Adjunction of Polymerase Chain Reaction in Screening for Hepatitis C virus RNA in Blood Donations:

Misuse of Principle of Caution

Sandrine LOUBIÈRE

INSERM Research Unit 379
"behavioral epidemiology in prevention and care for HIV infection", Marseilles, France.

Regional Center for Disease Control of South-Eastern, Marseilles, France.

E-mail : loubiere@marseille.inserm.fr
OBJECTIVES

Introduce Polymerase Chain Reaction (PCR) in the HCV screening of Blood donation is it cost effective?

Does it mean something to do all that is "technically possible" independently of any economic consideration?
## HYPOTHESIS (1) : residual risk

1 - 3 screening strategies to compare

<table>
<thead>
<tr>
<th>Strategies</th>
<th>EIA</th>
<th>EIA + PCR on each donation</th>
<th>EIA + PCR on pools</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Residual Risk</em></td>
<td>4.9 (1.9 - 10.3)</td>
<td>0.7 (0.3 - 1.5)</td>
<td>0.9 (0.4 – 1.9)</td>
</tr>
<tr>
<td><em>Nb of false negatives avoided</em></td>
<td>-</td>
<td>12 (4 - 24)</td>
<td>11 (4 – 22)</td>
</tr>
</tbody>
</table>
HYPOTHESIS (2) : Markov model

2. To take into account long term consequences

- Model of natural HCV history = Markov
NATURAL HISTORY OF HCV DISEASE

INFECTION

0.2% → Well
0.8% → Chronic Hepatitis

Well → Chronic Hepatitis

0.002 → Cirrhosis
0.059 → Cirrhosis

Cirrhosis → Cirrhosis

1 → Decomposed Cirrhosis
0.04 → Decomposed Cirrhosis

Decomposed Cirrhosis → Decomposed Cirrhosis

0.05 → Hepatocellular Carcinoma
0.03 → Hepatocellular Carcinoma

Hepatocellular Carcinoma → Hepatocellular Carcinoma

0.8 → Liver Transplantation
0.069 → Liver Transplantation

Liver Transplantation → Death

1 → Death

Death → Death
HYPOTHESES (2bis) : treatment option

2 - To take into account long term consequences

- Model of natural HCV history = Markov

- One treatment option available = IFN + Ribavirin
  - response rate : 40%
  - response rate in relapsers : 50%
HYPOTHESIS (3) : outcomes

3 - Effectiveness and cost outcomes:

**EFFECTIVENESS**

- HCV infection averted
- CHC averted
- Severe hepatic disease averted
- Years of life saved

**COSTS**

- Screening
  - PCR on donation 68
  - PCR on pools 6.09
  - Loss of the blood donation 79
- Treatment
  - IFN + RIBA 12m 12,000
  - IFN+RIBA 6m
- FOLLOW UP 10 y
  - Remission 152
  - CHC 580
  - Cirrhosis 1,370
  - DC 11,435
  - HCC 10,365
  - Transpl 7,930

Follow up: 10 years
Discount rate: 3% per year
RESULTS (1): effectiveness

- Infections avoided: 14
- CHC avoided: 1.7
- Severe hepatic disease avoided: 1.6
- Years of life saved: 0.2

< 1 severe hepatic disease avoided
< 1 year of life saved
### RESULTS (2) : Incremental CER

<table>
<thead>
<tr>
<th>Study</th>
<th>Effectiveness</th>
<th>Total costs</th>
<th>Strategies</th>
<th>Incremental cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loubière, Rotily, Durand-Zaleski, Costagliola</td>
<td>EIA + PCR on pools</td>
<td>+ €16.7 M</td>
<td>High / low HCV residual risk [€47.5 M – €277 M]</td>
<td>€84.6 M</td>
</tr>
<tr>
<td>Vox Sanguinis 2001 ;80 pp : 199-204</td>
<td>EIA + PCR on each donation</td>
<td>+ €150 M</td>
<td>High / low HCV residual risk [€415 M – €2496 M]</td>
<td>€891 M</td>
</tr>
</tbody>
</table>
RESULTS (2bis) : Incremental CER

CE ratio, MEuros

Baseline scenario
Optimistic scenario

PCR on each donation
PCR on pools

Low hypothesis for residual risk  Mean hypothesis  High hypothesis
## RESULTS (3) : Sensitivity analyses

<table>
<thead>
<tr>
<th>Transfusion recipients</th>
<th>PCR on each donation</th>
<th>PCR on pools</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Discount rate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (3%)</td>
<td>€ 891.1 M</td>
<td>€ 84.5 M</td>
</tr>
<tr>
<td>5%</td>
<td>€ 891.2 M</td>
<td>€ 84.6 M</td>
</tr>
<tr>
<td>10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cost of treatment and follow up</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>€ 891.3 M</td>
<td>€ 84.9 M</td>
</tr>
<tr>
<td>-50%</td>
<td>€ 890.7 M</td>
<td>€ 84.1 M</td>
</tr>
<tr>
<td>+50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cost of PCR test</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>€ 68</td>
<td>€ 6.09</td>
</tr>
<tr>
<td>-50%</td>
<td>€ 38.8 M</td>
<td>€ 41.8 M</td>
</tr>
<tr>
<td>+50%</td>
<td>€ 1,783 M</td>
<td>€ 1,920 M</td>
</tr>
<tr>
<td><strong>High effectiveness (29) and extremely low cost (€ 1)</strong></td>
<td></td>
<td>€ 5.3 M</td>
</tr>
</tbody>
</table>
MAGNITUDE ORDER

Hormonal therapy or Chemotherapy
Traffic road safety

≤ $7,000 / year of life saved
Hillner 1993

HCV treatment

≤ $20,000 / year of life saved

Socially acceptable threshold

≤ $70,000 / year of life saved
Gold 1996
<table>
<thead>
<tr>
<th>Studies</th>
<th>Population</th>
<th>Virus studied</th>
<th>Strategies</th>
<th>Effectiveness criteria</th>
<th>Total Cost</th>
<th>ICER</th>
<th>Average Cost (Euros)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Busch</strong></td>
<td>Blood donors</td>
<td>HCV (HBV)</td>
<td>ALT, EIA, EIA, ALT</td>
<td>QALY</td>
<td>?</td>
<td>-$87 900</td>
<td>$ 7 931 000</td>
</tr>
<tr>
<td><strong>1995</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>Vergnon</strong></td>
<td>Blood donors</td>
<td>HCV</td>
<td>ALT, HCV, HBV</td>
<td>True Positive</td>
<td>€ 5.8 M</td>
<td>€ 2,173</td>
<td>-</td>
</tr>
<tr>
<td><strong>1996</strong></td>
<td></td>
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<td></td>
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<tr>
<td><strong>Sailly</strong></td>
<td>Blood donors</td>
<td>HBV</td>
<td>EIA + confirmation test</td>
<td>Seroconversion avoided</td>
<td>€ 38 M</td>
<td>-</td>
<td>€ 4,878</td>
</tr>
<tr>
<td><strong>1997</strong></td>
<td></td>
<td>HCV HIV HTLV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>€ 10,976</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>€ 103,000</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>€ 915,000</td>
</tr>
<tr>
<td><strong>Djossou</strong></td>
<td>Blood donors</td>
<td>HIV</td>
<td>EIA + Ag p24</td>
<td>True Positive</td>
<td>€ 59 M</td>
<td>€ 1.5 M</td>
<td>-</td>
</tr>
<tr>
<td><strong>1999</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Pereira</strong></td>
<td>Blood donors</td>
<td>HCV</td>
<td>PCR</td>
<td>QALY Life years saved</td>
<td>$ 1 829 611</td>
<td>-</td>
<td>$1 100 000</td>
</tr>
<tr>
<td><strong>2000</strong></td>
<td></td>
<td></td>
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QUESTIONS

1 - What is the **opportunity cost** of the introduction of PCR in HCV blood screening?
   = How many people could be detected and treated?

2 - If Health Ministry decide PCR introduction
   = Does it mean "**risk aversion**"?
MISUSE OF THE PRINCIPLE OF CAUTION

1 - Principle of caution = a *legal rule* for whole ?
Or = a *tool* for policy makers ?

2 - Principle of caution applied to transfusion safety
= *Disregard the economic aspect*
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Results in the article: