The elimination of HCV: What data modelling predicts

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Conflicts of Interest

- I am an employee of the Center for Disease Analysis (CDA), Lafayette, Colorado, USA

- As an employee of CDA I am barred from receiving personal remuneration from outside sources

- CDA has received research grants from John C Martin Foundation, AbbVie, Boehringer Ingelheim, Gilead Sciences, Intercept Pharmaceuticals, National Academy of Sciences, World Health Organization (WHO)
What does it mean to eliminate hepatitis C?

“Elimination: Reduction to zero of the incidence of a specified disease/infection in a defined geographic area as a result of deliberate efforts; continued intervention measures are required” – Dowdle 1999

- Historically, blood transfusion and nosocomial sources were the predominant HCV transmission routes
- In Western Europe, incident cases occur primarily in high-risk populations, including people who inject drugs (PWID) and HIV+ men who have sex with men (MSM); immigration may also introduce new case (acute or viremic)

What types of models exist to inform the elimination of hepatitis C, and what questions do each of these models help us answer?

**Disease Transmission models**
- Inputs
  - Risk group population data
  - Scale of prevention efforts
  - Transmission probabilities
- Questions answered
  - Who is most at risk of acquiring or transmitting HCV?
  - Is transmission increasing, decreasing or stable?
  - What steps are necessary to prevent HCV transmission?

**Disease Burden models**
- Inputs
  - Background population data
  - HCV+ population data
  - Progression rates
- Questions answered
  - What is the current burden of HCV (prev., ESLD, death)?
  - Over the next 15+ years, how will the burden of HCV change?
  - What can be done to reduce the HCV disease burden?

**Cost-effectiveness models**
- Inputs
  - Cost data
  - DALY and/or QALY weights
  - Cost-effectiveness thresholds
- Questions answered
  - What is the cost of untreated HCV?
  - What costs will be incurred to implement HCV strategies?
  - How does curing HCV impact indirect measures of cost (DALYs and QALYs)?
In the EU in 2015, there were 3.2M (2.7M-4.0M) viremic infections with 1.2M diagnosed. Annually, there were 160K treated and 144K cured.

- The viremic prevalence of HCV in the EU-28 is 0.6% (95% UI: 0.4%-0.7%) with over one-third of infections already diagnosed.
- In 2015, an estimated 162,000 patients (or 5% of total infected) were treated.
- There were ~58,000 new infections (11.4 per 100,000) with an additional 30,000 HCV-RNA+ asylum seekers entering the EU-28, in 2015.

Source: Razavi 2016 – recent submission, ahead of print; Polaris Observatory (www.centerforda.com/polaris)
There is a wide range of prevalence, diagnosis, and treatment rates across the EU-28

**Source:** Razavi 2016 – recent submission, ahead of print; Polaris Observatory (www.centerforda.com/polaris)
The number of treated patients increased in 2014 and 2015 after a period of warehousing patients.

Total Number Treated in EU

Source: Razavi 2016 – recent submission, ahead of print; Polaris Observatory (www.centerforda.com/polaris)
WHO Targets – Increase screening, treatment and eligibility to achieve a 90% reduction in new infections

- Switch to direct acting antivirals with higher SVR, and increase treatment to achieve a ~5.5% treatment rate
- Expand screening to sustain treatment
- Prevent transmission through treatment of high-risk populations and individuals of all fibrosis stages (≥F0)

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Treated</td>
<td>78,700</td>
<td>162,400</td>
<td>170,500</td>
<td>173,900</td>
<td>173,900</td>
<td>173,900</td>
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<tr>
<td>Newly Diagnosed</td>
<td>88,770</td>
<td>88,770</td>
<td>88,770</td>
<td>94,540</td>
<td>119,590</td>
<td>166,230</td>
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<tr>
<td>Fibrosis Stage</td>
<td>≥F1</td>
<td>≥F2</td>
<td>≥F2</td>
<td>≥F0</td>
<td>≥F0</td>
<td>≥F0</td>
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<tr>
<td>New Infections</td>
<td>58,640</td>
<td>57,850</td>
<td>40,220</td>
<td>24,020</td>
<td>11,860</td>
<td>5,260</td>
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<td>Treated Age</td>
<td>15-64</td>
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<td>15-74</td>
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<tr>
<td>SVR</td>
<td>56%</td>
<td>89%</td>
<td>92%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
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</table>

Source: Razavi 2016 – recent submission, ahead of print; Polaris Observatory (www.centerforda.com/polaris)
Compared with 2015, total viremic infections is reduced by ~90%, LRD by 65%, HCC by 70% and DC by 60%

Source: Razavi 2016 – recent submission, ahead of print; Polaris Observatory (www.centerforda.com/polaris)
Curing HCV can reduce prevalence and incidence among PWID

- The way treatment is modeled has a substantial impact on outcomes (Figure 1) (Martin 2011)
- The impact of treatment is highly dependent on injecting duration and HCV prevalence (Figure 2) (Martin 2013)

Figure 1. a) Proportional treatment; b) Fixed treatment

Figure 2. One-way sensitivity analysis; % change from base-case scenario after 15 years

Sources:
However, secondary infections can be expected to occur until the viral pool is depleted

- In the absence of behavioral changes, the number of secondary infections should be expected to increase under all treatment scenarios
  - Re-exposure to the virus
- Under high level treatment, the number of secondary infections would peak and then drop corresponding with depletion of the viral pool

Source: Bruggmann 2016 - recent submission, ahead of print
Concerns of secondary infections shouldn’t change the decision to treat high-risk populations, and clear definitions should be employed.

- Out of 67,000 HCV infections in Belgium, ~64,000 are not active injectors (PWID) and can be treated without any risk of secondary infections.
- More than 75% of HCV+ PWID are on harm reduction.

CDA unpublished data
A one-size fits all approach doesn’t work when it comes to preventing HCV infections

New HCV Infections – Belgium

<table>
<thead>
<tr>
<th>Year</th>
<th>PWID</th>
<th>MSM</th>
<th>Vertical</th>
<th>Nosocomial</th>
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<tbody>
<tr>
<td>2013</td>
<td>181</td>
<td>64</td>
<td>7</td>
<td>6</td>
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<td>2015</td>
<td>149</td>
<td>64</td>
<td>6</td>
<td>6</td>
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<tr>
<td>2016</td>
<td>138</td>
<td>63</td>
<td>6</td>
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<tr>
<td>2017</td>
<td>130</td>
<td>63</td>
<td>6</td>
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<tr>
<td>2018</td>
<td>124</td>
<td>62</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>2019</td>
<td>115</td>
<td>61</td>
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<td></td>
</tr>
</tbody>
</table>

New Viremic HCV Cases

New HCV Infections – The Netherlands

<table>
<thead>
<tr>
<th>Year</th>
<th>All PWID</th>
<th>MSM</th>
<th>Vertical</th>
<th>Nosocomial</th>
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</thead>
<tbody>
<tr>
<td>2015</td>
<td>129</td>
<td>6</td>
<td>6</td>
<td>6</td>
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<tr>
<td>2016</td>
<td>129</td>
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<tr>
<td>2020</td>
<td>118</td>
<td>6</td>
<td></td>
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CDA unpublished data
Conclusions:

• HCV elimination is feasible in western countries
  » Many countries have already increased treatment so subsequent treatment increases can be modest; however, active screening is almost always necessary
  » To reduce new infections, screening and treatment has to encompass all HCV infected individuals (≥F0) – most new infections occur among younger individuals who are F0 or F1
  » To achieve elimination, a high level of treatment in high risk populations is required to reduce the viral pool
    ▪ Re-infection should be expected when treating high-risk populations, and elimination of HCV is not possible unless these populations are treated
    ▪ Prevention of HCV requires a thorough understanding of who is and who is not at risk of acquiring or transmitting HCV (country specific)

• Since treatments are curative, the number of treated patients and the associated costs is finite
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- **Croatia** – Hrstic I, Luksic B, Morovic M, Nonkovic D, Reic T, Vince A
- **Czech Republic** – Frankova S, Nemecek V, Sperl J, Urbanek P
- **Denmark** – Christensen P, Clausen M, Gerstoft J, Krarup H, Øvrehus A, Weis N
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- **Germany** – Alshuth U, Berg T, Cornberg M, Kautz A, Mauss S, Sarrazin C, Van Thié I, Wedemeyer H
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- **Hungary** – Horváth G, Hunyady B, Makara M
- **Ireland** – Bergin C, Houlihan D, Kieran J, Norris S, Thornton L, Walsh C
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- **United Kingdom** – Cramp M, Parkes J, Rosenberg W, Ryder S
References

- Polaris Observatory (www.centerforda.com/polaris)

Appendix

Thank you!