

**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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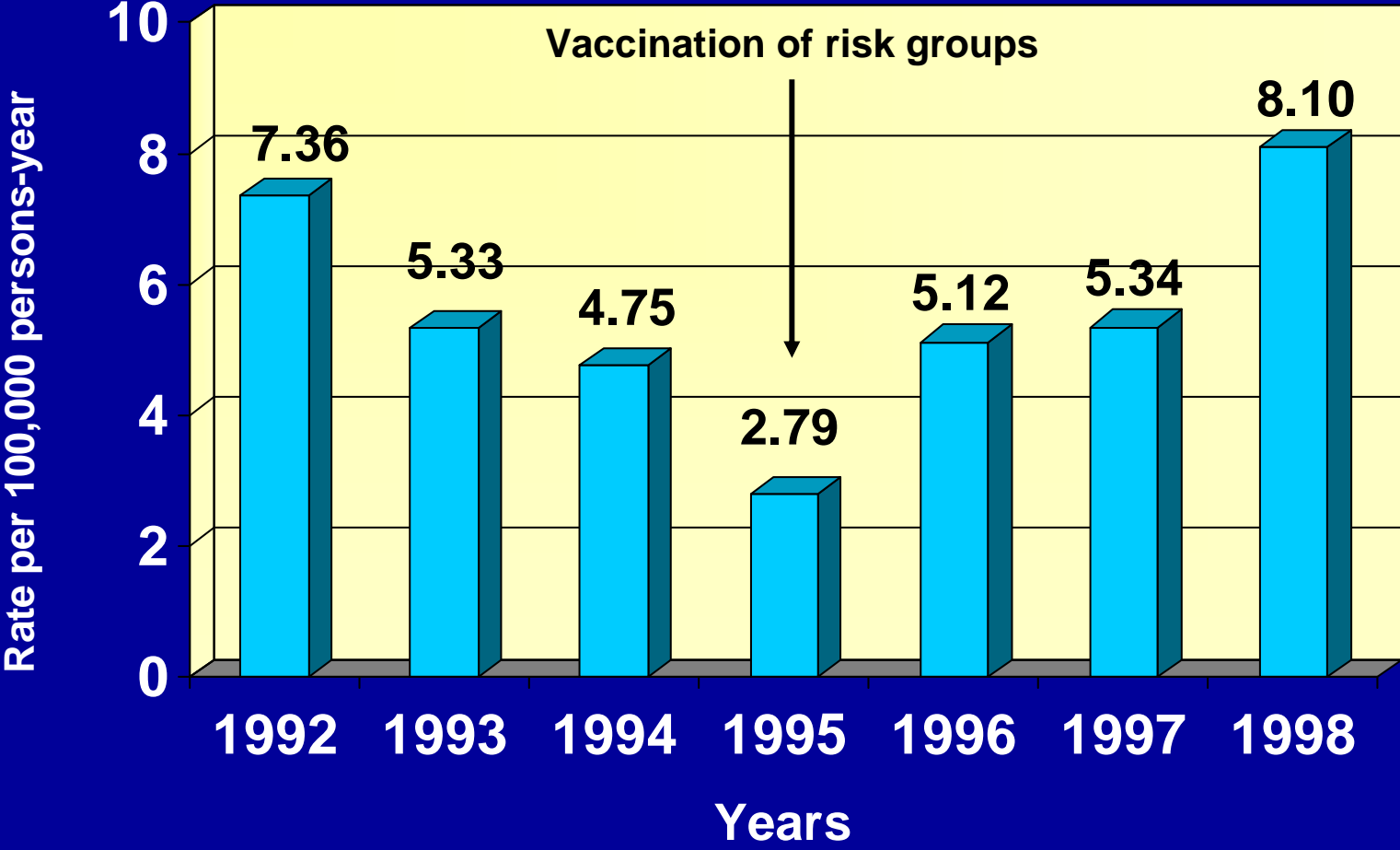


# RECOMMENDATIONS FOR HEPATITIS A VACCINATION IN CATALONIA

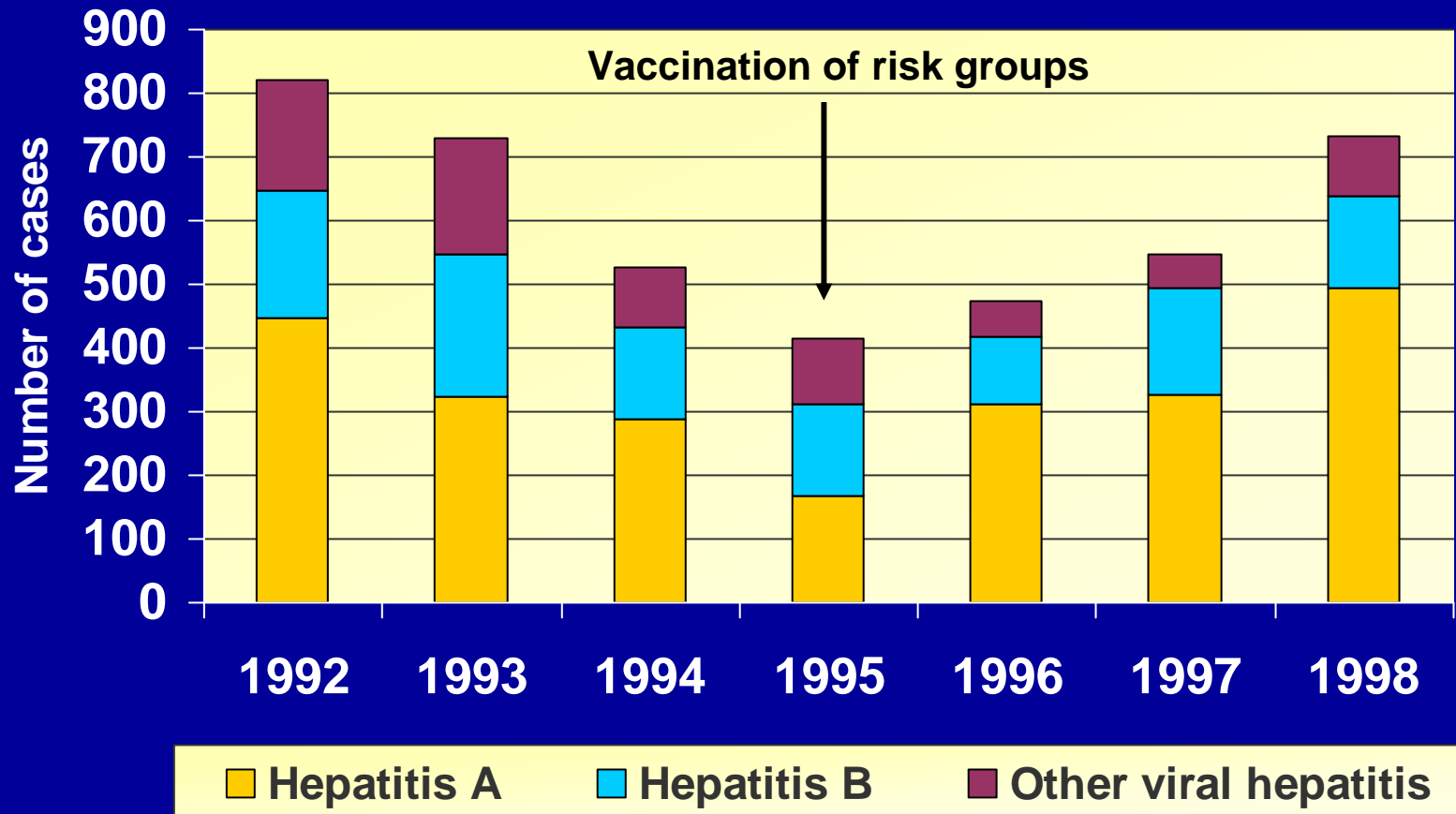
1995  Vaccination of risk groups

- ◆ 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



# EVOLUTION OF REPORTED VIRAL HEPATITIS. CATALONIA, 1992- 1998



# RECOMMENDATIONS FOR HEPATITIS A VACCINATION IN CATALONIA

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**1995 → Vaccination of risk groups**

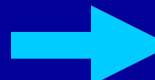
**1998 → Universal vaccination of preadolescents**

# **RATIONALE FOR HEPATITIS A UNIVERSAL VACCINATION**

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- ◆ **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



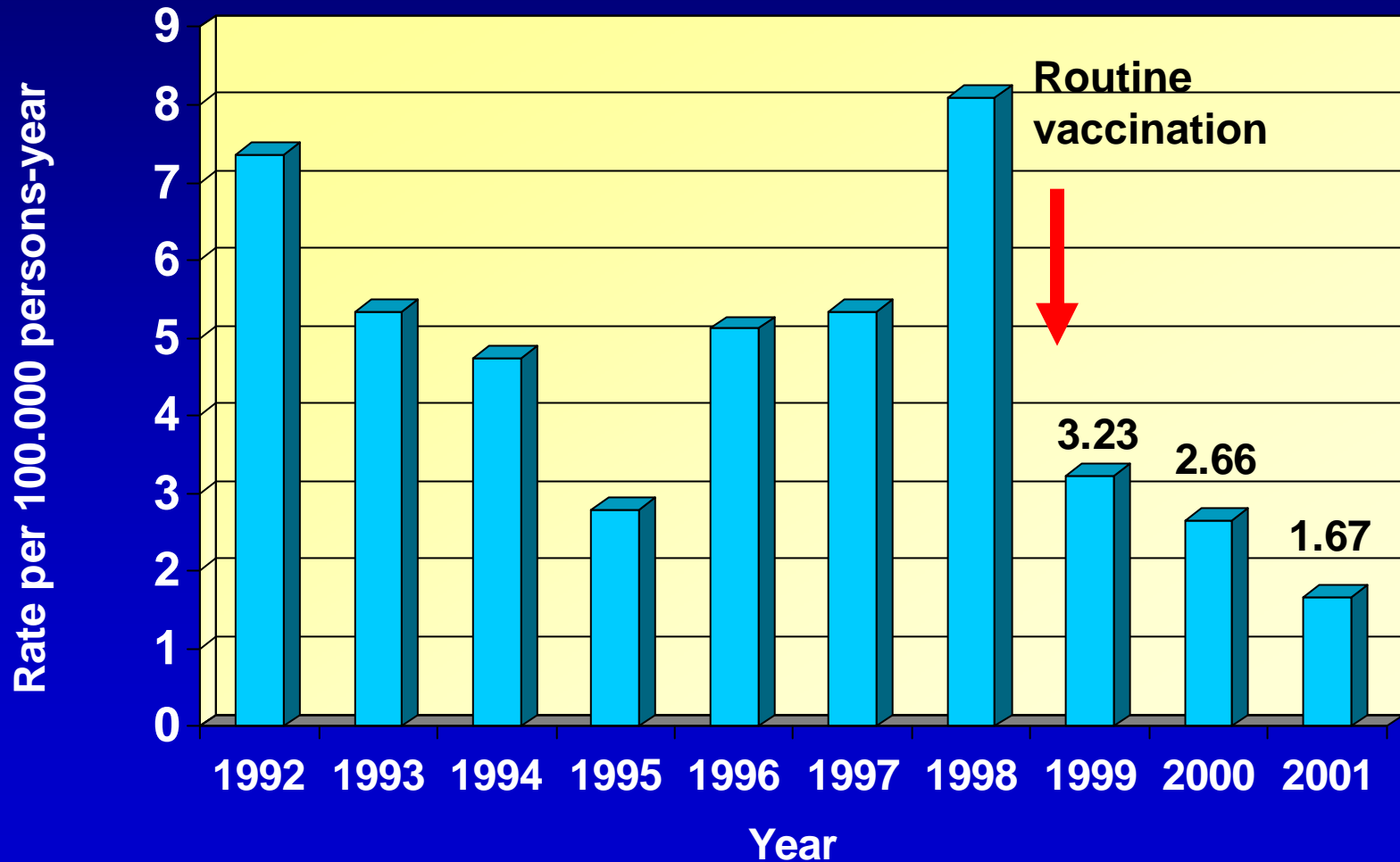
[cost of combined hepatitis A+B vaccine] - [cost of hepatitis B vaccine]



# SENSITIVITY ANALYSIS OF THE MAIN VARIABLES INFLUENCING THE RESULTS

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

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



# VACCINATION EFFECTIVENESS (I)

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- ◆ Vaccination effectiveness (VE)

$$VE = 1 - RR$$

$$RR = \frac{\text{Incidence rate in vaccinated cohorts}}{\text{Incidence rate in non vaccinated cohorts}}$$

- ◆ 95% CI of VE were calculated using Taylor series

# DISTRIBUTION OF HEPATITIS A CASES IN NON VACCINATED AND VACCINATED COHORTS

| BORN YEAR | CASES YEAR 1997                | CASES YEAR 1998                | CASES YEAR 1999                  | CASES YEAR 2000                 | CASES YEAR 2001                 |
|-----------|--------------------------------|--------------------------------|----------------------------------|---------------------------------|---------------------------------|
| 1984      | Children<br>13 years old<br>10 | Children<br>14 years old<br>13 |                                  |                                 |                                 |
| 1985      | Children<br>12 years old<br>5  | Children<br>13 years old<br>1  | Children<br>14 years old<br>1    |                                 |                                 |
| 1986      | Children<br>11 years old<br>6  | Children<br>12 years old<br>4  | Children<br>13 years old<br>1    | Children<br>14 years old<br>1   |                                 |
| 1987      |                                | Children<br>11 years old<br>3* | Children<br>12 years old<br>2*** | Children<br>13 years old<br>2** | Children<br>14 years old<br>0   |
| 1988      |                                |                                | Children<br>11 years old<br>0    | Children<br>12 years old<br>0   | Children<br>13 years old<br>0   |
| 1989      |                                |                                |                                  | Children<br>11 years old<br>0   | Children<br>12 years old<br>1** |

\* 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 |

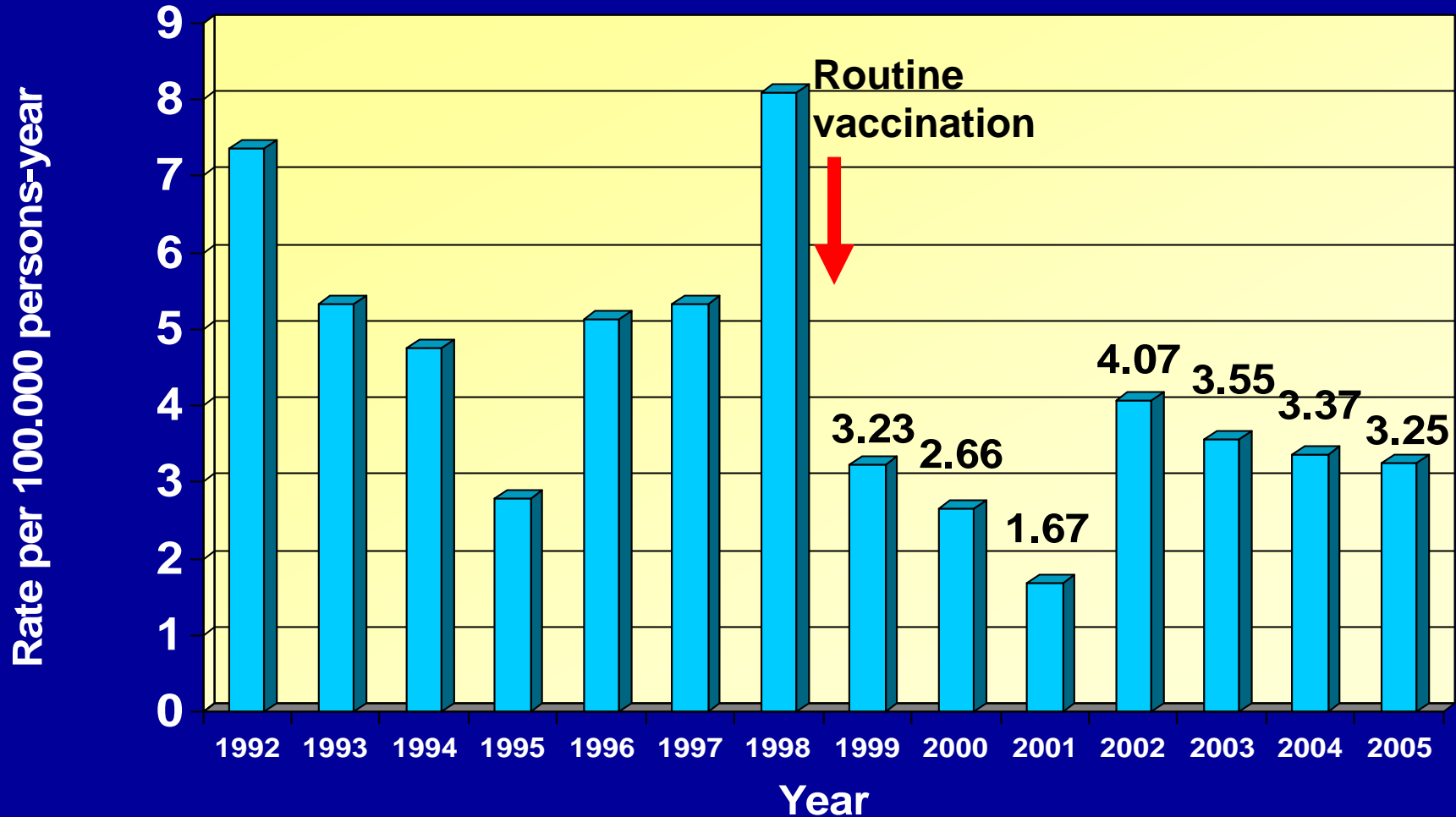
$$RR = 0.0296$$

$$VE = 97.0\%$$

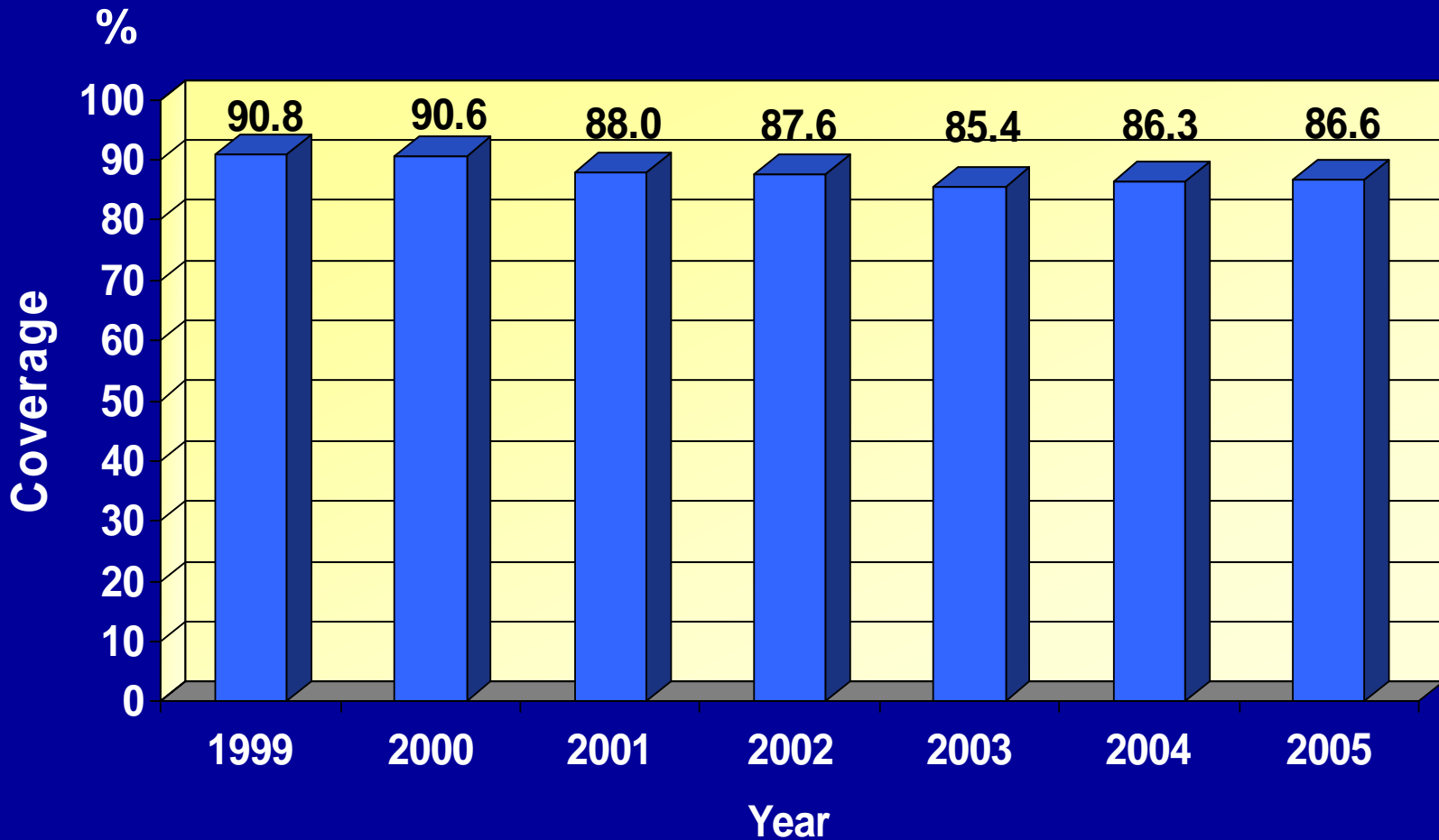
$$95\% \text{ CI} = 78.5\% - 99.6\%$$

**HOW HAS THE SITUATION EVOLVED?**

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



# REPORTED HEP A+B IMMUNIZATION COVERAGES (THREE DOSES). CATALONIA 1999-2005



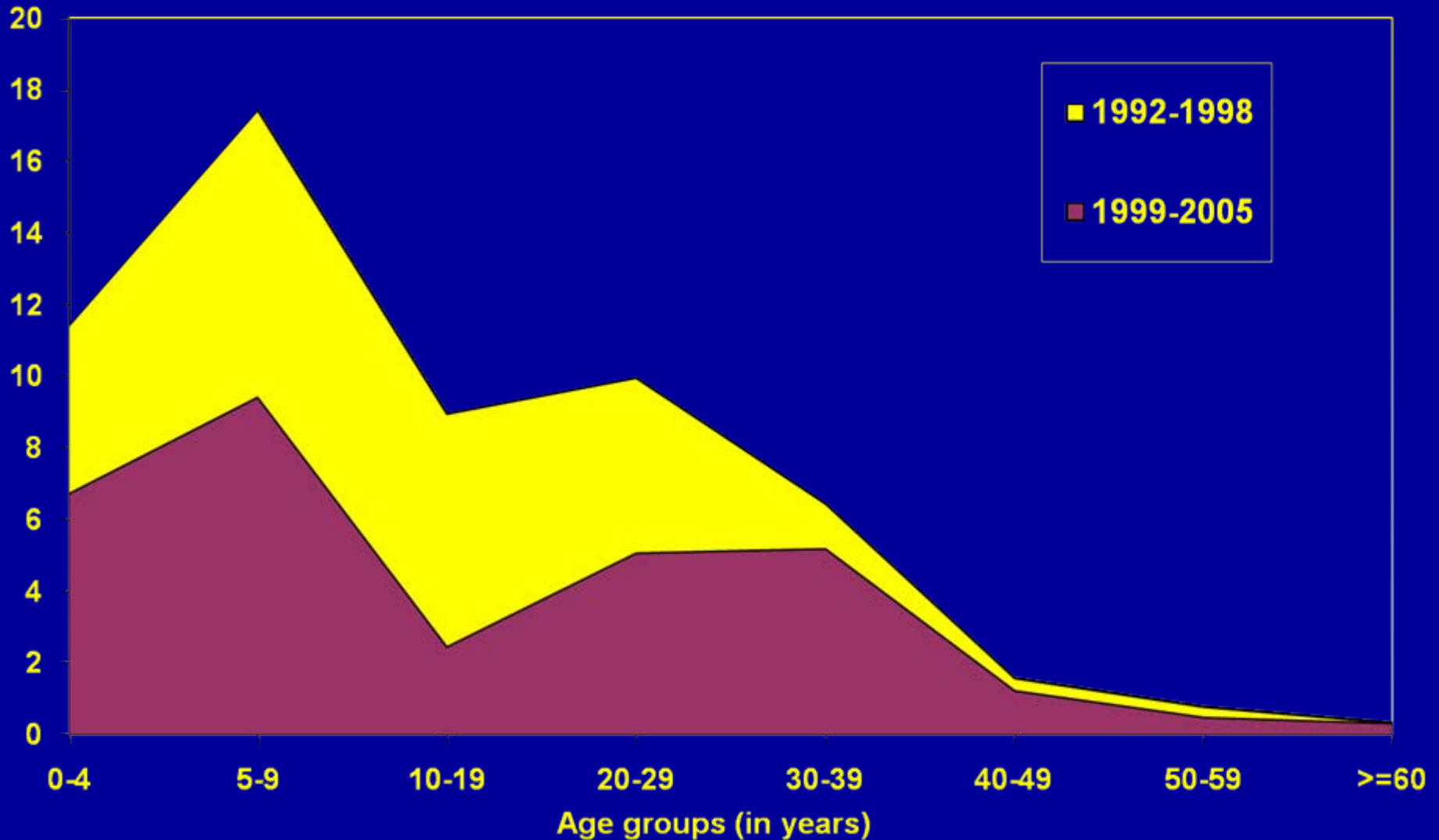


# DISTRIBUTION OF REPORTED RATES\* OF HEPATITIS A BEFORE AND AFTER ROUTINE VACCINATION

| Age group    | Before vaccination<br>1992 – 1998 |             | After vaccination<br>1999 – 2005 |             | Rate decline            |                  |
|--------------|-----------------------------------|-------------|----------------------------------|-------------|-------------------------|------------------|
|              | Rate                              | Cases       | Rate                             | Cases       | % (95% CI)              | P                |
| < 5          | 11.4                              | 219         | 6.7                              | 146         | 41.0 (27.3-52.2)        | <0.001           |
| 5 - 9        | 17.4                              | 353         | 9.4                              | 192         | 45.9 (35.6-54.7)        | <0.001           |
| 10 - 19      | 9.0                               | 511         | 2.5                              | 113         | 72.5 (66.3-77.6)        | <0.001           |
| 20 - 29      | 10.0                              | 695         | 5.1                              | 377         | 49.0 (42.2-55.0)        | <0.001           |
| 30 - 39      | 6.5                               | 416         | 5.2                              | 396         | 19.5 (7.7-29.9)         | 0.002            |
| 40 - 49      | 1.6                               | 92          | 1.3                              | 81          | 21.9 (5.3-42.0)         | 0.104            |
| 50 - 59      | 0.8                               | 38          | 0.5                              | 28          | 37.0 (2.6-61.4)         | 0.060            |
| ≥ 60         | 0.3                               | 32          | 0.3                              | 34          | 1.3 (-59.9-39.1)        | 0.957            |
| <b>TOTAL</b> | <b>5.5</b>                        | <b>2356</b> | <b>3.0</b>                       | <b>1367</b> | <b>45.9 (42.1-49.3)</b> | <b>&lt;0.001</b> |

\*Per 100,000 pers-yr

# DISTRIBUTION OF REPORTED INCIDENCE RATES OF HEPATITIS A INCIDENCE BEFORE AND AFTER ROUTINE VACCINATION



# VACCINATION EFFECTIVENESS

|   |                               |
|---|-------------------------------|
| Cases in vaccinated cohorts (born in 1987-1993) | 1                             |
| Pers-yr in vaccinated cohorts                   | 1,591,366 pers-yr             |
| Incidence rate in vaccinated cohorts            | $0.06 \times 10^{-5}$ pers-yr |

|  |                              |
|--|------------------------------|
| Cases in nonvaccinated cohorts (born in 1984-1986) | 131                          |
| Pers-yr in vaccinated cohorts                      | 2,023,121 pers-yr            |
| Incidence rate in non vaccinated cohorts           | $6.2 \times 10^{-5}$ pers-yr |

**RR: 0.0096**

**VE= 99.04%**

**95% 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**

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

$$\text{PF} = 0.91 \times 0.990 = 90.13\%$$

# CONCLUSIONS

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- 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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*\*CIBER, Epidemiology and Public Health (CIBERESP, SPAIN)*