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Additive impact of pneumococcal conjugate vaccines on pneumonia and empyema hospital admissions in England

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Summary *Objectives:* A wider spectrum 13-valent pneumococcal vaccine (PCV13) replaced PCV7 in the child immunization schedule in England from 2010. We assessed the additional impact of PCV13 over PCV7 on all-cause pneumonia and empyema admissions.
Methods: We extracted Hospital Episode Statistics data from 2001 to 2014 on all-cause pneumonia (ICD-10 codes J12-18) and empyema admissions (J86.0, J86.9) for children <16 years in England. Trend analysis and rate ratios (RR) were calculated comparing the Pre-vaccine era to September 2006, the PCV7 era and the PCV13 era from April 2010.
Results: Annual hospital admissions for pneumonia and empyema were increasing in the Pre-vaccine era peaking in 2005 at 15,733 pneumonia and 382 empyema cases (158.6 and 3.9 per 100,000 children, respectively). These rates fell following PCV7 introduction in 2006 but began to climb soon afterwards until PCV13 was introduced. By 2013, admission rates for pneumonia and empyema were 102.2 and 1.9 per 100,000 children, respectively. We found no added benefit of PCV13 over PCV7 on pneumonia admissions following PCV13 introduction but there was a significant decrease in empyema admissions in children aged <2 years (RR 0.58; 95% CI 0.34–0.99).
Conclusions: Additional serotypes covered by PCV13 may be more important in the aetiology of empyema and invasive disease than as a cause of uncomplicated pneumonia.

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Introduction

In the United Kingdom (UK), the 7-valent pneumococcal conjugate vaccine (PCV7) (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) was introduced into the immunization schedule from September 2006. National uptake rose from 84% to 91% within the first two years for primary vaccination (given at 2 and 3 months of age) and booster uptake of around 81% (given at 13 months), with a catch up campaign for older children.[1]

In England, hospital admission rates for bacterial pneumonia and empyema among children ≤15 years fell by 19% and 22%, respectively within the first two years after introduction.[2] Reductions in admissions were reported among older children, suggesting herd immunity.[2] PCV7 has been very effective in reducing the incidence of vaccine-type (VT) invasive pneumococcal disease (IPD) in both the target groups and older children in a variety of settings.[3] However, this reduction has been offset to a varying degree by an increase in IPD from non-vaccine serotypes (NVT) due to serotype replacement.[3,4] Key replacement serotypes in the UK post-PCV7 were 7F, 19A and 22F.[4]

PCV7 was subsequently replaced by PCV13 in many countries as vaccines with 6 additional serotypes (1, 3, 5, 6A, 7F, and 19A) became available in late 2009.[5] In the UK, PCV13 was introduced from April 2010, only three years after the PCV7 programme was rolled out. Uptake during 2010/11 was 94% for children at their first birthday and 91% for the booster at 13 months, with no catch up campaign. One year after its introduction, there was a 50% reduction of IPD cases in children <2 years due to one of the additional serotypes covered by PCV13.[6] Data from laboratory-based surveillance systems in Europe have demonstrated reductions in the incidence of VT IPD following the replacement of PCV7 by PCV13.[6–10] However, laboratory-based IPD surveillance is based on small numbers and does not provide information about other outcomes of interest, such as non-bacteremic community acquired pneumonia. Evaluating the clinical impact of PCV13 on pneumonia in the population is therefore important but currently there are few such studies published.[11] In the USA there were reductions in all-cause pneumonia and empyema admissions in children aged <2 years of 21% and 50%, respectively in the first 2 years after PCV13 was introduced, with smaller reductions in older age groups, indicating herd protection.[11]

Here we investigate the additional benefit of changing from PCV7 to PCV13 on hospital admissions rates for childhood pneumonia and empyema in England. We hypothesized that widening the spectrum of protection by providing cover for an additional six serotypes including 19A and 7F, which are important replacing serotypes,[4] would further reduce hospital admissions for pneumonia and empyema.

Methods

Data source

The Hospital Episodes Statistics (HES) database, holds records on all episodes of National Health Service (NHS) hospital care in England.[12] The data are recorded as finished consultant episodes, which are defined as the time period during which an admitted patient is under the care of a particular hospital consultant, which we grouped together into continuous spells in hospital. The primary diagnosis (main reason for admission) and up to 20 secondary diagnoses are coded using the International Classification of Diseases version 10 (ICD-10) codes.[13] We extracted HES data for unplanned admissions to NHS hospitals in children aged <16 years for financial years between April 2001 and March 2014.

Our main outcomes were hospital admission rates for all-cause pneumonia and empyema defined using ICD10 codes J12-18, and J86·0, J86·9, respectively (Supplementary Table A1) present in any diagnosis field in the admission record. Our case definition of all-cause pneumonia was deliberately broader than pneumococcal pneumonia because community acquired pneumonia is largely a clinical diagnosis.[14] Coding of hospital admissions is based on information recorded by clinicians on discharge. As many children with pneumonia will not have been tested or obtained a microbiological diagnosis before discharge, restricting our analysis to pneumococcal pneumonia admissions would substantially underestimate the clinical impact of PCV13 on pneumonia. A sensitivity analysis revealed that most pneumonias in HES are coded as "J18: pneumonia, organism unspecified" (89.8% of all pneumonia HES diagnoses in children aged <16 years) and the percentage of admissions with a specific 'pneumococcal pneumonia' code was small (1.5% of all pneumonia HES diagnoses in children aged <16 years) (Supplementary Table A2). Furthermore, our broad definition of pneumonia included codes for viral pneumonia (J12) because the distinction between viral and bacterial pneumonia diagnoses is potentially subject to misclassification bias within HES. British Thoracic Society guidelines state that it is not possible clinically or radiologically to distinguish bacterial and viral pneumonia in children.[14]

We excluded admissions where, in the secondary diagnosis fields, there was an ICD10 code for a comorbid diagnosis to avoid the risk of biased estimates of effect of PCV13 because children in these clinical risk groups are recommended to receive wider protection from PCV23 and are more likely to have frequent hospital admissions (Supplementary Table A3).

As a negative control we used data for all-cause unplanned hospital admissions (excluding admissions for all-cause pneumonia and empyema). We also obtained data for admissions for influenza-like illness (ILI) (ICD10 codes J10-11).

Data analysis

For the purposes of examining the impact of the pneumococcal vaccines the data were divided into three periods: Pre-vaccine (1st April 2001 to 31st August 2006), PCV7 era (1st September 2006 to 31st March 2010), and PCV13 era (1st April 2010 to 31st March 2014). We analysed the data by four age groups (<2 years, 2–4 years, 5–9 years and 10–15 years) whereby children aged <2 years were the target group for vaccination. Because HES data are reported in