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The effect of underlying clinical conditions on the risk of developing invasive pneumococcal disease in England

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Summary *Objective:* To inform national policy making on the use of the 13-valent pneumococcal vaccine among risk groups we estimated the increased risk of invasive pneumococcal disease (IPD) outcomes among clinical risk groups. Three years of post 7-valent pneumococcal conjugate vaccine (PCV7) data was included to investigate the herd protection effects.
Methods: Over 22,000 IPD patients in England (March 2002—March 2009 — aged 2 and over) were linked to their hospitalisation records. The prevalence of risk factors in these patients was compared to the prevalence of risk factors in the general population.
Results: There was an increased odds ratio (OR) for hospitalisation (OR 11.7 2—15 years; 7.6 16—64; 2.7 65+) and death (OR 2.4 2—15 years, 3.9 16—64, 1.2 65+) from IPD among risk group. The most important risk factors that predict IPD are chronic liver disease, immunosuppression, and chronic respiratory diseases. Herd protection effects due to introduction of the 7-valent vaccine were identical in both patient groups as shown by the similar decline in the proportion of IPD caused by PCV7 serotypes in risk and non-risk groups.
Conclusions: There is a marked increased risk of IPD among those with certain clinical conditions, suggesting potential benefit from a targeted vaccination approach. However, the indirect protection from conjugate vaccination of children suggests PCV vaccination of high-risk groups may not provide substantial additional benefit once herd immunity takes effect.

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Introduction

Development of evidence-based guidelines for the prevention of infectious disease by vaccination requires an understanding of the population groups most likely to become infected or to have severe disease or worse outcomes. Identification of high-risk groups allows a selective vaccination programme to be employed, as exemplified by the targeting of vaccination in the recent H1N1 (2009) pandemic to the most vulnerable.[1,2] The 23-valent pneumococcal polysaccharide (PPV23) vaccine has been recommended in the UK since 1992[3] for prevention of invasive pneumococcal disease (IPD) in those with various clinical conditions considered to be at increased risk of IPD[4] though uptake has been low.[3] There is however limited evidence on the magnitude of the increased risk for these various clinical groups by age compared with the general population. Moreover, there is little information on the degree and duration of protection from PPV23 in these targeted high-risk groups.[5,6] Pneumococcal conjugate vaccines (PCVs) that are more immunogenic than PPV23 may provide a better alternative for protection of high-risk patients.[7–9] However, they are more costly[10] and cover a lower proportion of the serotypes causing IPD than PPV23.

To help evaluate the potential utility of offering the 10-valent (PCV10) or 13-valent (PCV13) conjugate vaccine to individuals in high-risk groups, we identified patients with IPD admitted to hospital in England and compared the prevalence of risk factors in this group with that in the general population. Among the hospitalised patients with IPD we compare the case fatality ratio and the serotype distribution before and after the introduction of PCV7 in September 2006 and the coverage that would be achieved with higher valency vaccines for patients with high-risk conditions compared to those without.

Methods

Ascertainment of risk factors in the general population

Information on the prevalence of clinical risk factors in the general population was estimated from a Department of Health (DH) survey of the uptake of PPV23 using data extracted from 55.6% of the general practices in England, together covering 60% of the population.[11–13] Risk groups recommended for PPV23 vaccination in the Green Book (Immunisation Against Infectious Disease)[4] were identified from the diagnostic codes[14] used to record clinical conditions and medication in the electronic patient records of GP Practices. The clinical groups as extracted from the GP records are listed in Table 1. Patients with any of the clinical conditions comprise the "One or more risk factors" group in Table 2. The total number of patients registered in the participating practices and the number of patients with one of the risk group diagnostic codes by individual risk and age group were extracted (age groups 2–15, 16–64 and 65 years and over). The total estimated number of people in England by risk- and age group was extrapolated based on total population estimates.[15]

There are three groups that are in the Green Book risk group definitions but, due to the way the data are recorded at the GP are not included in the group with one or more risk factors. These are asthma patients on continuous or repeated steroids who have no other chronic respiratory disease code; other patients on steroids who have no other immunosuppression code; and patients with recently diagnosed malignancies (who are assumed to be receiving chemotherapy) who have no other risk factors. Those three risk groups are not included in this analysis. The number of individuals with no underlying risk factors was derived from the difference in number between the total population in the PPV23 uptake data extract and those flagged as having one or more risks.

Ascertainment of risk factors for hospitalised IPD cases

Risk factor information for hospitalised patients with IPD was obtained by linking the national dataset of laboratory confirmed IPD cases in England and Wales held by the Health Protection Agency (HPA)[16,17] with an extract from the Hospital Episode Statistics (HES) database (copyright © 2012, re-used with the permission of The Health and Social Care Information Centre. All rights reserved). A laboratory confirmed case of IPD is defined as identification by culture of *S. pneumoniae* or (more rarely) antigen detection or polymerase chain reaction (PCR), in a normally sterile site. Identification of the same invasive serotype in the same individual within 30 days was regarded as the same episode. The national IPD dataset covers all patients with IPD diagnosed by a laboratory in England and Wales. The HES dataset contains clinical information on all patients in National Health Service (NHS) hospitals in England,[18] this includes fifteen diagnostic fields in which the primary diagnosis and other clinical conditions of the patient are specified using the tenth revision of the International Classification of Disease coding system (ICD-10). As the HES dataset is too large to use in the linkage all hospital admissions with an ICD-10 code indicating possible acute pneumococcal disease (listed in online Appendix table 1) in any diagnostic field were extracted from HES between April 2002 and March 2009. Linkage was based on NHS number or postcode, date of birth and sex. Underlying clinical conditions were identified using an ICD-10 code list mapped to the READ codes used in the PPV23 uptake survey (see online Appendix table 2) to make sure we compared like with like. Because of the lack of medication codes in HES and the inability to identify patients with a recently diagnosed malignancy it was not possible to identify patients on steroids or chemotherapy. Patients with IPD in these groups and with no other risk group code are therefore included in the "no risk" group in line with the way patients are grouped in the PPV23 uptake survey. When multiple episodes in the HES database could be linked to a case in the national IPD dataset (based on an admission date between one week before to one month after the specimen date), diagnostic codes for all linked episodes were used. Deaths recorded in the HES dataset were considered to be related to the IPD episode if occurring within 30 days after the specimen date and were used to derive case fatality rates