

A Retrospective Database Analysis to Estimate the Burden of Pneumonia in Children <15 Years in the Veneto Region (Italy)

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Background

- Pneumonia continues to cause significant morbidity and mortality in children,¹ with *Streptococcus pneumoniae* as a leading bacterial cause²
- Heptavalent pneumococcal conjugate vaccine (PCV7) was introduced in the immunization schedule in the Veneto region of Italy in 2003 and was replaced by 13-valent PCV (PCV13) in 2010
- The Veneto region suspended all mandatory vaccinations for children during 2008–2017.³ During this period, vaccination coverage was 88–94%, 89–94%, and 85–93% for the first, second, and third dose, respectively⁴
- This study estimated the incidence rates (IRs) and regional expenditures of pneumococcal-specific and unspecified pneumonia following the introduction of PCV13

Methods

Study Design

- This retrospective observational study was conducted using data from:
 - Pedianet database⁵: Pedianet is an organized network of family pediatricians (FPs) across Italy. Data include patient demographic characteristics, prescriptions, vaccinations, diagnoses, and referrals to specialists and hospitals
 - Hospitalization and emergency room (ER) database: collects data on prescriptions, specialist visits, ER visits, and hospitalizations, can be linked to the Pedianet database for patients who provide informed consent

Data Analysis

- All pneumonia-related visits and hospitalizations in patients aged <15 years during 2010 and 2017 were identified in the databases using International Classification of Diseases, Clinical Modification, 9th revision (ICD-9-CM) codes and free text as summarized in **Table 1**
- Diagnostics to determine the pathogens causing pediatric pneumonia are extremely limited. Therefore, we include both pneumococcal specific and unspecified pneumonia codes

Table 1. Search Terms and Diagnoses of Pneumonia

Term	Description
ICD-9-CM 481	Pneumococcal pneumonia
ICD-9-CM 482.9	Bacterial pneumonia, unspecified
ICD-9-CM 485	Bronchopneumonia, organism unspecified
ICD-9-CM 486	Pneumonia, organism unspecified
olmon	Relating to <i>polmoni</i> (lungs) or <i>polmonite</i> (pneumonia)
bp	Relating to <i>bronchopolmonite</i> (bronchopneumonia)

ICD-9-CM, International Classification of Diseases, Clinical Modification, 9th revision.

References

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- An episode could comprise one or more related hospitalization, ER visits, and FP visits. A gap of 90 days between visits or hospitalizations defined the start of a new episode
- Annual incidence rates (IRs) were defined as numbers of episodes per 1000 person-years; 95% confidence intervals (CIs) were calculated
- Interrupted time series (ITS) analysis was conducted using a negative binomial regression model to assess differential trends in annual incidence rates in the early post-PCV13 (2010–2013) and late post-PCV13 (2014–2017) periods. The Mann–Kendall test was performed to examine whether the trend in annual IRs was monotonic or not
- Regional expenditures were calculated by multiplying the average cost per episode in 2017 with the standardized regional incidence rate and regional population <15 years old in each year

Results

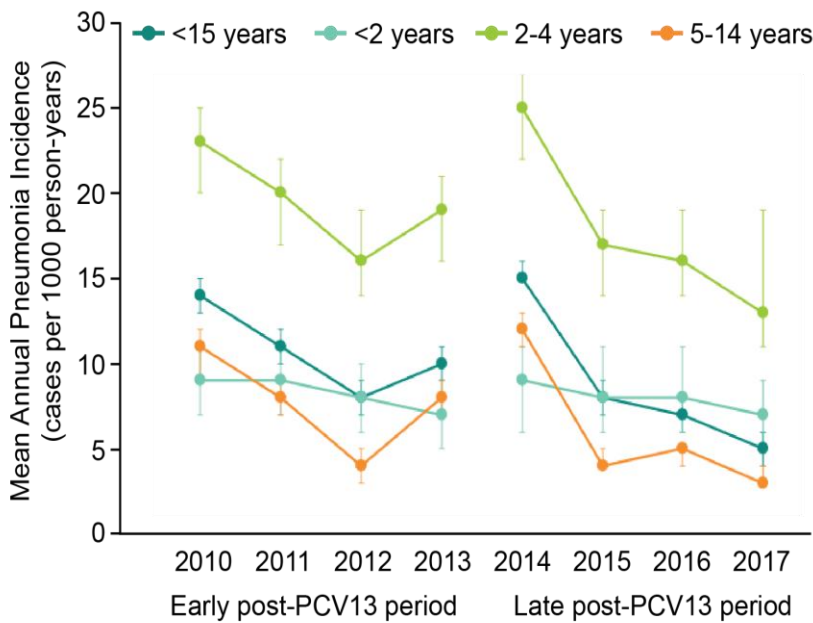
- 72,570 patients <15 years in the Veneto region were enrolled in the database during the study period
- There were 3,927 episodes from 2010–2017, with an annual IR of 10 per 1000 person-years (95% CI 9–10)
- In children <15 years, IRs decreased from 14 (95% CI 13–15) in 2010 to 5 per 1000 person-years (95% CI 4–6) in 2017
- The highest IRs from 2010–2017 were seen in children 2–4 years, (**Table 2** and **Figure 1**)

Table 2. Annual Mean Incidence Rate Estimates (per 1000 person-years) for Pneumonia Stratified by Age (95% CI in the parentheses)

Year	<2 Years	2-4 Years	5-14 Years
2010	9 (7–11)	23 (20–25)	11 (9–12)
2011	9 (7–11)	20 (17–22)	8 (7–9)
2012	8 (6–10)	16 (14–19)	4 (3–5)
2013	7 (5–9)	19 (16–21)	8 (7–9)
2014	9 (6–11)	25 (22–27)	12 (11–13)
2015	8 (6–11)	17 (14–19)	4 (4–5)
2016	8 (6–11)	16 (14–19)	5 (4–5)
2017	7 (5–9)	13 (11–15)	3 (3–4)

CI, confidence interval.

Figure 1. Changes in Annual Pneumonia Incidence Following Introduction of PCV13



- Results of ITS analysis indicated that in the early post-PCV13 period there was a non-significant downward trend with IRs decreasing by 1.54% per year ($P=0.119$; **Table 3**). After controlling for this trend, there was a non-significant level change with IRs increasing by 7.90% ($P=0.038$) between the early and late post-PCV13 periods. The trend of IRs in the late post-PCV13 period was significant, with rates decreasing by 2.80% ($P<0.001$) per year. According to the Mann–Kendall test, there was a monotonic decreasing trend (-0.64 , $P=0.026$) over the study period

Table 3. Interrupted Time Series Analysis of Annual IRs for Children <15 Years

	Early PCV13 period		Late PCV13 period	
	Coefficient	P-value	Coefficient	P-value
Trend	−1.54	0.119	−1.25	0.320
Change in trend	NA	NA	−2.80	<0.001
Change in level†	NA	NA	7.90	0.038

- When stratified by age, similar significant trends were observed for children aged 2–4 years and 5–14 years, with IRs decreasing by 3.54% ($P<0.001$) and 2.59% ($P=0.027$) per year in the late post-PCV13 period, respectively (**Figure 1**). In children aged <2 years, reduction of IRs was not significant ($P=0.070$; **Figure 1**)
- Total regional expenditure of pneumococcal and unspecified pneumonia decreased substantially following introduction of PCV13, from €8.97 million in 2010 to €3.59 million in 2017

Conclusions

- This study demonstrated a decline in the IRs of pneumococcal-specific and unspecified pneumonia in children <15 years following the introduction of PCV13, with the greatest benefit seen in older children. Regional expenditure also declined in children <15 years following the introduction of PCV13
- There remains a residual clinical and economic burden of pediatric pneumonia in Veneto, Italy

Disclosures

TH, TP, and GP are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, and MSD, Rome, Italy, and may own stock in the company.

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