1.8 *Streptococcus pneumoniae* (invasive)

Summary

Number of cases in 2011: 425
Number of cases in 2010: 391
Number of deaths in 2011: 11
Number of deaths in 2010: 14
Crude incidence rate, 2011: 9.3/100,000

Background

Invasive *Streptococcus pneumoniae* infection is a notifiable disease in Ireland; clinicians and laboratories are legally obliged to notify this infection. For the purposes of this report the term invasive pneumococcal disease (IPD) will be used to describe these infections. IPD includes meningitis and blood stream infection (BSI) with and without pneumonia.

A number of different initiatives are in place in Ireland for the surveillance of IPD. Data on IPD notifications are collated in the Computerised Infectious Disease Reporting (CIDR) system. Enhanced surveillance on IPD notifications is undertaken by Departments of Public Health particularly on children born since 2000 and these data are also collated in CIDR. A separate surveillance system (EARS-Net) involving the microbiology laboratories and the HPSC is used to monitor in detail the antimicrobial resistance profiles of invasive *S. pneumoniae* isolates from blood and/or CSF. Since April 2007, the National Pneumococcal Typing Project has been offering a typing service to Irish laboratories for all invasive *S. pneumoniae* isolates submitted. This is a collaborative project involving the RCSI/Beaumont Hospital, the Children's University Hospital, Temple Street and the HPSC.

In September 2008, the 7-valent pneumococcal conjugate vaccine (PCV7) was introduced into the Irish infant immunisation schedule at 2, 6 and 12 months of age. A catch-up campaign was also implemented at that time, targeting children <2 years of age. In December 2010, PCV13 replaced PCV7 in the infant schedule. Uptake of three doses of PCV by 24 months of age is currently 91%.

IPD notification data was extracted from CIDR on 16th October 2012. These figures may differ slightly from those previously published due to ongoing updating of notification data on CIDR. For the 2011 notifications, the 2003 HPSC case definition for IPD was used. In brief, isolation or detection of *S. pneumoniae* from a normally sterile site was classified as confirmed; detection of *S. pneumoniae* antigen from a normally sterile site was a probable case and a clinically

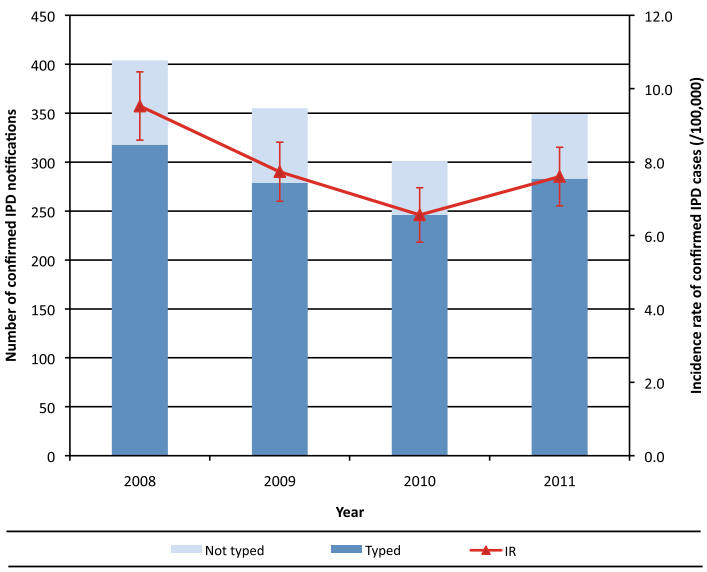

Figure 1. Number of confirmed invasive pneumococcal disease notifications by typing status and the incidence rate (IR) of confirmed IPD with 95% confidence intervals, 2008-2011
Data source: CIDR

compatible case without any laboratory confirmation or identification of *S. pneumoniae* from a non-sterile site (including urinary antigen positive) were classified as possible.

Results

All IPD notifications

In 2011, 425 cases of IPD (9.3/100,000) were notified in Ireland. This was an 8.7% increase in incidence compared with 2010 when 391 cases were notified (8.5/100,000). In 2011, 82% (n=349) of notifications were classified as confirmed, 1.9% (n=8) as probable and 16% as possible (n=68). The majority of the possible cases (85%, n=58/68) were notified by HSE-SE. These figures do not necessarily indicate a higher burden of IPD in this area relative to other areas, but rather it may reflect more consistent reporting of positive urinary antigen cases from that area.

Confirmed IPD notifications

For confirmed IPD notifications, 349 cases were notified in 2011 (7.6/100,000; 95% CI 6.8 - 8.4/100,000) (figure 1). Although this was a 16% increase in incidence compared with 2010 (6.6/100,000; 95% CI 5.3 – 7.3/100,000; 301 cases), overall the incidence of confirmed IPD in 2011 significantly declined by 20% compared with 2008 (9.5/100,000; 95% CI 8.6 – 10.5/100,000; 404 cases; p<0.05) (figure 1).
In 2011, 81% of the confirmed IPD notifications had an isolate submitted for serotyping which was similar to the proportion in 2010 and a slight improvement from 2008 and 2009 when 79% of notifications had an isolate typed (figure 1). In 2011 however, 41% of notifications (17/41) relating to children <5 years of age did not have an isolate submitted for serotyping. For 11 of the 17 an isolate was unavailable as the cases were confirmed by PCR only, while the remaining six did have an isolate from a sterile site.

Incidence rates by HSE area ranged from 5 per 100,000 in HSE-M and NE to 9 per 100,000 in HSE-MW, NW and S with the incidence highest in the HSE areas along the western seaboard (figure 2). However, the incidence rates in each of the eight HSE areas were not statistically different from the national one.

A clinical diagnosis was reported for just 127 of the 349 confirmed cases (36%), which included meningitis (n=23), BSI with pneumonia (n=69) and other BSI for the remainder.

More cases occurred in males than in females, 55% of cases in the former (n=193).

Cases ranged in age from 5 days to 97 years, with an average age of 54.6 years and a median age of 62 years. Those aged 65 years and older accounted for almost half of the cases (46%, n=160). The age specific incidence rate was highest in those 85 years of age and older (70/100,000; n=41), followed by 75-84 years age group (34/100,000; n=58) and then those aged between 65 and 74 years (20/100,000; n=61) (figure 3). In children < 2 years of age the age-specific incidence rate was 16 cases per 100,000 population (n=23). A statistically significant decline (62%) in IPD incidence was seen in this age group when compared with 2008 (42.8/100,000; n=52; p<0.0001), highlighting the positive impact the introduction of PCV7 to the infant schedule in September 2008 has had on reducing the burden of IPD in young children (figure 3).

The medical risk factor field was completed for 132 (38%) confirmed cases; for the remainder this information was either unknown or not specified. Based on the 132 cases with information reported, 96 (73%) had an underlying medical risk factor, with some patients having multiple ones. The main risk factors reported included immunosuppressive condition or therapies (n=29), chronic heart disease (n=22), chronic lung disease (n=18) and chronic liver disease (n=13). It should also be noted that being elderly, aged 65 years and older is also a recognised IPD risk factor; 160 cases in 2011 were in this age group. Apart from being elderly, 51 cases in this age group also had a reported medical risk factor.

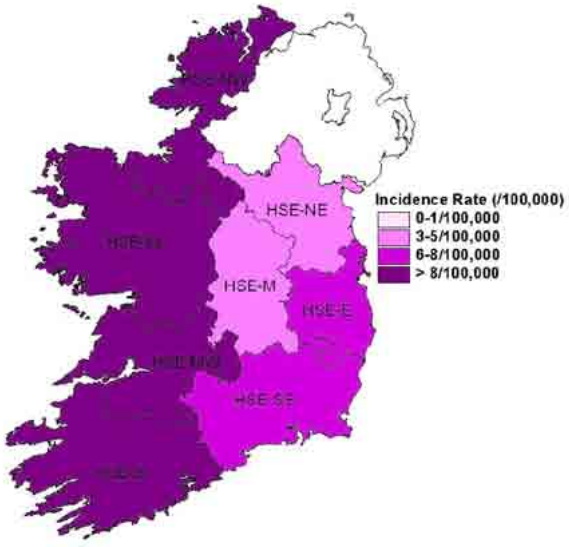

Figure 2. Incidence rate of confirmed invasive pneumococcal disease notifications by HSE area, 2011
Data source: CIDR

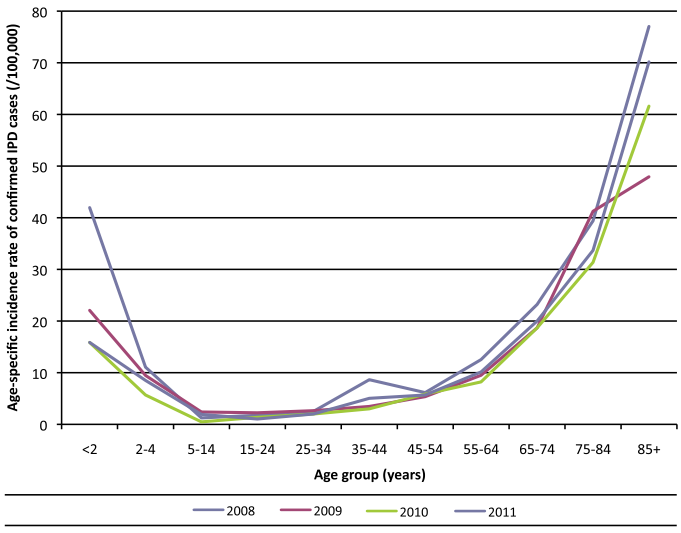

Figure 3. Age specific incidence rate of confirmed invasive pneumococcal disease notifications by age group, 2008-2011
Data source: CIDR

IPD death notifications

Outcome was reported on just 29% (n=123) of the IPD notifications in 2011. Therefore, these figures underestimate the burden of IPD in terms of mortality. Based on the data available, 19 deaths in individuals with IPD in 2011 were reported. The cause of death was reported as directly due to IPD in five cases, not due to IPD in eight cases and for the remaining six the cause of death was not specified or was unknown. Therefore, based on the outcome data available, IPD was potentially the cause of death in 11 patients, giving an IPD case fatality rate of 9%. All deaths occurred in adults, ranging in age from 49-94 years. Nine of the eleven deaths were in confirmed cases and one death each in a probable and possible IPD case.

Impact of pneumococcal conjugate vaccines (PCV)

Data from the National Pneumococcal Typing Project were used to assess the impact of introducing PCV on the distribution of *S. pneumoniae* serotypes associated with IPD and on the burden of IPD in Ireland. In 2011, isolates relating to 296 cases of IPD were typed, 99% (n=293) of these records had a corresponding notification in CIDR. Twenty percent of IPD infections were due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F), 36% were associated with the six additional serotypes included in PCV13 (1, 3, 5, 6A, 7F and 19A) and the remaining 44% of infections were due to non-vaccine types (NVTs, serotypes excluding the 13 covered by PCV13).

Since introducing PCV7 to the Irish childhood immunisation schedule towards the end of 2008, there has been a 20% reduction in the overall burden of IPD disease. In particular reductions in the incidence of IPD due to PCV7 serotypes have been seen in all age groups (figure 4a). Overall the incidence of IPD due to PCV7 serotype has significantly declined in 2011 compared with 2008 (70% decline, $p<0.001$). The greatest impact was seen in children <2 years of age where the incidence of the disease due to PCV7 serotypes has declined by 93% ($p<0.01$) (figure 4a). In 2011, the early impact of PCV13 was observed; the incidence of disease due to the additional six serotypes in PCV13 declined by over half in the <2 year olds compared with 2008 (figure 4b). This decline was not observed in any of the other age groups and in actual fact the incidence of disease increased compared with previous years (figure 4b). An increase in incidence due to the NVTs was also seen in 2011, particularly in the elderly, those aged 65 years and greater (figure 4c).

The predominant serotypes in circulation in 2011, were 7F and 19A (both included in PCV13) and then followed by serotypes 22F and 8 (both NVTs). In children <2 years of age, the predominant serotype was 19A, accounting for a third of the isolates serotyped in this age group (figure 5).

For ongoing updates, see "Slides – Impact of PCV in Ireland" at http://www.hpsc.ie/hpsc/A-Z/VaccinePreventable/PneumococcalDisease/PostersPresentations/

PCV vaccine failures

Based on data obtained through the IPD enhanced surveillance system, no PCV vaccine failures were reported in 2011. However, there were nine

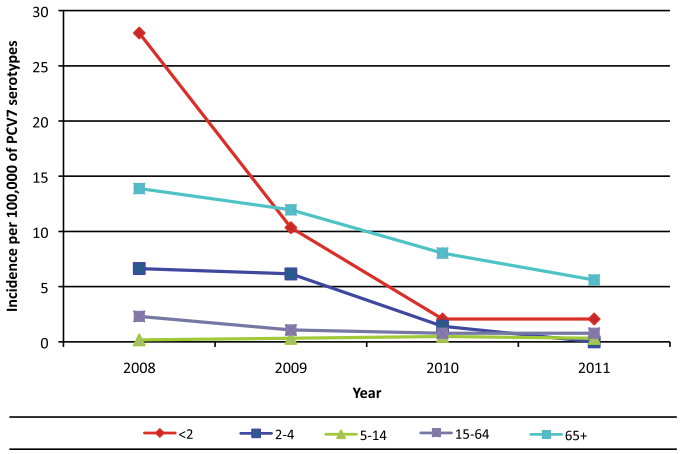

Figure 4a

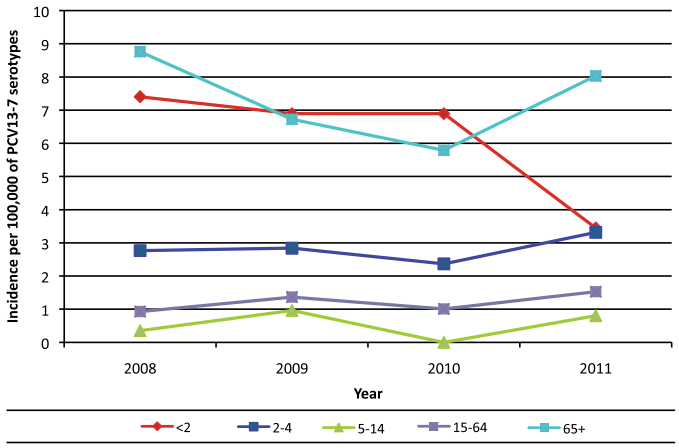

Figure 4b

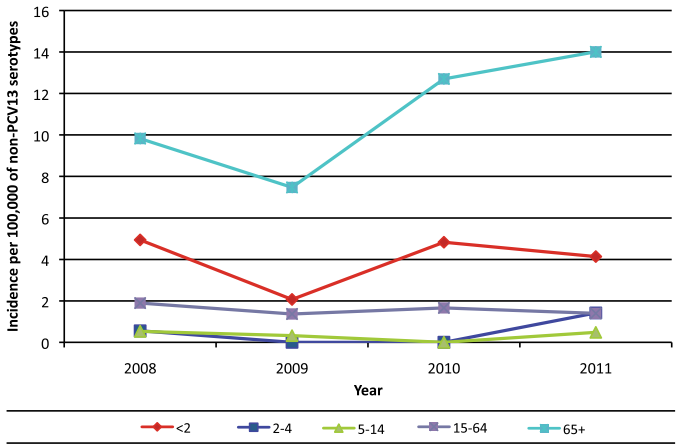

Figure 4c

Figure 4. Age specific incidence rate by age group of confirmed invasive pneumococcal disease cases due to (a) PCV7 serotypes, (b) the additional six serotypes covered by PCV13 (PCV13-7) and (c) non-vaccine types (non-PCV13 serotypes), 2008-2011
Data source: National Pneumococcal Typing Project

notifications where a child was reported as fully vaccinated but no serotype information was available to ascertain whether any of these cases were genuine vaccine failures or not. Since 2008, four vaccine failures have been reported, two due to serotype 14 and two due to 19F.

Penicillin non-susceptible S. pneumoniae (PNSP)

In 2011, the proportion of penicillin non-susceptible invasive *S. pneumoniae* (PNSP) was 19.6%, (6.1% and 13.5% with high and intermediate level resistance, respectively) while 18.9% of isolates were resistant to erythromycin (Data source: EARS-Net). In the UK, the PNSP proportion in 2011 was 5.5% (0.8% and 4.7%, with high and intermediate level resistance, respectively).

In 2011, Ireland had one of the highest proportions of PNSP in Europe ranking 7th out of 27 countries overall. Although, 35 different serotypes were identified in 2011, only 10 serotypes were associated with being penicillin non-susceptible. The predominant PNSP serotypes in 2011 were 19A and 6A whereas in 2008 serotypes 9V and 14 were the leading ones. For details on the antimicrobial resistance patterns of *S. pneumoniae*, please see the chapter on Antimicrobial Resistance within this report.

Discussion

Although the incidence of confirmed cases of IPD increased in Ireland in 2011 compared with 2010, PCV7 has had a significant impact in reducing the overall burden of the disease in the total population. There has been a decline in IPD in all age groups due to serotypes covered by PCV7, indicating the indirect/herd immunity effect the vaccine confers on the population. The greatest impact has been in children <2 years of age where the disease incidence due to PCV7 serotypes has been reduced by over 90%. Early indications that PCV13 introduced in December 2010, was beginning to have an impact was seen during 2011, when a reduction in the incidence of disease due to the additional six serotypes covered by PCV13 was observed in children <2 years of age.

However, despite these reductions in IPD burden, the incidence of disease due to non-PCV7 serotypes has increased in those > 2 years of age. There has been a shift in the prevalent serotypes associated with invasive disease. Serotypes 7F, 19A, and 22 have replaced 14, 4 and 9V (all covered by PCV7) as the predominant serotypes. The additional serotypes covered by PCV13 (particularly 7F and 19A) will hopefully tackle some of the serotype replacement issues observed in 2011.

To accurately assess the impact of PCV on immunisation programmes and to monitor for vaccine failures in Ireland, it is crucial that laboratories continue to send all invasive *S. pneumoniae* isolates for typing to the National Pneumococcal Typing Project. Although 81% of confirmed notifications had an isolate submitted for serotyping in 2011, 19% (n=66) did not, including 17 cases in children <5 years of age. In 11 of these 17 cases an isolate was not available for typing as confirmation was by PCR only. The overall concern is that serotype information is unavailable for 40% of confirmed notifications in this age group.

Continued good quality IPD surveillance including the monitoring of invasive *S. pneumoniae* serotypes is crucial in identifying any epidemiological changes in the disease, assessing the impact of PCV13 on public health and in guiding further vaccination strategies as newer expanded valency vaccines are made available. For example, due to the incomplete data we do not know the impact of IPD on mortality and this is a key metric in assessing the true impact of this disease and the effectiveness of interventions, including new vaccines. A properly resourced national reference laboratory service for pneumococcal typing is urgently required.

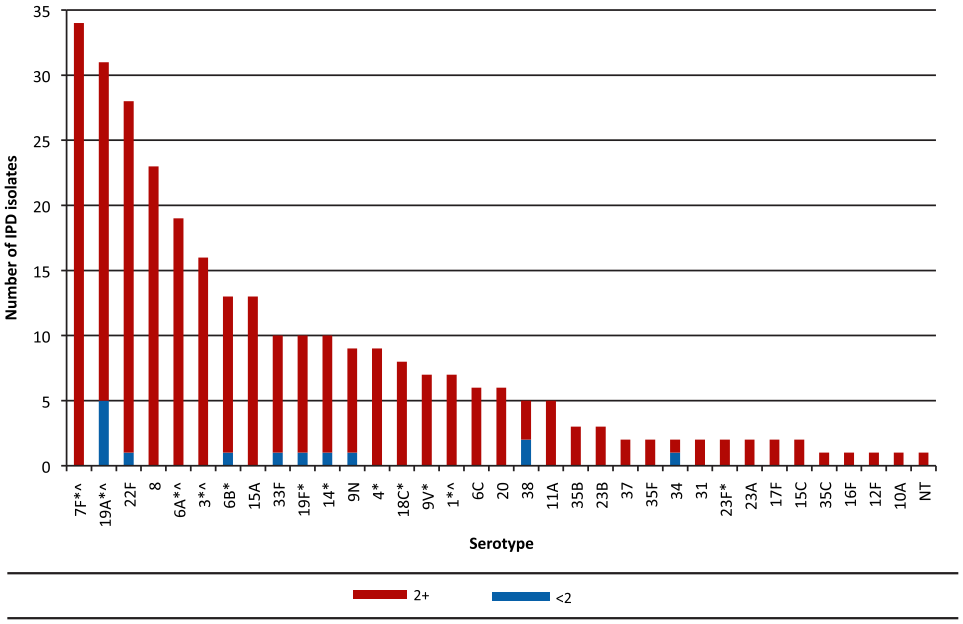

Figure 5. Serotype distribution of invasive Streptococcus pneumoniae isolates by age group (years) in Ireland, 2011
** Denotes serotypes included in PCV7*
**^ Denotes additional six serotypes included in PCV13 (PCV13-7)*
Data source: National Pneumococcal Typing Project