Epidemiology of Hepatitis C Virus: People Who Inject Drugs and Other Key Populations

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6.1 Introduction

Hepatitis C virus (HCV) infection is a serious public health problem, with globally 71 million people estimated to be chronically infected and at risk of long-term sequelae, including liver cirrhosis and hepatocellular carcinoma [1–3]. Acute infection is typically asymptomatic, and owing to HCV's ability to evade the immune system, 70–80% of infections become chronic [4–6]. In those chronically infected, it may be decades after initial infection before significant sequelae develop. If left untreated, chronic liver disease will progress to cirrhosis in 5–20%, and 1–5% will die from decompensated cirrhosis or hepatocellular carcinoma [7]. HCV infection contributes to around 27% of liver cirrhosis cases and 25% of primary liver cancers, and resulted in an estimated 400,000 deaths worldwide from these complications in 2015 [1, 8]. Co-infections with HIV are an increasing problem in countries with HIV

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epidemics in people who inject drugs (PWID), and among men who have sex with men (MSM), and underlying viral hepatitis is becoming a major cause of death among people with HIV [1, 9].

In May 2016, the World Health Assembly adopted the first Global Health Sector Strategy (GHSS) on viral hepatitis, aimed at eliminating hepatitis B and C as public health threats [10]. To achieve elimination, continued primary prevention efforts are needed as well as secondary prevention through screening, linkage to care and treatment of people with chronic HCV infection. There is currently no vaccine for HCV; however, research in this area is ongoing [11]. Although antiviral treatment for HCV has been available since 2001, the more recent development of highly effective direct-acting antiviral (DAA) therapy, which can cure more than 95% of persons with HCV infection, has now made elimination of HCV as a public health threat a possibility [3, 12, 13]. However, the largely asymptomatic nature of the infection until its later stages hinders early diagnosis, and access to treatment remains a problem in many countries. In Canada and the USA, it has been estimated that fewer than 5% of PWID have received treatment for chronic HCV [14, 15], while in Europe, this may be under 10% [3].

HCV is usually transmitted parenterally. Within high-income countries, HCV transmission through blood products has effectively been halted, leaving PWID as the group most affected by HCV infection [16, 17]. In these countries, HCV transmission is concentrated among PWID [18, 19], with between 50 to 80% chronically infected [3, 19]. In Europe, PWID, or people who have injected in the past, are now the main group affected [20–22]. In medium- and low-income countries, however, iatrogenic HCV transmission still accounts for a significant proportion of incident infections [23].

There are high numbers of PWID among most prison populations [24], and as a consequence, the burden of HCV is often high among prisoners, with a recent global meta-analysis estimating over one-quarter of inmates are positive for anti-HCV, equating to approximately 1.65 million with chronic HCV infection [25]. Furthermore, HCV transmission within prison is not an uncommon occurrence, often due to a lack of access to harm reduction interventions [25]. In many European countries, another population group at higher risk than the general population of having a chronic infection are migrants born in countries with high endemicity of HCV [26]. There is also increasing concern surrounding HCV among MSM, particularly those living with HIV. Although they contribute less towards the overall HCV epidemic than PWID, those who are co-infected are often in urgent need of HCV treatment and prevention interventions due to accelerated liver disease progression and increased mortality [27, 28]. Finally, there is still a significant fraction (up to 45% in some countries) of acute HCV infections for which the mode of transmission cannot be identified. Suggested explanations include undisclosed risk factors and possibly transmission by acupuncture, tattooing, piercing or shaving by barbers [29–31].

The aim of the chapter is to describe the epidemiology of HCV infection among PWID and other key risk groups and to identify knowledge gaps that are important for prevention and treatment. Given that data on specific risk groups are often scarce,

we have used both epidemiological data on HCV in general population groups and among these risk groups. Our sources have been key articles and reports already known to us, complemented by a search in PubMed on 'HCV epidemiology' limited to 'reviews' (resulting in 1623 items on August 1, 2017).

6.2 People Who Inject Drugs

6.2.1 Prevalence and Trends

A recent systematic review reported on the global prevalence of injecting drug use, the sociodemographic characteristics of PWID and prevalence of HIV, HBV and HCV in this group [32]. This review estimated that 52.3% (42.4–62.1%) of current PWID have been exposed to HCV (are anti-HCV positive), equating to 8.2 (4.7–12.4) million people. In most regions and countries, more than half of PWID have been exposed to HCV. PWID in sub-Saharan Africa had a lower prevalence of anti-HCV (21.8%, 17.6–26.5) compared with regions, such as Western Europe (53.2%, 48.4–57.9), where injecting drug use has been established for longer. High anti-HCV prevalence was estimated in some countries in east and Southeast Asia (e.g. Indonesia 89.2% (85.3–92.3), Taiwan 91.0% (89.5–92.4) and Thailand 88.5% (82.6–92.9)), although the regional estimated prevalence was lower (50.3%, 37.7–62.8), largely because HCV antibody prevalence among PWID in China (43.1%, 27.5–58.6) was estimated to be lower (Fig. 6.1) [32]. It is estimated that overall about 75% of those exposed to HCV infection will have an ongoing chronic infection and are at risk of long-term sequelae [33], although there may be sizeable variation in chronicity levels between countries and PWID populations [3].

Across Europe, the HCV antibody prevalence among PWID is high overall. A European review found the estimated anti-HCV prevalence in PWID was on average almost 50 times higher than that in the general population, in the 13 countries that had estimates of prevalence in both groups [34]. In more recent data obtained by the EMCDDA, 13 countries reported on anti-HCV prevalence among national samples of PWID for the years 2014 or 2015, with prevalence ranging from 15% to 84%, with prevalence in excess of 50% in five countries (Fig. 6.2) [36].

Monitoring of anti-HCV prevalence within populations over time provides an indication of possible changes in the transmission of the virus. Among EU countries reporting to EMCDDA with national trend data among PWID for the period 2010–2015, three observed an increase in HCV antibody prevalence, while four observed a decrease. Data at the subnational (local, regional) level are important as HCV prevalence can be very heterogeneous, and studies in Europe have shown local increases in prevalence in Budapest (Hungary), Sofia (Bulgaria) and Vienna (Austria) [37].

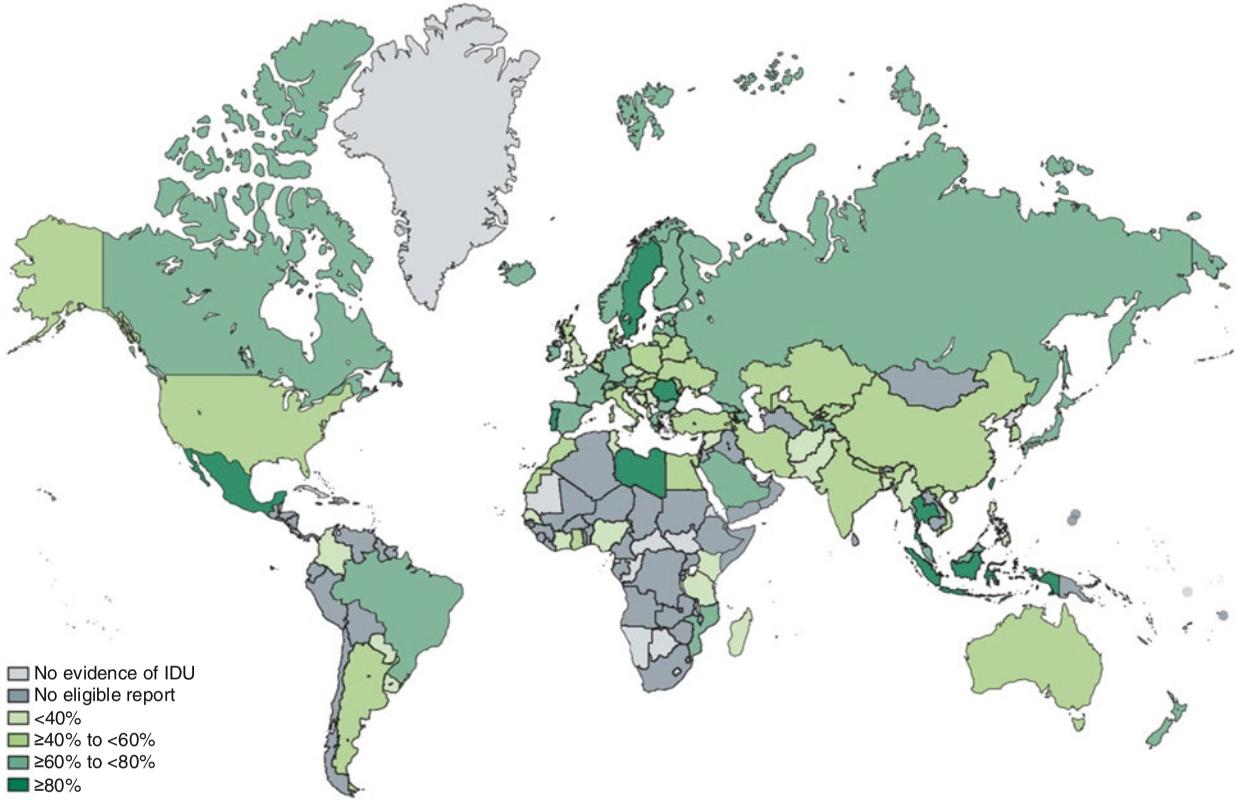


Fig. 6.1 Estimated anti-hepatitis C virus prevalence among people who inject drugs by country. Source: [32]. *IDU*: injecting drug use. No eligible report: evidence of IDU located, but no study of HCV antibody prevalence among people who inject drugs that met the eligibility criteria was located

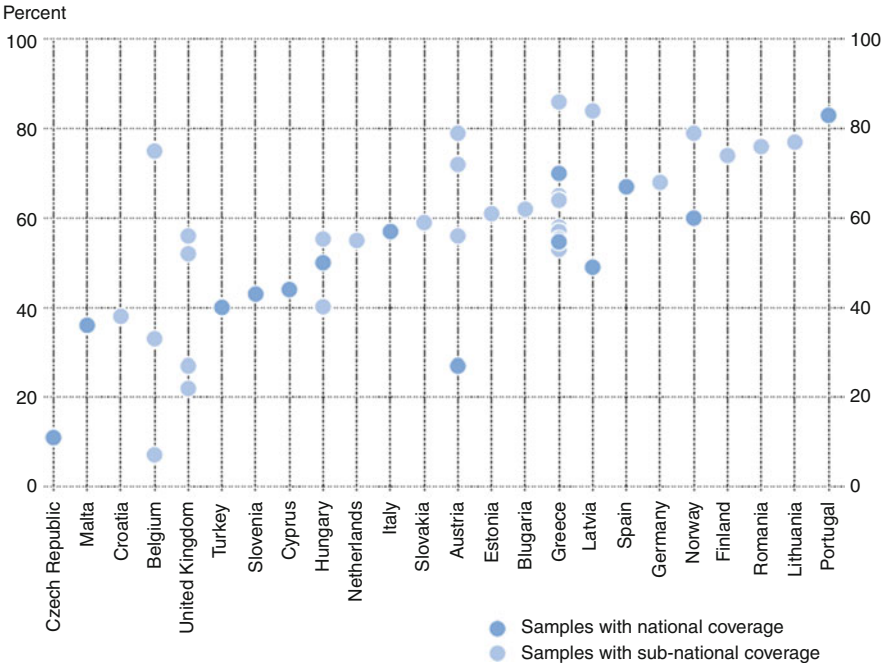


Fig. 6.2 Estimated anti-hepatitis C virus prevalence among people who inject drugs in Europe, 2014–2015. Source: [35]

6.2.2 Incidence

Incidence of new HCV infections is difficult to estimate directly as this requires studies that follow up those at risk over time; thus, globally, data on HCV incidence are not available for most countries. More recently, studies estimate incidence using biological markers of recent infection (e.g. HCV RNA in the absence of antibodies and antibody avidity) [38–44] and using indirect methods, such as back-calculations using the known number of total HCV infections in a given year and subtracting the number spontaneously cleared, cured and those who died in that year [45–47]. Globally, estimates of HCV incidence among PWID range from 5% to 45%/year [28]. As incidence in the general population is thought to mostly reflect incidence in PWID, both are discussed here.

A recent modelling study in 15 countries concluded that the overall annual incidence of HCV infection in the general population has reached its peak in most countries, although annual incidence seems to be still increasing in Russia [46]. Although surveillance data on reported diagnoses have to be interpreted with

great care, as they can reflect increases in testing and better reporting, a nationwide study from the USA for the period 2004–2014 found significant concurrent increases in reported cases of acute HCV infection and treatment admissions for injection of opioids [48]. The increase in incidence was largest in persons aged 18–29 years (400%) and 30–39 years (325%) and among non-Hispanic Whites and Hispanics. In the years 2011–2014, over 75% of the cases with acute HCV infection with risk factor data reported injecting drug use. In another study in the USA, a cohort study in five cities, the incidence of HCV infection in young PWID was 17.2 infections/100 person-years (PY) [49].

Studies reporting on the incidence of primary HCV infection among PWID in Europe have been reviewed by the EMCDDA [3]. In total, 27 studies were found that reported direct measurements of HCV incidence, covering only eight EU Member States (Czech Republic, Denmark, Finland, France, Ireland, Netherlands, Spain, Sweden) and the UK. In these studies, the incidence of HCV among PWID was often high (range 2.7–66/100 PY, median 13). The review found that studies of incidence of HCV infection among PWID were sparse across Europe, of variable quality and not easily comparable. Some of the studies had limitations such as being old, conducted in specific settings such as needle and syringe programmes or covering a small local area. While the review covered literature published from 2000 to 2012, studies published after 2005 were found only for the Netherlands and the UK [37].

As approximations of recently acquired infections or incidence, the EMCDDA monitors the prevalence of anti-HCV among young PWID (those under 25 years old) and among new PWID (those injecting for less than 2 years) among countries in Europe. Estimates for these subgroups of PWID are available only for a few countries and are often based on a small number of people. Overall, they indicate anti-HCV prevalence levels of between 20% and 60% in these groups. In common with the findings on anti-HCV prevalence among PWID of all ages and injection history, the highest estimates are among those in the south or east of Europe [37]. The latest data at the time of writing (2017) show that many of the countries reported samples where anti-HCV prevalence is 40% or more among young PWID, suggesting high levels of transmission in recent years (Fig. 6.3) [35, 36].

6.2.3 Genotypes

HCV can be classified into seven genotypes, numbered 1–7, and 67 subtypes [50]. Globally, genotype 1 (G1) is the most common (46%), followed by G3 (22%), G2 (13%) and G4 (13%) [51]. Some of the genotypes (1 and 3—in particular subtypes 1a, 1b and 3a) have become distributed widely because of transmission through blood transfusion and needle-sharing among PWID and now represent the vast majority of infections in developed countries [37, 52]. As new DAA treatments are effective across all genotypes, this variation in genotypes is now becoming less important; however, some variation in treatment success still exists by genotype [53]. Treatment regimens, duration of treatment and cure rates, as well as clinical

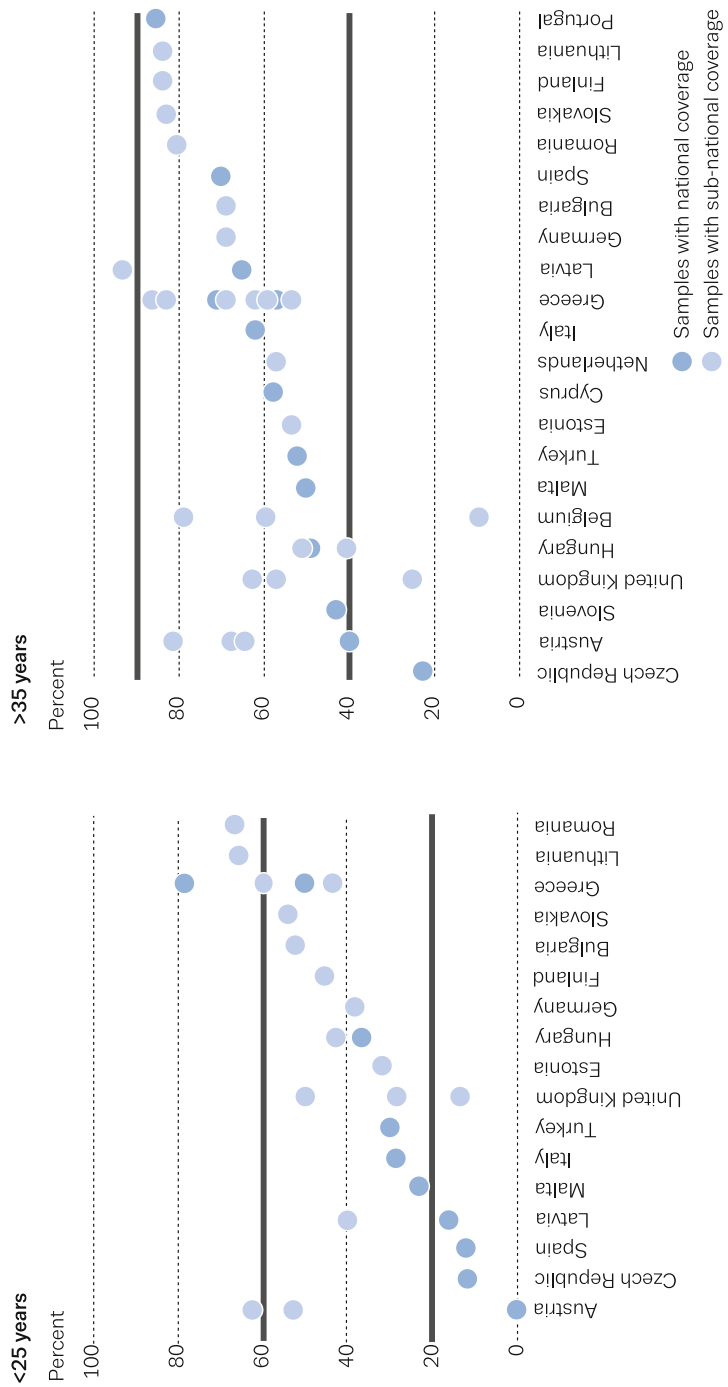


Fig. 6.3 Estimated anti-hepatitis C virus prevalence among people who inject drugs in Europe, by age; studies with national and subnational coverage, 2014–2015. Source: [35]
NB: The heavy lines in the graphics highlight the differences in the distributions of the two age groups. Studies with sample size of less than 10 are not available for all countries within artwork (similar to Fig. 6.12)

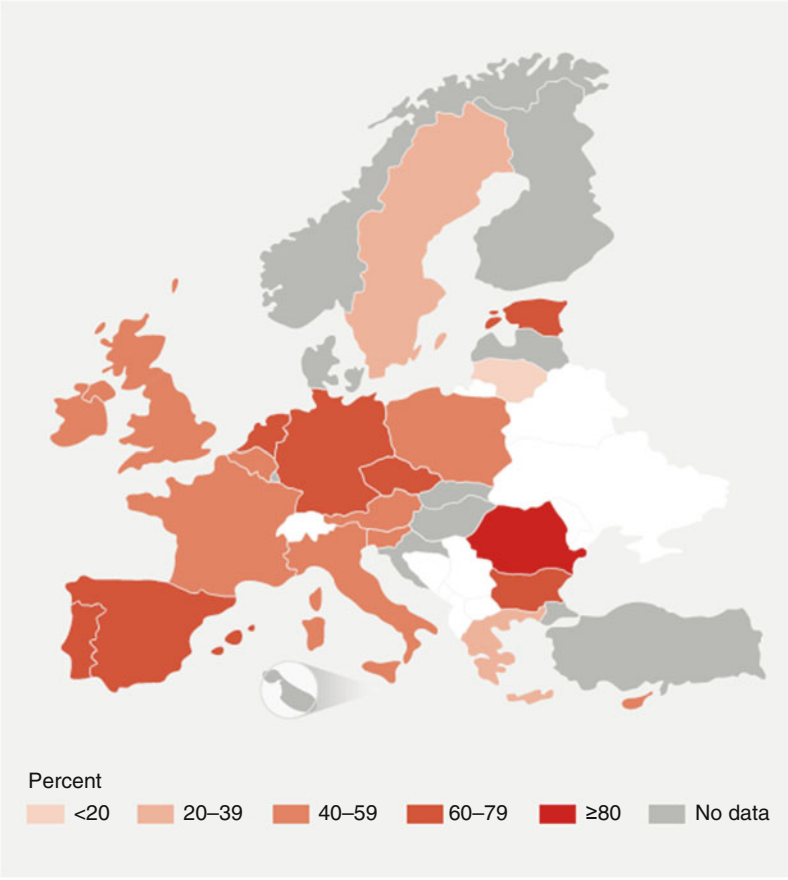


Fig. 6.4 Proportion (%) of HCV infections among people who inject drugs in Europe that are genotypes 1 or 4. Source: [3]

course, vary by genotypes, with genotype 3 being associated with an increased risk of cirrhosis and hepatocellular cancer [54, 55]. Genotyping is also an important tool to better understand the epidemiology of HCV [56].

In an EMCDDA review of HCV epidemiology among PWID in Europe [3], 36 studies with genotype data were identified from 20 EU countries, including samples for nearly 6000 HCV-infected PWID which were identified to the level of genotype or subtype. HCV genotypes 1 and 3 (subtypes 1a and 3a) are the most commonly identified among PWID in Europe. The data suggest that genotype 4, prevalent in the Middle East and Africa, particularly in Egypt [57], may be increasing. Distribution of the genotypes varied among PWID across Europe (Fig. 6.4) with genotypes 1 and 4 being predominant in certain EU countries (in particular Portugal, Romania and Spain), and showing a large variation across

the EU (prevalence of genotypes 1 or 4: 17–91%, median 53%) [3]. Caution must be exercised in interpreting these findings for a number of reasons: not all reports assessed mixed infections (to see if multiple genotypes are present); estimates for six of the countries are based on samples of fewer than 100 patients; for ten countries, only one study could be located; and some studies were based on selected populations (such as hospitalised patients) [37].

6.2.4 HIV Co-infection

Globally, it is estimated that there are approximately 2,278,400 (Interquartile range (IQR) 1,271,300—4,417,000) people living with HIV–HCV co-infections of which 59.8% (31.3—66.7%) are PWID [58]. In HIV-infected individuals, HCV co-infection is estimated at 2.4% (IQR 0.8–5.8) within general population samples, 4.0% (1.2–8.4) among pregnant women or heterosexuals, 6.4% (3.2–10.0) in MSM and 82.4% (55.2–88.5) in PWID [58]. Rates of co-infection are high in sub-Saharan Africa, with an average anti-HCV prevalence of 7% among those HIV-infected and with levels of HIV co-infection especially high among PWID [59].

A systematic review by the EMCDDA for PWID found 68 HIV–HCV co-infection estimates in Europe, among 33 published and 15 unpublished studies [3]. As HCV infection was not confirmed by RNA in many studies, antibody prevalence was used across all studies. Estimates of HIV–HCV co-infection prevalence were available for 22 countries in Europe with 11 countries having multiple estimates. Among HCV-infected PWID, co-infection with HIV ranged from 0% to 70%, with a median of 3.9%. The level of HIV-HCV co-infection correlated with the HIV prevalence. HIV prevalence among PWID differs greatly across Europe ranging from 0% to 30%. Levels of co-infection prevalence can be classed as low (not more than 4%) in 11 countries, moderate (5–15%) in three countries and high (over 15%) in seven countries (Fig. 6.5) [37].

An increase in HCV prevalence among PWID has previously been associated with an increased risk for injection-related HIV outbreaks, and therefore increases in HCV should be monitored carefully [37, 60–62].

6.2.5 Risk Factors

Sharing needle/syringes is the main route of HCV acquisition among PWID. Despite strong declines over time in some high-income countries globally, this risk behaviour generally persists among PWID [63–65]. In Europe, a similar decline has been seen in Western European countries [66–69]; however, the prevalence of sharing needles/syringes may remain high in Eastern Europe [70, 71].

The declines in needle/syringe sharing have helped reduce HIV incidence in PWID in many high-income countries, but not HCV incidence, as the shared use of other drug preparation materials persists [72, 73] and HCV is more easily transmitted than HIV [74]. The context in which PWID inject is characterised by a

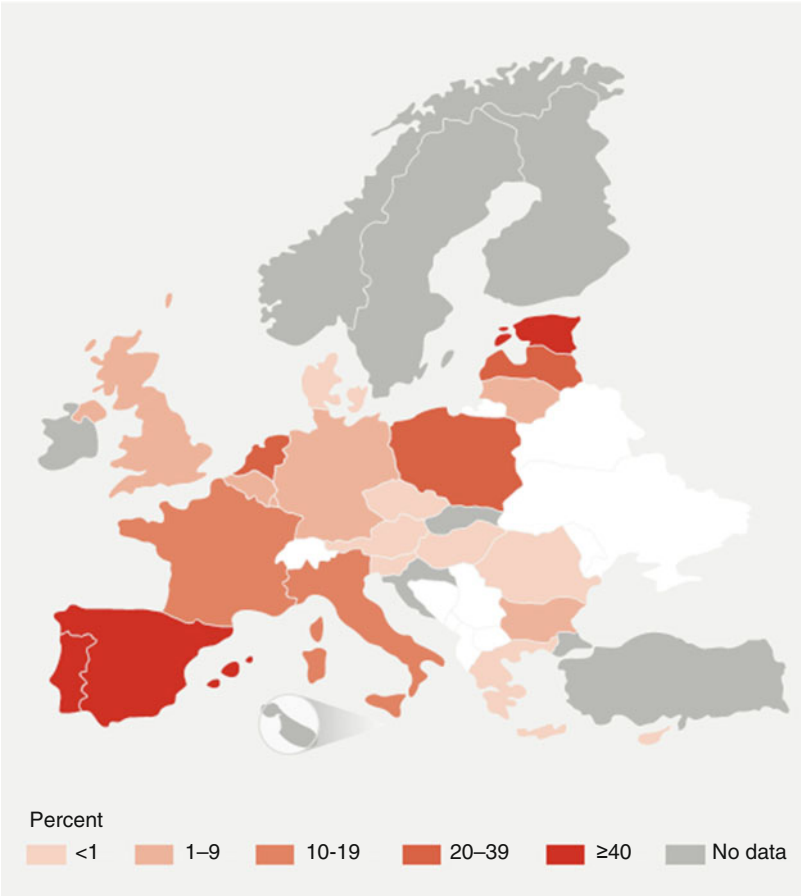


Fig. 6.5 Co-infection with HIV among HCV-infected people who inject drugs in Europe. Source: [3]

high prevalence of HCV and a wide range of injecting equipment that can transmit HCV [75]. The risk of sharing needle/syringes has been reasonably well established despite inconsistencies between individual studies. However, the discussion on the contribution of other injecting paraphernalia (e.g. cookers, filters) or behaviours (e.g. sharing drugs) and non-injecting drug paraphernalia (e.g. sniffing straws) has not yet been fully resolved.

A meta-analysis of 16 studies undertaken in Europe during 1990–2011 found that pooled prevalence and incidence of HCV were 59% and 11%, respectively, among PWID who reported never (in some studies: not recently) sharing needle/syringes. A pooled odds ratio (OR) of 3.3 (95% CI 2.4–4.6) was found, comparing HCV infection among those who ever (or recently) shared needle/syringes relative to those who reported never (or not recently) sharing. Differences were found when studies were stratified by recruitment setting (prison vs. drug treatment sites),

recruitment method (outreach vs. non-outreach), sample HCV prevalence and sample mean/median time since onset of injecting [76].

A prospective study in San Francisco in 2000–2001 found that sharing needle/syringes with an HCV-infected sex partner or a person who was not a sex partner, sharing non-sterile drug-preparation equipment, pooling money with another PWID to buy drugs, and exchanging sex for money were significantly associated with infection in young PWID [77]. In another cohort study in five cities in the USA (2002–2004), the incidence of HCV infection in young PWID was 17.2 infections/100 PY. Adjusting for confounders, the shared use of drug preparation equipment was significantly associated with HCV seroconversion (adjusted hazard ratio, 2.66; 95% confidence interval, 1.03–23.92), but needle/syringes sharing was not (adjusted hazard ratio, 0.91). It was estimated that 37% of HCV seroconversions in PWID were due to the sharing of drug preparation equipment [49]. Another analysis in a cohort of 317 PWID (1994–1997) found that among those who did not share needle/syringes, HCV seroconversion was associated with sharing drug cookers and filtration cotton (adjusted risk ratio 5.9; 95% confidence interval 1.1, 31.7); 54% of HCV infections in injection drug users who did not share needle/syringes were attributable to cooker/cotton sharing [78].

A recent experimental study suggests that the associations found in many studies with non-syringe equipment ('paraphernalia': cookers, filters) may actually reflect transmissions resulting from syringe-mediated sharing of drugs [79].

Equipment used for taking drugs by non-injecting routes might also be a risk for HCV transmission: using contaminated straws for snorting drugs might put people at risk of infection [80].

6.2.6 Disease Progression, Cirrhosis, Hepatocellular Carcinoma, Burden of Disease and Mortality

Information on the current and projected impact of HCV infection in terms of disease burden and mortality is necessary to inform public health planning and resource allocation. Burden of disease studies aim to quantify the effect of an illness in terms that are comparable across populations and between diseases. Data on the burden of disease due to HCV are however scarce, outdated or inconclusive [3, 37, 81].

Overall, an estimated 27% of liver cirrhosis cases and 25% of primary liver cancers result from HCV infection [8]. Approximately 400,000 people die each year from HCV, mostly from cirrhosis and hepatocellular carcinoma [11]. Between 1990 and 2013, global HCV deaths increased from 303,000 to 704,000 [82]. In the USA, mortality related to HCV nationally surpasses that from human immunodeficiency virus (HIV) infection [83, 84].

A systematic review of disease progression in PWID found that the pooled incidence rates of compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma were 6.6 (95% CI 4.8, 8.4), 1.1 (95% CI 0.8, 1.4) and 0.3 (95% CI 0.1, 0.6) events/1000 PY, respectively. Average time to cirrhosis using pooled stage-constant fibrosis progression rates is 34 years post-infection, and time to METAVIR stage F3 is 26 years; using stage-specific estimates, time to cirrhosis is 46 years and

time to F3 is 38 years. Thus, left untreated, many PWID with chronic HCV infection will develop liver sequelae in mid- to late adulthood [85]. A recent cohort study in England showed that liver disease (including viral hepatitis and cirrhosis) is one of the major causes of deaths among PWID [86].

A review conducted by the EMCDDA [3] of literature published 2000–2012 found seven studies that reported on the burden of disease or mortality related to HCV infection among PWID in the European Union and the UK. Where assessed, the disease burden of HCV was found to be substantial and was expected to rise in the next decade. Only 2 of the 27 countries included in the review appeared to have carried out a modelling study to estimate the effect of HCV treatment on the future burden of disease. Without treatment, a study in the Netherlands (Amsterdam) projected a 36% increase in the occurrence of decompensated cirrhosis or hepatocellular cancer, between 2011 and 2025 [87], whereas in Scotland, UK (Glasgow), increases of 56% in cirrhosis and 64% in mild liver disease were projected for 2010–2025. Both studies showed that HCV treatment would substantially reduce the burden of liver disease [88].

Mortality in HCV-infected PWID is dependent on competing mortality (e.g. due to HIV infection or overdose) and the duration of persistent HCV infection. In the review, all-cause mortality rates among HCV-infected PWID were estimated at 2.1–2.4/100 PY in Spain [89] and the Netherlands [90], while a much higher rate was estimated for PWID co-infected with HIV in Denmark, where all-cause mortality was estimated at 12.2/100 PY [91]. The high mortality rate in this Danish study may be explained by high local rates of overdose mortality and differences in antiretroviral therapy regimes compared to the Spanish study that reported a crude mortality rate of 2.4/100 person-years among HIV-co-infected PWID during a comparable study period. This suggests the existence of significant differences between countries in mortality rates among HIV-infected PWID, as is found for mortality among all PWID, and underlines the importance of obtaining country-specific mortality estimates.

The HCV disease burden among PWID translates to a significant burden in the general population. In Europe, annual mortality rates from hepatocellular cancer vary by country and are generally lower in countries in the north-west of Europe compared with those in the south-east, possibly reflecting historic differences in risk (Fig. 6.6). The main causes of hepatocellular cancer are HBV and HCV infections and alcohol consumption. In all countries, mortality from hepatocellular cancer is higher in males than in females [92]. Although these data are not specific to PWID, they provide the scale of morbidity and mortality related to liver cancer, a large proportion of which is accounted for by chronic viral hepatitis infection acquired through injecting drugs [37].

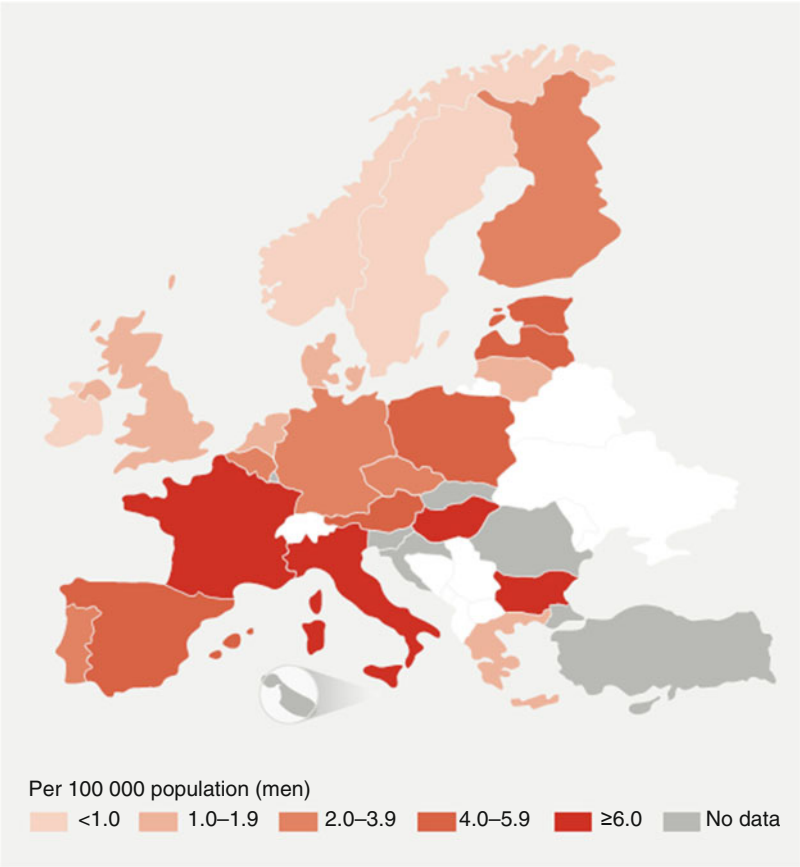


Fig. 6.6 Hepatocellular carcinoma-related mortality per 100,000 population (men). Source: [37]

6.2.7 Prevalence and Incidence of Injecting/Number of People Who Inject Drugs

Estimates of the numbers of PWID are important in projecting the future epidemiology of HCV infection and in planning and evaluating the public health responses [37]. A recent systematic review reported on the global prevalence of PWID [32], and as of June 2017, evidence of injecting drug use was reported in 179 of 206 countries or territories, an increase of 31 countries since a previous review of PWID prevalence [93]. The additional countries were mostly in sub-Saharan Africa ($n = 23$) and four Pacific Island states and territories. Globally, in 2015, an estimated 15.6 million people (95% uncertainty interval 10.2–23.7 million) injected drugs, amounting to approximately 0.33% (0.21–0.49) of those aged 15–64 years, and 21% of these were women (3.2 million, 1.6–5.1). At a regional level, prevalence varied

from 0.09% (0.07–0.11) in South Asia to 1.30% (0.71–2.15) in Eastern Europe. The largest populations of PWID were in East and Southeast Asia (4.0 million, 3.0–5.0 million), Eastern Europe (3.0 million, 1.7–5.0 million) and North America (2.6 million, 1.5–4.4 million). The proportion of women PWID varied substantially across regions—women were estimated to represent 30.0% (28.5–31.5) of PWID in North America and 33.4% (31.0–35.6) in Australasia, compared with 3.1% (2.1–4.1) among PWID in South Asia. The prevalence of injecting drug use among men was far higher than in women in all regions. The review found substantial variation in the estimated country-level prevalence of injecting drugs, with Georgia and Seychelles having the highest estimates; however, Russia, the USA and China contributed the largest proportions to the total number of PWID. Much lower prevalence was estimated for countries in Asia and sub-Saharan Africa than in other regions, though with some exceptions (Fig. 6.7) [32].

Relatively recent (2009–2015) national estimates of the prevalence of drug injecting among the general population are available in 16 of the 30 countries monitored by the EMCDDA [36]. Estimated prevalence varies across countries: from less than 1 to up to 9/1000 population aged 15–64 years (Fig. 6.8) although uncertainty intervals are often broad. Based on the available estimates, the highest absolute numbers of current PWID are reported in the UK (122,900), France (105,000), the Czech Republic (45,600), Finland (15,600), Portugal (14,400), Latvia (12,600) and Spain (9900). These numbers are important as they provide a proxy for the size of the group at potential risk of infection and transmission of HCV through injecting drug use. Combining estimates of injecting drug use with HCV prevalence estimates can enable us to understand the size and dynamic of the infection among this group [37].

6.2.8 Prevention and Harm Reduction for People Who Inject Drugs

Initiatives to reduce the spread of infectious diseases through the sharing of syringes and other drug injecting equipment by providing sterile drug use equipment to PWID date back to the mid-1980s [37, 94, 95]. This form of ‘prevention’ or ‘health protection’ activity is often in the policy context referred to as a ‘harm reduction’ approach, reflecting the fact that this response is not primarily focused on stopping the use of drugs but rather the prevention of harms associated with drug use. At present, most implemented interventions of this type are opiate substitution therapy (OST) and needle and syringe programmes (NSP). These two interventions when combined with high coverage have been associated with a reduction in the incidence of acute HCV infection [38, 96]. However, the coverage of these harm reduction responses, which are in place to some degree in a majority of the world’s countries, typically falls far short of what is needed to reach most PWID [97].

A recent systematic review reported on the global coverage of NSP and OST for PWID [98]. The study identified evidence of NSP operating in 93 of the 179 countries and territories where injecting drug use is known to occur (i.e. in 52% of countries where injecting drug use is reported). NSP was confirmed to be absent in 83 countries where injecting drug use occurs; the presence or absence of

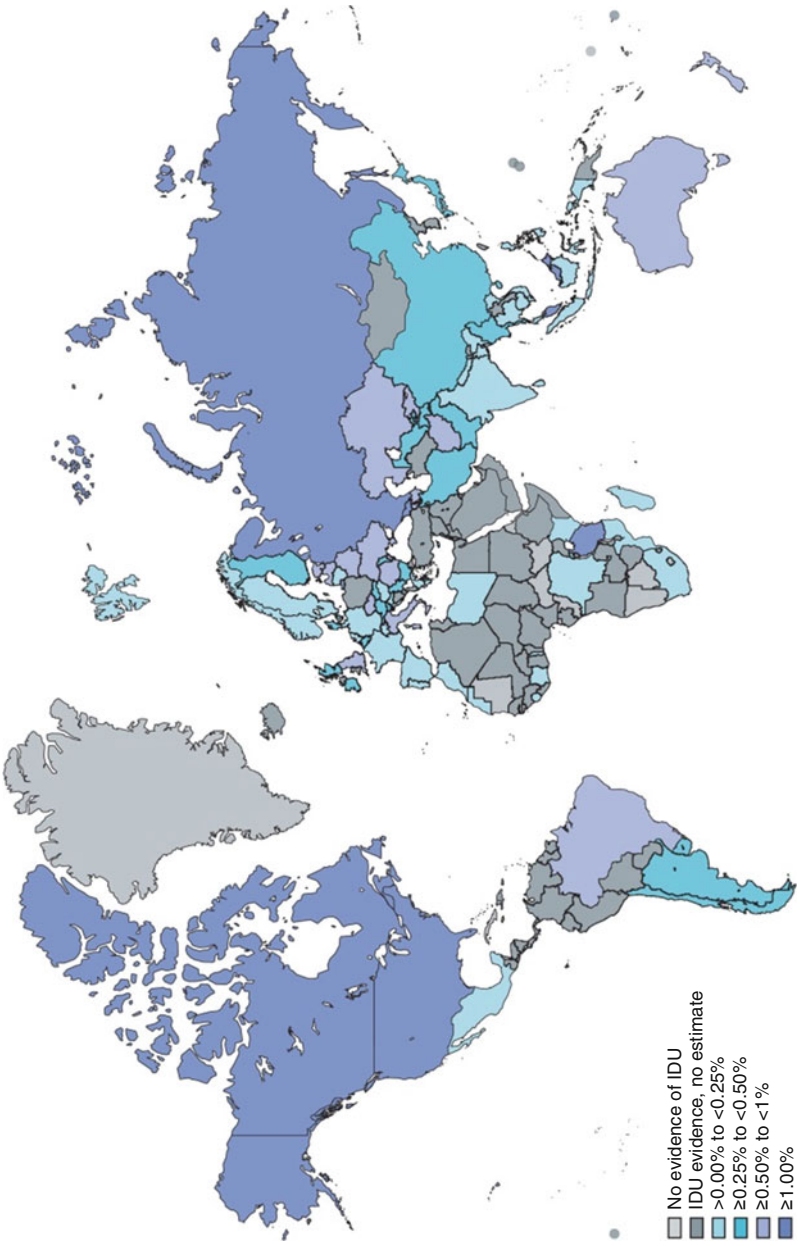


Fig. 6.7 Estimated prevalence of injecting drug use by country. Source: [32]. *IDU*: injecting drug use

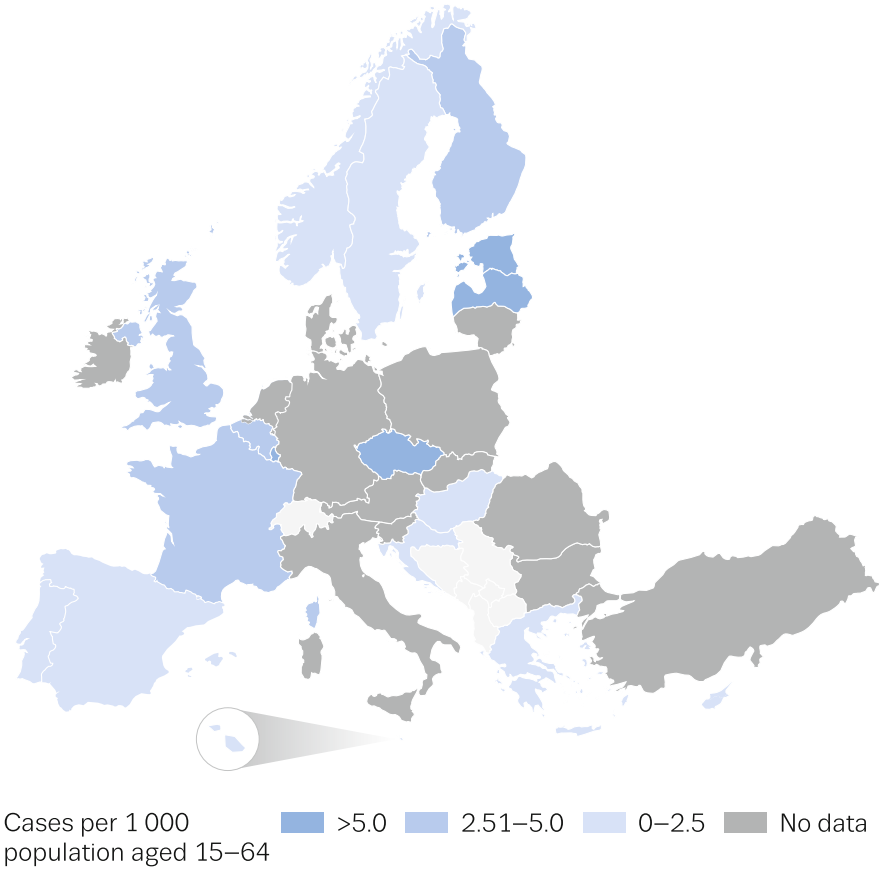


Fig. 6.8 Estimates of the prevalence of injecting drug use in Europe, 2009–2015 (most recent data). Source: [35]

NSP where injecting drug use is thought to occur could not be confirmed in three countries. OST was confirmed to be available in 86 countries where injecting drug use is known to occur (48% of countries where injecting drug use is reported), confirmed to be absent in 92 countries where injecting occurs, while the presence or absence of OST where injecting occurs could not be confirmed in one country. Methadone was the most frequently available medication used in OST, prescribed in 81 countries. Buprenorphine was prescribed for OST in 56 countries (of which 52 also prescribed methadone), and diamorphine was prescribed in seven countries (all of which also prescribed methadone and buprenorphine). Other forms of OST (e.g. tincture of opium, slow-release morphine) were prescribed in 12 countries. There were 79 countries implementing both NSP and OST (44% of countries where injecting drug use is reported) (Figs. 6.9 and 6.10) [98].

Fig. 6.9 Global coverage of needle and syringe programmes among people who inject drugs. Source: [32]. *NSP*: needle and syringe programmes, *PWID*: people who inject drugs

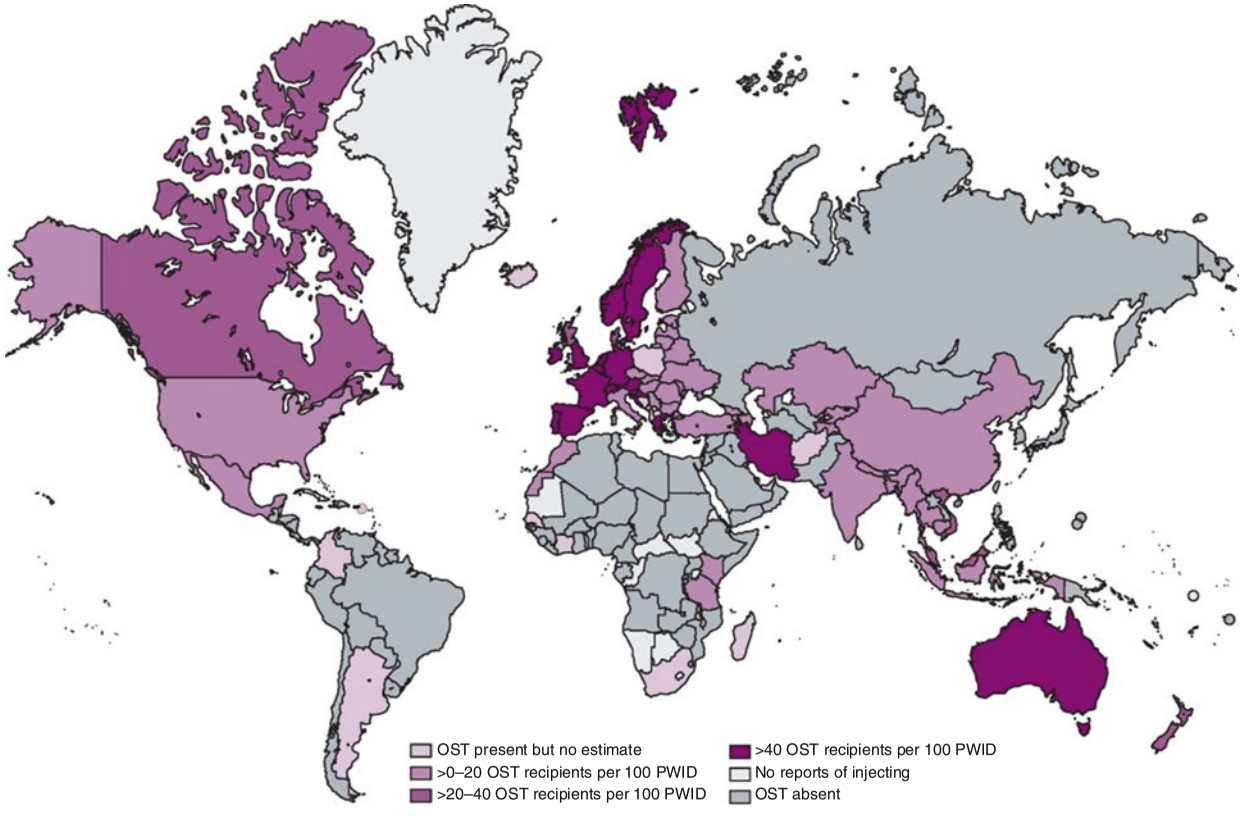


Fig. 6.10 Global coverage of opioid substitution therapy among people who inject drugs. Source: [32]. *OST*: opioid substitution therapy, *PWID*: people who inject drugs

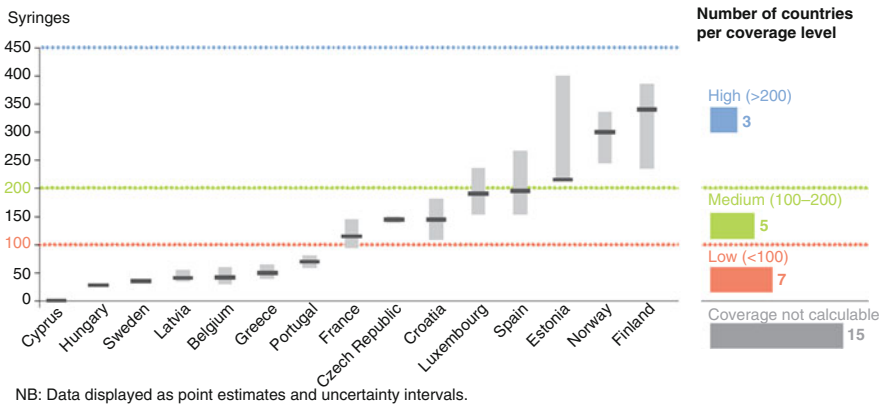
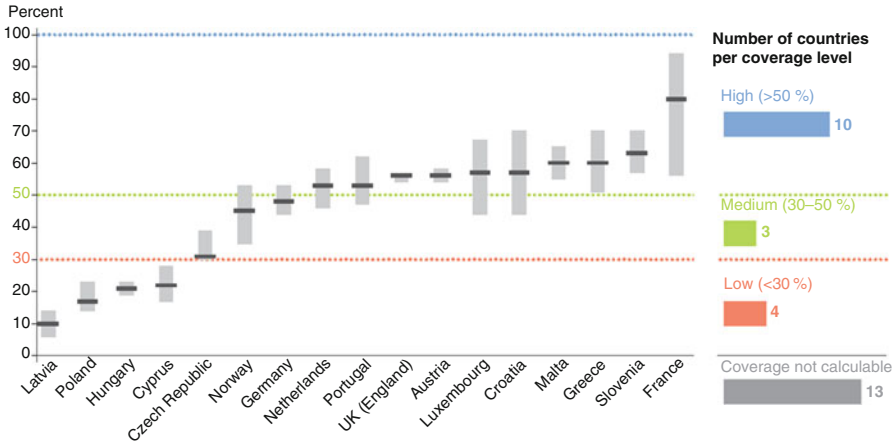


Fig. 6.11 Number of syringes provided through specialised needle and syringe programmes per estimated drug injector in 2015 or latest available year. Source: [36]

Coverage varied widely between countries, but was most often low according to WHO indicators (<100 needle-syringes distributed/PWID/year; <20 OST recipients/100 PWID/year). Globally, the study estimated that there are 33 (uncertainty interval 21–50) needle-syringes distributed via NSP per PWID annually and 16 (10–24) OST recipients/100 PWID. Less than 1% of PWID live in countries with high coverage of both NSP and OST (>200 needle-syringes distributed/PWID and >40 OST recipients/100 PWID) [98].

In Europe, needle and syringe programmes, integrated into multicomponent harm reduction interventions, distribute tens of millions of syringes each year. In addition to sterile syringes and needles, a range of other injecting paraphernalia, including alcohol pads, water, filters and mixing containers as well as equipment for inhaling drugs, are distributed by harm reduction facilities in order to prevent infections. The estimated number of syringes distributed each year per PWID through specialised programmes—excluding syringes sold by pharmacies outside of such programmes—ranged from less than 50 in Cyprus, Sweden, Belgium and Latvia to more than 350 in Estonia (Fig. 6.11). Comparing these estimates of syringe provision against international recommendations, less than a third of the countries that can be assessed provide syringes at a level judged to support effective harm reduction (at least 200 syringes/year/PWID [99]). Overall, it is estimated that approximately one in two high-risk opioid users in Europe received substitution treatment in 2014 [100]. This is the case for 10 of the 20 countries able to provide recent data allowing national coverage to be estimated. However, the available data indicate that in some countries, less than 10% of the estimated population of high-risk opioid users receive opioid substitution treatment (Fig. 6.12).

Exposure to disinfectants, including those containing alcohol, will effectively inactivate dried HCV on surfaces [75]. In a laboratory study simulating drug injection, containers (spoons or cookers) to prepare drugs for injection were contaminated with HCV in a water solution and heat was applied. The experiments



NB: Data displayed as point estimates and uncertainty intervals.

Fig. 6.12 Percentage of the estimated population of high-risk opioid users receiving substitution treatment in 2015. Source: [36]

showed that HCV could survive temperatures up to 65–70 °C, which required between 80 and 95 s of heating [75, 101].

In an earlier study in New York and Denver, ethnographers directly observed drug preparation in injection settings and measured heating times and temperatures applied to drug containers [102]. Only 12% of PWID heated drug solutions for >45 s, and nearly half heated for <15 s; they replicated these conditions in the laboratory and found that HIV was rapidly inactivated when heated, within 7–10 s. Thus, drug preparation practices that include heating may reduce the risk of HIV transmission via the shared use of containers, but HCV may still be transmitted [75].

This would also be consistent with substantial epidemiologic evidence that sharing containers is associated with HCV seroconversion [49, 77, 78]. However, it is not clear at present if this indicates direct transmission through contaminated injecting paraphernalia or if this association reflects syringe-mediated contamination when drugs are shared [79]. In a laboratory analysis of injection materials (syringes, drug cookers, filtration cotton, used water vials and alcohol and cotton swabs) collected from PWID in France, HCV RNA was not detected on used filters or water vials and was seldom detected on cups (9%). However, HCV RNA was frequently found on syringe pools (38%) and on swabs (82%) at high titres [75, 103]. Another laboratory study [104] demonstrated that HCV can survive for up to 3 weeks in bottled water and that HCV is also associated with filter material, in which around 10% of the viral inoculum was detectable. However, in a laboratory study attempting to replicate real-world injection practices, HCV could not be recovered from 'cookers', regardless of input syringe type or 'cooker' design. Recovery was higher when comparing detachable needles to fixed needles for residue in input syringes (73.8% vs. 0%), filters (15.4% vs. 1.4%) and receptive syringes (93.8% vs. 45.7%) [79].

A recent study [105] measured infectivity of laboratory clones of HCV recovered from used syringes and reported that 'HCV survival was dependent on syringe type, time and temperature'. Time and temperature may also have affected detection of HCV RNA in different types of equipment to a varying degree. Syringe type can determine the amount of blood remaining in a syringe when the plunger is fully inserted after injection, and this can range between 2 and 84 μl [75, 106].

Earlier studies of the use of disinfectant bleach to prevent HIV transmission via syringes shared by PWID suggested that, despite effectiveness claims in laboratory studies, this approach is ineffective in real-life settings [75, 107]. A recent study showed that HCV can be inactivated by microwave [108].

A project to assess tools to change the route of administration of drugs (e.g. heroin) from injecting to inhalation was conducted in Germany from 2011 to 2014 [109]. The aim of changing the route of administration was to reduce overdoses and the transmission of infections like HCV. A media campaign with posters, brochures, flyers and videos accompanied the project, and it was observed that PWID are willing to change their behaviour if well-equipped and sufficiently informed. Safer Smoke-Packs were developed, containing foil, straws and a flyer. Similar approaches have been piloted and are used in other countries [110].

A further intervention used to reduce drug use related harms, and often advocated for reducing drug overdose, is the provision of supervised injecting facilities. Such supervised injecting facilities are professionally run healthcare facilities where hygienic and safer use is promoted to reduce the morbidity and mortality associated with drug injecting [111, 112]. The facilities provide opportunities for health education and disease prevention and for immediate intervention by professionals in cases of overdose. Research has shown that supervised injecting facilities reach specific hard-to-reach target groups and that service users report substantial reductions in risk behaviour as well as improved health. Health promotion should include information which clarifies routes of transmission for diseases that are common among PWID. Information on infections like HIV, HCV and HBV should be provided, so that people understand that they can transmit the virus even if they show no symptoms [113].

6.2.9 HCV Treatment of People Who Inject Drugs

To date (2017), PWID in many countries have been excluded from HCV treatment. Despite multiple studies providing evidence that this population can be successfully treated [15, 114–121], HCV treatment rates among PWID are generally reported as low (<3%) even in high-income countries, due to concerns of poor adherence, psychiatric comorbidity and reinfection [122–125] and, especially since the introduction of DAAs, also costs. Prior to the introduction of DAAs, only 1–6% of HCV-infected current and former PWID in the USA, Canada and Australia were treated [3, 15, 28, 118, 119, 123, 126, 127]. International guidelines (such as the US National Institutes of Health, AASLD/IDSA, European Association for the Study of the Liver (EASL), International Network on Hepatitis in Substance Users and the

World Health Organization) all support treating HCV in people who use drugs [128–130]. Nevertheless, a recent study in the USA found that in 2014, 88% of states included drug and/or alcohol use in their HCV treatment eligibility criteria, with 50% requiring a period of abstinence and 64% requiring urine drug screening [28, 131].

A European review of treatment uptake before the widespread introduction of DAAs found that among groups of drug-using study participants who were HCV antibody-positive, the median treatment uptake level was 17%, and among those who were HCV RNA-positive, the median was 30%. In the 11 studies reporting specifically on treatment uptake among current and former PWID, HCV RNA-positive study populations had a median treatment uptake level of 32%. Only one study reported on HCV treatment uptake for people currently using drugs and found that uptake was relatively low among this group in several European countries and also pointed to considerable knowledge gaps regarding treatment uptake levels in this population [132]. A study from Germany however showed that direct-acting antiviral treatment of former or current drug users with or without opioid substitution therapy can achieve equally high sustained virologic response (SVR) rates as in patients with no history of drug use [133].

Since 2014, highly effective DAAs have been readily available. However, these treatments are costly and high costs could become a barrier to the widespread scale-up of HCV treatment. Guidelines issued by the European Association for the Study of the Liver (EASL) in 2015 recommend, for the first time, that treatment should be provided to PWID who are currently injecting on account of their risk of transmitting infection to others ('treatment as prevention'), irrespective of disease stage [134].

Several theoretical modelling studies have explored the potential impact and benefits of HCV treatment as prevention among PWID populations [28]. Modelling projections have indicated that achieving substantial reductions in HCV prevalence among PWID requires HCV treatment in addition to primary prevention. In addition to individual benefits, model projections have shown that HCV treatment for PWID could be an effective and cost-effective means of prevention in settings where chronic HCV prevalence among this group is less than 60% and that PWID should be prioritised after treating people with severe liver disease [135–141].

Interestingly, there is insufficient evidence to date of any impact of HIV treatment as prevention among marginal at-risk populations such as PWID [142, 143]. However, in theory, HCV treatment as prevention could be more effective than HIV treatment as prevention because HCV treatment is finite and curative. In particular, the dramatic improvement in SVR rates, once-daily dosing and short therapies (8–12 weeks) with interferon-free direct-acting antiviral therapies (IFN-free DAAs) has led many to speculate whether HCV treatment could feasibly be scaled up sufficiently to be used as an effective prevention strategy among those at risk of transmission [28, 144–148].

In most countries, it will be essential to scale up HCV treatment if the increasing trend in the prevalence of end-stage liver disease is to be reversed [45, 149]. However, targeting people with cirrhosis, as is the priority in many European countries, is unlikely to lead to substantial reductions in HCV transmission or the prevalence of

HCV infection among PWID [150, 151] as by the time cirrhosis has developed, injecting drug use behaviour has usually ceased. Although much of the HCV treatment as prevention modelling work has been done in a few countries (Australia, Canada, France, UK), the scenarios reflect the situation in many European cities and, therefore, can be generalised [141].

6.3 Men Who Have Sex with Men

Since 2000, outbreaks of acute HCV among HIV-positive MSM who have not reported injecting drug use have been published from Europe [152–159], the USA [160–162] and Australia [163]. The majority of these HCV infections were related to permucosal rather than parenteral risk factors, providing further evidence to support the role of sexual transmission [17]. These outbreaks have been associated with high-risk sexual practices, genital ulcer disease and illicit drug use including parenteral administration [17, 158, 164, 165]. However, a recent study in Amsterdam suggests that HIV-negative MSM may also be at risk of HCV infection, with the same HCV strains already circulating among HIV-positive MSM [166].

In 17 studies (from Australia, Canada, China, Denmark, Italy, Japan, the Netherlands, Spain, Switzerland, Taiwan, the UK and the USA), more than 13,000 HIV-positive MSM were followed for over 91,000 PY between 1984 and 2012; the pooled seroconversion rate was 0.53/100 PY. Calendar time was a significant moderator of HCV seroconversion, increasing from an estimated rate of 0.42/100 PY in 1991 to 1.09/100 PY in 2010 and 1.34/100 PY in 2012. Among those who seroconverted, a large proportion of infections were attributable to high-risk behaviours including mucosa-traumatic sex and sex while high on methamphetamine [167].

In Europe, during the past decade, the incidence of HCV in cohorts of HIV-positive MSM rose from 0.08/100 PY of follow-up (PYFU) to 4.1/100 PYFU [157, 168–171]. Currently, the epidemic appears to be declining in the Netherlands where a study in HIV treatment centres showed a decrease in incidence from 1.1 to 0.5/100 PFYU between 2014 and 2016 [172, 173]. However, in France, a study in a large cohort of people living with HIV found that despite a high HCV treatment uptake and cure rate, the incidence of new HCV infection (first infection or reinfection) regularly increased in French HIV-positive MSM between 2012 and 2016. First infection incidence in MSM rose from 0.5% to 0.92% patient-years, whereas the incidence of reinfection fluctuated but remained higher than the incidence of first infection (2.52–2.90% patient-years), suggesting that a subgroup of MSM pursued high-risk practices following cure of a first infection [174]. Outside Europe (the USA and Japan), no levelling off seems to be observed either, with recent reported incidence rates being between 0.2/100 PYFU and 2.5/100 PFYU [175, 176]. The acute HCV reinfection rate is even higher, with reported rates of 7.8 and 15.2/100 PYFU [31, 177, 178].

A supposed reason for this increase is the emergence of national and international networks of HIV-positive men who have unprotected sex with other HIV-positive

men ('serosorting') [179]. These could have arisen because of successful HIV treatment, widespread Internet use and low-budget travel possibilities [157, 180]. More recently, with effective ART, PreP and PEP serosorting may have declined, which could explain the emergence of HCV among HIV-negative MSM. Reported determinants for HCV transmission are sexualised drug use (including 'chemsex'); sharing of snorting straws; receptive fisting; ulcerative sexually transmitted infections, such as syphilis; group sex; and rectal trauma with bleeding [158, 164, 170, 181]. There are also a number of potential mechanisms related to HIV that might result in enhanced infectivity of and susceptibility to HCV, including increased HCV loads in serum and semen, and defects in the gastrointestinal immune system [17, 31].

6.4 Patients at Risk of Nosocomial Infection

Before the identification of HCV, transfusion of blood or blood-related products was one of the main routes of its transmission. Routine anti-HCV antibody screening in blood donations has almost eliminated the risk of HCV transmission from blood donations in many countries worldwide. However, there remains variation in routine testing for transfusion-related infections worldwide, and screening of blood donations is not conducted at all in around 40 countries due to financial restrictions with inconsistent testing in many other countries [182].

Unsafe injection, principally due to equipment reuse, in healthcare settings is also a risk for HCV. The WHO estimates that around two million new infections each year result from unsafe injections, accounting for 40% of all new infections [55, 183]. In 2015, it was estimated that, globally, 5% of healthcare-related injections remained unsafe [1].

The most dramatic example is Egypt, in which the iatrogenic transmission of HCV during the era of parenteral antischistosomal therapy mass treatment between 1960 and 1980 led to a nationwide epidemic. As a result, 10–20% of the total Egyptian population are currently infected, most of them with genotype 4. Because of inadequate sterilisation of healthcare equipment (and presumably other breaches in infection prevention and control in healthcare) and the high prevalence in the general population, HCV continues to spread in Egypt [29, 31].

Within the European healthcare systems, HCV transmission still occurs. For example, according to the national surveillance system in France, these infections (mainly from invasive procedures) account for up to 25% of all acute HCV infections diagnosed [184]. In this study, suspected healthcare procedures were mainly surgery, haemodialysis and endoscopy, a finding consistent with previous studies in France and Italy [184–188]. However, for hospitalised patients in Europe, the risk of acute HCV infection via blood transfusion or via medicinal use of contaminated needle injections has declined to low levels [31].

In most countries with available data, HCV prevalence is higher in men than women; this finding reflects the higher prevalence of risk factors (such as injecting drug use) in men than in women. In France, however, more women are

infected than men [189]. Similarly, in Germany, more women aged over 69 years have HCV infection than age-matched men [189]. In both countries, women were at risk of infection during childbirth in the late 1970s via contaminated blood or equipment. HCV is more common in women than men in Turkey; most infections in Turkey are nosocomial, with hospitalisation more common in women than in men [55, 189].

6.5 Migrants

Migrants born in countries with an intermediate or high HCV prevalence are at risk of having a chronic infection, mainly due to a higher risk of nosocomial transmission in the country of origin. A systematic review on the HCV prevalence among migrants worldwide showed the anti-HCV prevalence was high (>3%) in migrants from South Asia and sub-Saharan Africa, and intermediate (2–3%) in migrants from Eastern Europe and Central Asia [26].

The numbers of chronically infected migrants in the EU/EEA and the UK by country of birth and the contribution of migrants to the overall burden of disease have been estimated for the year 2013 [190]. In 2013, around 11% of the total population in the EU/EEA was foreign born to their country, of which 79% was born in HCV-endemic countries (anti-HCV prevalence ≥1%). The anti-HCV prevalence among migrants in the EU/EEA and the UK from HCV endemic countries was 2.3%, corresponding to around 580,000 chronic HCV infections. While 1 in 12 people in the EU/EEA and the UK is born in an HCV endemic country, migrants from endemic countries account for 1 in 7 (14%) of the total number of HCV infections in the EU/EEA and the UK. The relative contribution of migrants is higher in countries with a low HCV prevalence in the general population and with high numbers of migrants from countries of higher prevalence; in, for example, Germany and the Netherlands the proportion of all HCV infections that are among migrants is estimated to exceed 50% of the total number of chronic HCV infections [190].

6.6 Reinfection

The prospects of eliminating HCV could be counteracted by HCV reinfection in those successfully treated, and those who have naturally cleared infection, due to continued risks [71, 191]. This has been described in PWID and MSM [4, 165, 177, 192, 193].

Documentation of high rates of reinfection after treatment among HIV-HCV-co-infected MSM (8–15/100 PY) [165, 177, 178, 194] as well as evidence of a highly connected global network of HCV transmission due to travel may limit the effectiveness of treatment as prevention strategies in this key risk group [28]. Reinfection post-successful HCV treatment ($n = 2$ studies) among MSM was 20 times higher than initial seroconversion rates [167]. A study from eight HIV treatment centres in four European countries found a trend for lower incidence among MSM who had

spontaneously cleared their incident infection (5/100 PYFU) than among those who were treated (8/100 PYFU) [165].

Based on existing data from small and heterogeneous studies of interferon-based treatment, the incidence of reinfection after sustained virological response ranged from 2–6/100 PY among PWID to 10–15/100 PY among MSM with HIV [71].

In a recent meta-analysis of 61 studies published in 1990–2015, the 5-year risk of HCV reinfection in HIV-infected MSM was as high as 15% and higher than in studies on PWID [165, 195]. However, another recent study found that when accounting for frequency of risk behaviour, those reporting high-frequency injecting drug use had the highest risk (adjusted reinfection rate (per 1000 PYFU): 58, 95% credible interval [CrI], 18–134), followed by MSM reporting high-risk sexual activity (26, 95% CrI, 6–66) and low-frequency injecting drug use [196].

More recently, HCV reinfections have also been reported in phase III trials of DAA HCV compounds [197–199], nearly all of which have occurred among HIV-infected MSM [165].

6.7 Discussion

Globally, HCV incidence is mainly driven by two different mechanisms: in many developing countries, the use of unsafe invasive medical practice and lack of testing blood donations are key, while in many high- and middle-income countries, specific behaviours in high-risk groups such as PWID and MSM predominate. This calls for diversified prevention and monitoring strategies: in the first case, general population-based epidemiology and treatment with prevention focused on healthcare settings, while in the second case risk, group-based epidemiology, prevention and treatment are indicated.

Large-scale investment in awareness campaigns and education of the general public and healthcare staff about the risks associated with reuse of medical instruments might be one way to make inroads into this widespread ongoing problem. Another critical step in the control of the global burden of HCV is identifying and testing at-risk persons for HCV in each country. However, this task is daunting: it is estimated that 90% of the HCV-infected individuals worldwide are unaware of their infection status [55, 200, 201]. In 2017, the first WHO guidelines on hepatitis B and C testing were published recommending focused testing of individuals with (a history of) high-risk behaviour or who are part of a population with a higher seroprevalence [202]. A general population testing approach is recommended in settings with an anti-HCV prevalence of $\geq$2% or 'birth cohort' testing for specific age groups with a higher prevalence. A range of operational interventions that can enhance testing, linkage to care and treatment and thereby substantially optimise the continuum of care for chronic viral hepatitis were identified in a recent systematic review of studies, (all of which except one) from high-income countries. Findings included the following: clinician reminders to prompt HCV testing during clinical visits increased HCV testing rates; nurse-led

educational interventions improved HCV treatment completion and cure; and coordinated mental health, substance misuse and hepatitis treatment services increased HCV treatment uptake, adherence and cure compared with usual care [203].

The immediate priority is to scale up HCV treatment in people with severe liver disease to reduce HCV-related morbidity and mortality, as rapidly as possible. Thereafter, the question is which patients should be prioritised next for treatment—should countries target those with moderate liver disease (pre-cirrhotic) or those with HCV who are currently injecting drugs (or HIV-positive MSM), most of whom will have no or mild disease, as recommended by EASL. A recent EMCDDA publication emphasises the importance of HCV treatment in PWID—it is unlikely that the combination of opioid substitution treatment and needle and syringe programmes in itself will achieve substantial reductions in HCV prevalence in this group [141]. So far, economic modelling supports treatment for and prioritisation of PWID, as essential for achieving elimination targets. The evidence suggests that prioritising early HCV treatment on PWID can be highly cost-effective, depending on the prevalence of HCV [139]—but as yet we lack direct empirical evidence (i.e. that HCV transmission is reduced as a result of scaling up HCV treatment) [134].

While improvements in screening and treatment are becoming a priority in new HCV strategies in some countries, there is evidence that HCV is not being addressed in a comprehensive manner, as several countries still show important gaps in prevention coverage, and HCV treatment provision to PWID continues to be reported as low [37]. In high- and middle-income countries, it is clear that the highest proportion of infected individuals are former or current PWID and that treatment of infection is needed in this group. Substantial reductions in HCV incidence and prevalence can only be achieved with targeted DAA therapy among those at the highest risk of ongoing transmission [204]. However, despite the availability of novel treatment options with improved efficacy and tolerability, treatment is limited in this group. A recent study of the readiness in European countries to treat hepatitis C virus in individuals with opioid use disorder, on the basis of an expert-generated model assessment, showed that there are important limitations to successful HCV care in people with opioid use disorders, which most PWID are. According to the experts, specific actions should be taken: maintain/increase access to opioid use disorders treatment services/opioid agonist therapy, update HCV guidance, locate care in the same place and allow wider prescribing of anti-HCV medicines [205].

Regarding PWID and HIV-infected MSM, mathematical modelling predicts that if the required scale-up in treatment uptake with the new treatments is achieved, the result would be substantial reductions in HCV prevalence within a decade [138, 206]. Further benefits have been predicted if treatment is combined with an intervention to reduce behavioural risk, which makes the eradication of HCV an achievable goal in the HIV–HCV-coinfected population in Western Europe [165]. Among MSM, there is a lack of evidence-based behavioural interventions to reduce risk behaviours which have been associated with HCV transmission (such

as sexual and drug practices associated with mucosal trauma). Therefore, additional prevention interventions in these populations are urgently needed [28].

In contrast to PWID, the absolute numbers of HCV–HIV-coinfected MSM are small, and most diagnosed HIV-positive MSM are linked with care, closely monitored and frequently tested. Additionally, high uptake of HCV treatment among HIV-positive MSM has been reported, with over 40% of HIV–HCV-coinfected MSM being treatment experienced in European cohorts [153, 207, 208]. Hence, HCV treatment for prevention may be particularly feasible in this group [28].

However, according to WHO, other key populations need to be included in national strategies and need to be actively screened, diagnosed and linked to treatment and prevention of reinfection, e.g. migrant communities originating from countries with intermediate or high HCV prevalence [202].

Vaccinating key population groups at risk for HCV infection, or already infected, against other hepatitis viruses, in particular hepatitis B, should be considered by policy makers in accordance with local guidelines. Because of the possibility of a higher risk of hepatitis A outbreaks among PWID, the provision of a combined hepatitis A and B vaccination is suggested as the best way to prevent both infections in PWID and to avoid additional harm of the liver. This is particularly important for those who are HCV-positive.

Evidence indicates that the prevalence of HCV-related end-stage liver disease and mortality is increasing. However, the prevalence of severe liver disease among PWID with HCV remains largely unknown. Nor is it clear how many PWID have been treated for HCV infection. In addition, knowledge of the coverage of other key HCV primary interventions—opioid substitution treatment and needle and syringe programmes—is patchy in many countries, and in many European countries there are no reliable estimates of the population currently at risk of HCV infection through injecting drug use. Developing better surveillance and evidence on HCV is important and will require collaboration between international and regional organisations and among individual countries [134].

With the new treatments, national and international strategies are required to redesign and co-locate treatment services for managing HCV infection with specialist drug services for PWID. However, this is only the first step in addressing stigma and promoting patient-facing treatment services for PWID [209]. Certainly, there is now a window of opportunity to generate empirical data and conduct evaluations of the impact of scaling up HCV treatment among PWID in European settings, as treatment services are geared up to identify and deal with severe liver disease. Ideally, potential intervention sites will have established ‘HCV treatment-in-the-community’ services, integrated with other services that manage and support PWID, and critically sites will need to have mature systems for collecting data on behaviour, HCV transmission and HCV prevalence among this client group, and on HCV testing and treatment. In the context of the EASL guidelines and the changing therapeutic landscape of HCV, such an evaluation needs to be done as quickly as possible [134].

The burden of HCV is high and disproportionately affects PWID. In many countries with available data, more than half of PWID are infected, and current

data indicate ongoing transmission. The European picture is highly variable, with large variations in both the epidemiology of the infection and the prevention responses undertaken [3]. The coverage of interventions in some countries continues to be low when measured against international standards, and, in some instances, it has even been recently decreasing, significantly increasing the risk of HCV and other infections among PWID. There are significant gaps and also general limitations in the available data on notifications, prevalence estimates, estimates of the numbers of people injecting drugs and coverage of the main prevention interventions. Serious gaps also exist in estimates of incidence, co-infection, genotypes, undiagnosed fraction, treatment entry and burden of disease [3]. All these are valuable indicators for monitoring the continuum of care, and they should be promoted and their availability improved in several countries where they are still underdeveloped [3, 35, 37].

There is a need now to generate empirical data and conduct evaluations of the impact and cost-effectiveness of scaling up HCV treatment among people who inject drugs in European settings [141]. Constructive prevention strategies include acknowledgement of the problem without stigma and discrimination as a crucial first step, education and counselling, harm reduction optimisation, scaled-up treatment including treatment of injecting networks, post-treatment screening and rapid retreatment of reinfections [71].

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