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Global, regional, and country-level estimates of hepatitis C infection among people who have recently injected drugs

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ABSTRACT

Background and Aims People who have recently injected drugs are a priority population in efforts to achieve hepatitis C virus (HCV) elimination. This study estimated the prevalence and number of people with recent injecting drug use living with HCV, and the proportion of people with recent injecting drug use among all people living with HCV infection at global, regional and country-levels. **Methods** Data from a global systematic review of injecting drug use and HCV antibody prevalence among people with recent (previous year) injecting drug use were used to estimate the prevalence and number of people with recent injecting drug use living with HCV. These data were combined with a systematic review of global HCV prevalence to estimate the proportion of people with recent injecting drug use among all people living with HCV. **Results** There are an estimated 6.1 million [95% uncertainty interval (UI) = 3.4–9.2] people with recent injecting drug use aged 15–64 years living with HCV globally (39.2% viraemic prevalence; UI = 31.6–47.0), with the greatest numbers in East and Southeast Asia (1.5 million, UI = 1.0–2.1), eastern Europe (1.5 million, UI = 0.7–2.4) and North America (1.0 million, UI = 0.4–1.7). People with recent injecting drug use comprise an estimated 8.5% (UI = 4.6–13.1) of all HCV infections globally, with the greatest proportions in North America (30.5%, UI = 11.7–56.7), Latin America (22.0%, UI = 15.3–30.4) and eastern Europe (17.9%, UI = 8.2–30.9). **Conclusions** Although, globally, 39.2% of people with recent injecting drug use are living with hepatitis C virus (HCV) and 8.5% of all HCV infections occur globally among people with recent injecting drug use, there is wide variation among countries and regions.

Keywords Estimates, HCV, IDU, injecting drug use, PWID, viraemic.

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INTRODUCTION

The World Health Organization (WHO) has set a goal to eliminate hepatitis C virus (HCV) as a global public health threat by 2030 [1]. Between 2015 and 2030, WHO targets include reducing new HCV infections by 80%, the number of HCV deaths by 65% and increasing HCV diagnoses from 20 to 90%, and eligible people receiving HCV treatment from < 5 to 80%. People who inject drugs represent a priority population for HCV elimination, given the high prevalence and incidence in this group [2–7].

We previously estimated the global, regional and country-level prevalence of HCV (viraemic infections) [8]. In 2015, the global prevalence of HCV infection was estimated to be 1.0% [95% uncertainty interval (UI) = 0.8–1.1], corresponding to 71.1 million (62.5–79.4) people living with HCV [8]. We also estimated the global, regional and country-level HCV antibody prevalence among people with recent injecting drug use (previous 12 months). Among the estimated 15.6 million (UI = 10.2–23.7 million) people with recent injecting drug use aged 15–64 years globally, it is estimated

that 52.3% (UI = 42.4–62.1%) are HCV-antibody positive, representing 8.2 million people who have recently injected drugs (UI = 4.7–12.4 million) with past or present HCV [7]. Given that 25% of people clear HCV infection spontaneously [9], estimates are needed on the prevalence and numbers of people with recent injecting drug use who are living with HCV infection (viraemic infection).

There are no previous estimates at the global, regional and country levels of the HCV RNA (ribonucleic acid) prevalence among people with recent injecting drug use, the number of people with recent injecting drug use who are living with HCV infection (HCV RNA detectable or viraemic) or the proportion of people with recent injecting drug use among all people living with HCV infection. These data are crucial to monitor progress of global HCV elimination efforts and identify high-burden settings to enable appropriate targeting of prevention and treatment strategies to achieve the WHO HCV targets.

The aim of this study was to estimate the global HCV RNA prevalence (viraemic infections) among people who have recently injected drugs; the numbers of people with recent injecting drug use living with HCV infection; and the proportion of people who have recently injected drugs among all people living with HCV at global, regional and country levels.

METHODS

Study design and procedures

This analysis utilized data from two published studies. The first study was a systematic review to estimate the number of people with recent injecting drug use and the HCV antibody (anti-HCV) prevalence among people who have recently (previous 12 months) injected drugs [7]. The second study was a systematic review and modelling study to estimate the global viraemic HCV prevalence [8].

The first systematic review estimated global, regional and country-level prevalence of injecting drug use among people aged 15–64 years and the prevalence of HIV, HCV and hepatitis B virus (HBV) among people with recent injecting drug use in 2015 [7]. This review was performed consistent with the GATHER (Guidelines for Accurate and Transparent Health Estimates Reporting) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Multiple search strategies [7] were used to identify papers and reports published since previous reviews of IDU prevalence (from 2008) [10] and of HCV among people who inject drugs (PWID) (from 2011) [2]. Without language restrictions, peer-reviewed databases (MEDLINE, Embase and PsycINFO) and grey literature were searched systematically, and data requests disseminated to international experts and agencies. We searched for data on IDU prevalence and the prevalence of HIV, HCV and HBV among people with recent injecting drug use. Eligible data on prevalence of IDU, HIV antibody, HBsAg and HCV antibody among PWID were selected and, where multiple estimates were available, pooled for each country via random-effects meta-analysis. Data on HCV RNA prevalence among people with recent injecting drug use were also extracted. Global, regional and country-level estimates of the HCV antibody (anti-HCV) prevalence among people with recent injecting drug use were used for the current study [7].

The second systematic review estimated global, regional and country levels of viraemic HCV prevalence in 2015 [8]. Data published between 1 January 2000 and 31 March 2016 were identified through searches of electronic peer-reviewed literature databases, PubMed and Embase [8]. Non-indexed government reports, personal communication with country experts and additional studies identified through manual searches of references noted in publications were included where better data were not available. Papers were scored on the degree to which they could be extrapolated to the general population, the sample size and the year of analysis. A Microsoft Excel-based (version 2007) Markov-type model was populated with the highest-scoring epidemiological data for each country, used to estimate HCV prevalence over time (including in 2015). A Delphi process was used to gain country expert consensus and validate inputs. Further details of data extraction, scoring of data sources, Delphi process and modelling have been published [8]. Global, regional and country-level estimates of the numbers of people with viraemic HCV infection were used for the current study [7].

Statistical analysis

First, we sought to estimate the prevalence of viraemic HCV infection (detectable HCV RNA) among people with recent injecting drug use at global, regional and country levels. As shown in Table 1, 48% (98 of 206) of countries had available data on HCV antibody prevalence among people with recent injecting drug use (n = 374 studies) compared to only 9% (19 of 206) of countries with available data on HCV RNA prevalence among people with recent injecting drug use (n = 32 studies). Compared to studies of HCV antibody prevalence among people with recent injecting drug use (n = 374), studies of HCV RNA prevalence among people with recent injecting (n = 32) were less often estimate-grade A (multi-site seroprevalence study with > 1 sample types) (6.3 versus 21.9%) and national samples (6.2% versus 20.6%). Given the poor availability of data on HCV RNA prevalence, we sought to estimate the HCV viraemic proportion (those living with HCV infection) by using estimates of the prevalence of HCV antibodies among people with recent injecting drug use within each country [7] and multiplying by an

Table 1 Quality of evidence of countries with available hepatitis C virus (HCV) antibody prevalence and HCV RNA prevalence data among recent people who inject drugs (PWID).

	HCV antibody prevalence among recent PWID (n = 374)	*HCV RNA prevalence among recent PWID (n = 32)*
Countries with available data	98/206 (47.6%)	19/206 (9.2%)
Estimate-grade[b]		
A	82 (21.9%)	2 (6.3%)
B1	225 (60.2%)	20 (62.5%)
B2	13 (3.6%)	1 (3.1%)
C	54 (14.4%)	8 (25.0%)
U	–	1 (3.1%)
Geographic coverage		
National sample	77 (20.6%)	2 (6.2%)
Subnational sample	87 (23.3%)	11 (34.4%)
City sample	210 (56.1%)	19 (59.4%)
Literature type[a]		
A1	128 (34.2%)	30 (93.75%)
A2	4 (1.1%)	–
B2	147 (39.3%)	–
B3	81 (21.7%)	–
C	8 (2.2%)	2 (6.25%)
D	6 (1.6%)	–

[a]Grading for literature type: A1 = peer-reviewed journal article; A2 = abstract of published article only; B1 = published book/report/monograph from scholarly or commercial publisher; B2 = published book/report/monograph from international governmental or monitoring organization (e.g. UN, WHO, EMCDDA); B3 = published book/report/monograph from other source [e.g. government, non-governmental organization (NGO), university, research centre]; C = conference abstract; D = other unpublished report (including website downloads); E = e-mail and private correspondence; F = ARQ. [b]Grading for estimate grade: A = multi-site seroprevalence study with > 1 sample types (e.g. needle-syringe programmes, drug treatment centres, incarcerated IDUs); B1 = seroprevalence study, single sample type and multiple sites; B2 = seroprevalence study, multiple sample types and a single site; C = seroprevalence study, single sample type; D = registration or notification of cases of hepatitis/HIV infection; E = prevalence study using self-reported hepatitis/HIV status; ungraded = estimate with methodology unknown.

estimate of the proportion developing viraemic HCV infection [9]. The proportion with viraemic HCV infection among those who were HCV antibody-positive [75%; 95% confidence interval (CI) = 71%, 79%] was estimated using data from a well-characterized merged data set of nine international cohorts of people who had recently injected drugs who had acquired acute HCV infection, and were followed prospectively for spontaneous HCV clearance and viraemic infection [9]. The number of people with recent injecting drug use with viraemic HCV infection was then estimated by multiplying the number of people with recent injecting drug use who were HCV antibody positive by the HCV viraemic prevalence.

Ninety-five per cent UIs were estimated using Monte Carlo simulation taking 100 000 draws. A binomial distribution was used because the parameters of interest were proportions (product of IDU proportion among the population and HCV proportion among PWID). Estimated sample sizes were derived based on the 95% CIs and standard errors of proportion estimates in each country. The simulated UIs incorporated the uncertainty of estimates.

Following the collation of country-specific estimates, estimates of regional and global viraemic HCV infection among people with recent injecting drug use were derived. Region-specific, weighted estimates of the prevalence of HCV were made using all the observed estimates and 95% CI of estimates in each country within that region and deriving a weighted estimate and UI taking into account country population size. Regional estimates were then used to estimate the global prevalence.

The proportion of people with recent injecting drug use among all people living with HCV infection was computed by dividing the total number of people with recent injecting drug use living with HCV by the total number of all people living with HCV for countries where both estimates were available. As above, 95% UIs were simulated taking 100 000 draws carrying forward the standard errors for both people with recent injecting drug use living with HCV and the total HCV viraemic infection prevalence estimates.

RESULTS

Sufficient data were identified to enable estimates of the HCV viraemic prevalence among people with recent injecting drug use in 98 countries, and to estimate the population size of people with recent injecting drug use living with HCV in 76 countries. Sufficient data were identified to enable estimates of the number of people living with HCV overall in 98 countries. There were sufficient data to estimate the number of people with recent injecting drug use as a proportion of all people living with HCV in 55 countries.

Results are shown by region in Table 2 and by country in Table 3. Globally, we estimate that in 2015, 39.2% (UI = 31.6–47.0) of people with recent injecting drug use have HCV viraemic infection, representing 6.1 million (UI = 3.4–9.2) people with recent injecting drug use living with HCV infection globally. Of the 71.1 million (UI = 62.5–79.4 million) people living with HCV infection (Table 2), we estimate that 8.5% (UI = 4.6–13.1) are people with recent injecting drug use (Table 2).

At the regional level, HCV viraemic prevalence among people with recent injecting drug use varied from 16.3% (UI = 12.7–20.1) in sub-Saharan Africa to 48.6% (UI = 42.0–55.2) in eastern Europe (Table 2). The largest estimated numbers of people with recent injecting drug use living with HCV infection were in East and Southeast Asia (1.5 million, UI = 1.0–2.1), eastern Europe (1.5 million, UI = 0.7–2.4) and North America (1.0 million,

Table 2 Regional and global estimates of the prevalence of hepatitis C virus (HCV) viraemic infection among people with recent injecting drug use, the number of people with recent injecting drug use living with HCV viraemic infection, the total population living with HCV viraemic infection and the proportion of people with recent injecting drug use among the total population with HCV viraemic infection.

	Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Eastern Europe	48.6 (42.0, 55.2)	1 466 500 (699 500, 2 377 000)	8 181 000 (6 304 000, 8 250 000)	17.9 (8.2, 30.9)
Western Europe	39.9 (35.7, 44.1)	402 500 (264 500, 557 000)	2 347 000 (1 969 000, 3 289 000)	17.2 (9.9, 30.4)
East and Southeast Asia	37.7 (28.2, 47.5)	1 506 000 (1 019 500, 2 078 500)	16 313 000 (12 636 000, 17 242 000)	9.2 (5.8, 13.8)
South Asia	28.9 (13.4, 47.5)	296 000 (114 500, 518 000)	15 617 500 (13 341 000, 20 182 000)	1.9 (0.7, 3.6)
Central Asia	40.5 (36.5, 44.5)	114 000 (69 000, 165 000)	2 516 000 (2 010 000, 2 749 000)	4.5 (2.6, 6.9)
Caribbean	47.6 (40.2, 55.1)	37 500 (22 500, 55 000)	225 500 (183 000, 315 000)	16.7 (8.9, 30.6)
Latin America	46.4 (43.1, 49.8)	846 000 (617 500, 1 092 500)	3 854 000 (3 131 000, 3 948 000)	22.0 (15.3, 30.4)
North America	40.5 (29.2, 51.7)	960 000 (398 000, 1 679 500)	3 148 000 (2 429 000, 4 034 000)	30.5 (11.7, 56.7)
Pacific Island states and Territories[a]	41.4 (32.4, 50.5)	9000 (5500, 14 000)	117 500 (101 000, 376 000)	7.9 (1.9, 11.1)
Australasia	42.8 (38.9, 46.8)	49 500 (35 500, 65 000)	278 500 (220 000, 297 000)	17.7 (12.1, 25.2)
Sub-Saharan Africa	16.3 (12.7, 20.1)	225 000 (45 500, 458 500)	9 893 500 (7 605 000, 15 112 000)	2.3 (0.5, 5.9)
Middle East and North Africa	36.1 (29.2, 43.2)	126 000 (65 000, 199 500)	8 625 500 (6 838 000, 9,155 000)	1.5 (0.7, 2.4)
Global	39.2 (31.6, 47.0)	6 063 500 (3 434 500, 9 246 000)	71 146 000 (62 472 000, 79 404 000)	8.5 (4.6, 13.1)

UI = uncertainty interval (see Methods for details of estimation). Number of people with recent injecting drug use with viraemic HCV infection are rounded to the nearest 500. Total population number with viraemic HCV infection are rounded to the nearest 1000. [a]Note that no estimates of the prevalence of anti-HCV among people who inject drugs have been located for the Pacific Islands and Territories, so the weighted observed global prevalence was used here. Considerable caution should be used with these estimates.

Table 3 Country-level estimates of the prevalence of hepatitis C virus (HCV) viraemic infection among people with recent injecting drug use, the number of people with recent injecting drug use living with HCV viraemic infection, the total population living with HCV viraemic infection and the proportion of people with recent injecting drug use among the total population with HCV viraemic infection.

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Eastern Europe				
Armenia	32.0 (22.0, 42.3)	4000 (1500, 8500)	NK	NG
Azerbaijan	46.6 (34.9, 58.0)	20 000 (14 000, 27 000)	190 000 (125 000, 212 000)	10.6 (6.6, 17.3)
Belarus	43.7 (32.3, 55.1)	18 000 (7000, 31 500)	NK	NG
Bosnia and Herzegovina	30.0 (20.7, 39.5)	NK	NK	NK
Bulgaria	51.5 (47.3, 55.8)	9500 (7500, 11 500)	87 000 (46 000, 112 000)	11.0 (6.9, 20.4)
Czech Republic	13.7 (10.9, 16.7)	6500 (5000, 8000)	43 000 (22 000, 48 500)	15.0 (9.2, 28.6)
Estonia	59.4 (49.8, 68.4)	5000 (2500, 8500)	18 000 (11 500, 20 000)	28.2 (12.6, 53.0)
Georgia	51.8 (42.9, 60.5)	59 500 (12 500, 119 500)	165 000 (120 000, 169 000)	36.1 (7.4, 76.9)
Hungary	35.0 (22.9, 47.2)	1500 (500, 2500)	52 500 (28 500, 55 500)	2.7 (1.1, 5.6)
Latvia	55.8 (49.8, 61.7)	8000 (6000, 10 000)	43 000 (28 000, 50 000)	18.1 (11.8, 29.1)
Lithuania	30.8 (28.1, 33.7)	1500 (500, 2500)	32 500 (20 000, 38 500)	4.5 (2.0, 8.6)
Moldova	37.5 (25.5, 49.7)	4500 (2500, 7000)	NK	NG
Poland	44.0 (40.5, 47.6)	NK	184 000 (136 000, 224 000)	NK
Romania	62.9 (58.7, 67.0)	51 000 (36 000, 67 500)	547 000 (397 000, 566 000)	9.3 (6.0, 14.2)
Russian Federation	51.6 (44.2, 58.9)	969 500 (463 000, 1 570 500)	4 748 000 (3,238 000, 4 960 000)	20.4 (9.3, 37.2)
Slovakia	42.1 (26.6, 57.7)	8500 (3500, 14 500)	33 000 (20 000, 37 500)	25.4 (9.6, 52.0)
Ukraine	40.4 (36.3, 44.6)	129 000 (54 000, 222 000)	NK	NG
Western Europe				
Albania	25.5 (20.1, 31.1)	1500 (1000, 2500)	NK	NG
Andorra	NK	NK	NK	NK
Austria	45.7 (40.6, 50.9)	8500 (6000, 11 500)	21 000 (6000, 30 500)	40.2 (20.1, 100.0)
Belgium	43.8 (34.9, 52.6)	11 500 (7000, 16 500)	64 500 (23 000, 75 500)	17.8 (8.7, 45.8)
Croatia	27.5 (21.0, 34.2)	1500 (1000, 2500)	26 000 (16 500, 28 500)	6.7 (4.0, 11.3)
Denmark	31.9 (26.8, 37.2)	5500 (4000, 6500)	19 500 (14 500, 19 500)	27.2 (18.8, 39.5)
England	23.1 (20.0, 26.3)	48 500 (41 500, 56 000)	168 000 (91 000, 211 000)	28.9 (18.8, 51.8)
Finland	55.2 (51.2, 59.4)	9500 (7000, 12 500)	22 500 (16 000, 26 000)	41.6 (27.4, 62.8)
France	48.0 (44.5, 51.5)	39 500 (31 500, 47 500)	194 000 (92 500, 222 000)	20.2 (12.4, 40.1)
FYR (Former Yugoslav Republic) Macedonia	46.6 (43.4, 49.9)	2500 (1500, 3000)	NK	NG

(*Continues*)

Table 3. (Continued)

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Germany	48.7 (44.6, 53.0)	64 000 (13 500, 129 000)	205 000 (90 000, 313 000)	31.3 (6.2, 80.6)
Greece	49.2 (45.4, 53.1)	2500 (2000, 3000)	132 000 (82 000, 169 000)	1.9 (1.2, 3.1)
Greenland	–	–	NK	–
Iceland	47.3 (43.8, 50.8)	500 (< 500, 500)	1000 (1000, 1000)	NR
Ireland	56.0 (52.5, 59.4)	5000 (3500, 6000)	29 500 (20 000, 42 500)	16.2 (10.0, 28.9)
Italy	43.4 (38.8, 48.1)	148 500 (98 500, 205 000)	680 000 (455 000, 1 641 000)	21.8 (7.6, 33.9)
Liechtenstein	–	–	NK	–
Luxembourg	61.0 (55.9, 66.1)	1500 (1000, 1500)	5500 (3500, 6000)	25.2 (16.6, 41.1)
Malta	18.9 (10.4, 28.4)	< 500 (< 500, 500)	1000 (1000, 1500)	NR
Monaco	NK	NK	NK	NK
Montenegro	32.6 (29.4, 35.9)	500 (500, 500)	NK	NK
Netherlands	41.5 (36.7, 46.3)	1500 (1000, 2000)	16 500 (5000, 25 500)	8.3 (4.2, 22.9)
Northern Ireland	NK	NK	NK	NK
Norway	48.6 (44.5, 52.8)	4000 (3500, 5000)	21 000 (15 000, 24 500)	19.4 (13.8, 28.1)
Portugal	65.8 (59.1, 72.2)	10 500 (9000, 12 000)	89 000 (74 000, 120 000)	11.7 (8.2, 18.1)
San Marino	NK	NK	NK	NK
Scotland	39.1 (33.8, 44.5)	6000 (5000, 7500)	NK	NG
Serbia	19.4 (16.5, 22.6)	5500 (4500, 7000)	NK	NG
Slovenia	22.9 (19.6, 26.2)	1500 (1000, 2000)	6500 (4500, 7000)	21.3 (13.3, 33.5)
Spain	53.3 (50.2, 56.3)	5500 (2000, 9500)	386 000 (202 000, 620 000)	1.4 (0.5, 3.6)
Sweden	61.3 (57.6, 64.9)	5000 (< 500, 20 000)	37 500 (28 000, 43 500)	13.3 (0.0, 46.6)
Switzerland	55.9 (51.0, 60.9)	7500 (6000, 9500)	78 000 (45 500, 87 000)	9.7 (6.3, 16.7)
Wales	20.1 (17.2, 23.0)	NK	NK	NK
East and South East Asia				
Brunei Darussalam	NK	NK	NK	NK
Cambodia	NK	NK	257 000 (147 000, 272 000)	NK
China	32.3 (20.8, 44.3)	828 000 (493 000, 1 228 500)	9 795 000 (6 675 000, 10 832 000)	8.5 (4.6, 14.3)
Indonesia	66.9 (62.2, 71.5)	127 500 (103 000, 153 000)	1 289 000 (443 000, 2 046 000)	9.9 (5.5, 24.9)
Japan	48.6 (40.8, 56.3)	179 000 (130 500, 234 500)	857 000 (364 000, 1 024 000)	20.9 (11.7, 46.5)
Lao PDR	NK	NK	NK	NK
Malaysia	50.3 (46.2, 54.5)	142 000 (116 000, 169 500)	382 000 (240 000, 405 000)	37.1 (25.2, 59.2)

(*Continues*)

Table 3. (Continued)

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Mongolia	NK	NK	194 000 (131 000, 237 000)	NK
Myanmar	22.2 (19.9, 24.5)	38 500 (25 500, 53 000)	NK	NG
North Korea	–	–	NK	–
Philippines	26.4 (12.8, 41.6)	6500 (3000, 11 500)	614 000 (353 000, 651 000)	1.1 (0.4, 2.3)
Republic of Korea	36.3 (31.7, 41.0)	NK	231 000 (148 000, 261 000)	NK
Singapore	31.9 (28.9, 35.0)	NK	NK	NK
Taiwan	68.2 (64.4, 72.0)	NK	489 000 (310 000, 877 000)	NK
Thailand	66.4 (60.6, 71.9)	34 000 (12 500, 60 000)	463 000 (255 000, 487 000)	7.4 (2.6, 16.1)
Timor Leste	NK	NK	NK	NK
Viet Nam	43.8 (31.8,5 5.7)	70 500 (47 000, 98 000)	1 066 000 (580 000, 1 116 000)	6.6 (3.7, 12.5)
South Asia				
Afghanistan	28.4 (20.7, 36.3)	39 500 (23 000, 60 000)	183 000 (85 000, 258 000)	21.5 (10.5, 46.9)
Bangladesh	25.4 (16.9, 34.4)	17 500 (11 500, 24 000)	NK	NG
Bhutan	NK	NK	NK	NK
India	30.0 (25.2, 34.9)	59 000 (38 000, 84 000)	6,245 000 (4 748 000, 10 957 000)	0.9 (0.4, 3.0)
Iran	33.1 (21.4, 45.2)	52 000 (29 500, 81 000)	199 000 (129 000, 226 000)	26.2 (13.2, 47.0)
Maldives	0.5 (0.0, 1.4)	< 500 (< 500, < 500)	NK	NG
Nepal	33.4 (23.1, 43.8)	12 000 (8000, 15 500)	NK	NG
Pakistan	27.4 (0.0, 60.6)	116 000 (< 500, 173 500)	7 172 000 (5 363 000, 7 487 000)	1.6 (0.5, 3.1)
Sri Lanka	NK	NK	NK	NK
Central Asia				
Kazakhstan	44.1 (39.8, 48.4)	49 500 (30 000, 71 500)	508 000 (334 000, 572 000)	9.8 (5.4, 16.7)
Kyrgyzstan	32.9 (29.9, 36.0)	9500 (5500, 13 500)	NK	NG
Tajikistan	46.0 (41.9, 50.2)	11 000 (6500, 15 500)	NK	NG
Turkmenistan	NK	NK	NK	NK
Uzbekistan	38.8 (34.7, 43.0)	36 500 (22 500, 53 000)	1 292 000 (902 000, 1 524 000)	2.8 (1.6, 4.6)
Caribbean				
Antigua and Barbuda	–	–	NK	–
Bahamas	NK	NK	NK	NK
Barbados	–	–	NK	–
Bermuda	NK	NK	NK	NK

(*Continues*)

Table 3. (Continued)

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Commonwealth of Puerto Rico	58.8 (53.9, 63.7)	16 500 (10 000, 24 000)	35 500 (23 000, 60 500)	46.6 (22.1, 100.0)
Cuba	–	–	35 000 (13 500, 77 000)	–
Dominica	–	–	NK	–
Dominican Republic	NK	NK	68 000 (41 500, 108 000)	NK
Grenada	–	–	NK	–
Haiti	NK	NK	NK	NK
Jamaica	NK	NK	NK	NK
Saint Kitts and Nevis	–	–	NK	–
Saint Lucia	–	–	NK	–
St Vincent and the Grenadines	–	–	NK	–
Trinidad and Tobago	–	–	NK	–
Latin America				
Argentina	41.0 (37.5, 44.4)	33 000 (30 000, 36 000)	326 000 (144 000, 490 000)	10.1 (6.3, 21.0)
Belize	–	–	NK	–
Bolivia	NK	NK	NK	NK
Brazil	47.9 (44.3, 51.5)	461 000 (336 500, 596 500)	1 787 000 (1 293 000, 1 896 000)	25.8 (17.2, 38.5)
Chile	NK	NK	56 500 (31 000, 94 000)	NK
Colombia	21.6 (19.3, 24.0)	NK	409 000 (272 000, 436 000)	NK
Costa Rica	NK	NK	NK	NK
Ecuador	NK	NK	NK	NK
El Salvador	NK	NK	NK	NK
Guatemala	NK	NK	NK	NK
Guyana	NK	NK	NK	NK
Honduras	NK	NK	NK	NK
Mexico	71.5 (67.3, 75.5)	107 500 (70 500, 149 000)	532 000 (304 000, 557 000)	20.2 (11.4, 37.2)
Nicaragua	NK	NK	NK	NK
Panama	NK	NK	12 500 (7500, 13 500)	NK
Paraguay	7.4 (5.8, 9.0)	NK	NK	NK
Peru	NK	NK	167 000 (99 000, 182 000)	NK

(*Continues*)

Table 3. (Continued)

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Suriname	NK	NK	NK	NK
Uruguay	16.4 (14.1, 18.9)	1000 (< 500, 2500)	NK	NG
Venezuela	NK	NK	118 000 (58 500, 126 000)	NK
North America				
Canada	52.9 (44.5, 61.2)	65 000 (50 000, 82 000)	212 000 (136 000, 246 000)	30.7 (20.2, 49.3)
United States	39.8 (28.4, 51.3)	895 000 (353 500, 1 601 500)	2 936 000 (2 231 000, 3 826 000)	30.5 (10.9, 58.9)
Pacific Island States and Territories				
American Samoa	NK	NK	NK	NK
Federal States of Micronesia	NK	NK	NK	NK
Fiji	NK	NK	500 (< 500, 3000)	NK
French Polynesia	NK	NK	NK	NK
Guam	NK	NK	NK	NK
Kiribati	NK	NK	NK	NK
Marshall Islands	NK	NK	NK	NK
Nauru	–	–	NK	–
New Caledonia	NK	NK	NK	NK
Northern Mariana Islands	NK	NK	NK	NK
Palau	NK	NK	NK	NK
Papua New Guinea	NK	NK	94 500 (70 500, 328 000)	NK
Samoa	NK	NK	< 500 (< 500, 500)	NK
Solomon Islands	NK	NK	NK	NK
Tonga	NK	NK	NK	NK
Tuvalu	–	–	NK	–
Vanuatu	NK	NK	NK	NK
Australasia				
Australia	40.1 (36.9, 43.5)	37 500 (27 500, 48 500)	230 000 (178 000, 244 000)	16.2 (11.1, 23.2)
New Zealand	53.9 (46.8, 61.1)	12 000 (8000, 16 500)	48 500 (30 000, 62 500)	25.0 (14.7, 42.9)
Sub-Saharan Africa				
Angola	NK	NK	NK	NK
Benin	NK	NK	NK	NK
Botswana	–	–	NK	–

(*Continues*)

Table 3. (Continued)

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Burkina Faso	NK	NK	247 000 (189 000, 256 000)	NK
Burundi	NK	NK	120 000 (93 000, 459 000)	NK
Cameroon	NK	NK	164 000 (117 000, 184 000)	NK
Cape Verde	NK	NK	NK	NK
Central African Republic	–	–	15 500 (11 000, 17 500)	–
Chad	NK	NK	162 000 (111 000, 184 000)	NK
Comoros	–	–	NK	–
Congo (Kinshasa)	NK	NK	NK	NK
Cote d'Ivoire	1.3 (0.0, 7.1)	< 500 (< 500, < 500)	NK	NG
Djibouti	NK	NK	NK	NK
Equatorial Guinea	–	–	NK	–
Eritrea	–	–	NK	–
Ethiopia	NK	NK	647 000 (410 000, 726 000)	NK
Gabon	NK	NK	124 000 (90 000, 129 000)	NK
Gambia	NK	NK	17 000 (10 000, 27 000)	NK
Ghana	30.1 (25.8, 34.4)	NK	399 000 (305 000, 944 000)	NK
Guinea	NK	NK	NK	NK
Guinea-Bissau	–	–	NK	–
Kenya	12.3 (7.4, 17.7)	4000 (1000, 7500)	115 000 (42 500, 126 000)	3.3 (0.7, 9.7)
Lesotho	–	–	NK	–
Liberia	NK	NK	NK	NK
Madagascar	4.2 (1.8, 7.0)	500 (<500, 3000)	56 000 (39 000, 81 000)	1.2 (0.0, 5.2)
Malawi	NK	NK	NK	NK
Mali	NK	NK	NK	NK
Mauritania	–	–	NK	–
Mauritius	72.8 (68.8, 76.7)	5000 (1500, 9500)	NK	NG
Mozambique	50.3 (46.2, 54.4)	14 500 (< 500, 31 000)	NK	NG
Namibia	–	–	NK	–
Niger	NK	NK	NK	NK
Nigeria	4.3 (2.1, 6.8)	11 500 (2000, 27 000)	2 553 000 (1 902 000, 2 651 000)	0.5 (0.0, 1.1)
Republic of the Congo	–	–	NK	–

(*Continues*)

Table 3. (Continued)

Region and country	*Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)*	*Number of people with recent injecting drug use living with HCV viraemic infection (UI)*	*Total population living with HCV viraemic infection (UI)*	*Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)*
Rwanda	NK	NK	NK	NK
Sao Tome and Principe	–	–	NK	–
Senegal	29.5 (22.9, 36.3)	6500 (1500, 13 500)	NK	NK
Seychelles	31.5 (27.2, 36.0)	500 (500, 500)	NK	NG
Sierra Leone	NK	NK	NK	NK
Somalia	NK	NK	NK	NK
South Africa	NK	NK	356 000 (227 000, 441 000)	NK
Swaziland	NK	NK	NK	NK
Togo	NK	NK	NK	NK
Uganda	NK	NK	NK	NK
United Republic of Tanzania	20.8 (16.4, 25.4)	71 500 (41 000, 108 000)	NK	NG
Zambia	NK	NK	NK	NK
Zimbabwe	NK	NK	NK	NK
Middle East and North Africa				
Algeria	NK	NK	388 000 (140 000, 674 000)	NK
Bahrain	NK	NK	17 000 (11 000, 17 500)	NK
Cyprus	37.3 (32.9, 41.8)	< 500 (< 500, < 500)	NK	NG
Egypt	37.1 (26.7, 47.5)	NK	5 625 000 (4 007000, 6 044 000)	NK
Iraq	NK	NK	85 500 (60 500, 96 500)	NK
Israel	34.0 (28.3, 39.9)	NK	100 000 (60 000, 103 000)	NK
Jordan	NK	NK	24 500 (10 500, 29 000)	NK
Kuwait	NK	NK	NK	NK
Lebanon	17.6 (10.5, 25.2)	NK	7500 (3000, 18 000)	NK
Libyan Arab Jamahiriya	70.9 (66.4, 75.2)	1500 (500, 2000)	41 500 (32 000, 43 000)	3.3 (1.7, 5.5)
Morocco	40.4 (25.4, 55.8)	12 500 (5500, 21 000)	263 000 (190 000, 328 000)	4.7 (1.9, 8.5)
Occ. Palestinian Terr.	31.2 (26.3, 36.2)	NK	NK	NK
Oman	NK	NK	15 500 (12 000, 17 500)	NK
Qatar	NK	NK	37 500 (29 500, 40 000)	NK
Saudi Arabia	58.3 (53.7, 63.0)	NK	106 000 (78 500, 190 000)	NK
South Sudan	–	–	NK	–
Sudan	NK	NK	NK	NK

(*Continues*)

Table 3. (Continued)

Region and country	Prevalence of HCV viraemic infection among people with recent injecting drug use % (UI)	Number of people with recent injecting drug use living with HCV viraemic infection (UI)	Total population living with HCV viraemic infection (UI)	Proportion of people with recent injecting drug use among the total population with HCV viraemic infection % (UI)
Syrian Arab Rep.	2.5 (0.9, 4.3)	NK	554 000 (245 000, 653 000)	NK
Tunisia	21.8 (19.0, 24.7)	NK	108 000 (25 000, 123 000)	NK
Turkey	33.7 (30.7, 36.7)	NK	492 000 (271 000, 763 000)	NK
United Arab Emirates	NK	NK	131 000 (50 000, 159 000)	NK
Yemen	NK	NK	211 000 (143 000, 258 000)	NK

NK = no estimate of prevalence of that HCV was located, yet evidence of injecting drug use occurring in that country was identified; – = no evidence located that injecting drug use was occurring in this country; NR = uncertainty was not estimated around the estimate; NG = no estimate of HCV among the general population was available. PWID = people who inject drugs; UI = uncertainty interval (see methods for details of estimation).

UI = 0.4–1.7). The proportion of people with recent injecting drug use among all people living with HCV infection ranged from 1.5% (UI = 0.7–2.4) in the Middle East and North Africa to 30.5% (UI = 11.7–56.7) in North America (Table 2). Regions with people with recent injecting drug use comprising > 10% of all people living with HCV infection included Latin America (22.0%, UI = 15.3–30.4), eastern Europe (17.9%, UI = 8.2–30.9), Australasia (17.7%, UI = 12.1–25.2), the Caribbean (16.7%, 8.9–30.6) and western Europe (17.2%, UI = 9.9–30.4).

At the country level, there was very marked variation in the estimates of HCV viraemic prevalence between countries, ranging from 0.5% (UI = 0.0–1.4; Maldives) to 72.8% (UI = 68.8–76.7; Mauritius) (Fig. 1 and Table 3). The HCV viraemic prevalence was 60–80% in 10 countries, 40–< 60% in 38 countries and < 40% in 50 countries. The largest populations of people with recent injecting drug use living with HCV infection were in Russia (969 500; UI = 463 000–1 570 500), the United States (895 000; UI = 353 500–1 601 500), China (828 000; UI = 493 000–1 228 500) and Brazil (461 000, UI = 336 500–596 500) (Fig. 2 and Table 3); together, these countries accounted for 51% of people with recent injecting drug use living with HCV infection. The top 25 countries accounting for 82% of all people with recent injecting drug use living with HCV infection globally are shown in Fig. 3. The proportion of people with recent injecting drug use among all people living with HCV infection varied between 0.9% (UI = 0.4–3.0; India) and 46.6% (UI = 22.1–100.0; Commonwealth of Puerto Rico) (Fig. 4 and Table 3). The proportion of people with recent injecting drug use among all people living with HCV infection was < 10% in 21 countries, ≥ 10–< 20% in 11 countries and ≥ 20% in 23 countries.

DISCUSSION

This study estimated that there are 6.1 million (UI = 3.4–9.2) people with recent injecting drug use living with HCV infection world-wide, comprising 8.5% (UI = 4.6–13.1) of all HCV infections globally. There was considerable variation in the prevalence of HCV infection among people with recent injecting drug use at regional and country levels, and in the proportion of all HCV infection among people with recent injecting drug use. These findings highlight countries and regions where a focus upon HCV prevention and treatment among people with recent injecting drug use will be required if HCV elimination targets are to be met.

The greatest numbers of people with recent injecting drug use living with HCV infection are in eastern Europe, East and Southeast Asia and North America. Half of all people with recent injecting drug use living with HCV

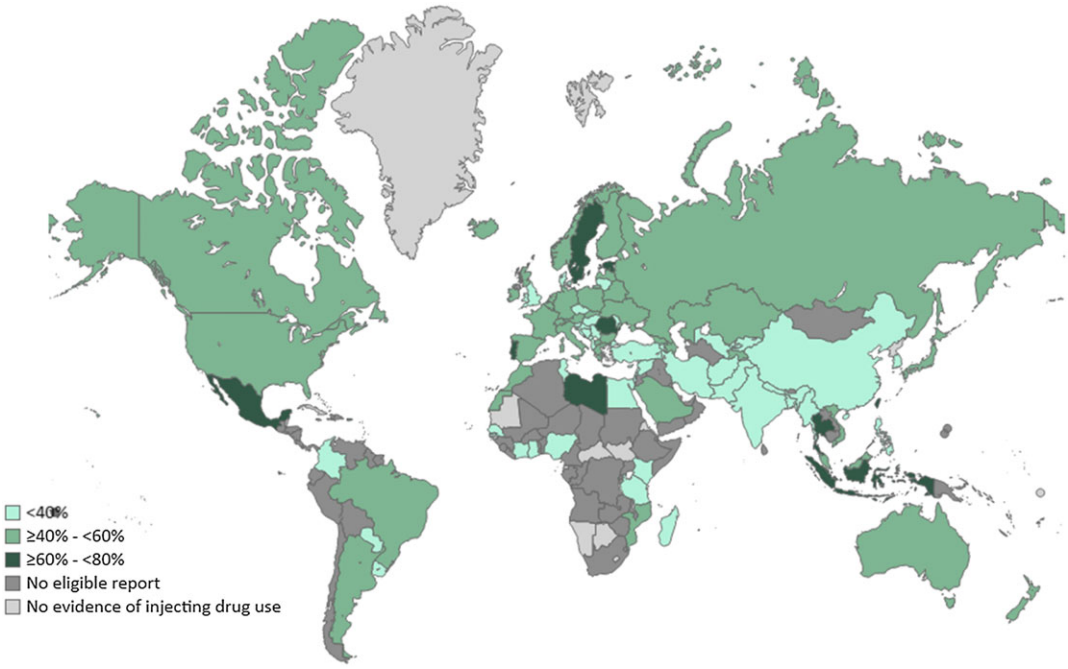

Figure 1 Estimated prevalence of hepatitis C virus (HCV) viraemic infection among people with recent injecting drug use, by country [Colour figure can be viewed at wileyonlinelibrary.com]

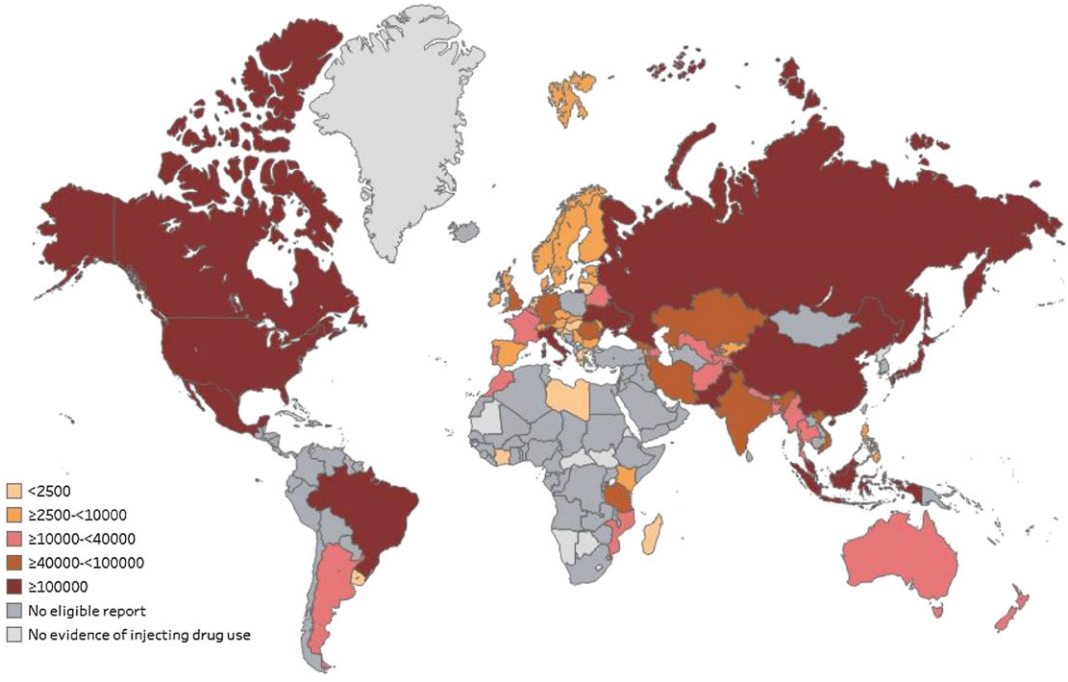

Figure 2 Estimated number of people with recent injecting drug use living with hepatitis C virus (HCV) viraemic infection, by country [Colour figure can be viewed at wileyonlinelibrary.com]

infection are from just four countries: the Russian Federation, the United States, China and Brazil. Further, the top 25 countries account for 82% of all people with recent injecting drug use living with HCV infection globally. Although PWID are a critical population for HCV elimination in many settings, concerted efforts to increase access to prevention and treatment for people with recent injecting drug use in these countries will be pivotal to the success of global HCV elimination efforts. Key among these will be harm reduction measures to prevent incident

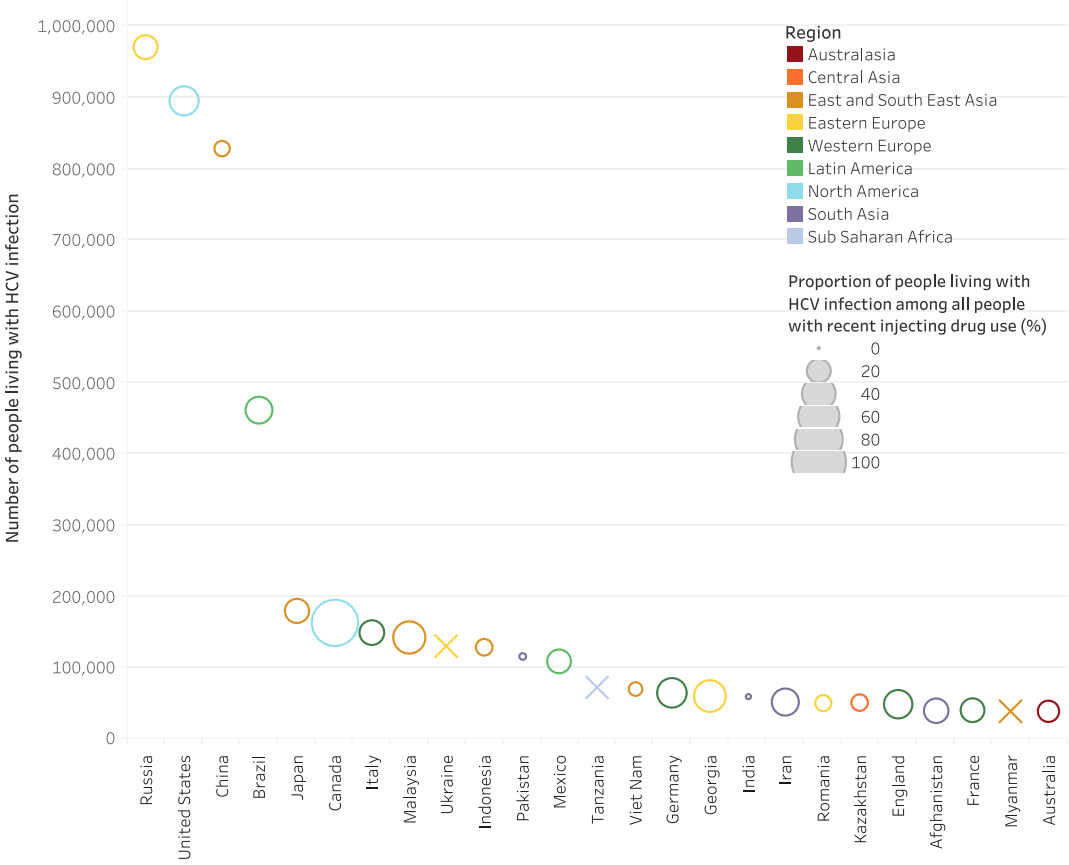

Figure 3 Countries with the greatest total number of people with hepatitis C virus (HCV) viraemic infection among people with recent injecting drug use globally. The size of the bubble represents the total proportion of hepatitis C viraemic infections that among people with recent injecting drug use. X indicates that data were not available to calculate the total proportion of viraemic HCV infections among people with recent injecting drug use [Colour figure can be viewed at wileyonlinelibrary.com]

infections [11] and increased testing, linkage to care and uptake of directly acting anti-viral therapy among people with recent injecting drug use [12,13].

Countries or territories where it is estimated that at least one-third of people living with HCV infection are people with recent injecting drug use include Georgia, Austria, Finland, Malaysia and Puerto Rico. In a further 16 countries, at least one-quarter of people living with HCV infection are people with recent injecting drug use. However, there are also 21 countries where the proportion of people living with HCV are people with recent injecting drug use is $< 10\%$. Collectively, these data highlight the variation in the proportion of overall viraemic HCV infection occurring among people with recent injecting drug use globally, reflecting the differing epidemiology of HCV in different settings. As such, different types of prevention, testing and treatment strategies will be needed to address HCV elimination targets according to the epidemiology within a given country. It should also be noted that there were 124 countries and territories where injecting drug use is known to occur, but no data were available to assess the proportion of people with HCV infection who are people with recent injecting drug use.

This study was limited to estimates among people with recent injecting drug use and will not include those who have even 'temporarily' or permanently ceased injecting. As such, this study underestimates the proportion of infections that occur among PWID within an overall epidemic, given that some infections due to injecting drug use will be among people with a history of injecting who have ceased injecting. It is critical to consider people who have recently injected drugs as well as those who have ceased injecting in the design of strategies to address HCV.

There are several limitations to this study. The search may have missed some literature (particularly grey literature), despite our wide scope of online searchers and requests for information from people across many countries. To address this possibility, we liaised with the WHO, Global Fund, United Nations Office on Drugs and Crime (UNODC) and Joint United Nations Programme on HIV and AIDS (UNAIDS) staff to contact experts within countries and obtain reports that were not available online. However, we doubt that any missed papers will alter these findings in a meaningful fashion.

Errors may have been made in data extraction and interpretation. To reduce such errors, all sources and data

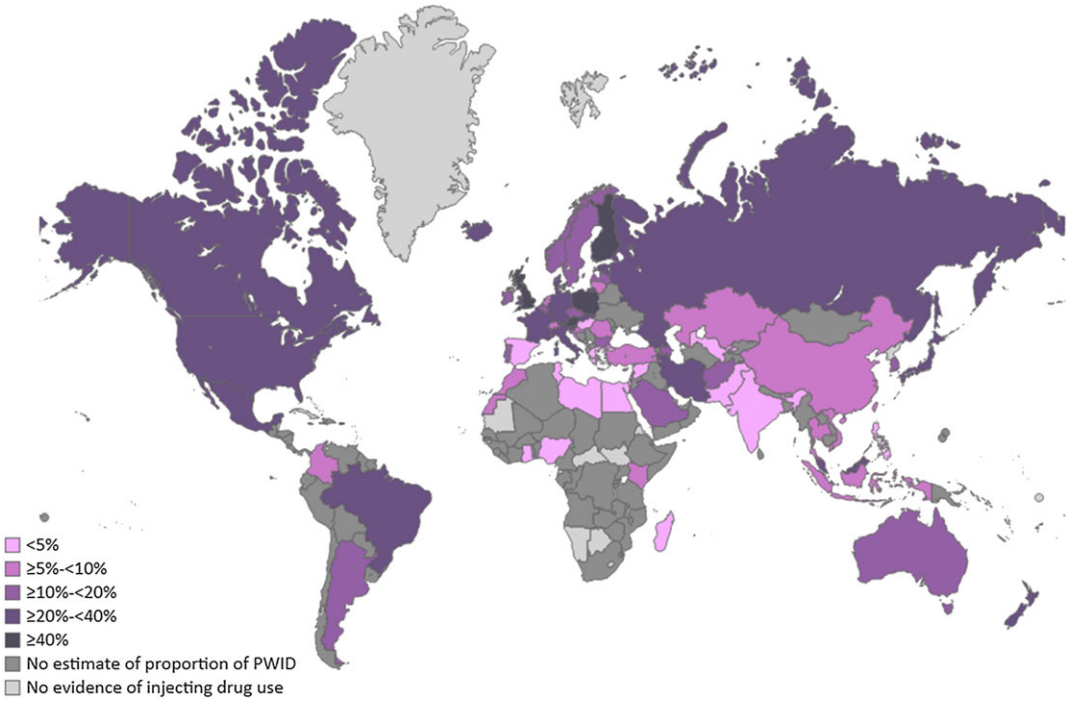

Figure 4 Estimated proportion of people with recent injecting drug use among the total population with hepatitis C virus (HCV) viraemic infection, by country [Colour figure can be viewed at wileyonlinelibrary.com]

from which the final estimates were derived were double-checked by at least two reviewers prior to inclusion with a further round prior to finalization with a third reviewer. We have online interactive presentations of these data at (https://ndarc.med.unsw.edu.au/resource/global-epidemiology-injecting-drug-use-2017) to ensure full transparency and to increase the potential for people to interact with the estimates and results, and suggest additional data sources. We encourage feedback at global.reviews@unsw.edu.au.

Although the review team searched for publications in multiple languages, we may have missed documents in languages in which we are not fluent. Those with access to data or papers/reports in other languages should contact us. It is also important to acknowledge a number of features of our approach to synthesis and imputation of estimates, driven by the gaps in data available. Although there has been a clear increase in efforts to quantify the extent of IDU and HCV among PWID, there are still major gaps in data in some regions. A hierarchical grading system was used to evaluate estimates based on geographical generalizability (e.g. from multiple sites) and across various populations of PWID (e.g. treatment and non-treatment samples). Exclusion of estimates based on a study's methodology grade was applied only to estimates of IDU and anti-HCV prevalence. Nonetheless, our recent approach, which involved pooling estimates, and our more sophisticated approach to estimating uncertainty around all our estimates, including our method of estimating uncertainty around imputed estimates, are both improvements upon previous reviews.

A limitation is the lack of country-level data to estimate the viraemic HCV prevalence (98 countries), numbers of people living with HCV (76 countries) and the proportion among the overall population living with HCV among people with recent injecting drug use (55 countries). Data were sparse in regions such as the Caribbean, Latin America, Pacific Island States and Territories, sub-Saharan Africa and the Middle East and North Africa. The estimates for these regions should be interpreted with caution, and highlights that further work is needed to improve estimates in countries from these regions.

In this study, data on HCV antibody prevalence [multiplied by an estimate of the proportion of people with HCV antibodies who would have active viraemia, 0.75 (95% CI = 0.71, 0.79)] was used to estimate the viraemic HCV prevalence, instead of actual data on HCV RNA prevalence. We opted for this approach because the data on HCV antibody prevalence were of higher quality and coverage, and there were few countries for which any data were available for HCV RNA (Table 1). Instead, we used data on the estimated viraemic prevalence from a well-defined series of nine prospective cohorts of acute HCV infection among people who inject drugs with well-characterized events of spontaneous clearance [9]. Although this provides an extremely accurate estimate of the proportion who progress to viraemic infection, the limitation is that this approach may have either over- or underestimated the true prevalence of viraemic infection in people with recent injecting drug use in various settings. In some regions, increased re-infection risk and/or higher HIV prevalence may result

in a higher viraemic prevalence, and our approach may have underestimated the viraemic prevalence [14]. Conversely, it is known that some factors (e.g. female sex) increase spontaneous clearance and can reduce the viraemic prevalence, which might have overestimated the viraemic prevalence observed. Also, these analyses did not take into consideration clearance due to HCV treatment, which might have led to an overestimation of the prevalence and numbers of people with recent injecting drug use living with HCV infection. However, this is also unlikely to have affected these estimates, as uptake of HCV treatment among PWID was very low prior to 2015 [15–19]. This study clearly demonstrates the need to integrate HCV RNA testing into future studies of HCV among people with recent injecting drug use to enable the evaluation of viraemic HCV RNA prevalence to improve national, regional and global estimates, particularly given that larger numbers of PWID are initiating HCV treatment (and will be anti-HCV positive, but HCV RNA-negative).

Denominator data are also subject to limitations. General population data may be in error for some countries where accurate census data are lacking. Population sizes of people with recent injecting drug use were based on the best available empirical estimates for each country, but there is often considerable uncertainty around estimates of this population, which translates to uncertainty in estimates of the number of PWID with HCV infection and the proportion of HCV infections occurring among people with recent injecting drug use. Estimates of HCV viraemia in people with recent injecting drug use incorporated the uncertainties in the IDU population size, anti-HCV prevalence estimate and viraemia multiplier. However, estimates of the prevalence of recent IDU and of HCV prevalence both in people with recent injecting drug use and in the general population are subject to biases, which may be responsible for some estimates that do not seem correct. Further, the extracted data were often from a single year and changes in injecting drug-user populations and HCV incidence could not be measured. This highlights the importance of continuing to improve country-level estimates of people with recent injecting drug use and those with viraemic HCV infection.

Irrespective of these limitations, this review advances our understanding of HCV prevalence and disease burden among people with recent injecting drug use. Accurate estimates of the prevalence and burden of viraemic HCV infection among people with recent injecting drug use are crucial to guide policy and practice and guide the development of strategies to enhance testing, linkage to care and treatment in this population. This review highlights that concerted efforts will be required in countries with large numbers of people infected with HCV to achieve global HCV elimination among PWID. Further, it highlights that strategies to achieve a reduction in HCV burden will need to be tailored to the individual country, based on the HCV epidemiology and the proportion of overall infections occurring in people with recent injecting drug use. Collectively, these data will inform mathematical modelling to identify strategies to increase diagnosis and treatment and reduce the number of new infections to achieve HCV elimination at a country level. Further work is needed to understand more clearly the population size of people with a history of injecting drug use and the prevalence of viraemic HCV infection and burden in those with former, but not recent, injecting drug use.

Declaration of interests

J.G. is a consultant/adviser and has received research grants from AbbVie, Bristol-Myers Squibb, Cepheid, Gilead Sciences and Merck/MSD. G.D. is a consultant/adviser and has received research grants from Abbvie, Abbot Diagnostics, Bristol Myers Squibb, Cepheid, Gilead, GlaxoSmithKline, Merck, Janssen and Roche. S.B. and H. R. have not received any remuneration. The CDA Foundation and the Polaris Observatory has not received any funding from commercial organizations. J.S. reports non-financial support from Gilead Sciences. During the past 3 years, LD has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior, Mundipharma, and Seqirus. S.L. has received investigator-initiated untied educational grants from Indivior. A.P. has received investigator-initiated untied educational grants from Mundipharma and Seqirus. E.B.C. received PhD funding from the Canadian Network on Hepatitis C. M.H. reports personal fees from Gilead, Abbvie and MSD.

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the position of the Australian Government. J.G. is supported by an NHMRC Career Development Fellowship. C. D. is supported by an NHMRC Practitioner Fellowship. J.S. acknowledges funding from a PhD scholarship from the Engineering and Physical Sciences Research Council (EPSRC). E.B.C. acknowledges funding from Canadian Network on Hepatitis C (CanHepC). A.T. has received PhD funding from the National Institute for Health Research (NIHR). M.H. and P.V. acknowledge support from NIHR Health Protection Research Unit (HPRU) in Evaluation of Interventions at the University of Bristol. P.V. acknowledges support from the NIHR HPRU in Blood-Borne and Sexually Transmitted Infections at University College London and National Institute for Drug Abuse (grant number R01 DA037773–01A1). We thank the research assistants who assisted with searches for and extraction of data from the eligible papers in this review: Erin Yong, Gabrielle Gibson, Griselda Buckland, Harriet Townsend, Julia Stadum and Laura Sergeant (NDARC, UNSW) and Diana Sergiienko (Ukrainian Institute of Public Health Policy). We also thank Mary Kumvaj, the librarian who provided specialist advice on our search strategy and search strings for the peer-reviewed literature searches. Finally, we thank the individuals who provided encouragement and support in various ways throughout the conduct of this study, including circulating requests for data, provision of in-country contacts and assistance with locating data: Annette Verster (WHO), Daniel Wolfe (Open Society Foundations), Andre Noor (EMCDDA), Eleni Kalamara (EMCDDA), Mauro Guarinieri (Global Fund), Christoforos Mallouris (UNAIDS), Susie McLean, Catherine Cook [Harm Reduction International(HRI)], Maria Phelan (HRI), Katie Stone (HRI), Riku Lehtovuori (UNODC), Keith Sabin (UNAIDS), Jinkou Zhao (Global Fund), Vladimir Poznyak (WHO) and Gilberto Gerra (UNODC). Assistance in sourcing and verifying data was provided by many individuals from government, non-government and research organizations around the world, for which we are thankful. These individuals are listed in the Appendix (p. 154).

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