Elimination of hepatitis C - a public health approach

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Disclosures

• Editorial: UpToDate, Clin Infect Dis, J Clin Invest
Elimination of hepatitis C

• What is elimination?
• How can elimination be achieved?
• How would long-acting treatments transform elimination?
Elimination differs from eradication

- **Eradication**: Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed. Example: smallpox.

- **Elimination**:

Dowdle WR. Bull World Health Organ 1998;76 Suppl 2:23-5
Heymann DL MMWR 1999
Eradication of hepatitis C using treatment

1. Every HCV-infected individual can be detected
   • HCV antibody and HCV RNA (or core antigen) in plasma

Smith CID 2011, Smith JID 2011, Grebley Lancet Gastro and Hep 2017
Eradication of hepatitis C is possible

- Every HCV-infected person can be detected AT THE POINT OF CARE

<table>
<thead>
<tr>
<th>Manufacturer (specimen type)</th>
<th>Sensitivity (95% CI, %)</th>
<th>Specificity (95% CI, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OraSure (blood)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seattle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SA (n = 266)</td>
<td>95.9 (91.6–97.6)</td>
<td>100 (94.9–100.0)</td>
</tr>
<tr>
<td>CDC (n = 265)</td>
<td>97.4 (94.1–98.9)</td>
<td>98.6 (92.9–99.8)</td>
</tr>
</tbody>
</table>

Smith CID 2011
Eradication of hepatitis C is possible

- Every HCV-infected person can be detected (and confirmed) at point of care

<table>
<thead>
<tr>
<th>Abbott RealTime HCV Viral Load</th>
<th>No. of Quantifiable</th>
<th>No. of Unquantifiable</th>
<th>No. of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert HCV VL FS (finger-stick)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of quantifiable</td>
<td>59</td>
<td>0</td>
<td>59</td>
</tr>
<tr>
<td>No. of unquantifiable</td>
<td>0</td>
<td>108</td>
<td>108</td>
</tr>
<tr>
<td>No. of total</td>
<td>59</td>
<td>108</td>
<td>167</td>
</tr>
<tr>
<td>Xpert HCV Viral Load (plasma)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of quantifiable</td>
<td>64</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>No. of unquantifiable</td>
<td>0</td>
<td>118</td>
<td>118</td>
</tr>
<tr>
<td>No. of total</td>
<td>64</td>
<td>118</td>
<td>182</td>
</tr>
</tbody>
</table>
Eradication of hepatitis C using treatment

1. Every HCV-infected individual can be detected
   • HCV antibody and HCV RNA (or core antigen) in plasma
   • Point of care detection of HCV antibodies and RNA with fingerstick

Smith CID 2011, Smith JID 2011, Grebley Lancet Gastro and Hep 2017
1. Every HCV-infected person can be detected
2. Every HCV infection can be cured
HCV can be eradicated with 12 weeks of well tolerated pills example: sofosbuvir and velpatasvir
Eradication of hepatitis C

1. Every HCV-infected person can be detected
2. Eradicate infection by stopping replication
3. Humans are only source
Humans are the only source of HCV

Kapoor PNAS 2011;
Baechlein J Virol 2015;
Drexler Plos Pathogens 2013
Eradication of hepatitis C

1. Every HCV-infected person can be detected
2. Eradicate infection by stopping replication
3. Humans are only source
4. Public health importance
Global health importance of hepatitis – mortality 1990-2013

Eradication of hepatitis C using treatment?

1. Every HCV-infected person can be detected
2. Eradicate infection by stopping replication
3. Humans are only source
4. Public health importance
5. Global eradication?
HCV is eradicated from those treated

- All oral
- PegIFN, RBV, and protease inhibitor
- PegIFN and ribavirin
- IFN and ribavirin
- IFN

But most are not treated

Lack of expanded use in infected people

Thomas Nat Med 2013
HCV viremic patients in 5 leading countries

Viremic HCV infections
2014 to 2017 (Aggressive Strategy)

Public health response to elimination of hepatitis C

WHO/UN: 2008 to 2017

✓ 2015 UN General Assembly adopts Sustainable Development Goals ‘to combat’ hepatitis
✓ 2016: WHO global health sector strategy for elimination
✓ 2017: Country-specific plans

USA elimination strategy

National Academy Recommendations

A NATIONAL STRATEGY FOR THE ELIMINATION OF HEPATITIS B AND C

The National Academies of Sciences • Engineering • Medicine

Buckley and Strom, NAM, 2017
# WHO HCV elimination goals

<table>
<thead>
<tr>
<th>Outcome</th>
<th>2015</th>
<th>2020</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>90% reduction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV incidence</td>
<td>1.75 million</td>
<td>1.23 million</td>
<td>175,000</td>
</tr>
<tr>
<td><strong>65% reduction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV liver mortality</td>
<td>400,000-600,000</td>
<td>200,000</td>
<td>140,000-210,000</td>
</tr>
</tbody>
</table>

*WHO Global Hepatitis Report 2017*
We need a public health approach to eliminate HCV infection

**WHO HCV targets to achieve elimination**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>2015</th>
<th>2020</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe injection</td>
<td>5%</td>
<td>50%</td>
<td>90%</td>
</tr>
<tr>
<td>Harm reduction</td>
<td>20%</td>
<td>50%</td>
<td>75%</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>&lt;5%</td>
<td>30%</td>
<td>90%</td>
</tr>
<tr>
<td>HCV treatment</td>
<td>1%</td>
<td>4%</td>
<td>80%</td>
</tr>
</tbody>
</table>

WHO Global Hepatitis Report 2017
We need a public health approach to eliminate new HCV infections

• Universal precautions for safe medical practices
• Expand harm reduction
• HCV vaccine
• Treatment for prevention: (e.g. MSM, PWID, inmates, women before pregnancy)

Canary CID 2017; Boerekamps CROI 2017; Platt Cochrane database 2016
Increasing HCV incidence in USA in young persons, 2000-2013

<table>
<thead>
<tr>
<th>Year</th>
<th>0-19 yrs</th>
<th>20-29 yrs</th>
<th>30-39 yrs</th>
<th>40-49 yrs</th>
<th>50-59 yrs</th>
<th>&gt; 60 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>3.0</td>
<td>1.5</td>
<td>1.0</td>
<td>0.5</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>2001</td>
<td>2.5</td>
<td>1.0</td>
<td>0.8</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>2002</td>
<td>2.0</td>
<td>0.8</td>
<td>0.6</td>
<td>0.3</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2003</td>
<td>1.5</td>
<td>0.6</td>
<td>0.4</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2004</td>
<td>1.0</td>
<td>0.4</td>
<td>0.2</td>
<td>0.1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2005</td>
<td>0.5</td>
<td>0.2</td>
<td>0.1</td>
<td>0.06</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2006</td>
<td>0.25</td>
<td>0.1</td>
<td>0.05</td>
<td>0.03</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2007</td>
<td>0.125</td>
<td>0.05</td>
<td>0.02</td>
<td>0.01</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2008</td>
<td>0.0625</td>
<td>0.02</td>
<td>0.01</td>
<td>0.005</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>2009</td>
<td>0.03125</td>
<td>0.01</td>
<td>0.005</td>
<td>0.0025</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2010</td>
<td>0.015625</td>
<td>0.005</td>
<td>0.0025</td>
<td>0.00125</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2011</td>
<td>0.0078125</td>
<td>0.0025</td>
<td>0.00125</td>
<td>0.000625</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2012</td>
<td>0.00390625</td>
<td>0.00125</td>
<td>0.000625</td>
<td>0.0003125</td>
<td>0.0</td>
<td>0.0</td>
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Source: National Notifiable Diseases Surveillance System (NNDSS)
We need a public health approach to eliminate HCV infection

**WHO HCV targets to achieve elimination**

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<td>HCV treatment</td>
<td>1%</td>
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<td>80%</td>
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WHO Global Hepatitis Report 2017
Global Distribution of 71 million HCV infections

Global cascade of HCV care and 2030 WHO elimination goals: 90/80 target

WHO Global Hep Report 2017
HCV care cascade in USA

HCV Care Cascade in Iceland 2015

HCV Microelimination in Iceland 2016

Gottfredsson IDWEEK AB 1694

Worldwide HCV cure rarely exceeds new infections

Hill J Virus Erad 2017
HCV viremic patients in 5 leading countries

Viremic HCV infections
2014 to 2017 (Aggressive Strategy)

We need a public health approach to eliminate HCV infection

• New models of health care
• Public health infrastructure
• Prevention
• Testing
• Treatment (longer acting and lower cost)
Global cascade of HCV care and 2030 WHO elimination goals: 90/80 target
Point of care HCV testing will improve diagnosis but not treatment

WHO Global Hep Report 2017
Point of care HCV testing will improve diagnosis but not treatment

2024 Projection

2030 Target

WHO Global Hep Report 2017
Point of care HCV testing will improve diagnosis but not treatment

If all tested are treated using long-acting injectable

WHO Global Hep Report 2017
Eight weeks of oral HCV treatment can cure most* infections

Genotype 1

% Cured

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Cured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glecaprevir-pibrentasvir, 12 wk</td>
<td>99.7</td>
</tr>
<tr>
<td>(331/332)</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir-pibrentasvir, 8 wk</td>
<td>99.1</td>
</tr>
<tr>
<td>(332/335)</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir-pibrentasvir, 12 wk</td>
<td>100</td>
</tr>
<tr>
<td>(331/331)</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir-pibrentasvir, 8 wk</td>
<td>100</td>
</tr>
<tr>
<td>(332/332)</td>
<td></td>
</tr>
</tbody>
</table>

Genotype 3

% Cured

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Cured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glecaprevir-pibrentasvir, 12 wk</td>
<td>95</td>
</tr>
<tr>
<td>(222/233)</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir-pibrentasvir, 8 wk</td>
<td>97</td>
</tr>
<tr>
<td>(111/115)</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir-daclatasvir, 12 wk</td>
<td>95</td>
</tr>
<tr>
<td>(149/157)</td>
<td></td>
</tr>
</tbody>
</table>

Zeuzem NEJM 2018
Extended release HCV treatment would transform elimination: public health model

Glecaprevir
- HCV protease inhibitor
- Liver metabolized; renal safe
- Tmax 5 hrs
- Mol Wt 838 g/mol
- Water sol <0.1 to 0.3 mg/ml
- Charge 0; Polar surface 204 Å²

Pibrentasvir
- HCV NS5A
- Liver metabolized; renal safe
- Tmax 5 hrs
- Mol Wt 1113 g/mol
- Water sol <0.1 mg/ml
- Charge 0; Polar surface 200 Å²

We need a *well-resourced* public health approach to eliminate HCV infection

“The key is the commitment” DA Henderson
We need a well-resourced public health approach to eliminate HCV infection

• Public health response to HIV
  – ART given to 20 million persons
  – Cost of HIV ~20 billion USD/year
We need a well-resourced public health approach to eliminate HCV infection

• Public health response to HIV
  – 20 million persons getting 240 million months of treatment in 2017
  – Cost of HIV ~20 billion USD/year

• Public health responses to HCV
  – 71 million persons need 213 million months of treatment
  – HCV elimination: 11.9 billion USD for 2016-2021
We need a well-resourced public health approach to eliminate HCV infection

- Public health response to HIV
  - 20 million persons getting 240 million months of treatment in 2017
  - Cost of HIV $\sim$20 billion USD/year

- Public health responses to HCV
  - 71 million persons need 213 million months of treatment
  - HCV elimination: 2.2 billion USD/year (2016-2021)
Elimination of HCV

1. We can eradicate HCV with treatment
2. We should eliminate HCV
3. We need a public health approach to a public health problem