Funding Innovation in Hepatitis C Treatment

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LSHTM, 5 June 2015
Outline

• The economic and social impact of Hepatitis C

• New treatments in Hepatitis C

• Funding models for new hepatitis C treatments
  • From efficacy to effectiveness
  • Funding models and using innovative approaches
HCV is a major public health issue

Hepatitis C is a blood-borne infectious disease. It is caused by the hepatitis C virus (HCV) which lives and replicates in the liver.

About 170 million people are chronically infected with hepatitis C virus (HCV) worldwide.

4 OUT OF 5 BECOME CHRONIC

Acute
Can resolve within 6 months

Chronic
Can last a lifetime and cause a considerable impact on quality of life

For Every 100 People Infected with the Hepatitis C Virus

75–85 Will Develop Chronic Infection

60–70 Will Develop Chronic Liver Disease

5–20 Will Develop Cirrhosis

1–5 Will Die of Cirrhosis or Liver Cancer

More than 350,000 people die each year from hepatitis C-related liver disease.
A growing number of people are living with HCV-related sequelae

Estimated number of people living with HCV-related cirrhosis and decompensated cirrhosis/HCC in England 1995–2020 (95% CI)

<table>
<thead>
<tr>
<th>Year</th>
<th>Compensated cirrhosis</th>
<th>Decompensated cirrhosis and HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>11,630 (9,060, 14,700)</td>
<td>4,210 (3,910, 4,520)</td>
</tr>
<tr>
<td>2015</td>
<td>9,550 (7,360, 12,040)</td>
<td>3,330 (3,150, 3,520)</td>
</tr>
<tr>
<td>2010</td>
<td>7,240 (5,600, 9,160)</td>
<td>2,430 (2,310, 2,550)</td>
</tr>
<tr>
<td>2005</td>
<td>5,090 (3,900, 6,430)</td>
<td>1,640 (1,560, 1,720)</td>
</tr>
<tr>
<td>2000</td>
<td>3,290 (2,520, 4,190)</td>
<td>1,020 (950, 1,090)</td>
</tr>
<tr>
<td>1995</td>
<td>1,960 (1,490, 2,510)</td>
<td>590 (530, 640)</td>
</tr>
</tbody>
</table>

The incidence of HCV-related liver cancer and death is also expected to peak in the coming decades

- At peak in the USA:
  - 38,600 cases of end-stage liver disease; 3,200 referrals for transplant; 36,100 deaths

Numbers of liver transplants have been increasing in Europe over the past two decades.

HCV-related cirrhosis is the commonest indication for liver transplantation in Europe.

- Virus-related disease = single largest indication for liver transplant in Europe
- 63% HCV-related

At a substantial cost for treating consequences of chronic HCV

Analysis included patients with HCV infection (n=286; 139 treatment-naïve) from France, Germany, UK, Italy and Spain, matched with control subjects without HCV

*Ps<0.002

ER: emergency room
Whilst, unlike HIV and HBV, HCV can be cured and this can be achieved faster and with fewer side effects

\[\text{The beginning of the end of hepatitis C?}\]

Unlike chronic infection with HBV or HIV, where a reservoir of virus always remains once the infection is established, HCV can be eradicated in the vast majority of patients\(^1\)

- SVR is defined as undetectable HCV RNA in the blood after completion of therapy\(^2\)
  - SVR24 has been the gold standard measure of treatment success in the past
  - SVR12 is now an established primary endpoint and measure of treatment success accepted by clinical and regulatory agencies

New therapies are recommended by leading organisations

WHO issues its first hepatitis C treatment guidelines

News release

9 APRIL 2014 | LONDON, UNITED KINGDOM - WHO has issued its first guidance for the treatment of hepatitis C, a chronic infection that affects an estimated 130 million to 150 million people and results in 350 000 to 500 000 deaths a year.

The publication of the "WHO Guidelines for the screening, care and treatment of persons with hepatitis C infection" coincides with the availability of more effective and safer oral hepatitis medicines, along with the promise of even more new medicines in the next few years.

"The WHO recommendations are based on a thorough review of the best and latest scientific evidence," says Dr Stefan Wiktor, who leads WHO's Global Hepatitis Programme. "The new guidance aims to help countries to improve treatment and care for hepatitis and thereby reduce deaths from liver cancer and cirrhosis."

LSE
But at what cost?

Sovaldi, a new hepatitis C treatment, can cure up to 90 percent of patients within three months. There’s just one problem: The drug costs $1,000 a day. That price tag has thrown the biotechnology world into turmoil, as lawmakers and insurance companies complain that Sovaldi’s maker is trying to milk desperate patients.

How Much Should Hepatitis C Treatment Cost?
Patient segments and potential interventions

1. **Prisoner populations: Prevention treatment**
   ① Assure access for an undertreated segment, leverage closed system to improve public health and cure by release from prison
   ② Support routine diagnosis of high-risk population
   ③ Early intervention in closed system to reduce long-term cost burden

2. **Methadone maintenance programs: Prevention treatment**
   ① Assure access for an undertreated segment and decrease HCV transmission to society
   ② Support routine diagnosis of high-risk population
   ③ Cure and prevention of transmission in high-risk population

3. **Non-marginalised populations: Develop integrated care models**
   ① Rapid cure with limited side-effects
   ② Higher societal benefits

4. **An EU-wide HCV prevention program**
   ① Target key causes of spread by supporting IC programs
How do we pay for all this?

1. Are treatments effective (not only efficacious)?
2. What are the target populations and in what ways can we target them?
Evidence development:

The importance of registries in showcasing benefit and effectiveness and some evidence of how it can be used to gauge effectiveness and promote efficiency

Example: Monitoring registries in Italy
Clinical and anthropometric baseline data of cases analyzed

<table>
<thead>
<tr>
<th></th>
<th>Exenatide</th>
<th>Liraglutide</th>
<th>Saxagliptin</th>
<th>Sitagliptin</th>
<th>Sitagliptin/ Met</th>
<th>Vildagliptin</th>
<th>Vildagliptin/ Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/ F)</td>
<td>8,196/ 8,565</td>
<td>10,436/ 9,713</td>
<td>6,427/ 5,198</td>
<td>8,835/ 7,847</td>
<td>4,211/ 3,479</td>
<td>2,790/ 2,568</td>
<td>3,671/ 2,840</td>
</tr>
<tr>
<td>Age in years, mean</td>
<td>57.4</td>
<td>58.0</td>
<td>62.8</td>
<td>61.0</td>
<td>61.1</td>
<td>61.5</td>
<td>61.1</td>
</tr>
<tr>
<td>Body Mass Index (Kg/m²), mean</td>
<td>36.2</td>
<td>39.0</td>
<td>29.9</td>
<td>30.9</td>
<td>30.9</td>
<td>30.7</td>
<td>30.8</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl), mean</td>
<td>187.8</td>
<td>179.4</td>
<td>162.0</td>
<td>169.7</td>
<td>166.2</td>
<td>178.2</td>
<td>168.0</td>
</tr>
<tr>
<td>HbA₁c (%) , mean</td>
<td>8.8</td>
<td>8.5</td>
<td>8.0</td>
<td>8.2</td>
<td>8.1</td>
<td>8.3</td>
<td>8.1</td>
</tr>
</tbody>
</table>
Total treatment costs and mean cost/patient from the Antidiabetics AIFA Monitoring Registry

<table>
<thead>
<tr>
<th></th>
<th>Total costs (Thousand €)</th>
<th>% of total cost</th>
<th>Mean treatment duration (days)</th>
<th>Mean cost per patient (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide</td>
<td>22,184.60</td>
<td>26.4%</td>
<td>272.0</td>
<td>1,323.60</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>26,851.30</td>
<td>32.0%</td>
<td>282.7</td>
<td>1,332.60</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>6,550.90</td>
<td>7.8%</td>
<td>255.0</td>
<td>563.52</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>15,093.90</td>
<td>18.0%</td>
<td>351.0</td>
<td>921.40</td>
</tr>
<tr>
<td>Sitagliptin/Met</td>
<td>4,313.50</td>
<td>5.1%</td>
<td>229.1</td>
<td>560.90</td>
</tr>
<tr>
<td>Vildagliptin</td>
<td>4,467.60</td>
<td>5.3%</td>
<td>351.0</td>
<td>833.80</td>
</tr>
<tr>
<td>Vildagliptin/Met</td>
<td>4,506.40</td>
<td>5.4%</td>
<td>232.7</td>
<td>692.12</td>
</tr>
</tbody>
</table>
HCV patient population – Overview

Example: In Spain 1/3 of the HCV population is F3-F4 with patient management mainly taking place by specialists

<table>
<thead>
<tr>
<th>Mode of transmission</th>
<th>Patient setting</th>
<th>Prisoners</th>
<th>Active and past IDUs</th>
<th>BT infected</th>
<th>HCP</th>
<th>Other*</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Stage F1-F2</td>
<td>≈ 70%</td>
<td>≈ 70%</td>
<td>≈ 70%</td>
<td>≈ 70%</td>
<td>≈ 70%</td>
<td>≈ 30%</td>
</tr>
<tr>
<td></td>
<td>2. Stage F3-F4</td>
<td>≈ 30%</td>
<td>≈ 30%</td>
<td>≈ 30%</td>
<td>≈ 30%</td>
<td>≈ 30%</td>
<td>≈ 70%</td>
</tr>
<tr>
<td>Primary attention</td>
<td>23k</td>
<td>7k</td>
<td>27k</td>
<td>13k</td>
<td>58k</td>
<td>~130k</td>
<td></td>
</tr>
</tbody>
</table>

| Specialists (Office based and Uni. clinics) | n.a. | 30k | 110k | 51k | 232k | ~421k |
| Total                                  | 23k | 37k | 137k | 63k | 290k | ~550k |

Other: Incl. other high-risk groups (e.g. men-having sex with men and unknown mode of transmission)
Most new cases of HCV arise from IDU

Applying filters to set treatment priorities: Treatment decisions contingent on patient willingness to comply

### Risk factors for acute HCV infection

- Injecting illicit drug use (IDUs): 53%
- High-risk behavior in the past: 25%
- Sexual activity: 10%
- Unknown: 7%
- Blood transfusion/hemodialysis: 3%
- Health care employment: 2%

### Treatment decision – HCV

- **Treat**
  - Rehabilitated IDUs
  - Patients with symptoms of liver disease
  - GT/GT3 patients
- **Wait**
  - Recovering IDUs
  - Young patients
  - GT1 patients
- **Don't treat**
  - Current IDUs
  - Elderly
  - Decompensated liver disease
  - Psychiatric illness

**Decision levers**

1. **Ability** of patient to comply with treatment
2. **Willingness** of patient to undergo treatment
3. **Likelihood** of treatment success (e.g. genotype)
Payment models: Paying for value

• Clinical benefit assessment
  • Ranking of technologies based on their clinical benefit in relation to current standards of care

• Clinical and cost effectiveness
  • New treatments can be highly cost-effective driven by high clinical benefit or QALY gain

• But, high budget impact
  • Treating entire patient population could require expenditure 3-5 times greater than total drug spend

• And, uncertainty about outcome in the community
Financing models for HCV innovation

A mix of models to suit different patient populations

1. Social/Health impact bonds
   - A financing mechanism where investor returns are aligned with social outcomes
   - Based on contract with public sector in which it commits to pay for improved social outcomes (re-payments from public sector plus a financial return)
   - Adolescent Behavioral Learning Experience (US/NYC): evidence-based intervention to adolescents after release in the community

<table>
<thead>
<tr>
<th>Outcome improvement [%]</th>
<th>IRR [%]</th>
<th>City net savings [USD m]</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 20.0</td>
<td>8.1</td>
<td>20.5</td>
</tr>
<tr>
<td>≥ 16.0</td>
<td>5.3</td>
<td>11.7</td>
</tr>
<tr>
<td>≥ 13.0</td>
<td>3.1</td>
<td>7.2</td>
</tr>
<tr>
<td>≥ 12.5</td>
<td>2.7</td>
<td>6.4</td>
</tr>
<tr>
<td>≥ 12.0</td>
<td>2.3</td>
<td>5.6</td>
</tr>
<tr>
<td>≥ 11.0</td>
<td>2.0</td>
<td>1.7</td>
</tr>
<tr>
<td>≥ 10.0</td>
<td>0.0</td>
<td>≥ 1.0</td>
</tr>
<tr>
<td>≥ 8.5</td>
<td>-25.94</td>
<td>≥ 1.0</td>
</tr>
</tbody>
</table>
Financing models for HCV innovation

A mix of models to suit different populations: Non-marginalised populations

1 Risk sharing and Managed Entry Schemes

- Disagreement or uncertainty on therapeutic value
- Very high cost and budget impact
- Uncertainty as to who might benefit most and possibly larger patient numbers
- Reduce decision uncertainty, enable effectiveness evidence to enter decision-making, improve affordability (through P/Q or discounting, etc.)
Examples of risk sharing types and risks addressed by individual schemes

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Right patients</th>
<th>Uncertain clinical value</th>
<th>Low cost effectiveness</th>
<th>Budget overspend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coverage with ED</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>x</td>
</tr>
<tr>
<td>Conditional coverage</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Outcome guarantee</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>x</td>
</tr>
<tr>
<td>Price-volume deal</td>
<td>x</td>
<td>x</td>
<td>X</td>
<td>Yes</td>
</tr>
</tbody>
</table>
“Innovative” payor schemes

• Why?
  – Disagreement or uncertainty on therapeutic value
  – Uncertainty on dose in daily practice
  – Possibility to drive to larger patient access

• Main types of strategies
  – Portfolio deals
  – One price per patient
  – Targeting the patient out-of-pocket burden
  – Disease management, integrated care and service agreements
The role of Managed Entry Schemes in delivering value to health systems: Evidence of how Risk Sharing and Managed Entry Schemes are used in practice
Main objectives of MEAs

BI: Budget impact
CE: Cost-effectiveness
Use: utilisation
U: Uncertainty of treatment

Ferrario & Kanavos, 2013
Common elements of MEAs

PVAs: Price-volume agreements
pp: per person

Ferrario & Kanavos, 2013
**Therapeutic classes**

**ATC groups** (according to ATC-index 2011)
A: Alimentary tract and metabolism
B: Blood and blood forming organs
C: Cardiovascular system
D: Dermatologicals
G: Genito urinary system and sex hormones
H: Systemic hormonal preparations, excl. sex hormones and insulins
J: Anti-infectives for systemic use
L: Antineoplastic and immuno-modulating agents
M: Musculo-skeletal system
N: Nervous system
R: Respiratory system
S: Sensory organs;
V: Various

ATC_Mix: There was one case in Italy where a particular AIFA-note contained medicines from different ATC-groups.

Ferrario & Kanavos, 2013
Conclusions

• HCV: a big public health concern
• The importance of prevention, also at EU level
• New funding models for certain populations
• Risk sharing and Managed Entry Schemes
• From Efficacy to Effectiveness & registries
• Bold moves in policy terms, but evidence that they can happen