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Univariable associations between a history of incarceration and HIV and HCV prevalence among people who inject drugs across 17 countries in Europe 2006 to 2020 - is the precautionary principle applicable?

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Background: People who inject drugs (PWID) are frequently incarcerated, which is associated with multiple negative health outcomes. Aim: We aimed to estimate the associations between a history of incarceration and prevalence of HIV and HCV infection among PWID in Europe. Methods: Aggregate data from PWID recruited in drug services (excluding prison services) or elsewhere in the community were reported by 17 of 30 countries (16 per virus) collaborating in a European drug monitoring system (2006–2020; n=52,368 HIV+/-; n=47,268 HCV+/-). Country-specific odds

ratios (OR) and prevalence ratios (PR) were calculated from country totals of HIV and HCV antibody status and self-reported life-time incarceration history, and pooled using meta-analyses. Country-specific and overall population attributable risk (PAR) were estimated using pooled PR. Results: Univariable HIV OR ranged between 0.73 and 6.37 (median: 2.1; pooled OR: 1.92; 95% CI: 1.52-2.42). Pooled PR was 1.66 (95% Cl 1.38-1.98), giving a PAR of 25.8% (95% Cl 16.7–34.0). Univariable anti-HCV OR ranged between 1.06 and 5.04 (median: 2.70; pooled OR: 2.51; 95% CI:

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2.17–2.91). Pooled PR was 1.42 (95% CI: 1.28–1.58) and PAR 16.7% (95% CI: 11.8–21.7). Subgroup analyses showed differences in the OR for HCV by geographical region, with lower estimates in southern Europe. **Conclusion:** In univariable analysis, a history of incarceration was associated with positive HIV and HCV serostatus among PWID in Europe. Applying the precautionary principle would suggest finding alternatives to incarceration of PWID and strengthening health and social services in prison and after release ('throughcare').

Background

People who inject drugs (PWID) are frequently incarcerated, with an estimated 58% of PWID ever incarcerated and prison populations including up to 50% PWID in many countries [1-3]. Incarceration of PWID is associated with higher risks of drug-related problems [4,5] including human immunodeficiency virus (HIV) and hepatitis C virus (HCV) transmission [6-9], fatal overdose [10,11], mental illness and social disruption [5] and poor or no access to care and treatment [12] including for women [13] - as well as unfavourable HIV treatment (anti-retroviral treatment (ART)) outcomes [14-16]. However, prisons may also provide an important opportunity for treatment and care [5,12,14,17,18]. Incarceration is associated with increases in HIV- and HCV-related risk behaviour among PWID both in prison and after release [19-22], and may be a driver of HCV and HIV transmission among PWID [6,7,19,23,24]. Incarceration is associated with self-reported transitions to injecting drug use, sharing of injecting equipment inside prison (because of their scarcity), sharing tattooing and shaving materials, and unprotected sex [19,20,25-27]. Injecting and other risks (e.g. sex work, nonfatal overdose and death) have been found to increase immediately after release from prison [21,28-31]. This may be due to the disruption of protective factors and social conditions (e.g. interruption of OST, unemployment), which could be especially marked in countries with repressive policies and insufficient needle and syringe programmes (NSP), opioid substitution treatment (OST), ART and HCV treatment and other services [23,28,32,33].

While a minority of countries (many of these in Europe) have expanded services such as OST, NSP and ART/HCV treatment in the community, services in prisons are still mostly lacking [34-37]. There is limited access to OST for incarcerated PWID, an almost complete absence of NSP and a lack of options for stimulant users, in prison and/or after release [36,38]. 'Throughcare', the uninterrupted provision of services to an individual from community to prison and back to community after release, is seldom in place [33,39,40].

Law enforcement and incarceration may not be effective in reducing drug use, while resulting in high public health and social costs [41,42]. Abolishing incarceration for use and possession of illicit drugs can result in a major reduction of incarceration episodes and in important health improvements among people who use drugs [6,42-47]. For example, decriminalisation of minor drug offences in Portugal has resulted in important reductions in the number of individuals incarcerated for drug law offences, significant savings in legal system costs, large public health benefits and declines in problem drug use (i.e. a shift from heroin use to cannabis use) [43,46,48,49].

To assess the degree to which a history of incarceration may be associated with a positive HIV and HCV antibody status among PWID in countries in Europe, we used data from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) drug monitoring system. Using the population attributable risk (PAR), we estimated the proportion of HIV and HCV seropositivity among PWID that can be attributed to a history of incarceration if these associations are causal. This gives an estimate of the degree to which HIV and HCV transmission among PWID could potentially have been avoided through decarceration-oriented drug policies.

Methods

Data sources

The EMCDDA monitoring system receives aggregate data on HIV and HCV prevalence in PWID annually from collaborating countries. For the time period reported here (2006 to 2020), this system covered 28 countries of the European Union (EU) plus Turkey and Norway, with 17 of the 30 countries (16 per virus) being able to provide the data required for this analysis. Fifteen countries provided data for both viruses, Belgium only for HIV and Turkey only for HCV (the United Kingdom (UK) provided data for 2006 to 2015, when it was an EU Member State). The data for this analysis include information on HIV and HCV antibody test result and a self-reported history of incarceration, except for all HIV data from Belgium and part of the HIV data from Latvia, which are based on self-reported test status. PWID include ever and recent injectors recruited at drug services (excluding prison services) or elsewhere in the community. For more information on data sources, see the Supplement (primary study characteristics in Tables S1 and S2 and references) and https://www. emcdda.europa.eu/data/stats2021/drid_en.

Aggregate HIV and HCV testing data (not individual case records) were available for analysis as two separate datasets, one for HIV and one for HCV (thus totals tested are different per virus). Each dataset contained only total counts by country (number tested, number and percentage seropositive and -negative for HIV or HCV) broken down by self-reported prison history (ever/never in prison). In addition, we obtained study-level data on recruitment method and setting.

Statistical analyses

Univariable country-level odds ratios (OR), prevalence ratios (PR – analogous to a relative risk [50]) and PAR and their 95% confidence intervals (CI) were calculated

HIV prevalence by self-reported past incarceration among people who inject drugs in 16 European countries, 2006-2020 (n = 52,368)

Country	Year	n	Ever in prison				Never in prison		
				%	Positive	% positive		Positive	% positive
Cyprus	2006-15	888	362	40.8	1	0.3	526	2	0.4
United Kingdom	2006-15	29,061	20,323	69.9	234	1.2	8,738	114	1.3
Austria	2006-15	608	220	36.2	1	0.5	388	2	0.5
Croatia	2007	397	167	42.1	0	0.0	230	0	0.0
Portugal	2010-15	1,901	966	50.8	216	22.4	935	149	15.9
Romania	2015	522	199	38.1	71	35.7	323	80	24.8
Latvia	2007-14	3,047	1,552	50.9	424	27.3	1,495	256	17.1
Estonia	2012-14	1,277	739	57.9	473	64.0	538	256	47.6
France	2011	898	542	60.4	92	17.0	356	30	8.4
Germany	2011-14	2,069	1,672	80.8	91	5.4	397	10	2.5
Sweden	2013-20	8,512	4,326	50.8	154	3.6	4,186	60	1.4
Greece	2006-15	934	164	17.6	11	6.7	770	18	2.3
Poland	2009	181	88	48.6	24	27.3	93	10	10.8
Belgiumª	2008-11	363	210	57.9	12	5.7	153	2	1.3
Lithuania	2012-14	530	420	79.2	54	12.9	110	3	2.7
Hungary	2014-15	1,180	574	48.6	3	0.5	606	0	0.0
Total ^b		52,368	32,524	62.1	1,861	5.7	19,844	992	5.0
Median (unweighted) ^c		916	481	50.8	63	6.2	462	14	2.4

EMCDDA: European Monitoring Centre for Drugs and Drug Addiction; PWID: people who inject drugs.

Countries are listed in the order of increasing odds ratio. For sample characteristics see Supplementary Table S1. Given varying recruitment methods and settings and geographical coverage, the data should not be interpreted as being representative for all PWID in the country, only for the sample studied. Data for Belgium and part of the data for Latvia concern self-reported HIV status. Data for Hungary were not controlled for double counting between the two study years and may include duplicates. Data for Sweden were obtained directly from the Swedish author, not through the EMCDDA monitoring system.

^a In Belgium, data were from the French-speaking community only.

^b Pooled percentages are the weighted average.

^c Unweighted medians are not necessarily consistent with one another as they merely reflect the midpoint of the 16 country values in that column (unlike the pooled data that all describe the same sample of n = 52,368 each median only describes one column with 16 country level values, thus providing an alternative unweighted central value. For the percentages these can be interpreted as if all countries had the same sample size).

between a history of incarceration and HIV and HCV infection. The OR and PR were pooled using random effects meta-analysis (DerSimonian-Laird methodology), with a continuity correction of 0.5 applied where countries contained a zero cell. We evaluated between-study heterogeneity using the I² statistic and the p value for heterogeneity (Cochran's *Q* statistic). The proportion of PWID ever incarcerated was used with the pooled PR to estimate a 'pooled PAR'. We calculated the correlation coefficients between the country-specific OR for HIV and HCV and between the country-specific PAR for HIV and HCV, to assess consistency in the associations between each of these infections and a history of incarceration (Pearson's r, using the CORREL function in MS Excel).

We carried out a sensitivity analysis to examine the extent to which the pooled OR was affected by differences in the prevalence of: (i) history of incarceration, (ii) HIV or (iii) HCV in the PWID population, (iv) recruitment method, (v) recruitment setting, (vi) gross domestic product (GDP) per capita, (vii) national incarceration rate and (viii) region (as defined by the United Nations [51]). We grouped countries as follows: (i) percentage of PWID reporting a history of incarceration: <45% = low, 45-55% = medium and >55% = high, (ii) HIV prevalence: <5% = low, 5-20% = medium and > 20% = high, (iii) HCV prevalence: $\langle 45\% = low, 45-65\% = medium$ and>65%=high, (iv) recruitment method: 'seroprevalence studies' (in which an unbiased estimate of prevalence is attempted) vs 'diagnostic testing' studies (that use test results from routine testing in services), (v) recruitment setting 'exclusively low-threshold services such as NSP, and/or on the street', 'both low-threshold services/street and drug treatment settings' and 'exclusively drug treatment settings', (vi) GDP per capita (World bank data), using the median across all countries in our analysis: < USD 20,000 (the equivalent of EUR 17,478 on 15 November 2021) = low and ≥ USD 20,000 = high, (vii) national incarceration rate [52], using the median across all countries: <107 per 100,000 = low and \geq 107 per 100,000 = high, and (viii) United Nations region: northern Europe, eastern Europe, western Europe and southern Europe (with Cyprus and Turkey classified as southern Europe).

HCV antibody prevalence by self-reported past incarce ration among people who inject drugs in 16 European countries, 2006-2020 (n = 47,268)

Country	Year	n	Ever in prison				Never in prison		
				%	Positive	% positive		Positive	% positive
Portugal	2010-15	1,518	762	50.2	648	85.0	756	637	84.3
Turkey	2008	168	25	14.9	2	8.0	143	7	4.9
Cyprus	2006-15	894	363	40.6	193	53.2	531	206	38.8
United Kingdom	2006-15	28,536	19,914	69.8	10,164	51.0	8,622	2,800	32.5
Poland	2009	180	87	48.3	61	70.1	93	47	50.5
Croatia	2007	397	167	42.1	99	59.3	230	87	37.8
Germany	2011-14	2,071	1,674	80.8	1,131	67.6	397	178	44.8
Austria	2006-15	608	220	36.2	126	57.3	388	129	33.2
Greece	2006-15	583	108	18.5	74	68.5	475	212	44.6
Sweden	2013-20	8,512	4,326	50.8	3,453	79.8	4,186	2,485	59.4
Latvia	2014	383	164	42.8	150	91.5	219	174	79.5
Romania	2015	521	199	38.2	172	86.4	322	223	69.3
France	2011	898	542	60.4	402	74.2	356	176	49.4
Lithuania	2014	200	125	62.5	106	84.8	75	48	64.0
Hungary	2014-15	1,124	548	48.8	356	65.0	576	199	34.5
Estonia	2013-14	675	409	60.6	356	87.0	266	152	57.1
Totalª		47,268	29,633	62.7	17,493	59.0	17,635	7,760	44.0
Median (unweighted) ^b		641	292	48.5	183	69.3	372	177	47.1

EMCDDA: European Monitoring Centre for Drugs and Drug Addiction; PWID: people who inject drugs.

Countries are listed in the order of increasing odds ratio. For sample characteristics see Supplementary Table S2. Given varying recruitment methods and settings and geographical coverage, the data should not be interpreted as being representative for all PWID in the country, only for the sample studied. Data for Hungary were not controlled for double counting between the two study years and may include duplicates. Data for Sweden were obtained directly from the Swedish author, not through the EMCDDA monitoring system.

^a Pooled percentages are the weighted average.

^b Unweighted medians are not necessarily consistent with one another as they merely reflect the midpoint of the 16 country values in that column (unlike the pooled data that all describe the same sample of n = 47,268 each median only describes one column with 16 country level values, thus providing an alternative unweighted central value. For the percentages these can be interpreted as if all countries had the same sample size).

A chi-squared test for heterogeneity across subgroup estimates was performed to test for statistical differences between the groups. Analyses were done in MS Excel (v. 14.5.7) and Stata (StataCorp. 2019. Stata Statistical Software: Release 16. StataCorp LLC, College Station, US).

Results

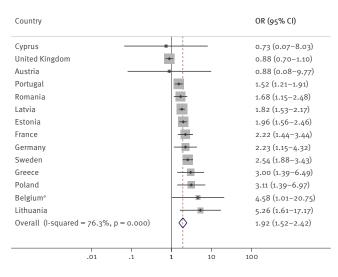
The total number tested for HIV was 52,368 and for HCV 47,268. Sample sizes for HIV were large in most countries, with a median of 916 (interquartile range (IQR): 528–1,943) and a mean of 3,273, although they varied considerably, from 181 PWID tested in Poland to 29,061 in the UK (Table 1 and Supplementary Table S1). Of those tested for HIV, 62.1% (n=32,524) had ever been in prison, of whom 5.7% (95% Cl: 5.5-6.0; n = 1,861) were HIV-positive. Among those ever in prison, HIV prevalence also varied greatly across countries (0-64%), with a pooled average of 5.7% (median: 6.2%; IQR: 1.0–23.6). HIV prevalence among those with no history of incarceration (37.9% of all those tested for HIV; n = 19,844) had a pooled average of 5.0% (95% CI: 4.7-5.3; n = 992), with similarly wide variation across countries (range: 0–48; median: 2.4%; IQR: 1.1–12.0).

For HCV, total sample sizes were somewhat smaller than those reported for HIV (mostly provided by the same studies, see Supplement), with a median of n = 641 (IQR: 393.5-1,222.5) and a mean of 2,954, ranging from 168 PWID tested in Turkey to 28,536 in the UK (Table 2 and Supplementary Table S2). Of those tested for HCV, 62.7% (n=29,633) had ever been in prison, of whom 59.0% (95% Cl: 58.5-59.6; n=17,493) were HCV antibody-positive. The HCV antibody prevalence among those with no history of incarceration (37.3% of all those tested for HCV; n = 17,635) was 44.0% (95%) CI: 43.3–44.7; n=7,760). HCV prevalence among those ever in prison varied greatly across countries (8-92%)with the median at 69.3% (IQR: 58.8–84.9). HCV prevalence among those never in prison also varied widely (5–84%), with a median of 47.1% (IQR: 37.0–60.5).

Levels of self-reported history of incarceration ('ever in prison') also diverged across countries. In the HIV testing dataset, having ever been in prison ranged from 17.6% in Greece to 80.8% in Germany, with a pooled average across countries of 62.1% (unweighted median: 50.8%; IQR: 41.7–58.5). A similar pattern was observed in the HCV testing dataset (ranging from 14.9% in Turkey to 80.8% in Germany) with a pooled

FIGURE 1

Odds ratios of HIV infection among PWID reporting a history of incarceration vs PWID not reporting a history of incarceration in Europe, 2006–2020 (n = 52,368)



Cl: confidence interval; OR: odds ratios; PWID: people who inject drugs.

Data from Belgium and part of the data for Latvia concern selfreported HIV status by the PWID.

^a In Belgium, data were from the French-speaking community only.

average of 62.7% (unweighted median: 48.5%; IQR: 40.0-60.4) (Tables 1 and 2).

Association between HIV or HCV serostatus and history of incarceration

The OR between a positive HIV serostatus and a history of incarceration showed strong and consistent univariable associations in most countries although with important variation across countries (from 0.73 in Cyprus to 6.37 in Hungary – although these extremes were both not statistically significant) and in some cases wide CI. Eleven of the 16 countries with available data showed a positive association that was statistically significant, while none showed a statistically significant negative association (in five countries, the OR was not statistically significant: two above and three below OR = 1.00). The pooled OR across countries showed a statistically significant positive association (OR = 1.92; 95% CI: 1.52-2.42) (Figure 1 and Table 3) with substantial heterogeneity between countries $(I^2 = 76.3\%; p = 0.000).$

The OR for a positive HCV serostatus and a history of incarceration also showed strong and consistent univariable associations in most countries although, similarly to HIV, with wide variation between countries (from 1.06 in Portugal to 5.04 in Estonia – although the estimate for Portugal was not statistically significant) and in some cases wide CI. Fourteen of the 16 countries with available data showed a statistically significant positive association, two showed a non-significant

Population attributable risk of HIV or HCV seropositivity

The estimated PAR of HIV seropositivity, that is the fraction of positive cases attributable to a history of incarceration if the association are causal, varied from 14.4% in Romania to 74.6% in Lithuania, with an overall pooled PAR of 25.8% (95% CI: 16.7–34.0) (Table 3). For HCV, it ranged from 6.0% in Latvia to 30.0% in Hungary, with an overall pooled PAR of 16.7% (95% CI: 11.8–21.7) (Table 4).

The correlation coefficient between the OR for HIV and HCV was low (r=0.3, based on the 15 countries with information on both viruses) as was the correlation coefficient between the PAR for HIV and HCV (r=0.35, based on nine countries with PAR available for both viruses) (not shown in Tables), suggesting differences between the level of HIV and HCV transmission associated with a history of incarceration. In most countries, the OR was higher for HCV than for HIV (10 of 15 countries), while the PAR was mostly lower for HCV than for HIV (eight of nine countries).

Sensitivity analyses

In sensitivity analyses, the OR for HCV differed significantly based on geographical region, with pooled estimates greatest in northern (OR = 2.85; 95% CI: 2.26-3.59), eastern (OR = 3.21; 95% CI: 2.62-3.95) and western Europe (OR = 2.70; 95% CI: 2.31-3.15) and lowest in southern Europe (OR = 1.82; 95% CI: 1.23-2.68) (Table 5). A similar but weaker pattern was found for HIV – with the pooled OR not significantly different. No other statistical differences were detected, owing to low statistical power at country level (for these subanalyses, the sample size is 16 countries per virus).

Discussion

Our findings suggest that past incarceration is associated in univariable analysis with a positive HIV and HCV serostatus among PWID in Europe. We estimate that the PAR, i.e. the percentage of infections attributable to a history of incarceration if these associations are causal, would be around one in four infections (25.8%) for HIV and one in six (16.7%) for HCV.

The country-specific PAR ranged from 14.4% in Romania to 74.6% in Lithuania for HIV and from 6.0% in Latvia to 30.0% in Hungary for HCV. This seems to align well with other epidemiological evidence. In Lithuania, a large HIV outbreak in prisons has occurred [53], and new HIV diagnoses in prisons were increasing until 2017 [54]. In Estonia (with a PAR for HCV of 24.0%) high prevalence of HCV and HIV were found in prisons,

Associations between HIV prevalence and self-reported past incarceration among people who inject drugs in 16 European countries, 2006-2020 (n = 52,368)

Country	Year	OR	95% CI	PR	95% CI	PAR (%)	95% CI
Cyprus	2006-15	0.73ª	0.07-8.03	0.73ª	0.07-7.98		NA ^a
United Kingdom	2006-15	0.88ª	0.70-1.10	0.88ª	0.71-1.10		NAª
Austria	2006-15	0.88ª	0.08-9.77	0.88ª	0.08-9.67		NAª
Croatia	2007	(1.38) ^a	(0.03-69.9)	NA ^a		NAª	
Portugal	2010-15	1.52	1.21-1.91	1.40	1.16-1.69	16.9	7.52-26.0
Romania	2015	1.68	1.15-2.48	1.44	1.10-1.88	14.4	3.67-25.1
Latvia	2007-14	1.82	1.53-2.17	1.60	1.39-1.83	23.4	16.6-29.7
Estonia	2012-14	1.96	1.56-2.46	1.35	1.21-1.49	16.8	10.8-22.1
France	2011	2.22	1.44-3.44	2.01	1.36-2.97	37.9	17.8-54.3
Germany	2011-14	2.23	1.15-4.32	2.16	1.14-4.11	48.4	10.2-71.5
Sweden	2013-20	2.54	1.88-3.43	2.48	1.85-3.34	42.9	30.2-54.3
Greece	2006-15	3.00	1.39-6.49	2.87	1.38-5.96	24.7	6.26-46.6
Poland	2009	3.11	1.39-6.97	2.54	1.29-4.99	42.8	12.4-66.0
Belgium ^₅	2008-11	4.58	1.01-20.8	4.37ª	0.99-19.3		NAª
Lithuania	2012-14	5.26	1.61-17.2	4.71	1.50-14.8	74.6	28.4-91.6
Hungary 2014–15		(6.37)ª	(0.32–127)	NAª		NAª	
Total (pooled) ^c		1.92	1.52-2.42	1.66	1.38-1.98	25.8	16.7-34.0
Median (unweighted)		2.09	NA	1.81	NA	37.9	NA

CI: confidence interval; EMCDDA: European Monitoring Centre for Drugs and Drug Addiction; NA: not applicable; OR: odds ratio; PAR: population attributable risk; PR: prevalence ratio (necessary to calculate PAR); PWID: people who inject drugs.

^a Not statistically significant (two-sided p>0.05). NA: Country-specific PAR was not calculated where PR was not statistically significant or NA. Country-specific OR shown in brackets, PR not calculated and countries excluded from the pooled totals where OR was estimated with adjustment for an empty cell (Croatia, Hungary).

^b In Belgium, data were from the French-speaking community only.

^c OR and PR pooled using random effects meta-analysis to account for heterogeneity between countries, excluding Croatia and Hungary. Data for Belgium and part of the data for Latvia concern self-reported HIV status. Data for Hungary were not controlled for double counting between the two study years and may include duplicates. Data for Sweden were obtained directly from the Swedish author, not through the EMCDDA monitoring system.

Countries are listed in order of increasing odds ratio. For sample characteristics see Supplementary Table S1. Given varying recruitment methods and settings and geographical coverage, the data should not be interpreted as being representative for all PWID in the country, only for the sample studied.

and very low HCV treatment rates, with HCV seropositivity strongly associated with a history of drug use, HIV co-infection, previous incarceration and increasing age [55]. Conversely, the weak association for HIV in Romania (with the lowest PAR at 14.4%), may reflect high transmission unrelated to incarceration, possibly a consequence of a recent HIV outbreak among PWID in the community and high heterosexual transmission in the general population following an earlier large nosocomial HIV outbreak [56]. Portugal showed one of the weakest associations for HIV (and one of the lowest PAR at 16.9%), and no association for HCV, more than a decade after decriminalising minor drug offences (in 2001) and introducing widespread harm reduction measures (since around 1996). Similarly, the UK, which historically has had strong harm reduction policies (although more recently it has lagged behind some other European countries e.g. in introduction of drug consumption rooms), showed no association for HIV and one of the weakest for HCV. However, it should be noted that the data we used were from England and Wales, where HIV prevalence is very low, whereas a very strong association between HIV and a history of incarceration has been found during a recent HIV

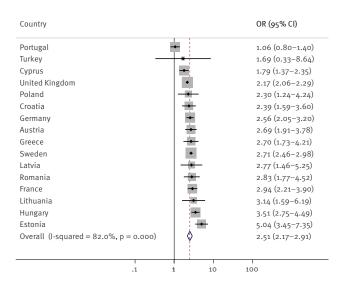
outbreak among PWID in Scotland [57]. By contrast, Sweden, a country with a traditionally more repressive drug policy and low levels of harm reduction (although with a major increase in NSP and OST in the last decade), showed strong associations both for HIV and HCV.

The strength of most of the (positive) associations we found between a history of incarceration and a positive HIV or HCV serostatus, and the fact that we observed these associations across a large number of countries, should strengthen confidence in our results. Moreover, no country showed a statistically significant negative association, and the associations were seen across studies using different recruitment methods and for two blood-borne viruses.

However, our study has important limitations. Notably, using aggregate data, we were unable to adjust for potential individual-level confounders such as the number of years injecting or age, which have been shown to be strongly related to HIV and HCV infection as well as a history of incarceration, thus potentially resulting in overestimated or even spurious associations [58]. Further, we do not have information on

FIGURE 2

Odds ratio of HCV antibodies among PWID reporting a history of incarceration vs PWID not reporting a history of incarceration in Europe, 2006-2020 (n = 47,268)



CI: confidence interval; OR: odds ratios; PWID: people who inject drugs.

when infection occurred, before, during or after incarceration, and we are unable to analyse the effects of the number of times incarcerated or total time spent in prison. Therefore, our findings remain inconclusive, and need to be interpreted in the context of a wealth of similar findings from other studies [7,33,57,59-69].

Individual level variables may play a further role in the causal pathway between incarceration and HIV/ HCV infection, such as having ever shared needles/ syringes or number of lifetime sexual partners (e.g. through sex work because of temporary homelessness) or tattooing, and structural variables including national drug policies (existence of sustainable harm reduction policy, access to ART and HCV treatment for PWID, law enforcement regarding drug use etc). Therefore, multivariate adjustment for injecting risks such as injecting frequency and sharing needles/syringes may also result in biased findings, such as underestimating or obscuring a true association between a history of incarceration and HIV/HCV prevalence, if these injecting risks are part of the causal pathway [19-22,33]. Moreover, although different confounders and effect modifiers (e.g. national drug and incarceration policies) are likely to result in different effect sizes in different countries and studies (as we find in our data), the general consistency in our results and with other studies makes it seem unlikely that the causal mechanism for these associations would be fundamentally different, i.e. driven by different factors, between countries and studies. This provides further support for our findings, despite their limitations, and with special relevance for the countries here studied.

We are less confident about some of the lowest levels of incarceration history among PWID in our data and suspect it may have been under-reported in some countries (possibly because it is highly stigmatised), especially where these seem inconsistent with overall population incarceration rates [70]. However, misclassification of incarceration history because of underreporting would lead to underestimating the strength of the associations with HIV or HCV, the PR and PAR, thus strengthening the validity of our findings. Some of our data are not recent (since 2006) or based on only one calendar year, while since 2007, there has been much effort with respect to bringing down incidences of HCV and HIV and there have been downward trends in the general population and among PWID. However, reductions in prevalence would not necessarily affect the associations here reported, while in one country, we were able to verify that the strong associations in a recent (2013–2020) and large dataset here reported already existed in a smaller independent dataset from 2007 (not shown).

PWID reported life-time prison experience, thus our findings may relate to incarcerations that took place well before the study years. However, we have little indication that incarceration polices for PWID (and services in prisons) have substantially changed across most countries, with the few exceptions here discussed (e.g. Portugal decriminalised in 2001, so that effects of that change should be reflected in our data). Data collection methods and sample representativity varied across countries and findings can probably not be generalised to all PWID at the national level, however, our findings are consistent despite this limitation. Finally, our analysis is cross-sectional so that we are unable to establish the direction (temporality) of potential causality, and while it may be more likely that incarceration leads to HIV and HCV infections rather than the other way round, it is possible that high-risk PWID may be more likely to get incarcerated and to acquire HIV or HCV, thus potentially resulting in selection bias and confounding [71].

Given their consistency across countries and with other studies, our findings may have implications for health and drug policies regarding incarceration of PWID and HIV and HCV infection, even without considering other outcomes such as overdose and mortality. They add further evidence for strengthening service provision throughout incarceration and on release ('throughcare') and for considering alternatives to incarceration such as decarceration and decriminalisation (depenalisation, police diversion) policies, which have already been successfully introduced [43,48,49,72,73]. The COVID-19 pandemic has provided additional urgency to reducing the potential negative public health impact resulting from incarcerating people who use drugs, and decarceration has already been applied as a precaution to limit the spread of COVID-19 [74-76].

Associations between HCV antibody prevalence and self-reported past incarceration among people who inject drugs in 16 European countries, 2006-2020 (n = 47,268)

Country	Year	OR	95% CI	PR	95% CI	PAR (%)	95% CI
Portugal	2010-15	1.06ª	0.80-1.40	1.01	0.97-1.05		NA ^a
Turkey	2008	1.69ª	0.33-8.64	1.63	0.36-7.42		NA ^a
Cyprus	2006-15	1.79	1.37-2.35	1.37	1.19-1.58	13.1	7.16-19.1
United Kingdom	2006-15	2.17	2.06-2.29	1.57	1.52–1.61	28.5	26.6-29.9
Poland	2009	2.30	1.24-4.24	1.39	1.09-1.77	15.9	4.17-27.1
Croatia	2007	2.39	1.59-3.60	1.57	1.27-1.93	19.3	10.2-28.1
Germany	2011-14	2.56	2.05-3.20	1.51	1.34–1.69	29.2	21.6-35.8
Austria	2006-15	2.69	1.91-3.78	1.72	1.44-2.07	20.7	13.7-27.9
Greece	2006-15	2.70	1.73-4.21	1.54	1.31–1.81	9.09	5.43-13.0
Sweden	2013-20	2.71	2.46-2.98	1.34	1.31–1.38	14.9	13.6-16.2
Latvia	2014	2.77	1.46-5.25	1.15	1.06-1.25	6.04	2.50-9.67
Romania	2015	2.83	1.77-4.52	1.25	1.14-1.37	8.72	5.08-12.4
France	2011	2.94	2.21-3.90	1.50	1.34–1.69	23.2	17.0-29.4
Lithuania	2014	3.14	1.59-6.19	1.33	1.10-1.59	17.1	5.88-26.9
Hungary	2014-15	3.51	2.75-4.49	1.88	1.65-2.14	30.0	24.1-35.7
Estonia	2013-14	5.04	3.45-7.35	1.52	1.36-1.70	24.0	17.9-29.8
Total (pooled) ^b		2.51	2.17-2.91	1.42	1.28–1.58	16.7	11.8-21.7
Median (unweighted)		2.70	NA	1.51	NA	18.2	NA

CI: confidence interval; EMCDDA: European Monitoring Centre for Drugs and Drug Addiction; NA: not applicable; OR: odds ratio; PAR: population attributable risk; PR: prevalence ratio (necessary to calculate PAR); PWID: people who inject drugs.

^a Not statistically significant (two-sided p>0.05). NA: Country-specific PAR was not calculated where PR was not statistically significant.

^b OR and PR pooled using random effects meta-analysis to account for heterogeneity between countries. Data for Hungary were not controlled for double counting between the two study years and may include duplicates. Data for Sweden were obtained directly from the Swedish author, not through the EMCDDA monitoring system.

Countries are listed in order of increasing odds ratio. For sample characteristics see Supplementary Table S2. Given varying recruitment methods and settings and geographical coverage, the data should not be interpreted as being representative for all PWID in the country, only for the sample studied.

Despite the limitations with respect to analyses performed and the data available, the precautionary principle states that in a situation of incomplete evidence, it is important to weigh potential costs of inaction (here: continued infections and other harms that are potentially due to incarceration) against costs of action (here: the costs of strengthening services and/or introducing alternatives to incarceration) [77,78]. Thus, (i) if the precautionary principle is applicable to this policy area and (ii) given the potential on-going health costs if our findings and similar findings from other studies do reflect true associations through a common causal process, it would be important to review public health harms among PWID related to incarceration policies even before final conclusive evidence may become available. This would need to address mechanisms to avoid the incarceration of PWID, as well as strengthening services in prisons and after release [43]. If our findings are not confirmed in future work, the established benefits of such service provision and alternatives to incarceration on the health and well-being of PWID, and their cost-effectiveness, are still likely to result in important health improvements among PWID [43,79].

Conclusion

A history of incarceration was found in univariable analysis to be associated with an increased risk of HIV and HCV seropositivity among community-recruited PWID in Europe. Owing to study limitations these findings should be interpreted with caution. However, our findings are in agreement with other evidence and suggest a need for further in-depth studies. If the precautionary principle is applied, they already suggest a need for reviewing incarceration policies affecting PWID and strengthening health services for PWID, both in prison and after release ('throughcare').

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Conflict of interest

MK has received honoraria for lectures/consultancy from AbbVie, Gilead, MSD, Mundipharma, DnE Pharma and Nordic Drugs and has received research grants from Gilead and Nordic Drugs.

Authors' contributions

Pooled odds ratios from sensitivity analyses, by study characteristics, HIV (n = 51,627 tests^a) and HCV (n = 47,268 tests) among people who inject drugs related to past incarceration, 16 European countries, 2006–2020

	HIV				HCV		
	OR	95% CI	p value for difference	OR	95% CI	p value for differenc	
HIV/HCV prevalence							
Low (< 5%)	1.89	1.02-3.49		2.13	1.54-2.96		
Medium (5–20%)	2.22	1.49-3.31	0.743	2.62	2.20-3.12	0.513	
High (>20%)	1.85	1.62-2.10		2.61	1.69-4.05		
Incarceration prevalence							
Low (<45%)	1.83	1.30-2.56		2.31	1.98-2.71		
Medium (45–55%)	1.96	1.53-2.50	0.933	2.2	1.37-3.55	0.386	
High (>55%)	2.02	1.22-3.33		2.91	2.21-3.82		
Recruitment method							
Seroprevalence studies	1.86	1.37-2.53	- (-(2.86	2.36-3.46	a a 9 /	
Diagnostic studies	2.09	1.42-3.08	0.656	2.04	1.42-2.92	0.084	
Recruitment setting ^b							
Exclusively in LTS	2.04	1.75-2.39		2.89	2.45-3.41		
LTS and DTS	1.37	0.55-3.40	0.635	2.69	2.05-3.52	0.143	
Exclusively in DTS	1.86	1.19-2.93		1.9	1.22-2.94		
GDP per capita ^c							
Low (<usd 20,000)<="" td=""><td>2.09</td><td>1.58-2.75</td><td>0.442</td><td>2.96</td><td>2.52-3.47</td><td>0.077</td></usd>	2.09	1.58-2.75	0.442	2.96	2.52-3.47	0.077	
High (>USD 20,000)	1.76	1.26-2.47	0.442	2.37	1.96-2.86	0.077	
National incarceration rate							
Low (<107/100,000)	2.19	1.80-2.66	0.208	2.55	2.26-3.59	0.094	
High (≥107/100,000)	1.81	1.32-2.50	0.308	2.54	1.87-3.45	0.981	
Region							
Eastern Europe	2.06	1.17-3.62		3.21	2.62-3.95		
Northern Europe	2.09	1.70-2.58	0.011	2.85	2.26-3.59	0.044	
Southern Europe	1.79	1.06-3.00	0.911	1.82	1.23-2.68	0.044	
Western Europe	1.73	0.90-3.33		2.70	2.31-3.15		

CI: confidence interval; DTS: drug treatment services/settings; GDP: gross domestic product; HCV: hepatitis C virus; LTS: low threshold setting; OR: odds ratio.

^a Croatia and Hungary were excluded from the HIV analysis for consistency with Table 3 (instability of the OR due to zero /low number of HIV cases), therefore HIV sample size was reduced by n = 741.

 $^{\rm b}$ LTS such as needle and syringe programmes, street recruitment.

^c World Bank data, approximate value is EUR 17,478 using conversion rate per 15 November 2021.

p value for chi-squared test for heterogeneity between sub-groups.

LW: conceptualisation, methodology. LW, EK, BG, TS: development and coordination EU data collection system, data acquisition and management. LW, JS, PV, AU, BG, EK: statistical analysis and interpretation. LW: writing - original draft preparation and revisions. AF, AKU, AT, BK, IH, IY, JG, LJ, LL, LS, LVB, MJR, MK, MR, PA, RZ, VH: national and sub-national studies/data collection. LW, AF, AK, AKU, AT, AU, BG, BK, DJG, EK, IH, IY, JG, JS, KD, LJ, LL, LM, LS, LVB, MF, MJR, MK, MR, PA, PV, RZ, TS, VH, VS: interpretation of results, reviewing draft versions and approval of final version.

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