

REDUCTION OF INVASIVE DISEASE IN CHILDREN TWO DECADES AFTER THE INTRODUCTION OF *HAEMOPHILUS INFLUENZAE* TYPE B CONJUGATE VACCINATION IN APULIA REGION, ITALY

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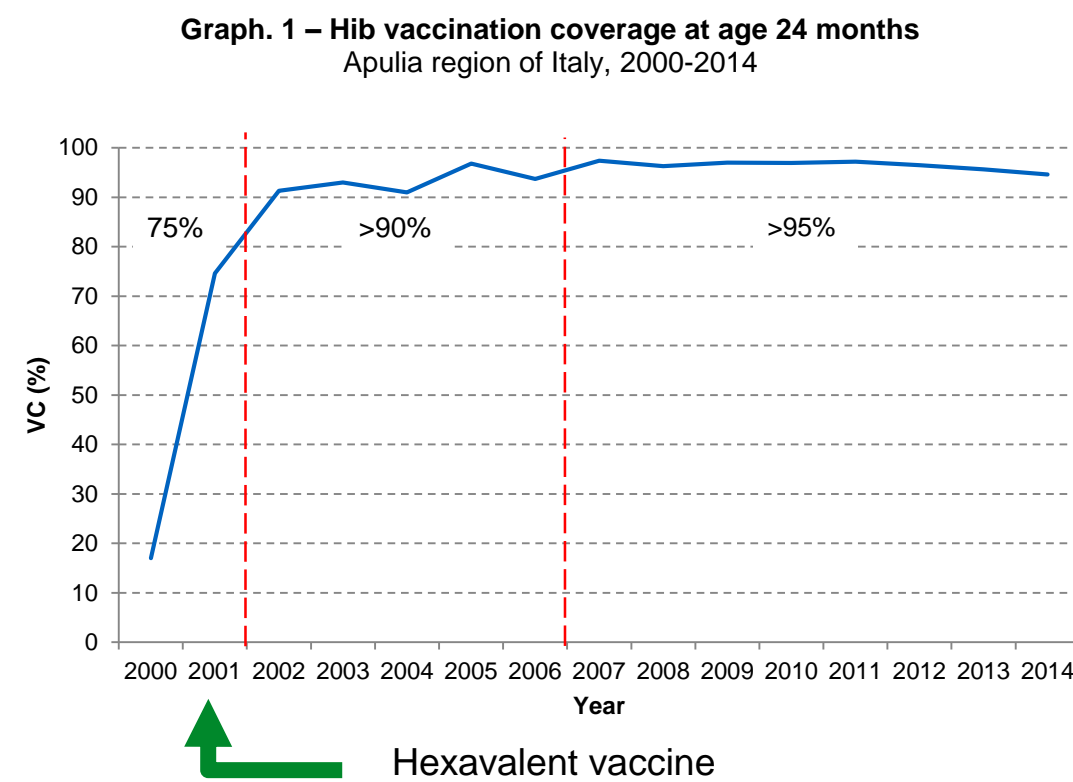
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Background

Haemophilus influenzae type b conjugate (Hib) monovalent vaccination, consisting of 2p+1 doses at 3, 5, and 11 months of age, was introduced in the Italy's infant immunization schedule in 1999 and included in the DTaP-HBV-IPV/Hib hexavalent vaccine since 2001. The estimated vaccination coverage was 83.4% in 2002, >90% by 2005, and >95% by 2011 [1-4].

In the Apulia region of Italy (about 4,000,000 inhabitants), vaccination coverage for 3 doses reached 75% in 2001, >90% by 2002, and >95% by 2007 (Graph. 1).



This study aimed at estimating the decline in incidence of *Haemophilus influenzae* invasive disease requiring hospitalization in children aged <5 years in Apulia, by calculating the attributable benefit ($A_{Ie}B$) and the prevented fraction ($P_{ed}F$) of Hib universal routine vaccination.

Methods

We considered annual age-specific hospitalization rates in infants <1 year and children 1-4 years as a proxy for incidence in the period 1996-2014. The attributable benefit was calculated as the reduction in incidence of *Haemophilus influenzae* invasive disease among vaccinated children attributable to the routine use of Hib monovalent vaccine during 1999-2000 (“Hib-monovalent period”) and of the hexavalent DTPa-HBV-IPV/Hib vaccine in the period 2001-2014 (“DTPa-HBV-IPV/Hib period”). The prevented fraction was calculated as the proportion of hypothetical total cases that were prevented by the use of monovalent and hexavalent vaccine, respectively (Panel A) [5].

Panel A

Attributable benefit
Reduction in incidence of the disease among vaccinated individuals attributable to the introduction of vaccination, calculated as:

$$A_{Ie}B = I_{\text{vaccinated}} - I_{\text{unvaccinated}}$$

Prevented fraction
Proportion of hypothetical total cases that were prevented by the introduction of vaccination, calculated as:

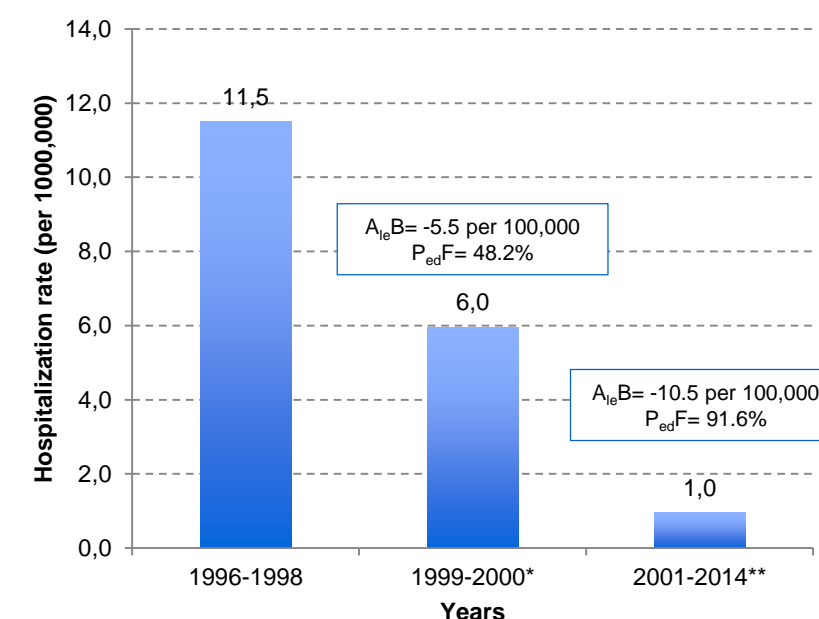
$$P_{ed}F = \frac{I_{\text{unvaccinated}} - I_{\text{population}}}{I_{\text{unvaccinated}}}$$

Results

The hospitalization rate for *Haemophilus influenzae* invasive disease among infants decreased from 11.5 (95% CI= 1.4-21.6) per 100,000 in the 1996-1998 pre-vaccination period to 6 (95% CI= -1.4-13.3) per 100,000 in the “Hib-monovalent period”, with an estimated $A_{Ie}B$ of -5.5 per 100,000 and a $P_{ed}F$ of 48.2%. It declined further to 1 (95% CI= -2.2-4.1) per 100,000 in the “DTaP-HBV-IPV/Hib period”, with an $A_{Ie}B$ of -10.5 per 100,000 and a $P_{ed}F$ of 91.6% (Graph. 2).

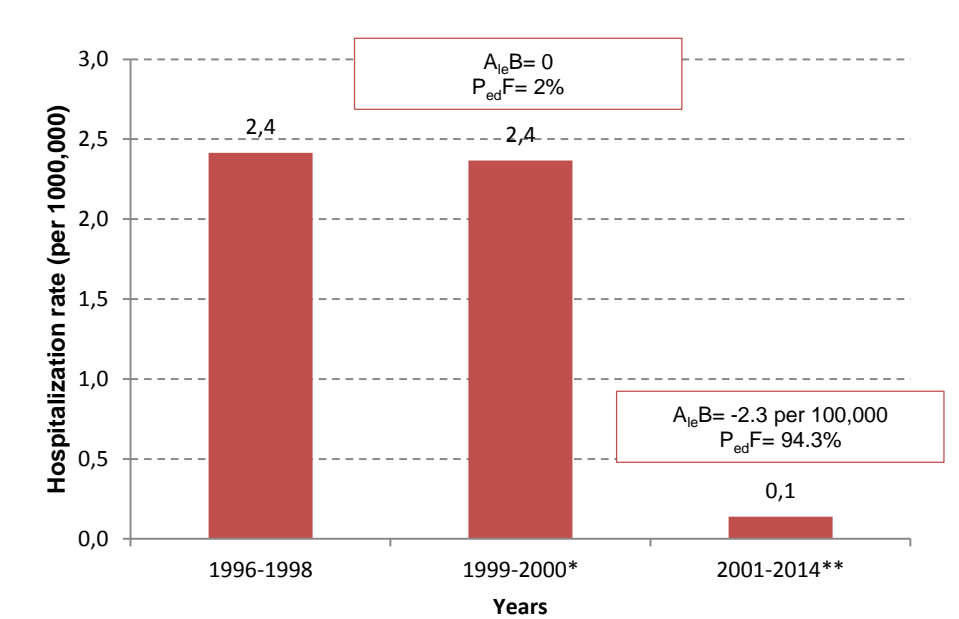
The rate of hospitalization among children aged 1-4 year remained stable at 2.4 per 100,000 from the pre-vaccination period through “Hib-monovalent period” ($A_{Ie}B=0$; $P_{ed}F=2\%$) and declined to 0.1 (95% CI= -0.4-0.7) per 100,000 in the “DTaP-HBV-IPV/Hib period”, with an $A_{Ie}B$ of -2.3 per 100,000 and a $P_{ed}F$ of 94.3% (Graph. 3).

Graph. 2 - Hospitalization rates for invasive *H. influenzae* disease in infants <1 year in the pre- and Hib vaccination periods
Apulia region of Italy



* Hib-monovalent period - ** DTPa-HBV-IPV/Hib period

Graph. 3 - Hospitalization rates for invasive *H. influenzae* disease in children 1-4 years in the pre- and Hib vaccination periods
Apulia region of Italy



Conclusions

In the Apulia region of Italy, the proportion of *Haemophilus influenzae* invasive disease requiring hospitalization in children aged <5 years presumably prevented by the introduction of Hib universal vaccination amounted to more than nine in ten cases. These findings are consistent with increased vaccine coverage rates as a result of the wide use of the hexavalent combination vaccines.

Conflict of interest

Domenico Martinelli reports grants from GSK and non-financial support from Sanofi Pasteur MSD, GSK and Pfizer, outside this work. Rosa Prato has served in advisory committees related to Hib vaccine for Sanofi Pasteur MSD. She also reports grants, personal fees and non-financial support from Sanofi Pasteur MSD, Pfizer and GSK, outside this work.



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