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

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CONTEXT			METHODS	
 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) 	 Search strategy and selection criteria: MEDLINE, Embase, and PsycINFO for stand Dec 19, 2021 Population: people with a history of information of people susceptible to infection, or Data extraction HIV/HCV incidence overall (recent an stratified by gender and age Study characteristics (e.g., inclusion/method of incidence estimation, test Participant characteristics (e.g., mea on OST, background HIV/HCV prevale Data analysis (pre-specified: PROSPERC) Random-effects meta-analysis and m Incidence rates of HIV and HCV Relative risk (RR)⁺ of HIV and HCV PWID RR⁺ of HIV and HCV acquisition at Multi—level meta-regression⁺⁺ to ex HIV and HCV incidence 	systematic literature search ^{5,6} of udies published between Jan 1, 2000 fection drug use in assessed either through repeat follow- in through tests of recent infection and non-recent, where available ⁺⁺) and fexclusion criteria, recruitment scheme, ting schedule, follow-up duration) in age/duration of injection, % women, % ence) D 2020 CRD42020220884) heta-regression to synthesise: W acquisition among younger vs older among women vs men who inject drugs plore temporal and geographic trends in	5363 potentially eligible records identified via database search over Sept 14, 2020 – Dec 12, 2021 1569 via MEDLINE; 3651 via Embase; 143 via PsychiNFO (1183 duplicates rem (4180 records identified for title and abstract screening (4180 records eligible for full-text screening (122 eligible records (94 published & 28 unpublished) 68 records on HCV incidence (51 published & 17 unpublished) 67 records on HIV incidence (52 published & 16 unpublished)	Figure 1: Study Selection 377 potentially eligible records identified via prior database search over Jan 1, 2000 – Sept 14, 2020 moved udded or unpublished data 430 records excluded: 140 did not report eport eport HCV or HIV incidence 45 did not report report HCV or HIV incidence exclusively in people who inject drugs 31 suthors were contacted to request 140 did not report HCV or HIV incidence exclusively in people who inject drugs 31 suthors are duplicate exclusively in people who inject drugs 31 suthated only HCV reinfection or primary HCV and HCV reinfection combined 1 submated only HCV incidence and people who inject drugs in prison 124 presented duplicate data 11 were duplicate data 124 presented duplicate data 127 records on the RR of HCV infection by age (15 published & 17 unpublished) 27 records on the RR of HCV infection by age (11 published & 16 unpublished)
		RESU	JLTS	
Figure 2: Forest plot of HIV in	cidence rate, by WHO region	Figure 3: Forest	t plot of HCV incidence rate, by WHO region	Figure 4: Temporal and geographic trends in HIV and HCV incidence
First author/year Country City/Cities Calend African Region Kurth AE/Walker JG Kenya Nairobi, Western Region 2012-4 Overall Heterogeneity: not applicable Kenya Kenya Kenya Kenya	dar period Rate per 100 py [95% Cl] -2015 2.6 [1.8; 3.7] 2.6 [1.8; 3.7]	First author/yearCountryCity/CitleEastern Mediterranean Region Todd CS 2015AfganistanKabul CairoMohamed R 2021EgyptCairoOverall Heterogeneity: $I^2 = 96.9\%$, $\tau^2 = 1.3$, $p < 0.001$ City/Citle	es Calendar period Rate p 2007–2009 2016–2019	per 100 py [95% Cl] Image: Second
Eastern Mediterranean RegionTodd CS 2015AfghanistanKabul2007-3Anwar S 2021EgyptCairo2013-3Samo RN 2013PakistanKarachi2009-3Iversen J 2021Pakistanmulti-city2012-3OverallHeterogeneity: l^2 = 90.6%, t^2 = 1.3, $p < 0.001$ European RegionLucidarme D 2004FranceNorthern and Eastern regions 1999-3Aladashvili MGeorgiaTbilisi, Poti, BatumiSubatini A 2004FranceNorthern and Eastern regions 1999-3Aladashvili MGeorgiaTbilisi, Poti, BatumiSypsa VGreeceAthensSaybatini A 2011ItalyMulti-city199-3Sabbatini A 2011RussiaSt. Petersburg2004-Kozlov A 2016RussiaSt. Petersburg2004-Kozlov A 2016RussiaSt. Petersburg2004-Kozlov AP 2006RussiaSt. Petersburg2004-Biome MA 2011SwedenStockholm </th <th>$\begin{array}{cccccccccccccccccccccccccccccccccccc$</th> <th>European RegionMravcik V 2009Czechiamulti-cityLucidarme D 2004FranceNorthernAladashvili MGeorgiaTbilisi, PoSypsa V 2017GreeceAthensSmyth B 2003IrelandDublinPeles E 2011IsraelTel AvivSpada E 2018Italymulti-cityPuoti M 2017Italymulti-cityVan Santen DK/Prins MNetherlandsAmsterdaSmit, BoydNetherlandsmulti-citySilva MJ 2015PortugalLisbonVallejo F 2015SpainBarcelonaLa Rosa JV 2018SpainMadridBlome MA 2011SwedenMalmoKaberg MSwedenStockholrCroxford SUK (England, Wales, N Ireland)multi-cityBalogun MA 2009UK (England)London, FFoley S 2009UK (England)London, SIreland G 2019UK (Scotland)GlasgowRoy KM 2001UK (Scotland)GlasgowPalmateer NEUK (Scotland)multi-cityOverallHeterogenetty: $l^2 = 97.6\%, r^2 = 0.5, p < 0.001$Heterogenetty: $l^2 = 97.6\%, r^2 = 0.5, p < 0.001$</th> <th>$\begin{array}{cccccccccccccccccccccccccccccccccccc$</th> <th>$\begin{array}{c} 112[6.9; 18.3]\\ 9.0[5.5; 14.6]\\ 14.6[120; 17.7]\\ 56.3[34.5; 92.0]\\ 65.9[51.9; 83.8]\\ 3.9[2.5; 6.2]\\ 11.3[5.6; 22.6]\\ 7.2[5.3; 9.7]\\ 0.9[0.1; 14.4]\\ 0.2[0.1; 0.4]\\ 12.1[9.8; 15.0]\\ 39.8[294; 53.9]\\ 72.5[46.6; 108.2]\\ 38.3[33.1; 44.2]\\ 19.8[17.5; 22.4]\\ 11.0[6.5; 18.6]\\ 41.8[31.9; 54.7]\\ 9.1[4.6; 18.2]\\ 8.7[8.1; 9.3]\\ 6.3[4.4; 8.9]\\ 28.4[15.7; 51.2]\\ 10.6[8.7; 12.9]\\ 5.9[3.7; 9.5]\\ 19.2[17.0; 21.6]\\ 12.8[0.5; 17.2]\\ \end{array}$</th>	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	European RegionMravcik V 2009Czechiamulti-cityLucidarme D 2004FranceNorthernAladashvili MGeorgiaTbilisi, PoSypsa V 2017GreeceAthensSmyth B 2003IrelandDublinPeles E 2011IsraelTel AvivSpada E 2018Italymulti-cityPuoti M 2017Italymulti-cityVan Santen DK/Prins MNetherlandsAmsterdaSmit, BoydNetherlandsmulti-citySilva MJ 2015PortugalLisbonVallejo F 2015SpainBarcelonaLa Rosa JV 2018SpainMadridBlome MA 2011SwedenMalmoKaberg MSwedenStockholrCroxford SUK (England, Wales, N Ireland)multi-cityBalogun MA 2009UK (England)London, FFoley S 2009UK (England)London, SIreland G 2019UK (Scotland)GlasgowRoy KM 2001UK (Scotland)GlasgowPalmateer NEUK (Scotland)multi-cityOverallHeterogenetty: $l^2 = 97.6\%, r^2 = 0.5, p < 0.001$ Heterogenetty: $l^2 = 97.6\%, r^2 = 0.5, p < 0.001$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 112[6.9; 18.3]\\ 9.0[5.5; 14.6]\\ 14.6[120; 17.7]\\ 56.3[34.5; 92.0]\\ 65.9[51.9; 83.8]\\ 3.9[2.5; 6.2]\\ 11.3[5.6; 22.6]\\ 7.2[5.3; 9.7]\\ 0.9[0.1; 14.4]\\ 0.2[0.1; 0.4]\\ 12.1[9.8; 15.0]\\ 39.8[294; 53.9]\\ 72.5[46.6; 108.2]\\ 38.3[33.1; 44.2]\\ 19.8[17.5; 22.4]\\ 11.0[6.5; 18.6]\\ 41.8[31.9; 54.7]\\ 9.1[4.6; 18.2]\\ 8.7[8.1; 9.3]\\ 6.3[4.4; 8.9]\\ 28.4[15.7; 51.2]\\ 10.6[8.7; 12.9]\\ 5.9[3.7; 9.5]\\ 19.2[17.0; 21.6]\\ 12.8[0.5; 17.2]\\ \end{array}$
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Yang YC 2016ChinaDehong Prefecture2004-3Wei L 2006ChinaHeng County2002-3Yang Y 2017ChinaLiangshan2015Zhang Y 2007ChinaUrumqi2002-3Ruan Y 2013ChinaXichang2006-3Yen, YF 2012TaiwanTaipei2007-3Des Jarlais DC 2020VietnamHai Phong2016-3Go VF 2015VietnamThai Nguyen Province2009-3OverallHeterogeneity: $I^2 = 97.3\%$, $\tau^2 = 1.8$, $p < 0.001$ 2007-3Metzger DS 2015China and Thailand multi-city2007-4	2015 + 1.6 [1.4; 1.9] 2003 3.1 [1.8; 5.2] 2003 8.8 [6.5; 12.0] 2008 0.6 [0.2; 1.7] 2010 + 2019 1.2 [0.4; 3.6] 2015 1.0 [0.1; 7.4] 2015 + 2014 + 2011 +	Van Den Boom W/Dietze FAustraliaMelbournSacks-Davis RAustraliaMelbournIversen J 2013Australiamulti-cityMaher L 2006AustraliaNew SoutIversen J/Maher LAustraliaSydneyThe Kirby Institute 2020AustraliaSydneyLuo W 2021ChinaBaoshanJackson JB1 2014ChinaHeng CouGarten RJ 2004ChinaPingxiangRuan Y 2013ChinaXichangBrunton CR 2000New Zealandmulti-cityMoles JP 2020VietnamHai PhonClatts MC 2010VietnamHanoi	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	13.1 [8.6; 19.8] 9.7 [6.9; 13.6] 30.8 [24.3; 39.0] 6.6 [4.7; 9.3] 9.6 [6.7; 13.7] 0.3 [0.0; 1.8] 22.0 [15.3; 31.7] 52.6 [40.1; 69.1] 30.3 [22.5; 40.8] 13.0 [6.8; 25.1] 19.4 [12.2; 30.8] empirical estimates of HIV or HCV incidence (measured using direct methods) among people
Overall Heterogeneity: not applicable Overall Heterogeneity: $I^2 = 98.4\%$, $\tau^2 = 1.3$, $p = 0$	 0.5 [0.3; 1.1] 0.5 [0.3; 1.1] 1.7 [1.2; 2.3] 0 2 4 6 8 10 12 14 HIV incidence rate per 100 person-years 	Overall Heterogeneity: $l^2 = 94.3\%$, $\tau^2 = 0.6$, $p < 0.001$ Overall Heterogeneity: $l^2 = 97.2\%$, $\tau^2 = 0.6$, $p = 0$	0 10 20 30 40 50 60 HCV incidence rate per 100 person-vears	14.1 [9.0; 21.9] who inject drugs are unavailable in most 12.4 [10.3; 15.0] countries, and of those available, many are not recent or are not nationwide > Considerable efforts needed to develop

	Table 1:	Pooled H	HV and HCV	incide	nce, stratified by	y key metrics	5		
Variable		No. of estimates	HIV incidence (/100py; 95% Cl)	l² (%)	Variable		No. of estima tes	HCV incidence (/100py; 95% Cl)	l² (%
World Bank Income	High income	28	0.8 (0.6 - 1.2)	94.1	World Bank Income	High income	52	12.1 (9.7–15.1)	97.4
classification	Low or middle income	34	3.1 (2.1 - 4.4)	98.5	classification	Low or middle income	14	14.2 (10.1- 20.1)	94.7
≥80% of participants	Yes	45	1.5 (1.0 - 2.3)	98.5				,	
reported injecting within the past year	No	7	1.1 (0.4 - 2.8)	96.5	≥80% of participants	Yes	46	15.0 (11.9 - 18.9)	97.1
. ,	Not available	10	2.8 (1.7 - 4.4)	97.5	within the past year	No	6	10.0 (8.2 - 12.1)	45.5
Recruitment venues	Community	23	1.1 (0.7 - 1.8)	97.8		Not available	14	7.7 (5.5 - 10.9)	95.8
	Medical	13	1.6 (0.9 - 2.8)	96.4	Recruitment venues	Community	22	16.6 (13.0 - 21.3)	95.2
	Network	12	4.0 (2.1 - 7.9)	98.7		Medical	15	7.6 (5.1 - 11.4)	96.5
	Mix	14	1.7 (0.9 - 3.2)	97.2		Network	8	17.3 (12.8 - 23.3)	88.5
Risk of bias score ⁺	Low	28	1.5 (0.9 - 2.4)	98.3	Risk of bias score [†]	Mix Low	21 27	11.6 (7.5 - 18.0) 10.5 (7.3 - 15.1)	97.7 97.0
	Moderate-to-high	34	1.8 (1.2 – 2.8)	98.6		Moderate-to-high	39	13.9 (11.1 - 17.4)	96.1
Study start year	≥2010	27	1.9 (1.2-2.9)	98.7	Study start year	≥2010	18	13.7 (10.7 – 15.7)	94.7
	<2010	35	1.6 (1.0 24)	97.7		<2010	48	12.2 (9.5 – 15.7)	97.7

	HIV		HCV	
	Pooled relative risk	l ² (%)	Pooled relative risk	l ² (%)
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

Fonds de recherche

Santé

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- 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%



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



