four countries: Russia, Brazil, China, the United States, all of which will need to make concerted efforts to reduce this burden. Only 44% of countries where injecting drug use is known to occur had sufficient data to estimate national population sizes of PWID living HIV, highlighting the need for more and higher quality data to inform our understanding of the size of the global epidemic of HIV among PWID.

HIV prevalence among PWID was associated with anti-HCV prevalence in this population, corroborating evidence that HCV prevalence is a key indicator of HIV epidemic potential. Greater income inequality was associated with higher HIV prevalence amongst PWID, although the causal mechanism of the relationship requires further work to be understood. Reducing the burden of HIV infection among PWID will require attention to structural determinants of health in addition to individual-level prevention interventions.

CRediT author statement

Sarah Larney: Conceptualisation, methodology, investigation, writing – original draft, project administration. **Janni Leung**: Methodology, software, formal analysis, investigation, writing – review & editing. **Jason Grebely**: Methodology, investigation, writing – review & editing. **Matthew Hickman:** Methodology, writing – review & editing. **Peter Vickerman:** Methodology, writing – review & editing. **Amy Peacock**: Conceptualisation, methodology, investigation, writing – review & editing. **Jack Stone:** Methodology, investigation, writing – review & editing. **Adam Trickey:** Methodology, investigation, writing – review & editing. **Kostyantyn V. Dumchev:** Methodology, investigation, writing – review & editing. **Samantha Colledge:** Software, investigation, data curation, writing – review & editing, visualisation. **Evan B. Cunningham**: Software, investigation, visualisation, writing – review & editing. **Michael Lynskey:** Writing – review & editing. **Richard P. Mattick:** Methodology, writing – review & editing. **Louisa Degenhardt:** Conceptualisation, methodology, investigation, writing – review & editing, supervision, project administration, funding acquisition.

Declaration of interests

SL has received investigator-initiated untied educational grants from Indivior. LD has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Reckitt Benckiser, Indivior, Mundipharma and Seqirus. AP has received investigator-initiated untied educational grants from Mundipharma and Seqirus. JG is a consultant/advisor and has received research grants from Abbvie, Cepheid, Gilead Sciences and Merck/MSD. MH reports honoraria for speaking at meetings from Gilead, Abbvie, and MSD. JS reports non-financial support from Gilead Sciences, outside the submitted work.

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Table 1: Summary of data available to estimate population sizes of PWID living with HIV

Region	**N countries where IDU is known to occur**	**N (%) countries with estimates of IDU prevalence**	**N (%) countries with estimates of HIV prevalence among PWID**	**N (%) countries with estimates of population size of PWID living with HIV**
Eastern Europe	17	15 (88%)	17 (100%)	15 (88%)
Western Europe	31	21 (68%)	24 (77%)	20 (65%)
East and Southeast Asia	16	10 (63%)	11 (69%)	8 (50%)
South Asia	9	8 (89%)	8 (89%)	6 (67%)
Central Asia	5	4 (80%)	4 (80%)	4 (80%)
Caribbean	6	1 (17%)	1 (17%)	1 (17%)
Latin America	19	5 (26%)	8 (42%)	4 (21%)
North America	2	2 (100%)	2 (100%)	2 (100%)
Pacific Islands	15	0 (0%)	3 (20%)	0 (0%)
Australasia	2	2 (100%)	2 (100%)	2 (100%)
Sub-Saharan Africa	36	12 (33%)	13 (36%)	10 (28%)
Middle East and North Africa	21	3 (14%)	15 (71%)	3 (14%)
Global	**179**	**83 (46%)**	**108 (60%)**	**78 (44%)**

Notes: IDU: injecting drug use. PWID: people who inject drugs. Percentages use the number of countries where IDU is known to occur as the denominator.

Table 2: National prevalence of injecting drug use, and prevalence and population size of HIV infection among people who recently (past 12 months) injected drugs

	Prevalence of injecting drug use % (95% CI)*	HIV prevalence among PWID % (95% CI)*	Number of current PWID living with HIV (95% UI)
Eastern Europe			
Armenia	0.62 (0.41-1.35)	5.4 (2.2-8.5)	500 (<500-1500)
Azerbaijan	0.61 (0.49-0.74)	9.7 (5.6-13.8)	4000 (2500-6500)
Belarus	0.59 (0.22-0.96)	25.6 (17.9-33.2)	10500 (4000-18500)
Bosnia & Herzegovina	NK	0.3 (0.0-0.6)	NE
Bulgaria	0.38 (0.30-0.45)	7.0 (3.2-1.1)	1500 (1000-1500)
Czech Republic	0.64 (0.61-0.67)	0.3 (0.2-0.4)	<500 (<500-<500)
Estonia	0.94 (0.69-1.73)	53.4 (44.4-62.5)	4500 (2000-7500)
Georgia	4.19 (0.48-7.90)	2.2 (1.5-2.9)	2500 (500-5500)
Hungary	0.06 (0.03-0.08)	0.2 (0.0-0.4)	<500 (0-<500)
Latvia	0.92 (0.73-1.17)	26.9 (24.1-29.6)	4000 (3000-5000)
Lithuania	0.22 *(0.12, 0.34)*	8.0 (1.7-14.4)	500 (<500-1000)
Moldova	0.40 (0.25-0.54)	29.5 (12.9-46.0)	3500 (1500-6000)
Poland	NK	18.0 (15.3-20.9)	NE
Romania	0.62 (0.46-0.84)	20.5 (7.0-34.1)	16500 (6500-29500)
Russian Federation	1.78 *(0.94, 2.71)*	30.4 (17.9-43.0)	572500 (235500-1036500)
Slovakia	0.49 (0.35-0.89)	0.01 (0.0-0.03)	<500 (0-<500)
Ukraine	0.97 (0.52-1.79)	19.1 (16.1-22.2)	61000 (24500-106000)
Western Europe			
Albania	NK	0.5 (0.0-2.8)	NE
Andorra	NK	NK	NK
Austria	0.32 (0.22-0.42)	0.6 (0.3-1.0)	<500 (<500-<500)
Belgium	0.35 (0.24-0.49)	4.3 (3.3-5.4)	1000 (500-1500)
Croatia	0.23 (0.18-0.29)	0.4 (0.0-0.8)	<500 (0-<500)
Denmark	0.45 (0.35-0.52)	1.3 (0.3-3.6)	<500 (0-500)
England	0.59 (0.55-0.63)	0.8 (0.1-1.5)	1500 (500-3500)
Finland	0.46 (0.41-0.67)	1.2 (0.5-2.4)	<500 (<500-500)
FYR Macedonia	NK	NK	NK
France	0.20 (0.16-0.23)	8.7 (5.3-12.1)	7000 (4500-10500)
Germany	0.24 (0.03-0.45)	4. (2.3-6.4)	6000 (1000-12500)
Greece	0.07 (0.06-0.09)	6.9 (4.2-9.6)	500 (<500-500)
Iceland	NK	NK	NK
Ireland	0.27 (0.20-0.33)	5.8 (4.2-7.4)	500 (500-500)
Italy	0.83 (0.57-1.14)	6.1 (4.7-7.5)	21000 (13000-30500)
Luxembourg	0.57 (0.45-0.69)	1.5 (0.5-2.5)	<500 (<500-<500)
Malta	NK	0.5 (0.0-1.2)	NE
Monaco	NK	NK	NK
Montenegro	NK	0.2 (0.0-0.6)	NE
Netherlands	0.03 (0.02-0.04)	2.3 (1.9-2.6)	<500 (<500-<500)
Northern Ireland	NK	NK	NK
Norway	0.24 (0.21-0.29)	0.7 (0.0-1.5)	<500 (0-<500)
Portugal	0.22 (0.19-0.25)	18.0 (15.4-20.6)	3000 (2500-3500)
San Marino	NK	NK	NK
Scotland	0.44 (0.38-0.49)	0.8 (0.5-1.3)	<500 (<500-<500)
Serbia	0.49 (0.41-0.58)	0.0 (0.0-<0.1)	0 (0-0)
Slovenia	0.42 (0.30-0.55)	0.5 (0.1-1.0)	<500 (<500-<500)
Spain	0.03 (0.01-0.05)	32.6 (31.6-33.6)	3500 (1000-6000)

	Prevalence of injecting drug use % (95% CI)*	HIV prevalence among PWID % (95% CI)*	Number of current PWID living with HIV (95% UI)
Sweden	0.13 (0.03-0.62)	0.2 (0.0-0.5)	<500 (0-<500)
Switzerland	0.24 (0.19-0.29)	1.4 (0.6-2.2)	<500 (<500-500)
Wales	NK	NK	NK
East and Southeast Asia			
Brunei Darussalam	NK	NK	NK
Cambodia	0.11 (0.10-0.23)	24.4 (17.0-33.1)	2500 (1000-4500)
China	0.25 (0.19-0.31)	12.4 (6.8-17.9)	316500 (171500-493500)
Hong Kong (China)	NK	NK	NK
Indonesia	0.11 (0.09-0.13)	44.5 (34.0-55.0)	84500 (61000-111500)
Japan	0.47 *(0.36, 0.58)*	NK	NK
Lao PDR	NK	17.4 (7.8-31.4)	NE
Malaysia	1.33 (1.11-1.56)	17.8 (16.6-19.1)	50500 (41000-60000)
Mongolia	NK	NK	NK
Myanmar	0.48 (0.32-0.65)	23.4 (19.0-27.7)	40500 (26000-57500)
Philippines	0.04 (0.03-0.05)	20.3 (13.0-27.6)	5000 (3000-7500)
Republic of Korea	NK	0.0 (0.0-<0.1)	NE
Singapore	NK	NK	NK
Taiwan	NK	12.4 (8.1-16.8)	NE
Thailand	0.11 (0.03-0.18)	24.5 (17.4-31.7)	12500 (4500-23500)
Timor Leste	0.01 (<0.01-0.02)	NK	NK
Viet Nam	0.25 *(0.19, 0.31)*	16.6 (13.1-20.1)	26500 (19000-36000)
South Asia			
Afghanistan	0.80 (0.50-1.09)	4.0 (2.2-5.8)	5500 (3000-9000)
Bangladesh	0.07 (0.06-0.07)	0.5 (0.2-0.7)	500 (<500-500)
Bhutan	NK	NK	NK
India	0.02 (0.01-0.03)	15.6 (12.9-18.2)	30500 (19500-43500)
Iran	0.28 (0.19-0.37)	14.0 (9.2-18.7)	22000 (13000-33500)
Maldives	0.60 (0.26-0.94)	0.0 (0.0-<0.1)	0 (0-0)
Nepal	0.20 (0.19-0.21)	9.6 (6.3-12.9)	3500 (2500-4500)
Pakistan	0.37 (0.32-0.42)	32.3 (25.5-39.1)	136500 (103500-172500)
Sri Lanka	<0.01 (<0.01-<0.01)	0.0 (0.0-<0.1)	0 (0-0)
Central Asia			
Kazakhstan	0.96 *(0.64, 1.42)*	9.2 (8.0-10.4)	10500 (6500-15000)
Kyrgyzstan	0.74 *(0.50, 1.11)*	12.4 (10.3-14.7)	3500 (2000-5000)
Tajikistan	0.45 *(0.30, 0.66)*	27.0 (21.0-33.7)	6500 (3500-9500)
Turkmenistan	NK	NK	NK
Uzbekistan	0.47 *(0.32, 0.70)*	7.3 (5.8-9.1)	7000 (4000-10500)
Caribbean			
Bahamas	NK	NK	NK
Bermuda	NK	NK	NK
Puerto Rico	1.15 *(0.77, 1.71)*	6.0 (3.7-9.3)	1500 (1000-3000)
Dominican Republic	NK	NK	NK
Haiti	NK	NK	NK
Jamaica	NK	NK	NK
Latin America			
Argentina	0.29 (0.29-0.30)	49.7 (35.4-64.0)	40000 (29000-51500)
Bolivia	NK	NK	NK
Brazil	0.67 *(0.51, 0.87)*	48.0 (18.0-78.0)	462000 (283500-674500)
Chile	0.38 *(0.29, 0.50)*	NK	NK

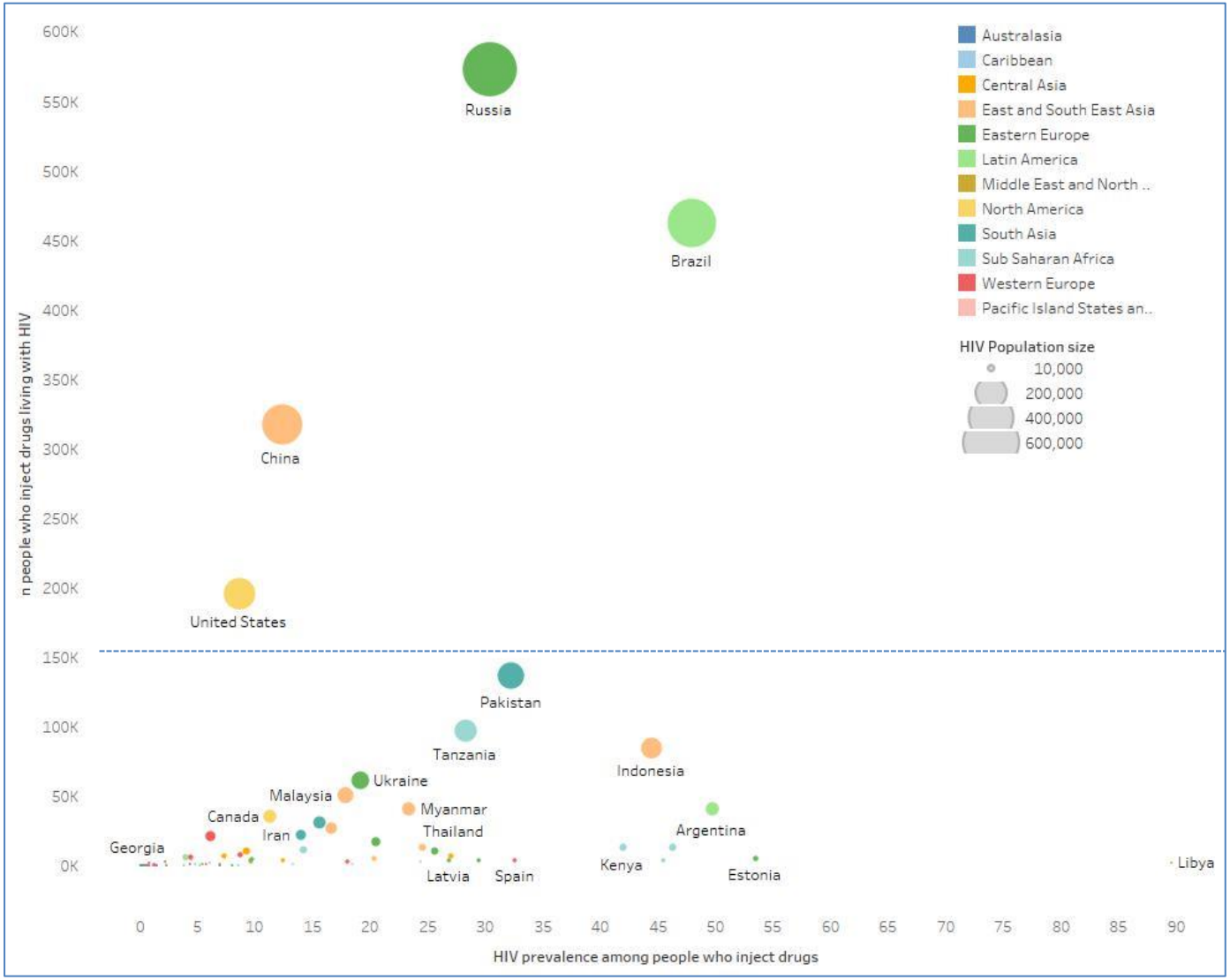
	Prevalence of injecting drug use % (95% CI)*	HIV prevalence among PWID % (95% CI)*	Number of current PWID living with HIV (95% UI)
Colombia	NK	4.6 (2.7-6.4)	NE
Costa Rica	NK	NK	NK
Ecuador	NK	NK	NK
El Salvador	NK	NK	NK
Guatemala	NK	NK	NK
Guyana	NK	NK	NK
Honduras	NK	NK	NK
Mexico	0.18 (0.12-0.25)	4.0 (3.0-4.9)	6000 (3500-9000)
Nicaragua	NK	2.4 (0.1-12.9)	NE
Panama	NK	NK	NK
Paraguay	NK	9.4 (3.7-15.0)	NE
Peru	NK	13.0 (10.9-15.1)	NE
Suriname	NK	NK	NK
Uruguay	0.30 (0.10-0.87)	18.5 (16.1-21.0)	1000 (0-3000)
Venezuela	NK	NK	NK
North America			
Canada	0.39 (0.31-0.47)	11.3 (8.5-14.2)	14000 (25500-46000)
United States	1.04 (0.57-1.88)	8.7 (6.8-10.7)	195500 (80000-343000)
Pacific Islands			
American Samoa	NK	NK	NK
Fed. States of Micronesia	NK	NK	NK
Fiji	NK	NK	NK
French Polynesia	NK	NK	NK
Guam	NK	NK	NK
Kiribati	NK	NK	NK
Marshall Islands	NK	NK	NK
Nauru	NK	NK	NK
New Caledonia	NK	NK	NK
Palau	NK	NK	NK
Papua New Guinea	NK	NK	NK
Samoa	NK	0.0^	NE
Solomon Islands	NK	0.0^	NE
Tonga	NK	0.0^	NE
Vanuatu	NK	NK	NK
Australasia			
Australia	0.60 (0.43-0.76)	1.3 (1.0-1.6)	1000 (1000-1500)
New Zealand	0.73 (0.49-0.97)	0.1 (0.0-0.8)	<500 (0-<500)
Sub Saharan Africa			
Angola	NK	NK	NK
Benin	NK	5.1 (3.2-7.0)	NE
Burkina Faso	NK	NK	NK
Burundi	NK	NK	NK
Cameroon	NK	NK	NK
Cape Verde	NK	NK	NK
Chad	NK	NK	NK
Dem. Rep. Congo	0.01 (<0.01-0.40)	13.3 (7.3-21.6)	500 (0-19000)
Cote d'Ivoire	0.01 (<0.01-0.01)	5.3 (1.1-14.6)	<500 (0-<500)
Djibouti	NK	NK	NK
Ethiopia	NK	NK	NK

	Prevalence of injecting drug use % (95% CI)*	HIV prevalence among PWID % (95% CI)*	Number of current PWID living with HIV (95% UI)
Gabon	NK	NK	NK
Gambia	NK	NK	NK
Ghana	NK	NK	NK
Guinea	NK	NK	NK
Kenya	0.12 (0.03-0.20)	42.0 (21.1-62.8)	13000 (4000-24500)
Liberia	NK	NK	NK
Madagascar	0.12 (0.02-0.59)	4.8 (0.2-9.4)	500 (0-3500)
Malawi	NK	NK	NK
Mali	NK	NK	NK
Mauritius	0.78 (0.39-1.54)	45.5 (42.4-48.6)	3000 (1000-6000)
Mozambique	0.20 (0.00-0.41)	46.3 (41.9-50.7)	13500 (0-29000)
Niger	NK	NK	NK
Nigeria	NK	3.1 (1.8,4.4)	NE
Rwanda	0.03 (0.00-0.07)	NK	NK
Senegal	NK	9.3 (5.0,15.4)	NE
Seychelles	2.30 (1.54-3.43)	3.8 (2.0-6.4)	<500 (<500-<500)
Sierra Leone	0.04 (0.04-0.04)	8.5 (5.4-12.6)	<500 (<500-<500)
Somalia	NK	NK	NK
South Africa	0.21 (0.06-0.74)	14.2 (11.1-17.8)	11000 (0-32000)
Swaziland	NK	NK	NK
Tanzania	1.24 (0.72-1.76)	28.3 (16.3-40.4)	97000 (47000-163000)
Togo	0.06 (0.01-0.49)	NK	NK
Uganda	NK	NK	NK
Zambia	NK	NK	NK
Zimbabwe	NK	NK	NK
Middle East & North Africa			
Algeria	NK	1.1 (0.0-5.7)	NE
Bahrain	NK	4.6 (1.9-9.3)	NE
Cyprus	0.08 (0.04-0.12)	1.2 (0.6-1.7)	<500 (<500-<500)
Egypt	NK	2.6 (0.6-4.5)	NE
Iraq	NK	NK	NK
Israel	NK	0.0 (0.0-<0.1)	NE
Jordan	NK	NK	NK
Kuwait	NK	NK	NK
Lebanon	NK	0.0 (0.0-0.1)	NE
Libya	0.05 *(0.01, 0.10)*	89.6 (85.8-92.7)	2000 (1000-2500)
Morocco	0.13 (0.07-0.20)	9.6 (0.0-20.6)	3000 (500-6500)
Occ. Palestinian Terr.	NK	0.0 (0.0-<0.1)	NE
Oman	NK	11.8 (5.0-18.6)	NE
Qatar	NK	NK	NK
Saudi Arabia	NK	9.8 (7.0-13.2)	NE
Sudan	NK	0.0^	NE
Syrian Arab Rep.	NK	0.0 (0.0-<0.1)	NE
Tunisia	NK	3.5 (2.6-4.4)	NE
Turkey	NK	0.2 (0.1-0.4)	NE
United Arab Emirates	NK	NK	NK
Yemen	NK	NK	NK

Population size estimates are rounded to the nearest 500. Where confidence intervals are presented in italics, the original source provided a point estimate only and uncertainty was estimated using uncertainty around

other estimates from countries in that region. * Data originally published in Degenhardt et al., 2017.[1] ^Confidence intervals unable to be estimated as no sample size was available. CI: confidence interval. UI: uncertainty interval. NE: Injecting drug use has been documented in this country and estimates of HIV prevalence among people who inject drugs were located, but no estimates of IDU prevalence were located. NK: Injecting drug use has been documented in this country, but no estimates of HIV prevalence among people who inject drugs were located. Countries with no reports of injecting drug use identified were excluded from this table, including: Greenland, Liechtenstein (Western Europe), North Korea (East and southeast Asia), Antigua & Barbuda, Barbados, Cuba, Dominica, Grenada, Saint Kitts & Nevis, Saint Lucia, St Vincent & the Grenadines, Trinidad & Tobago (Caribbean), Belize (Latin America), Northern Mariana Islands, Tuvalu (Pacific Islands), Botswana, Central African Republic, Comoros, Equatorial Guinea, Eritrea, Guinea-Bissau, Lesotho, Mauritania, Namibia, Republic of Congo, Sao Tome & Principe (Sub-Saharan Africa), South Sudan (Middle East and North Africa).

Figure 1: Estimated national HIV prevalence among people who inject drugs and number of people who inject drugs living with HIV.



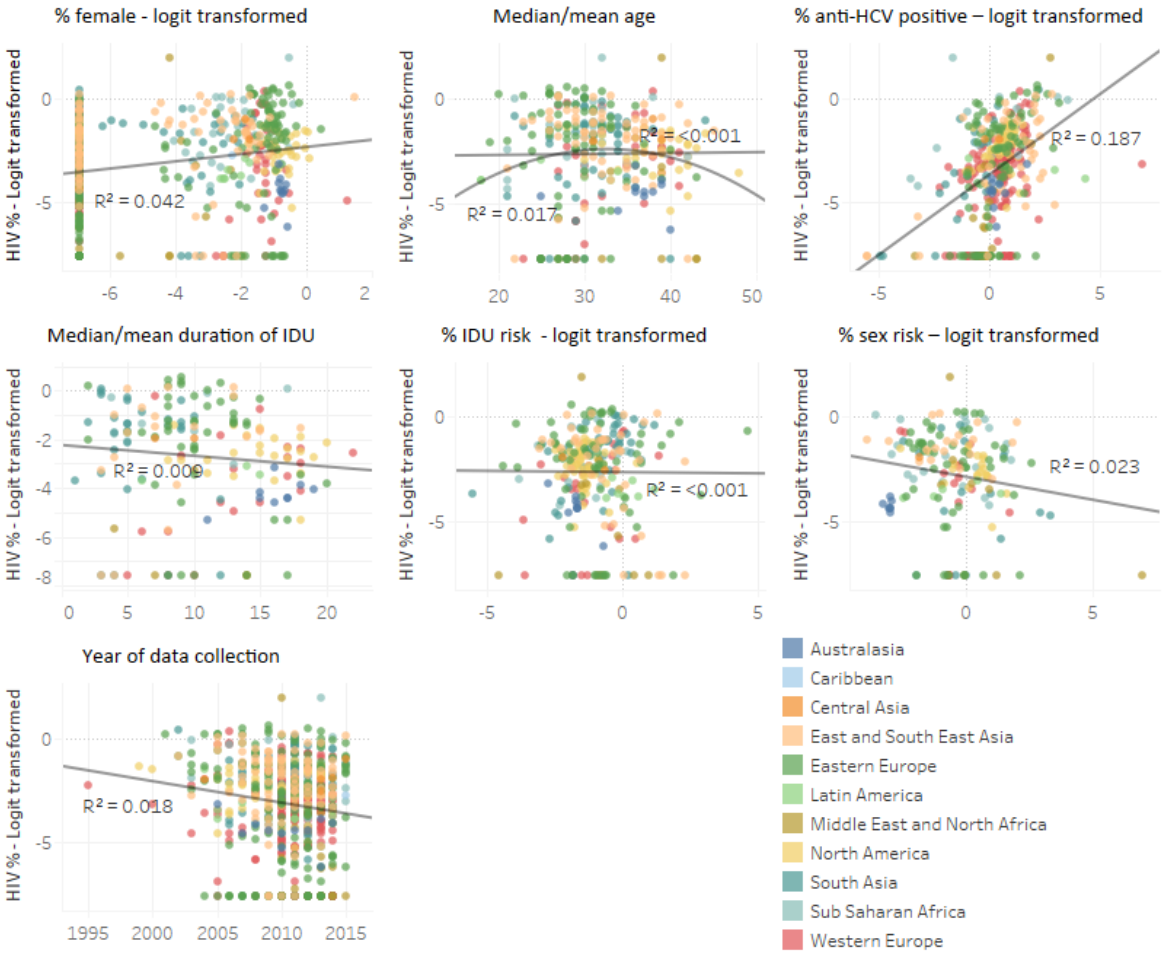
55% of estimated global population of PWID living with HIV

Note: HIV prevalence data and global population of PWID living with HIV originally published in Degenhardt et al.[1]

Table 3: Summary of studies included in analysis of demographic and behavioural factors associated with HIV prevalence in PWID

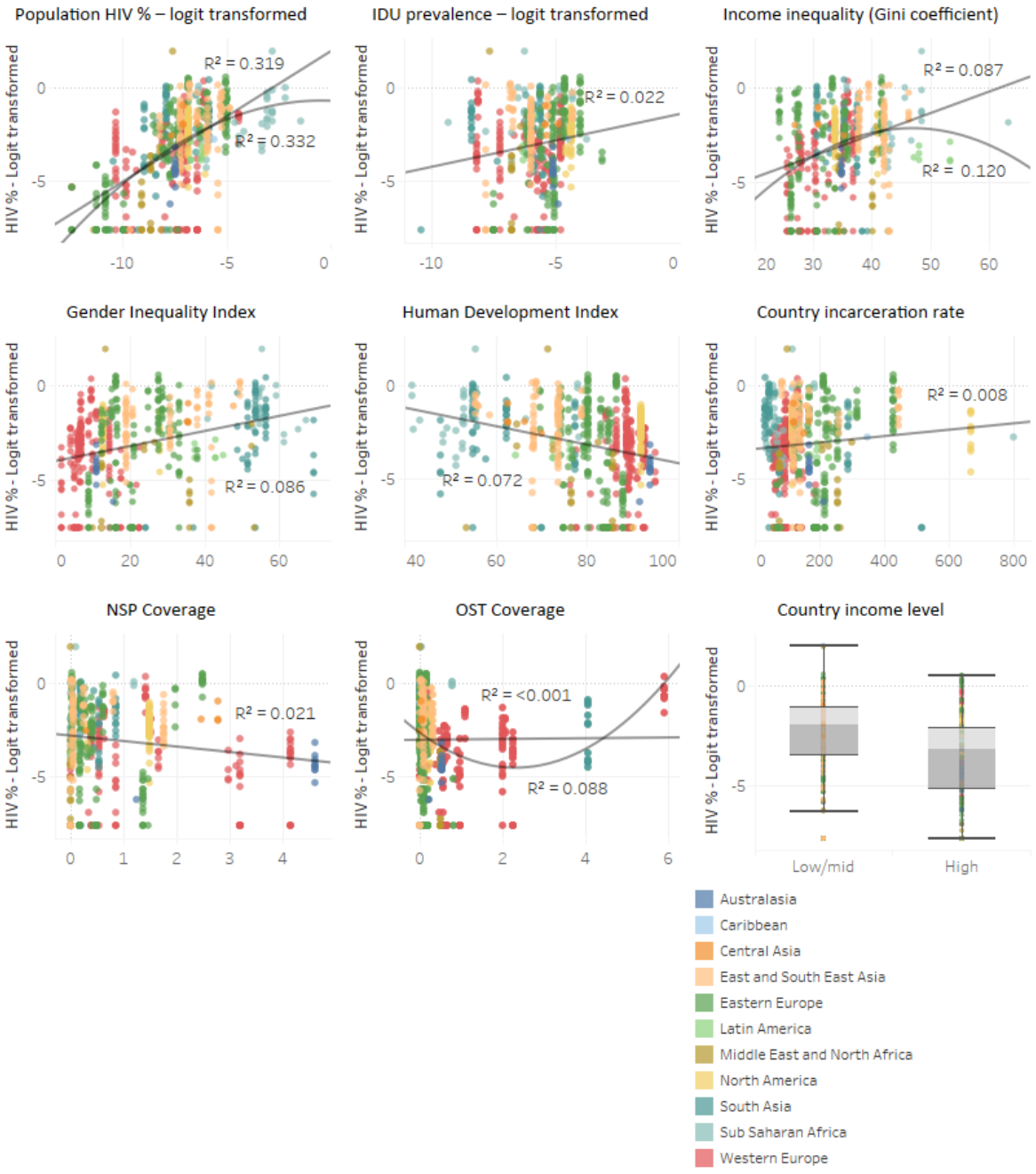
Region	N estimates of HIV prevalence	Estimates from N countries	N participants in included studies	Minimum reported HIV prevalence (%)	Maximum reported HIV prevalence (%)
Eastern Europe	157	18	218479	0.0	64.0
Western Europe	182	20	277401	0.0	58.1
East and Southeast Asia	88	11	65903	0.0	55.0
South Asia	59	8	81043	0.0	59.
Central Asia	5	3	3595	7.3	27.0
Caribbean	1	1	315	6.0	6.0
Latin America	8	4	4167	2.0	18.5
North America	58	2	35814	0.5	25.7
Pacific Islands	0	-	-	-	-
Australasia	11	2	18000	0.2	4.0
Sub-Saharan Africa	30	12	13742	1.4	87.5
Middle East and North Africa	27	9	21481	0.0	87.1
Global	626	93	739940	0.0	87.5

Figure 2: Associations of study-level demographic and behavioural profiles of PWID with HIV prevalence in PWID



Notes: Anti-HCV – hepatitis C antibody. IDU – injecting drug use. Curved lines represent quadratic trends

Figure 3: Associations of environmental variables and HIV prevalence in PWID



Notes: IDU – injecting drug use. NSP – needle and syringe programs. OST – opioid substitution therapy

Table 4: Ecological analysis of study-level and country-level associations with HIV prevalence in PWID

Models of HIV prevalence in current PWID	N*	Unadjusted models				Adjusted for population HIV prevalence			
		β	SE	95% CIs	p	β	SE	95% CIs	p
Study-level exposure variables									
Percentage of sample female	619	0.17	0.07	(0.04,0.31)	.012	0.07	0.06	(-0.06,0.19)	.289
Median/mean age of sample	303	0.00	0.04	(-0.06,0.07)	.899	0.03	0.03	(-0.03,0.08)	.331
Median/mean age of sample in model with quadratic term	303	0.47	0.21	(0.05,0.89)	.027	0.53	0.20	(0.14,0.92)	.007
Quadratic term	--	-0.01	0.00	(-0.01,0.00)	.024	-0.01	0.00	(-0.01,0.00)	.010
Prevalence of anti-HCV+	385	0.77	0.12	(0.54,1.00)	<.001	0.60	0.11	(0.38,0.81)	<.001
Median/mean duration of injecting	167	-0.04	0.05	(-0.14,0.05)	.353	-0.02	0.05	(-0.12,0.09)	.772
Percentage of sample reporting injecting risk behaviours	276	-0.01	0.16	(-0.33,0.30)	.940	-0.04	0.16	(-0.36,0.28)	.817
Percentage of sample reporting sexual risk behaviours	165	-0.23	0.15	(-0.53,0.06)	.122	-0.14	0.11	(-0.36,0.09)	.230
Year of data collection	626	-0.11	0.04	(-0.19,-0.02)	.016	-0.07	0.04	(-0.14,0.01)	.075
Country-level exposure variables									
Population HIV prevalence	626	0.70	0.09	(0.53,0.87)	<.001	--	--	--	--
Population HIV prevalence in model with quadratic term	626	-0.04	0.30	(-0.62,0.54)	.882	--	--	--	--
Quadratic term	--	-0.05	0.02	(-0.09,-0.01)	.022	--	--	--	--
Population IDU prevalence	582	0.28	0.23	(-0.16,0.73)	.216	0.17	0.16	(-0.15,0.49)	.287
Income inequality (Gini Coefficient)	598	0.11	0.04	(0.03,0.19)	.005	0.02	0.03	(-0.05,0.09)	.508
Income inequality in model with quadratic term	598	0.49	0.30	(-0.10,1.08)	.105	0.48	0.14	(0.21,0.74)	<.001
Quadratic term	--	-0.01	0.00	(-0.01,0.00)	.175	-0.01	0.00	(-0.01,0.00)	<.001
Gender Inequality Index	610	0.04	0.01	(0.02,0.06)	<.001	0.02	0.01	(-0.01,0.04)	.127
Human Development Index	621	-0.05	0.02	(-0.08,-0.02)	.002	-0.02	0.02	(-0.05,0.01)	.260
National incarceration rate	624	1.70	1.66	(-1.56,4.96)	.308	0.55	1.19	(-1.77,2.88)	.641
Country income level (Low/middle vs high)	626	1.27	0.47	(0.35,2.19)	.007	0.61	0.40	(-0.18,1.40)	.129
NSP coverage	523	-0.29	0.23	(-0.73,0.16)	.207	-0.28	0.23	(-0.73,0.17)	.227
NSP coverage in model with quadratic term	523	0.44	0.71	(-0.96,1.84)	.539	0.66	0.51	(-0.35,1.66)	.201

Quadratic term	--	-0.20	0.15	(-0.50,0.11)	.205	-0.25	0.11	(-0.46,-0.04)	.017
OST coverage	583	0.02	0.25	(-0.46,0.50)	.935	0.16	0.16	(-0.15,0.47)	.321
OST coverage in model with quadratic term	583	-1.60	0.50	(-2.59,-0.62)	.001	-0.79	0.71	(-2.19,0.61)	.267
Quadratic term	--	0.35	0.09	(0.17,0.52)	<.001	0.20	0.13	(-0.05,0.46)	.120

*Maximum number of data points in each model is 626 (the number of estimates of HIV prevalence among people who inject drugs). SE: standard error. CI: confidence interval. Anti-HCV: hepatitis C virus antibody positive. NSP coverage and OST coverage are in hundreds. Adjusted models for each variable are independent and adjusted for HIV prevalence only.