Seirbhís Sláinte Níos Fearr á Forbairt | Building a Better Health Service

hpsc

Annual Epidemiological Report

June 2019

Streptococcus Pneumoniae (invasive) in Ireland, 2018

Key Facts

- In 2018, 510 confirmed cases of invasive pneumococcal diseases (IPD) were reported in Ireland, among which there were 73 (14%) IPD related deaths; case fatality ratio among all IPD notifications was 17.3% (88/510).
- The incidence rate was 10.7 per 100,000 population, an increase compared to 2017 (8.7 per 100,000 population).
- Age specific incidence rates (ASIR) were highest in those aged 85 years and over (99.2 per 100,000 population), followed by those aged 75-85 and 65-75 years (48.3 and 27.6 per 100,000 population respectively).
- In 2018, 87% of the confirmed IPD notifications had an isolate submitted for serotyping.
- The most common serotypes in adults were 8, 19A, 12F, 9N, 3 and 22F. In children <5 years of age, the predominant serotypes were 23B, 15B/C, 19A and followed by serotypes 12F, 33F, 22F, 24F and 10A.
- In 2018, compared to 2008, the greatest impact due to PCV has been seen in children <5 years of age where the incidence due to PCV7 serotypes has declined by 100% (p<0. 001). The incidence of disease due to the additional six serotypes covered by the PCV13 declined by 80% (p<0. 001) in those <2 years of group.
- A significant indirect impact was also observed in those aged 65 years and older with declines in incidence of serotypes from the PCV7 serotypes in 2018, compared with 2008 (90%; p<0. 001).
- An increase in incidence due to non-vaccine types was also seen in all age groups in 2018 compared with 2008. In particular the incidence rate increased in those aged 65 and over.

Suggested citation: HSE Health Protection Surveillance Centre. *Streptococcus pneumoniae* (invasive) in Ireland, 2018. Dublin: HSE HPSC; 2019

Table of Contents

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 of other sterile sites.

For this report notification data for IPD was extracted from Computerised Infectious Disease Reporting (CIDR) system on 20th June 2019. 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 incidence rates we have used 2016 census data from the Central Statistics Office (CSO) for calculating rates for 2014-2017 and 2018. This has resulted in differences from rates calculated in previous years' reports as CSO 2011 data were used in those reports.

Surveillance

A number of different initiatives are in place in Ireland for the surveillance of IPD. Data on IPD notifications are collated using CIDR. Enhanced surveillance (including outcome, risk factors, vaccination, serotype) 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 cerebrospinal fluid (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 ESBSI 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, Children's Health Ireland at 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+ (Integrated Monitoring of Vaccines in Europe). 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, with particular focus on children less than five years of age and in adults aged 65 years and over. The I-MOVE+ study is now also studying the effectiveness of the pneumococcal polysaccharide vaccine which offers protection against 23 serotypes (PPV23) and is recommended for those at risk of IPD and those 65 years and older. For more information please see following links to I-MOVE+: http://www.i-moveplus.eu/wp3 and SpIDnet (Epiconcept): http://www.epiconcept.fr/. In 2019 HPSC was invited to participate in a collaborative project between the World Health Organization (WHO) and International Vaccine Access Centre (IVAC) at Johns Hopkins Blomberg School of Public Health (JHSPH) in the USA called PSERENADE (Pneumococcal Serotype Replacement and Distribution Estimation). This project aims to assess the impact of pneumococcal conjugate vaccine (PCV) on IPD incidence and serotype distribution in the setting of mature PCV10/PCV13 programmes on a global level.

Pneumococcal conjugate vaccine

In September 2008, the 7-valent pneumococcal conjugate vaccine (PCV7) (protects against seven types of pneumococcal bacteria) 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 (protects against 13 types of pneumococcal bacteria) (PCV13) replaced PCV7 in the infant schedule. (1) In December 2016, due to the introduction of the new meningococcal B vaccine (Men B) into routine immunisation, the third dose of PCV13 was shifted to 13 months of age for children born on or after 1st October 2016.

Since January 2014 one dose of PCV13 is recommended for individuals of all ages at high risk of invasive pneumococcal disease (including those with asplenia, splenic dysfunction, complement deficiency, immunosuppressive conditions and therapies, CSF leaks, intracranial shunt, candidates for, or recipients of a cochlear implant, post haematopoietic stem-cell transplant, solid organ transplant, and cancer patients under hospital supervision). Two doses of PCV13 two months apart is recommended for those if response may be blunted e.g. asplenia/hyposplenia. (1)

Vaccine uptake

National PCV vaccination coverage is monitored in children at 12 and 24 months of age. Following PCV introduction in 2008, uptake of the recommended number of doses among the first cohorts vaccinated was high, at 88% and 89% for children aged 12 months in 2009 and 2010, respectively. Higher uptake was reported for subsequent birth cohorts, with between 90-92% of children at 12 and 24 months of age reported as being age appropriately vaccinated since 2011. Uptake of three doses of PCV by 12 and 24 months of age for 2017 was 90% and 91%, respectively. (2)

Pneumococcal polysaccharide vaccine

One dose of pneumococcal polysaccharide vaccine (PPV23) is recommended for all those aged 65 years and older, and for those other age groups at increased risk of pneumococcal infection since 1996. (1)

Methods

Case definition of IPD

IPD case classification has changed over time. Between 2004 and 2011, in individuals with clinically compatible symptoms, the isolation or detection of *S. pneumoniae* from a normally sterile site was classified as a confirmed case; detection of *S. pneumoniae* antigen from a sterile site was classified as probable and detection from non-sterile site was classified as a possible case. In 2012, the previously used probable case definition became no longer applicable and any case in which *S. pneumoniae* antigen was detected from a normally

sterile site was classified as confirmed and detection in urine was classified as possible. In July 2015, the case definition of *S. pneumoniae* was again amended; only those cases of IPD meeting the laboratory criteria were classified as confirmed cases, and urinary antigen detection (possible cases) is no longer notifiable.(3)

Definition of vaccine failure

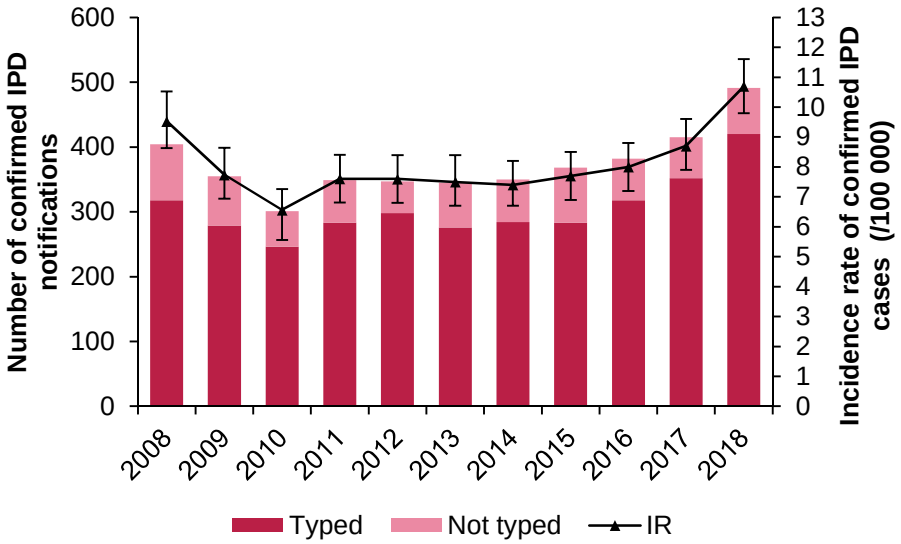
PCV vaccine failure was defined as a confirmed IPD case in a child caused by a PCV-serotype who has completed a PCV immunisation course appropriate for his/her age and disease onset is ≥14 days after last dose of PCV.

Epidemiology

Focusing on the confirmed IPD notifications, 510 cases were notified in 2018 (10.7/100,000; 95% CI 9.8 - 11.6/100,000), a significant increase of 23% (p=0.0009) in the number of cases compared with 2017 (8.7/100,000; CI 7.9 - 8.8/100,000; 415 cases) (Figure 1). In 2018, the incidence of confirmed IPD increased 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 2018, 87% (422/487) of cases had an isolate submitted for serotyping, more than the proportion of cases in 2017 (85%) and 2016 (84%), and in 2008 and 2009, when 79% of notifications had an isolate typed. Twenty-three cases were confirmed by PCR only. In 2012, 86% of all isolates were typed (Figure 1). In 2018, 91% of notifications (31/34) relating to children <5 years of age had an isolate submitted for serotyping.

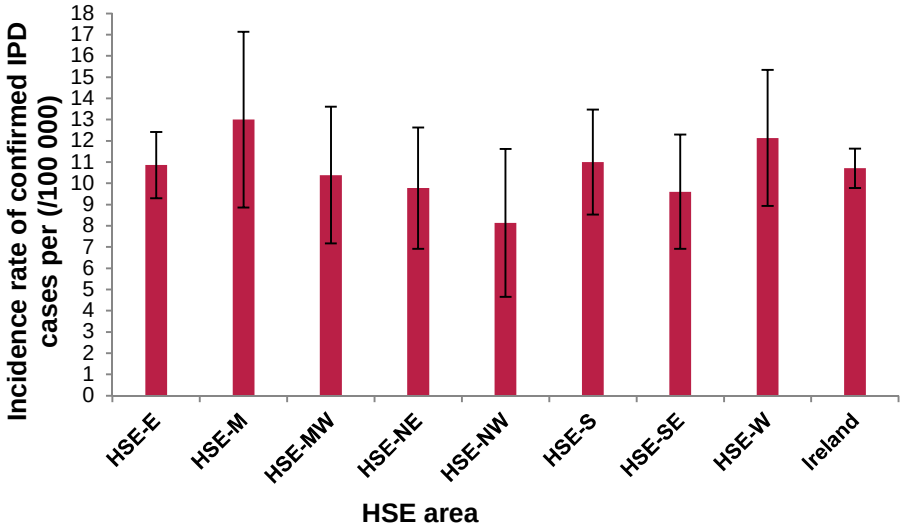
Figure 1. Number of confirmed invasive pneumococcal disease (IPD) notifications by typing status and the incidence rate (IR) of confirmed IPD with 95% confidence intervals, in Ireland, 2008-2018



Data source: CIDR

During 2018, the incidence rates by HSE area ranged from 8.1 per 100,000 (HSE NW) to 13 per 100,000 (HSE M) (Figure 2). However, the incidence rates in each of the eight HSE areas were not statistically different from the national rate.

Figure 2. Crude incidence rate of confirmed invasive pneumococcal disease notifications by HSE area, 2018

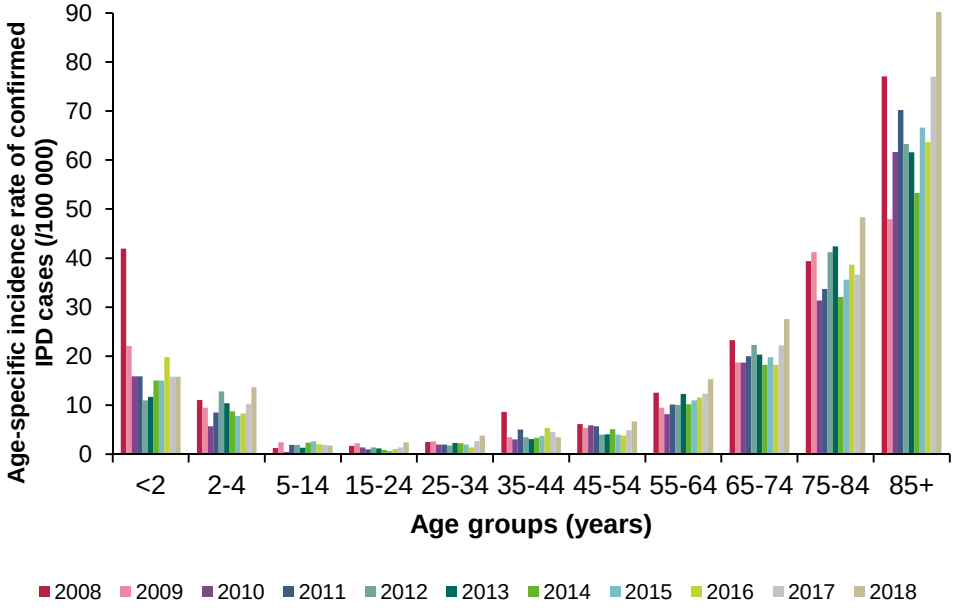


Data source: CIDR

In 2018, a clinical diagnosis was reported for 438 of the 510 confirmed cases (86%), which included BSI with pneumonia (n=325), meningitis (n=40), from these 17 had meningitis and BSI; and other BSI for the remainder (n=73). This reflects the constant improvement in the completeness of data provided in comparison to previous years, although in 2018 the percentage of information on clinical diagnosis and risk factors slightly decreased. In 2017, 2016, 2015 and 2014, the clinical diagnosis was reported for 388 of the 415 (94%), 313 of the 381 (82%), 229 of the 368 (62%) and 168 of the 350 (48%) confirmed cases, respectively).

Slightly more females (n=265, 52%) than males were reported with IPD. The median age of cases was 66 years (range 1 month to 95 years). Those aged 65 years and older accounted for half of cases (52%, n=264). Within this age category the age specific incidence rate (ASIR) was highest in the oldest age groups; ≥85 years of age (99.2/100,000; n=67); 75-84 year age group (48.3/100,000; n=95); 65-74 year age group (27.6/100,000; n=103) (Figure 3). In children <2 years of age the ASIR was 15.8 cases per 100,000 population (n=20). A statistically significant decline (70%) 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, in Ireland, 2008-2018



Data source: CIDR

Medical risk factors for IPD were reported for 360 (71%) confirmed cases; 87 cases (17%) did not have an identified risk factor; for the remaining 63 cases this information was either unknown or not specified. The main medical risk factors reported included chronic lung disease (n=140; 27%), chronic heart disease (n=122; 24%), immunosuppressive condition or therapies (n=84; 16%), chronic liver disease (n=18; 3%) and renal diseases (n=39; 8%). It should also be noted that being aged 65 years and older is also a recognised IPD risk factor; 265 (52%) cases in 2018 were in this age group, of whom 213 (80%) also reported a medical risk factor.

IPD death notifications

The outcome field was completed in 100% (n=510) of the IPD notifications in 2018, versus 97% in 2017, 85% in 2016, 56% in 2015 and 39% in 2014. Among those whose outcome was reported, case fatality ratio among IPD notifications overall was 17.3% (88/510); for 46 (63%) patients who died, the cause of death was reported as directly due to IPD, in 15 patients it was not due to IPD, for nine patients cause of death was pending or awaiting a coroner's report. For the remaining 18, the cause of death was not specified or was unknown. Most of these deaths (n=86) occurred in adults (age range 42-95 years) and two in adolescents under 18 years of age.

The increased completion in the reported outcome field since 2014 reflects improved 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).

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 2018, of the 510 confirmed IPD notifications reported in CIDR, 23 were confirmed by PCR only, 422 (87% 422/487) had isolates sent for serotyping; 4% of IPD infections were due to PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F and 23F); 19% were associated with the six additional serotypes included in PCV13 (1, 3, 5, 6A, 7F and 19A); the remaining 77% of infections were due to non- PCV13 vaccine types.

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 associated with serotypes included in the vaccines in use. 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 2018 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 2018 the incidence of disease due to the additional six serotypes covered by the PCV13 declined by 80% in children <2 years of age compared with 2008 (p<0.001) (Figure 4b). However the increase was observed in the 65 years and older age group with these additional six serotypes compared with 2008 (10%; p=0.3965) (Figure 4b). An increase in incidence due to non-vaccine types (NVTs) was also seen in 2018 compared with 2008. In those aged 2-4 years and 65 years and older there was a significant increase (p<0. 001) in incidence rates. An increase in incidence was also observed in those aged <2 years in 2018 compared with 2017. There has been little change in the incidence of NVTs among other age groups (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, in Ireland, 2008-2018.

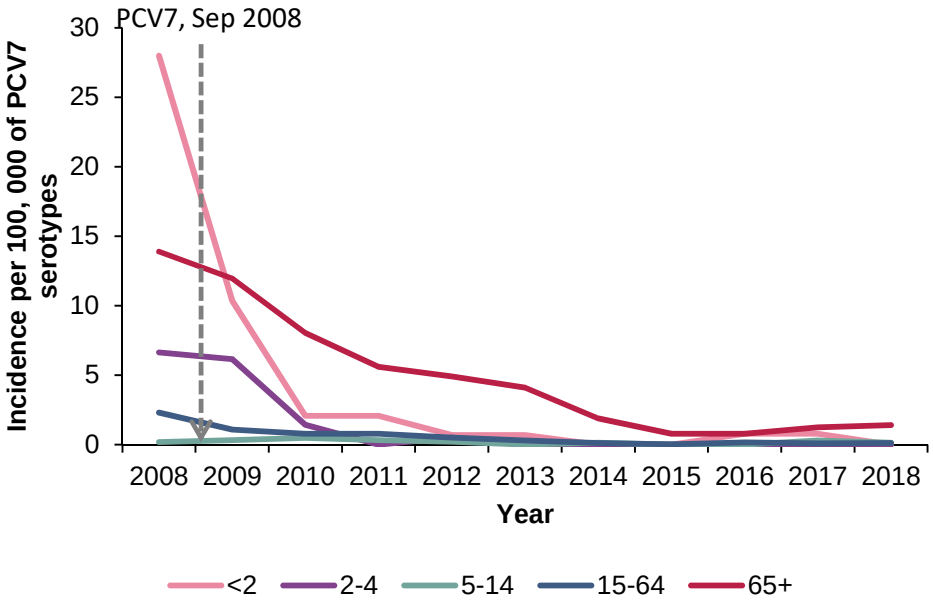


Figure 4a

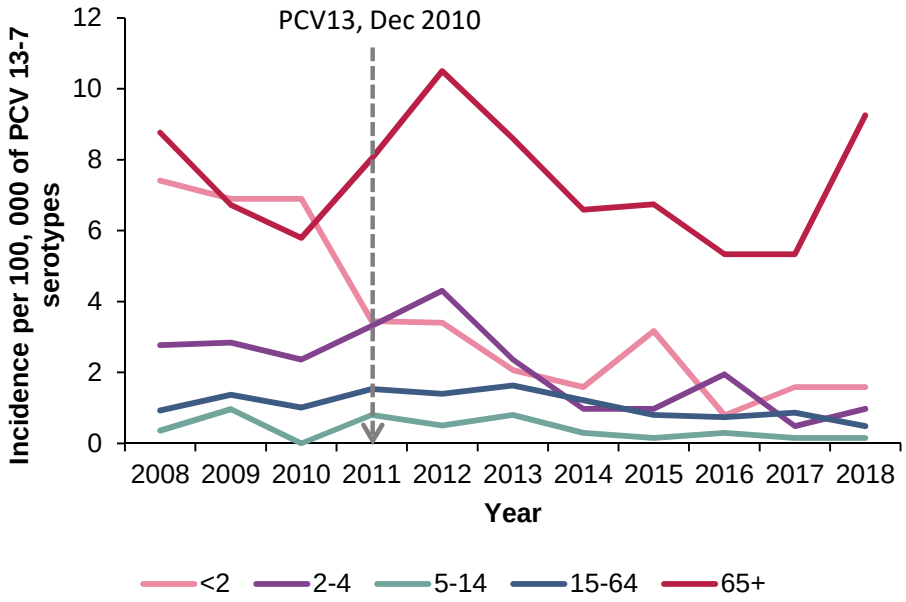


Figure 4b

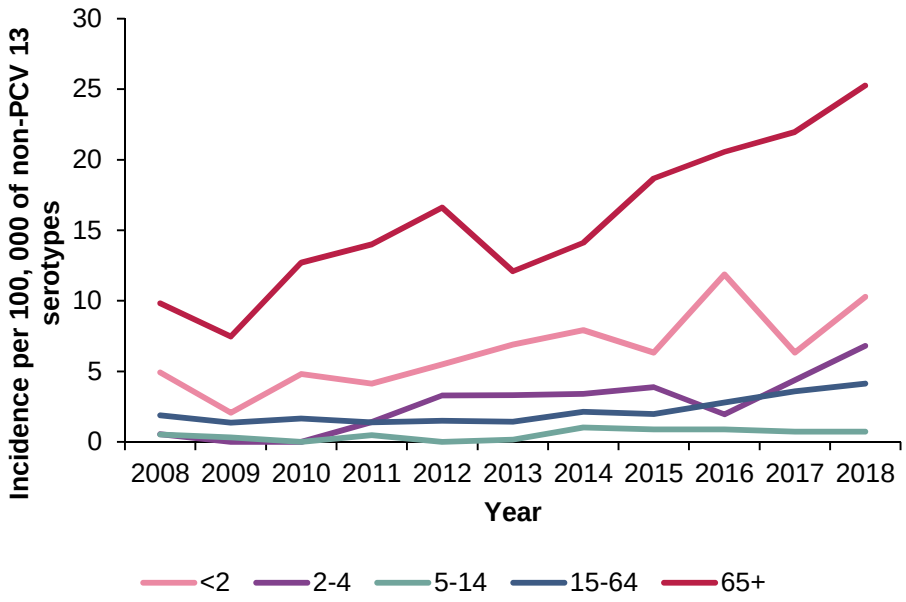


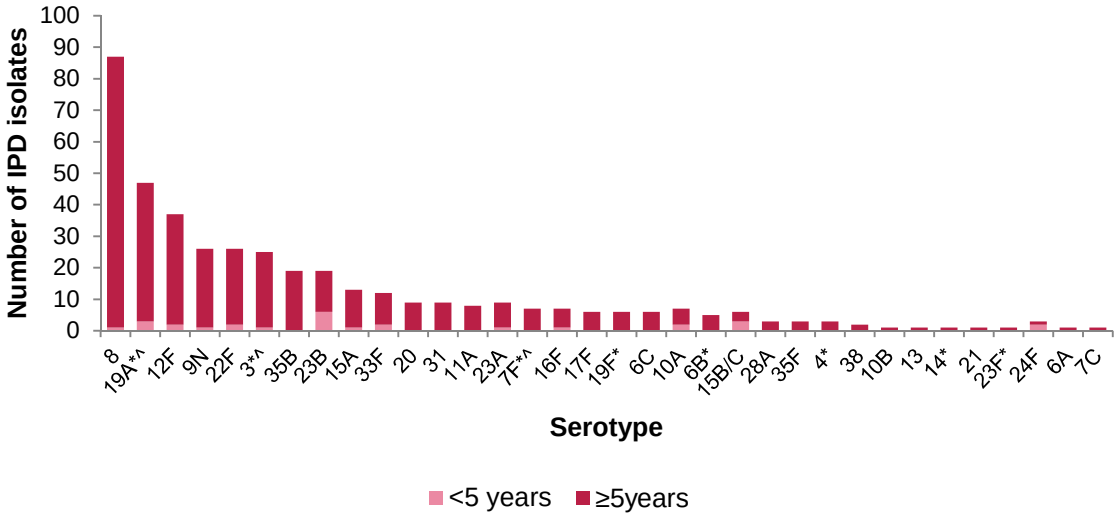
Figure 4c

Data source: Irish Pneumococcal Reference Laboratory

The predominant serotypes in circulation in 2018, were 8 and 12F (both included to PPV23, not included in PCV13 vaccine), 19A and 3 (both included in PCV13), followed by serotypes 9N (non vaccine type; NVT) and 22F (included in PPV23, not included to PCV13 vaccine). In children <5 years of age, the predominant serotypes were 23B, 15B/C, 12F, 33F, 22F, 24F, and 10A (all NVTs) and 19A (included in PCV13). All these serotypes accounted for 71% of the isolates serotyped in this age group (Figure 5).

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

Figure 5. Serotype distribution of invasive *Streptococcus pneumoniae* isolates by age group (<5 or ≥5 years) in Ireland, 2018



* 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 2018, one due to serotype 19A, one due to serotype 3 (both included in PCV 13, not in PCV7). Since 2009, 17 vaccine failures have been reported in total in Ireland (Table 1) with 19A the most commonly reported (n=10; 59%). Six of the 17 had a risk factor indicated.

Table 1. Number of vaccine failures by serotype in Ireland in 2009-2018

	Vaccine failures	Serotype
2009	0	-
2010	2	14, 19F
2011	0	-
2012	2	19A,19F
2013	3	19A
2014	2	19A
2015	2	19A
2016	2	19A, 7F
2017	2	6B, 3
2018	2	3,19A

Data source: CIDR

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

In 2018, the proportion of penicillin non-susceptible invasive *S. pneumoniae* (PNSP) was 20.2%, (2.2% and 18.0% with high and intermediate level resistance, respectively) while 13.4% of isolates were resistant to erythromycin (Data source: HPSC/EARS-Net Ireland). The proportion of PNSP and isolates resistant to erythromycin increased from 2017, when 15.8% and 12.9% had high and intermediate resistance, respectively. However, the overall trend in 2014-2017 has been downward, despite the increase observed in 2018.

In 2018, the proportion of *S. pneumoniae* with resistance to erythromycin slightly increased compared to 2017, despite a declining trend from 2014-2017.

For details on the antimicrobial resistance patterns of *S. pneumoniae*, please see the link on EARS-Net Report, Quarters 1-4 2018 https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/ears-netdataandreports/

Discussion

There was a significant increase in the incidence of confirmed cases of IPD in Ireland in 2018 compared with 2017. Increase in the number of cases coincided with the period of high influenza incidence during the 2017-18 influenza season. Since its introduction in

2008, PCV7 has had a significant impact in reducing the overall burden of the disease in the total population with a decline in IPD in all age groups due to serotypes covered by PCV7. This indicates both a direct and indirect/herd immunity effect which 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 80%.

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, 12F, 9N, 22F and 3 were the predominant serotypes identified in 2018.

Ireland's (HPSC's) participation in the EU funded projects, SpIDnet (since 2012) and I-MOVE+ (2015- 2018) is supporting efforts to strengthen IPD surveillance in Ireland. Through this project's additional support for the collection of enhanced surveillance data, this 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, overall 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 and understand vaccine failures in Ireland, it is crucial that samples from sterile sites are obtained for culture and susceptibility testing. 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 with patient details to enable linkage with CIDR notification data at laboratory level. Although 87% of confirmed notifications had an isolate submitted for serotyping in 2018, 13% (n=65) did not.

The dramatic impact of PCV on the epidemiology of IPD in Ireland is similar to that being seen in other European countries, most of which have introduced this vaccine into their national immunisation programmes in the past 15 years. The emergence of serotype replacement being seen in Ireland is also being seen elsewhere in Europe. (4) In North

America, non-vaccine serotype emergence has not been reported from the USA (CDC publications relating to 2015 data), but has been reported in Canada (5,6). On-going monitoring of serotypes in the post-implementation vaccine era is an integral part of surveillance for all countries with PCV vaccination programmes.

Public health implications

Continued good quality IPD surveillance, including the monitoring of invasive *S. pneumoniae* serotypes, is crucial in order to identify any epidemiological changes in the disease, assess the impact of PCV13 on public health, and guide further vaccination strategies, as newer expanded valency vaccines become available and changes are made to PCV coverage, e.g. age or risk factor related. Striving to improve data quality is an essential part of IPD surveillance. A pneumococcal polysaccharide vaccine which offers protection against 23 serotypes (PPV23) is already recommended for elderly and risk groups and is important to give additional protection despite a lower vaccine efficacy than the PCV.

Technical notes

Activities key to the surveillance of IPD in Ireland

Notifications: Clinicians and laboratories should notify all cases of IPD to the relevant Department of Public Health and data are inputted to the national Computerised Infectious Diseases reporting (CIDR) system for notifiable infectious diseases.

Typing: Laboratories should submit **all** invasive *S. pneumoniae* isolates to Temple Street Children's University Hospital for typing by address:

Irish Pneumococcal Reference Laboratory
which is housed with
Irish Meningitis & Sepsis Reference Laboratory,
Temple Street Children's University Hospital,
Temple Street, Dublin 1

Note: For each isolate sent to the IPRL, the patient's details are required on the form submitted in order that the results sent to the laboratory can be linked to the notification already made in CIDR.

Enhanced surveillance: Departments of Public Health perform enhanced surveillance on cases of IPD notifications and enter these data on CIDR.

Antimicrobial resistance: Laboratories should report data on antimicrobial resistance profiles of invasive *S. pneumoniae* isolates (from blood and CSF) to the European Antimicrobial Resistance Surveillance System Network (EARS-Net) at HPSC.

Laboratories: Submission of isolates for typing

For details regarding the submission of invasive *Streptococcus pneumoniae* isolates for typing, please contact:

Dr Mary Corcoran
Tel.: 01 878 4854
Email: mary.corcoran@cuh.ie

Link to sample request form:
https://www.cuh.ie/wp-content/uploads/2019/06/IMSRL-Request-Form-Edition-04.pdf

Address:
Irish Pneumococcal Reference Laboratory,
Irish Meningitis & Sepsis Reference Laboratory,
Temple Street Children's University Hospital,
Temple Street, Dublin 1

Departments of Public Health: IPD surveillance

IPD **enhanced surveillance form** is available at: https://www.hpsc.ie/a-z/vaccinepreventable/pneumococcaldisease/surveillanceforms/

Protocol for the enhanced surveillance of IPD is available at: https://www.hpsc.ie/a-z/vaccinepreventable/pneumococcaldisease/informationforhealthprofessionals/

Further information available on HPSC website

For further details on the surveillance and epidemiology of IPD in Ireland, please see:

Biannual Reports on invasive *Streptococcus pneumoniae* infection available at:

https://www.hpsc.ie/A-Z/VaccinePreventable/PneumococcalDisease/Publications/QuarterlyReportsonInvasivePneumococcalDisease/

Annual Reports on invasive *Streptococcus pneumoniae* infection available at:

https://www.hpsc.ie/a-z/vaccinepreventable/pneumococcaldisease/publications/annualreportsoninvasivepneumoccaldisease/

Articles published in Epi-Insight available at: https://www.hpsc.ie/a-z/vaccinepreventable/pneumococcaldisease/publications/articles/

Posters and Presentations available at: https://www.hpsc.ie/a-z/vaccinepreventable/pneumococcaldisease/posterspresentations/

Quarterly and Annual EARSS Reports available at: https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/ears-netdataandreports/

Acknowledgements

Thanks are due to all the health care professionals involved in the surveillance of IPD in Ireland. In particular, we wish to thank all the laboratory scientists, consultant microbiologists, public health doctors/nurses/surveillance scientists, and others for forwarding pneumococcal isolates and for the work involved in the surveillance of pneumococcal disease in Ireland. We are also grateful for the assistance of staff in the Departments of Clinical Microbiology at the Royal College of Surgeons in Ireland and Temple Street Children's University Hospital, Dublin, Ireland. In addition, we would like to thank Epiconcept for the opportunity to participate in the European Networks such as SpIDnet and I-MOVE+, which allowed us to improve quality of surveillance data.

Report prepared by:

Jolita Mereckiene[3], Meadhbh Hunt[3], Breda O'Loughlin[3], Mary Corcoran[1], Prof Hilary Humphreys[2], Robert Cunney[1, 3], Stephen Murchan[3], Suzanne Cotter[3]

[1]Irish Pneumococcal Reference Laboratory, Irish Meningitis & Sepsis Reference Laboratory, Temple Street Children's University Hospital, Temple Street, Dublin 1

[2]Education and Research Centre, Royal College of Surgeons in Ireland and Beaumont Hospital

[3]Health Protection Surveillance Centre (HPSC), Dublin.

References

(1) National Immunisation Advisory Committee. Immunisation Guidelines for Ireland. http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/immunisationguidelines.html . 2018. Access date: 26-6-2019.

(2) Health Protection Surveillance Centre. Early Childhood Immunisation Uptake Statistics Q1 1999-Q4 2017 Summary. https://www.hpsc.ie/a-z/vaccinepreventable/vaccination/immunisationuptakestatistics/immunisationuptakestatisticsat12and24monthsofage/Summary%20Immunisation%20Uptake%20Statistics-%20National,%20CHO%20&%20LHO.pdf. 2017. Access date: 26-6-2018.

(3) Health Protection Surveillance Centre. Case Definitions for Notifiable Diseases. [28-05-2018]. http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/referenceandeducationalresourcematerial/spneumoniae/casedefinition/ 2018. Access date: 26-6-2019.

(4) European Centre for Disease Prevention and Control. Invasive pneumococcal disease - Annual Epidemiological Report 2017 [2017 data]. https://www.ecdc.europa.eu/sites/portal/files/documents/AER_for_2017-invasive-pneumococcal-disease.pdf Access date: 26-6-2019.

(5) Government of canada. National Laboratory Surveillance of Invasive Streptococcal Disease in Canada – Annual Summary 2014**.** http://www.healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/2014-streptococcus/alt/surveillance-streptococca-eng.pdf. Access date: 26-6-2019.

(6) Center for Disease Control and Prevention. Surveillance and Reporting. https://www.cdc.gov/pneumococcal/surveillance.html Access date: 26-6-2019.