1.8 *Streptococcus pneumoniae* (invasive)

Summary

Number of cases in 2012: 427
Number of cases in 2011: 425
Number of deaths in 2012: 37
Number of deaths in 2011: 11
Crude incidence rate, 2012: 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 and adolescents <15 years and these data are also collated in CIDR. A separate surveillance strand (EARS-Net project) 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 Laboratory 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 addition, since August 2012 Health Protection Surveillance Centre (HPSC) is participating in a European Centre for Disease Prevention and Control (ECDC) project called SpID-net. The project aims to strengthen or set up long term active population based IPD surveillance in order to estimate the impact of the pneumococcal conjugate vaccines in children less than five years of age in Europe.

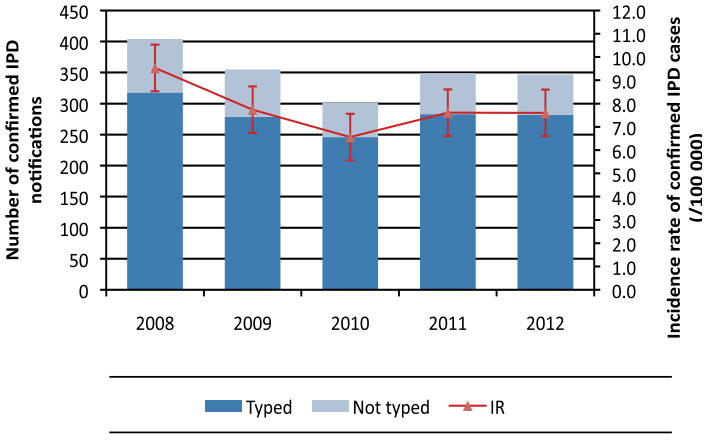

Figure 1. Number of confirmed invasive pneumococcal disease notifications by typing status and the incidence rate (IR) of confirmed IPD with 95% confidence intervals, 2008-2012
Data source: CIDR

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 for 2012 was 91%.

IPD notification data was extracted from CIDR on 26th June 2012. These figures may differ slightly from those previously published due to ongoing updating of notification data on CIDR. For the 2012 notifications, the 2012 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 urine was classified as possible case. Since 2012 the previously used probable case definition is no longer applicable used and any case in which *S. pneumonia* antigen is detected from a sterile site is now categorized as confirmed.

Results

All IPD notifications

In 2012, 427 cases of IPD (9.3/100,000) were notified in Ireland. There was no significant increase in IPD notifications in 2012 compared with 2011 (425 cases; 9.3/100000).

In 2012, 81% (n=347) of notifications were classified as confirmed and 19% (n=80) as possible. The majority of possible cases (72%, n=58/80) 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

Focusing specifically on the confirmed IPD notifications, 347 cases were notified in 2012 (7.6/100,000; 95% CI 6.8 - 8.4/100,000) (figure 1). There was no increase in incidence compared with 2011 (7.6/100,000; 95% CI 6.8 - 8.4/100,000; 349 cases). However the incidence of confirmed IPD in 2012 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 2012, 85% of the confirmed IPD notifications had an isolate submitted for serotyping, a slight improvement to the proportion in 2011 (81%) and a marked improvement from 2008 and 2009 when 79% of notifications had an isolate typed (figure 1). In 2012 however, 37% of notifications (16/43) relating to children <5 years of age did not have an isolate submitted for serotyping. For six of the 16 the cases were confirmed by PCR only and no isolate was available. For the remaining ten no isolate from a sterile site was available for typing.

Incidence rates by HSE area ranged from 6.4 per 100,000 in HSE-NE to 10.5 per 100,000 in HSE-MW with the incidence higher in the HSE NW and HSE S and highest in HSE MW (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 176 of the 347 confirmed cases (51%), which included meningitis (n=36), blood stream infection (BSI) with pneumonia (n=80) and other BSI for the remainder (n=60).

More cases occurred in males than in females, 52% of cases in the former (n=182). Cases ranged in age from 1 month to 96 years, with an average age of 55.6 years (median age 65 years). Those aged 65 years and older accounted for more than half of cases (51%, n=160). The age specific incidence rate (ASIR) was highest in those 85 years of age and older (63/100,000; n=37), followed by those in the 75-84 years age group (41/100,000; n=71) and 65 and 74 year age group (22/100,000; n=68) (figure 3). In children < 2 years of age the ASIR was 11 cases per 100,000 population (n=16). A statistically significant decline (74%) in IPD incidence was seen in this age group when compared with 2008 (42/100,000; n=52; p<0.0001), highlighting the positive impact the introduction of PCV7 in September 2008 to the infant schedule and replaced by PCV13 in December 2010 has had on reducing the burden of IPD in young children (figure 3).

The medical risk factor field was completed for 123 (35%) confirmed cases; for the remainder this information was either unknown or not specified. Based on the 123 cases with information reported, 85 (69%) had an underlying medical risk factor, with some patients having multiple risk factors. The main risk factors reported included immunosuppressive condition or therapies (n=45), chronic lung disease (n=35), chronic heart disease (n=31) chronic liver disease (n=19) and renal diseases (n=17). It should also be noted that being elderly, aged 65 years and older is also a recognised IPD risk factor; 176 cases in 2012 were in this age group. Apart from being elderly, 69 cases in this age group also had a reported medical risk factor.

IPD death notifications

Outcome was reported on 47% (n=202) of the IPD notifications in 2012. Therefore, these figures may underestimate the burden of IPD in terms of mortality. Based on the data available, 37 deaths in individuals with IPD in 2012 were reported. The cause of death was reported as directly due to IPD in six cases, not due to IPD in five cases and for the remaining 26 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 32 patients, giving an IPD case fatality rate of 16% (32/202). Twenty nine

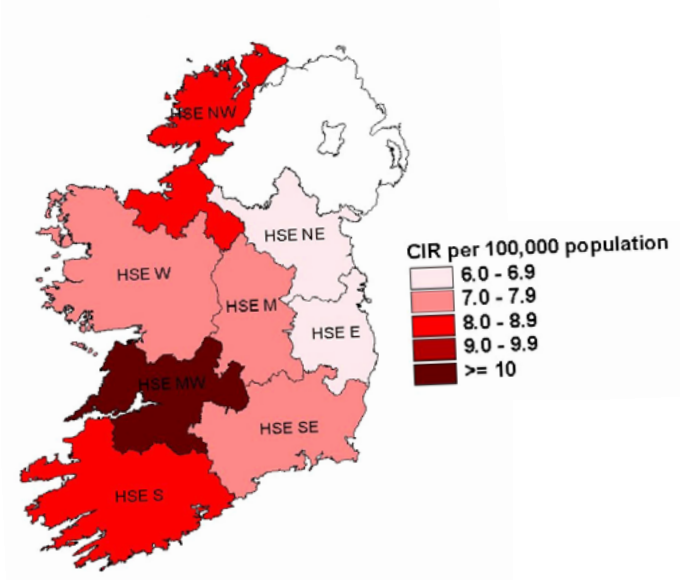

Figure 2. Incidence rate of confirmed invasive pneumococcal disease notifications by HSE area, 2012
Data source: CIDR

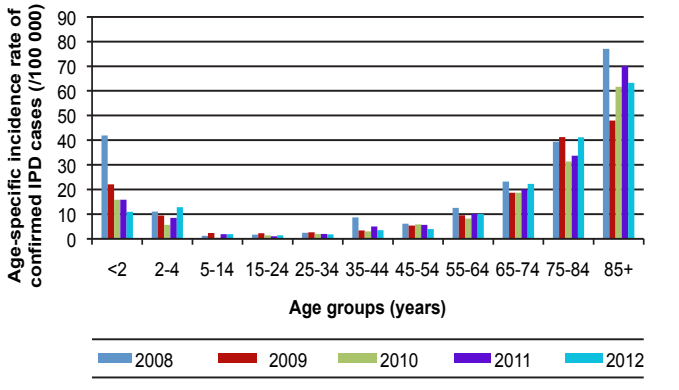

Figure 3. Age specific incidence rate of confirmed invasive pneumococcal disease notifications by age group, 2008-2012
Data source: CIDR

deaths occurred in adults, ranging in age from 46-91 years and three deaths occurred in children (aged 6 months; one and 11 years). Thirty of the 32 deaths were in confirmed cases and two deaths each in a possible IPD cases.

The apparent increase in IPD death notifications in 2012 (37 cases in 2012 versus 11 cases in 2011) is most likely related to the additional information that was available by linking CIDR data to the Enhanced Surveillance of Blood Stream Infections (ESBI) database. Missing information on outcome in CIDR was identified and then the CIDR database was updated by HSE areas.

Impact of pneumococcal conjugate vaccines (PCV)
Data from the National Pneumococcal Typing Laboratory 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 2012, of the 347 confirmed IPD notifications reported in CIDR, 296 had isolates sent for typing (85%). Fourteen percent of IPD infections were due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F), 38% were associated with the six additional serotypes included in PCV13 (1, 3, 5, 6A, 7F and 19A) and the remaining 48% 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 17% 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 2012 compared with 2008 (76% 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 97% ($p<0.01$) (figure 4a). In 2012 the incidence of disease due to the additional six serotypes in PCV13 declined by 44% in the <2 year olds compared with 2008 (figure 4b). This decline was not observed in any of the other age groups, but rather the incidence of disease increased compared with previous years (figure 4b). An increase in incidence due to the NVTs was also seen in 2012, particularly in those aged 65 years and greater with an increase in incidence evident since 2009. There has been little change in the incidence of NVTs among other age groups (figure 4c).

The predominant serotypes in circulation in 2012, were 7F and 19A (both included in PCV13) and then followed by serotypes 22F, 8 (both NVTs) and 3 (included in PCV13). In children <2 years of age, the predominant serotypes were 19A, 15A and 7F accounting for a half 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

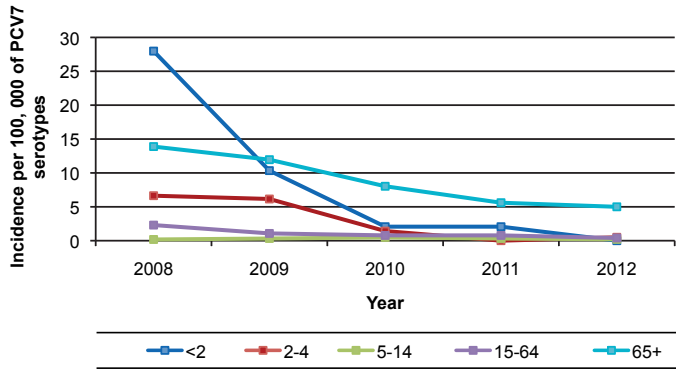

Figure 4a

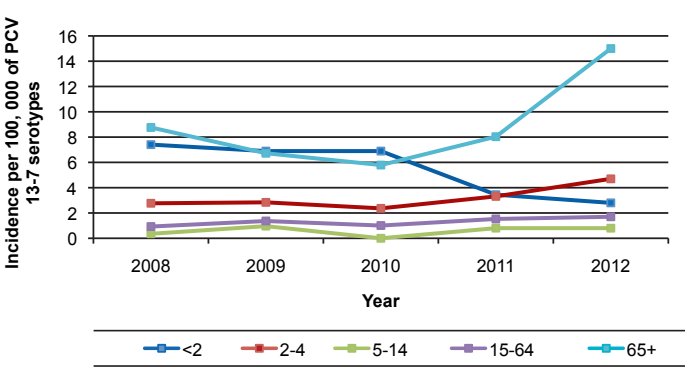

Figure 4b

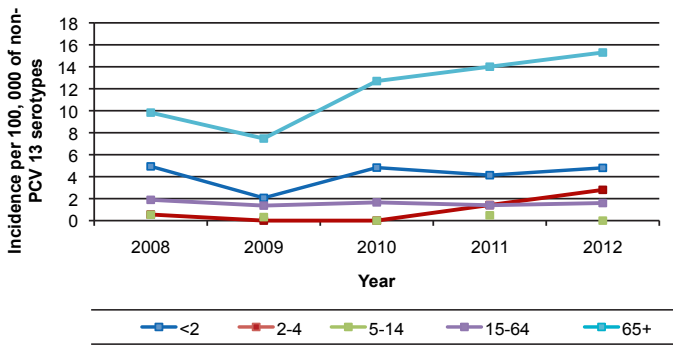

Figure 4c

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), 2008-2012
Data source: National Pneumococcal Typing Laboratory

surveillance system, two PCV vaccine failures were reported in 2012. One vaccine failure was due to serotype 19F (PCV7); another due to serotype 19A (PCV 13).In addition, 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 2012, the proportion of penicillin non-susceptible invasive *S. pneumoniae* (PNSP) was 19.6%, (4.0% and 15.6% with high and intermediate level resistance, respectively) while 16.9% of isolates were resistant to erythromycin (Data source: HPSC/EARS-Net Ireland). In the UK, the PNSP proportion in 2012 was 4.9% (0.7% and 4.2%, with high and intermediate level resistance, respectively).

In 2012, Ireland had one of the highest proportions of PNSP in Europe ranking 9th out of 28 countries overall. Although, 34 different serotypes were identified in 2012, only 15 serotypes were associated with being penicillin non-susceptible. The predominant PNSP serotypes in 2012 were 19A, 35B and 6B 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 there was no significant changes in the incidence of confirmed cases of IPD in Ireland in 2012 compared with 2011, 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 97%.

The impact due to PCV13 vaccine, which was introduced in December 2010 was observed in children <2 years of age amongst whom the reduction in the incidence of disease due to the additional six serotypes covered by PCV13 was 44%, the same as in 2011.

However, despite these reductions in IPD burden, the incidence of disease due to non-PCV7 serotypes has increased in all age groups. There has been a shift in the prevalent serotypes associated with invasive disease. Serotypes 7F, 19A, and 22F have been predominant serotypes as 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 Laboratory. Although 85% of confirmed notifications had an isolate submitted for serotyping in 2012, 15% (n=51) did not, including 16 cases in children <5 years of age. In six of these 16 cases an isolate was not available for typing and confirmation was by PCR only. The overall concern is that serotype information is unavailable for 37% 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.

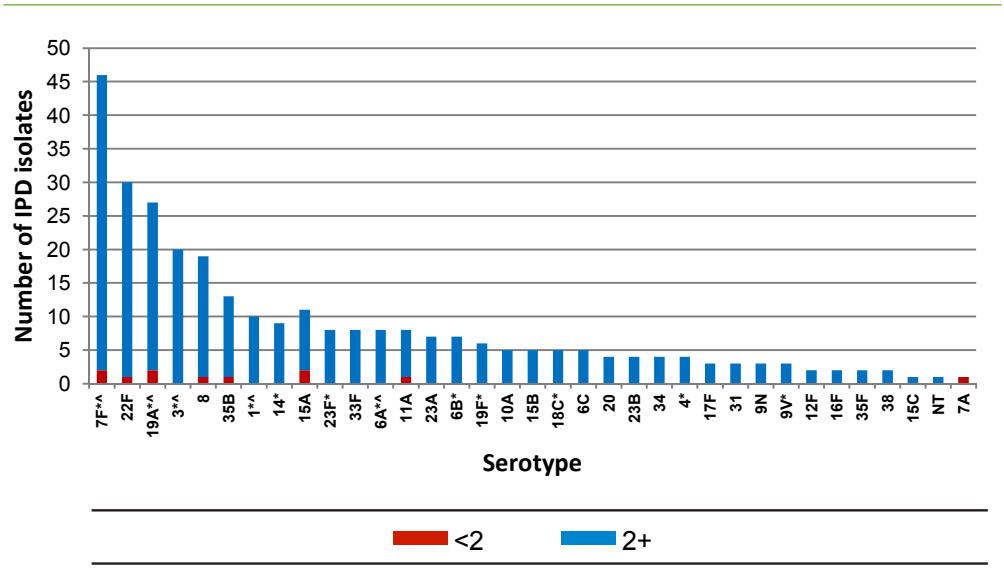

Figure 5. Serotype distribution of invasive Streptococcus pneumoniae isolates by age group (years) in Ireland, 2012
** Denotes serotypes included in PCV7*
**^ Denotes additional six serotypes included in PCV13 (PCV13-7)*
Data source: National Pneumococcal Typing Laboratory