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Incidence of invasive pneumococcal disease in 5–15 year old children with and without comorbidities in Germany after the introduction of PCV13: Implications for vaccinating children with comorbidities

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ABSTRACT

Objective: To describe the burden of suffering from IPD in children aged 5–15 years with and without comorbidities up to 5 years after the introduction of PCV13 in Germany and to identify the potential benefit for PCV13 and PPV23 vaccination.
Methods: The surveillance of IPD for children <16 years was based on two independently reporting sources: active surveillance in pediatric hospitals and a laboratory-based sentinel surveillance system. Case definition: IPD with cultural detection of pneumococci at a physiologically sterile site in children from 2010 to 2014 in Germany. Incidence was estimated by capture–recapture analysis with stratification by absence/presence of comorbidities. Coverage of the observed serotypes by different vaccines was assessed.
Results: 142 (Capture recapture-corrected: 437) cases were reported: 72.5% were healthy children and 27.5% had a comorbidity. The incidence of IPD related to children with comorbidities was 0.2 per 100,000. One third of these cases had serotypes not included in either vaccine. The remaining cases might benefit from pneumococcal vaccination but one third of all cases was not vaccinated. The additional potential benefit of PPV23 compared to PCV13 with respect to coverage was 10%.
Conclusion: The incidence of IPD in children with comorbidities in Germany is low. Pneumococcal vaccination uptake in children with comorbidities should be increased, although only about two-thirds of the cases might be preventable by presently available vaccines.

1. Introduction

A recent paper [1] reported on the difficulty of finding an adequate pneumococcal vaccination strategy for school-aged children with comorbidities: effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPV23) against invasive pneumococcal disease (IPD) could not be established, possibly due to lack of power, whereas the number of cases who might benefit from 13-valent pneumococcal conjugate vaccine (PCV13) vaccination was substantial. These analyses were based on cases collected between July 2009 and July 2011, i.e. before and after introduction of PCV13 (April 2010) into the national infant immunization program in the UK.

In Germany, universal infant immunization with PCV7 was first recommended in 2006. In December 2009, PCV7 was replaced by PCV13. PCV10 is also available, but not often used. Here, we present data on cases of IPD in children aged 5–15 years up to 5 years after the introduction of PCV13 in Germany. Specifically, we addressed the question whether children with comorbidities are possibly protected from IPD by PCV13 or PPV23 vaccination.

2. Methods

We used data from a German-wide surveillance program of IPD for children <16 years based on two independently reporting data sources [2]. On data source is based on active surveillance

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in pediatric hospitals, German pediatric surveillance unit (Erhebungseinheit für seltene pädiatrische Erkrankungen [ESPED]). In ESPED all pediatric wards and children's hospitals in Germany ($n = 423$) are monthly asked to report on IPD cases. Case reports are verified by means of a detailed questionnaire [2]. The second data source "PneumoWeb" is laboratory based sentinel surveillance system for IPD cases of all ages in Germany. In neither system reporting is compulsory by law. Cases were children 5–15 years of age treated for IPD from 2010 to 2014 in Germany. IPD was defined as the detection of pneumococci by culture at a physiologically sterile site [2]. Serotyping was performed by the Neufeld Quellung reaction using type and factor sera provided by the Statens Serum Institute, Copenhagen, Denmark. Three categories of comorbidities, as defined by the German Standing Committee on Vaccination (Ständige Impfkommission, STIKO), were applied: (1) congenital or acquired immune deficiency or immunosuppression, e.g. T-Cell deficiency, antibody deficiency, splenectomy or neoplastic disease; (2) other chronic diseases; (3) anatomic or foreign body associated risks like cochlear implant or liquor fistula [3].

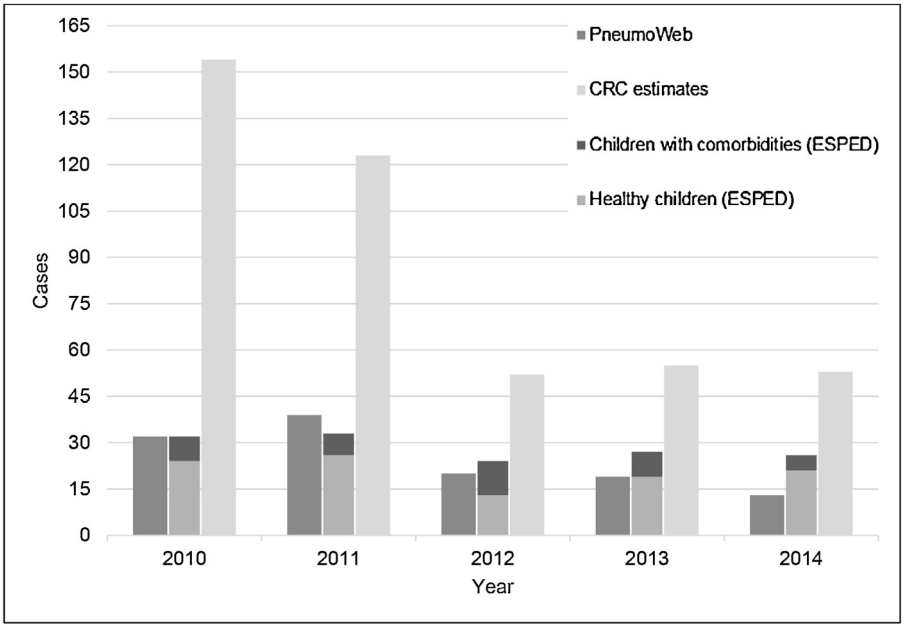
We report cases identified by ESPED (first data source) with correction for underreporting by capture-recapture (CRC) calculation using "PneumoWeb" (second data source). The number of cases not included in either of the sources was estimated by applying Bayes' probability theory. Overlapping cases between ESPED and PneumoWeb were identified by four variables: age in months, sex, postal code of the child's address (first three digits) and date of hospital admission or respective date of specimen sampling. We calculated the total number of IPD cases (N) and 95% confidence intervals using conventional CRC formulas [4]. Since comorbidities were only reported in the ESPED data source, the prevalence of children with comorbidities in the ESPED data source is extrapolated to the CRC estimates. To convert the annual CRC estimates into incidence rates (per 100,000 children) the age specific (5–15 years) population denominator, provided by the German Federal Statistical Office, was used [5].

Descriptive statistics, Pearson's Chi-square test or Fisher's Exact Test, as appropriate, and Cochran–Armitage trend test were calculated using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

The total number of cases reported in PneumoWeb was 123 and 142 in ESPED. There was a clear decrease in the total number of reported cases in PneumoWeb but not in ESPED. Applying CRC correction, a decrease was only observed in the first 3 years with constant numbers thereafter (Fig. 1). The CRC estimate yielded a total number of 322 healthy children and 115 children with comorbidities, resulting an annual overall IPD incidence of 1.1/100,000 (Table 1). The incidence in the first 2 years was higher: 2010–2011 1.6/100,000 vs. 2012–2014 0.6/100,000.

For the 142 children reported in ESPED we had information as to whether they had a comorbidity or not: 103 (72.5%) of these were healthy children, whereas 39 (27.5%) had a comorbidity according to the STIKO risk factors for IPD: 11 had congenital or acquired immune deficiency or immunosuppression with acquired immune deficiency accounting for the majority of cases ($n = 6$), 26 had chronic diseases such as neurological disease ($n = 10$) and cardiovascular diseases and diseases of the lung ($n = 10$), and two had a



Year	2010	2011	2012	2013	2014	total
PneumoWeb	32	39	20	19	13	123
ESPED total	32	33	24	27	26	142
Children with comorbidities	8	7	11	8	5	39
Healthy children	24	26	13	19	21	103
CRC estimates	154	123	52	55	53	437

Fig. 1. Cases of invasive pneumococcal disease (IPD) in children aged 5–15 years in Germany 2010–2014 by reporting system: PneumoWeb, ESPED and CRC. Only ESPED allows to distinguish children with comorbidities and healthy children. Abbreviations: CRC, Capture recapture; ESPED, German pediatric surveillance unit (Erhebungseinheit für seltene pädiatrische Erkrankungen).

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