How to make an effective response to viral hepatitis in PWID?

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Estimated prevalence of injecting drug use by country

15.6 million PWID globally (0.33% of those aged 15 – 64 years)
Estimated prevalence of injecting drug use by country

15.6 million PWID globally (0.33% of those aged 15 – 64 years)

<table>
<thead>
<tr>
<th>Europe</th>
<th>PWID Prevalence</th>
<th>PWID N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western</td>
<td>0.34 %</td>
<td>1 million</td>
</tr>
<tr>
<td>Eastern</td>
<td>1.3 %</td>
<td>3 million</td>
</tr>
</tbody>
</table>

Europe

<table>
<thead>
<tr>
<th>Europe</th>
<th>Age &gt;25 y</th>
<th>Inject opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western</td>
<td>70%</td>
<td>78.3 %</td>
</tr>
<tr>
<td>Eastern</td>
<td>58%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Estimated anti-HCV prevalence among PWID by country

15.6 million PWID globally
52.3% anti-HCV positive (= 8.2 million)

Worldwide Prevalence of HCV Infection in HIV-positive PWID


<table>
<thead>
<tr>
<th>Population</th>
<th>Proportion of HIV-positive individuals co-infected with HCV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No high-risk behaviour</td>
<td>2.4%</td>
</tr>
<tr>
<td>PWID</td>
<td>82.4%</td>
</tr>
</tbody>
</table>

* Systematic review and meta analysis of 783 studies, resulting in 902 estimates of the prevalence of HIV/HCV co-infection.
Current Key Populations for HCV infection in EU/EEA

- HCV infection in migrants is higher compared to general population
  
- Risk of transmission disproportionately affects prisoners, particularly due to IDU
  
- Men who have sex with men (particularly HIV-positive) are at increased risk of contracting HCV
  
People who inject drugs account for the majority of new cases of HCV in developed countries

PWID are the driving force of HCV epidemic in EUROPE

- **80%** of new HCV infections
- **60%** of existing HCV infections

Source:
Anti-HCV seroprevalence among PWID in Europe
Period 2016/17

HCV infection in prisons throughout Europe

Risk of transmission disproportionately affects prisoners, particularly due to IDU

Age distribution of HCV-infected persons in EU in 2015

The population of HCV-infected has been ageing – reaching a critical period for life-threatening conditions to develop.

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Polaris Observatory. Accesses at: http://www.polarisobservatory.com/
The natural course of HCV infection with no treatment:
It takes >20 years of infection to develop life-threatening conditions

For every 100 people infected...
- 75-80 will develop chronic infection...
- 60-70 will develop chronic liver disease...
- 5-20 will develop cirrhosis...
- 1-5 will die of cirrhosis or HCC...

+ more will die of extrahepatic manifestations
The burden of hepatitis C virus (HCV)-related morbidity and mortality continues to rise. Progression to advanced liver disease among HCV-infected individuals generally requires decades, but we are entering an era where those infected with HCV in the 1970s and 1980s are at significant risk of mortality. Liver disease has overtaken drug-related harm as the major cause of mortality in HCV-infected individuals in many settings. Direct-acting antiviral therapies have provided renewed optimism, but HCV treatment uptake will need to increase markedly to reduce liver-related mortality. This review provides updated information on the natural history of HCV and its specific causes of mortality and drug-related disease, and strategies to combat HCV among people who inject drugs will be outlined.

20-25% of deaths among PWID result from advanced liver disease

15-30% of deaths among PWID directly related to drug use

Response to DAAs among ongoing drug users and people on opioid treatment agonists (OTA)

Deaths due to life-threatening conditions of chronic HCV infection after 20-years of follow up

PWID attending needle/syringe programs nationally between 2015 and 2017 in Australia

Immediate introduction of DAAs and decline in HCV RNA prevalence
PWID attending needle/syringe programs nationally between 2015 and 2017 in Australia

Immediate introduction of DAAs and decline in HCV RNA prevalence

HCV prevalence 43%

HCV prevalence 25%

Prevalence of HCV RNA among prisoners in Iceland

When TraPHepC was initiated in 2016:
- All inmates were screened, diagnosed and subsequently treated with DAAs

HCV prevalence dropped from **29%** to **7%** (a 76% decrease!)

International guidelines call for HCV treatment in PWID
HCV treatment with DAAs
EASL 2018 Guidelines

People who inject drugs and patients receiving opioid substitution therapy

People who inject drugs include former injectors who have ceased injecting and recent/current PWIDs.

Some people with a history of injecting drug use receive opioid substitution therapy (OST), e.g., methadone or buprenorphine, for the management of their opioid dependence. In Europe, two-thirds of the HCV burden is attributable to the use of injection drugs.

The prevalence of chronic HCV infection in people who inject drugs is approximately 1-3% who recently injected drugs is approximately 1-3%.

Recommendations for HCV testing is based on the high prevalence of infection in PWIDs.

Clinical Practice Guidelines

- PWIDs should be routinely and voluntarily tested for anti-HCV antibodies and HCV RNA. PWIDs who are HCV RNA-negative should be tested for HCV RNA annually and following any high-risk injecting episode (A1).
- PWIDs should be provided with appropriate access to OST and clean drug injecting equipment as part of widespread comprehensive harm reduction programs, including in prisons (A1).
- All PWIDs who are infected with HCV have an indication for antiviral therapy, as DAA-based therapies are safe and effective in HCV-infected patients receiving OST, those with a history of injecting drug use and those who recently injected drugs (A1).
- HCV treatment should be offered to HCV-infected patients in prison (B1).
- Pre-therapeutic education should include discussions of HCV transmission, risk factors for fibrosis progression, treatment, reinfection risk, and harm reduction strategies (B1).
- In patients on OST, DAA-based anti-HCV therapy does not require methadone or buprenorphine dose adjustment (A1).
- Harm reduction, education and counselling should be provided to PWIDs in the context of HCV treatment to prevent HCV reinfection following successful treatment (B1).
- Following SVR monitoring for HCV reinfection ideally through bi-annual, at least annual HCV RNA assessment should be undertaken in PWIDs with an ongoing risk behaviour (A1).
- Retreatment should be made available, if reinfection is identified during post-SVR follow-up (A1).
Eliminating Hepatitis C – An Action Plan

Globally, there are an estimated 71 million people actively infected with HCV, and 11-14 million of these reside in Europe.

EASL Recommends:

1. Increasing awareness amongst HCPs, patients, policy-makers, the media and the public (especially high risk groups), whilst combating the stigma and discrimination that is associated with HCV infection.

2. Implementing harm reduction strategies, such as access to opioid substitution therapy, safe injecting equipment for drug users and safe sex education.

3. Making DAAs available at reasonable prices, to avoid any further reimbursement restrictions and to allow governments to implement a comprehensive elimination strategy.

4. Improving access to treatment and care by increasing the number of authorised prescribers, promoting telemedicine and by increasing input from AHPs during and after treatment.

5. Treating every Hepatitis C patient at the earliest opportunity, especially those at high risk.

6. Providing rapid testing, in all relevant settings, with priority given to high-risk persons.

The continuum of services and a cascade-of-care for HCV management

HCV cascade-of-care in PWID

Barriers to HCV treatment access in the IFN-era

Barriers to access to HCV care in the IFN-free era

Direct acting antivirals:
Highly effective, simple, safe, patient/doctor friendly

Major barriers to access to care:
Policy, System

Reported presence of the national strategies, action plans and clinical guidelines for the treatment of hepatitis C from 34 European countries in 2016

#Scotland was treated separately from the UK.
$The countries in gray participated in the study in 2013. The countries in gray and white participated in the study in 2016.

The policy of HCV management in PWUD in 33 European countries:
PWUD were still excluded in some countries

<table>
<thead>
<tr>
<th>Policy</th>
<th>PWID included</th>
<th>PWID not included</th>
<th>Not existing/na</th>
<th>Excluded from study</th>
</tr>
</thead>
<tbody>
<tr>
<td>National strategies 2016</td>
<td>11</td>
<td>2</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>National strategies 2013</td>
<td>6</td>
<td>0</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>National action plans 2016</td>
<td>8</td>
<td>4</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>National action plans 2013</td>
<td>4</td>
<td>0</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>National treatment guidelines 2016</td>
<td>22</td>
<td>6</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>National treatment guidelines 2013</td>
<td>20</td>
<td>2</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

Number of countries

Restrictions on access to HCV treatment with DAAs include PWID in several European countries (N=27)

The number of countries with a **national hepatitis plan** increased in the WHO Europe:

- In 2013: **13**
- In 2018: **27**
SYSTEM barriers to access to HCV care in key populations

PWID are **difficult to engage in formal healthcare services**

- Lack of services/inconvenient location
- Lack of co-ordination/collaboration between services
- Lack of training programmes to work with key populations
- Criminalisation of PWID
- High treatment fees

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Restrictions on access to HCV treatment with DAAs in 2017 in European countries

By prescriber type

In **94%** of countries prescribed **only by specialists**
Traditional referral model for HCV care

Modified from John Dillon. INHSU, September 2018.
The long journey to HCV diagnosis

Visit #1: Anti-HCV test (Central Lab) 1-2 wks
Visit #2: Phlebotomy (Phlebotomist)
Visit #3: Receive diagnosis (Physician)
Visit #4: Phlebotomy (Phlebotomist) 1-2 wks
Visit #5: HCV RNA test (Central Lab)

...the long journey from HCV diagnosis to HCV treatment and cure
Simplification of existing models of care to access HCV treatment

This is all that we need !!!
We know direct-acting antiviral (DAA) therapies work, so now what?

Hepatitis C

Patient-Centred Care

Chronically HCV-infected individuals—from testing to cure and subsequent care and monitoring.

Redefining models of HCV testing, linkage-to-care and treatment with DAAs

- Sexual health
- Pharmacies
- Community health centers
- Drug and alcohol clinics
- Prisons
- Primary healthcare / GPs
- Needle/syringe programs

Bring HCV care to the community where patients simply access services

Modified from John Dillon. INHSU, September 2018.
Redefining models of HCV testing, linkage-to-care and treatment with DAAs

Sexual health

Pharmacies

Community health centers

Drug and alcohol clinics

Primary healthcare / GPs

Tertiary care hospital

Prisons

Needle/syringe programs

Bring HCV care to the community where patients simply access services

Modified from John Dillon. INHSU, September 2018.
Coverage of OST and Needle/Syringe programmes throughout Europe
Period 2017/18

The implementation of WHO HCV recommendations - dosing the gaps between policy and practice in 25 European countries

Adaptation of HCV services to Key populations

Hepatitis C interventions by organizations providing Harm reduction services in 27 European countries

Fig. 16 ~ Number of applicant organizations according to their self-identified capacity to deliver HCV services (N=60)

- My organization is equipped to deliver comprehensive HCV services but we needed additional resources to meet the requirements / existing demand: 52
- My organization can not support HCV services any further as it is not within our formal purpose: 11
- My organization is fully equipped to deliver comprehensive HCV services matching the current requirements, and does not need of additional resources: 14

Hepatitis C interventions by 55 organizations providing Harm reduction services from 27 European countries

Fig. 12 - Number of applicant organizations according to the type of support offered for clients with an active HCV infection* (N=55)

- Offering treatment externally: 35
- We don’t offer any HCV support, but refer externally: 21
- Disease self-management control: 20
- Liver health monitoring / assessment: 20
- Offering HCV treatment onsite: 13
- Other: 13
- We don’t offer any support, and can’t refer externally: 2

* positive HCV Ag and/or HCV-RNA test result

Model of care for HCV
Theoreticaly

A setting specific framework involving a continuum of services for a cascade of care:

- prevention
- testing
- treatment
- chronic care

Model of care:

- **WHAT?** - services
- **WHERE?** - setting
- **WHO?** - providers
- **HOW?** - integration approach

## Successfull real-life models of care

### WHOM?

<table>
<thead>
<tr>
<th>Key populations (n)</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWID / on OST (42/3)</td>
<td>Australia; Belgium; Canada; Denmark; France; Georgia; Greece; Ireland; Norway; Portugal; Spain; Switzerland; UK; USA</td>
</tr>
<tr>
<td>Prisoners (11)</td>
<td>Australia; France; Ireland; Portugal; Romania; Spain; Sweden; UK</td>
</tr>
<tr>
<td>Homeless (7)</td>
<td>Australia; Canada, France; Romania; Scotland; Spain; UK</td>
</tr>
</tbody>
</table>

# Successful real-life models of HCV care

## WHERE?

<table>
<thead>
<tr>
<th>Setting (n)</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-threshold setting (25)</td>
<td>Australia; Belgium; Canada; Denmark; France; Georgia; Greece; Italy; Ireland; Norway; Portugal; Romania; Spain; UK; USA</td>
</tr>
<tr>
<td>Primary care (20)</td>
<td>Australia, Canada, Ireland, Mexico, Pakistan, Romania, Scotland, Spain, UK, USA</td>
</tr>
<tr>
<td>Prison (9)</td>
<td>Australia, Ireland, Romania, Spain, Sweden, Portugal, UK</td>
</tr>
<tr>
<td>High-threshold setting (6)</td>
<td>Belgium, Denmark, Switzerland, USA</td>
</tr>
<tr>
<td>Hospital (4)</td>
<td>Australia, Canada, India</td>
</tr>
<tr>
<td>Rural (4)</td>
<td>Canada, Egypt, France</td>
</tr>
<tr>
<td>Regional setting (3)</td>
<td>Canada, Egypt, UK</td>
</tr>
<tr>
<td>Pharmacy (3)</td>
<td>Scotland, USA</td>
</tr>
<tr>
<td>Mobile van (4)</td>
<td>Australia, France, USA</td>
</tr>
<tr>
<td>Other (2)</td>
<td>Multi-country reviews</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Setting (n)</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multidisciplinary (22)</td>
<td>Australia; Canada; Denmark; Egypt; France; Greece; Ireland; Portugal; Romania; Spain; Switzerland; UK; USA</td>
</tr>
<tr>
<td>Medical specialists (26)</td>
<td>Australia; Belgium; Canada; France; India; Norway; Pakistan; Portugal; Sweden; UK; USA</td>
</tr>
<tr>
<td>General practitioners (12)</td>
<td>Australia; Belgium; Canada; France; India; Norway; Pakistan; Portugal; Sweden; UK; USA</td>
</tr>
<tr>
<td>Telemedicine (7)</td>
<td>Australia; Spain; Canada; Mexico; USA</td>
</tr>
<tr>
<td>Nurse-led (14)</td>
<td>Australia; Belgium; Canada; Georgia; Sweden; UK; USA</td>
</tr>
<tr>
<td>Specialist nurse (but not nurse-led) (12)</td>
<td>Australia; Belgium; Canada; Norway; UK; USA</td>
</tr>
<tr>
<td>Peer-support (3)</td>
<td>Australia; Belgium</td>
</tr>
<tr>
<td>Pharmacists (3)</td>
<td>Pakistan; UK; USA</td>
</tr>
<tr>
<td>Non-governmental organization (1)</td>
<td>Pakistan</td>
</tr>
<tr>
<td>Not reported/Not specified (8)</td>
<td>Australia; Egypt; Spain; USA</td>
</tr>
<tr>
<td>Other (reviews) (3)</td>
<td>Multi-country reviews</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study, project, and location</th>
<th>Where (setting)</th>
<th>What (services)</th>
<th>Who (providers)</th>
<th>How (integration approach)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radley et al., 2017 Directly Observed Therapy for Hepatitis C (DOT-C), Dundee, Scotland, United Kingdom</td>
<td>Community pharmacies</td>
<td>Dried blood spot testing, OST, DAA therapy</td>
<td>Pharmacists, physicians</td>
<td>Community pharmacies referring patients who test positive for HCV to clinics for assessment and treatment</td>
<td>HCV testing and treatment is feasible in community pharmacies, especially for patients already receiving OST there. Compared to nurse-practitioners, pharmacists were much more likely to get patients to take a rapid HCV test, and for clients with reactive tests, the pharmacist were much more successful in getting them to attend a clinic for assessment and treatment.</td>
</tr>
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# VALID (vulnerable adults liver disease) Study, Southeast England, UK

<table>
<thead>
<tr>
<th>Study, project, and location</th>
<th>Where (setting)</th>
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<th>Who (providers)</th>
<th>How (integration approach)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hashim A et al, 2019</td>
<td>Hostels, Community clinics</td>
<td>Point of care testing, liver fibrosis assessment (Fibroscan), alcohol and substance misuse counseling/social support (provided by primary care physician) and HCV treatment. A specialist registrar runs the clinics under the supervision of a Hepatologist.</td>
<td>General practitioner, medical specialist</td>
<td>One stop HCV clinic at two major homeless hostels in Southeast England.</td>
<td>72 attended the clinic, 71 (99%) were included in the program, 28 (39.4%) were anti-HCV positive, 26/28 consented to further testing, 20/26 were HCV RNA positive, 5/20 started DAA treatment. Results in 2019: 131 individuals approached, 127/131 individuals enrolled in the program, 59/127 were HCV Ab positive, 48/59 were HCV RNA positive, 28/48 initiated HCV treatment, 14/17 achieved SVR12, 13 still on treatment/waiting SVR results, 1 discontinued the treatment.</td>
</tr>
<tr>
<td>Study, project, and location</td>
<td>Where (setting)</td>
<td>What (services)</td>
<td>Who (providers)</td>
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</tr>
<tr>
<td>Cuadrado et al., 2018</td>
<td>El Dueso Prison healthcare facility</td>
<td>HBV, HCV and HIV screening and diagnosis; DAA therapy, teleconsultation; phylogenetic analysis of nonresponders, followed by targeted retreatment</td>
<td>Prison health team (physicians, nurses, pharmacist); addiction specialists; social service providers; hospital team (infectious disease specialists, hepatologists, specialized nurses, radiologists, ID specialists, pharmacists, psychologists); Telemedicine expert</td>
<td>A video collaboration tool was used for consultations between prison and hospital teams, as well as between treatment recipients and a hospital hepatologist, also after any inmate release. Treatment was prescribed by the hepatologist and administered by the prison healthcare providers. Prisoners were consulted on study design, and their input contributed to the use of telemedicine and the choice of the quickest treatment regimen (non-ribavirin).</td>
<td>A test-and-treat strategy enabled the prison to screen 99.5% of its inmates for HCV, treated everyone who was infected and would be in prison more than 30 days, established a teleconsultation programme for those who were released. The programme achieved SVR in 97% of the treated prisoners. At the end of the programme, no inmate had any detectable HCV RNA.</td>
</tr>
</tbody>
</table>

SLOVENIA 2007-2018
National healthcare network for managing HCV in PWID
An integrated approach


Counselling to prevent HCV infection

Testing for HCV infection (every 6–12 months)

HBV/HAV vaccination

Identification of HCV treatment eligible patients

Transient elastography on the spot (Fibroscan*)

Motivation, assessment

Linkage-to-care

18 Drug treatment centres

DAA treated: N=173

Treatment success: mITT

PWID: SVR=97%

Medical evaluation/assessment
Clinical management
Counselling, motivation
Treatment (DAAs)

5 Viral hepatitis centres

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A TAKE-HOME MESSAGE
How to make an effective response to viral hepatitis in PWID?

• HCV care in PWID needs to be patient-centered
• Access to HCV care needs to be re-defined and de-centralised
• One size does not fit all
• Multiple models and interventions adapted to specific settings are needed