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

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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, with the largest numbers found in Iran at 68 526 and in Pakistan at 46 554. There was no statistically significant evidence for a decline in HCV antibody prevalence over time. Genotype diversity was moderate (Shannon Diversity Index of 1.01 out of 1.95; 52.1%). The pooled mean percentage for each HCV genotype was highest in genotype 3 (42.7%) and in genotype 1 (35.9%). **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.

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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, 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 46 493 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]	2006–8	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
Mohsen, 2015 [54]	2002–12	Clinical setting	CC	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 rehabilitation center	CS	Conv	42	35.7
Alipour, 2013 [58]	NS	Drop-in or rehabilitation center	CS	Conv	226	38.1
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	Coh[a]	Conv	150	69.3
Ataei, 2010 [63]	2008–09	Drop-in or rehabilitation center	CS	Conv	3284	38.0
Ataei, 2011 [64]	NS	Prison	CS	Conv	1485	43.4
Ataei, 2011 [65]	NS	Drop-in or rehabilitation center	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 rehabilitation center	CS	Conv	258	65.1
Honarvar, 2013 [69]	2012–13	Drop-in and rehabilitation centers	CS	Conv	233	40.3
Hosseini, 2010 [70]	2006	Prison	CS	Conv	417	80.1
Imani, 2008 [71]	2004	Drop-in or rehabilitation center	CS	Conv	133	11.3
Ismail, 2005 [72]	NS	Clinical setting	CS	Conv	65	16.9
Kaffashian, 2011 [73]	NS	Prison	CS	Conv	951	41.9
Kassaian, 2012 [74]	2009	Prison	CS	Conv	943	41.6
Keramat, 2011 [75]	2005–07	Drop-in or rehabilitation center	CS	Conv	199	63.3

(***Continues***)

Table 1. (Continued)

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-Movaghar, 2010 [90]	2006–07	Drop-in or rehabilitation center	CS	Snowball sampling	859	34.1
Rahimi-Movaghar, 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
Sharifi-Mood, 2006 [99]	2000–05	Clinical setting	CS	Conv	31	22.6
Sofian, 2012 [100]	2009	Prison	CS	Conv	153	59.5
Soudbakhsh, 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***)

Table 1. (Continued)

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	Drop-in or rehabilitation center	CS	Conv	94	23.4
Ramia, 2003 [109]	NS	Clinical setting	CS	Conv	40	5.0
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	NS	CS	RDS	269	45.6
Integrated behavioral and biological survey, 2012 [111]	NS	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	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
Altaf, 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[a]	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
Shobokshi, 2003 [133]	1998–2002	Clinical setting	CS	Conv	9137	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)						
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. [a]In cohort studies the extracted HCV antibody prevalence measure was the cross-sectional baseline HCV antibody prevalence measure.

city, town, village, etc.), clinical setting (such as a hospital), drop-in center or rehabilitation center, voluntary counselling and testing center, prison or were not specified. The majority of studies used non-probability-based sampling (approximately 75%) to recruit study subjects, and had a sample size ≥ 100 (approximately 70%).

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 (I^2 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 Total N	Samples Total N	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[g]
			Median (%)	Range (%)	Mean (%)	95% CI	Q (P-value)[a]	I^2 (confidence limits)[b]	Prediction interval (%)[c]			
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%)	4.9–70.4	18 820 (12 435–23 000)	6192 (3134–9453)	4360 (2207–6657)
Algeria	0	–	–	–	–	–	–	–	–	40 961 (26 333–55 590)	20 194 (11 692–30 074)[f]	14 220 (8233–21 178)
Bahrain	0	–	–	–	–	–	–	–	–	1937 (1369–15 506)	955 (608–8388)[f]	672 (428–5907)
Djibouti	0	–	–	–	–	–	–	–	–	821 (616–1026)	405 (273–555)[f]	285 (193–391)
Egypt	2	243	51.8	40.6–63.0	51.6[d]	30.0–73.0	–	–	–	90 809 (71 485–119 633)	46 857 (21 446–87 332)	32 997 (15 102–61 499)
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%)	17.0–86.7	185 000 (135 000–300 000)	97 310 (64 260–172 500)	68 526 (45 252–121 475)
Iraq	0	–	–	–	–	–	–	–	–	34 673 (23 115–46 230)	17 094 (10 263–25 010)[f]	12 037 (7227–17 612)
Jordan	0	–	–	–	–	–	–	–	–	4850 (3200–6500)	2391 (1421–3517)[f]	1684 (1001–2476)
Kuwait	0	–	–	–	–	–	–	–	–	4050 (1850–8750)	1997 (821–4734)[f]	1406 (578–3334)
Lebanon	3	240	23.4	5.0–52.8	25.0	4.4–54.5	42.6 ($P < 0.01$)	95.3% (89.6–97.9%)	0.0–100	3207 (1506–4908)	802 (66–2675)	565 (47–1884)
Libya	1	328	94.2	94.2	94.2[e]	90.8–96.7	–	–	–	4446 (2948–5943)	4188 (2677–5747)	2949 (1885–4047)
Mauritania	0	–	–	–	–	–	–	–	–	6908 (5181–8635)	3406 (2300–4672)[f]	2398 (1620–3290)
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%)	0.0–100	18 000 (13 500–22 500)	9540 (4469–16 290)	6718 (3147–11 471)
Oman	1	512	48.1	48.1	48.1[e]	43.8–52.4	–	–	–	4250 (2800–5700)	2044 (1226–2987)	1440 (864–2103)
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%)	1.6–100	117 632 (89 500–510 000)	66 109 (32 399–239 700)	46 554 (22 815–168 797)
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%)	24.9–59.3	1850 (1200–2500)	770 (497–1753)	542 (350–1234)
Qatar	0	–	–	–	–	–	–	–	–	1190 (780–1600)	587 (346–866)[f]	413 (244–610)
	5	12 298	69.0		55.5				0.0–100.0		9324 (2324–19 503)	6566 (1636–13 734)

(*Continues*)

Table 2. (Continued)

Country	Studies Total N	Samples Total N	HCV antibody prevalence Median (%)	HCV antibody prevalence Range (%)	Pooled HCV antibody prevalence Mean (%)	Pooled HCV antibody prevalence 95% CI	Heterogeneity measures Q (P-value)[a]	Heterogeneity measures I^2 (confidence limits)[b]	Heterogeneity measures Prediction interval (%)[c]	Population size [32–42]	Estimated number of HCV antibody-positive current PWID	Estimated number of HCV chronically infected current PWID[g]
Saudi Arabia				14.4–77.8		20.5–87.6	3674.4 ($P < 0.01$)	99.9% (99.9–99.9%)		16 800 (11 336–22 264)		
Somalia	0	–	–	–	–	–	–	–	–	1000 (750–1250)	493 (53–676)[f]	347 (37–476)
Sudan	0	–	–	–	–	–	–	–	–	37 828 (24 319–51 337)	18 649 (10 798–27 773)[f]	13 133 (7604–19 558)
Syria	2	95	40.8	12.0–23.0	39.6[d]	7.0–78.5	–	–	–	8000 (5750–10 250)	3168 (403–8046)	2231 (283–3738)
Tunisia	1	23	21.7	21.7	21.7[e]	4.9–38.6	–	–	–	11 000 (8462–13 750)	2387 (415–5308)	1681 (292–3738)
UAE	0	–	–	–	–	–	–	–	–	4800 (3200–6400)	2366 (1421–3462)[f]	1666 (1001–2438)
Yemen	0	–	–	–	–	–	–	–	–	19 770 (12710–26 830)	9747 (5643–14 515)[f]	6864 (3974–10 221)
MENA	118	46 493	45.5	5.0–94.4	49.3	44.4–54.1	12 232.4 ($P < 0.01$)	99.1% (99.0–99.1%)	6.0–93.3	638 602 (459 345–1 270 101)	314 831 (203 949–687 125)	221 704 (143 621–483 873)

CI = confidence interval; UAE = United Arab Emirates. [a]Q = Cochran Q statistic assessing the existence of heterogeneity in HCV antibody prevalence estimates. [b]I^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. [c]Prediction interval: a measure estimating the 95% interval in which the true HCV antibody prevalence in a new study will lie. [d]Weighted average calculated as too few studies were available (< 3) to perform a meta-analysis. [e]The mean is reflective of the point study in the only study that is available. [f]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. [g]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).

		Univariable analysis					*Multivariable analysis*[a]	
		Number of studies	*OR (95% CI)*	*P-value*	*LR test P-value*	*Variance explained adj R^2 (%)*	*aOR (95% CI)*	*P-value*
Country	Afghanistan	17	1	–			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			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
	Others[b]	13	1.7 (0.8–3.8)	0.173	0.054	5.1	2.0 (0.7–5.2)	0.170
Study site	Community	14	1	–			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			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)	0.434	0.434	0.0	–	–
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. [a]The adjusted *R*-squared for the full model was 7.7%. [b]Countries 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).

			Percentage (actual studies)		*Percentage (meta-analysis)*		*Heterogeneity measures*		
Genotype	*Studies Total N*	*Samples n (%)*	*Median (%)*	*Range (%)*	*Mean (%)*	*95% CI*	*Q (P-value)*[a]	*I^2 (confidence limits)*[b]	*Prediction interval (%)*[c]
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. [a]Q = Cochran Q statistic assessing the existence of heterogeneity in HCV genotype proportion estimates. [b]I^2 = 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. [c]Prediction interval = estimates the 95% interval in which the true HCV genotype proportion estimate in a new HCV genotype study will lie.

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 conducive 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 conducive 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 accessibility to HCV testing and treatment and to offset decades of stigma and criminalization of this population.

Declaration of interests

None.

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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.

