

**Trends in *Streptococcus pneumoniae* invasive diseases in children in 5 Italian regions in the era of glycoconjugate vaccines, 2008-2013**

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**Objectives:** Following glycoconjugate vaccine use, *Streptococcus pneumoniae* epidemiology is constantly evolving as regards invasive diseases incidence, serotypes distribution and the related antibiotic resistance phenomenon. In Italy the use of the 7-valent vaccine PCV7 for children immunization was gradually implemented in the Italian regions starting from 2006 and was replaced by the 13-valent vaccine PCV13 between 2010 and 2011.

The aim of this study was to evaluate the impact of vaccine use on pneumococcal invasive diseases (IPD) and to provide insight into the evolution of the pneumococcal population in children in 5 Italian regions, representing approximately one third of the Italian population, during the shift from PCV7 to PCV13.

**Methods:** All cases of pneumococcal invasive diseases (IPD) in children aged 0-4 years from 5 Italian regions (Emilia-Romagna, Lombardia, Piemonte, P. A. Bolzano, P. A. Trento) and reported in the nationwide surveillance system of invasive bacterial diseases (<http://www.simi.iss.it>) in the period 2008-2013 were included in this study. Serotyping was performed by latex agglutination and the Quellung reaction; susceptibilities to penicillin, erythromycin and ceftriaxone were determined by the Etest using the EUCAST breakpoints.

**Results:** Overall, 298 cases of IPD were reported over the study period. The incidence of IPD in children declined from 7.5 in 2008 to 4.2 cases/100,000 inhabitants in 2013.

A total of 228 (76.5%) pneumococcal strains were available for serotyping. PCV13 serotypes represented approximately 75% of the isolates in the years 2008-2009 and 2010-2011, and decreased substantially to 48.4% in 2012-2013. Conversely, non vaccine serotypes increased from 21.6 and 24.4% in 2008-2009 and 2010-2011 respectively, to 51.6% in 2012-2013. In the last two-year period the most frequent serotypes were 1 (11.3%), 7F (9.7%), 14 (8.1%), 19A and 24F (6.4% each), 12F, 23B, and 33F (4.8% each). The rates of penicillin non-susceptibility and of resistance to ceftriaxone increased from 15.5% and 6.0% in 2008-2011 to 28.2% and 12.5% in 2012-2013, respectively. On the contrary, in the same periods, the rate of erythromycin resistance decreased from 37.0% to 26.6%. Overall, in 2012-2013, PCV13 serotypes accounted for 66.6%, 100% and 52.9%, of the penicillin non-susceptible, ceftriaxone resistant and erythromycin resistant strains, respectively.

**Conclusions:** The use of glycoconjugate vaccines led to a substantial decrease in IPD incidence in children throughout the study period. The effect of PCV13 was apparent during 2012-2013 when PCV13 serotypes decreased in frequency, although some PCV13 serotypes were still the predominant serotypes causing IPD and were responsible for the majority of antibiotic-resistant infections. Since new epidemiological changes are expected to occur in the next years continuous surveillance is required to evaluate the long-term impact of PCV13 on IPD and on the evolution of pneumococcal population.