Global Hepatitis A meeting
Miami, 30 November-1 December 2007

Country and regional examples of hepatitis A prevention: The experience of Catalonia (Spain)

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## RECOMMENDATIONS FOR HEPATITIS A VACCINATION IN CATALONIA

### 1995 Vaccination of risk groups

- International travellers to regions of endemic disease
- Homosexual men
- Users of intravenous drugs
- Sewage workers
- Patients receiving factor VIII concentrates
- Exposed to non-human primates
- Staff of day-care centres
- Staff of institutions for developmentally disabled persons
- People >30 years old with chronic liver disease
- People infected by hepatitis C virus
REPORTED MORBIDITY OF HEPATITIS A.
CATALONIA, 1992-1998

Rate per 100,000 persons-year

Vaccination of risk groups

Years
7.36 5.33 4.75 2.79 5.12 5.34 8.10
EVOLUTION OF REPORTED VIRAL HEPATITIS. CATALONIA, 1992-1998

Vaccination of risk groups

- Hepatitis A
- Hepatitis B
- Other viral hepatitis
RECOMMENDATIONS FOR HEPATITIS A VACCINATION IN CATALONIA

1995 → Vaccination of risk groups

1998 → Universal vaccination of preadolescents
RATIONALE FOR HEPATITIS A
UNIVERSAL VACCINATION

- Limited impact of selective vaccination of risk groups
- Immediate impact of universal vaccination on clinical cases
- Potential of mass vaccination to eliminate the disease
- Combined A+B vaccine available
- Well-established hepatitis B vaccination program of preadolescents in schools
- Low cost of the program
- Acceptable cost-effectiveness and cost-benefit ratios of the program
NET PRESENT VALUE AND COST-BENEFIT RATIO*

Length of protection: 25 years. Cohort of 67,441 pre-adolescent vaccinated at 12 years and followed for 25 years. Discount rate: 5%

Cost of vaccination program 336,567 €
Cost of hepatitis A without vaccination 995,096 €
Cost of hepatitis A with vaccination 124,821 €
Benefit of vaccination program 870,275 €
Net present value +533,708 €
Cost-benefit ratio 2.58

*Cost of hepatitis A vaccine= 1.98 euros

[cost of combined hepatitis A+B vaccine] - [cost of hepatitis B vaccine]

# Sensitivity Analysis of the Main Variables Influencing the Results

<table>
<thead>
<tr>
<th>Variations in the Variables</th>
<th>Cost per case avoided</th>
<th>Cost per year of life gained</th>
<th>Cost per year of life adjusted for disability gained</th>
<th>Benefit/Cost Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BASE CASE</strong></td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>2.58</td>
</tr>
<tr>
<td><strong>INCREMENTAL PRICE OF A+B VACCINE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.31 euros/dose</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>1.54</td>
</tr>
<tr>
<td>5.05 euros/dose</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>1.0</td>
</tr>
<tr>
<td>11.12 euros/dose</td>
<td>3,229</td>
<td>37,152</td>
<td>31,478</td>
<td>0.45</td>
</tr>
<tr>
<td>15 euros/dose</td>
<td>5,219</td>
<td>60,047</td>
<td>50,875</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>INCIDENCE RATE OF HEPATITIS A</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.5 per 100,000</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>1.01</td>
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<tr>
<td>22.5 per 100,000</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>3.87</td>
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<tr>
<td>30 per 100,000</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>5.17</td>
</tr>
<tr>
<td>37.5 per 100,000</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>&lt;0 (saving)</td>
<td>6.45</td>
</tr>
</tbody>
</table>

IMPACT OF ROUTINE HEPATITIS A VACCINATION ON THE GLOBAL INCIDENCE OF THE DISEASE

![Graph showing the impact of routine hepatitis A vaccination on the global incidence of the disease. The graph displays data from 1992 to 2001, with the rate per 100,000 persons-year indicated for each year. The data shows a significant decrease in the incidence of the disease after the implementation of routine vaccination.]
VACCINATION EFFECTIVENESS (I)

- Vaccination effectiveness (VE)
  \[ \text{VE} = 1 - \text{RR} \]

  - Incidence rate in vaccinated cohorts
  \[ \text{RR} = \text{Incidence rate in non vaccinated cohorts} \]

- 95% CI of VE were calculated using Taylor series
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td>Children 13 years old 10</td>
<td>Children 14 years old 13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1985</td>
<td>Children 12 years old 5</td>
<td>Children 13 years old 1</td>
<td>Children 14 years old 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1986</td>
<td>Children 11 years old 6</td>
<td>Children 12 years old 4</td>
<td>Children 13 years old 1</td>
<td>Children 14 years old 1</td>
<td></td>
</tr>
<tr>
<td>1987</td>
<td></td>
<td>Children 11 years old 3*</td>
<td>Children 12 years old 2***</td>
<td>Children 13 years old 2 **</td>
<td>Children 14 years old 0</td>
</tr>
<tr>
<td>1988</td>
<td></td>
<td></td>
<td>Children 11 years old 0</td>
<td>Children 12 years old 0</td>
<td>Children 13 years old 0</td>
</tr>
<tr>
<td>1989</td>
<td></td>
<td></td>
<td></td>
<td>Children 11 years old 0</td>
<td>Children 12 years old 1**</td>
</tr>
</tbody>
</table>

* All three cases occurred before the beginning of vaccination
** The cases had not been vaccinated
*** Vaccination status unknown in one case; the other had not been vaccinated.
VACCINATION EFFECTIVENESS (II)

Cases in vaccinated cohorts 1
Pers-yr in vaccinated cohorts 446,995 pers-yr
Incidence rate in vaccinated cohorts $0.2 \times 10^{-5}$ pers-yr

Cases in non vaccinated cohorts 49
Pers-yr in non vaccinated cohorts 648,591 pers-yr
Incidence rate in non vaccinated cohorts $7.55 \times 10^{-5}$ pers-yr

$\text{RR} = 0.0296$

$\text{VE} = 97.0\%$
$95\% \text{ CI} = 78.5\% - 99.6\%$

HOW HAS THE SITUATION EVOLVED?
IMPACT OF ROUTINE HEPATITIS A VACCINATION ON THE GLOBAL INCIDENCE OF THE DISEASE

![Graph showing the impact of routine hepatitis A vaccination on the global incidence of the disease from 1992 to 2005. The graph indicates a significant decrease in the incidence rate after the implementation of the vaccination program.](image-url)
REPORTED HEP A+B IMMUNIZATION COVERAGES (THREE DOSES). CATALONIA 1999-2005

Year | Coverage
--- | ---
1999 | 90.8
2000 | 90.6
2001 | 88.0
2002 | 87.6
2003 | 85.4
2004 | 86.3
2005 | 86.6
### DISTRIBUTION OF REPORTED RATES* OF HEPATITIS A BEFORE AND AFTER ROUTINE VACCINATION

<table>
<thead>
<tr>
<th>Age group</th>
<th>Before vaccination 1992 – 1998</th>
<th>After vaccination 1999 – 2005</th>
<th>Rate decline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate</td>
<td>Cases</td>
<td>Rate</td>
</tr>
<tr>
<td>&lt; 5</td>
<td>11.4</td>
<td>219</td>
<td>6.7</td>
</tr>
<tr>
<td>5 - 9</td>
<td>17.4</td>
<td>353</td>
<td>9.4</td>
</tr>
<tr>
<td>10 - 19</td>
<td>9.0</td>
<td>511</td>
<td>2.5</td>
</tr>
<tr>
<td>20 - 29</td>
<td>10.0</td>
<td>695</td>
<td>5.1</td>
</tr>
<tr>
<td>30 - 39</td>
<td>6.5</td>
<td>416</td>
<td>5.2</td>
</tr>
<tr>
<td>40 - 49</td>
<td>1.6</td>
<td>92</td>
<td>1.3</td>
</tr>
<tr>
<td>50 - 59</td>
<td>0.8</td>
<td>38</td>
<td>0.5</td>
</tr>
<tr>
<td>≥ 60</td>
<td>0.3</td>
<td>32</td>
<td>0.3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>5.5</td>
<td>2356</td>
<td>3.0</td>
</tr>
</tbody>
</table>

*Per 100,000 pers-yr
DISTRIBUTION OF REPORTED INCIDENCE RATES OF HEPATITIS A INCIDENCE BEFORE AND AFTER ROUTINE VACCINATION
## VACCINATION EFFECTIVENESS

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Cases</th>
<th>Pers-yr</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated (born 1987-1993)</td>
<td>1</td>
<td>1,591,366</td>
<td>$0.06 \times 10^{-5}$</td>
</tr>
<tr>
<td>Nonvaccinated (born 1984-1986)</td>
<td>131</td>
<td>2,023,121</td>
<td>$6.2 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

Relative Risk (RR): 0.0096

Vaccine Effectiveness (VE): 99.04%

95% Confidence Interval (CI): 93.11% - 99.88%
PREVENTED FRACTION (PF)

Proportion of the hypothetical load of disease (in the 12-19 years age group) that has been prevented by vaccination

\[ PF = \text{Coverage} \times (1 - \text{RR}) \]

\[ PF = 0.91 \times 0.990 = 90.13\% \]
CONCLUSIONS

1. The incidence rate of hepatitis A in the general population has fallen by 46% in the seven years following introduction of vaccination compared with the seven previous years.

2. By age group, the greatest fall in hepatitis A incidence (73%) occurred in the 10-19 years age group (corresponding to the vaccinated cohorts) followed by the 20-29 years age group (49%)
3. The effectiveness of the vaccination programme 7 years after the beginning was 99% and the prevented fraction of hepatitis A in children 12-19 years old is estimated at 90%.

4. The reduction in the incidence in non-vaccinated age groups supports the indirect effects of the vaccination program suggested by other authors.
STUDY PARTICIPANTS

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