Hepatitis C virus infection: monitoring of end-stage liver disease and prediction of disease burden

Sharon Hutchinson

VHPB meeting, 17-18th November 2005
Outline

• Monitoring of end-stage liver disease
  – Scotland

• Prediction of HCV disease burden
  – Scotland
  – England and Wales
Hepatitis C virus: Natural History

- Acute Infection - 5% symptomatic disease
  - 60-85% develop chronic infection

- Chronic Infection - 5-10% develop cirrhosis by 20 years

- Factors affecting disease progression
  - Age, alcohol and HIV

- Cirrhosis
  - Decompensation (4-9% per annum)
  - Carcinoma (2-4% per annum)
Annual and cumulative HCV diagnoses in Scotland
(to end of 2003)

By Risk Group

- Other
- NK
- IDU

Year of first positive specimen

Cumulative HCV diagnoses

Annual HCV diagnoses

0
500
1000
1500
2000
5,000
10,000
15,000
20,000
Record-linkage study to determine severe disease burden related to HCV in Scotland, data to Dec 2001

HCV Diagnoses
Database (HPS)*
N=12,096

Hospital Discharge Records (ISD)**
Cancer Registrations (ISD)**
Death Records (GRO/ISD)**

* Limited identifiers
** Full identifiers
Data Linkage Results: Epidemiological Characteristics of 12,096 HCV diagnosed persons in Scotland 1991-2001

Dead: 12%
High Deprivation*: 56%
Alcohol-related hospitalisation/death: 17%
Diagnosed HIV +ve: 5%
Injecting Drug User: 88%

* Carstairs 6/7 based on postcode
### Data Linkage Results: End-Stage Liver Disease among 12,096 HCV diagnoses in Scotland 1991-2001

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>134 (26%)</td>
<td>171 (33%)</td>
<td>209 (41%)</td>
<td></td>
</tr>
<tr>
<td>Health-board of residence</td>
<td>Glasgow</td>
<td>Lothian</td>
<td>Elsewhere</td>
<td></td>
</tr>
<tr>
<td></td>
<td>173 (34%)</td>
<td>142 (28%)</td>
<td>199 (39%)</td>
<td></td>
</tr>
<tr>
<td>Age at presentation</td>
<td>&lt; 30</td>
<td>33 (6%)</td>
<td>325 (63%)</td>
<td>156 (31%)</td>
</tr>
<tr>
<td></td>
<td>30-49</td>
<td>197 (38%)</td>
<td>304 (60%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥50</td>
<td>166 (32%)</td>
<td>301 (60%)</td>
<td></td>
</tr>
<tr>
<td>Alcohol-related hospitalisation/death</td>
<td>Yes</td>
<td>364 (71%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>150 (29%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>312 (61%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died from decompensated cirrhosis</td>
<td>163 (32%)</td>
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</table>
Modelling the burden of HCV among IDUs in Scotland: overview of projection model

Designed to incorporate the knowledge and uncertainty about major parameters relating to:

(1) the IDU population (e.g. incidence of injecting),
(2) the characteristics of IDUs affecting HCV disease progression (e.g. HIV co-infection and heavy alcohol use),
(3) the incidence of HCV infection among current IDUs,
(4) the rate of HCV disease progression

Outline of stages in HCV projection model

- Resolved HCV
- Chronic HCV
  - Mild disease
  - Moderate disease
  - Cirrhosis
  - Decomp. cirrhosis
  - HCC
  - Transplant
- Death unrelated to HCV among current & former IDUs
- Death related to HCV
Modelled prevalent number of IDUs in Scotland, 1960-2000

- Current & Former IDUs
- Current IDUs

Living IDUs (thousands)

Year

Modelled prevalent number of IDUs with HCV in Scotland, 1960-2000

- All IDUs
- All IDUs with HCV
- All IDUs with chronic HCV

Year

Living IDUs (thousands)
Natural history of HCV disease

No infection

HCV

Infection

Mild disease

Moderate disease

Severe disease (cirrhosis)

Liver failure

15-40% recover

40-70% by 20 years

5-10% by 20 years

4-9% per year

Transplantation
## Current burden of HCV among IDUs in Scotland, 2005

<table>
<thead>
<tr>
<th>Stage</th>
<th>All IDUs</th>
<th>Former IDUs</th>
</tr>
</thead>
<tbody>
<tr>
<td>No infection</td>
<td>45,000</td>
<td>35,000</td>
</tr>
<tr>
<td>Infection</td>
<td>22,900</td>
<td>16,000</td>
</tr>
<tr>
<td>Mild disease</td>
<td>9,000</td>
<td>8,000</td>
</tr>
<tr>
<td>Moderate disease</td>
<td>1,900</td>
<td>1,800</td>
</tr>
<tr>
<td>Severe disease (cirrhosis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver failure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:**
- HCV infection occurs at a rate of 1,000-2,000 per year among all IDUs.
- Liver failure occurs at a rate of 100 per year.
Observed and modelled annual incidence of liver failure among HCV infected IDUs in Scotland, 1980-2030
Modelled prevalent number of HCV infected IDUs in Scotland according to stage of HCV disease, 1960-2030

- Recovered from HCV
- Cleared HCV from treatment
- Mild disease
- Moderate disease
- Cirrhosis

Calendar year

Living IDUs (thousands)
Modelled distribution of former IDUs in Glasgow in 2005 by stage of HCV disease and current age

Mean percentage of former IDUs

- HCV uninfected
- Recovered from HCV
- Cleared HCV
- Mild disease
- Moderate disease
- Cirrhosis

Age in years (% of 22,500 former IDUs)

- <30 (18%)
- 30-39 (57%)
- 40-49 (23%)
- 50+ (2%)
Modelled % of severe HCV disease prevented among IDUs in Glasgow (2006-2030) from different antiviral treatment scenarios

<table>
<thead>
<tr>
<th>Stage of HCV disease initiated on therapy</th>
<th>Uptake of therapy by former IDUs (N per year)</th>
<th>Modelled % of severe HCV disease prevented according to these response rates to antiviral therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>45% response*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75% response*</td>
</tr>
<tr>
<td>Mild or Moderate disease</td>
<td>75 500 1,000</td>
<td>3% 17% 30%</td>
</tr>
<tr>
<td></td>
<td>75 500 1,000</td>
<td>5% 29% 50%</td>
</tr>
<tr>
<td>Moderate disease</td>
<td>75 500 1,000</td>
<td>5% 28% 38%</td>
</tr>
<tr>
<td></td>
<td>75 500 1,000</td>
<td>8% 47% 63%</td>
</tr>
<tr>
<td>Moderate disease or compensated cirrhosis</td>
<td>75 500 1,000</td>
<td>6% 35% 42%</td>
</tr>
<tr>
<td></td>
<td>75 500 1,000</td>
<td>10% 58% 69%</td>
</tr>
</tbody>
</table>

* Represents compliance to therapy & clearance of the virus from therapy
Modelling the burden of HCV in England and Wales: back-calculation approach

Data on HCC deaths with HCV

+ estimated rates of HCV disease progression

Generate data on the incidence of HCV

+ estimated rates of HCV disease progression

Generate data on the incidence and prevalence of HCV-related disease

Source: Sweeting M, DeAngelis D, Ramsay M, Brant L, Harris H. The burden of hepatitis C in England and Wales. *In preparation*

* Estimated based on % of HCC deaths with mention of HCV on death and hospital data (1996-2004) and extrapolated to earlier years.
Estimated number of people living with HCV-related cirrhosis/decomp cirrhosis/HCC in England/Wales (1990-2010)

<table>
<thead>
<tr>
<th>Year</th>
<th>Compensated cirrhosis</th>
<th>Decompensated cirrhosis &amp; HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>6,000</td>
<td>1,000</td>
</tr>
<tr>
<td>2005</td>
<td>5,000</td>
<td>2,000</td>
</tr>
<tr>
<td>2000</td>
<td>4,000</td>
<td>1,000</td>
</tr>
<tr>
<td>1995</td>
<td>3,000</td>
<td>1,000</td>
</tr>
<tr>
<td>1990</td>
<td>2,000</td>
<td>1,000</td>
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</table>
Summary (1)

- HCV-related end stage liver disease is not uncommon, is increasing and is usually associated with an alcohol problem.

- The young age of decompensated patients presenting to hospital with both HCV and alcohol suggests that the combined effect of these 2 factors accelerates liver disease progression.
Summary (2)

• Thousands of past injectors (mostly aged 30-49 years) have chronic HCV and are undiagnosed.

• Identifying the above group and considering individuals for therapy should be regarded a priority.

• If current low levels of antiviral therapy do not increase in the future, the numbers developing severe HCV disease will increase considerably.
Acknowledgements

Scotland

- **HPS**: David Goldberg, Kirsty Roy, Sarah Wadd, Glenn Codere, Louise Shaw
- **MRC Biostatistics Unit**: Sheila Bird
- **ISD**: Record Linkage Team
- **Regional Virus Laboratories**: Sheila Cameron (Glasgow), Sheila Burns (Edinburgh), Pamela Molyneaux (Grampian), Paul McIntyre (Tayside)

England and Wales

- **HPA/MRC Biostatistics Unit**: Daniela DeAngelis, Michael Sweeting
- **HPA**: Mary Ramsay, Lisa Brant, Helen Harris
Influence of age, alcohol and HIV co-infection on the development of decompensated cirrhosis (DC) following HCV diagnosis for persons referred from non-hospital settings in Scotland

<table>
<thead>
<tr>
<th></th>
<th>Person yrs (py)</th>
<th>Number of DC (rate/1000 py)</th>
<th>Relative Hazard* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>7331</td>
<td>8 (1.1)</td>
<td>1.0 (baseline)</td>
</tr>
<tr>
<td>30-49</td>
<td>12348</td>
<td>79 (6.4)</td>
<td>4.6 (2.2 - 9.6)</td>
</tr>
<tr>
<td>50-69</td>
<td>1070</td>
<td>14 (13.1)</td>
<td>8.8 (3.5 - 22.0)</td>
</tr>
<tr>
<td>70+</td>
<td>254</td>
<td>4 (15.7)</td>
<td>10.7 (3.1 - 37.5)</td>
</tr>
<tr>
<td><strong>Hospitalised for alcohol abuse</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2062</td>
<td>40 (19.4)</td>
<td>6.1 (4.0 - 9.1)</td>
</tr>
<tr>
<td>No</td>
<td>18941</td>
<td>65 (3.4)</td>
<td>1.0 (baseline)</td>
</tr>
<tr>
<td><strong>Diagnosed HIV +ve</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1018</td>
<td>20 (19.7)</td>
<td>3.9 (2.2 - 7.0)</td>
</tr>
<tr>
<td>No</td>
<td>19986</td>
<td>85 (4.3)</td>
<td>1.0 (baseline)</td>
</tr>
</tbody>
</table>

* Cox PH regression adjusted for these factors and gender, healthboard and risk group.