A GLOBAL SYSTEMATIC REVIEW AND META-ANALYSIS OF THE INCIDENCE OF HIV AND HEPATITIS C VIRUS (HCV) AMONG PEOPLE WHO INJECT DRUGS, AND ASSOCIATIONS WITH AGE AND GENDER

Adelina Artenie[1,2], Jack Stone[1,2], Hannah Fraser[1,2], Chiedozie Arum[1,2], Aaron G Lim[1,2], Anna McNaughton[1,2], Daniel Stewart[3], Adam Trickey[1,2], Zoe Ward[1,2], Malvina Aladashvili[4], Michel Alary[5,6], Jacquie Astemborski[7], Tasnim Azim[8], Julie Bruneau[9,10], Kora DeBeck[11,12], Steven J Clipman[7], Carla S Coffin[13], Sara Croxford[14], Paul Dietze[15], Kostyantyn Dumchev[16], Jennifer R Havens[17], Kanna Hayashi[18], Margaret Hellard[15], Matthew Hickman[1,2], Jennifer Iversen[19], Ali Judd[20], Martin Kåberg[21,22], Anne Kurth[23], Gisela Macphail[13,24], Lisa Maher[19], Allison M. McFall[7], Shruti Mehta[7], Viktor Mravčík[25], Norah E Palmateer[26,27], Maria Prins[28,29], Rachel Sacks-Davis[15], Sunil S Solomon[7,30], Steffanie A Strathdee[31], Vana Sypsa[32], Catherine S Todd[33], Wijnand Van Den Boom[15], Daniela K van Santen[15,28], Jorge Valencia[34], Josephine G Walker[1,2], Ernst Wisse[35], Peter Vickerman[1,2]

[1]Population Health Sciences, University of Bristol, Bristol, UK; [2]National Institute for Health Research Health Protection Research Unit in Behavioural Science and Evaluation, University of Bristol, Bristol, UK; [3]UK Health Security Agency, London, UK; [4]Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia; [5]Centre de recherche du CHU de Québec, Québec City, QC, Canada; [6]Département de médecine sociale et préventive, Université Laval, Québec City, QC, Canada; [7]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, US; [8]BRAC University, Dhaka, Bangladesh; [9]Département de Médecine Familiale et Médecine d'Urgence, Université de Montréal, Montréal, QC, Canada; [10]Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; [11]School of Public Health, Simon Fraser University, Burnaby, BC, Canada; [12]BC Centre on Substance Use, Vancouver, BC, Canada; [13]Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; [14]Public Health and Clinical Directorate, UK Health Security Agency, London, UK; [15]Burnet Institute, Melbourne, Australia; [16]Ukrainian Institute on Public Health Policy, Kyiv, Ukraine; [17]Department of Behavioral Science, University of Kentucky College of Medicine, Lexington, KY, US; [18]Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada; [19]Kirby Institute for Infection and Immunity, UNSW Sydney, NSW, Australia; [20]MRC Clinical Trials Unit at UCL, London, UK; [21]Stockholm Needle Exchange, Stockholm Centre for Dependency Disorders, Stockholm, Sweden; [22]Department of Medicine Huddinge, Karolinska Institute, Karolinska University Hospital Huddinge, Stockholm, Sweden; [23]Yale School of Nursing, Orange, CT, US; [24]Infectious Diseases, CUPS Liver Clinic, Calgary, AB, Canada; [25]Society Podané ruce, Brno, Czech Republic; [26]School of Health & Life Sciences, Glasgow Caledonian University, Glasgow, Scotland; [27]Public Health Scotland, Glasgow, Scotland; [28]Department of Infectious Diseases, Public Health Service of Amsterdam, Amsterdam, Netherlands; [29]Division of Infectious Diseases, Amsterdam Infection and Immunity Institute, Amsterdam University, Amsterdam, Netherlands; [30]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, US; [31]School of Medicine, University of California, San Diego, CA, US; [32]Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [33]PROMISE Zambia, Durham, NC, US; [34]Harm Reduction Unit "SMASD", Department of Addictions and Mental Health, Madrid, Spain; [35]Medécins du Monde France, Paris, France

CONTEXT

- People who inject drugs are one of the populations most affected by HIV and HCV infection[1,2]
- International public health agencies have called for the elimination/end of these epidemics as public health problems by 2030[1,2]
- Incident HIV/HCV infection can be a difficult metric to measurex[3,4], yet **it is key to monitoring the course of the epidemic, to informing the need for interventions and to tracking the elimination goals**
- **Aim:** to systematically review and synthesize global data on HIV and HCV incidence among people who inject drugs
  - Explore differences in HIV and HCV incidence, with a focus on **geographic location, calendar time and basic demographic characteristics of the participants (age and sex or gender)**

METHODS

Search strategy and selection criteria: systematic literature search[5,6] of MEDLINE, Embase, and PsycINFO for studies published between Jan 1, 2000 and Dec 19, 2021

Population: people with a history of injection drug use

Measures: HIV or HCV incident infection assessed either through repeat follow-up of people susceptible to infection, or through tests of recent infection

Data extraction

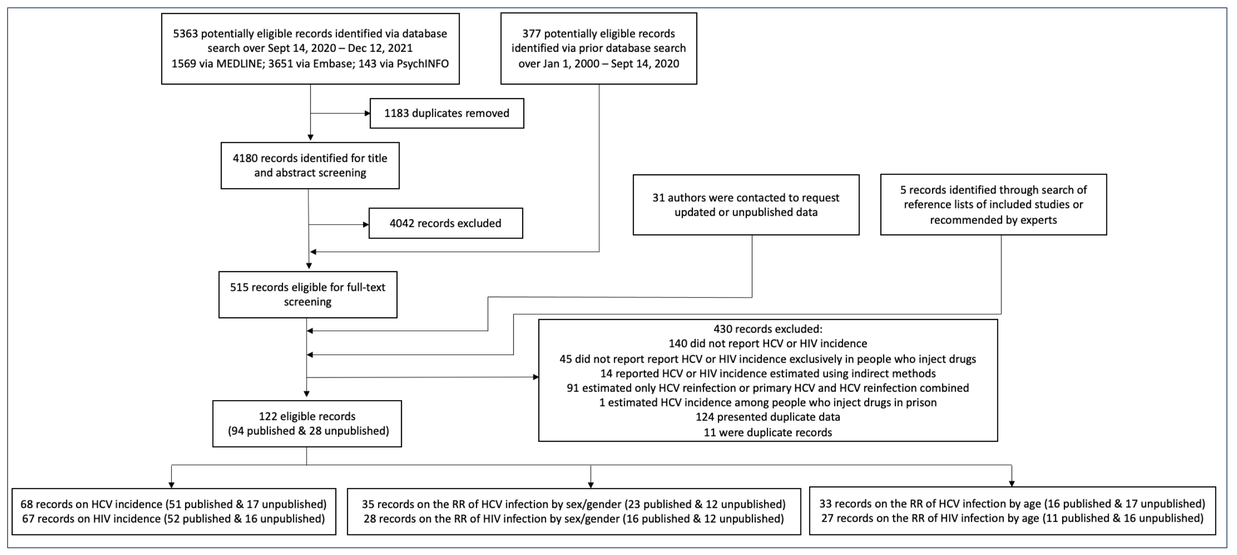
- HIV/HCV incidence overall (recent and non-recent, where available[††]) and stratified by gender and age
- Study characteristics (e.g., inclusion/exclusion criteria, recruitment scheme, method of incidence estimation, testing schedule, follow-up duration)
- Participant characteristics (e.g., mean age/duration of injection, % women, % on OST, background HIV/HCV prevalence)

Data analysis (pre-specified: PROSPERO 2020 CRD42020220884)

- Random-effects meta-analysis and meta-regression to synthesise:
  - Incidence rates of HIV and HCV
  - Relative risk (RR)[†] of HIV and HCV acquisition among younger vs older PWID
  - RR[†] of HIV and HCV acquisition among women vs men who inject drugs
- Multi—level meta-regression[††] to explore temporal and geographic trends in HIV and HCV incidence

[††]Incidence trend data from the same study were included where available

Figure 1: Study Selection



RESULTS

Figure 2: Forest plot of HIV incidence rate, by WHO region

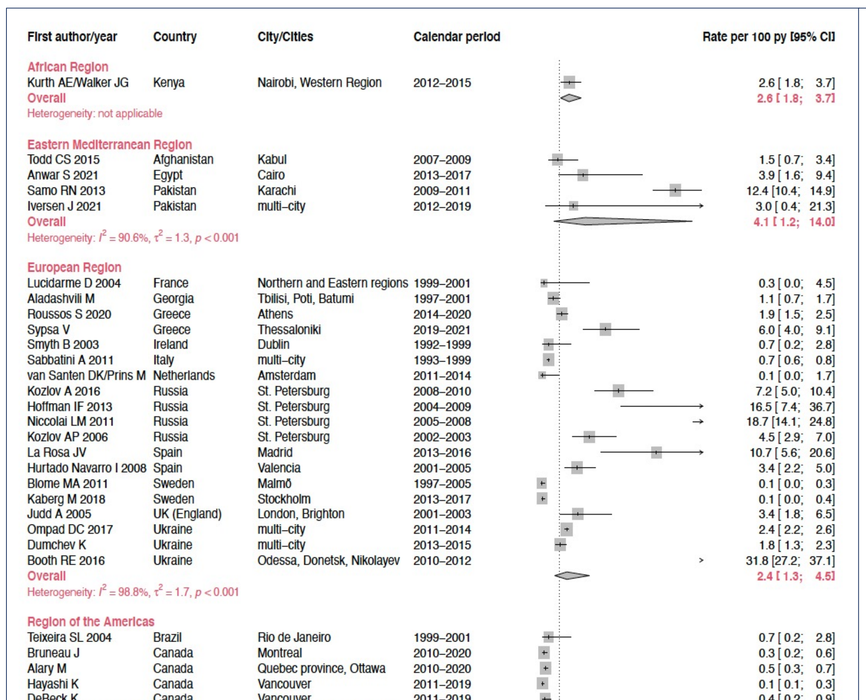


Figure 3: Forest plot of HCV incidence rate, by WHO region

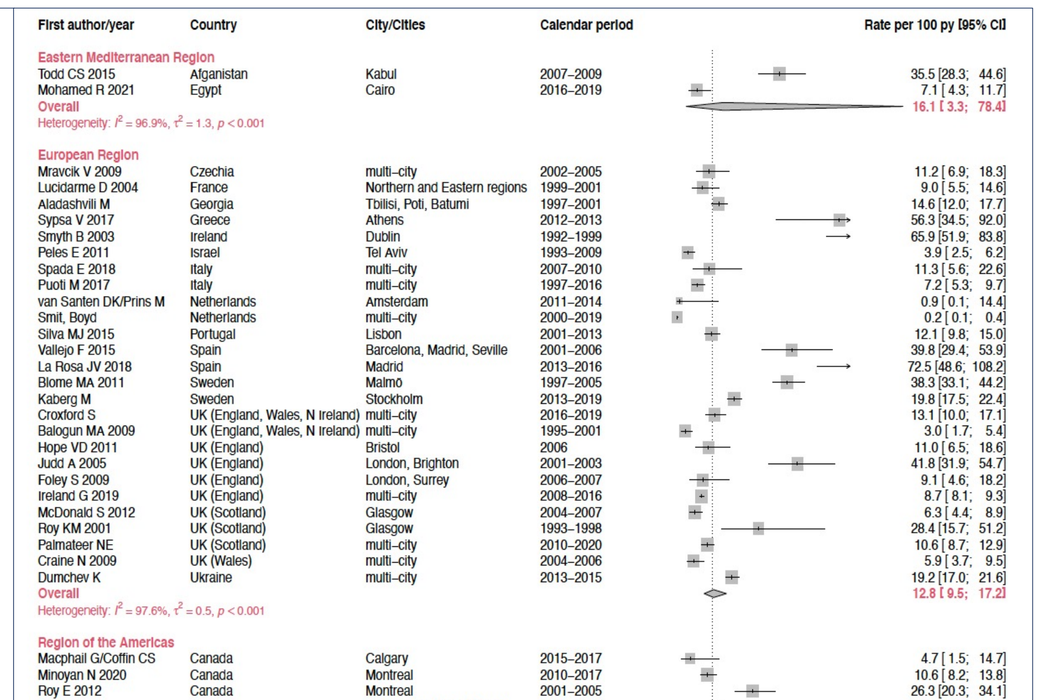
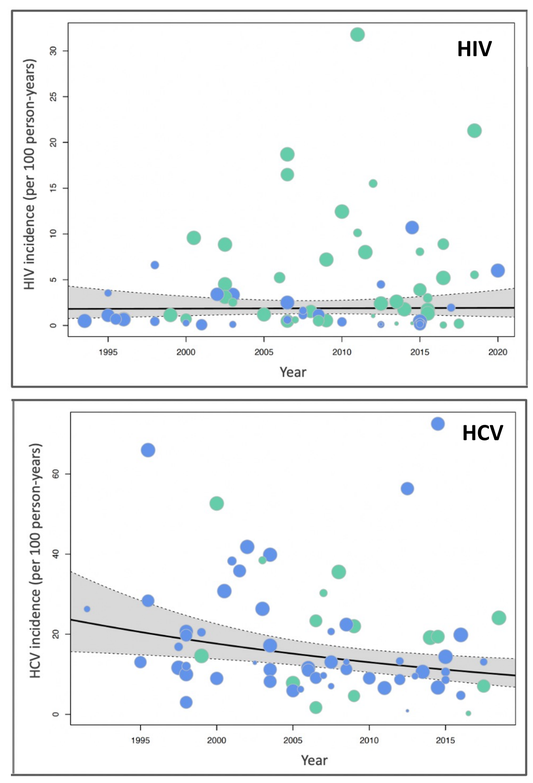


Figure 4: Temporal and geographic trends in HIV and HCV incidence



Blue: high-income countries; Green: low- and middle-income countries

Variable	Category	Adjusted incidence rate ratio*	
		HIV[†]	HCV[††]
Year**	1-year increase	0.97 (0.92 – 1.03)	0.96 (0.94 – 0.99)
World Bank Income classification	High income	Ref	Ref
	Low or middle income	3.41 (1.49 - 7.80)	0.96 (0.55 – 1.68)

**Based on multivariable multi-level meta-regression*
***Defined as the midpoint of the time period over which incidence was estimated; if follow-up was >10 years, the estimate was excluded from the model*
[†] Based on 70 estimates and 58 unique studies
[††]Based on 67 estimates and 57 unique studies

Table 1: Pooled HIV and HCV incidence, stratified by key metrics

Variable		No. of estimates	HIV incidence (/100py; 95% CI)	I² (%)
World Bank Income classification	High income	28	0.8 (0.6 - 1.2)	94.1
	Low or middle income	34	3.1 (2.1 - 4.4)	98.5
≥80% of participants reported injecting within the past year	Yes	45	1.5 (1.0 - 2.3)	98.5
	No	7	1.1 (0.4 - 2.8)	96.5
	Not available	10	2.8 (1.7 - 4.4)	97.5
Recruitment venues	Community	23	1.1 (0.7 - 1.8)	97.8
	Medical	13	1.6 (0.9 - 2.8)	96.4
	Network	12	4.0 (2.1 - 7.9)	98.7
	Mix	14	1.7 (0.9 - 3.2)	97.2
Risk of bias score[†]	Low	28	1.5 (0.9 - 2.4)	98.3
	Moderate-to-high	34	1.8 (1.2 – 2.8)	98.6
Study start year	≥2010	27	1.9 (1.2-2.9)	98.7
	<2010	35	1.6 (1.0 2-.4)	97.7

Variable		No. of estimates	HCV incidence (/100py; 95% CI)	I² (%)
World Bank Income classification	High income	52	12.1 (9.7–15.1)	97.4
	Low or middle income	14	14.2 (10.1-20.1)	94.7
≥80% of participants reported injecting within the past year	Yes	46	15.0 (11.9 - 18.9)	97.1
	No	6	10.0 (8.2 - 12.1)	45.5
	Not available	14	7.7 (5.5 - 10.9)	95.8
Recruitment venues	Community	22	16.6 (13.0 - 21.3)	95.2
	Medical	15	7.6 (5.1 - 11.4)	96.5
	Network	8	17.3 (12.8 - 23.3)	88.5
	Mix	21	11.6 (7.5 - 18.0)	97.7
Risk of bias score[†]	Low	27	10.5 (7.3 - 15.1)	97.0
	Moderate-to-high	39	13.9 (11.1 - 17.4)	96.1
Study start year	≥2010	18	13.7 (10.7 – 15.7)	94.7
	<2010	48	12.2 (9.5 – 15.7)	97.7

Table 2: Pooled relative risks comparing HIV and HCV acquisition in women who inject drugs vs men who inject drugs and young PWID vs older PWID

	HIV		HCV	
	Pooled relative risk	I² (%)	Pooled relative risk	I² (%)
Women who inject drugs vs men who inject drugs	1.4 (1.1 - 1.6)	54.9	1.2 (1.1 - 1.3)	43.2
Young PWID vs older PWID	1.4 (1.2 - 1.8)	66.3	1.5 (1.3 - 1.8)	70.0

- **No. of countries with incidence data: 27 (HIV) and 24 (HCV)**
- **Incidence estimates measured over: 1987-2021 (HIV) and 1992-2021 (HCV)**
- **Proportion of incidence estimates derived from a single city rather than multi-city/nationwide:** HIV: 65%; HIV: 66%

CONCLUSIONS

- **Empirical estimates of HIV or HCV incidence (measured using direct methods) among people who inject drugs are unavailable in most countries, and of those available, many are not recent or are not nationwide**
  - Considerable efforts needed to develop systems for monitoring HIV and HCV incidence
  - Probably need indirect methods to keep track of epidemics to validate elimination goals or use alternative indicators to validate elimination
- Available data indicate that HIV incidence and primary HCV incidence are generally high but pooled estimates carry a substantial level of heterogeneity
- Taking all countries together, primary HCV incidence appears to have decreased over time (~4%/year); no evidence of a temporal change in HIV incidence
- No evidence of a difference in primary HCV incidence between low- or middle-income (LMIC) and high-income countries (HIC) (although few studies in LMIC); HIV incidence appears >3x greater in LMIC compared to HIC
- Younger people who inject drugs and women who inject drugs have a higher risk of both HCV and HIV acquisition suggesting that targeted efforts are needed to engage these groups in prevention programs

[1]WHO. Global health sector strategy on viral hepatitis 2016-2021. 2016; [2]Joint UNAIDS. An ambitious treatment target to help end the AIDS epidemic. 2014; [3]Artenie A et al. Lancet Gastroenterol Hepatol 2022; [4]Hallet TB. Current opinion in HIV and AIDS 2011; [5]Stone J et al. Lancet Infect Dis 2018; [6]Arum C et al. Lancet Public Health 2021