Annual Report*

Typing & Antimicrobial Susceptibilities of isolates causing Invasive Pneumococcal Disease (IPD) in Ireland – Results from 2019-2021

Published April 2022

***This report covers three years (2019-2021) as collection and analysis of data was delayed by the pandemic during 2020-21.**

Executive Summary

This report summarises the results from invasive pneumococcal disease (IPD) isolates submitted to the Irish Meningitis and Sepsis Reference Laboratory (IMSRL) for typing from 2019 to 2021 and compares the serotype distribution to 2018 and previous years.

The number of IPD isolates typed decreased significantly from 2019 to 2021 (n=374, 181 and 160) in comparison to previous years (*n*=448, 391 in 2018 and 2017 respectively). It is likely that the increased influenza activity reported in 2018, which was the highest since surveillance began, may have also contributed to the high incidence of IPD in 2018 [1]. Therefore a decline back to 374 in 2019 is similar to what was observed in other years. The decline in 2020 and 2021 was associated with the emergence of the SARSCoV-2 (COVID-19) pandemic. This was also observed with other respiratory pathogens and observed in many countries across the globe [2]. Ireland contributed to the international study co-ordinated by Brueggemann *et al.* to examine the impact of COVID-19 on the incidence of other respiratory pathogens. The results of which indicated that while particular "lock-down" measures could not be directly correlated with the decline in respiratory illness, it is likely that changes in practice such as mask wearing and reduced social mixing, reduced the transmission of respiratory pathogens such as *Streptococcus pneumoniae*.

Overall, there was a continued decline of vaccine associated serotypes in 2020 and 2021 confirming the success of the current paediatric immunisation schedule which currently recommends three doses of a 13-valent pneumococcal conjugate vaccine (PCV13) to young children. However, there was an increase in the serotypes not covered in the PCV13. In late 2021 - early 2022, two new pneumococcal conjugate vaccines (PCV15 and PCV20) were approved for use in adults by the European Medicines Agency (EMA). While these are not part of the current vaccine schedule in Ireland, the vaccine-serotype coverage (i.e. potential protection) offered by the current and future vaccines is examined in this report. Some of the non-PCV13 serotypes that have emerged in recent years such as serotypes 22F, 33F (covered in both vaccines) and serotypes 8, 10A and 15B/C which are covered in PCV20. However, other serotypes such as 23B which is not covered in the current or newly approved vaccines have become predominant serotypes in children and are also associated with antimicrobial resistance.

The recent changes in serotype epidemiology and the continual emergence of non-vaccine serotypes highlight the vital role of national surveillance of IPD to assess the effectiveness of the current vaccines and potential impact of additional vaccines that have recently been approved for use in Europe.

Background

The bacterium

Streptococcus pneumoniae is a major cause of life-threatening infections such as meningitis and bloodstream infection, i.e. invasive pneumococcal disease (IPD). Pneumonia remains a leading cause of death in children worldwide and accounts for up to 14% of deaths of children < 5 years of age [3]. *S. pneumoniae* is the leading bacterial pathogen associated with pneumonia in this cohort. The population groups at highest risk of pneumococcal infection are young children and the elderly [4]. The Centers for Disease Control and Prevention (CDC) in the USA estimate that the mortality rate due to IPD is much greater in adults ≥65 years of age (18/100,000 population) than in children <2 years (0.4/100,000) in the post vaccine-era [5].

S. pneumoniae is a successful pathogen in part due to the diversity of the circulating capsular serotypes. The continued identification of new serotypes based on the chemical composition of the polysaccharide capsule, indicates that over 90 immunologically distinct serotypes exist [6]. Immune responses elicited by current pneumococcal vaccines are also directed towards the polysaccharide capsule [7]. The conjugate vaccines were developed to reduce the burden of the predominant serotypes circulating in paediatric populations at the time of development. However, serotype prevalence data varies depending on patient demographics, vaccination schedules and the geographical area. Therefore, it is critical that IPD clinical notification, laboratory surveillance including serotype and antimicrobial resistance data, are continually monitored at a national level to inform vaccine and antimicrobial use and policies.

Laboratory surveillance

The National IPD surveillance programme is a collaborative project between the Royal College of Surgeons in Ireland (RCSI) Education and Research Centre, Beaumont Hospital, The Irish Meningitis and Sepsis Reference Laboratory (IMSRL); based at Children's Health Ireland (CHI) at Temple Street, and the Health Protection Surveillance Centre (HPSC). The programme was established in April 2007 to provide reference laboratory support for the investigation of IPD in advance of the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2008. However, changes in serotype epidemiology in the wake of an increase in serotypes not covered in the vaccines have meant that IPD surveillance remains an essential component of public health surveillance.

The vaccine schedule in Ireland

In September 2008, PCV7 was introduced to the Irish infant immunisation schedule at 2, 6 and 12 months of age. A catch-up programme was offered to children who were < 2 years of age at that time. The PCV7 vaccine offered protection against seven serotypes 4, 6B, 9V, 14, 18C, 19F and 23F which were commonly associated with invasive disease in children at that time. In December 2010, PCV7 was replaced by the 13-valent pneumococcal conjugate vaccine (PCV13), which offers protection against six additional serotypes; 1, 3, 5, 6A, 7F and 19A. In December 2016, the schedule for children born on or after October 1st, 2016 was changed to a dose of PCV13 at 2, 6 and 13 months. This was done to accommodate vaccination with the newly introduced *Neisseria meningitis* type B vaccine at 12 months. The uptake of the three doses of PCV13 at 24 months of age is ranging between 84-87% [8]. A 23-valent polysaccharide vaccine (PPV23) is recommended for adults ≥65 or for high-risk adults < 65 years with immunosuppressive conditions or co-morbidities. However uptake in adults in Ireland is low in comparison to the paediatric schedule (27-36% v's >90%), therefore it is difficult to assess any impact this may have had on serotype epidemiology in Ireland. Since 2015, a single dose of PCV13 prior to PPV23 administration is recommended for those with immunosuppressive conditions or co-morbidities. All vaccine information is available on http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter3.pdf.

Table 1 summarises current and newly approved vaccines against IPD. The two new pneumococcal conjugate vaccines (PCV15 and PCV20) were approved for use in adults only by the European Medicine Agency (EMA). It is likely that both will be approved for use in paediatrics in subsequent years. While these are not part of the current vaccine schedule in Ireland, the vaccine-serotype coverage (i.e. potential protection) offered by the current and future vaccines is examined in this report.

Table 1: Summary of Pneumococcal Vaccines currently approved for use

Type	Serotypes	Introduced	Schedule	Uptake
PCV7	4, 6B, 9V, 14, 18C, 19F and 23F	Sept 2008	2, 6 and & 12 months. Catch up for those < 2 years.	90-92% (HPSC)
PCV13	PCV7 + 1, 3, 5, 6A 7F and 19A	Dec 2010	2, 6 and 13 months. No catch up.	
PPV23	PCV13* + 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F (**excluding 6A*)	Recommended since 1980s	Those ≥65 years of age. Additional 1 dose of PCV13 for high-risk adults i.e. immunosuppressive conditions, co-morbidities (Aug.2015)	27-36% (Giese et al. 2016)
PCV15	PCV13 and 22F + 33F		Not currently part of the Irish vaccination schedule. Approved for use in adults in December 2021.	
PCV20	PCV13 and 8, 10A, 11A, 12F, 15B, 22F + 33F		Not currently part of the Irish vaccination schedule. Approved for use in adults in February 2022	

1. Methods

Invasive *S. pneumoniae* isolates (from blood, cerebrospinal fluid and occasionally other sterile sites) are referred by clinical microbiology laboratories throughout the Republic of Ireland to the IMSRL. Typing is performed using a combination of serological co-agglutination using antisera from the Statens Serum Institute and multiplex PCR, as previously described [9]. Susceptibility to antimicrobials is assessed using the E-test method (bioMérieux), and the results are interpreted using the European Union Criteria for Antimicrobial Susceptibility Testing (EUCAST) criteria [10]. The EUCAST breakpoints of MIC >0.06 µg/ml for penicillin, >0.5 µg/ml for cefotaxime and >0.25 µg/ml for erythromycin were considered as non-susceptible [10]. Typing based on whole genome sequencing (WGS) analysis and antimicrobial susceptibility testing (AST) using broth micro-dilution (BMD) are both currently under validation review. However, due to WGS lead times, serology which is still considered the gold standard for definitively serotyping *S. pneumoniae,* remains the main typing method.

Due to the COVID-19-related fall in IPD, in some instances when comparing the serotype trends, the results will be presented as a percentage of proportion of IPD cases typed within that period, in addition to absolute numbers or incidence rates. Incidence rates represent the incidence rates (IR) of typed isolates referred to the IMSRL using data from the 2016 census of the population (http://www.cso.ie/en/census/) and rates are expressed as the number of serotyped isolates from cases per 100,000 population (/100,000).

2. Results

Overall number of isolates

More *S. pneumoniae* isolates were referred for typing in 2019 (*n*=487) than 2020 (*n*=202) and 2021 (*n*=180). The numbers for 2020 and 2021 are a notable decline in comparison to previous years 350-460. In 2021, eleven isolates were not culturable on receipt and a repeat culture was referred: this is a significant improvement from previous years. A faster turn-around time for referring isolates rather than sending in batches has contributed to the improved recovery of *S. pneumoniae* from slopes. Duplicate isolates from different sites from the same patient i.e. blood and cerebrospinal fluid (CSF), repeat isolates from the same patient, multiple isolates from one patient but referred from different hospitals, or multiple isolates from the same patient within the same week were typed, and reported to the referring laboratory, but are not included in the summary of this report. Once all duplicate isolates and non-invasive query isolates were removed, the total number of typed IPD isolates (based on isolation date) was compared with other years using the same criteria. The number of IPD isolates typed in 2019, 2020 and 2021 were *n*=374, *n*=181 and *n*=160, respectively.

The number of isolates per sample patent group, sample type, quarter and geographical region

Fifty-five to fifty-four per cent of the isolates typed were from female patients in 2019-2021. From 2019-2021, most samples were from blood (*n*=96-97%) followed by CSF samples (1-2%) and other sterile sites (2-3%). The total number of isolates typed in 2019 (n=374) was much greater than 2020 (n=181) and 2021 (n=160). This was much lower than 2018 (*n*=448) and previous years, i.e. 2015-2017, *n*=299-389. As indicated in **Figure 1**, more samples were received in quarter 1 (January to March) than other quarters, with the exception of 2021, which increased each quarter as the year progressed. There was no difference in the number of samples typed in Q1 of 2019 and Q2 of 2020 (n=108), however, there was a notable decline in all other quarters of 2020 and 2021, which coincides with the introduction of COVID-19 restrictions in **Figure 1**. The number of isolates typed in Q4 of 2021 (n=81) was much greater than any of the other three quarters of 2021 (n=22-29) and more comparable to what was typed in in the pre-pandemic period (Q4 2018, 2019 *n*=119, 117). The number of isolates typed per Health Service Executive (HSE) area based on referring hospital location is displayed in **Figure 2**. The largest proportion of isolates was received from the HSE-East area (**Figure 2**), which is reflective of the larger population within this region. The number of isolates typed from all regions decreased in 2020 and 2021, with no major changes in the distribution.

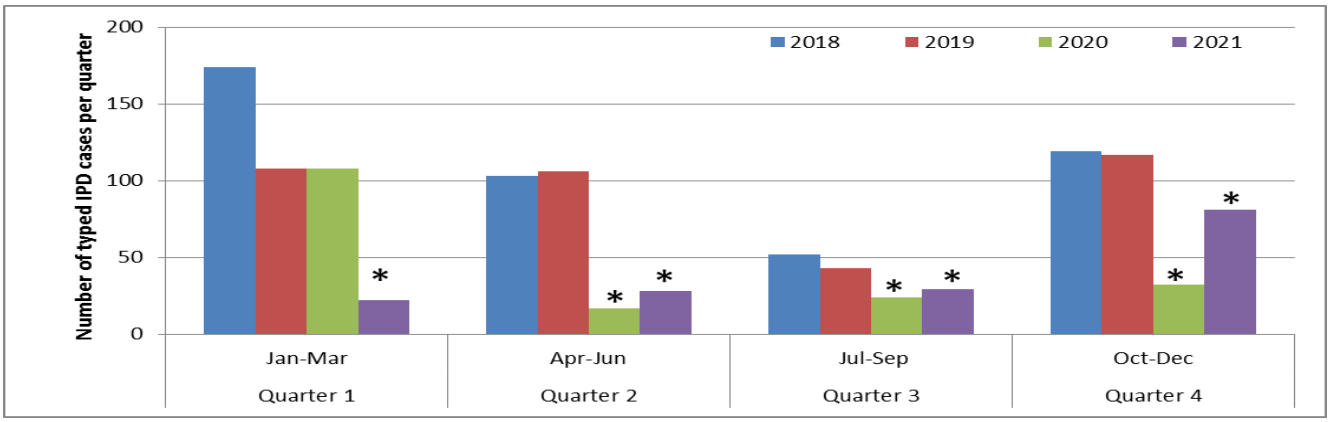

Figure 1. Number of IPD isolates in all patient age groups typed per quarter from 2018 to2021
The * denotes the COVID-19 pandemic period.

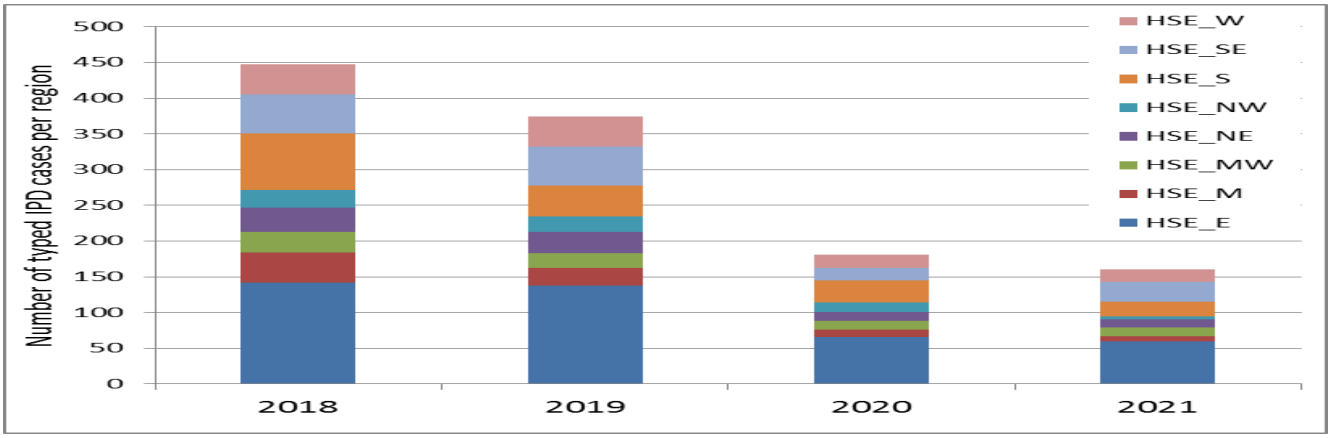

Figure 2. Number of IPD isolates typed from each HSE area and from 2018 to 2021.

The number of isolates in each age group

The number of IPD cases has fallen in Ireland post-pandemic and is similar to what was observed elsewhere [2]. Overall, the total number of IPD cases fell by 57% in 2021 in comparison to 2019, with the largest decline observed in those aged ≥65 years (64%, *n*=181,66 from 2019 to 2021) and those aged 5-16 years (64%, n=11,4) (**Figure 3A**). There was less of a decline in adults aged 35-64 years (49%), those aged < 2 years of age (55%) and those aged 2-4 years (47%). Young children < 5 years of age are known to have high asymptomatic *S. pneumoniae* carriage rates and were also less impacted by COVID related changes such as mask wearing due to young age whereas older adults were required to adhere to mask wearing recommendations and asked to restrict movement during the pandemic. It is likely that both of these factors could have influenced IPD rates within this cohort. However, it is difficult to pinpoint why the number of cases fell less in some adult age groups in comparison to others, particularly in countries like Ireland with a small population. The long-term impact of COVID-19 is remains under investigation as part of the global collaborative project with reference laboratories (https://pubmlst.org/projects/iris).

Based on incidence rates (IR per 100, 000), adults ≥65 years of age remain at highest risk of IPD with an incidence rate of 8.89/100,000 in 2021 (**Figure 3B**). This is much lower than the IR in previous years, which peaked in 2018 (IR=36.68/100,000) and during the pre-pandemic period of 2019 (IR=23.00/100,000). After older adults, the next highest incidence rate was observed in children < 2 years of age which ranged from IR=16.22/100,000 in 2019 to IR=7.90/100,000 in 2021. The overall incidence rate in children < 2 years of age ranged from a peak in 2008 IR=34.66/100,000 (year PCV7 was introduced) to the lowest rate of IR=9.20/100,000 in 2015, prior to the pandemic decline. The third highest disease incidence was in children aged between 2-4 years of age which ranged from IR=8.86/100,000 in 2019 to IR=3.16/100,000 and IR=4.77/100,000 in 2020 and 2021 respectively. Prior to this, the highest incidence was in 2009 (IR=9.97/100,000 and fell to as low as IR=3.32/100,000 in 2014). Based on the incidence rate trends, it is clear that paediatric IPD incidence rates were not impacted by the pandemic as much as adult cases. This was also confirmed when the proportion of cases per age group (as percentage of total received) was examined. Based on **Figure 3C** those aged < 16 years of age represented 12-14% of all IPD cases in 2020-2021, in comparison to 9-13% in 2018 and 2019. Conversely the proportion of cases from those ≥65 years of age was lower in 2020 (47%) and 2021 (42%) in comparison to previous years following PCV introduction when ≥50% of the IPD cases were from adults ≥65 years of age.

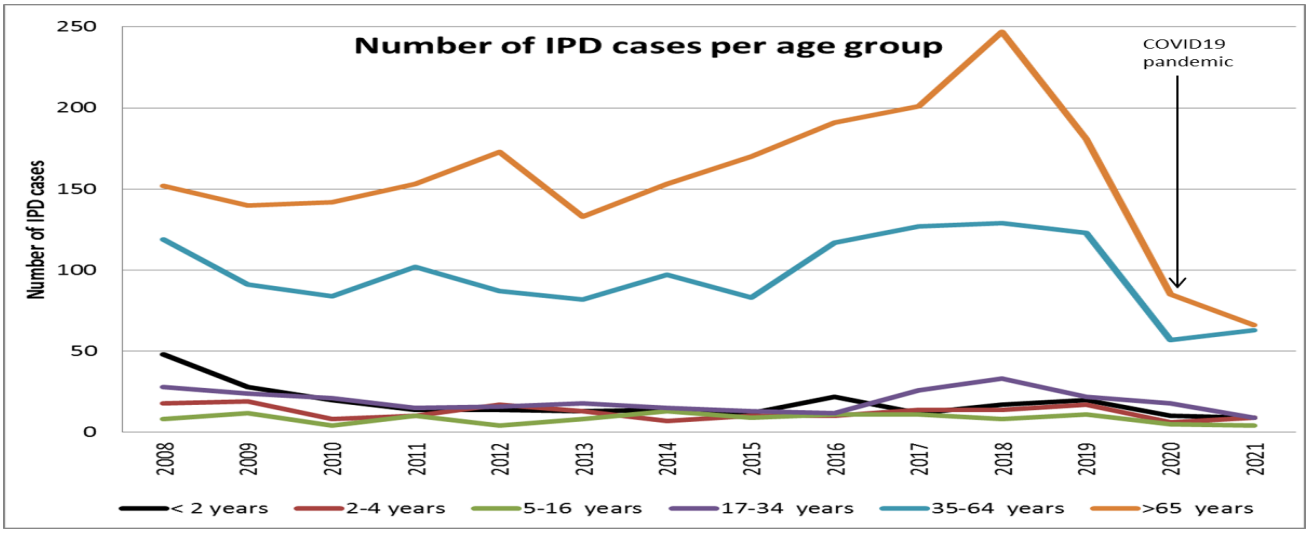

Figure 3A. Number of IPD isolates typed based on patient age from 2008-2021

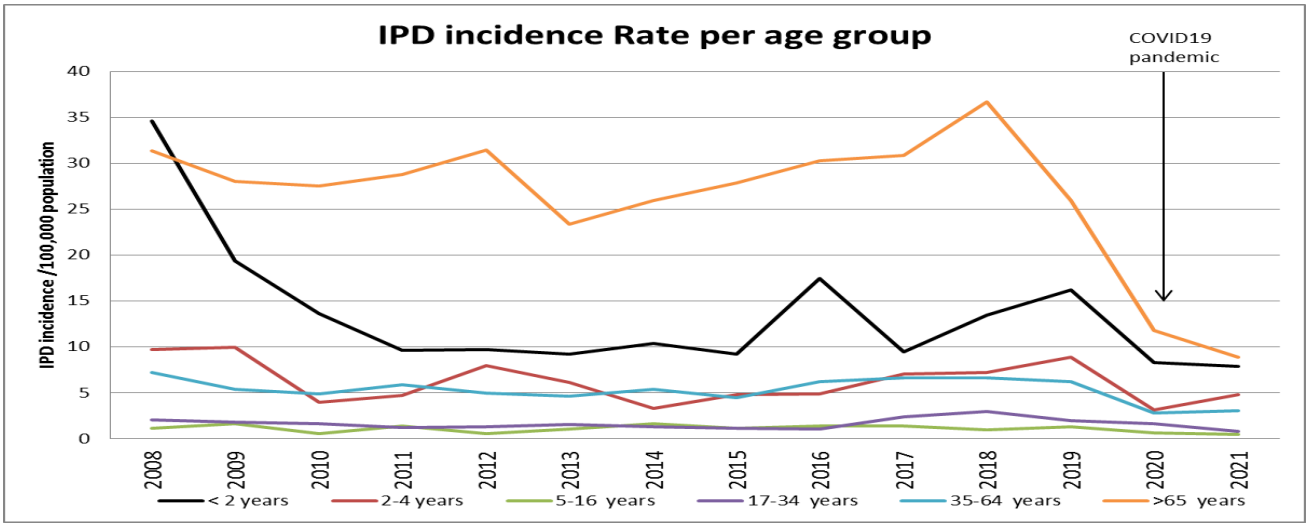

Figure 3B. Incidence Rate of IPD isolates typed based on patient age from 2008-2021

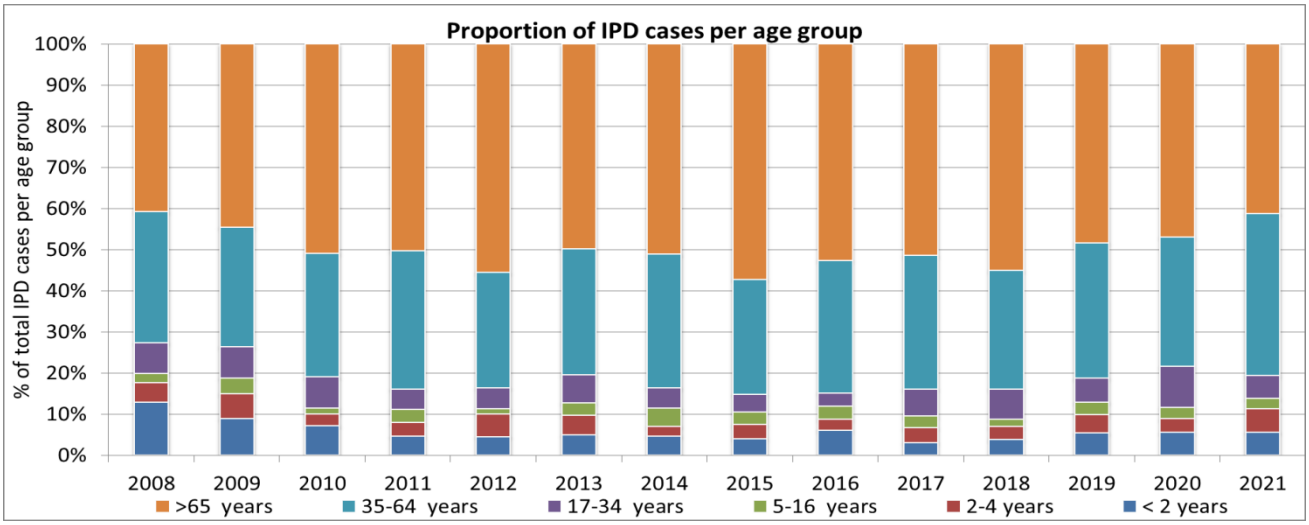

Figure 3C. Proportion of IPD isolates typed based on patient age from 2008-2021

The distribution of predominant serotypes associated with disease – All age groups

The most common serotypes in 2021 were 8 (*n*=36, 22% of IPD), 3 (*n*=16, 10%), 23B (*n*=15, 9%), 15A (*n*=12, 8%) and 19A (*n*=10, 6%). Similarly in 2019 and 2020 the predominant serotypes were 8 (*n*=98, 36; 26-30%), 19A (*n*=38, 17, 9-10%), 3(*n*=34, 13, 7-9%), 22F (*n*=18, 16, 5-9%) and 12F (*n*=27, 5; 3-7%). These predominant serotypes accounted for over half of all IPD isolates typed annually from 2019 to 2021.

Figure 4A displays the number of isolates typed in relation to PCV7 PCV13 serotypes. The proportion of PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) in 2019-2021 remained low. Similarly, the proportion of PCV13-7 serotypes (i.e. the additional serotypes in PCV13, 1, 3, 5, 6A, 7F and 19A) remained low, with the exception of serotype 3 (10% of IPD in 2021) and 19A (6%). It is also important to note that when surveillance commenced in 2008, PCV7 and PCV13-7 serotypes accounted for 48% and 23% of infection in circulation in comparison to non-PCV13 serotypes (48%). This confirms that the both PCV7 and PCV13 have offered protection against these predominant serotypes in circulation as the PCV7 and PCV13-7 serotypes accounted for only 4% and 16% of infections respectively in 2021.

However, the increase in non-vaccine types requires close monitoring. These include 22F and 33F which accounted for 5% and 4% of IPD isolates in 2021 and are covered in PCV15 and PCV20. Serotypes 8 and 15B/C, are covered in the PCV20 vaccine and accounted for 23% and 4% of IPD cases in 2021. There was also an increase in the proportion of particular serotypes not covered in any of the current (PCV7/PCV13) or new (PCV15/PCV20) vaccines**. Figure 4B** displays the predominant non-PCV20 serotypes *i.e.* serotypes not covered in PCV20, PCV15, PCV13 nor PCV7. These include an increase in serotype 35B (5% of cases in 2021), serotype 15A (7% of IPD cases in 2021) and most notably serotype 23B which increased from 3% of cases in 2019-2020 to 9% of cases in 2021). There were 15 different non-PCV20 serotypes (including not typable (NT) strains with capsular modifications) that were associated with IPD in recent years. It is possible that any of these serotypes may become predominant serotypes in the future in the same manner that serotype 23B emerged as a leading serotype in 2021. The continual change in predominant serotypes associated with IPD needs to be considered when examining current and future vaccine development and implementation.

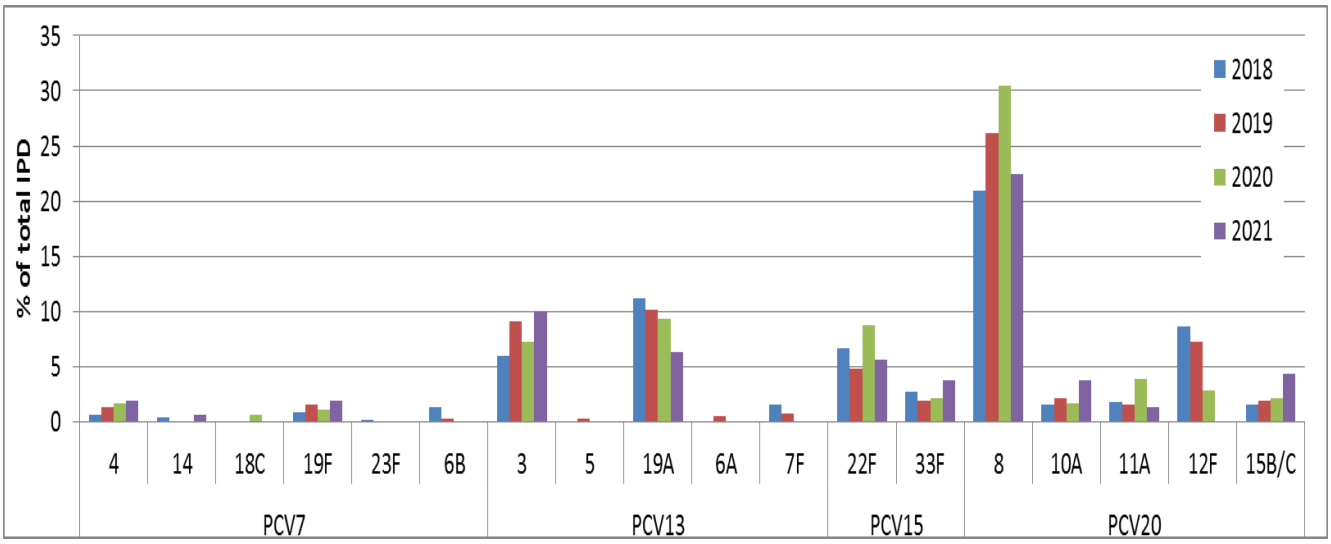

Figure 4A. Proportion of total number of isolates typed annually based on associated pneumococcal conjugate vaccines (PCV7 and PCV13-7, PCV15 and PCV20) from 2018-2021

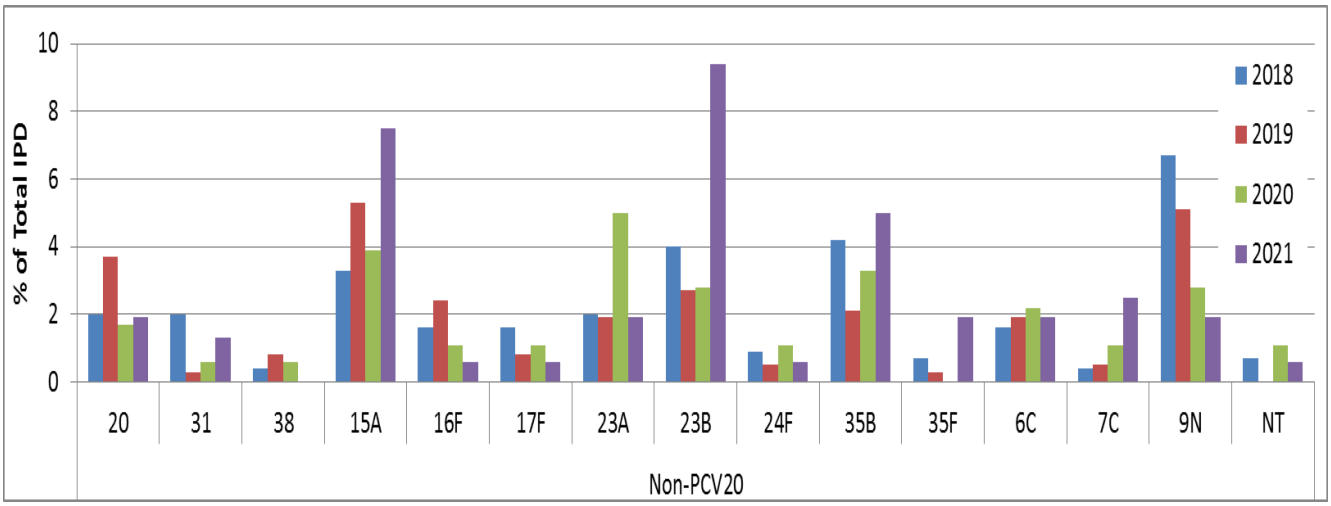

Figure 4B. Proportion of predominant non-PCV (PCV7/13/15/20) serotypes typed annually from 2018 to 2021

IPD and the distribution of serotypes amongst children

The number of IPD cases in children < 2 years decreased in 2020 (n=10) and 2021 (n=9) in comparison to 2019 (n=20). However, it was similar to other post PCV years including 2015 and 2017 (n=12 each year). A similar pattern was observed in older children aged 2-4 years and those aged 5-16 years. The incidence of IPD in children ≤ 16 years of age fell from IR=4.2/100,000 in 2019 to IR=2.0/100,000 in 2021 (**Figure 5**). Overall, the incidence rate in children ≤ 16 years fell from IR=7.2/100,000 when PCV7 was introduced in 2008 to between IR=2.8-3.4/100,000 from 2010 to 2018. This demonstrates the very positive benefits of PCV7 and PCV13 introduction to the paediatric vaccine schedule. This was further evident by examining the proportion of PCV serotypes associated with disease in young children. When PCV7 was introduced in 2008, these serotypes

accounted for over 60% of cases in children, but since 2019, PCV7 serotypes have accounted for only 0-5% of cases. The proportion of cases covered in PCV13 (which includes PCV7 serotypes) has also declined from 78% of cases in 2010 to 23% of cases by 2019 and 5% by 2021.

Based on the data from 2021, the two new vaccines (PCV15 and PCV20) would also offer limited protection to children as the proportion of PCV15 serotypes fell from 29% in 2019 to 9% in 2021 and PCV20 serotype coverage fell from 63% in 2019 to 36% in the same period (**Figure 5**). This was mainly due the rise of the non-vaccine serotype 23B which emerged post-vaccine introduction and represented 3% of paediatric cases in 2012 (n=1/35) but represented 10% (n=2/21) and 41% of cases (n=9/22) in 2020 and 2021, respectively (**Figure 6**). The isolates were mainly associated with young children aged from <2 years (n=4) and 2-5 years (n=4), with only one isolate being from an older child. Of the nine cases in 2021, there was no indication of potential clusters or outbreaks as the isolates were from seven different hospitals at different time periods. Serotype 23B has emerged as a vaccine replacement serotype elsewhere [11, 12]. Conversely serotype 12F, which was previously a predominant vaccine-replacement serotype and represented 10% in 2019 in children <16 years was not isolated in children in neither 2020 nor 2021.

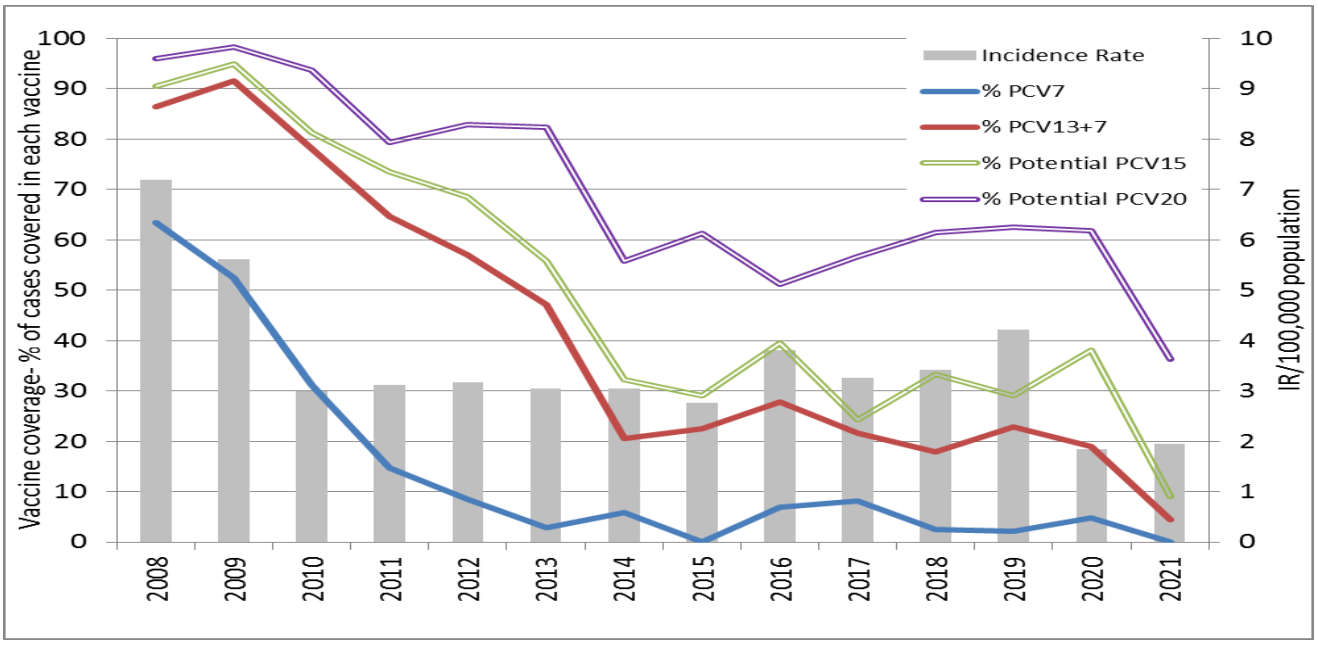

Figure 5. Vaccine coverage for children ≤16 years of age based on proportion of IPD cases caused by a vaccine-preventable serotypes (PCV7, PCV13, PCV15, PCV20) from 2008 to 2021

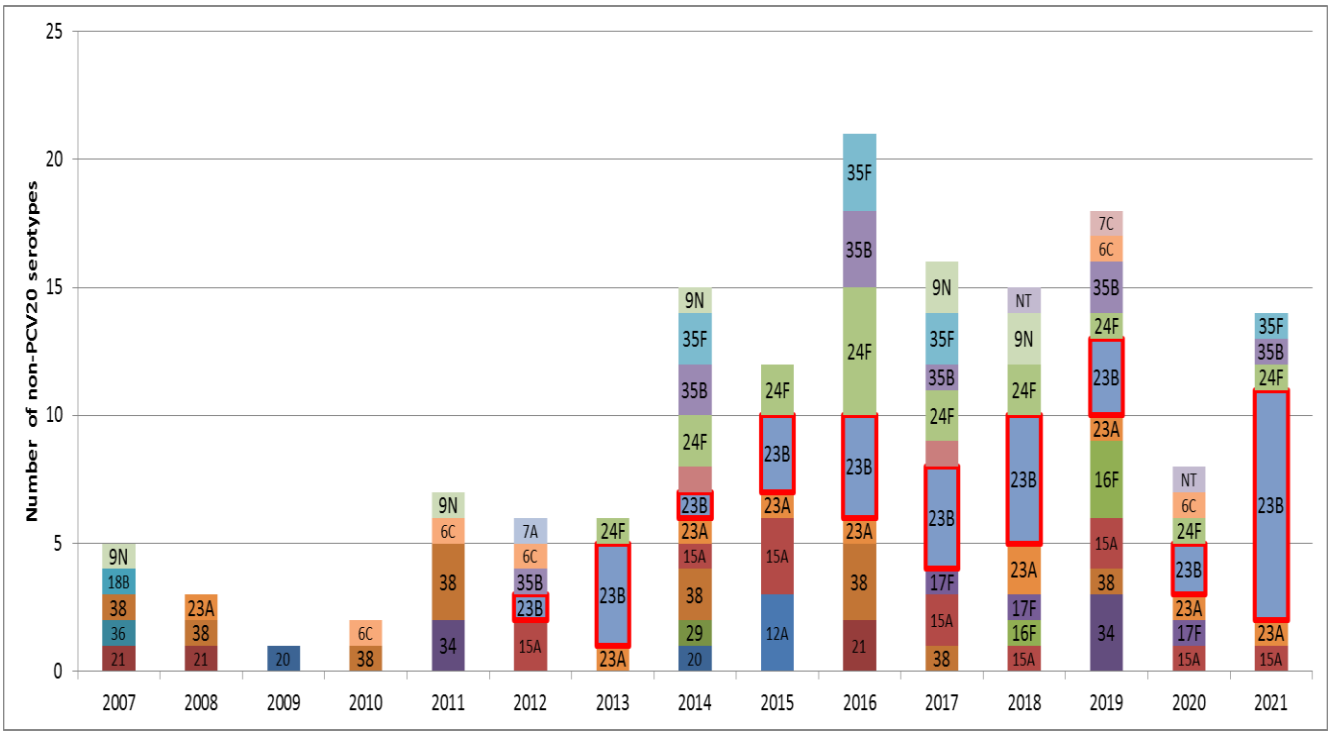

Figure 6. Predominant serotypes associated with IPD in children ≤16 years of age not associated with PCV20 (i.e. also not covered in PCV7, PCV13, PCV15) from 2008 to 2021

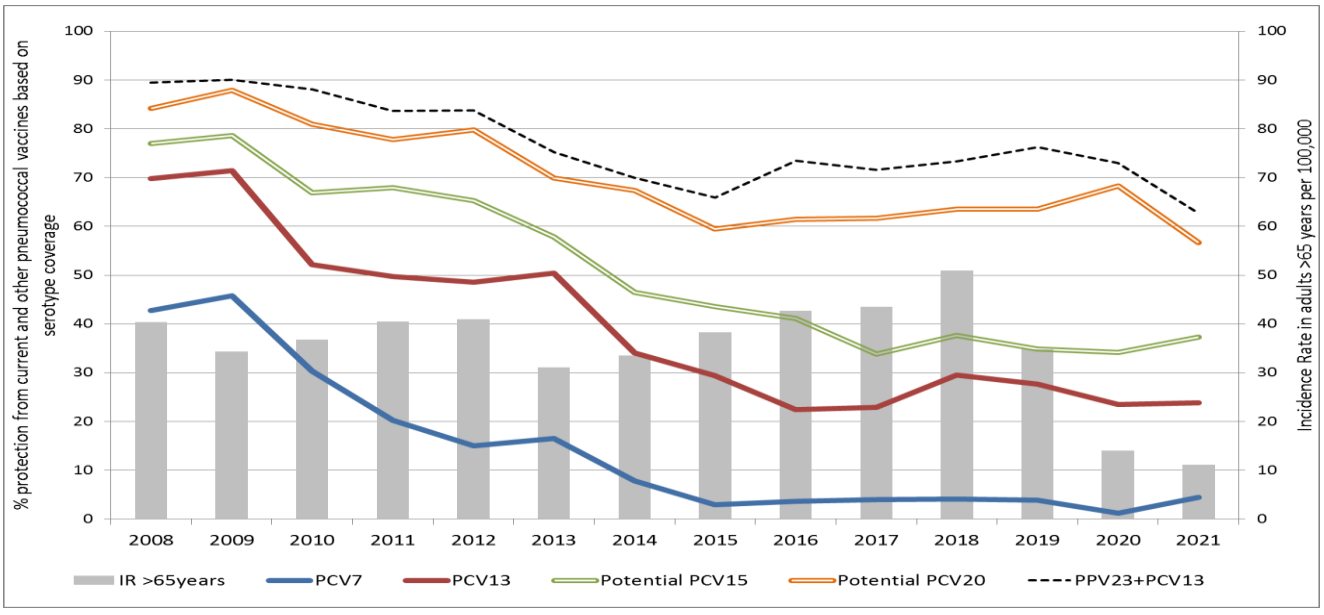

Figure 7. Vaccine coverage for adults ≥65 years of age based on proportion of IPD cases caused by a vaccine-preventable serotypes (PCV7, PCV13, PCV15, PCV20, PPV23) from 2008 to 2021.

IPD and the distribution of serotypes associated with adults ≥65 years of age

The number of cases and IR in adults ≥65 years declined in 2020 and 2021 (**Figure 7**). With uptake of PPV23 markedly low in Ireland (27-36%), it is difficult to assume that vaccination may have impacted serotype epidemiology. Similar to the results in children, the number of PCV7 cases dropped after the vaccine was introduced to the paediatric schedule, which was indicative of herd immunity which has been discussed elsewhere. While most PCV13 cases declined in recent years, two predominant PCV13 serotypes persisted in 2020 and 2021. Serotype 19A represented 15% and 7% of cases in older adults in 2020 and 2021 while serotype 3 represented 7% and 12% in 2020 and 2021, respectively. Aside from those serotypes most other IPD cases were associated with non-PCV13 serotypes.

Overall the predominant non-PCV13 serotypes in adults ≥65 years of age in 2020 and 2021 included serotype 22F (7% and 8%) which is covered in PCV15 and PCV20, serotype 8 (28%, 12%) which is covered in PCV20 and 35B (5%,9%) which is not covered in any of the PCV's. Serotype 23B, which emerging in the paediatric cases also increased from 1% in 2020 to 6% of cases in 2021 in older adults. As displayed **Figure 7** increased vaccination uptake (PPV23) or changes in the vaccine schedule (to include PCV15 or PCV20) could provide protection against IPD serotypes associated with older adults. In 2021, 37%, 57% and 63% of IPD cases were caused by serotypes covered in PCV15, PCV20 and PPV23, respectively. While polysaccharide vaccines are not reported to provide as effective immune response in older adults in comparison to conjugate vaccines (PCVs), a single dose of PCV13 prior to PPV23 immunisation was initially recommended for older adults in the US to improve the immune response. These recommendations have now changed to include recommendations of PCV15 and PCV20 [13]. In Ireland, a single dose of PCV13 prior to PPV23 administration is recommended for those with immunosuppressive conditions or co-morbidities. However, based on the IPD data from 2021, between 24-57% of IPD cases were PCV15-PCV20 vaccine preventable. Therefore direct immunisation, rather than herd protection from PCV13 in children could reduce the burden of disease in this population. While PPV23 coverage was also high in this population (63% coverage in 2021), low uptake and waning immunity reported elsewhere, direct vaccination with a PCV may provide greater protection to older adults who now bear the highest disease burden. There may also be a case for including one of the new PCVs in the immunisation of older people and immunosuppressed adults, with or without the continued use of PPV23 in the same age categories.

The distribution of serotypes associated with antimicrobial resistance

Overall, 17-19% of IPD isolates in 2020 and 2021 displayed reduced susceptibility to penicillin using the EUCAST breakpoints. This is a marked decline in comparison to 22% in 2018 and may reflect the changes in serotype epidemiology, such as a decline in 19A. A similar trend was observed with erythromycin with a reduced susceptibility rate of 20% in 2020 and 15% in 2021, this had increased in comparison to other years such as 2018 (16%). The number of isolates with reduced susceptibility to cefotaxime continued to fall in 2020 and 2021 and remained at ≤ 5% since 2014. Similar to previous years, a small number of serotypes are responsible for most reduced susceptibility to antimicrobials as displayed in **Figure 8**. The isolates with reduced susceptibility to penicillin in 2020 and 2021 included PCV7 serotypes 19F, PCV13 serotype 19A, PCV20 serotype 15B/C and a number of non-PCV serotypes including 15A, 23B and 35B.

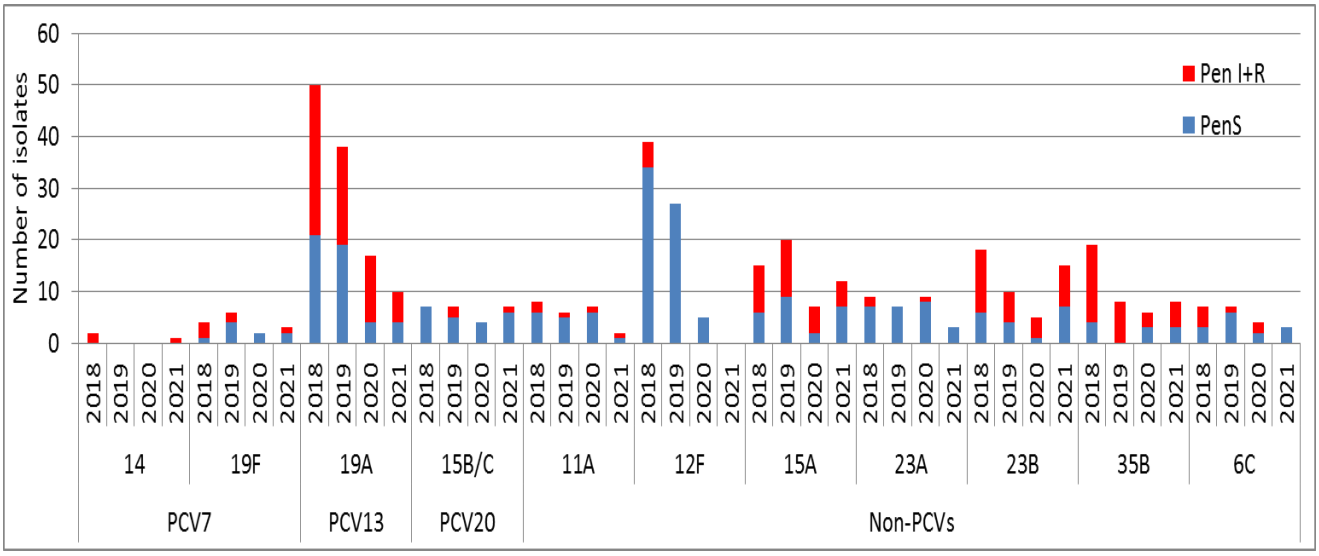

Figure 8. The number of penicillin non-susceptible *S. pneumoniae* (PNSP) isolates categorised by serotype in 2018-2021

As indicated in **Figure 9**, the PNSP prevalence rate increased in children increase, particularly in children < 2 years of age which increased from 10% (n=2/20) in 2019 to 33% (n=3/9) in 2021. Similarly the percentage of cases in children aged 5-16 years of age increased from 9% in 2019 (n=1/11) to 50% (n=2/4) in 2021. This increase was accompanied by an overall drop in the number of isolates received. However, an increase in PNSP isolates such as 23B, 35B and 15B/C is of particular concern as serotypes 23B and 35B are not covered in the current new vaccines currently approved for use in Europe. There was a decline of PNSP isolates in older adults, which fell from 28% (*n*=69/247) in 2019 to 18% (*n*=12/66) in 2021. This was mainly due to a decline in 19A in 2021, in particular. Overall, there were limited differences between the HSE areas aside from an

increase in PNSP isolates from the Mid-West region in 2020 and in the Western region in 2018 and 2021. However when the mean for each area was calculated (**Figure 9**), there was very little variation annually.

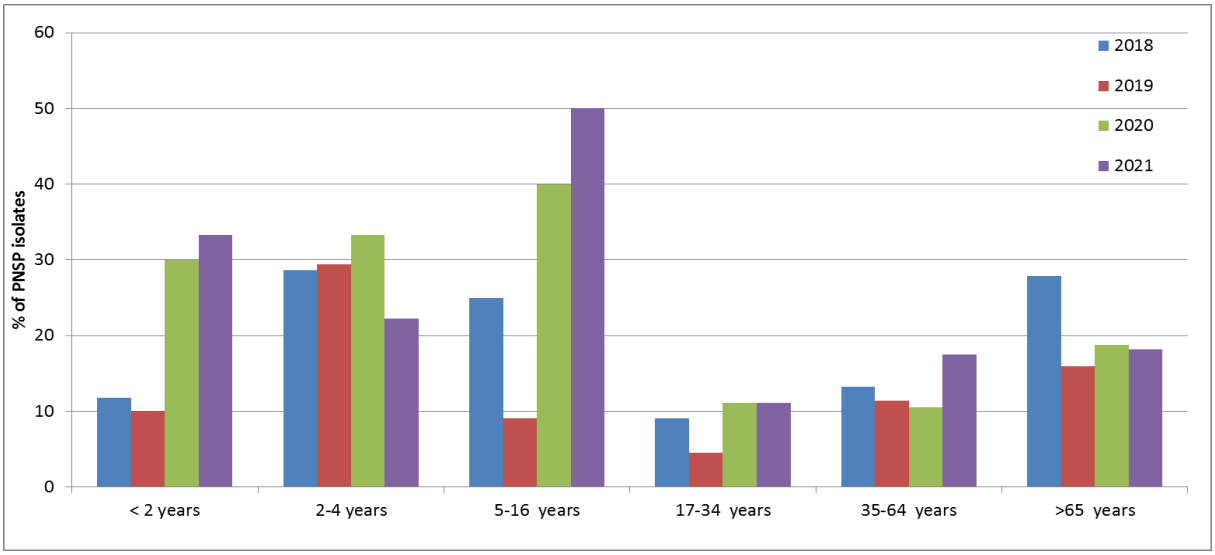

Figure 9. The percentage of penicillin non-susceptible pneumococci (PNSP) per age group from 2018 to 2021

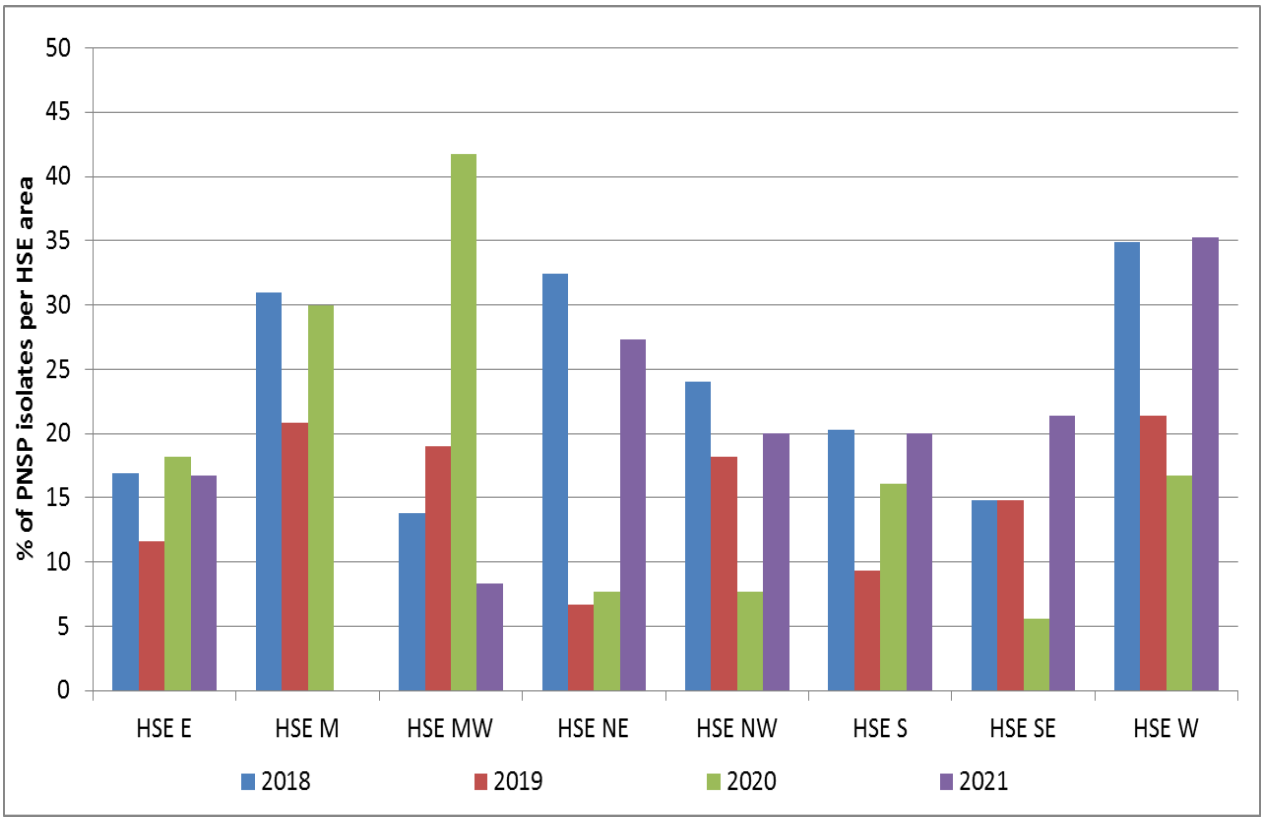

Figure 10. The percentage of penicillin non-susceptible pneumococci per HSE area from 2018 to 2021

3. Implications and the future

Continued national surveillance of serotypes causing IPD is necessary to: monitor the epidemiology of IPD in Ireland, assess the effectiveness of the national vaccination programme in Ireland, detect the presence of non-vaccine serotypes and monitor the emergence of replacement serotypes, and their association with antibiotic resistance. All this also contributes to European IPD surveillance networks and to public health.

Ireland has a relatively high incidence of PNSP isolates in comparison to other EU countries, and we need to monitor these rates in conjunction with improvements in antimicrobial prescribing practices. The results of this report demonstrate that the introduction of the PCV7/13 resulted in a reduction in the number of IPD isolates and led to the reduction in the PNSP rate in subsequent years. However, the proportion of PNSP isolates is unstable with an increase in number of PNSP isolates in children. The emergence of non-vaccine associated serotypes that are also associated with resistance, particularly those not covered in the two vaccines (PCV15/PCV20) recently approved for use in Europe is of concern. However, it is important to note that these new vaccines could still reduce the burden of disease in older adults as PCV15 and PCV20 serotypes still account for 37-57% of cases in this patient group.

4. Acknowledgements

We wish to thank all the laboratory scientists and consultant microbiologists in Irish hospitals for forwarding pneumococcal isolates, and departments of public health and all involved with surveillance of pneumococcal disease in Ireland. We are also grateful for the assistance of the staff of the Departments of Clinical Microbiology, RCSI, and CHI at Temple Street. This work was funded by the HPSC and previously with support from Pfizer Healthcare Ireland. A WGS research study was funded by an Investigator Initiated Research grant from Pfizer (W1243730). Pfizer did not have a role in data collection, study design, writing or decision to submit manuscripts for publication. Surveillance work was also supported by the ECDC (SpIDnet project) and the European Commission (Horizon 2020).Additional data on IPD in Ireland is available on the HPSC website: http://www.hpsc.ie/A-Z/VaccinePreventable/PneumococcalDisease/

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Recent Manuscripts with Irish IPD data

- Corcoran, M., Mereckiene, J., Cotter, S., Murchan, S., Lo, S.W., McGee, L., Breiman, RF., **Cunney, R.,** Humphreys, H., Bentley, S.D., Gladstone, R.A. Using genomics to examine the persistence of *Streptococcus pneumoniae* serotype 19A in Ireland and the emergence of a sub-clade associated with vaccine failures. *Vaccine* 2021 Jul 20;S0264-410X(21)00741-6. https://doi.org/10.1016/j.vaccine.2021.06.017
- Corcoran, M., Mereckiene, J., Cotter, S., Murchan, S., Cunney, R. and Humphreys, H. Invasive *Streptococcus pneumoniae* Infections and Vaccine Failures in Children in Ireland from the postvaccine Era From 2007 to 2018. The Pediatric Infectious Disease Journal 2020 April; 39(4): 339-344
- **As part of The Pserenade Team.** Serotype Distribution of Remaining Pneumococcal Meningitis in the Mature PCV10/13 Period: Findings from the PSERENADE Project. *Microorganisms* 2021, 9, 738. https://doi.org/10.3390/microorganisms9040738
- **As part of The Pserenade Team.** Global Landscape Review of Serotype-Specific Invasive Pneumococcal Disease Surveillance among Countries Using PCV10/13: The Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) Project *Microorganisms* 2021, 9, 742. https://doi.org/10.3390/microorganisms9040742
- **As part of the The IRIS Consortium:** Changes in the incidence of invasive disease due to *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis* during the COVID-19 pandemic in 26 countries and territories in the Invasive Respiratory Infection Surveillance Initiative: a prospective analysis of surveillance data. *Lancet Digital Health* 2021 Jun;3(6):e360-e370. http://dx.doi.org/10.1016/S2589-7500(21)00077-7.
- **As part of SpIDnet team**. Serotype replacement after the introduction of 10 and 13-valent pneumococcal conjugate vaccines in 10 European countries: results from the SpIDnet multicentre study. *Emerging Infectious Diseases* 2022 Jan;28(1):137-138. DOI: 10.3201/eid2801.210734

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May 2022