The status of hepatitis C virus infection among people who inject drugs in the Middle East and North Africa

Sarwat Mahmud1, Ghina R. Mumtaz1,2, Hiam Chemaitelly1, Zaina Al Kanaani1, Silva P. Kouyoumjian1, Joumana G. Hermez3 & Laith J. Abu-Raddad1,4,5

Infectious Disease Epidemiology Group, Weill Cornell Medicine-Qatar, Cornell University, Qatar Foundation, Education City, Doha, Qatar, 1 Department of Epidemiology and Population Health, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon, 2 Department of Communicable Diseases, HIV/Hepatitis/STIs Unit, World Health Organization, Regional Office for the Eastern Mediterranean, Cairo, Egypt, 3 Department of Healthcare Policy and Research, Weill Cornell Medicine, Cornell University, New York, NY, USA 4 and College of Health and Life Sciences, Hamad bin Khalifa University, Doha, Qatar 5

ABSTRACT

Background and aims People who inject drugs (PWID) are a key population at high risk of hepatitis C virus (HCV) infection. The aim of this study was to delineate the epidemiology of HCV in PWID in the Middle East and North Africa (MENA).

Methods Syntheses of data were conducted on the standardized and systematically assembled databases of the MENA HCV Epidemiology Synthesis Project, 1989–2018. Random-effects meta-analyses and meta-regressions were performed. Meta-regression variables included country, study site, year of data collection and year of publication [to assess trends in HCV antibody prevalence over time], sample size and sampling methodology. Numbers of chronically infected PWID across MENA were estimated. The Shannon Diversity Index was calculated to assess genotype diversity.

Results Based on 118 HCV antibody prevalence measures, the pooled mean prevalence in PWID for all MENA was 49.3% [95% confidence interval (CI) = 44.4–54.1%]. The country-specific pooled mean ranged from 21.7% (95% CI = 4.9–38.6%) in Tunisia to 94.2% (95% CI = 90.8–96.7%) in Libya. An estimated 221 704 PWID were chronically infected across MENA were estimated. The Shannon Diversity Index was calculated to assess genotype diversity.

Conclusion Half of people who inject drugs in the Middle East and North Africa appear to have ever been infected with hepatitis C virus, but there are large variations in antibody prevalence among countries. In addition to > 200 000 chronically infected current people who inject drugs, there is an unknown number of people who no longer inject drugs who may have acquired hepatitis C virus during past injecting drug use. Harm reduction services must be expanded, and innovative strategies need to be employed to ensure accessibility to hepatitis C virus testing and treatment.

Keywords Drug injection, genotype, HCV, MENA, prevalence, epidemiology, infection.

INTRODUCTION

The Middle East and North Africa (MENA) region is reported to have the highest prevalence of hepatitis C virus (HCV) infection globally, with approximately 20% of all chronically infected individuals residing in MENA [1,2]. Chronic HCV infection may lead to several morbidities, such as liver fibrosis, cancer and cirrhosis [3], placing a burden on health-care systems [4]. Recent development of the highly effective direct-acting antivirals (DAA) provides promising new opportunities in controlling HCV transmission and its disease burden [5]. As such, a global target for elimination of HCV infection by 2030 has been set by the World Health Organization (WHO) [6,7].

HCV is a blood-borne pathogen that is transmitted predominantly parenterally [3]. As a consequence of practices such as sharing of needles and/or syringes, people who inject drugs (PWID) are a key population at high risk of HCV infection.
infection, half of whom are estimated to have been infected with HCV globally [8]. MENA is particularly vulnerable to injecting drug use, being at the epicenter of major drug production sites and trade routes [9,10]. Recent evidence has suggested that targeting PWID for HCV screening is critical for program efficiency in identifying HCV infections [11]. A comprehensive characterization of HCV epidemiology in PWID in this region is essential to inform the expansion of harm reduction services and development of population-specific and cost-effective screening and treatment programs for HCV infection.

The aim of this study was to delineate HCV epidemiology among PWID in MENA by: (1) estimating the country-specific pooled mean HCV antibody prevalence in PWID, (2) estimating the country-specific number of chronically infected PWID, (3) identifying predictors and trends of HCV antibody prevalence in PWID as well as sources of between-study heterogeneity and (4) estimating the pooled mean proportions and diversity of HCV genotypes in PWID. This study was conducted as part of the MENA HCV Epidemiology Synthesis Project [2], an ongoing undertaking to characterize HCV epidemiology and inform key public health research, policy and programming priorities in the region.

METHODS

Data sources

All studies reporting on HCV measures in PWID in MENA were retrieved from the MENA HCV Epidemiology Synthesis Project database [2]. This comprehensive database includes several subdatabases, such as an HCV antibody prevalence subdatabase comprised of 2614 antibody prevalence studies among 49,821,739 participants, an HCV genotype frequency subdatabase comprised of 338 HCV genotype studies among 82,257 participants and an HCV ribonucleic acid (RNA) prevalence (among antibody-positive people) subdatabase comprised of 179 RNA prevalence studies among 19,680 participants.

The Synthesis Project database was developed through a series of systematic reviews for HCV infection throughout MENA [12–19]. Additional data in PWID were searched for by performing a search update of PubMed and Embase, following similar methodologies to these systematic reviews [12–19]. In brief, to perform the update, all records reporting HCV antibody prevalence and/or incidence in PWID in MENA up to November 2018 were systematically reviewed and included in this study, as informed by the Cochrane Collaboration handbook [20], and reported using the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines (Supporting information, Table S1). Broad search criteria with no language restrictions were used in all these reviews (Supporting information, Fig. S1) [12–19]. All records reporting HCV measures after 1989, the year in which existence of HCV as a virus was established [21,22], were included in these reviews [12–19].

All data included in the reviews [12–19] were identified through literature searches using international databases (PubMed and Embase), regional and country-level databases (WHO Index Medicus for the Eastern Mediterranean Region and the Iraqi Academic Scientific Journals, Iran’s Scientific Information, among others), MENA HIV/AIDS Epidemiology Synthesis Project database [23,24], abstract archives of non-indexed international conferences and gray literature comprised of public health reports and routine data reporting.

Duplicate records were excluded and the remaining unique records underwent two rounds of screening. The titles and abstracts were screened for relevance, and full texts of potentially relevant records were retrieved and further screened. References of all included full texts were also screened for additional data that may have been missed. Any document reporting primary data on HCV antibody prevalence and/or incidence was included. All records were included in an additional independent screening for HCV genotype information, regardless of whether or not they had reported HCV antibody prevalence.

In this study, MENA consists of 24 countries: Afghanistan, Algeria, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Mauritania, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, the United Arab Emirates (UAE) and Yemen.

The analysis in this study was not pre-registered and the results should be considered exploratory.

Pooled mean HCV antibody prevalence

Country-specific meta-analyses to pool HCV antibody prevalence measures were performed whenever three or more prevalence measures were available, with a minimum sample size of 25 participants for each measure. HCV antibody prevalence for the total sample was replaced with stratified measures if the sample size requirement was held for each stratum. Only one stratification level for each study was included based on an a priori sequential order of prioritizing nationality followed by sex, year and age.

All meta-analyses were performed using DerSimonian–Laird random-effects models with inverse variance weighting to pool measures [25]. Variance of each measure was stabilized using the Freeman–Tukey-type arcsine square root transformation [26]. Heterogeneity was characterized using several statistical measures [25,27]. Forest plots were visually inspected and Cochran’s Q-test was conducted, where a P-value < 0.10 was considered to indicate statistical significance [25,27]. $I^2$ and its confidence interval (CI) were calculated [25]. Prediction intervals were also
calculated to discern the distribution of true effects around the estimated mean [25,28]. Statistical analyses were performed using R version 3.4.3 [29].

**Estimation of number of HCV-infected PWID**

The country-specific number of HCV antibody-positive PWID was calculated by multiplying the country-specific pooled HCV antibody prevalence by the country-specific population size of PWID. If the country-specific pooled HCV antibody prevalence was unavailable, the pooled HCV antibody prevalence for MENA as a whole was used. This was subsequently multiplied by the region’s pooled mean fraction of HCV RNA positivity among antibody-positive PWID (i.e. the ‘viremic rate’ [30,31]) to attain the number of chronically infected PWID in each country and in MENA as a whole.

The viremic rate was estimated by performing a meta-analysis of proportion for all HCV RNA positivity data among antibody-positive PWID in MENA. The country-specific population size of PWID was derived from a systematic review and synthesis in which PWID population proportion and population size were extracted and synthesized from publications in the peer-reviewed literature, United Nations Office on Drugs and Crime (UNODC) estimates and data provided by the WHO Eastern Mediterranean Regional Office (EMRO) [32]. In countries with multiple population-size estimates, the median of these estimates was used. The estimates were subsequently updated with recent data [33–42] identified through a data and literature search.

**Predictors, trends and sources of between-study heterogeneity for HCV antibody prevalence**

Based on established methodology, [20] univariable and multivariable random-effects meta-regressions were performed to assess the predictors of HCV antibody prevalence in PWID, trend in prevalence over time and sources of between-study heterogeneity. A priori-relevant independent variables included country, study site, year of data collection and year of publication (to assess trend in HCV antibody prevalence over time), sample size (< 100 or ≥ 100) and sampling method (probability-based versus non-probability-based). Countries with three or fewer studies were lumped together as one category referred to as ‘Others’. Variables with a likelihood ratio test P-value of < 0.20 in the univariable analysis were included in the final multivariable model. Variables with a P-value of < 0.05 in the multivariable model were deemed statistically significant.

In studies where the year of data collection variable was unavailable, missing observations were imputed. This was performed by using the median of the values calculated by subtracting the year of data collection from the year of publication for each study.

Separate meta-regressions were performed in countries with ≥ 15 studies to assess the trend in HCV antibody prevalence over time.

Meta-regressions were performed on Stata version 13, using the metan command [43].

**Genotype proportions and diversity**

Individuals with untypeable genotypes were removed from the sample size of each study. Individuals with mixed genotypes contributed separately to the enumeration of each genotype. Frequency of each genotype was calculated. The pooled mean proportion for each genotype and the corresponding 95% CI were also estimated by performing random-effects meta-analyses. Diversity of genotypes was assessed by calculating the Shannon Diversity Index, with higher score indicating higher diversity [44]. Assuming highest diversity, i.e. equal distribution among the seven main genotypes [44], the largest Shannon Diversity Index score possible is 1.95 [45].

**RESULTS**

**Overview of evidence**

Supporting information, Figs S2 and S3 outline the process by which HCV incidence and/or prevalence studies and HCV genotype studies were selected in the update, as per the PRISMA flow diagram. Relative to the previous systematic reviews, the update identified no additional incidence reports, 10 additional prevalence reports and one additional genotype report.

Results using all searches combined were generated based on analysis of 118 HCV antibody measures among a total of 46493 PWID (Table 1), seven HCV RNA positivity measures among a total of 920 antibody-positive PWID (Supporting information, Table S2) and 15 genotype frequency measures among a total of 969 HCV RNA-positive PWID (Supporting information, Table S3).

PWID data were available for 12 of the 24 MENA countries. No studies were available for Algeria, Bahrain, Djibouti, Iraq, Jordan, Kuwait, Mauritania, Qatar, Somalia, Sudan, UAE and Yemen. Iran contributed the largest number of data points of HCV antibody prevalence measures (n = 60), followed by Pakistan (n = 19). HCV RNA positivity measures were available for only four countries: Afghanistan, Iran, Lebanon and Pakistan. Genotype frequency measures were available for only seven countries: Afghanistan, Iran, Lebanon, Morocco, Pakistan and Saudi Arabia.

Studies identified their samples from various study sites, such as in the community (a geographical area, such as a
Table 1: Studies reporting hepatitis C virus (HCV) antibody prevalence among people who inject drugs (PWID) across the Middle East and North Africa (MENA).

| Author, year (citation) | Year(s) of data collection | Study site | Study design | Study sampling procedure | Sample size | HCV antibody prevalence (%) |
|-------------------------|-----------------------------|------------|--------------|--------------------------|-------------|-----------------------------|
| Afghanistan (n = 17)    |                             |            |              |                          |             |                             |
| Afghanistan NACP, 2010 [46] | 2009 NS              | CS         | RDS          | 286                      | 37.1        |
| Afghanistan NACP, 2010 [46] | 2009 NS              | CS         | RDS          | 159                      | 57.9        |
| Afghanistan NACP, 2010 [46] | 2009 NS              | CS         | RDS          | 102                      | 25.5        |
| Afghanistan NACP, 2012 [47] | 2012 NS              | CS         | RDS          | 369                      | 27.6        |
| Afghanistan NACP, 2012 [47] | 2012 NS              | CS         | RDS          | 185                      | 70.8        |
| Afghanistan NACP, 2012 [47] | 2012 NS              | CS         | RDS          | 254                      | 23.6        |
| Afghanistan NACP, 2012 [47] | 2012 NS              | CS         | RDS          | 236                      | 15.3        |
| Afghanistan NACP, 2012 [47] | 2012 NS              | CS         | RDS          | 117                      | 28.2        |
| Bautista, 2010 [48]    | 2005–06 VCT            | CS         | Conv         | 153                      | 36.0        |
| Bautista, 2010 [48]    | 2005–06 VCT            | CS         | Conv         | 159                      | 37.0        |
| Bautista, 2010 [48]    | 2005–06 VCT            | CS         | Conv         | 147                      | 37.0        |
| MENA HIV Epidemiology Synthesis Project, 2011 [23,49] | 2011 NS | CS         | NS          | 4866                     | 15.7        |
| Nasir, 2011 [50]       | 2006–08 VCT            | CS         | Conv         | 340                      | 49.1        |
| Nasir, 2011 [50]       | 2006–08 VCT            | CS         | Conv         | 96                       | 12.5        |
| Nasir, 2011 [50]       | 2006–08 VCT            | CS         | Conv         | 187                      | 24.1        |
| Todd, 2007 [51]        | 2005–06 VCT            | CS         | Conv         | 458                      | 36.9        |
| Todd, 2011 [52]        | 2007–09 NS             | CS         | Conv         | 483                      | 36.1        |
| Egypt (n = 2)          |                            |            |              |                          |             |                             |
| el-Ghazzawi, 1995 [53] | NS NS                   | CC         | Conv         | 100                      | 63.0        |
| Molsen, 2015 [54]      | 2002–12 Clinical setting | CS         | Conv         | 143                      | 40.6        |
| Iran (n = 60)          |                            |            |              |                          |             |                             |
| Abadi, 2018 [55]       | 2013–14 Clinical setting | CS         | Conv         | 173                      | 53.5        |
| Alavi, 2007 [56]       | 2001–03 Clinical setting | CS         | Conv         | 104                      | 74.0        |
| Alavi, 2009 [57]       | 2001–06 Clinical setting | CS         | Conv         | 142                      | 52.1        |
| Alipour, 2013 [58]     | NS Drop-in or            | CS         | Conv         | 42                       | 35.7        |
| Alipour, 2013 [58]     |Drop-in or rehabilitation center | | | | |
| Alizadeh, 2005 [59]    | 2002 Prison              | CS         | SRS          | 149                      | 31.5        |
| Amini, 2005 [60]       | NS Blood transfusion center | CS         | Conv         | 34                       | 64.7        |
| Amiri, 2007 [61]       | 2003 Prison              | CS         | Conv         | 81                       | 88.9        |
| Asl, 2013 [62]         | 2003–5 Prison            | CS         | Conv         | 150                      | 69.3        |
| Ataei, 2010 [63]       | 2008–09 Drop-in or       | CS         | Conv         | 3284                     | 38.0        |
| Ataei, 2010 [63]       | rehabilitation center    | | | | |
| Ataei, 2011 [64]       | NS Prison                | CS         | Conv         | 1485                     | 43.4        |
| Ataei, 2011 [65]       | NS Drop-in or            | CS         | Conv         | 136                      | 19.9        |
| Davoodian, 2009 [66]   | 2002 Prison              | CS         | SRS          | 249                      | 65.5        |
| Doosti-Irani, 2017 [67] | 2015 Community        | CS         | Conv         | 119                      | 80.7        |
| Eskandarieh, 2013 [68] | NS Drop-in or            | CS         | Conv         | 258                      | 65.1        |
| Honarvar, 2013 [69]    | 2012–13 Drop-in and       | CS         | Conv         | 233                      | 40.3        |
| Hosseini, 2010 [70]    | 2006 Prison              | CS         | Conv         | 417                      | 80.1        |
| Imani, 2008 [71]       | 2004 Drop-in or          | CS         | Conv         | 133                      | 11.3        |
| Imani, 2008 [71]       | rehabilitation center    | | | | |
| Ismail, 2005 [72]      | NS Clinical setting      | CS         | Conv         | 65                       | 16.9        |
| Kaffashian, 2011 [73]  | NS Prison                | CS         | Conv         | 951                      | 41.9        |
| Kassouli, 2012 [74]    | 2009 Prison              | CS         | Conv         | 943                      | 41.6        |
| Keramat, 2011 [75]     | 2005–07 Drop-in or       | CS         | Conv         | 199                      | 63.3        |
| Keramat, 2011 [75]     | rehabilitation center    | | | | |

(Continues)
| Author, year (citation) | Year(s) of data collection | Study site | Study design | Study sampling procedure | Sample size | HCV antibody prevalence (%) |
|------------------------|----------------------------|------------|--------------|--------------------------|-------------|-----------------------------|
| Khani, 2003 [76]       | 2001                       | Prison     | CS           | Conv                     | 346         | 50.9                        |
| Kheirandish, 2009 [77] | 2006                       | Prison     | CS           | Conv                     | 61          | 67.2                        |
| Kheirandish, 2009 [77] | 2006                       | Prison     | CS           | Conv                     | 229         | 80.8                        |
| Kheirandish, 2009 [77] | 2006                       | Prison     | CS           | Conv                     | 103         | 82.5                        |
| Kheirandish, 2009 [77] | 2006                       | Prison     | CS           | Conv                     | 49          | 87.8                        |
| Khorvash, 2008 [78]    | 2005                       | Clinical setting | CS       | Conv                     | 92          | 71.0                        |
| Mehrjerdi, 2014 [79]   | 2011                       | Drop-in or rehabilitation center | CS     | Conv                     | 209         | 26.8                        |
| Meydani, 2009 [80]     | 2007–08                    | Clinical setting | CS       | Conv                     | 150         | 26.0                        |
| Mirahmadizadeh, 2004 [81] | NS                  | NS         | CS           | Conv                     | 186         | 80.1                        |
| Mirahmadizadeh, 2009 [82] | NS                  | Drop-in or rehabilitation center | CS   | SRS                      | 936         | 43.4                        |
| Mir-Nasseri, 2005 [83] | 2001–02                    | Drop-in or rehabilitation center | CS     | NS                       | 42          | 50.0                        |
| Mir-Nasseri, 2005 [83] | 2001–02                    | Drop-in or rehabilitation center | CS     | NS                       | 425         | 67.5                        |
| Mir-Nasseri, 2008 [84] | 2001–02                    | Drop-in or rehabilitation center | CS     | Conv                     | 54          | 38.9                        |
| Mir-Nasseri, 2008 [84] | 2001–02                    | Drop-in or rehabilitation center | CS     | Conv                     | 464         | 61.9                        |
| Mir-Nasseri, 2011 [85] | 2001–02                    | Drop-in or rehabilitation center | CS     | Conv                     | 518         | 69.3                        |
| Moradi, 2018 [86]      | 2015                       | Prison     | CS           | Multi-stage cluster sampling | 678         | 42.5                        |
| Momen-Heravi, 2012 [87]| NS                         | Drop-in or rehabilitation center | CS     | Multi-stage cluster sampling | 300         | 47.3                        |
| Pourahmad, 2007 [88]   | 2003                       | Prison     | CC           | Conv                     | 401         | 76.8                        |
| Rahbar, 2004 [89]      | 2001                       | Prison     | CC           | Conv                     | 101         | 59.4                        |
| Rahimi-Movahghar, 2010 [90] | 2006–07                  | Drop-in or rehabilitation center | CS     | Snowball sampling        | 859         | 34.1                        |
| Rahimi-Movahghar, 2010 [90] | 2006–07                  | Drop-in or rehabilitation center | CS     | Snowball sampling        | 36          | 44.4                        |
| Ramezani, 2014 [91]    | 2012                       | Drop-in or rehabilitation center | CS     | Conv                     | 100         | 56.0                        |
| Rostami-Jalilian, 2006 [92] | 2002–04                | Clinical setting | CS       | Conv                     | 76          | 34.2                        |
| Rostami-Jalilian, 2006 [92] | 2002–04                | Clinical setting | CS       | Conv                     | 72          | 45.8                        |
| Saleh, 2011 [93]       | 2007–08                    | Clinical setting | CC       | Conv                     | 94          | 60.6                        |
| Salehi, 2015 [94]      | 2006–11                    | Community   | CS           | Conv                     | 1327        | 13.5                        |
| Sarkari, 2012 [96]     | 2009–10                    | NS          | CS           | Conv                     | 158         | 42.4                        |
| Shahrani, 2017 [97]    | 2017                       | Drop-in or rehabilitation center | CS     | Snowball sampling        | 606         | 54.8                        |
| Sharif, 2009 [98]      | 2001–06                    | Clinical setting | CS       | Conv                     | 200         | 12.0                        |
| Shariff-Mood, 2006 [99] | 2000–05                | Clinical setting | CS       | Conv                     | 31          | 22.6                        |
| Soalian, 2012 [100]    | 2009                       | Prison     | CS           | Conv                     | 153         | 59.5                        |
| Soudabakhsh, 2008 [101] | NS                    | Clinical setting | CS       | Conv                     | 26          | 88.5                        |
| Tavanaee, 2012 [95]    | 2007–09                    | Clinical setting | CS       | Conv                     | 62          | 71.0                        |
| Tayeri, 2008 [102]     | 2000–07                    | Clinical setting | CS       | Conv                     | 106         | 75.5                        |
| Aminzadeh, 2007 [103]  | 2007                       | NS          | CS           | Conv                     | 70          | 35.7                        |
| Zali, 2001 [104]       | 1995                       | Prison     | CS           | SRS                      | 402         | 45.3                        |
| Zamani, 2007 [105]     | 2004                       | Mixed       | CS           | Conv                     | 202         | 52.0                        |
| Zamani, 2010 [106]     | 2008                       | Drop-in or rehabilitation center | CS     | Snowball sampling        | 117         | 60.7                        |

(Continues)
| Author, year (citation) | Year(s) of data collection | Study site | Study design | Study sampling procedure | Sample size | HCV antibody prevalence (%) |
|-------------------------|----------------------------|------------|--------------|---------------------------|-------------|----------------------------|
| Lebanon (n = 3)          |                            |            |              |                           |             |                            |
| Mahfoud, 2010 [107]      | 2007–08                    | NS         | CS           | RDS                       | 106         | 52.8                       |
| Merabi, 2016 [108]       | 2013                       | CS         | Conv         |                           | 94          | 23.4                       |
| Libya (n = 1)            |                            |            |              |                           |             |                            |
| Mirzoyan, 2013 [110]     | 2010–10                    | Community  | CS           | RDS                       | 328         | 94.2                       |
| Morocco (n = 3)          |                            |            |              |                           |             |                            |
| Integrated behavioral and biological survey, 2012 [111] | NS | CS | RDS | 269 | 45.6 |
| Integrated behavioral and biological survey, 2012 [111] | NS | CS | RDS | 278 | 79.2 |
| Moroccan Ministry of Health, 2014 [112] | 2013–14 | NS | CS | RDS | 212 | 45.4 |
| Oman (n = 1)             |                            |            |              |                           |             |                            |
| EMRO, 2011 [113]         | NS                         | CS         | Conv         |                           | 512         | 48.1                       |
| Pakistan (n = 19)        |                            |            |              |                           |             |                            |
| Kuo, 2006 [114]          | 2003–03                    | Clinical setting | CS | Conv | 351 | 88.0 |
| Achakzai, 2007 [115]     | 2004                       | Community  | CS           | Conv                      | 50          | 60.0                       |
| Alnaf, 2007 [116]        | 2003                       | Drop-in or rehabilitation center | CS | Conv | 161 | 94.3 |
| Abbasi, 2009 [117]       | 2003                       | Community  | CS           | Conv                      | 300         | 44.7                       |
| Butt, 2011 [118]         | NS                         | Prison     | CS           | Conv                      | 76          | 84.2                       |
| Platt, 2009 [119]        | 2007                       | Community  | CS           | RDS                       | 302         | 17.3                       |
| Platt, 2009 [119]        | 2007                       | Community  | CS           | RDS                       | 102         | 8.0                        |
| Rehan, 2009 [120]        | 2004                       | Community  | CS           | SRS                       | 399         | 87.0                       |
| Rehan, 2009 [120]        | 2004                       | Community  | CS           | SRS                       | 380         | 91.8                       |
| Rehman, 2011 [121]       | NS                         | Community  | CS           | Conv                      | 100         | 35.0                       |
| Rehman, 2011 [121]       | NS                         | Community  | CS           | Conv                      | 60          | 25.0                       |
| Rehman, 2011 [121]       | NS                         | Community  | CS           | Conv                      | 40          | 32.5                       |
| Memon, 2012 [122]        | 2007–08                    | Laboratory | CS           | Conv                      | 407         | 68.3                       |
| Daud, 2014 [123]         | 2008                       | Drop-in or rehabilitation center | CS | Conv | 81 | 77.8 |
| Akhtar, 2016 [124]       | 2012–13                    | Community  | CS           | Conv                      | 241         | 36.1                       |
| Mansha, 2017 [125]       | 2013                       | Laboratory | CS           | Conv                      | 100         | 55.0                       |
| Waheed, 2017 [126]       | 2016                       | Community  | CS           | Conv                      | 72          | 83.3                       |
| Ali, 2011 [127]          | NS                         | Mixed      | CS           | Conv                      | 42          | 14.3                       |
| Rasool, 2014 [128]       | 2009                       | Clinical setting | Coh<sup>a</sup> | Conv | 40 | 42.0 |
| Palestine (n = 4)        |                            |            |              |                           |             |                            |
| Stulhofer, 2012 [129]    | 2010                       | Other      | CS           | RDS                       | 192         | 43.8                       |
| Stulhofer, 2016 [130]    | 2013                       | NS         | CS           | TLS                       | 100         | 39.0                       |
| Stulhofer, 2016 [130]    | 2013                       | NS         | CS           | TLS                       | 83          | 33.7                       |
| Stulhofer, 2016 [130]    | 2013                       | NS         | CS           | TLS                       | 105         | 47.6                       |
| Saudi Arabia (n = 5)     |                            |            |              |                           |             |                            |
| Njoh, 1997 [131]         | 1995–96                    | Drop-in or rehabilitation center | CS | Conv | 1909 | 74.6 |
| Iqbal, 2000 [132]        | NS                         | Clinical setting | CS | Conv | 574 | 69.0 |
| Shobokshl, 2003 [133]    | 1998–2002                  | Clinical setting | CS | Conv | 913 | 14.4 |
| Alshomrani, 2015 [134]   | 2006–12                    | Clinical setting | CS | Conv | 378 | 77.8 |
| Alibrahim, 2018 [135]    | 2012                       | Drop-in or rehabilitation center | CS | Conv | 300 | 42.7 |
| Syria (n = 2)            |                            |            |              |                           |             |                            |
| Syrian Ministry of Health, 2008 [136] | 2006 | NS | CS | Snowball sampling | 57 | 21.0 |
| Othman, 2002 [137]       | NS                         | NS         | CS           | Conv                      | 38          | 60.5                       |

(Continues)
Table 1. (Continued)

| Author, year (citation) | Year(s) of data collection | Study site | Study design | Study sampling procedure | Sample size | HCV antibody prevalence (%) |
|-------------------------|----------------------------|------------|--------------|--------------------------|-------------|----------------------------|
| Tunisia (n = 1)          |                            |            |              |                          |             | 21.7                       |
| Belarbi, 2013 [138]     | 2012                      | Clinical setting | CS          | Conv                    | 23          | 21.7                       |

NACP = National AIDS Control Program; EMRO = Eastern Mediterranean Regional Office; NS = not specified; VCT = voluntary counselling and testing; CS = cross-sectional; CC = case-control; Coh = cohort; RDS = respondent-driven sampling; Conv = convenience; SRS = simple random sampling; TLS = time-location sampling. In cohort studies the extracted HCV antibody prevalence measure was the cross-sectional baseline HCV antibody prevalence measure.

HCV antibody prevalence among PWID

HCV antibody prevalence ranged from 5.0% in a study from Lebanon [109] to 94.3% in a study from Pakistan [116] (Table 1). The median HCV antibody prevalence among all studies was 45.5%, with an interquartile range of 34.4–67.4%. Table 2 lists the estimated pooled mean antibody prevalence among PWID across MENA. The country-specific estimate ranged from 21.7% (95% CI = 4.9–38.6%) in Tunisia to 94.2% (95% CI = 90.8–96.7%) in Libya. Egypt, Iran, Libya, Morocco, Pakistan and Saudi Arabia had a prevalence estimate > 50%. The pooled mean for MENA as a whole was 49.3% (95% CI = 44.4–54.1%).

Evidence for heterogeneity in HCV antibody prevalence was observed in the majority of meta-analyses (P < 0.01; Table 2). Most of the variation in prevalence was due to true variation in prevalence across studies rather than sampling variation (I² was most often > 90%; Table 2). This was also confirmed by the wide prediction intervals (Table 2).

Estimated number of infections among PWID

Based on a total of seven identified studies (Supporting Information, Table S2), the pooled mean viremic rate was 70.4% (95% CI = 53.7–84.9%). This estimate was used in calculating the number of chronic infections for each country and for MENA as a whole.

Table 2 lists the estimated number of HCV antibody-positive PWID and the estimated number of chronically infected PWID in each country and in MENA as a whole. The largest number of chronically infected PWID was found in Iran at 68 526, followed by Pakistan at 46 554 and Egypt at 32 997. The remaining countries had a substantially smaller number of chronically infected PWID. In MENA as a whole, 314 831 PWID were estimated to be antibody-positive and 221 704 PWID were estimated to be chronically infected.

HCV antibody prevalence predictors, trends and sources of between-study heterogeneity

Table 3 lists the results of the univariable and multivariable meta-regressions. The variables country, study site and year of data collection were found to be statistically significant predictors (P < 0.2), and were therefore included in the final multivariable analysis.

In the multivariable analysis, year of data collection lost significance (P > 0.05); here, only country and study site remained statistically significant. Pakistan had a statistically significant higher HCV antibody prevalence among PWID than in Afghanistan; the adjusted OR was 5.0 (95% CI = 1.4–18.0). Prison study site had a statistically significant higher antibody prevalence among PWID than in the community; the adjusted OR was 2.6 (95% CI = 1.0–6.7).

Notably, no small-study effect, i.e. studies with smaller sample size yielding different antibody prevalence, [139] was found. Similarly, the sampling method had no effect on observed antibody prevalence. The model explained 7.7% of the variability in antibody prevalence.

Separate meta-regressions were performed for Afghanistan, Iran and Pakistan (countries with ≥ 15 studies), all of which showed no statistically significant evidence for a declining or increasing trend in antibody prevalence over time.

A sensitivity analysis was performed using only the non-imputed observations to assess the impact of the imputation on the results, and the results confirmed the results of the original meta-regression.

Genotype proportions and diversity

Table 4 lists the frequency of each HCV genotype as well as its pooled mean proportion estimate. The pooled mean proportion (expressed as a percentage) was 42.7% (95%
### Table 2 Results of the meta-analyses of hepatitis C virus (HCV) antibody prevalence measures among people who inject drugs (PWID) across the Middle East and North Africa (MENA).

| Country | Studies | Samples | HCV antibody prevalence | Pooled HCV antibody prevalence | Heterogeneity measures | Estimated number of HCV antibody-positive current PWID | Estimated number of HCV chronically infected current PWID |
|---------|---------|---------|--------------------------|--------------------------------|------------------------|-----------------------------------------------|-------------------------------------------------|
|         | Total N | Total N | Median (%) | Range (%) | Mean (%) | 95% CI Q (P-value) | Prediction interval (%) | Population size [32–42] |                                                      |
| Afghanistan | 17     | 8597   | 36.0        | 9.5–70.0 | 32.9 | 25.2–41.1 | 711.6 (P < 0.01) | 97.8% (97.2–98.2%) | 18 820 (12 435–23 000) | 6192 (3134–9453) |
| Algeria | 0      | –      | –           | –        | –   | –          | – | – | 40 961 (26 333–55 590) | 20 194 (11 692–30 074) |
| Bahrain | 0      | –      | –           | –        | –   | –          | – | – | 19 377 (13 691–25 010) | 405 (273–555) |
| Djibouti | 0      | –      | –           | –        | –   | –          | – | – | 821 (616–1026) | 32 997 (15 102–61 499) |
| Egypt | 2      | 243    | 51.8        | 40.6–63.0 | 51.6 | 30.0–73.0 | 2716.0 (P < 0.01) | 97.9% (97.6–98.1%) | 185 000 (135 000–233 000) | 97 310 (64 260–172 500) |
| Iran | 60     | 19 614 | 52.0        | 11.3–88.9 | 52.6 | 47.6–57.5 | 2716.0 (P < 0.01) | 97.9% (97.6–98.1%) | 185 000 (135 000–300 000) | 97 310 (64 260–172 500) |
| Iraq | 0      | –      | –           | –        | –   | –          | – | – | 34 673 (23 115–46 230) | 17 094 (10 263–25 010) |
| Jordan | 0      | –      | –           | –        | –   | –          | – | – | 4850 (3200–6500) | 34 673 (23 115–46 230) |
| Kuwait | 0      | –      | –           | –        | –   | –          | – | – | 40 500 (1850–8750) | 197 203 (1241–2473) |
| Lebanon | 3      | 240    | 52.8        | 5.0–52.8 | 52.8 | 4.4–54.5 | 42.6 (P < 0.01) | 95.3% (89.6–97.9%) | 3207 (1506–4908) | 802 (66–2675) |
| Libya | 1      | 328    | 94.2        | 94.2–96.7 | 94.2 | 90.8–96.7 | – | – | 3207 (1506–4908) | 4446 (2948–5943) |
| Mauritania | 0     | –      | –           | –        | –   | –          | – | – | 6908 (5181–8635) | 4188 (2677–5747) |
| Morocco | 3      | 759    | 46.2        | 40.9–71.9 | 53.0 | 33.1–72.4 | 63.6 (P < 0.01) | 96.9% (93.6–98.5%) | 18 000 (13 500–22 500) | 4446 (2948–5943) |
| Oman | 1      | 512    | 48.1        | 48.1–52.4 | 48.1 | 43.8–54.8 | – | – | 4250 (2800–5700) | 2044 (1226–2987) |
| Pakistan | 19     | 3304   | 55.0        | 8.0–93.8 | 56.2 | 41.4–70.1 | 1297.1 (P < 0.01) | 98.6% (98.3–98.8%) | 117 632 (89 500–150 000) | 66 109 (32 399–239 700) |
| Palestine | 4    | 480    | 41.4        | 33.7–47.6 | 41.6 | 36.2–47.0 | 4.3 (P = 0.23) | 29.8% (0.0–74.4%) | 1850 (1200–2500) | 770 (497–1753) |
| Qatar | 0      | –      | –           | –        | –   | –          | – | – | 1190 (780–1600) | 587 (346–866) |
| 5      | 12 298 | 69.0   | 55.5        | 0.0–100.0 | 55.5 | – | – | – | 9324 (2324–19 503) | 6566 (1636–13 734) |

(Continues)
| Country       | Total N | Total N | Median (%) | Range (%) | HCV antibody prevalence | Pooled HCV antibody prevalence | Heterogeneity measures | Population size [32–42] | Estimated number of HCV antibody-positive current PWID | Estimated number of HCV chronically infected current PWID |
|---------------|---------|---------|------------|-----------|--------------------------|-------------------------------|------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|
| Saudi Arabia  | 14.4    | 77.8    | 20.5–77.8  | 36.7–4.4  | 99.9% (99.9–99.9%       | 99.9% (P < 0.01)             |                        | 16 800 (11 336–22 264)  | 347 (53–676)                                  | 13 133 (7604–19 558)                               |
| Somalia       | 0       | –       | –          | 0–0       | –                        | –                            |                        | 1000 (750–1250)                | 18 649 (10 798–27 773)                           | 13 133 (7604–19 558)                               |
| Sudan         | 0       | –       | –          | –         | –                        | –                            |                        | 37 828 (24 319–51 337)            | 27 773 (5374–10 221)                             | 19 558 (P < 0.01)                                 |
| Libya         | 2       | 95      | 40.8       | 12.0–23.0 | 39.6                    | 7.0–78.5                     |                        | 8000 (5750–10 250)              | 3168 (403–8046)                                | 2231 (283–3738)                                  |
| Tunisia       | 1       | 23      | 21.7       | 21.7      | 4.9–23.0                 | 4.9–78.5                     |                        | 11 000 (8462–13 750)             | 2387 (435–5308)                                | 1681 (292–3738)                                  |
| UAE           | 0       | –       | –          | –         | –                        | –                            |                        | 4800 (3200–6400)                | 2366 (1421–3462)                               | 1666 (1001–2438)                                 |
| Yemen         | 0       | –       | –          | –         | –                        | –                            |                        | 19 770 (12 710–26 830)           | 9747 (5643–14 315)                              | 6864 (3974–10 221)                               |
| MENA          | 118     | 46 493  | 45.5       | 5.0–94.4  | 49.3–54.1                | 12 232.4–1270 (P < 0.01)    |                        | 638 602 (459 345–1270 101)       | 314 831 (203 949–687 125)                       | 221 704 (143 621–483 873)                         |

CI = confidence interval; UAE = United Arab Emirates; *Q* = Cochran Q statistic assessing the existence of heterogeneity in HCV antibody prevalence estimates. \( \chi^2 \) = a measure assessing the magnitude of between-study variation that is due to true differences in HCV antibody prevalence estimates across studies rather than chance. \( \beta^2 \) = prediction interval: a measure estimating the 95% interval in which the true HCV antibody prevalence in a new study will lie. \( \gamma^2 \) = weighted average calculated as too few studies were available (< 3) to perform a meta-analysis. The mean is reflective of the point study in the only study that is available. For countries with no data available, the regional pooled mean HCV antibody prevalence estimate was used to estimate the number of HCV antibody-positive current PWID. Confidence intervals were calculated based on the uncertainty intervals of the population size and the confidence intervals of the pooled mean HCV antibody prevalence estimate.
Table 3 Univariable and multivariable meta-regression models for hepatitis C virus (HCV) antibody prevalence in people who inject drugs (PWID) across the Middle East and North Africa (MENA).

| Country       | Number of studies | OR (95% CI) | P-value | LR test P-value | Variance explained adj R² (%) | aOR (95% CI) | P-value |
|---------------|-------------------|-------------|---------|-----------------|-------------------------------|--------------|---------|
| Afghanistan   | 17                | 1           | –       |                 |                               |              | –       |
| Iran          | 60                | 2.4 (1.3–4.2) | 0.004  |                |                               | 2.5 (0.8–7.8) | 0.109   |
| Pakistan      | 19                | 2.8 (1.4–5.8) | 0.005  |                |                               | 5.0 (1.4–18.0) | 0.014   |
| Palestine     | 4                 | 1.5 (0.4–4.8) | 0.525  | 0.054           | 5.1                           | 1.5 (0.4–5.2) | 0.531   |
| Saudi Arabia  | 5                 | 2.6 (0.9–7.7) | 0.084  |                 |                               | 3.5 (0.8–15.8) | 0.109   |
| Othersb       | 13                | 1.7 (0.8–3.8) | 0.173  | 0.054           | 5.1                           | 2.0 (0.7–5.2) | 0.170   |
| Community     | 14                | 1           | –       |                 |                               |              | –       |
| Clinical setting | 24          | 0.8 (0.4–1.7) | 0.580  |                |                               | 1.2 (0.5–2.7) | 0.713   |
| Drop-in or rehabilitation center | 26 | 0.9 (0.4–1.8) | 0.787  |                |                               | 1.4 (0.6–3.4) | 0.438   |
| VCT           | 7                 | 0.4 (0.2–1.1) | 0.086  | 0.188           |                               | 1.8 (0.4–8.3) | 0.478   |
| Prison        | 19                | 1.7 (0.8–3.5) | 0.173  |                |                               | 2.6 (1.0–6.7) | 0.041   |
| Not specified | 25                | 0.6 (0.3–1.3) | 0.223  | 0.034           | 6.3                           | 1.9 (0.6–5.7) | 0.269   |
| Year of data collection | 118 | 1.0 (0.9–1.0) | 0.188  | 0.188           | 0.6                           | 1.0 (0.9–1.0) | 0.643   |
| Year of publication | 118 | 1.0 (0.9–1.0) | 0.188  | 0.188           | 0.6                           | 1.0 (0.9–1.0) | 0.643   |
| Sample size   | < 100             | 34          | 1       | –               |                               |              | –       |
| ≥ 100         | 84                | 1.1 (0.7–1.7) | 0.702  | 0.702           | 0.0                           |              | –       |
| Sampling method | Non-probability-based | 91 | 1 | – | | | – |
| Probability-based | 27          | 0.9 (0.5–1.4) | 0.525  | 0.525           | 0.0                           |              | –       |

Adj=adjusted; CI = confidence interval; LR = likelihood ratio; OR = odds ratio; aOR = adjusted odds ratio; VCT = voluntary counselling and testing. aThe adjusted R-squared for the full model was 7.7%. bCountries with three or fewer studies (Egypt, Lebanon, Libya, Morocco, Oman, Syria and Tunisia) were combined into the ‘Others’ category.

Table 4 Frequency and pooled mean proportion for each hepatitis C virus (HCV) genotype across the Middle East and North Africa (MENA).

| Genotype | Studies Total | Samples n (%) | Percentage (actual studies) Median Range (%) | Percentage (meta-analysis) Mean 95% CI | Heterogeneity measures |
|----------|--------------|---------------|---------------------------------------------|---------------------------------------|-----------------------|
|          | N            |               |                                             |                                       | Q (P-value)  I² (confidence limits) Prediction interval (%) |
| Genotype 1 | 15           | 449 (46.3%)   | 41.7 (0.0–64.9) 35.9 (23.5–49.1) | 163.5 (P < 0.01) 91.4% (87.6–94.1%) 0.1–85.9 |
| Genotype 2 | 15           | 48 (5.0%)     | 0.0 (0.0–41.5) 0.5 0.0–4.2 | 85.2 (P < 0.01) 83.6% (74.2–89.5%) 0.0–23.4 |
| Genotype 3 | 15           | 422 (43.6%)   | 50.0 (0.0–100) 42.7 (31.7–54.0) | 114.0 (P < 0.01) 87.7% (81.4–91.9%) 6.2–83.9 |
| Genotype 4 | 15           | 47 (4.9%)     | 27.4 (0.0–75.0) 4.1 (0.1–11.7) | 144.0 (P < 0.01) 90.3% (85.7–93.4%) 0.0–44.7 |
| Genotype 5 | 15           | 3 (0.3%)      | 0.0 (0.0–2.9) 0.0 0.0–0.0 | 9.9 (P = 0.77) 0.0% (0.0–0.0%) 0.0–0.0 |

CI = confidence interval. aQ = Cochran Q statistic assessing the existence of heterogeneity in HCV genotype proportion estimates. bI² = A measure assessing the magnitude of between-study variation that is due to true differences in HCV genotype proportion estimates across studies rather than chance. cPrediction interval = estimates the 95% interval in which the true HCV genotype proportion estimate in a new HCV genotype study will lie.

© 2020 The Authors. Addiction published by John Wiley & Sons Ltd on behalf of Society for the Study of Addiction.
CI = 31.7–54.0%) for genotype 3, 35.9% (95% CI = 23.5–49.1%) for genotype 1, 4.1% (95% CI = 0.1–11.7%) for genotype 4, 0.5% (95% CI = 0.0–4.2%) for genotype 2 and 0.0% (95% CI = 0.0–0.0%) for genotype 5. Genotypes 6 and 7 were not found (among PWID) in any of the available studies. Genotype diversity was moderate for MENA as a whole (Shannon Diversity Index = 1.01 out of 1.95; 52.1%). Most PWID were infected by a single genotype: only 2.1% of them were coinfected by multiple genotypes.

**DISCUSSION**

We have presented a comprehensive characterization of HCV epidemiology among PWID in MENA. Generally, we found very high HCV antibody prevalence among PWID, which varied by country. Approximately half (49.3%) of PWID have ever been infected with HCV, with more than two-thirds (70.4%) of those ever being infected being chronically infected—findings that are similar to the global epidemiology of HCV in PWID [8,31]. The variables country (Pakistan, with an OR of 5.0) and study site (prison, with an OR of 2.6) were identified as statistically significant predictors of higher antibody prevalence; there was no evidence that sampling method or sample size affected the observed prevalence. No evidence was also found for any change in antibody prevalence over time. Moderate genotype diversity was observed in MENA as a whole. The pooled mean percentages of genotypes were highest in genotype 3 (42.7%), followed by genotype 1 (35.9%).

We estimated that there are approximately 221,000 chronically infected PWID in MENA (Table 2). As this estimate is only for those currently injecting, this number represents the lower bound for the number of chronically infected people who acquired HCV through injecting drug use in this region. As available studies normally investigate PWID who are currently injecting, we are unable to estimate the number of chronic infections among ex-PWID, people who injected drugs in the past, but are no longer injecting at present. In the United States, for example, the number of HCV-infected ex-PWID was found to be sevenfold higher than that of HCV-infected current PWID [140]. Therefore, the number of chronic infections due to injecting drug use in MENA could be substantially greater than the estimated 221,000 for current PWID, although probably not sevenfold higher as it is in the United States, as injecting drug use in this region appears to be more of a recent phenomenon compared to the United States [2,32].

The identified very high HCV antibody prevalence, at 49% (Table 2), among PWID indicates that there is high epidemic potential for concentrated HIV epidemics. A recent mathematical modeling study [141] as well as ecological analyses [32,142], suggest that an antibody prevalence level > 45% indicates an epidemic potential for sustainable and concentrated HIV epidemics. Indeed, reviews of the HIV epidemic among PWID in MENA [9,23,24,32,143], as well as modeling estimates [144–146], indicate emerging HIV epidemics with often high levels of infection incidence.

HCV antibody prevalence in PWID varied throughout, and within, countries (Table 1). In Afghanistan, for example, antibody prevalence showed subnational variation [18]. This variability may be reflective of variation in the local injecting environment, impact of expansion of harm reduction services [147] or the natural HCV epidemic dynamics among recently formed injecting networks.

Variations in antibody prevalence across MENA may also be attributed to differences in the typologies of the PWID populations and nature of their social and injecting networks [23,148]. For example, in Lebanon, where antibody prevalence was on the lower range of that observed in MENA, PWID appear to form closed small networks, with most injecting occurring in private residences and among friends [2,32,149], and thus not conducing for HCV (or HIV) transmission. In contrast, in Iran and Pakistan, where antibody prevalence was in the higher range of that observed in MENA, PWID networks appear to be well connected, with instances of injecting occurring among individuals not necessarily socially related, such as in shooting galleries [2,32,148,150], and thus conducing for infection transmission. In Pakistan, specifically, much of the injecting appears to occur in public places among groups, and with the reported use of professional injectors or ‘street doctors’, who frequently re-use injecting equipment [2,32,151–155].

Our results suggest that prisons are a setting predictive of higher HCV antibody prevalence (Table 3), possibly because of higher-risk injecting in prisons, or that this setting tends to be frequented with higher-risk PWID. Other evidence supports this conjecture, and indicated an important role for incarceration in the dynamics of HCV and HIV transmission in MENA [9,23,156,157]. This highlights the need for harm reduction and HCV/HIV testing and treatment services in prisons.

Genotype 3 was found to be the major circulating strain among PWID (Table 4), in concordance with the global association between injecting drug use and this genotype [158]. This finding, however, also reflects the fact that genotype 3 is the dominant circulating strain in Afghanistan [18,159] and Pakistan [19,159,160], also with a large presence in Iran [14,159], countries that contributed most of the genotype studies.

Despite the observed high burden of HCV and the emerging and, at times, large HIV epidemics among PWID in MENA [9,23,24,32,143,144], harm reduction services remain overall limited or essentially non-existent across countries, hindered by poor availability, quality and coverage of services, stigma, fear of legal prosecution, ineffective
governance, limited resources and competing national priorities. By 2016, needle and syringe exchange programs (NSPs) were available only in 10 countries of the region, and opioid substitution therapy (OST) in only five [161]. Such programs, when they attain high coverage, have proved successful in reducing both HCV and HIV incidence in other regions [162–164].

Within the socio-cultural and politico-legal context of the region, and with the overall reluctance of political leaders to acknowledge and deal with most affected communities, harm reduction in MENA is still the realm of non-governmental organizations (NGOs). Experience in several countries such as Morocco, Iran, and Lebanon, among others, has proved that this is a successful and feasible model to access and reach hard-to-reach communities such as PWID [23,165]. Scale-up of harm reduction and further integration of NGO services within national policies are needed to strengthen the response to the high burden of HCV and the growing burden of HIV among PWID in MENA. Recent evidence has emphasized the effectiveness of HCV DAA treatment as prevention (HCV-TasP) in achieving HCV elimination by 2030 [166,167], even in countries with very large epidemics such as Egypt and Pakistan [12,13,19,160,167,168]. Essentially, HCV-TasP effectively reduces the pool of HCV chronically infected individuals, thereby curtailing the onward transmission of the infection. Several countries, most prominently Egypt [169,170], have initiated and implemented ambitious and large DAA treatment programs to achieve elimination [171]. Evidence has highlighted the potency of combining HCV-TasP, which reduces the prevalence of chronic infection and onward transmission, with harm reduction services, such as NSP and OST programs, which reduce HCV incidence [167,172]. Integrating HCV testing and treatment in harm reduction services is integral to overcoming difficulties in accessing PWID for HCV interventions and to effectively reduce the number of chronically infected PWID.

A review of HCV, HBV and HIV among PWID globally has been recently published, in which the reported HCV antibody prevalence among PWID (48.1%) was similar to that found in this study (49.3%) [8]. However, as a consequence of our comprehensive systematic approach, including searches of national journals and databases and the gray literature, this study identified more data for MENA, covered more countries for this region, analytically examined trends and associations and reported more outcome measures and analyses (such as for genotype distribution).

This study identified key gaps in the epidemiological evidence for HCV infection among PWID in MENA. Evidence varied substantially by country, with no studies identified for 12 of the 24 MENA countries (Table 1). Several countries that reported high HCV antibody prevalence also had too few available studies, such as for Libya, with only one identified study (of high quality), but at a very high antibody prevalence of 94.2% [110]. Some studies were limited to a single metropolitan area or study site, and therefore may not be representative of the wider PWID population in the country. Indeed, from countries where there was a high number of studies, such as Iran (Table 1), there was wide variation in antibody prevalence, suggesting the possibility of bias in estimating country-specific antibody prevalence for countries with too few studies.

Only seven studies reported HCV RNA among antibody-positive PWID. Accordingly, the estimated viremic rate may not be representative of the wider PWID population in the region. However, a systematic meta-analysis of viremic rates in different populations in MENA arrived at similar values for the viremic rate, irrespective of subregion or population [30]. Similar values were also reached in the probability-based and nationally representative surveys in Egypt [173,174], in the National Health and Nutrition Examination Surveys in the United States [175] and in other population-based surveys such as in India [176], Ireland [177] and Latvia [178].

Only 15 studies reported HCV genotypes among PWID, and therefore available genotype data may not have captured the true genotype distribution and diversity in PWID. For example, the HCV epidemic in Egypt [12,13,167], the largest in MENA, is very dominated by genotype 4 [159], but there were few studies from Egypt for PWID, thus possibly underestimating the frequency of this genotype in all of PWID in MENA.

Most studies employed non-probability-based sampling; however, the results of the meta-regression indicated that this had no discernable effect on observed HCV antibody prevalence (Table 3)—this may not have limited the representativeness of these studies. High heterogeneity in antibody prevalence was observed (Table 2), but most of it remained unexplained by the considered factors in the meta-regressions (Table 3). As indicated above, we were unable to assess the number of chronically infected ex-PWID, as available studies investigated only current PWID—our estimate for the number of chronically infected PWID represents the lower bound.

Despite these limitations, we were able to identify a substantial volume of evidence on HCV infection in PWID in MENA, which facilitated diverse analyses leading to informative inferences. However, further research is needed to address the gaps in evidence. Expanding existing surveillance systems and conducting repeated integrated bio-behavioral surveillance (IBBS) surveys for HCV (and HIV) in PWID is critical in delineating HCV epidemiology in this population in countries with limited or no data [2,143,179]. These surveys need also to have a wider geographic coverage with multi-sites included, and must
incorporate innovative sampling methodologies, such as respondent-driven sampling or time-location sampling, to reach PWID populations. PWID size estimation studies and mapping is also critical in delineating the typologies of PWID injecting and sexual networks [32]. More studies of HCV viremic rate are also warranted, especially so that the viremic rate could be used to monitor the progress in scaling-up HCV treatment [30]. Addressing these gaps is critical to inform the expansion of harm reduction services and testing and treatment programs.

CONCLUSION

Our findings indicated high HCV antibody prevalence among PWID in MENA, approximately half of whom have ever been infected with this infection and one-third are chronically infected. There was no evidence for any decline in antibody prevalence in recent years. Most infections among PWID were either by genotypes 3 or 1. In addition to 221,000 chronically infected current PWID, there is an unknown number of ex-PWID who may have acquired the infection during their past injecting drug use.

The evidence collectively, and overwhelmingly, attests to the immediate need for a robust response to the epidemic among PWID. The lack of evidence of a decline in antibody prevalence and the high viremic rate emphasize that interventions are either non-existent or have not reached sufficient effectiveness, coverage and/or quality to impact the epidemiology. Without an appropriate response, elimination of HCV by 2030 may not be possible. Harm reduction and testing and treatment services must be expanded in the wider PWID community as well as in prisons, and innovative strategies need to be employed to ensure accessiblity to HCV testing and treatment and to offset decades of stigma and criminalization of this population.

Declaration of interests

None.

Acknowledgements

This publication was made possible by NPRP grant number 12S-0216-190094 and NPRP grant number 9-040-3-008 from the Qatar National Research Fund (a member of Qatar Foundation). The statements made herein are solely the responsibility of the author(s). The authors are also grateful for support provided by the Biostatistics, Epidemiology, and Biomathematics Research Core at Weill Cornell Medicine-Qatar.

References

1. World Health Organization (WHO). Global Hepatitis Report, 2017. Available at: http://www.who.int/hepatitis/
publications/global-hepatitis-report2017/en/. (accessed 3 September 2018).
2. The epidemiology of hepatitis C virus in the World Health Organization Eastern Mediterranean Region: Implications for strategic action. Eastern Mediterranean Hepatitis C Virus Epidemiology Synthesis Project. Cairo: Regional Office for the Eastern Mediterranean; 2020. ISBN: 978-92-9022-286-6 (online).
3. Lauer G. M., Walker B. D. Hepatitis C virus infection. N Engl J Med 2001; 345: 41–52.
4. Adler M., Goubau P., Nevens E., Van H. V. Hepatitis C virus: the burden of the disease. Acta Gastroenterol Belg 2002; 65: 83–6.
5. European Association for the Study of the Liver (EASL) EASL recommendations on treatment of hepatitis C 2014. J Hepatol 2014; 61: 373.
6. World Health Organization (WHO). Global Health Sector Strategy on Viral Hepatitis 2016–2021. Towards ending viral hepatitis. Geneva: WHO; 2016.
7. World Health Organization (WHO) Combating Hepatitis B and C to Reach Elimination by 2030: Advocacy Brief. Geneva: WHO; 2016.
8. Degenhardt L., Peacock A., Colledge S., Leung J., Grebely J., Vickerman P., et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Lancet Glob Health 2017; 5: e1192–e1207.
9. Mumtaz G. R., Weiss H. A., Abu-Raddad L. J. Hepatitis C virus and HIV infections among people who inject drugs in the Middle East and North Africa: a neglected public health burden J Int AIDS Soc 2015; 18: 20582.
10. United Nations Office on Drugs Crime (UNODC) World Drug Report 2010. Geneva: United Nations Publications; 2010.
11. Chemaiteilly H., Mahmoud S., Kouyoumjian S. P., Al Kanaani Z., Abu-Raddad L. J. Who to test for hepatitis C virus in the Middle East and North Africa? Pooled analyses of 2500 prevalence measures including 49 million tests. Hepatol Commun 2019; 3: 325–39.
12. Mohamoud Y. A., Mumtaz G. R., Riome S., Miller D., Abu-Raddad L. J. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. BMC Infect Dis 2013; 13: 288.
13. Kouyoumjian S., Chemaiteilly H., Abu-Raddad L. J. Characterizing hepatitis C virus epidemiology in Egypt: systematic reviews, meta-analyses, and meta-regressions. Sci Rep 2018; 8: 1661.
14. Mahmoud S., Akbarzadeh V., Abu-Raddad L. J. The epidemiology of hepatitis C virus in Iran: systematic review and meta-analyses. Sci Rep 2018; 8: 150.
15. Chemaiteilly H., Chaabna K., Abu-Raddad L. J. The epidemiology of hepatitis C virus in the Fertile Crescent: systematic review and meta-analysis. PLOS ONE 2015; 10: e0135281.
16. Fadlalla E. A., Mohamoud Y. A., Mumtaz G. R., Abu-Raddad L. J. The epidemiology of hepatitis C virus in the Maghreb region: systematic review and meta-analyses. PLOS ONE 2015; 10: e0121873.
17. Chaabna K., Kouyoumjian S. P., Abu-Raddad L. J. Hepatitis C virus epidemiology in Djibouti, Somalia, Sudan, and Yemen: systematic review and meta-analysis. PLOS ONE 2016; 11: e0149966.
18. Chemaiteilly H., Mahmoud S., Rahmani A. M., Abu-Raddad L. J. The epidemiology of hepatitis C virus in Afghanistan.
21. Choo Q.-L., Kuo G., Weiner A. J., Overby L. R., Bradley D. W., Houghton M. Isolation of a cDNA clone derived from a blood-borne non-a, non-B viral hepatitis genome. *Science* 1989; 244: 359–62.

22. Kuo G., Choo Q.-L., Alter H., Gitnick G., Redeker A., Purcell R., et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. *Science* 1989; 244: 362–4.

23. Abu-Raddad L., Akala F. A., Semini I., Riedner G., Wilson D., Tawil O. The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. *BMC Infect Dis* 2015; 15: 54–63.

24. Abu-Raddad L., Akala E. A., Semini I., Riedner G., Wilson D., Tawil O. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa: time for strategic action. *Washington DC: The World Bank Press; 2010.*

25. Borenstein M., Hedges L. V., Higgins J. P. T., Rothstein H. R. *Introduction to Meta-Analysis.* Chichester, UK: John Wiley & Sons; Ltd; 2005.

26. Freeman M. F., Tukey J. W. Transformations related to the Box-Cox transformation. *Biometrika* 1964; 51: 233–52.

27. Higgins J. P., Thompson S. G., Deeks J. J., Altman D. G. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327: 557–60.

28. Higgins J. P., Thompson S. G., Spiegelhalter D. J. A re-evaluation of random-effects meta-analysis. *J R Stat Soc A Stat Soc 2009; 172: 137–59.*

29. Schwarzer G. *General Package for Meta-Analysis, version 4.1–0.* Available at: http://cran.r-project.org/web/packages/meta/meta.pdf. (Accessed on November 5, 2018).

30. Harfouche M., Chemaitelly H., Kanaani Z., Mahmud S., Kouyoumjian S. P., Abu-Raddad L. J. The epidemiology of hepatitis C virus infection in Lebanon. *BMC Infect Dis* 2014; 14: 282.

31. Ayoub H. H., Chemaitelly H., Omon R., Abu-Raddad L. J. Hepatitis C virus infection spontaneous clearance: has it been underestimated? *Int J Infect Dis* 2015; 2018; 75: 60–6.

32. Mumtaz G. R., Weiss H. A., Thomas S. L., Riome S., Setayesh A., Horyniak D., Saifi N., et al. Updated data on the size of the people who inject drugs population in the Eastern Mediterranean Region. Cairo, Egypt: Eastern Mediterranean Regional Office of the World Health Organization; 2016.

33. Johnston GL. HIV Integrated Behavioral and Biological Surveillance Surveys—Injecting Drug Users in Tanger and Nadir, Morocco. *Kingdom of Morocco Ministry of Health and National STI/AIDS Programme.* Rabat, Morocco: Joint United Nations Programme on HIV/AIDS, and Gland Fund Unit; 2012.
and associated risk behavior in injection drug users, Kabul, Afghanistan. *Emerg Infect Dis* 2007; 13: 1327.

52. Todd C. S., Nasir A., Stanekzai M. R., Fieker K., Rasuli M. Z., Vlahov D., et al. Prevalence and correlates of HIV, syphilis, and hepatitis B and C infection and harm reduction program use among male injecting drug users in Kabul, Afghanistan: a cross-sectional assessment. *Harm Reduct J* 2011; 8: 22.

53. El-Ghazzawi E., Drew L., Hamdy L., El-Sherbini E., Sadek S.-D., Saleh E. Intravenous drug addicts: a high risk group for infection with human immunodeficiency virus, hepatitis viruses, cytomegalovirus and bacterial infections in Alexandria Egypt. *J Egypt Public Health Assoc* 1995; 70: 127–50.

54. Mohsen A., Bernier A., LeFouler L., Delarocque-Astagneau et al. HIV, hepatitis B, and hepatitis C infection among injecting drug users in Al-Farabi City, Kazakhstan. *Arch Dermatol Res* 2011; 303: 127–32.

55. Molsen A., Bernier A., LeFouler L., Delarocque-Astagneau E., El-Daly M., El-Kafrawy S., et al. Hepatitis C virus acquisition among Egyptians: analysis of a 10-year surveillance of acute hepatitis C. *Trop Med Int Health* 2015; 20: 89–97.

56. Esfahangi Mosa Abadi B., Kandelouei T., Eslami G., Asl M., Vaezjafari M. Prevalence and risk factors for occult hepatitis B and HIV infections among HCV infected intravenous drug users, Tehran, Iran. *Arch Clin Infect Dis* 2018; 13: e67968.

57. Alavi S. M., Etemadi A. HIV/HBV, HIV/HCV and HIV/HTLV-I co-infection among injecting drug users patients hospitalized at the infectious disease ward of a training hospital in Iran. *Pakistan J Med Sci* 2007; 23: 510.

58. Alavi S. M., Alavi L. Seroprevalence study of HCV among hospitalized intravenous drug users in Ahvaz, Iran (2001–2006). *J Infect Public Health* 2009; 2: 47–51.

59. Allpour A., Haghdoost A. A., Sajadi L., Zolali E. HIV prevalence and related risk behaviours among female partners of male injecting drugs users in Iran: results of a behavioural survey. *2010. Sex Transm Infect* 2013; 89: iii41–iii44.

60. Alizadeh A. H. M., Alavian S. M., Jafari K., Yazdi N. Prevalence and risk factors. *Hepatitis C virus infection and risk factors of drug using prisoners in Guilan province.* *Iran J Med Sci* 2010; 35: 609–13.

61. Amini S., Mahmoodabadi S. A., Lamian S., Joulaie M., Ahmadian M. S., Majidi A. Hepatitis C virus acquisi- tion among Zanjan prisoners. *Arch Iran Med* 2003; 6: 1–4.

62. Amini Z. M., Rezvani M., Shakib R. J., Shakib A. J. Prevalence of hepatitis C virus infection and risk factors of drug using prisoners in Guilan Province. *East Mediterr Health J* 2007; 13: 250–6.

63. Asl R. T., Esbrati B., Dell C. A., Taylor K., Afshar P., Kamali M., et al. Outcome assessment of a triangular clinic as a harm reduction intervention in Rajaei-Shahr prison, Iran. *Harm Reduct J* 2013; 10: 41.

64. Ataei B., Adibi P., Yaran M., Kassaian N., Nokhdian Z., Meshkaty M., et al. Seroepidemiology of hepatitis C in cases with history of intravenous drug use in Isfahan province, Iran. *Clin Microbiol Infect* 2010; 16: S314.

65. Ataei B., Babak A., Yaran M., Kassaian N., Nokhdian Z., Meshkaty M., et al. Hepatitis C in intravenous drug users: seroepidemiology and risk factors. *J Isfahan Med Sch* 2011; 28: 1537–45.

66. Ataei B., Meshkati M., Karimi A., Yaran M., Kassaian N., Nokhdian Z., et al. Hepatitis C screening in intravenous drug users in Golpayegan, Isfahan through community announcement: pilot study. *J Isfahan Med Sch* 2011; 28: 1581–6.

67. Davoodian P., Dadvand H., Mahoori K., Amoozandeh A., Salavati A. Prevalence of selected sexually and blood-borne infections in injecting drug user inmates of Bandar Abbas and roodan correction facilities, Iran, 2002. *Br J Infect Dis* 2009; 13: 356–8.

68. Doosti-Iranii A., Mokhhaer H., Chegini Sharafi A., Aghasadeghi M. R., Hajimiragha M., Saki M., et al. Prevalence of HIV, HBV, and HCV and related risk factors amongst male homeless people in Lorestan Province, the west of Iran. *J Res Health Sci* 2017; 17: e00373.

69. Eksandarzieh S., Nikfarjam A., Tarjoman T., Nasahi A., Jafari E., Saberi-Zaaraghandi M.-B. Descriptive aspects of injection drug users in Iran’s national harm reduction program by methadone maintenance treatment. *Iran J Public Health* 2013; 42: 588–93.

70. Honarvar B., Odoomi N., Moghadami M., Kazerooni P. A., Hassanabadi A., Dolatabadi P. Z., et al. Blood-borne hepatitis B in opiate users in Iran: a poor outlook and urgent need to change nationwide screening policy. *PLoS ONE* 2013; 8: e82230.

71. Hosseini M., Seyed A. N. S., Kheyr J. G. R., Shirkad H., Karami N. et al. Prevalence and correlates of co-infection with human immunodeficiency virus and hepatitis C virus in male injection drug users in Iran. *Archives of Iranian Medicine.* 2010; 13: 318–23.

72. Imani R., Kariati A., Rouzbahani R., Rouzbahani A. Sero-prevalence of HBV, HCV and HIV infection among intravenous drug users in Shahre-e-Kord, Islamic Republic of Iran. *East Mediterr Health J* 2008; 14: 1136–41.

73. Ismail H., Rouhollah Y., Noorah S., Masoud S., Ali K., Fateme M., et al. Investigation of intravenous drug users and determining the rate of HIV and hepatitis virus in Loghman Hakim hospital [in Persian]. *Iran J Surg* 2005; 13: 89–94.

74. Kaffashian A., Nokhodian Z., Kassaian N., Babak A., Yaran M., Shouei P., et al. The experience of hepatitis C screening among prison inmates with drug injection history. *J Isfahan Med Sch* 2011; 28: 1571–5.

75. Kassaian N., Adibi F., Kafashalina A., Yaran M., Nokhdian Z., Shouei P., et al. Hepatitis C virus and associated risk factors among prison inmates with history of drug injection in Isfahan, Iran. *Int J Prev Med* 2012; 3: S156.

76. Keramat F., Eini F., Majooabi M. Seroprevalence of HIV, HBV and HCV in persons referred to Hamadan behavioral counseling center, west of Iran. *Iran Red Crescent Med J* 2011; 13: 42.

77. Khvostov V., Zaimova V. A., Gereshchuk O. A., editors. Paracutaneous disorders and prevalence of viral infections in injection drug users. 1st National Congress of Infection in Addicts. *J Oziev Univ Med Sci* 2009; 13: 23–9.

78. Alam Mehrjerdi Z., Abarashi Z., Noroozi A., Arshad L., Zarghami M. Correlates of shared methamphetamine injection among methamphetamine-injecting treatment seekers: the first report from Iran. *Int J STD AIDS* 2014; 25: 420–7.

79. Meydani M., Fardad H., Hasanzadeh A. Sero-prevalence of HTLV-I. 2 virus among injection drug addicts in Isfahan, 2007–2008. *J Shahid Sadoughi Univ Med Sci* 2009; 17: 286–90.
81. Mirahmadizadeh A, Kadivar M, Hemmati A, Javadi A editors. Infection with HIV and hepatitis C and B viruses among injecting drug users in Shiraz, Southern Iran. International Conference on AIDS, Bangkok, Thailand: 2004.

82. Mirahmadizadeh A R, Majdzadeh R, Mohammad K, Forouzanfar M. Prevalence of HIV and hepatitis C virus infections and related behavioral determinants among injecting drug users of drop-in centers in Iran. *Iran Red Crescent Med* 2009; 11: 325–9.

83. Mir-Nasseri M, Poustchi H, Nasser-Moghadam S, Nouriaie S, Tahughoghli S, Ashfar P, et al. HCV in intravenous drug users. *Gouresh* 2005: 10: 80–6.

84. Mir-Nasseri M M, Poustchi H, Nasser-Moghadam S, Tavakkoli H, Mohammadkhani A, Ashfar P, et al. Hepatitis C seroprevalence among intravenous drug users in Tehran. *J Res Med Sci* 2008; 13: 295–302.

85. Mir-Nasseri M M, Mohammadkhani A, Tavakkoli H, Ansari E, Poustchi H. Incarceration is a major risk factor for blood-borne infection among intravenous drug users: incarceration and blood borne infection among intravenous drug users. *Hepat Monthly* 2011; 11: 19.

86. Moradi G, Gouya M M, Azimian Zavareh F, Mohamadi Bolbanabadi A, Darvishi S, Aghasaelehgi M R, et al. Prevalence and risk factors for HBV and HCV in prisoners in Iran: a national bio-behavioral surveillance survey in 2015. *Trop Med Int Health* 2018; 23: 641–9.

87. Momen-Heravi M, Afzali H, MoosaviPanah H, editors. Prevalence of anti HIV, ANTIHCV and HBSAG positive among injection drug users in Kashan-Iran. *J Clin Immunol* 2012; 32: S248.

88. Pourahmad M, Javady A, Karimi L, Ataei B, Kassaei N. Seroprevalence of and risk factors associated with hepatitis B, hepatitis C, and human immunodeficiency virus among prisoners in Iran. *Infect Dis Clin Pract* 2007; 15: 368–72.

89. Rahbar A R, Rooholamin S, Khoshnood K. Prevalence of HIV infection and other blood-borne infections in incarcerated and non-incarcerated injection drug users (IDUs) in Mashhad, Iran. *Int J Drug Policy* 2004; 15: 151–5.

90. Rahimi-Movaghar A, Raavan E M, Sohimi-Isaeddin E, Amin-Esmaili M. HIV, hepatitis C virus, and hepatitis B virus co-infections among injection drug users in Tehran. *Iran J Infect Dis* 2010; 14: e28–e13.

91. Ramenani A, Amirmoeezi R, Volki J E, Aghakhani A, Zarinfar N, McFarland W, et al. HCV, HBV, and HIV seroprevalence, coinfections, and related behaviors among male injection drug users in Arak. *AIDS Care* 2014; 26: 1122–6.

92. Rostamaljallilian M, Omid G M, Kassaei N. Relationship of hepatitis B and C with deep vein thrombosis in IV drug abusers. *Military Med* 2006; 8: 78–81.

93. Saleh M, Mohammad K, Saleh A, Asghar H, Rasool S. Prevalence of HIV, hepatitis B and C seropositivity in expired IV drug abusers in Hamedan. *Sci J Forens Med* 2011; 16: 253–7.

94. Salehi A, Naghshehrivian M, Marzban M, Bagheri Lankarani K. Prevalence of HIV, HCV, and high-risk behaviors for substance users in drop in centers in southern Iran. *J Addict Med* 2015; 9: 181–7.

95. Tavaneae S A, Khaleghi N M. Epidemiological evaluation and some species in injection drug users that admitted in infectious department of Imam Reza Hospital (2007–2009). *J Med Council* 2012; 30: 155–61.

96. Sarkari B, Ellami O, Khosravani A, Sharifi A, Tabatabaeae M, Fararouei M. High prevalence of hepatitis C infection among high risk groups in Kohgiloyeh and Boyer Ahmad Province, Southwest Iran. *Archives of Iranian Medicine* 2012;15: 271–4.

97. Sharhani A, Mehrabi Y, Noroozi A, Nasirian M, Higgs P, Hajeji A, et al. Hepatitis C virus Seroprevalence and associated risk factors among male drug injectors in Kermanshah, Iran. *Hepat Monthly* 2017; 17: e58739.

98. Shari’i M, Sherif A, Sayyah M. Frequency of HBV, HCV and HIV infections among hospitalized injecting drug users in Kashan. *Indian J Sex Transm Dis* 2009; 30: 28.

99. Shari’i-Mood B, Metamat M. Infection among hospitalized injection drug users. *J Med Sci* 2006; 6: 686–9.

100. Sofian M, Aghakhani A, Banilaz M, Azadmanesh K, Farazi A A, McFarland W, et al. Viral hepatitis and HIV infection among injection drug users in a central Iranian City. *J Addict Med* 2012; 6: 292–6.

101. Soudbakhs A, Namli S, Hadi-Jabadi-Baghi M, Kazemi B. Transfusion Transmitted Virus prevalence rate Infection Drug Users (IDUs): a cross sectional study. *Tehran University Medical Journal*. 2008;66:113–7.

102. Tayeri K, Kasaeian N, Fadaei N R, Ataei B. The prevalence of hepatitis B, hepatitis C and associated risk factors in intravenous drug addicts (IVDA) with HIV in Isfahan. *Isfahan Med School J* 2008; 26: 273–7.

103. Aminzadeh Z, Aghazadeh Sarhangi K. Seroepidemiology of HIV, syphilis, hepatitis B and C in intravenous drug users at Lohghan Hakim hospital, *J Iran Med Microbiol* 2007: 1: 53–6.

104. Zali M R, Aghazadeh R, Nowroozi A, Amir-Rasouly H. Anti-HCV antibody among Iranian IV drug users: is it a serious problem? *Arch Iran Med* 2001; 4: 115–9.

105. Zamani S, Ichikawa S, Nassirimanesh B, Vazirian M, Ichikawa K, Gouya M M, et al. Prevalence and correlates of hepatitis C virus infection among injecting drug users in Tehran. *Int J Drug Policy* 2007; 18: 359–63.

106. Zamani S, Radfar R, Nematiollahi P, Fadaie R, MeshkatFinder M, Mortazavi S, et al. Prevalence of HIV/HCV/HBV infections and drug-related risk behaviours amongst IDUs recruited through peer-driven sampling in Iran. *Int J Drug Policy* 2010; 21: 493–500.

107. Mahfouz Z, Kasak K, Kreidhe K, Shamra S, Ramia S. Distribution of hepatitis C virus genotypes among injecting drug users in Lebanon. *Viril J* 2010; 7: 96.

108. MerabZ, Najia W J, Souli M, Yabek J C, Rabeh W, Salem B A, et al. Intranasal heroin use—an emerging trend in Lebanon: a single institution study presenting sociodemographic profiles of intranasal versus intravenous users. *J Subst Abuse* 2017; 22: 391–6.

109. Ramia S, Klayme S, Namian R. Infection with hepatitis B and C viruses and human retroviruses (HTLV-I and HIV) among high-risk Lebanese patients. *Ann Trop Med Parasitol* 2003; 97: 187–92.

110. Mirzoyan L, Berendes S, Jeffery C, Thomson J, Othman H. New evidence on the HIV epidemic in Libya: why countries must implement prevention programs among people who inject drugs. *J AIDS* 2013; 62: 577–83.

111. Global Fund to Fight Aids Tuberculosis and Malaria (GATM). Joint United Nations Program on HIV/AIDS (UNAIDS), Ministry of Health (Morocco), National AIDS Control Program (Morocco), National Institute for Hygiene (INH) (Morocco), Morocco HIV Integrated Behavioral and Biological Surveillance Survey 2011–2012.
112. Observatoire National des Drogues et Addictions. Enquête integree de surveillance bio-comportementale auprès des usagers de drogues injectables à Tetouan [Morocco—Tetouan Integrated Bio-Behavioral Surveillance Surveys for Injectable Drug Users 2013–2014]. Tanger et à Nador, Morocco: Observatoire National des Drogues et Addictions; 2015.

113. Eastern Mediterranean Regional Office/World Health Organization (EMRO/WHO) Annual HIV/STI Reporting from Oman: Injecting Drug Users. Cairo, Egypt; WHO Regional Office for the Eastern Mediterranean; 2011.

114. Kuo L, Galai N, Thomas D L, Zafar T, Ahmed M A, Stratthdee S A. High HCV seroprevalence and HIV drug use risk behaviors among injection drug users in Pakistan. Harm Reduct J 2006; 3: 26.

115. Achakzi M., Kassi M., Kasi P. M. Seroprevalences and co-infections of HIV, hepatitis C virus and hepatitis B virus in injecting drug users in Quetta, Pakistan. Trop Doct 2007; 37: 43–5.

116. Altuf A., Shah S. A., Zaidi N. A., Memon A., Wray N. High risk behaviors of injection drug users registered with harm reduction programme in Karachi, Pakistan. Harm Reduct J 2007; 4: 7.

117. Abbas et S., Faqir E., Khan S., Zaidi S. K., Ahmad S. Q., Iqbal A., Khan S., Zaidi S. K. Prevalence of hepatitis C in people who inject drugs in the cities of Rawalpindi and Islamabad, Pakistan. Biomed Rep 2017; 7: 263–6.

118. Ali I., Siddique L., Rehman I. U., Khan N. U., Iqbal A., Munir I., et al. Prevalence of HCV among the high risk groups in Khyber Pakhtunkhwa. Virol J 2011; 8: 296.

119. Rehan N., Bokhari A., Nizamani N. M., Jackson D., Naqvi H. Active hepatitis C infection and HCV genotypes prevalence among injection drug users in a Saudi Arabian hospital: a point cross sectional survey. J Public Health Africa 2018; 9: 726.

120. Shobokshi O. A., Serebou F. E., Al-Drees A. Z., Mitwally A. H., Qahtani A., Shaikani I. L. Hepatitis C virus seroprevalence rate among Saudis. Saad Med J 2003; 24: 81–6.

121. Alshomrani A. T. Prevalence of human immunodeficiency virus, hepatitis C virus, and hepatitis B virus infection among heroin injectors in the central region of Saudi Arabia. Saudi Med J 2015; 36: 802–6.

122. Rehan N., Bokhari A., Nizamani N. M., Jackson D., Naqvi H. R., Quayyum K., et al. National study of reproductive tract infections among high risk groups of Lahore and Karachi. J Coll Physicians Surg Pak 2009; 19: 228–31.

123. Rehan N., Nizamani N. M., Jackson D., Naqvi H. R., Qahtani A., Shaikani I. L. Hepatitis C virus seroprevalence rate among injecting drug users in Rawalpindi and Abbottabad, Pakistan: evidence for an emerging infection-related HIV epidemic. Sex Transm Infect 2009; 85: ii17–ii22.

124. Rehan N., Bokhari A., Nizamani N. M., Jackson D., Naqvi H. R., Qahtani A., Shaikani I. L. Active hepatitis C infection and HCV genotypes prevalent among the IDUs of Khyber Pakhtunkhwa. Virol J 2011; 8: 327.

125. Memon A. R., Shalique K., Memon A., Draz A. U., Rauf M. U. A., Afzar S. Hepatitis B and C prevalence among the high risk groups of Pakistani population. A cross sectional study. Arch Public Health 2012; 70: 9.

126. Mansha S., Imran M., Shah A. M. U. H., Jamal M., Ahmed F., Atif M., et al. Hepatitis B and C virus infections among human immunodeficiency virus-infected people who inject drugs in Lahore, Pakistan. Viral Immunol 2017; 30: 366–70.

127. Ali I., Siddique L., Rehman I. U., Khan N. U., Iqbal A., Munir I., et al. Prevalence of HCV among the high risk groups in Khyber Pakhtunkhwa. Virol J 2011; 8: 296.

128. Alshomrani A. T. Prevalence of hepatitis C virus in drug-dependent patients in Jeddah, Saudi Arabia. East Afr Med J 1997; 74: 89–91.

129. S. Prevalence of antibodies to hepatitis C virus in drug-dependent patients in Jeddah, Saudi Arabia. East Afr Med J 2000; 21: 51–7.

130. Alshomrani A. T. Prevalence of hepatitis C viral infection among injecting drug users in a Saudi Arabian hospital: a point cross sectional survey. J Public Health Africa 2018; 9: 726.

131. Alshomrani A. T. Prevalence of hepatitis C viral infection among injecting drug users in a Saudi Arabian hospital: a point cross sectional survey. J Public Health Africa 2018; 9: 726.

132. Alshomrani A. T. Prevalence of hepatitis C viral infection among injecting drug users in a Saudi Arabian hospital: a point cross sectional survey. J Public Health Africa 2018; 9: 726.

133. Alshomrani A. T. Prevalence of hepatitis C viral infection among injecting drug users in a Saudi Arabian hospital: a point cross sectional survey. J Public Health Africa 2018; 9: 726.

134. Alshomrani A. T. Prevalence of hepatitis C viral infection among injecting drug users in a Saudi Arabian hospital: a point cross sectional survey. J Public Health Africa 2018; 9: 726.
175. National Health and Nutrition Examination Survey (NHANES). National Health and Nutrition Examination Survey, 1999–2012. Available at: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx (Accessed on September 15, 2018).

176. Lee M. H., Yang H. I., Yuan Y., L’Italien G., Chen C. J. Epidemiology and natural history of hepatitis C virus infection. World J Gastroenterol 2014; 20: 9270–80.

177. Thornton L., Murphy N., Jones L., Connell J., Dooley S., Gavin S., et al. Determination of the burden of hepatitis C virus infection in Ireland. Epidemiol Infect 2012; 140: 1461–8.

178. Tolmane I., Rozentale B., Keiss J., Arsa F., Brigis G., Zvaigzne A. The prevalence of viral hepatitis C in Latvia: a population-based study. Medicina 2011; 47: 76.

179. Bozicevic I, Riedner G, Calleja JM. HIV surveillance in MENA: recent developments and results. Sex Transm Infect 2013;89(Suppl 3):iii11–iii6.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist [1].

Table S2 Studies reporting hepatitis C virus (HCV) viremic rate among people who inject drugs (PWID) across countries of the Middle East and North Africa (MENA).

Table S3 Studies reporting on hepatitis C virus (HCV) genotype distribution among people who inject drugs (PWID) in the Middle East and North Africa (MENA).

Figure S1 Search criteria for systematically reviewing hepatitis C virus (HCV) data in people who inject drugs (PWID) in the Middle East and North Africa (MENA).

Figure S2 Flow chart adapted from the PRISMA 2009 guidelines [1] outlining the article selection process by which hepatitis C virus (HCV) incidence and/or prevalence studies were identified in the reviews update.

Figure S3 Flow chart adapted from the PRISMA 2009 guidelines [1] outlining the article selection process by which hepatitis C virus (HCV) genotype studies were identified.