Cost effectiveness of case finding for hepatitis C in former injecting drug users

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  Hepatologist

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Background

• UK policy supports active case finding
  – All Party Parliamentary Group on Hepatitis
  – Royal College of Physicians (here)
  – EASL

• Treatment options have improved
  – Pegylated interferon + ribavirin are standard
  – NICE guidance

• Previous HTA of case finding
  – GUM and drug services
  – Emphasised importance of drug services
  – Case finding in GUM probably not cost effective unless restricted to former drug users
  – No evidence of behavioural change from knowledge of HCV infection
  – More case finding in GUM than drug services
Objectives

- Estimate the clinical and cost effectiveness (cost utility) of case finding for hepatitis C among former injecting drug users in the UK
- Explore cost effectiveness in different settings
  - Drug and alcohol services
  - Prisons
  - General practice
Methods

• Former injecting drug users
• Testing and diagnosis – decision tree
• Treatment and disease progression – Markov
• Spontaneous presentation and “re-presentation”
• Discounting – 6% & 1.5% (3.5% in S/A)
• Cohort: mean age 37
• Outputs – Cost/consequence; Cost per LYG; Cost per QALY; PSA; EVPI
Case finding scenarios

• General case
  – 2 minute consultation along with offer of testing

• General practice
  – Search for IDUs in practice systems
  – General population approach

• Prisons
  – Offer at induction based on existing empirical data on acceptance and prevalence in tested prisoners

• Drug and Alcohol services
  – Offer to all people in contact with services not currently injecting
Methods

• Obtaining data inputs
  – Initial searches in wide range of databases:
    • Epidemiology
    • Natural history
    • Acceptability of testing and adherence
    • Effectiveness of treatment
    • Costs of treatment and long term consequences
    • Quality of life
Methods

- Testing uses ELISA and PCR (not RIBA)
- Biopsy only in genotype 1 or 4
  - Treatment only in moderate/severe
- Treatment without biopsy in G2/3
- Treatment with pegylated interferon and ribavirin for 48 weeks
- Response in mild disease is as for moderate/severe
- Progression to cirrhosis is sequential and linear
- Decompensation and HCC lead to transplant
Key sources

• Freeman (2003)
  – meta-analysis of progression to cirrhosis

• Trent HCV Cohort Database
  – Age at diagnosis (37 years)
  – Treatment eligibility and acceptance
  – severity of hepatitis at diagnosis (HAI score)
  – ALT levels

• Hutchinson et al (2005)
  – Gender and alcohol consumption

• Progression to HCC
  – Literature review inconclusive (2.5% per annum)

  – Effectiveness of combination therapy
Key sources

• Bird *et al* (2005)
  – Number of undiagnosed cases
• HTA Mild HCV Trial
  – costs and utilities for relevant health states
• Mortality
  – state specific and *general population*
• Prisons
  – Horne et al & Rosenberg et al
• General practice
  – Anderson et al
• Drug services
  – Serfaty et al, Plymouth Drug & Alcohol Action Team
## Treatment effectiveness

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Manns&lt;sup&gt;43&lt;/sup&gt;(N=511)</td>
</tr>
<tr>
<td>SVR, Overall (ITT)</td>
<td>%</td>
</tr>
<tr>
<td>SVR, Genotype 1 or 4 (ITT)</td>
<td>54</td>
</tr>
<tr>
<td>SVR, Genotype 2 or 3 (ITT)</td>
<td>82</td>
</tr>
<tr>
<td>SVR, Patients with cirrhosis (ITT)</td>
<td>44</td>
</tr>
<tr>
<td>Adherence to treatment</td>
<td>97</td>
</tr>
<tr>
<td>Genotype 1 or 4, (treatment completers)</td>
<td>43</td>
</tr>
<tr>
<td>Genotype 2 or 3, (treatment completers)</td>
<td>85</td>
</tr>
<tr>
<td>Cirrhosis (treatment completers)</td>
<td>45</td>
</tr>
</tbody>
</table>
# Different scenarios

<table>
<thead>
<tr>
<th>Setting</th>
<th>ELISA acceptance rate (%)</th>
<th>Proportion of positive results (%)</th>
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</thead>
<tbody>
<tr>
<td>General case</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>Prison scenario 1</td>
<td>8.5</td>
<td>16</td>
</tr>
<tr>
<td>Prison scenario 2</td>
<td>12</td>
<td>42</td>
</tr>
<tr>
<td>General practice</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>Targeted approach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General practice</td>
<td>10</td>
<td>12.5</td>
</tr>
<tr>
<td>Population approach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug and alcohol services</td>
<td>49</td>
<td>68</td>
</tr>
</tbody>
</table>
Testing & Diagnosis

Refuse biopsy

Infected, staging unknown

Death from biopsy

Infected, staging known

Consider eligibility for treatment

Follow Natural history (stratified by presumed stage)

Fals e - ve

ELISA + ve

PCR at attendance in secondary care (with repeat ELISA)

Genotype

Genotype 1 or 4

Offer Liver Biopsy

Genotype 2 or 3

Not infected

Follow Natural history (stratified by presumed stage)

Unidentified infection

Not infected

PCR – ve

Genotype

Follow Natural history (stratified by presumed stage)

Lost to Follow Up

Accept ELISA test

ELISA – ve

PCR – ve

False – ve

Not infected

Follow Natural history (stratified by presumed stage)

Follow Natural history (stratified by presumed stage)
Disease progression

Progression stratified by Gender, Alcohol consumption, ALT levels, Ishak

Population stratified by untreated, SVR, no SVR

Mild → Moderate → Severe → Cirrhosis

Hepatocellular carcinoma

Waiting for transplant → Liver transplant → Well post-transplant

Encephalopathy

Ascites

Variceal bleeding

Decompensated cirrhosis

Decompensation post-transplant

Re-infection post-transplant

Well post-transplant

Liver transplant

Waiting for transplant

DEATH

= entry points
Analysis of uncertainty

• One way sensitivity analyses
• Probabilistic sensitivity analysis
  – All parameters
• Scenario analyses
  – Settings
  – Age groups (proxy for severity)
• Value of information analysis
  – 15 year decision duration
  – 100,000 people
Initial results of case finding

- Initial yield from case finding is low
  - 490 accept of testing
  - 240 ELISA +ve
  - 94 attend for specialist investigation
  - 77 PCR +ve (i.e. chronic infection)
    - 10 with absolute contraindications
    - 35 genotype 2 or 3 – offer treatment
    - 32 genotype 1 or 4
      - biopsy 88% and treat moderate to severe hepatitis only
  - 25 patients treated
Longer term outcomes

Consequences averted:

- Decompensated cirrhosis = 3.5
- Hepatocellular Ca = 1.5
- Liver transplants = 0.14
- Deaths due to HCV = 3

• Cost of case finding
  - £760,000
  - Highest costs in group with mild hepatitis (£242,000)
Cost effectiveness analysis

- Incremental costs and benefits are small
- £20,000 per LYG
- £16,514 per QALY

By duration of infection:
- 0-9 years: £23,000 per QALY
- 20-29 years: £15,000 per QALY
- 30+ years: £17,000 per QALY

By setting:
- Prisons: £20,000 per QALY
- Family practice: £16,500 per QALY
- Drug services: £17,500 per QALY
One way sensitivity analyses

- Not influential
  - Acceptance of testing and treatment
  - Test characteristics and costs
  - Incidence of long term complications
- Some influence
  - Distribution of severity at presentation
  - Response to treatment
  - Background mortality
- Influential
  - Discount rate (£29,000 per QALY @ 3.5%)
  - Prevalence of HCV
  - Differential and absolute rates of spontaneous and re-presentation
Probabilistic analysis

<table>
<thead>
<tr>
<th>Incremental cost (£)</th>
<th>Incremental benefit (QALYs/patient)</th>
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<tbody>
<tr>
<td>£1,200</td>
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<td>£600</td>
<td>0.15</td>
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<tr>
<td>£400</td>
<td>0.20</td>
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<table>
<thead>
<tr>
<th>Threshold (£)</th>
<th>P(x)</th>
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</thead>
<tbody>
<tr>
<td>£1,000</td>
<td>1.00</td>
</tr>
<tr>
<td>£3,000</td>
<td>0.95</td>
</tr>
<tr>
<td>£5,000</td>
<td>0.90</td>
</tr>
<tr>
<td>£7,000</td>
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<tr>
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<td>0.80</td>
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<td>0.60</td>
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<tr>
<td>£19,000</td>
<td>0.55</td>
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<tr>
<td>£21,000</td>
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<td>0.05</td>
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<tr>
<td>£41,000</td>
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</tbody>
</table>

- **ICER**, Central Estimate
- Case finding
- Non-case finding
Value of information

Population Expected value of Information (£, millions)

Threshold (£)

EVPI Population
Partition of benefits

Discounted incremental QALYs over time case finding vs. non-case finding
(showing component contributions)

- Total
- Treatment Decrement
- Presentation Decrement
- Sustained Viral Resp. Benefit
- Residual (long-term benefits)
Summary

• Case finding for HCV is probably cost effective
• Less striking than cost effectiveness of treatment
• Data are very limited in specific settings and for IDU population
• Further empirical (probably observational) studies are urgently required