Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

hpsc

2006

EPIDEMIOLOGY OF INVASIVE *STREPTOCOCCUS PNEUMONIAE* INFECTION, IN IRELAND

cidr

Table of Contents

Acknowledgements

The authors wish to thank all who participated in the surveillance of invasive pneumococcal disease in Ireland and provided data for this report – Departments of Public Health, Microbiology Laboratories and Clinicians.

Authorship:
This report was written by Dr Margaret Fitzgerald and edited by Dr Suzanne Cotter, HPSC.

Citation:
Epidemiology of invasive *Streptococcus pneumoniae* infection in Ireland, 2006. Health Protection Surveillance Centre, October 2007.

Further information:
For further details on invasive pneumococcal disease in Ireland, please see http://www.ndsc.ie/hpsc/A-Z/VaccinePreventable/PneumococcalDisease/

Summary

Two data sources are used in this report to describe the epidemiology of invasive pneumococcal disease (IPD) in 2006 in Ireland, namely the infectious disease notifications and data from the European Antimicrobial Surveillance System (EARSS).

Based on the notification data, 293 (6.9/100,000) cases of IPD were notified in 2006, increasing from 271 (6.4/100,000) and 175 (4.1/100,000) in 2005 and 2004, respectively. In 2006, more cases occurred in males than in females (1.3:1.0). Cases ranged in age from 1 month to 100 years; median age 52.5 years. The burden of disease was highest in the very young and the very old. The age specific incidence rate in infants (<1 year old) was 44.2 per 100,000 while in the elderly adults, 85 years of age and older, it was 45.8 per 100,000. Seven deaths due to IPD were reported in 2006, all occurred in adults. However, this figure may be an underestimate of the true IPD mortality since outcome was not reported for 90% of the notifications.

Based on the EARSS data similar trends were noted with respect to gender and age. However, the overall incidence of the disease was higher when compared with notification data. Through EARSS, 407 cases of IPD were reported (9.6/100/000) in 2006, which is similar with previous years when 401 and 400 cases were notified in 2005 and 2004, respectively. Therefore, notification data underestimates by as much as 39% the burden of IPD in Ireland when compared with EARSS data.

In 2006, just 15% of all *Streptococcus pneumoniae* isolates reported through EARSS were typed. The 23-valent pneumococcal polysaccharide vaccine, PPV23, would have covered 98% of the isolates typed while 55% would have been covered by the 7-valent conjugate vaccine, PCV7. In children under 2 years of age, 79% of isolates typed would have been covered by the PCV7 formulation and in adults 65 years of age or older, 95% of the isolates typed were covered by PPV23.

Introduction

Invasive infections due to *Streptococcus pneumoniae* include conditions such as septicaemia and meningitis. For the purposes of this report the term invasive pneumococcal disease (IPD) will be used to describe these infections. IPD is a disease mainly of young children and older adults. Individuals with severe chronic conditions or immunodeficiencies are also at increased risk of this disease. The treatment of IPD is complicated by the emergence of *S. pneumoniae* strains resistant to penicillin. The prescribing of broad-spectrum antibiotics or third or fourth line antibiotics in the community have been identified as likely contributors to the rising levels of antimicrobial resistance in *S. pneumoniae*. The proportion of penicillin non-susceptible *S. pneumoniae* (PNSP) in some European countries is now over 35%.[1] In Ireland, the annual trends now indicate that the proportion of PNSP has increased from just over 10% in 2004 to almost 16% in 2006.[2]

A substantial proportion of IPD can be prevented by vaccination. Two types of pneumococcal vaccine are available. The pneumococcal polysaccharide vaccine contains capsular antigens to 23 serotypes (PPV23), which are associated with 90% of pneumococcal infections. This vaccine is not recommended for children under 2 years of age, as it is poorly immunogenic in this age group. The 7-valent pneumococcal conjugate vaccine (PCV7) contains capsular polysaccharide antigens to seven serotypes associated with approximately 70% of pneumococcal infections. The polysaccharide component of this vaccine is conjugated to a carrier protein (non-toxic diphtheria CRM_{197} protein); it thereby elicits a T-cell dependent response and immunological memory even in infants and thus protects infants and young children against pneumococcal disease.

Following the introduction of PCV7 to the universal childhood immunisation programme in the United States in August 2000, reports have demonstrated that PCV7 is highly effective in reducing the burden of pneumococcal disease in children <5 years of age, and there is evidence of a herd immunity as well as a decrease in antibiotic resistant strains causing disease.[3-4] Therefore, the indications are that preventing the occurrence of IPD through vaccination may help alleviate the challenges of antibiotic resistance due to this organism.
In 2006, both the Netherlands and the United Kingdom introduced PCV7 to their respective routine infant immunisation schedules. Canada, Australia, Norway, Italy, Greece, Spain, Austria, Switzerland also offer universal pneumococcal vaccination in their infant schedules. Other countries, including Ireland, have selective immunisation programmes at present whereby PCV7 is offered to infants and children considered to be at increased risk of IPD.
In a recent position paper published, the World Health Organisation (WHO) considers it a priority to include PCV7 in national immunisation programmes, taking into account the heavy burden of IPD occurring in young children and the availability now of a safe, effective vaccine for this age group.[5]

In this report the epidemiology of IPD in Ireland in 2006 is reviewed.

Case Definitions [6]

For the purposes of surveillance cases of invasive *Streptococcus pneumoniae* infections are classified as confirmed, probable or possible.

Clinical description – *S. pneumoniae* causes many clinical syndromes, depending on the site of infection.

A **Confirmed** case is a clinically compatible case that has been laboratory confirmed by one of the following:

- Isolation of *S. pneumoniae* from a normally sterile site (e.g. blood, cerebrospinal fluid, joint, pleural or pericardial fluid)
- Detection of *S. pneumoniae* nucleic acid from a normally sterile site.

A **Probable** case is a clinically compatible case with detection of *S. pneumoniae* antigen from a normally sterile site.

A **Possible** case is a clinically compatible case without any laboratory confirmation or with identification from a non-sterile site.

Materials and Methods

Two data sources are used by HPSC in examining the epidemiology of invasive pneumococcal disease (IPD) in Ireland, namely notifiable infectious disease data and data from the European Antimicrobial Surveillance System (EARSS).

Invasive pneumococcal disease has been a notifiable disease in Ireland since 1st January 2004, when the Infectious Diseases (Amendment) (No. 3) Regulations 2003 (SI No. 707 of 2003) came into effect. Laboratories and clinicians are legally obliged to notify. In 2006, for areas using the Computerised Infectious Disease Reporting (CIDR) system, IPD data were entered directly by the regions. For areas not yet on the system, notifications were sent weekly to HPSC from where the data were entered on CIDR. Following year-end, data cleaning and validation were undertaken between HPSC and the Departments of Public Health in the HSE areas. The IPD notification data were extracted from CIDR on the 9th August 2007. These figures may differ from those published previously due to ongoing updating of notification data on CIDR.

In 2006, 42 laboratories participated in the EARSS project in Ireland, giving an estimated population coverage of 98%. In the case of *S. pneumoniae*, the participating laboratories collected data on the first invasive isolate per patient per quarter from blood or CSF. These data were submitted quarterly to HPSC where data were collated in the WHONET database, from which the data for this report were extracted in August 2007.

Denominator data used for the calculation of incidence rates were taken from the 2006 Census of Population.

Results

Infectious Disease Notification Data

IPD Notifications

In 2006, 293 cases of IPD (6.9/100,000) were notified in Ireland through the weekly infectious disease notification system. This was an increase from both 2005 and 2004, when 271 (6.4/100,000) and 175 (4.1/100,000) cases were notified respectively (figure 1).

In 2006, 247 cases were classified as confirmed, 34 as probable and 12 as possible. The clinical diagnosis was reported in just 55 of the cases. The clinical manifestations of the disease were meningitis (n=18), septicaemia (n=17), meningitis and septicaemia (n=5), pneumonia (n=14) and peritonitis (n=1). Clinical diagnosis was not reported for the remaining 238 IPD notifications (81%).

More IPD cases occurred in males (n=166) than in females (n=127) in 2006, the male to female ratio was 1.3:1.0. Cases ranged in age from 1 month to 100 years, with a median age of 52.5 years. Over half of the IPD cases notified in 2006 occurred in the very young or the very old, 19.5% (n=57) of cases were in children <5 years of age and 34.1% (n=100) were in elderly adults ≥65 years.

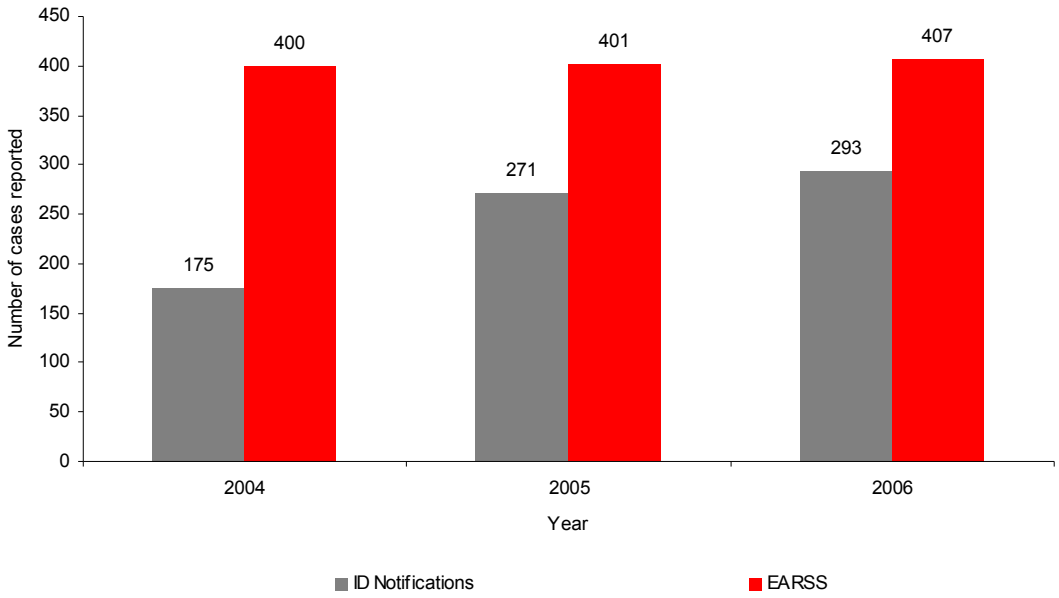

Figure 1. *Number of invasive pneumococcal disease (IPD) cases reported through the infectious disease notification system and EARSS, 2004-2006*

IPD notifications by age

In children the burden of IPD was highest in infants <1 year of age (44.2/100.000), followed by the 1-2 year olds (19.0/100,000). Thereafter, the incidence dropped to <10 cases per 100,000 population for those in the 3-59 years age groups (figure 2). From the age of 60 onwards the incidence of IPD increased with increasing age, from 11 cases per 100,000 population in 60-64 year olds, rising to 23.8 per 100,000 in 75-79 year olds and reaching the highest incidence rate in those 85 years and older, at 45.8 cases per 100,000.

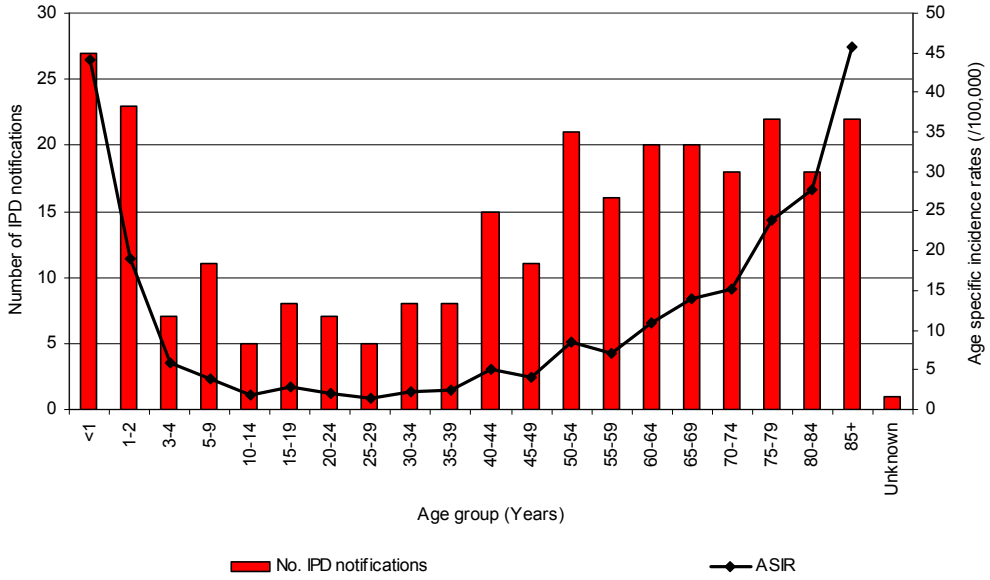

Figure 2. *Number and age specific incidence rates of IPD by age group, 2006*

Looking more closely at IPD incidence rates in infants and children in 2006 the age specific incidence rates were highest by far in the 6-11 month olds (58.9/100,000), followed by the <6 month olds (29.5/100,000). The latter was followed closely by the 12-17 and 18-23 months olds, both age groups had incidence rates of 23.2/100,000. Thereafter, the incidence of IPD declined (figure 3).

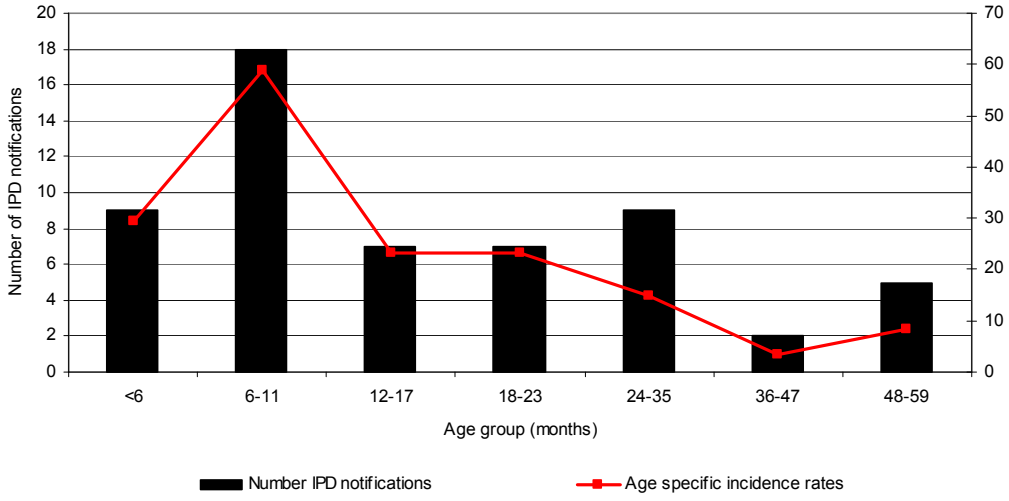

Figure 3. *Number and age specific incidence rates of IPD in infants and children, 2006*

IPD notifications by HSE area

The national crude incidence rate of IPD in 2006 was 6.9 per 100,000 total population. The incidence of IPD was highest in HSE-NW (20.2/100,000) and HSE-SE (15.2/100,000) and lowest in HSE-M (1.2/100,000) (table 1).

The high incidence of IPD notifications in HSE-NW can partly be attributed to an outbreak due to *S. pneumoniae*, which occurred in a residential institution in June/July of 2006, involving mainly middle aged and elderly patients. The total number of people ill was 19. Individual notifications were received for 18 of these cases (2 confirmed, 5 probable and 11 possible). The cases associated with this one outbreak accounted for 38% of IPD notifications from HSE-NW in 2006.

The high incidence rates of IPD in HSE-SE may be a reflection of the range of diagnostic methods used and reported on. In addition to culture and PCR methods (confirmed cases), the urinary antigen test is also used (probable cases) and positive results notified. Forty one percent of notifications (29/70) from HSE-SE in 2006 were classified as probable based on positive urinary antigen tests for *S. pneumoniae* taken from patients with clinical symptoms suggestive of invasive pneumonia. Apart from HSE-NW no other HSE area reported probable IPD cases (table 1).

Table 1. *Number of IPD notifications by case classification, 2006*

	Confirmed	Probable	Possible	Total	CIR*
HSE-E	104	0	0	**104**	6.9
HSE-M	3	0	0	**3**	1.2
HSE-MW	21	0	0	**21**	5.8
HSE-NE	20	0	0	**20**	5.1
HSE-NW	32	5	11	**48**	20.2
HSE-SE	41	29	0	**70**	15.2
HSE-S	19	0	1	**20**	3.2
HSE-W	7	0	0	**7**	1.7
Ireland	**247**	**34**	**12**	**293**	6.9

*CIR, crude incidence rate per 100,000 population

IPD deaths

Seven deaths due to IPD were reported in 2006. Three occurred in patients with meningitis, three with pneumonia and one with septicaemia. All deaths were in adults, age range 43-80 years, and five of these deaths were in elderly adults >65 years of age. It should be noted that outcome was not reported or reported as unknown for the vast majority of the notifications (90%, 264/293). Therefore, the figures presented in this report may underestimate mortality due to IPD in Ireland, in 2006.

EARSS Data

EARSS ~ IPD by age

The number of *S. pneumoniae* isolates reported through the European Antimicrobial Surveillance System (EARSS) has remained stable over the last three years, ranging between 400 reports in 2004 and 407 in 2006 (9.4-9.6/100,000) (figure 1). As with the notification data, predominantly more male than female cases of IPD were reported through EARSS in 2006 with the same male to female ratio being reported by both systems, 1.3:1.0.

The age-specific incidence rates of IPD as reported through EARSS in 2006 followed a similar trend as the notification data with the very young and the very old being most affected (figure 4). The incidence rate was 40 per 100,000 or greater in the <1 year olds (49.1/100,000) and the 75-79 year olds (40/100,000), 80-84 year olds (58.6/100,000) and 85 year olds and older (85.4/100,000). For the vast majority of the age groups, the incidence of IPD was higher when reported through EARSS than by the notification system. The difference in incidence rates reported between the two systems was small for infants, children and young to middle-aged adults whereas with increasing age, especially from the age of 55 years onwards the differences were substantial, with considerably more cases reported through EARSS than via the infectious disease notification process (figure 4).

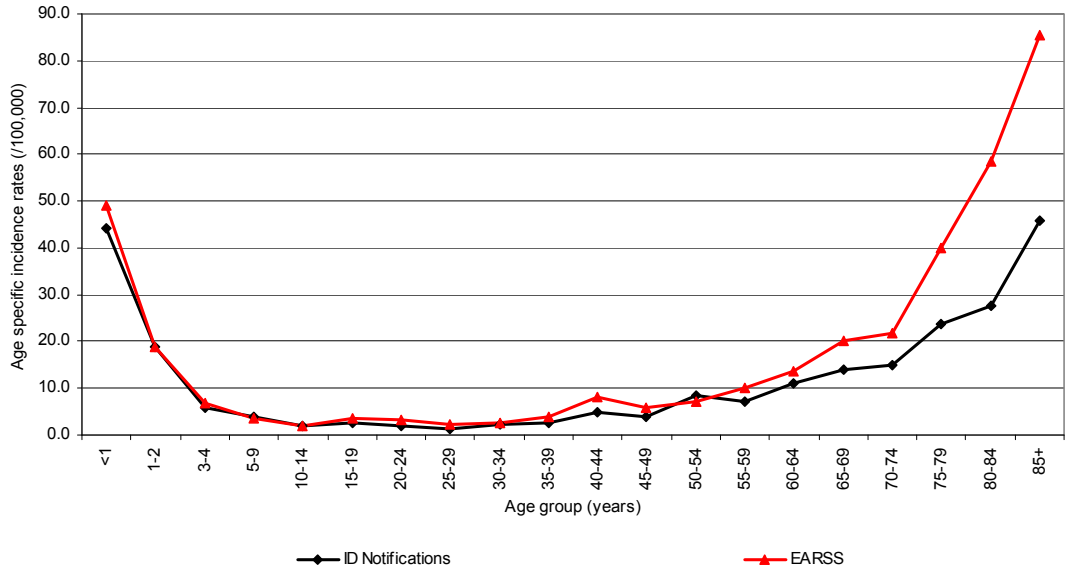

Figure 4. *Age specific incidence rates of IPD cases reported in 2006 through the infectious diseases notification process and EARSS*

EARSS ~ IPD by HSE area

Based on the EARSS data, the incidence of IPD was highest in HSE-NW (14.3/100,000) and HSE-E (13.0/100,000) and lowest in HSE-NE (3.8/100,000). The low HSE-NE incidence rate was due to a reporting artefact as one laboratory in this area is not currently participating in EARSS. Thus, the true burden of IPD in this area is most likely to be underestimated (figures 5a-5b).

So that EARSS and notification data are comparable by area, only confirmed cases are included for the latter. Compared with the EARSS data, the notification data underestimates the burden of IPD in five of the eight HSE areas (figures 5a and 5b). In four of these areas the magnitude of this underestimation ranges between 88-633%. Overall, the burden of confirmed cases of IPD is 65% higher when determined using EARSS data (figure 5b).

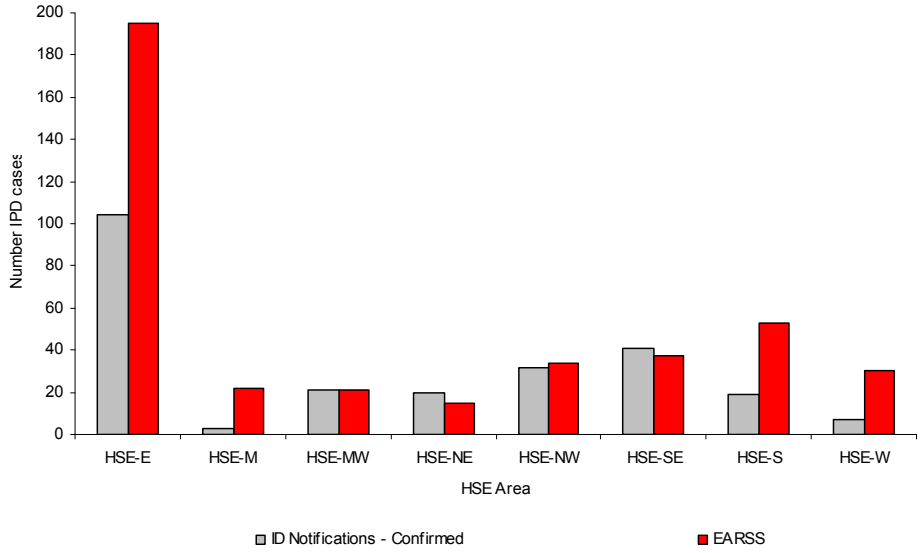

***Figure 5a**. Number of IPD cases by HSE area in 2006 reported through the infectious disease notification system and EARSS*

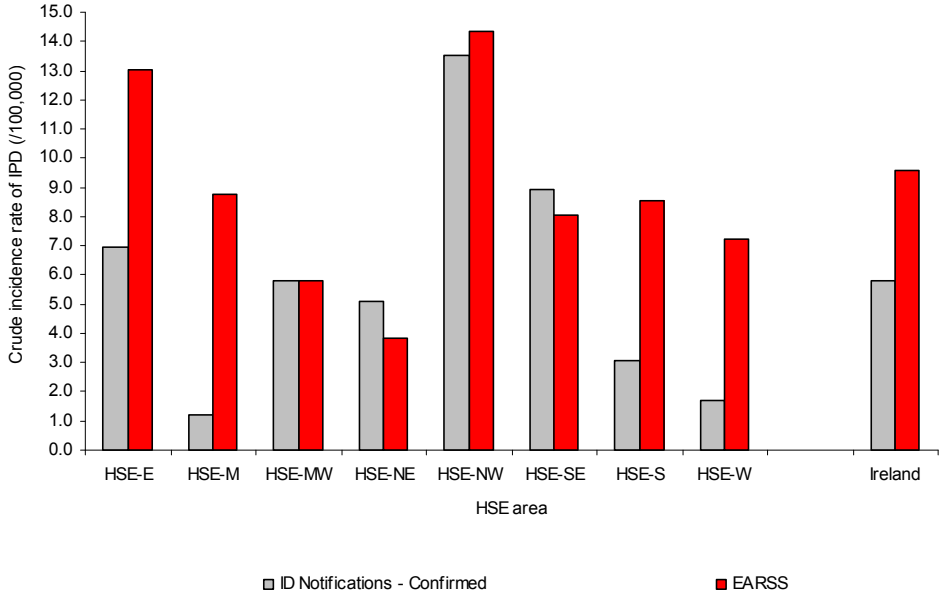

***Figure 5b**. Crude incidence rates (per 100,000) of IPD cases by HSE area in 2006 reported through the infectious disease notification system and EARSS*

EARSS – IPD by serotype

In 2006, just 15% (60/407) of all *S. pneumoniae* isolates reported through EARSS were typed, with five of the 42 laboratories participating. The predominant types identified were 6B, 4, 1, 3, 9V and 14 (table 1). These accounted for 58% of the typed isolates. The 23-valent pneumococcal polysaccharide vaccine, PPV23, would have covered 98% of the isolates typed while 55% would have been covered by the 7-valent conjugate vaccine, PCV7. In children under 2 years of age, 79% of isolates typed would have been covered by the PCV7 formulation and in adults 65 years of age or more, 95% of the isolates typed would have been covered by PPV23.

Table 1. Number of *Streptococcus pneumoniae* isolates by type, 2006

	Number of isolates			Types covered by	
Serotype	**All ages**	**<2 years**	**65 years +**	**PPV23**	**PCV7**
1	6	0	0	**Yes**	No
3	5	0	3	**Yes**	No
4	6	0	2	**Yes**	**Yes**
6B	8	4	3	**Yes**	**Yes**
7F	3	2	1	**Yes**	No
8	3	0	1	**Yes**	No
9N	1	0	0	**Yes**	No
9V	5	1	2	**Yes**	**Yes**
10A	2	0	1	**Yes**	No
14	5	3	1	**Yes**	**Yes**
15A	1	0	1	No	No
18C	4	2	1	**Yes**	**Yes**
19A	3	1	0	**Yes**	No
19F	1	1	0	**Yes**	**Yes**
22F	2	0	2	**Yes**	No
23F	4	0	2	**Yes**	**Yes**
33F	1	0	1	**Yes**	No
Total	**60**	**14**	**21**	**Yes**	No
% PPV23*	**98.3**	**NA**	**95.2**		
% PCV7*	**55.0**	**78.6**	**NR**		

* % isolates typed covered by pneumococcal vaccines
NA – Not applicable, since PPV23 not immunogenic in children <2 years of age
NR – Not relevant, since PCV7 not recommended in adults as PPV23 effective in this age group and is also protective against greater number of serotypes

Discussion

Notification data underestimates the burden of IPD in Ireland when compared with the EARSS data. In particular, the incidence of IPD in older adults was considerably underestimated by the notification data. Although the number of IPD notifications increased each year since 2004, the fact that the number of cases reported through EARSS remained stable, it would indicate that the increase in notifications seen over this period is more than likely a reflection of improved reporting rather than any change in the IPD trends *per se.* Despite the differences between the two systems the overall trends were the same with the very young and the very old being most being most vulnerable.

Based on the notification data, the highest incidence rates occurred in HSE-NW and HSE-SE. A number of factors accounted for the high rates in these areas: (1) all labs are not consistently reporting IPD cases through the notification system in addition to EARSS, whereas labs in above areas are (2) labs in these two areas are testing for and reporting positive urinary antigen tests for *S. pneumoniae* (probable cases as per case definitions) and (3) an IPD outbreak occurred in HSE-NW in mid-2006 and thereby further augmenting the incidence rate for the disease there.

Data received on clinical diagnosis of IPD cases and outcome were sketchy. Clinical diagnosis was not reported for 81% of the notifications and outcome was unavailable for 90% of notifications. Details on the case's risk factors for disease and vaccination status (where applicable) are not routinely reported. The gaps in such vital data highlight the importance of an enhanced surveillance system for this disease.

Based on the 2002 Immunisation Guidelines by the National Immunisation Advisory Committee in Ireland, pneumococcal vaccination is recommended for certain at-risk groups which included vaccination of the elderly aged 65 years of age and older with PPV23 and PCV7 for infants and children <2 years of age considered to be at increased risk of IPD. Therefore, infants and children in this age group not considered at risk from this disease are not offered PCV7 vaccination at present. This policy has recently been reviewed by NIAC and the inclusion of PCV7 in the routine childhood immunisation schedule has been recommended. The expectation is that this recommendation will be implemented in 2008.

Serotyping data were available on only 15% of *S. pneumoniae* isolates in 2006. Based on the data available, PCV7 would have covered 79% of the typed isolates in the <2 year olds and in adults 65 years of age and older 95% of the isolates typed would have been covered by PPV23. More comprehensive serotyping data are required on invasive *S. pneumoniae* isolates in order to determine the distribution of *S. pneumoniae* isolates in Ireland by serotype, to firstly ascertain serotype distribution of isolates prior to implementation of universal infant vaccination, secondly to fully evaluate the impact of any vaccine programmes and finally to ascertain the serotypes associated with penicillin non-susceptible *S. pneumoniae*. To bridge this gap, a pilot project for

the serotyping and further molecular typing of invasive *S. pneumoniae* isolates in Ireland commenced in April 2007 in collaboration with Beaumont Hospital, the Children's University Hospital, Temple Street and HPSC.

In conclusion, the surveillance of IPD needs strengthening in Ireland. Clinicians and laboratories are statutorily obliged to notify cases of this disease through the weekly infectious disease notification system as well as through EARSS. Implementation of a standardised enhanced surveillance system is required involving the Departments of Public Health, the laboratories and clinicians. Furthermore, a recognised streptococcal reference facility is required where services such as pneumococcal typing can be offered. Such surveillance initiatives will provide improved and more in-depth information on the epidemiology of IPD in Ireland. This information in turn can be used to inform public health policy, monitor the impact of any pneumococcal vaccination programmes and to measure vaccine efficacy. This information will also be vital in ascertaining serotype distributions of *S. pneumoniae* isolates in advance of and after implementation of any future vaccination initiatives.

References

1. EARSS Annual Report 2005 for Europe. Available at http://www.rivm.nl/earss

2. HPSC. EARSS Report for Q4 2006. Available at http://www.hpsc.ie

3. CDC. Direct and indirect effects of routine vaccination of children with 7-valent pneumococcal conjugate vaccine on incidence of invasive pneumococcal disease – United States, 1998-2003. *MMWR Morb Mortal Wkly Rep* 2005; **54:** 893-97.

4. Kyaw MH *et al.* Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae. N Engl J Med* 2006; **354:** 1455-63.

5. WHO. Pneumococcal conjugate vaccine for childhood immunisation – WHO position paper. *Wkly Epidemiol Rec* 2007; **82:** 93-104.

6. Case Definitions for Notifiable Diseases. Infectious Diseases (Amendment No. 3) Regulations 2003 (SI No. 707 of 2003). Available at http://www.hpsc.ie