Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

hpsc

Streptococcus pneumoniae (invasive)

Summary

Number of confirmed cases in 2016:	381
Number of confirmed cases in 2015:	368
Number of deaths in 2016:	48
Number of deaths in 2015:	37
Crude incidence rate of confirmed cases in 2016:	8.3/100,000

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, bloodstream infection (BSI) with and without pneumonia, and invasive disease from other sterile sites.

Surveillance

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 the 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 patient notified with *S. pneumoniae* isolate. These data are collated by HPSC through the Enhanced Surveillance of Bloodstream Infection (ESBSI) system. In order to improve data quality, regular processes for cross-checking CIDR data with other data sources were established in 2012. To identify missing IPD notifications and/or missing information CIDR data were linked to both the typing and ESBI databases and additional information on either of these systems which is missing or incomplete in CIDR was collated.

Since April 2007, the Irish Pneumococcal Reference Laboratory (IPRL) 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 the 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+. Both projects aim to strengthen or set up long term active population-based IPD surveillance in order to estimate the direct and indirect impact of the pneumococcal conjugate vaccines (PCV) in all age groups. children less than five years of age, in those aged 5-64 years of age and in adults aged 65 and over in Europe. The I-Move+ study is now also studying the effectiveness of pneumococcal polysaccharide vaccine which offers protection against 23 serotypes (PPV23) and is recommended for those at risk of IPD and those older than 65 years. For more information please see following links to I-Move+: http://www.i-moveplus.eu/wp3 and SpIDnet (Epiconcept): http://www.epiconcept.fr/

Pneumococcal conjugated vaccine – use in national immunisation programme

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, the 13-valent PCV vaccine (PCV13) replaced PCV7 in the infant schedule. Due to the introduction of Men B vaccine in to routine immunisation the third dose of PCV 13 was shifted to 13 months of age in December 2016 for children born on or after 1st October 2016. Uptake of three doses of PCV by 24 months of age for 2016 was 91%.

Definitions

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 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.

PCV vaccine failure was defined as confirmed IPD case in a child caused by a PCV-serotype who has completed a PCV immunisation course appropriate for his age and diseases onset is ≥ 14 days after last dose of PCV.

For this report notification data for IPD was extracted from CIDR on 3rd May 2017. 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. For calculation of incidences 2011 CSO data were used.

Results

All IPD notifications

In 2016, 381 cases of IPD (8.3/100,000) were notified in Ireland, a decrease compared with 2015 (549 cases; 12.0/100000). This decrease is related to an absence of possible cases notified in 2016 in comparison to 2015 due to case definition changes. Since July 2015 only confirmed cases have been notifiable. Consequently, in 2016 all notifications were classified as confirmed.

Confirmed IPD notifications

Focusing specifically on the confirmed IPD notifications only, 381 cases were notified in 2016 (8.3/100,000; 95% CI 7.5 - 9.1/100,000), a slight increase (not significant) in the number of cases compared with 2015 (8.0/100,000; 95% CI 7.2 - 8.8/100,000; 368 cases) (Figure 1). In 2016, the incidence of confirmed IPD decreased by 10% compared with 2008 (9.5/100,000; 95% CI 8.6 – 10.5/100,000; 404 cases; p<0.05) (Figure 1).

In 2016, 84% of the confirmed IPD notifications had an isolate submitted for serotyping, more than the proportion of cases in 2015 (77%), 2014 (81%), and 2008 and 2009 when 79% of notifications had an isolate typed. In 2012, 86% of all isolates were typed (Figure 1). In 2016, 40% of notifications (17/42) relating to children <5 years of age did not have an isolate submitted for serotyping. For six of the 17 cases IPD was confirmed by PCR only and no isolate was available. For the remaining eleven isolates (26%; 11/42) from a sterile site, no sample was available for typing.

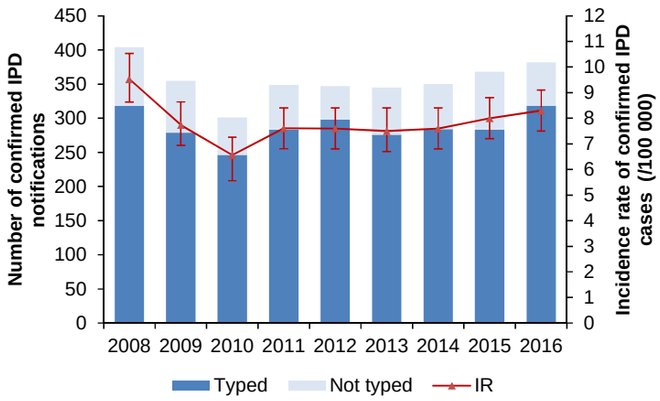

Figure 1. Number of confirmed invasive pneumococcal disease (IPD) notifications by typing status and the incidence rate (IR) of confirmed IPD with 95% confidence intervals, 2008-2016
Data source: CIDR

During 2016, incidence rates by HSE area ranged from 6.1 per 100,000 (HSE W) to 10.2 per 100,000 (HSE SE,) (Figure 2). However, the incidence rates in each of the eight HSE areas were not statistically different from the national one.

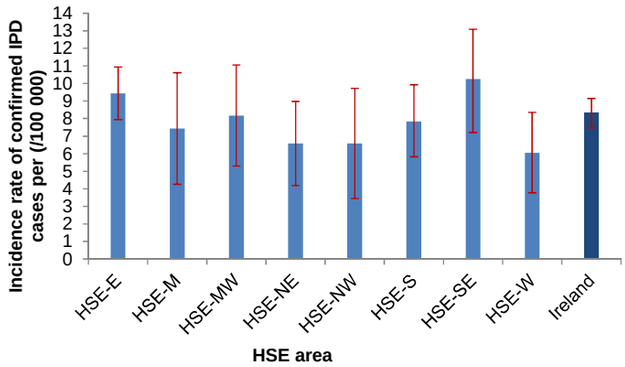

Figure 2. Crude incidence rate of confirmed invasive pneumococcal disease notifications by HSE area, 2016
Data source: CIDR

In 2016, a clinical diagnosis was reported for 313 of the 381 confirmed cases (82%), which included BSI with pneumonia (n=222), meningitis (n=37), and other BSI for the remainder (n=54). This reflects an improvement in completeness of data provided in comparison to 2015 and 2014, when the clinical diagnosis was reported for 229 of the 368 (62%) and 168 of the 350 (48%) confirmed cases respectively, 20% more than in 2015 and 34% than in 2014.

More cases occurred in males (n=207, 54%) than in females. The median age of cases was 64 years (range 1 month to 94 years). Those aged 65 years and older accounted for half of the cases (49%, n=188). Within this age category the age specific incidence rate (ASIR) was highest in the oldest age groups; ≥85 years of age (75.3/100,000; n=44); 75-84 year age group (43.6/100,000; n=75); 65-74 year age group (22.3/100,000; n=68) (Figure 3). In children < 2 years of age the ASIR was 17.2 cases per 100,000 population (n=26). 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 and PCV13 in 2008 and 2010 respectively (Figure 3).

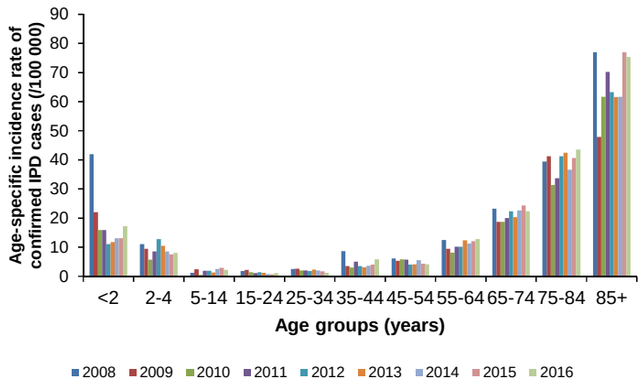

Figure 3. Age specific incidence rate of confirmed invasive pneumococcal disease notifications by age group, 2008-2016
Data source: CIDR

Medical risk factor for IPD was reported for 256 (67%) confirmed cases; 65 cases (17%) did not have an identified risk factor; for the remaining 60 cases this information was either unknown or not specified. The main medical risk factors reported included immunosuppressive condition or therapies (n=54; 21%), chronic lung disease (n=59; 41%), chronic heart disease (n=101; 39%), chronic liver disease (n=21; 8%) and renal diseases (n=19; 7%). It should also be noted that being aged 65 years and older is also a recognised IPD risk factor; 188 (49%) cases in 2016 were in this age group, of whom 153 (81%) also reported a medical risk factor.

IPD death notifications

Outcome was reported in 85% (n=323) of the IPD notifications in 2016 versus 56% in 2015 and 39% in 2014. Among those whose outcome was reported, case fatality among IPD notifications was overall 18.8% (61/323); for 27 (8.3%) case-patients the cause of death was reported as directly due to IPD, in 13 case-patients it was not due to IPD and for the remaining 21, the cause of death was not specified or was unknown. Most of these deaths (60) occurred in adults (age range 36-94 years) and one in a child (< 3 years of age). All deaths were in confirmed cases.

The increased completion in the reported outcome field since 2014 reflects improve enhanced data collection undertaken by the public health staff in the HSE areas as well as the input of a HPSC based research nurse who is funded by the EU projects (SpIDnet and IMOVE+). Additionally by linking CIDR data to the ESBI database it has been possible to identify missing outcome information in CIDR which can then be updated by HSE areas.

Impact of pneumococcal conjugate vaccines (PCV)

Serotyping data from the IPRL were used to assess the impact of the PCV programme on the distribution and burden of *S. pneumoniae* serotypes associated with IPD. In 2016, of the 381 confirmed IPD notifications reported in CIDR, 318 (84%) had isolates sent for serotyping; 4% of IPD infections were due to PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F and 23F); 20% were associated with the six additional serotypes included in PCV13 (1, 3, 5, 6A, 7F and 19A); the remaining 76% 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 substantial 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 2016 compared with 2008 (90% 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 2016 the incidence of disease due to the additional six serotypes covered by the PCV13 declined by 90% 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 2016 compared with 2008. In those aged <2 years and 65 years and older, an increase in incidence was observed in 2016 compared with 2015. There has been little change in the incidence of NVTs among other age groups (Figure 4c).

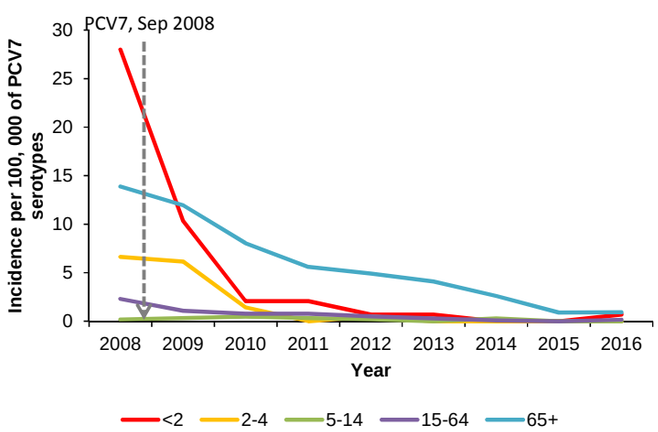

Figure 4a

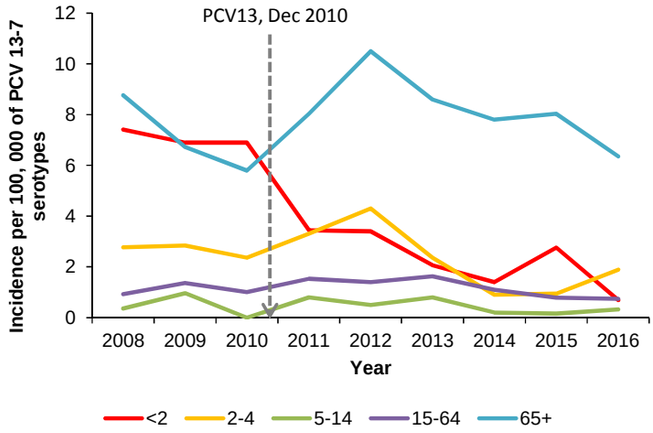

Figure 4b

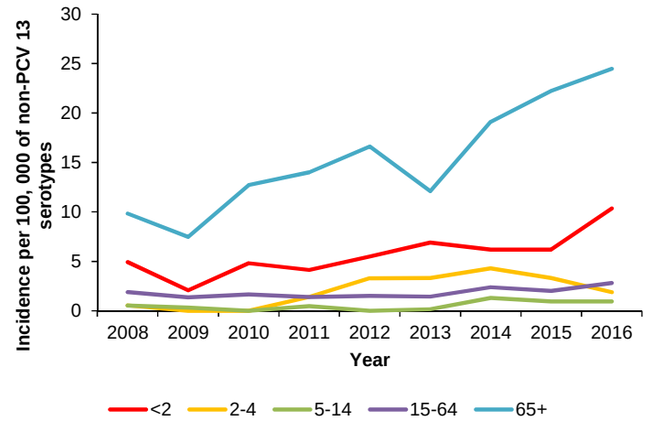

Figure 4c

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 , 2008-2016.
Data source: Irish Pneumococcal Reference Laboratory

The predominant serotypes in circulation in 2016, were 8 and 12F (NVT), 19A and 3 (both included in PCV13), followed by serotypes 33F and 22F (both NVT). In children <5 years of age, the predominant serotypes were 19A and 3 (included in PCV13); 24F, 38, 33F, 35F and 23B (all NVTs). All these serotypes accounted for 69% 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/

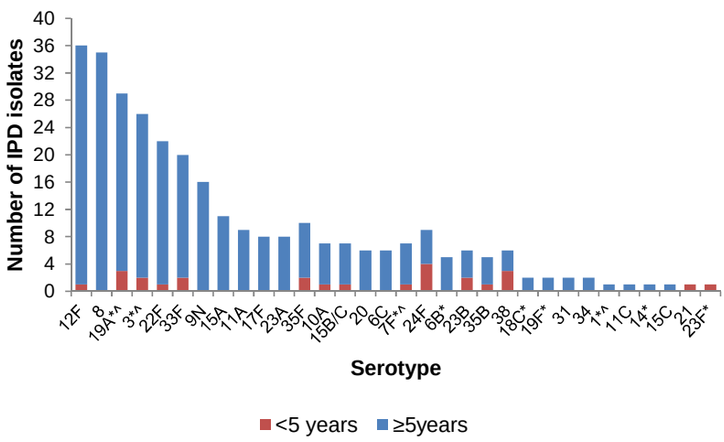

Figure 5. Serotype distribution of invasive *Streptococcus pneumoniae* isolates by age group (years) in Ireland, 2016
* Denotes serotypes included in PCV7
*^ Denotes additional six serotypes included in PCV13 (PCV13-7)
Data source: Irish Pneumococcal Reference Laboratory

PCV vaccine failures

Based on data obtained through the IPD enhanced surveillance system, two PCV vaccine failures were reported in 2016, one due to serotype 19A and one due to serotype 7F(both included in PCV 13). Since 2008, a total of 13

vaccine failures have been reported in addition to the two reported in 2016, two in 2015 (19A) 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 2016, the proportion of penicillin non-susceptible invasive *S. pneumoniae* (PNSP) was 16.5%, (0% and 16.5% with high and intermediate level resistance, respectively) while 13.2% of isolates were resistant to erythromycin (Data source: HPSC/EARS-Net Ireland). This compares to 17.5% and 15.2% in 2015, respectively. In 2016, the proportion of PNSP decreased slightly compared to 2015, and the overall trend for the past four years has been downward. In 2016, the proportion of *S. pneumoniae* with resistance to erythromycin decreased compared to 2015, and the overall trend for the past four years has been downward.

The predominant PNSP serotypes in 2016 were 8, 12F, 3 and 19A, 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 2016 https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/earsssurveillancereports/2016reports/EARS-Net%20annual-quarterly%20data%20summary%20sheet_website_2016Q4.pdf

Laboratory survey

During 2016, in collaboration with the IPRL we undertook a survey of Irish clinical laboratories in relation to testing, diagnosis and notification of IPD in order to assess the quality and completeness of the national IPD surveillance programme.

Thirty-five of the 39 clinical microbiology laboratories participated (response rate 89.7%). Most laboratories (94%) had notification systems and processes in place to ensure that all IPD cases were notified. Most (91.4%) sent isolates to the IPRL for serotyping, with most (71.4%) sending isolates as soon as culture was positive. Based on the results of this survey it is evident that national IPD surveillance is comprehensive, however some potential gaps in notification and referral for serotyping were identified which will be addressed in 2017, with all laboratories encouraged to send isolates on a timely and regular basis to the IPRL.

Discussion

There was a slight increase (not significant) in the incidence of confirmed cases of IPD in Ireland in 2016 compared with 2015. Since its 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 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 12F were the predominant serotypes identified in 2016.

Ireland's (HPSC's) participation in the EU funded projects, SpIDnet (since 2012) and I-Move+ (since 2015) is supporting efforts to strengthen IPD surveillance in Ireland. Through this project additional support for the collection of enhanced surveillance data that has been possible in a number of HSE regions. This has resulted in improved data collection for all cases (paediatric and adults). As a result, at national level it is evident that a greater proportion of IPD notifications now have data on clinical presentation, risk factors, outcome and vaccination history.

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 susceptibility. 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 IPRL. Although 84% of confirmed notifications had an isolate submitted for serotyping in 2016, 16% (n=64) did not, including 17 cases in children <5 years of age. In six of these 17 cases, an isolate was not available for typing and confirmation was by PCR only. Serotype information is unavailable for 26% 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 and PPV23 on public health and in guiding further vaccination strategies, including expanded valency vaccines.