Epidemiologic impact of expanding chronic hepatitis C (CHC) treatment in people who inject drug (PWID) in the United States (US): a mathematical model using data from the C-EDGE CO-STAR Study

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Background

- Hepatitis C is caused by the infection of hepatitis C virus (HCV). It is estimated that in 70-85% of HCV-infected individuals (Micallef et al, 2006; Page et al, 2009), hepatitis C will become chronic infection, which may lead to severe consequences such as cirrhosis and hepatocellular carcinoma (HCC).

- In the United States (US), it is estimated that 2.7-3.9 million individuals are living with chronic hepatitis C (CHC). Injection drug use is found to be the most common route of HCV transmission (CDC FAQs, 2017). Nevertheless, people who inject drug (PWID) are not widely treated when compared to non-PWID, in the fear of reinfections due to their risky behaviour.

- The current analysis aimed to develop a simple dynamic transmission model (DTM), to assess the impact of treating all genotype 1 CHC patients regardless of transmission route, leveraging the data from the only clinical trial in the PWID population (C-EDGE CO-STAR Study, elbasvir/grazoprevir vs. placebo; Dore et al, 2016).
Methods

- A dynamic transmission model was developed in R, comprising of 70 differential equations. In the model, uninfected individuals are at risk of acute HCV infection. Those who are acutely infected may experience spontaneous clearance of the infection, become chronically infected, recovered or re-infected. Individuals who are chronically infected follow the natural history of the disease.

- The population was stratified by risk into non-PWID and PWID. Individuals in one group may move to the other group at any time, and may be infected by individuals within the same group, or by those from the other group.

- The analysis assumed the number of individuals and the number of PWIDs were constant over time (Shah et al, 2006), and individuals were tracked from 2017 onwards for 50 years.

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**Figure: model schematics**

- Individuals can be undiagnosed, diagnosed, treated, failed, re-treated, unsuccessfully retreated.

* Unlike F0-F3, those F4 who are successfully will still be at risk of disease progression despite at a lower rate; ** Individuals may die from any state; DC: decompensated cirrhosis; LT: liver transplantation; HCC: hepatocellular carcinoma
Methods (cont’d)

• Parameterization
  – Population and HCV transmission parameters were sourced from the US and international literature.
  – Progression of CHC was based on a previously published cost-effectiveness analysis (Elbasha et al, 2017).
  – Contact rates, rates of HCV clearance and time to HCV clearance were calibrated using a reduced model, which excluded treatment-related calculation. The calibration targets were epidemiology of HCV infection and CHC prior to 1992 (Alter et al, 1999; Amon et al, 2008; Armstrong et al, 2006; Chak et al, 2011), before the introduction of any CHC treatment. It was also assumed that these targets were at equilibrium.
  – Diagnosis rate and treatment rates were taken from a previously published epidemiology model (Durham et al, 2016).
  – Sustained virologic response (SVR) rates, the measurement for treatment success, were taken from the aforementioned C-EDGE CO-STAR trial (Dore et al, 2016) for PWIDs, and the label of elbasvir/grazoprevir (Merck & Co., Inc, 2017).

• The model assessed two treatment strategies
  – Differential scenario: treatment rate was lower in PWIDs (as in the table).
  – Non-differential scenario: treatment rate was the same in two groups (i.e. 2.5%).

Table: diagnosis, treatment and SVR rates

<table>
<thead>
<tr>
<th></th>
<th>Non-PWID</th>
<th>PWID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis rate</td>
<td>5.9%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Treatment rate</td>
<td>2.5%</td>
<td>0.6%</td>
</tr>
<tr>
<td>SVR rate</td>
<td>0.9355-0.9798*</td>
<td>0.9511</td>
</tr>
</tbody>
</table>

* Depending on treatment history and cirrhosis status.
Results

• Following the US population from 2017 for 50 years
  – Non-differential strategy was expected to avoid a total of 81,298 new CHC cases, 51,867 F4 cases, 14,414 DC cases, 18,279 HCC cases, 103 LT cases and 22,365 liver-related deaths. Roughly half of the reduction came from reduced infection in the PWID population.
  – The prevalence of HCV infection and CHC in the PWID population was expected to decrease by 2.7% and 2.5% (relative to differential strategy), respectively.

<table>
<thead>
<tr>
<th>Number of cases over 50 years</th>
<th>Differential strategy</th>
<th>Non-differential strategy</th>
<th>Cases avoided under non-differential strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In non-PVID</td>
<td>PWID</td>
<td>Total</td>
</tr>
<tr>
<td>CHC</td>
<td>1,598,820</td>
<td>2,519,426</td>
<td>4,118,245</td>
</tr>
<tr>
<td>F4</td>
<td>1,801,125</td>
<td>300,079</td>
<td>2,101,204</td>
</tr>
<tr>
<td>DC</td>
<td>846,036</td>
<td>65,782</td>
<td>911,818</td>
</tr>
<tr>
<td>HCC</td>
<td>1,082,324</td>
<td>80,047</td>
<td>1,162,371</td>
</tr>
<tr>
<td>LT</td>
<td>172,300</td>
<td>10,430</td>
<td>182,730</td>
</tr>
<tr>
<td>Liver deaths</td>
<td>1,638,822</td>
<td>97,039</td>
<td>1,735,861</td>
</tr>
</tbody>
</table>
Results (cont’d)
Conclusion

• Despite higher re-infection rates in the PWID population, the current analysis shows that increasing CHC treatment rate in this population can markedly reduce numbers of new CHC and liver-related disease cases due to herd immunity and high efficacy level observed in the C-EDGE CO-STAR trial.

• The current analysis only looked at dichotomous risk groups. Nevertheless, resource allocation and prioritization in real-world settings are more complex, especially given the budget constraint. Further studies are warranted to assess which high-risk population(s) to be focused on in order to achieve the goals set out in the National Viral Hepatitis Action Plan.


