Barriers to HCV treatment: A need for a public health approach

Slides adapted from Dr Hélène Fontaine, Hepatology Unit, Hôpital Cochin, Paris
Hepatitis C: A dynamic epidemic

- **Prevalence:** 71 million infected
- **Incidence:** 1.75 million/year (unsafe health care injections, and drug use)
Viral Hepatitis-Related Mortality

10th cause of mortality in 2013

Global Report on Hepatitis, WHO, 2017

Stanaway, Lancet 2016
WHO Objective: Elimination of viral hepatitis by 2030

Global Report on Hepatitis, WHO, 2017

Stanaway, Lancet 2016
Cascade of care

World cascade of care

Figure 2: Cascade of care in the European Union, 2015
The error bars represent 95% uncertainty intervals.

Global Report on Hepatitis, WHO, 2017
Reducing Incidence
Exemple of effective strategies in PWIDs in Montréal

Mathematic models estimating the effect of TasP strategies on HCV transmission and related morbidity, according to variations of components of the HCV cascade of care

**Incidence of HCV at 10 years**  **Prevalence of HCV at 10 years**  **Decrease of cirrhosis complications at 10 and 40 y**

**Scenario 7:**
- Time of contamination to diagnosis = 6 months vs 2 years
- Time to linkage-to-care = 6 months vs 1.7 years
- Decrease of loss to follow-up = 5%/year vs 10.2%/year
- Beginning of treatment = 20% vs 5% of cases
- Treatment whatever the stage of fibrosis
- SVR rate >90%

Cousien, BMC Inf Dis 2017
Exemple of effective strategies in MSM in the UK

- Difficult to reduce low incidence by 90% (i.e. to less than 0.14%)

- Requires:
  - All treated after diagnosis (currently 88% tested/year) plus 25% behavior reduction
  - Enhanced testing and treatment: all tested every 6 months and treated

Reducing Mortality through better access to care
Barriers to HCV elimination in the US

Analysis of the care pathway in US HCV patients identifying the barriers to management in the care cascade in the real life (National laboratory database)

974,000/17 millions (5,7 %) were screened positive

338,000 had HCV RNA testing

390,000 had fibrosis severity assessment

18,000 were treated

Rege S et al, PS66, EASL 2019
Barriers to HCV elimination in the US

Analysis of the care pathway in US HCV patients identifying the barriers to management in the care cascade in the real life (National laboratory database)

Origin of prescriptions
Barriers to HCV elimination in the US

- Several barriers, mainly between screening and diagnosis and between diagnosis and treatment
- One third of screenings are prescribed by general practitioners, but the patients are treated by specialists
- Improving linkage-to-care would facilitate HCV elimination

Reau S et al, PS066
Lifting barriers in the cascade of care?

People living with chronic viral hepatitis
- Testing
- Linkage to care
- Treatment uptake
- Treatment adherence
- Viral suppression
- Cure (HCV) or viral suppression (HBV)

Operational interventions to optimise engagement and retention along care continuum
- Improved access to testing
- Education about testing
- Facilitated referral to specialist care
- Programmes to help patients meet criteria for treatment eligibility
- Education about treatment
- Co-located testing and care services
- Psychological therapy and counselling for comorbid patients
- Resources for primary care providers to manage treatment
- Coordinated treatment for hepatitis and other comorbidities
- Directly observed therapy
- Directly observed therapy

Zhou K et al, Lancet Infect Dis 2016
Best approach: «Test and treat»!

Visit #1
- Anti-HCV antibody (Physician)
- Rapid anti-HCV antibody test (Health care worker)
- Dried blood spot sample (Health care worker)
- Point-of-care HCV RNA test and diagnosis (Health care worker)

Visit #2
- Phlebotomy (Phlebotomist)
- Central Lab Antibody test 1-2 weeks

Visit #3
- Phlebotomy (Phlebotomist)
- RNA test 1-2 weeks
- Receive diagnosis (Physician)

Visit #4
- Phlebotomy (Phlebotomist)
- RNA test 1-2 weeks
- Receive diagnosis (Physician)

Visit #5
- Receive diagnosis (Physician)

Test
- Increased time, visits and lost of follow up

Treat

Test

© ESCMID eLibrary by author

HCV RNA/Core Ag Screening

GenXpert

POCT

GenDrive

HCV core Ag quantification

- Small (23cm)
- Light (1kg)
- Rechargeable battery
- Wireless connection
- LOD/LLOQ: ‘0 IU/mL
- CE marked and WHO prequal.

Abbott/Alere

Samba semi-Q

Developed for HIV, adapted for HCV

Others

Chevaliez & Pawlotsky. J Hepatol 2018

Duchesne, J Int AIDS Soc 2017

LOD: 1000 IU/mL

© ESCMID eLibrary by author
Integrated HIV-HBV-HCV screening

• 2018 EASL recommandation to implement 3-virus screening in at-risk populations

• Recommandation in the French general population to screen the 3 blood-borne viruses once in a lifetime (AFEF 2018)

Ex: Portable « POC » ELISA device from MAGIA
Self-testing

• Concept of remote testing acceptable
• But evidence of tension associated with outcomes:
  • value of autonomy
  • fear of dealing with positive result in isolation
  • linkage to care
Test-and-treat: Where? By whom?

- Sexual health
- Drug and alcohol clinics
- Primary health care / GPs
- Community health centres
- Prisons
- Needle and syringe programmes
- Tertiary care hospital
- Laboratories
- Pharmacies

© ESCMID eLibrary by author
Screening in an anesthesia consultation

Systematic screening (HBsAg and HCV Ab) in 3,000 patients

Characteristics of the 12 HCV RNA + patients

Already known (n = 10)
At least one risk factor of infection (n = 9)

Newly diagnosed (n = 2)

2 new patients

HBsAg+ = 0.26%
Anti-HBc+ = 4.32%
HBV DNA + = 0.13%
HCV Ab+ = 0.44%
HCV RNA + = 0.07%
The experience of drug user centers in Australia

Observatory in 15 centers managing 1,001 patients with addiction (drugs/alcohol)

<table>
<thead>
<tr>
<th>Last injection (frequency)</th>
<th>HCV testing</th>
<th>Treatment uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last month (≥daily)</td>
<td>Included</td>
<td>Chronic HCV</td>
</tr>
<tr>
<td></td>
<td>Serology Performed</td>
<td>Management began</td>
</tr>
<tr>
<td>32 % 13 % 20 % 35 %</td>
<td>862 86 %</td>
<td>511 85 %</td>
</tr>
<tr>
<td>1-12 months</td>
<td>HCV Ab +</td>
<td>Treatment</td>
</tr>
<tr>
<td></td>
<td>734 85 %</td>
<td>353 59 %</td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>HCV RNA done</td>
<td></td>
</tr>
<tr>
<td></td>
<td>550 75 %</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Management from screening and fibrosis evaluation to treatment in drug user centers increases the number of cured patients

Valerio H, Australie, EASL 2019, Abs. PS-070
Management of migrants at arrival (Italy)

Cascade of care for screened patients

2,639 screening migrants

**HBV infected**
- HBS Ag+ (n = 257)
- Chronic hepatitis B (n = 70)
- Treatment initiated (n = 55)
- Undetectable HBV DNA (n = 47)

**HCV infected**
- Anti-HCV+ (n = 24)
- HCV RNA+ (n = 18)
- Treatment initiated (n = 15)
- SVR12 (n = 14)

**HIV infected**
- HIV+ (n = 57)
- Treatment initiated (n = 57)
- Undetectable HIV RNA at 1 year (n = 34)

➡ Early management is not only possible, but also efficient

© ESCMID eLibrary by author
Simplification of prescription and DAA treatment follow-up

- Reimbursement in all patients
- Near the patient (prison, drug user centers, migrant centers, sexual health centers...)
- Prescription by a medical doctor
- Follow-up by a medical doctor or a nurse, a pharmacist, a social worker, etc...
- By-phone or on-line consultations

Expanding the treater pool +++
Task Shifting

Gave informed consent (n=681)

LTFU before day 0 (n=45)

Excluded or received treatment through insurance (n=36)

Started LDV-SOF treatment (n=600)

Received treatment from nurses (n=150)

Received treatment from general practitioners (n=160)

Received treatment from specialist (n=290)

 Included in analysis (n=150)* With SVR data: 141 (94%)

 Included in analysis (n=160)* With SVR data: 147 (91.9%)

 Included in analysis (n=290)* With SVR data: 263 (90.7%)
International randomized trial evaluating an intervention based on a simplified follow-up schedule of patients treated with glecaprevir/pibrentasvir

Chronic HCV treatment naïve patients without cirrhosis, genotypes 1-6
N=375

Baseline (Week 0)
Randomisation (1:2 Standard ; Simplified)

Standard Arm
Week 4
Phone contact visit*
On-site visit
EOT (Week 8)
Phone contact visit*
On-site visit
SVR12 (Week 20)
On-site visit

Simplified Arm
Week 4
Phone contact visit*
On-site visit
EOT (Week 8)
Phone contact visit*
On-site visit
SVR12 (Week 20)
On-site visit

Conclusion: non inferiority of the simplified vs standard follow-up

Dore et al, EASL 2019
Conclusion
Global Predictive Timing of HCV Elimination

Markov model assessment of the progress made in 45 high-income countries towards meeting the WHO 2030 HCV elimination targets for incidence, mortality, diagnosis and treatment of chronic HCV infection.

Estimated Year of Elimination

- Countries on track by 2030
- Countries on track by 2040
- Countries on track by 2050
- Countries not on track to achieve elimination by 2050

Razavi et al, EASL 2019, Abs. SAT-260