Access to direct-acting antiviral availability and reimbursement restrictions in high-income countries: The European landscape

Prof Jeffrey V. Lazarus [Jeffrey.Lazarus@isglobal.org]
Barcelona Institute of Global Health (ISGlobal), Hospital Clínic, University of Barcelona
CHIP, Rigshospitalet, University of Copenhagen, WHO Collaborating Centre on HIV and Viral Hepatitis
Editor-in-Chief, Hepatology, Medicine and Policy
Disclosures

Personal consultancy/speaker fees from AbbVie, Gilead Sciences, MSD. Institution research grants from AbbVie and Gilead Sciences.

Research grants from European Liver Patients Association and World Hepatitis Alliance.

Former employee of World Health Organization, The Global Fund
Looking at two viral hepatitis studies published in 2017:

Restrictions for reimbursement of interferon-free direct acting antiviral therapies for HCV infection in Europe

Alison D. Marshall, Stine Nielsen, Evan B. Cunningham, Alessio Aghemo, Hannu Alho, Markus Backmund, Philip Bruggmann, Olav Dalgard, Robert Flisiak, Graham Foster, Liana Gheorghe, David Goldberg, Ioannis Goulis, Matthew Hickman, Patrick Hoffmann, Ligita Jancorienė, Peter Jarčuška, Martin Kåberg, Mihály Makara, Matti Maimets, Rui Marinho, Mojca Matičič, Suzanne Norris, Sigurður Ólafsson, Anne Øvrehus, Jean-Michel Pawlotsky, James Pocock, Geert Robaeys, Carlos Roncero, Marieta Simonova, Jan Sperl, Michele Tait, Ieva Tolmane, Stefan Tomaselli, Marc van der Valk, Adriana Vince, Gregory J. Dore, Jeffrey V. Lazarus*, and Jason Grebely* on behalf of the International Network on Hepatitis in Substance Users (INHSU) Network

*contributed equally

The 2016 Hep-CORE Report
Monitoring European policy responses to viral hepatitis

Jeffrey V. Lazarus, Samya R. Stumo, Kelly Safreed-Harmon, on behalf of the Hep-CORE Study Group (Charles Gore (World Hepatitis Alliance), Hande Harmanci (World Health Organization), Magdalena Harris (London School of Hygiene and Tropical Medicine, United Kingdom), Greet Hendrickx (Viral Hepatitis Prevention Board), Marie Jauffret-Roustide (Paris Descartes University, France), Achim Kautz (European Liver Patients Association), Mojca Matičič (University Medical Centre Ljubljana, Slovenia), Luis Mendão (Grupo de Ativistas em Tratamentos (GAT), Portugal), Antons Mozalevskis (WHO Regional Office for Europe), Raquel Peck (World Hepatitis Alliance), Tatjana Reic (European Liver Patients Association), Eberhard Schatz (Correlation Network), Kaarlo Simojoki (A-Clinic Foundation, Finland), Joan Tallada (European AIDS Treatment Group)
WHO Global Health Sector Strategy on Viral Hepatitis 2016–2021

28 May 2016: The first of its kind, WHO publishes a global strategy aiming for elimination of viral hepatitis as a major public health threat by 2030

Some countries may achieve the WHO targets by or even before 2030

Iceland

National plan to treat all HCV patients according to Icelandic guidelines over 3 years
- Prioritisation of active PWID and patients with moderate-to-severe fibrosis
- Jan to Dec 2016, 1/3 of the HCV population were treated

Georgia

Georgia HCV Elimination Program
- Prioritisation of patients with advanced liver disease
- April 2015 to April 2016, 8448 people treated, a 400% increase in the number patients treated over the previous 4 years

Australia

Public health policy
- Access for all to highly effective HCV treatment was made a priority
- March to July 2016, 11% (26,360 patients) of the HCV population were treated

Eliminating HCV requires national plans

A viral hepatitis resolution approved by the World Health Assembly in 2014 called on all countries to develop and implement national strategies for preventing, diagnosing and treating viral hepatitis.
Background on policy implications for restrictions on treatment of PWID

- Many countries have developed national hepatitis plans…but are they comprehensive? Do they cover treatment, for ex?
- Interferon-free HCV DAAs have cure rates of >90%, fewer side-effects & shorter treatment duration
- List price of DAA therapies has led governments to place restrictions on reimbursement criteria
- Universal HCV DAA coverage = immense challenges
- Prior evidence on reimbursement restrictions:
  - Marshall et al. 2016 (Canada)
  - Barua et al. 2015 (US)
Aims

To review the availability of interferon-free DAA therapy among EU/EEA countries and Switzerland

- sofosbuvir + ribavirin (Sovaldi®)
- sofosbuvir/ledipasvir + ribavirin (Harvoni®)
- sofosbuvir/velpatasvir + ribavirin (Epolusa®)
- ombitasvir/paritaprevir/ritonavir + dasabuvir + ribavirin (Viekirax®)
- elbasvir-grazoprevir + ribavirin (Zepatier®)
- sofosbuvir + daclatasvir + ribavirin (Daklinza®)
- sofosbuvir + simeprevir + ribavirin

To review national criteria for interferon-free DAA therapy reimbursement among EU/EEA countries and Switzerland

To review European national policies with regards to:

- awareness & engagement,
- monitoring & data collection,
- prevention,
- testing & diagnosis,
- clinical assessment,
- treatment.

To inform efforts to monitor countries’ implementation of the WHO GHSS on viral hepatitis from 2016

To engage European patient groups in monitoring of viral hepatitis policy response


Methods in brief

**Primary outcomes**
- Minimum fibrosis stage required
- Drug and alcohol restrictions
- Prescriber-type restrictions
- HIV co-infection restrictions

**Data collection (Nov 2016 – July 2017)**
- National experts, Ministry of Health websites; online drug formularies

**Prospective cross-sectional study**
- 39-item questionnaire
- Administered to 25 European countries, 24 European Liver Patients’ Association (ELPA) member patient organizations
- Questionnaire items on treatment asked about clinical guidelines, availability, cost, treatment settings, and restrictions on treatment access
- Online data collection (Jul 2016 – Oct 2016)
  - ELPA member groups
Reimbursement of DAAs

- The most common DAA reimbursed was PrOD ± RBV (94%)

### Table 1. Reimbursement of interferon-free DAAs for HCV infection in Europe

<table>
<thead>
<tr>
<th>HCV DAA Therapy</th>
<th>SOF + RBV</th>
<th>SOF/RBV</th>
<th>SOF/TEC/RBV</th>
<th>PRD + RBV</th>
<th>EBR + GZR</th>
<th>SOF + DCV ± RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Belgium</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Croatia</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Cyprus</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Denmark</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>England</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Estonia</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Finland</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>Y</td>
<td>NO</td>
</tr>
<tr>
<td>France</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Germany</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Greece</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Hungary</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Iceland</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Ireland</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Italy</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Latvia</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Liechtenstein</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Lithuania</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Malta</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Netherlands</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>N. Ireland</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Norway</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Poland</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Portugal</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Romania</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Scotland</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Slovakia</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Slovenia</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Spain</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Sweden</td>
<td>YES*</td>
<td>YES*</td>
<td>YES</td>
<td>YES</td>
<td>YES*</td>
<td>YES*</td>
</tr>
<tr>
<td>Switzerland</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES*</td>
<td>YES*</td>
</tr>
<tr>
<td>Wales</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES*</td>
<td>YES*</td>
</tr>
</tbody>
</table>

**Source:** Marshall, AD et al. Restrictions for reimbursement of interferon-free direct acting antiviral therapies for HCV infection in Europe. Poster presented at The International Liver Congress. 19-23 April 2017. Amsterdam, The Netherlands.
DAAs available to all patients diagnosed with HCV?

- 64% (n=25) of patient groups surveyed reported access in their country to all below DAA therapies
- 16% of groups reported no DAAs (though this has changed since mid-2016), and the remaining 20% reported varying availability

**Patient groups reporting HCV treatment available to all HCV diagnosed patients in their country by drug**

<table>
<thead>
<tr>
<th>HCV DRUGS AVAILABLE FOR ALL HCV DIAGNOSED PATIENTS</th>
<th>NUMBER OF COUNTRIES REPORTING HCV DRUG AVAILABILITY (N=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir</td>
<td>Available: 17, Not available: 8</td>
</tr>
<tr>
<td>Dasabuvir</td>
<td>Available: 18, Not available: 7</td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>Available: 20, Not available: 5</td>
</tr>
<tr>
<td>Ombitasvir/Paritaprevir/Ritonavir</td>
<td>Available: 20, Not available: 5</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>Available: 20, Not available: 5</td>
</tr>
<tr>
<td>None of the above</td>
<td>Available: 4, Not available: 21</td>
</tr>
</tbody>
</table>

Minimum fibrosis stage required for DAA reimbursement

57% (n=20) of countries required evidence of ≥F2

*Fibrosis stage restrictions based on HCV genotype

Fibrosis stage is included in a point system for prioritisation of DAA therapy

Fibrosis stage restrictions based on HCV genotype and IL28B polymorphism

Drug/alcohol restrictions for DAA reimbursement

83% (n=29) of countries had no drug or alcohol use restrictions

97% (n=34) of countries had no additional restrictions for HIV-HCV co-infection

88% (n=25) of patient groups surveyed reported some level of restrictions on access to DAAs in their country.

72% cited fibrosis level (unspecified level), second only to restriction on people currently injecting drugs (13 patient groups, 48%).

### Restrictions on access to direct-acting antivirals for the treatment of HCV

<table>
<thead>
<tr>
<th>Type of Restriction</th>
<th>Number of Countries Reporting Restrictions (N=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>3</td>
</tr>
<tr>
<td>Fibrosis level</td>
<td>18</td>
</tr>
<tr>
<td>People currently injecting drugs</td>
<td>13</td>
</tr>
<tr>
<td>People who have abstained from injecting drugs for a specified time</td>
<td>8</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>8</td>
</tr>
<tr>
<td>Quotas</td>
<td>7</td>
</tr>
<tr>
<td>Past or present drug users only if receiving OST</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
</tr>
<tr>
<td>People who injected drugs in the past</td>
<td>1</td>
</tr>
<tr>
<td>Do not know</td>
<td>1</td>
</tr>
</tbody>
</table>

94% (n=33) of countries required specialists to prescribe DAA therapy.

Licensing requirements for DAA prescription

- 24% (n=25) of patient groups surveyed reported that non-specialists are able to prescribe DAAs to HCV patients in their country and in only two cases were they GPs
- The majority (64%) require at least a gastroenterologist

Expanding prescriber base

- In countries without prescriber restrictions, such as Australia, general practitioners and non-specialists have greater access to reach patients in need of treatment

- 5-15% of individuals initiating DAAs had treatment prescribed by a GP

**Source:** Hajarizadeh B, Grebely J, Matthews GV, Martinello M, Dore GJ. The path towards hepatitis C elimination in Australia following universal access to interferon-free treatments. Poster to be presented at: International Liver Congress. 2017; Amsterdam, Netherlands.
Is HCV treatment provided in prisons in your country?

- **Yes**
- **No**
- **Unknown / Unavailable**

Percentage of prisons providing HCV treatment:

- AT: 10-19%
- DK: 40-49%
- FR: 0-9%
- DE: 0-9%
- HU: 20-29%
- PT: 0-9%
- SK: 100%
- SV: 100%

All other countries responding affirmatively were unable to specify percentages of prisons.

68% (n=25) of patient groups surveyed reported that HCV treatment is not available in prisons.

Do HCV patients in your country have the option of being treated in non-hospital settings?

- Yes
- No
- Unknown / Unavailable

80% (n=25) of patient groups surveyed reported that HCV treatment is not available outside of a hospital setting.

Discussion (1)

- Global elimination of HCV now a possibility
- Findings highlighted considerable variability in DAA therapy restrictions across Europe, particularly with respect to fibrosis stage and injecting drug status
- Restricting DAA prescribing to specialists is a considerable barrier to broad access
- Access to HCV treatment outside of hospital settings is limited yet key for reaching and treating high-risk patient populations
- Future studies would benefit from triangulation, eg having participants from multiple stakeholders groups
Discussion (2)

Implications for health policy-makers and health service delivery with evidence of some countries not following EASL HCV treatment guidelines (2016)

- A shift is required from individual management of HCV to population management:
  - Improve screening, especially among those at high risk of HCV infection, through healthcare access points
  - Scale-up treatment including by broadening the HCV prescriber base
  - Expand models of care to include screening, assessments, treatment, harm reduction and re-screening for those with continued high-risk behaviors

- To achieve global HCV elimination, partnership is required between HCPs, policy-makers, patient organizations, and industry to develop and implement local strategies
Central elements for HCV elimination

- Increase screening and diagnosis
- Increase uptake of effective treatment
- Expanded models of HCV management
- Political leadership
- National HCV strategies
- Policy change
Acknowledgements

**Study Authors**

*In particular:* Alison Marshall, Jason Grebely, Stine Nielsen, Evan Cunningham

*and* Samya R. Stumo, Kelly Safreed-Harmon

**Student Scholarships**

**Hep-CORE study countries / ELPA members**

- Austria
- Belgium
- Bosnia & Herzegovina
- Bulgaria
- Croatia
- Denmark
- Egypt
- Finland
- France
- Germany
- Greece
- Hungary
- Israel
- Italy
- Macedonia
- Netherlands
- Poland
- Portugal
- Romania
- Serbia
- Slovakia
- Slovenia
- Spain
- Sweden
- Turkey
- Ukraine
- United Kingdom

**Hep-CORE study group**

- Charles Gore (World Hepatitis Alliance)
- Hande Harmanci (WHO)
- Magdalena Harris (LSHTM)
- Greet Hendrickx (Viral Hepatitis Prevention Board)
- Marie Jauffret-Roustide (Paris Descartes University)
- Achim Kautz (ELPA)
- Mojca Matičič (University Medical Centre Ljubljana)
- Luis Mendão (Grupo de Ativistas em Tratamentos (GAT))
- Antons Mozalevskis (WHO Euro)
- Raquel Peck (World Hepatitis Alliance)
- Tatjana Reic (ELPA)
- Eberhard Schatz (Correlation Network)
- Kaarlo Simojoki (A-Clinic Foundation, Finland)
- Joan Tallada (European AIDS Treatment Group)

Hep-CORE funding to ELPA provided by AbbVie, Gilead Sciences, MSD.

For more information or questions about these two studies:

- amarshall@kirby.unsw.edu.au
- Jeffrey.Lazarus@isglobal.org