Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

hpsc

Streptococcus pneumoniae (invasive)

Summary

Number of confirmed cases in 2015:	368
Number of confirmed cases in 2014:	350
Number of deaths in 2015:	37
Number of deaths in 2014:	37
Crude incidence rate of confirmed cases in 2015:	8.0/100,000

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 bloodstream 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 of IPD notifications is undertaken by Departments of Public Health. A separate surveillance strand (EARS-Net project) involving the microbiology laboratories and HPSC is used to monitor in detail the antimicrobial resistance profiles of invasive *S. pneumoniae* isolates from blood and/or CSF. EARS-Net laboratories can also collect additional information, including risk factors, admission and outcome for each *S. pneumoniae* isolate reported and these data are collated by HPSC through the Enhanced Surveillance of Bloodstream Infection (ESBSI) system. To improve data quality regular processes for cross-checking CIDR data with other data sources was established in 2012; CIDR data are linked to the typing and ESBSI databases and additional information on either of these systems but missing or incomplete in CIDR is collated on an annual basis.

Since April 2007, the Irish Pneumococcal Reference Laboratory has provided a typing service to Irish laboratories for all invasive *S. pneumoniae* isolates. This is a collaborative project involving the Royal College of Surgeons in Ireland/Beaumont Hospital, the Children's University Hospital, Temple Street and HPSC. In addition, since August 2012 HPSC has participated in a European Centre for Disease Prevention and Control (ECDC) project called SpIDnet and since 2015 HPSC has joined the ECDC project I-MOVE plus. Both projects aim 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 those aged 5-64 years of age and in adults aged 65 and over in Europe.

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 2015 was 93%.

Notification data for IPD was extracted from CIDR on 30th May 2016. These figures may differ slightly from those previously published due to ongoing updating of notification data on CIDR. For the 2012-2014 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 a possible case. Since 2012, the previously used probable case definition is no longer applicable and any case in which *S. pneumonia* antigen was detected from urine (previously defined as a probable case) was classified as possible, and antigen detection from a sterile site was categorised as confirmed. Since July 2015, the case definition of *S. pneumoniae* was amended and only those cases of IPD meeting the laboratory criteria for laboratory confirmed are now notifiable and urinary antigen detection (possible cases) are no longer notifiable.

Results

All IPD notifications

In 2015, 549 cases of IPD (12.0/100,000) were notified in Ireland, a decrease compared with 2014 (681 cases; 14.8/100000). This decrease is related to a decrease in the number of possible cases notified in 2015 in comparison to 2014 due to definition changes.

In 2015, 67% (n=368) of notifications were classified as confirmed and 33% (n=181) as possible. The majority of possible cases (83%) were notified by HSE E, HSE SE and HSE MW (n=47/181; n=59/181 and n=44/181, respectively).

Confirmed IPD notifications

Focusing specifically on the confirmed IPD notifications, 368 cases were notified in 2015 (8.0/100,000; 95% CI 7.2 - 8.8/100,000), a slight increase in the number of cases was observed compared with 2014 (7.6/100,000; 95% CI 6.8 - 8.4/100,000; 350 cases) (Figure 1). In 2015, the incidence of confirmed IPD decreased 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 2015, 77% of the confirmed IPD notifications had an isolate submitted for serotyping, less than the proportion of cases in 2014 (81%) and in 2013 (80%), but similar to the proportions reported in 2008 and 2009 when 79% of notifications had an isolate typed. In 2012, 86% of all isolates were typed (Figure 1). In 2015, 37% of notifications (13/35) relating to children <5 years of age did not have an isolate submitted for serotyping. For two of the 13 cases IPD was confirmed by PCR only and no isolate was available. For the remaining eleven isolates from a sterile site, no sample was available for typing.

Incidence rates by HSE area ranged from 5.8 per 100,000 in HSE W to 8.8 per 100,000 in HSE E, with the highest incidence in the HSE MW, HSE S and HSE-SE (Figure 2). However, the incidence rates in each of the eight HSE areas were not statistically different from the national one.

In 2015, a clinical diagnosis was reported for 229 of the 368 confirmed cases (62%), which included BSI with pneumonia (n=163), meningitis (n=29), and other BSI for the remainder (n=37). This reflects an improvement in completeness of data provided in comparison to 2014, when clinical diagnosis was reported for 168 of the 350 confirmed cases (48%), 14% less than in 2015.

More cases occurred in males (n=194, 53%) than in females. Cases ranged in age from 1 month to 99 years, with an average age of 57.3 years (median age 65.5 years). Those aged 65 years and older accounted for half of the cases (51%, n=189). The age specific incidence rate (ASIR) was highest in those 85 years of age and older (77.0/100,000; n=45), followed by those in the 75-84 years age group (40.7/100,000; n=70) and the 65-74 year age group (24.3/100,000; n=74) (Figure 3). In children <2 years of age the ASIR was 13.1 cases per 100,000 population (n=19). A statistically significant decline (60%) 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 of the introduction of PCV7 in September 2008 to the infant schedule followed by PCV13 in December 2010 (Figure 3).

The medical risk factor field was completed for 178 (48%) confirmed cases; 37 cases (16%) did not have an identified risk factor; for the remaining 131 cases this information was either unknown or not specified. Based on the 178 cases for whom this information was reported, 144 (81%) of them had an underlying medical risk factor, with some patients having multiple risk factors. The main medical risk factors reported included immunosuppressive condition or therapies (n=58; 40.3%), chronic lung disease (n=59; 41%), chronic heart disease (n=64; 44.4%), chronic liver disease (n=15; 10.4%) and renal diseases (n=21; 14.6%). It should also be noted that being aged 65 years and older was also a

recognised IPD risk factor; 189 (51%) cases in 2015 were in this age group. Apart from their age, 103 (54%) cases in this age group also had a reported medical risk factor.

IPD death notifications

Outcome was reported in 56% (n=309) of the IPD notifications in 2015 versus 39% in 2014. Therefore, these figures may not accurately estimate the burden of IPD in terms of mortality. Based on the data available in 2015, 41 deaths in individuals with IPD were reported; for seven cases the cause of death was reported as directly due to IPD, not due to IPD in four cases and for the remaining 30, the cause of death was not specified or was unknown. Forty deaths occurred in adults, ranging in age from 50-99 years and one in an infant three months of age. Forty deaths were in confirmed cases.

The apparent increase in IPD death notifications in 2012-2015 (41 cases in 2015 and also in 2014, 24 cases in 2013 and 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 (ESBSI) database. Using BSI data it was possible to identify missing information on outcome in CIDR 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 2015, of the 368 confirmed IPD notifications reported in CIDR, 283 had isolates sent for typing (77%). Two percent of IPD infections were due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F), 26% were associated with the six additional serotypes included in PCV13 (1, 3, 5, 6A, 7F and 19A) and the remaining 72% of infections were due to non-vaccine types (NVTs).

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. 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 serotypes has significantly declined in 2015 compared with 2008 (99% decline, $p<0.001$). The greatest impact has been seen in children <5 years of age where the incidence due to PCV7 serotypes has declined by 100% ($p<0.001$) (Figure 4a). In 2015 the incidence of disease due to the additional six serotypes covered by the PCV13 declined by 60% in children <2 years of age compared with 2008 (Figure 4b). The decline was also observed in the other age groups with these additional six serotypes compared with 2008; however, this decline was not significant (Figure 4b). An increase in incidence due to NVTs was also seen in 2015 compared with 2008. In those aged 65 years and older, an increase in incidence was observed in 2015 compared with 2014. There has been little change in the incidence of NVTs among other age groups (Figure 4c).

The predominant serotypes in circulation in 2015, were 8 (NVT), 19A, 7F and 3 (all included in PCV13) and followed by serotypes and 12F and 22F (both NVT). In children <5 years of age, the predominant serotypes were 19A (included in PCV13), 12F, 15A, 23B, 12A and 15B/C (all NVTs); all these serotypes accounted for 91% 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/A-Z/VaccinePreventable/PneumococcalDisease/PostersPresentations/

PCV vaccine failures

Based on data obtained through the IPD enhanced surveillance system, two PCV vaccine failures were reported in 2015, both due to serotype 19A (PCV 13). Since 2008, a total of 11 vaccine failures have been reported in addition to the two reported in 2015, two in 2014 (19A), three in 2013 (19A), two in 2012 (19F and 19A) and two in 2010 (19F and 14).

Penicillin non-susceptible *S. pneumoniae* (PNSP)

In 2015, the proportion of penicillin non-susceptible invasive *S. pneumoniae* (PNSP) was 17.5%, (0.3% and 17.2% with high and intermediate level resistance, respectively) while 15.2% of isolates were resistant to erythromycin (Data source: HPSC/EARS-Net Ireland). This compares to 17.1% and 13.8% in 2014, respectively. In 2015, the proportion of PNSP increased slightly compared to 2014, but the overall trend for the past 3 years has been downward. In 2015, the proportion of *S. pneumoniae* with resistance to erythromycin increased compared to 2014, but the overall trend for the past four years has been downward.

The predominant PNSP serotypes in 2015 were 8, 19A and 12F whereas in 2008 serotypes 9V and 14 were the predominant serotypes associated with PNSP. For details on the antimicrobial resistance

patterns of *S. pneumoniae*, please see the link on EARS-Net Report, Quarters 1-4 2015: http://www.hpsc.ie/A-Z/MicrobiologyAntimicrobialResistance/EuropeanAntimicrobialResistanceSurveillanceSystemEARSS/EARSSSurveillanceReports/2015Reports/

Discussion

Although there was slight increase in the incidence of confirmed cases of IPD in Ireland in 2015 compared with 2014, since vaccine introduction in 2008, 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 <5 years of age where disease incidence due to PCV7 serotypes has fallen by 100%. The impact due to the additional six serotypes covered by PCV13 vaccine was observed in children <2 years of age, amongst whom the reduction in the incidence of disease was 60%.

However, despite reductions in the IPD burden during childhood, the incidence of disease due to non-PCV7 serotypes has increased in other age groups. There has been a shift in the prevalent serotypes associated with invasive disease. Serotypes 8, 19A and 7F were the predominant serotypes identified in 2015.

Ireland (HPSC) is participating in ECDC funded projects, SpIDnet (since 2012) and I-Move plus (since 2015). Participation in these projects allows the strengthening of the IPD surveillance system in Ireland. As part of SpIDnet project since January 2013 enhanced surveillance was extended to all children and adolescents aged <15 years of age and since December 2014 enhanced surveillance was undertaken in one of the HSE regions on all adult IPD cases particularly focusing on data collection for clinical presentation, risk factor, outcome and vaccination history. This approach has improved data quality, completeness and timeliness. All HSE regions are striving to improve the quality of enhanced data collection for all cases (paediatric and adults).

To accurately assess the impact of PCV on immunisation programmes and to monitor for vaccine failures in Ireland, it is crucial that samples from sterile sites are obtained for culture and sensitivity. Isolates obtained by culture are required for serotyping and antibiotic susceptibility. Furthermore it is crucial that laboratories continue to send all invasive *S. pneumoniae* isolates for typing to the National Pneumococcal Typing Laboratory. Although 77% of confirmed notifications had an isolate submitted for serotyping in 2015, 23% (n=85) did not, including 13 cases in children <5 years of age. In two of these 13 cases, an isolate was not available for typing and confirmation was by PCR only. Serotype information is unavailable for 37% of confirmed notifications in this age group and the absence of this data is of concern.

Continued good quality IPD surveillance including the monitoring of invasive *S. pneumoniae* serotypes is crucial in identifying any epidemiological changes in the disease, in assessing the impact of PCV13 on public health and in guiding further vaccination strategies, as newer expanded valency vaccines become available and changes to recommendations of PCV are made e.g. age related. 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.

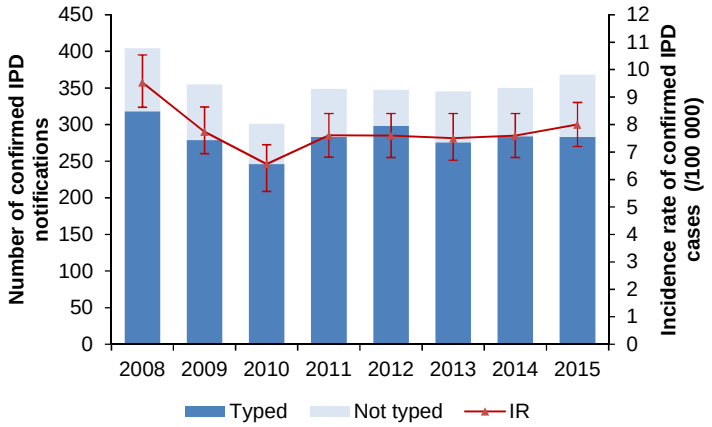

Figure 1. Number of confirmed invasive pneumococcal disease (IPD) notifications by typing status and the incidence rate (IR) of confirmed IPD with 95% confidence intervals, 2008-2015
Data source: CIDR

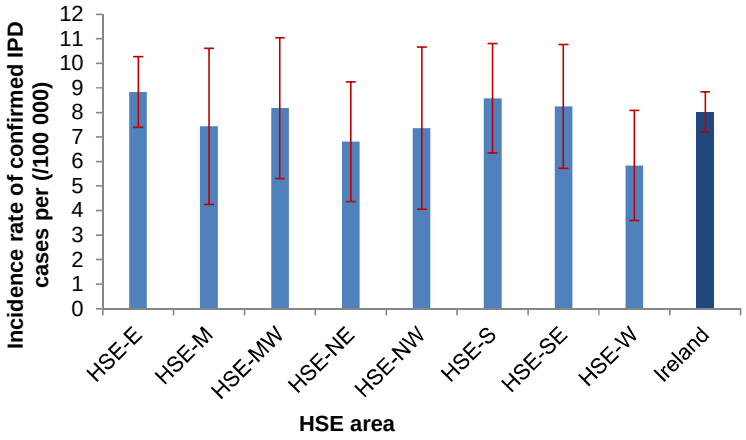

Figure 2. Crude incidence rate of confirmed invasive pneumococcal disease notifications by HSE area, 2015
Data source: CIDR

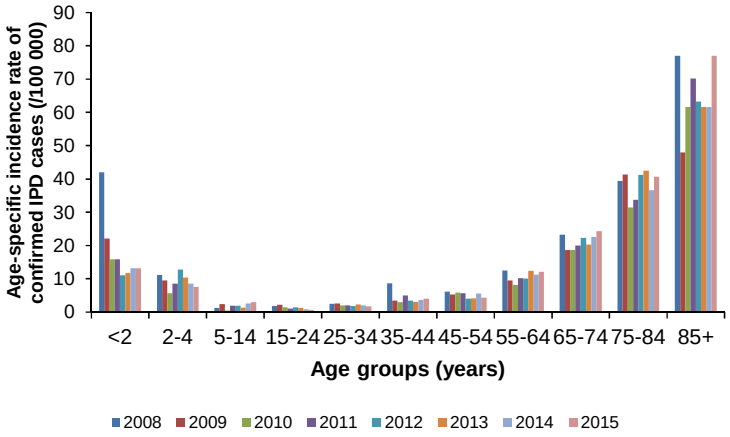

Figure 3. Age specific incidence rate of confirmed invasive pneumococcal disease notifications by age group, 2008-2015
Data source: CIDR

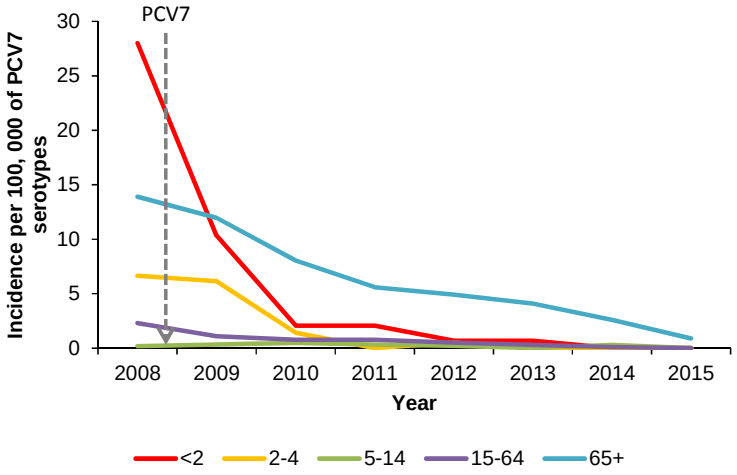

Figure 4a

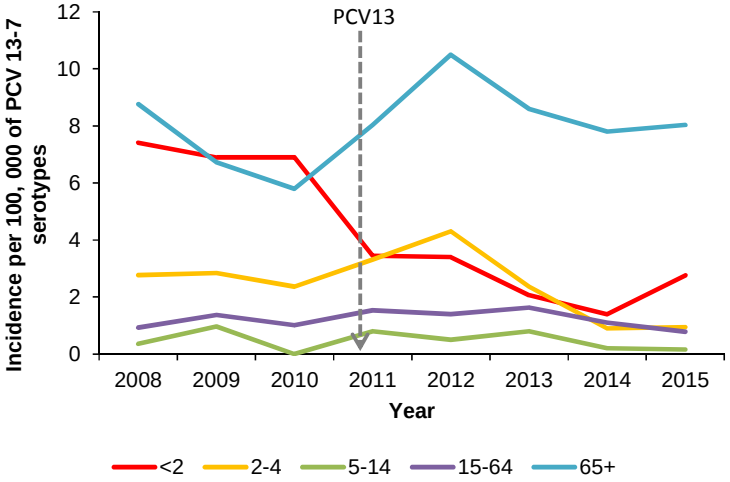

Figure 4b

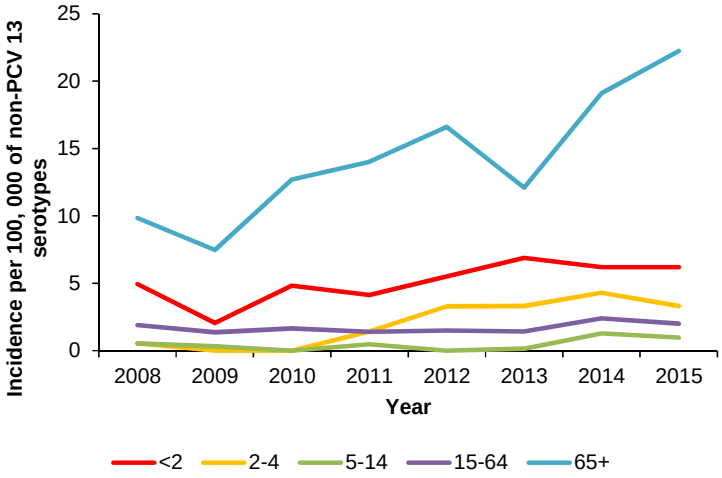

Figure 4c

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 and (c) non-vaccine types, 2008-2015.
Data source: Irish Pneumococcal Reference Laboratory

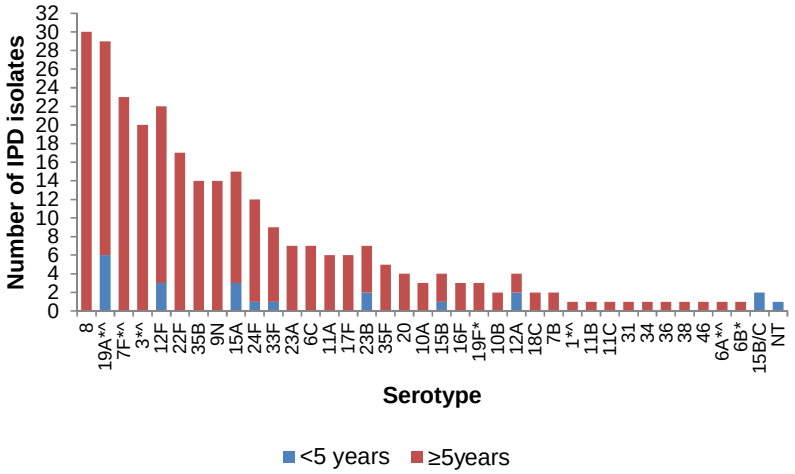

Figure 5. Serotype distribution of invasive *Streptococcus pneumoniae* isolates by age group (years) in Ireland, 2015

* Denotes serotypes included in PCV7

*^ Denotes additional six serotypes included in PCV13 (PCV13-7)

Data source: Irish Pneumococcal Reference Laboratory