Economic issues in Hepatitis C

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Acknowledgements

• Mild Hepatitis C study
• Principal Investigators:
  – Howard Thomas, Janice Main
• Centre co-ordinators
  – William Rosenberg; Maggie Bassendine
• Statisticians
  – Daniela DeAngelis; Michael Sweeting
Summary of talk

- Cost-effectiveness analysis (CEA) of antiviral treatment
- CEA of antiviral treatment for mild hepatitis C
- Emerging issues
  - Sub groups
  - Changing treatment regimens
Challenges for Cost-effectiveness analysis in hepatitis C

• Slowly progressive disease
• Antiviral treatment has high initial cost
  – (48 weeks pegylated interferon+ ribavirin~ = 20,000 Euro)
• Are initial treatment costs offset by?
  – Improved life expectancy
  – Gains in quality of life (QOL)
  – Lower costs of subsequent disease
• Estimation of quality-adjusted life years (QALYS)
• Lifetime costs per QALY gained from intervention
  – NICE < 30,000 per QALY
Cost-effectiveness analysis in hepatitis C requires evidence..

- Interventions’ effectiveness in routine clinical practice (RCTs)
- Disease progression (observational studies)
- QOL and costs (RCTs, observational studies or expert opinion)
- *Lifetime* costs/QALY (from a model)
Previous studies in hepatitis C

• Interferon alpha + ribavirin cost-effective for chronic hepatitis C (<15,000 Euro per QALY)

• Pegylated Interferon alpha + ribavirin is cost-effective for chronic hepatitis C (<20,000 Euro per QALY)
Cost-effectiveness analysis and policy

• NICE concluded for patients with moderate to severe chronic hepatitis C
  – a) Interferon alpha and ribavirin is cost-effective and should be provided (2000)
  – b) Pegylated interferon alpha and ribavirin cost-effective and should be provided (2003)
  – c) Decision on mild chronic hepatitis C delayed (Guidance expected August 2006)
    • Lack of evidence
    • Currently not recommended for treatment
NHS Health Technology assessment on mild hepatitis C

• Cost-effectiveness of antiviral treatment at a *mild* stage vs only treating those who progress to *moderate disease*?
  – Interferon alpha and ribavirin
  – Pegylated interferon alpha and ribavirin

• Final results
Evidence to address study questions

• Interventions’ effectiveness:
  – Alpha interferon and ribavirin NHS RCT (Wright et al 2005)
  – Pegylated interferon and ribavirin: multinational RCTs adjusted estimates (Manns et al)

• Disease progression
  – Reanalysis of observational studies (Wright et al 2005; Sweeting et al 2005)

• HRQOL and costs
  – NHS RCT, observational study (Wright et al 2005)
  – Lifetime costs/QALY from model (Grieve and Roberts 2002)
Markov Model for Hepatitis C
Treatment for mild HCV

Virological response → 1000 mild cases

1000 mild cases → Moderate

Moderate → cirrhosis

cirrhosis → Death

Death → Liver transplant, Decompensated cirrhosis, Hepatocellular carcinoma

Liver transplant → 1000 mild cases

Decompensated cirrhosis → Death, Hepatocellular carcinoma

Hepatocellular carcinoma → Death
Markov Model for Hepatitis C
Treatment for moderate HCV

Virological response

1000 mild cases

Moderate

Death

Liver transplant

Decompensated cirrhosis

Hepatocellular carcinoma
## Model inputs

### Transition Probabilities

<table>
<thead>
<tr>
<th>State Transition</th>
<th>Mean estimate</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild-moderate</td>
<td>0.025</td>
<td>Wright et al 2005</td>
</tr>
<tr>
<td>Moderate-cirrhotic</td>
<td>0.037</td>
<td>Wright et al 2005</td>
</tr>
<tr>
<td>Cirrhotic-decomp</td>
<td>0.039</td>
<td>Fattovitch 1997</td>
</tr>
<tr>
<td>Decompensated-HCC</td>
<td>0.01</td>
<td>Fattovitch 1997</td>
</tr>
<tr>
<td>Decompensated-death</td>
<td>0.13</td>
<td>Fattovitch 1997</td>
</tr>
</tbody>
</table>
Model inputs: Effectiveness alpha interferon and ribavirin

- Overall sustained viral response (SVR) of 33% (Wright et al 2005)
  - 18% genotype 1
  - 49% genotype non-1
- Previous estimates higher SVRs (Manns et al 2001, McHutchison et al 1998)
- No evidence lower SVR because mild rather than moderate HCV (Manns et al 2001)
- So used overall SVR of 33% for moderate disease
- Context NHS pragmatic RCT vs multinational RCT
Effectiveness: pegylated interferon and ribavirin

• No available estimates from NHS RCTs
• Effectiveness of pegylated interferon + ribavirin vs alpha interferon + riba from multinational RCT (Manns et al)
• Used to derive ‘NHS’ effectiveness of pegylated interferon and ribavirin
  – Genotype 1 SVR: 24%
  – Genotype non-1 SVR: 55%
Quality of life at different stages of hepatitis C
(Euroqol EQ-5D scores; scale: 0 death to 1 perfect health)

<table>
<thead>
<tr>
<th>Stage</th>
<th>source</th>
<th>N</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild HCV</td>
<td>RCT</td>
<td>185</td>
<td>0.77(0.25)</td>
</tr>
<tr>
<td>Treatment mild HCV</td>
<td>RCT</td>
<td>80</td>
<td>0.66(0.32)</td>
</tr>
<tr>
<td>Post SVR</td>
<td>RCT</td>
<td>24</td>
<td>0.82(0.21)</td>
</tr>
<tr>
<td>Moderate HCV</td>
<td>Observational</td>
<td>71</td>
<td>0.66(0.21)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Observational</td>
<td>40</td>
<td>0.55(0.34)</td>
</tr>
</tbody>
</table>
Mean Health service costs (£) per year at different stages of hepatitis C

<table>
<thead>
<tr>
<th>Stage</th>
<th>source</th>
<th>N</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild HCV</td>
<td>RCT</td>
<td>39</td>
<td>138 (170)</td>
</tr>
<tr>
<td>Treatment* mild HCV</td>
<td>RCT</td>
<td>44</td>
<td>7,141 (2,852)</td>
</tr>
<tr>
<td>Moderate HCV</td>
<td>Observational</td>
<td>183</td>
<td>717 (1,029)</td>
</tr>
<tr>
<td>cirrhosis</td>
<td>Observational</td>
<td>24</td>
<td>1,138 (2,479)</td>
</tr>
<tr>
<td>Decompensated Cirrhosis</td>
<td>Observational</td>
<td>64</td>
<td>9,121 (9,610)</td>
</tr>
</tbody>
</table>

*alpha interferon and ribavirin for mean of 38 weeks
Results of cost-effectiveness analysis: Overview

- Projected results are based on the trial population
- Results are based on lifetime analysis
- Presented for “average” 40 year old trial patient
- Costs and outcomes discounted at 3.5%
- Key Assumptions tested in subsequent sensitivity analysis
Costs per QALY gained (£)

• Interferon alpha+ ribavirin at mild vs moderate stage
  – Overall £9,535 per QALY
  – genotype non-1 £4,535 per QALY
  – genotype 1 £25,188 per QALY
Costs per QALY gained (£)

• Pegylated interferon alpha and ribavirin at mild vs moderate stage
  – genotype non-1 £7,821 per QALY
  – genotype 1 £28,409 per QALY
Costs per QALY gained (£)

- Pegylated interferon alpha and ribavirin at mild stage vs interferon alpha + ribavirin at mild stage
  - Genotype non-1  £32,226 per QALY
  - Genotype 1     £32,896 per QALY
Uncertainty in parameter estimates: Probabilistic sensitivity analysis

- aged 40 genotype non-1
- aged 40 genotype 1

Value ceiling ratio (£/QALY gained)

Probability (cost-effective)
Probabilistic sensitivity analysis by genotype and age

![Graph showing probability of cost-effectiveness by genotype and age]
Alternative scenarios: alpha interferon and ribavirin for mild HCV

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Genotype 1</th>
<th>Genotype non-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base</td>
<td>25,188</td>
<td>4,535</td>
</tr>
<tr>
<td>Viral kinetics</td>
<td>17,051</td>
<td>1,425</td>
</tr>
<tr>
<td>Transition probabilities from more gen popl't'ion</td>
<td>36,040</td>
<td>6,604</td>
</tr>
<tr>
<td>Effectiveness McHutchison RCT</td>
<td>12,622</td>
<td>2,686</td>
</tr>
</tbody>
</table>
Conclusions from HTA study

- Overall more cost-effective to provide antiviral treatment (either alpha or peg interferon combined with ribavirin) at a mild rather than a moderate stage.
- Not cost-effective at a mild stage for older patients (>65) with genotype 1.
- More conservative than previous estimates:
  - Earlier stage of the disease
  - Lower estimates of disease progression
  - Lower SVRs based on pragmatic NHS RCT
  - Empirical estimates of QOL and cost
Further areas research arising

• Which sub groups patients should have priority for antiviral treatment?
  – Disease stage, age, genotype, co-morbidities
  – Efficiency vs equity

• How can treatment be made more cost-effective?
  – Shorter treatment regimens, nurse-led care, fewer liver biopsies

• HRQOL and cost data useful for cost-effectiveness of prevention strategies
  – How much should we invest in treatment vs prevention?