Bacteremic Pneumococcal Community-acquired Pneumonia in Children Less Than 5 Years of Age in Italy

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Background: This study was designed to determine the proportion of bacteremic pneumococcal cases in a group of pediatric subjects with community-acquired pneumonia (CAP), the importance of the different serotypes and the impact of the currently available pneumococcal conjugate vaccines (PCVs).

Methods: The study involved children who were ≤5 years with radiographically confirmed CAP admitted to hospital in Italy between September 2008 and March 2011. A diagnosis of laboratory-confirmed bacteremic pneumococcal CAP was made in the presence of a culture and/or real-time polymerase chain reaction (PCR) positive for Streptococcus pneumoniae.

Results: A total of 510 children were included in the study. Pneumococcal CAP was diagnosed in 73 cases (14.3%); *S. pneumoniae* was identified by means of positive real-time PCR in 67 cases (91.8%), a positive blood culture in 1 (1.4%) and both in 5 (6.8%). Complicated pneumonia was observed significantly more often in the pneumococcal-positive cases (P = 0.02) and empyema was the main complication (P = 0.007). Serotype 19A was most frequently encountered (17 cases; 25.8%), followed by serotypes 14 (10 cases, 15.1%), 4 (5 cases, 7.6%) and 3 (4 cases, 6.1%). The theoretical coverage offered by the available PCVs was calculated to be 31% for PCV7, 37% for PCV10 and 71% for PCV13.

Conclusions: In Italy, bacteremic pneumococcal CAP accounts for a significant number of CAP cases in children who were ≤5 years, with serotypes 19A and 14 being the most frequent. This suggests that PCV13 is the best means of preventing pneumococcal CAP.

Key Words: children, community-acquired pneumonia, pneumococcal conjugate vaccines, pneumococcal serotypes, Streptococcus pneumoniae

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Community-acquired pneumonia (CAP) due to *Streptococcus pneumoniae* is one of the most important causes of morbidity and mortality in children worldwide. The inclusion of the heptavalent pneumococcal conjugate vaccine (PCV7) in the immunization program of younger children in several countries has led to a significant reduction in the incidence of the disease. However, many infants in the first years of life continue to develop pneumococcal CAP with severe clinical, social and economic consequences. A number of reasons explain the partial coverage offered by PCV7. First, a considerable number of cases of pediatric pneumococcal CAPs (particularly those with a severe clinical picture) are due to serotypes such as 1 and 3 that are not included in PCV7. Second, the so-called replacement phenomenon means that the eradication of colonizing pneumococci of the vaccine serotypes included in PCV7 from the nasopharynx creates the setting for an increase in the role of nonvaccine serotypes as the cause of disease. Finally, and at least partially independently of the selective pressure of PCV7, serotype 19A has emerged as the most important because of its increased frequency as the cause of disease, virulence and frequent resistance to the most widely used antibiotics. To overcome these problems, 2 new vaccines have been developed that contain many of the serotypes possibly causing pneumococcal CAP and invasive pneumococcal disease (IPD) not included in PCV7. In addition to the serotypes included in PCV7, PCV10 contains serotypes 1, 5 and 7F, whereas PCV13 includes serotypes 1, 3, 5, 6A, 7F and 19A.

The circulation and microbiological characteristics of the pneumococcal serotypes that cause CAP can vary geographically, as demonstrated by the differences in the incidence of pneumococcal disease and *S. pneumoniae* antibiotic resistance in European children from different countries. It is therefore necessary to have data concerning the distribution of serotypes in every geographical area to evaluate the potential impact of PCV10 and PCV13 on pediatric CAP. Unfortunately, etiological studies of CAP in younger patients are complicated by the difficulty in obtaining adequate sputum specimens, the reluctance to perform lung aspiration and bronchoalveolar lavage, and the low yield of blood cultures. However, it has been clearly demonstrated that the limitations of blood culture can be overcome by using recently developed molecular methods, particularly real-time polymerase chain reaction (PCR), that do not require viable bacteria, require small sample volumes and appear to be more sensitive. Consequently, they can be useful in diagnosing and serotyping pneumococcal CAP.

This study was designed to evaluate the proportion of pneumococcal bacteremic cases in otherwise healthy young children with radiographically confirmed CAP, their clinical and laboratory characteristics, the importance of the different serotypes and the potential impact of the recently marketed PCVs.

**PATIENTS AND METHODS**

**Study Design**

This study was carried out during the 30 months between September 2008 and March 2011 and involved children aged ≤5 years with radiographically confirmed CAP admitted to 1 of 5 pediatric hospitals located in 5 different regions of Italy: Ospedale
Maggiore Policlinico, Milan, Lombardy; Azienda Ospedaliera Maggiore della Carità, Novara, Piemonte; Ospedale Giannina Gaslini, Genoa, Liguria; Ospedale Bambino Gesù, Rome, Lazio; and Azienda Ospedaliera di Padova, Padua, Veneto. These hospitals are among the most important pediatric hospitals in Italy and are the reference centers for pediatric diseases in the Regions where they are sited. Consequently, pediatric population that is admitted to them can be considered representative of the pediatric population of the whole Region. The study was approved by the Institutional Review Board of each center, and the written informed consent of a parent or legal guardian of all of the study participants was obtained.

**Patient Enrollment**

Otherwise healthy children aged ≤5 years with clinical signs such as tachypnea and abnormal breath sounds, and a chest radiograph consistent with CAP were considered eligible for the study. The exclusion criteria were chronic diseases increasing the risk of respiratory infections, including premature birth; chronic disorders of the pulmonary or cardiovascular systems, including asthma and cystic fibrosis; chronic metabolic diseases, including diabetes mellitus; neoplasia; kidney or liver dysfunction; hemoglobinopathies; immunosuppression, diseases requiring long-term aspirin therapy and genetic or neurological disorders. The children with presumed nosocomial pneumonia (ie, those who had been evaluated in an outpatient clinic or day-hospital, or had been discharged from hospital within the preceding 2 weeks) were also excluded.

All of the chest radiographs were initially evaluated by an independent expert radiologist who was unaware of the patients’ clinical and laboratory findings in accordance with the World Health Organization criteria for the standardized interpretation of pediatric chest radiographs for a diagnosis of pneumonia. Subsequently, the radiologist made standardized and mutually exclusive diagnoses that included focal, segmental or lobar consolidation with or without pleural effusion, interstitial pneumonia, atelectasis or necrotizing pneumonia. Complicated CAP was defined as the presence of more than one of the following conditions: parapneumonic effusion, defined as loculated pleural fluid; any pleural fluid parameters consistent with empyema; atelectasis and necrotizing pneumonia.8,10

Data regarding pneumococcal vaccination status were recorded in all cases. The children were considered fully vaccinated against pneumococcal disease if they had completed the national vaccination schedule, including 3 doses of the vaccine at 3, 5 and 11–12 months of age, or 2 doses after the first year of life, or a single dose in children aged ≥24 months. They were considered to be incompletely vaccinated if they had started but not completed the vaccine schedule.

Blood was drawn from all of the children as soon as possible after hospital admission, and the sample was divided in 2 parts: about 4 mL of whole blood were used for culture purposes and immediately sent to the laboratory of each center; and about 1.5–2 mL of whole ethylenediaminetetraacetic acid blood was reserved for molecular diagnoses and shipped in a refrigerated box to the central laboratory (DISC Microbiology Section, University of Genoa, Genoa, Italy).

**Diagnosis of Bacteremic Pneumococcal CAP**

Laboratory-confirmed bacteremic pneumococcal CAP was diagnosed in the presence of a culture positive for *S. pneumoniae* and/or real-time PCR for both the *LytA* and wzc (*cpsA*) genes. The blood was cultured using a BacT/ALERT (bioMérieux, Florence, Italy) or BacTec 9240 (Becton Dickinson, Bucinasco, Italy). The blood samples sent to the central laboratory were immediately extracted to avoid the possible degradation of pneumococcal DNA. The primers and probes (TIB Molbiol, Genoa, Italy) used to detect the *LytA* and wzc (*cpsA*) genes were those, respectively, described by Sheppard et al22 and Tarragó et al,21 with small changes in the reaction mixture and cycling conditions. DNA was amplified using a LightCycler 2.0 (Roche, Monza, Italy). All of the runs included a negative water control and a positive control (an appropriate dilution of *S. pneumoniae* ATCC 49619 genomic DNA). The *S. pneumoniae* genomic DNA was prepared as described by Park et al.23 A standard curve was created using concentrations from approximately 10 million genomic copies of *S. pneumoniae*, and if no increase in fluorescent signal was observed after 45 cycles, the amplification was assumed to be negative. The 45 cycles threshold was choosen on the basis of previously tested probes performances. Each sample was tested in triplicate. A sample was considered positive if at least 2 of the 3 tests yielded positive results. An internal amplification control was deliberately not used in the reaction to maximize sensitivity, because it has been shown that an internal amplification control reduces assay sensitivity due to the intrinsic competitive nature of the technique.23 An external control was also used. In all runs, the negative controls never gave false-positive results.

**Determination of Pneumococcal Serotypes**

The *S. pneumoniae* were serotyped using primers and probes designed on the basis of the sequences of serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F in the GenBank database (www.ncbi.nlm.nih.gov) and synthesized by TIB Molbiol. Their analytical specificity was pre-evaluated by means of computer-aided analysis using Primer-BLAST (www.ncbi.nlm.nih.gov/tools/prime-blast) and BLAST (blast.ncbi.nlm.nih.gov/Blast.cgi) and comparing all of the used sequences with all of the sequences in “bacteria” and “homo sapiens.” The GenBank primers and probes used in this study, their target genes, the numbered base positions of the probes and the cycling conditions of each serotype have been reported by us in a previous study.24

**Statistical Analysis**

Descriptive statistics of the history and the clinical and laboratory data were generated. The continuous variables are given as mean ± SD, and analyzed using a 2-sided Student’s *t* test if the data were normally distributed (on the basis of the Shapiro-Wilk statistic) or a 2-sided Wilcoxon’s rank-sum test if they were not. The categorical variables are given as numbers and percentages and were compared between groups using contingency table analysis with the χ² test or Fisher’s exact test, as appropriate.

**RESULTS**

The study involved a total of 510 children with radiographically confirmed CAP (277 males [54.3%]; median age 2.3 years, range 1 month to 5 years). Their demographic and clinical characteristics are shown in Table 1. Pneumococcal CAP was diagnosed in 73 cases (14.3%): *S. pneumoniae* was identified by means of real-time PCR in 67 cases (91.8%), a positive blood culture in 1 (1.4%) and both in 5 (6.8%). The proportion of pneumococcal CAP cases was similar among the children aged more and less than 2 years.

Complicated pneumonia was observed significantly more often in the pneumococcal cases (odds ratio of complications = 1.96; 95% confidence interval = 1.09–3.52; *P* = 0.02): empyema was the main complication and was significantly more frequent in the pneumococcal-positive patients (odds ratio = 18.6; 95% confidence interval = 1.9–179.0; *P* = 0.007). Laboratory data including C-reactive protein levels, white blood cell (WBC) counts and the percentage of neutrophils were similarly modified in both groups, with no difference between pneumococcal-positive patients complicated and uncomplicated CAP.

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TABLE 1. Characteristics of Subjects With Radiographically Confirmed Community-acquired Pneumonia

<table>
<thead>
<tr>
<th></th>
<th>All Subjects</th>
<th>Real-time PCR and/or Blood Culture Negative for Streptococcus pneumoniae</th>
<th>Real-time PCR and/or Blood Culture Positive for S. pneumoniae</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD, yrs</td>
<td>2.4 ± 1.4</td>
<td>2.4 ± 1.4</td>
<td>2.3 ± 1.2</td>
<td>0.60</td>
</tr>
<tr>
<td>Median age (range), yr</td>
<td>2.3 (1–5 yr)</td>
<td>2.3 (1 mo–5 yr)</td>
<td>2.2 (15–4.8 yr)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>277 (54.3)</td>
<td>241 (55.2)</td>
<td>36 (49.3)</td>
<td>0.35</td>
</tr>
<tr>
<td>Female</td>
<td>233 (45.7)</td>
<td>196 (44.8)</td>
<td>37 (50.7)</td>
<td></td>
</tr>
<tr>
<td>Previous antibiotic administration</td>
<td>403 (78.0)</td>
<td>349 (78.4)</td>
<td>60 (82.1)</td>
<td>0.57</td>
</tr>
<tr>
<td>Complications of pneumonia*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>85/507 (16.8)</td>
<td>66/434 (15.2)</td>
<td>19/73 (26.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>75/85 (88.2)</td>
<td>59/66 (89.4)</td>
<td>16/19 (84.2)</td>
<td>0.69</td>
</tr>
<tr>
<td>Necrotising pneumonia</td>
<td>5/85 (5.9)</td>
<td>1/86 (1.5)</td>
<td>4/18 (22.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>Atelectasia</td>
<td>1/85 (1.2)</td>
<td>1/86 (1.5)</td>
<td>0/19 (0.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Laboratory data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-reactive protein, mean ± SD (mg/dL)</td>
<td>8.1 ± 15.2</td>
<td>8.1 ± 15.8</td>
<td>7.9 ± 11.0</td>
<td>0.84</td>
</tr>
<tr>
<td>White blood cells, mean ± SD (cell/μL)</td>
<td>12,942 ± 9090</td>
<td>12,838 ± 8929</td>
<td>12,682 ± 10,484</td>
<td>0.68</td>
</tr>
<tr>
<td>Neutrophils, mean ± SD (%)</td>
<td>55.0 ± 21.3</td>
<td>54.7 ± 21.4</td>
<td>56.9 ± 20.7</td>
<td>0.42</td>
</tr>
<tr>
<td>Real-time PCR S. pneumoniae detection</td>
<td>438 (85.9)</td>
<td>437 (100.0)</td>
<td>1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>72 (14.1)</td>
<td>0 (–)</td>
<td>72 (98.6)</td>
<td></td>
</tr>
<tr>
<td>Blood culture S. pneumoniae isolation</td>
<td>489 (98.8)</td>
<td>437 (100.0)</td>
<td>67 (91.8)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>6 (1.2)</td>
<td>0 (–)</td>
<td>6 (8.2)</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal vaccination†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>173 (33.9)</td>
<td>147 (33.6)</td>
<td>26 (35.6)</td>
<td></td>
</tr>
<tr>
<td>1 dose before 1 yr</td>
<td>10 (1.9)</td>
<td>9 (2.1)</td>
<td>1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>2 doses before 1 yr</td>
<td>86 (16.9)</td>
<td>71 (16.2)</td>
<td>15 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Fully vaccinated (≥3 doses, 2 doses at 1–2 yr or 1 dose at ≥2 yr)</td>
<td>241 (47.2)</td>
<td>210 (48.0)</td>
<td>31 (42.5)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

*The sum of subjects and/or percentage do not add up to the total because of a few missing values.
†All subjects received 7-valent pneumococcal conjugate vaccine only, except for 5 who received a dose of 13-valent vaccine (all of them were PCR negative).
PCR indicates polymerase chain reaction.

Two hundred forty-one children (47.2%) were fully vaccinated with PCV7, and 269 (52.8%) were not vaccinated or were incompletely vaccinated [86 children (16.9%) had received 2 doses, 10 (1.9%) had received 1 dose before the age of 1 year and 173 (33.9%) had not received any dose]. PCV7 was used in all of the subjects except 5, who had received 1 dose of PCV13 and were negative for S. pneumoniae.

Real-time PCR serotyping was carried out in 66 of the 72 patients in whom molecular methods diagnosed pneumococcal CAP, including 18 cases with complicated CAP; there was insufficient blood for serotyping the remaining 6. Table 2 summarizes the distribution of the serotypes in the real-time PCR-positive subjects by the presence of complications. The most frequent serotype was 19A (17 cases; 25.8%), followed by serotype 14 (10 cases; 15.1%), serotype 4 (5 cases; 7.6%) and serotype 3 (4 cases; 6.1%). Serotyping was not possible in 19 cases (28.8%) because the serotype of the detected S. pneumoniae was different from those that could be identified with the method used. Among the complicated cases, 6 (33.3%) were due to serotype 19A and 6 (33.3%) due to untypeable serotypes; in the other cases, different serotypes were identified. The prevalence of serotype 19A in complicated cases was not significantly different from that of other serotypes (P = 0.53). In children with pneumococcal infection and empyema, in whom thoracocentesis was performed, serotypes 1, 3, 14 and 19A were identified in the blood. Unfortunately, no evaluation of pleural fluid was available.

Table, Supplemental Digital Content 1, http://links.lww.com/INF/B133 shows distribution of serotypes by vaccination status. Pneumococcal CAP occurred in 41 children (62.1%) who were incompletely vaccinated with PCV7 [27 (65.8%) had received no dose or only 1 dose of the vaccine, and 14 (34.2%) received 2 doses in the first year of life], and 25 (35.9%) of the fully vaccinated children. The CAP was due to serotypes included in PCV7 in 15

TABLE 2. Distribution of Pneumococcal Serotypes in 66 Real-time PCR-positive Subjects* by Complications

<table>
<thead>
<tr>
<th>Serotype</th>
<th>All Subjects</th>
<th>Uncomplicated Pneumonia</th>
<th>Complicated Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>19A†</td>
<td>17</td>
<td>25.8</td>
<td>11</td>
</tr>
<tr>
<td>14‡</td>
<td>10</td>
<td>15.1</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>7.6</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>6.1</td>
<td>2</td>
</tr>
<tr>
<td>7F</td>
<td>3</td>
<td>4.6</td>
<td>2</td>
</tr>
<tr>
<td>19F</td>
<td>3</td>
<td>4.6</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1.5</td>
<td>—</td>
</tr>
<tr>
<td>6A</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>6B</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>9V</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>23F</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>Untypeable, other serotype</td>
<td>19</td>
<td>28.8</td>
<td>13</td>
</tr>
</tbody>
</table>

*Seven subjects had an untypeable serotype because the blood sample was insufficient (n = 6) or was positive at blood culture but not real-time PCR (n = 1) and are therefore not included in the Table.
†Serotype 19A did not differ significantly from the other serotypes in terms of complications (P-value = 0.53) or severity of CAP (P-value = 0.35).
‡Serotype 14 did not differ significantly from the other serotypes in terms of complications (P-value = 0.26) or severity of CAP (P-value = 0.58). The other serotypes were not tested because the numbers were too small.
CAP indicates community-acquired pneumonia; PCR, polymerase chain reaction.
The streptococci different use of real-time PCR in children hospitalized for CAP.

Unfortunately, real-time PCR is not routinely performed in Italy and can at least partially be attributed to the phase reactants and WBC counts seem to be useless in this regard, as previously reported by some of us.

The analysis of serotype distribution showed that serotypes 19A and 14 were the most common _S. pneumoniae_ associated with bacteremic CAP, that the frequency of serotypes 1 and 3 was limited and that about 30% of the cases were due to serotypes not included in any of the currently available conjugate vaccines. The importance of serotype 19A in causing IPD has been widely demonstrated in many countries, including Italy.

**DISCUSSION**

This study evaluated the proportion and characteristics of bacteremic pneumococcal cases among children aged ≤ 5 years admitted to hospital because of radiographically confirmed CAP over a period of 30 months during which only PCV7 was used in Italy for the first 24 months, after which it was replaced by PCV10 or PCV13. However, PCV10 was practically not used and the period of administration of PCV13 was too short to have a substantial impact on the circulation of _S. pneumoniae_. Consid-ering that the hospitals in which the study was performed can be considered representative of the pediatric population living in the regions in which they are sited, we believe that the reported data reflect the real proportion of pneumococcal bacteremic cases and provide reliable information as to which serotypes play the greatest role in an area, such as that of the 5 Italian regions involved, in which PCV7 vaccination coverage is, about 50%; they also provide information concerning the theoretical coverage of both PCV10 and PCV13.

This view is supported by the fact that, in addition to blood cultures, molecular methods based on the amplification of 2 genes, _lytA_, which encodes the major pneumococcal autolysin, and _cpsA_, a conserved gene in the capsular polysaccharide biosynthesis locus, were used to identify _S. pneumoniae_. The streptococci different from _S. pneumoniae_ that have the _lytA_ gene are not encapsulated and therefore do not have the _cpsA_ gene, and so the combined evaluation of both genes excludes false-positive results.

Furthermore, recent studies have shown that real-time PCR targeting the _lytA_ gene cannot detect pneumococcal DNA in the blood of healthy carriers, and so the risk of confusing children suffering from pneumococcal CAP with simple carriers of the pathogen was also avoided.

Bacteremic pneumococcal CAP was diagnosed in about 15% of the enrolled children as a whole, and the proportion of cases was similar among the children aged more and less than 2 years. Most of the cases were diagnosed molecularly as only 1.2% of the patients had positive blood cultures, a proportion that is in line with the findings of previous studies. The superiority of real-time PCR in identifying the bacterial etiology of CAP has long been known, and many experts consider such findings in otherwise healthy children as paradigmatic of pneumococcal infection. Our study confirms this conclusion and suggests that antibiotic therapy against _S. pneumoniae_ should be prescribed while awaiting the results of a specific microbiological evaluation of pleural effusion or empyema. On the contrary, acute phase reactants and WBC counts seem to be useless in this regard, as previously reported by some of us.

The frequencies of serotypes 1, 3 and 14 in our study population are quite different from those observed by Resti et al in a similar study recently carried out in Italy. They found a large preponderance of serotype 1, that serotype 3 was the third most frequently identified serotype and that serotype 14 was involved in only a few cases. These differences are probably related to the characteristics of enrollment: we enrolled all patients with radiographically confirmed CAP who were hospitalized in a given period without any selection, whereas Resti et al evaluated a selected population including a large number of complicated cases. As serotypes 1 and 3 are frequently associated with complications, PCV10 or PCV13 is usually found in mild cases, the differences in their prevalence between the 2 studies are easily explained.

More than 25% of _S. pneumoniae_ found in our patients could not be serotyped, and this suggests that these pathogens belonged to serotypes different from the 13 that could be identified with the method used in this study and that are included in the 13-valent PCV. Moreover, one third of this unknown serotypes were associated with severe clinical presentation. This means that even the use of the PCV with the highest number of serotypes does not exclude the development of a nonmarginal number of complicated CAP cases in children ≤ 5 years of age. Further studies are needed to understand which serotypes are involved in the determination of these cases to favor the development of more protective vaccines. However, at the moment the theoretical coverage offered by PCV13 is significantly higher than that of PCV10, which in our study population does not seem to have a significantly greater effect than PCV7.

Some of the bacteremic pneumococcal CAP cases in this study due to serotypes included in PCV7 occurred in children who were fully vaccinated. However, their incidence was significantly lower than that found in the children who had received no dose or only 1 dose of the vaccine, and a little lower than that in the children...
who had received 2 doses. Although this study was not designed to quantify the efficacy of PCV7 in preventing bacteremic CAP, these findings seem to indicate that full immunization with PCV7 was effective and that only 2 doses of PCV7 can reduce the risk of the disease. Furthermore, an evaluation of the immunogenicity of PCV7 in otherwise healthy full-term infants has shown that, with the exception of 23F, mean levels of antibodies against all of the serotypes remained significantly higher than the correlate of protection (20.35 μg/mL) 6–7 months after the second dose, thus suggesting long-term protection against IPD. Among children who received no dose or only 1 dose of PCV7, the frequency of cases due to serotypes not included in the vaccine was 47.7%, whereas in those fully vaccinated it was 24%, which suggests a protective efficacy of about 40%. This is lower than that reported in studies of the efficacy of PCV7 administered using the 2 plus 1 schedule, but these considered all IPDs together and possible differences in protection depending on the site of infection were not evaluated. However, the small number of cases with bacteremic pneumococcal CAP due to serotypes included in PCV7 in this study does not allow any firm conclusions to be drawn concerning the protective effect of PCV7 against this disease, and further studies are required.

In conclusion, our findings indicate that bacteremic pneumococcal CAP accounts for a significant proportion of all CAP cases in children aged ≤5 years admitted to hospital in Italy. They also show that, in a country in which only about 50% of children are vaccinated, serotypes 19A and 14 are the most frequent causes of the disease, followed by other serotypes (including some that are covered by all the PCVs currently on the market). The circulation and antibiotic resistance of these serotypes need to be carefully and continuously monitored. On the basis of these epidemiological data and the composition of the new vaccines, it can be concluded that PCV13 seems the best solution at the moment available to overcome the limitations of PCV7, whereas the theoretical protection offered by PCV10 against bacteremic CAP is only slightly higher than that of PCV7.

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26. Azzari C, Cortimiglia M, Moriondo M, et al. Pneumococcal DNA is not continuously monitored. On the basis of these epidemiological data and the composition of the new vaccines, it can be concluded that PCV13 seems the best solution at the moment available to overcome the limitations of PCV7, whereas the theoretical protection offered by PCV10 against bacteremic CAP is only slightly higher than that of PCV7.


