INVASIVE PNEUMOCOCCAL DISEASE IN NEW ZEALAND, 2010

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SUMMARY

A 4-dose schedule of the 7-valent pneumococcal conjugate vaccine (PCV-7), Prevenar®, was added to the New Zealand childhood immunisation schedule in June 2008, with a catch-up programme for all children born on or after 1 January 2008. Since 17 October 2008, invasive pneumococcal disease (IPD) has been notifiable to medical officers of health under the Health Act 1956.

In this report, the data presented for 2009 and 2010 is based on IPD case notifications supplemented with serotype and antimicrobial susceptibility data from ESR's national laboratory-based surveillance of invasive *Streptococcus pneumoniae* isolates. Data for earlier years is solely from ESR's laboratory-based surveillance. For this laboratory-based surveillance, diagnostic microbiology laboratories are requested to refer all invasive isolates of *S. pneumoniae* to ESR for serotyping and antimicrobial susceptibility testing.

There were 535 cases of IPD notified in 2010, which equates to a rate of 12.2 cases per 100 000. A *S. pneumoniae* isolate from an invasive site was received at ESR for serotyping and susceptibility testing for 514 (96.1%) of the notified cases.

The incidence of IPD in infants <2 years old has reduced 70.9% since the introduction of PCV-7: from an average annual incidence of 100.4 cases per 100 000 in 2006 and 2007 to 29.2 per 100 000 in 2010. The reduction in IPD caused by PCV-7 serotypes in this age group is even more striking than the reduction in all IPD, with a 90.5% decrease from an average annual incidence of 83.2 per 100 000 in 2006 and 2007 to 7.9 per 100 000 in 2010.

In 2010, IPD also decreased in the 2-4 year age group: from a rate of 23.0 cases per 100 000 in 2009 to 15.1 per 100 000. This is as expected, as some of the vaccine-eligible children would have been in this age group in 2010 (ie, the 2 year olds born throughout 2008). Also in 2010 for the first time there was evidence of the indirect or herd immunity effect of PCV-7 infant immunisation, with a significant ($P \leq 0.05$) decrease in the rate of IPD due to PCV-7 serotypes in the ≥65 year age group between 2009 and 2010 with the rate falling from 26.4 to 17.7 cases per 100 000.

In 2010 the all-age rate of pneumococcal meningitis was 0.7 cases per 100 000. The highest rate of meningitis occurred in the <1 year age group (7.8 per 100 000). There were no cases of pneumococcal meningitis in the 1-2 year age group. The case-fatality rate was 5.3%.

Rates of IPD in Pacific Peoples and Māori were 5.9 and 3.6 times, respectively, the rate among Europeans. The rate of disease in the most deprived NZDep quintile (indices 9-10) was 3.1 times that in the least deprived quintile (indices 1-2).

52.8% of IPD cases, for whom the information was reported, were recorded as having a chronic illness, 52.6% of cases <5 years of age were in childcare, and 42.9% of cases <5 years of age were exposed to smoking in the household.

continued

SUMMARY *continued*

There were no significant regional differences ($P \leq 0.05$) in the incidence of IPD in 2010, but within the Northern region disease rates were significantly higher in Counties Manukau District Heath Board (DHB) than in the other three DHBs in the region.

Among the 34 cases who had received ≥1 dose of PCV-7, and for whom the serotype causing disease was known, 27 (79.4%) had IPD due to a non-PCV-7 type. Of the seven cases who had received ≥1 dose of PCV-7 and had disease due to a PCV-7 type, five had serotype 19F disease, one had type 6B disease and one had type 14 disease.

There has been some increase in IPD caused by non-PCV-7 serotypes since the introduction of PCV-7. This increase has been predominantly due to serotype 1 disease. An increase in serotype 1 IPD was first noted in 2007 and appears to have peaked in 2009, with the rate of type 1 disease halving between 2009 and 2010. Except for 2009, most of the serotype 1 disease has been in cases 5-34 years of age. In 2009, this type also became common among infants <2 years old, although this did not continue into 2010 when the type only accounted for 5.6% (2) of cases in this age group. With ethnicity data available for IPD cases the first time in 2009, it became clear that this type was associated with cases in Māori and Pacific Peoples. In 2010, serotype 1 accounted for 29.5% and 23.1%, respectively, of all IPD cases in Māori and Pacific Peoples, and 64.0% and 63.2%, respectively, of cases in Māori and Pacific People aged 5-34 years.

Serotype 19A is the non-PCV-7 type that is most frequently reported to have increased in other countries following the introduction of the vaccine. In New Zealand there have been no significant changes in the rate of disease due to type 19A in any age group. There was, however, a notable but not significant increase in the rate of type 19A disease in the ≥65 year age group in 2010.

Although there was a decrease in penicillin and cefotaxime resistance between 2008 and 2009, there was no further decrease between 2009 and 2010. In 2010, 18.1% of isolates were categorised as penicillin resistant according to the Clinical and Laboratory Standards Institute's meningitis interpretive criteria. No isolates were categorised as penicillin resistant according to the interpretive criteria for the parenteral treatment of non-meningitis infections. 2% of isolates were cefotaxime resistant according to the meningitis interpretive criteria and 1.6% were resistant according to the non-meningitis interpretive criteria. There is no indication that resistance is increasing in non-PCV-7 serotypes in this country, with PCV-7 types still accounting for over 80% of the penicillin and cefotaxime resistance in 2010.

In late 2011, PCV-7 will be replaced with PCV-10 (Synflorix®) on the childhood immunisation schedule. PCV-10 will give additional coverage for serotypes 1, 5 and 7F. Hopefully, the serotype 1 coverage will prevent future outbreaks of this type such as that we have recently experienced in New Zealand.

1. INTRODUCTION

Prior to 2009, the national surveillance of invasive pneumococcal disease (IPD) in New Zealand was solely laboratory based, with diagnostic laboratories referring invasive isolates of *Streptococcus pneumoniae* to the Institute of Environmental Science and Research Ltd (ESR) for serotyping and antimicrobial susceptibility testing. This laboratory-based surveillance provided information on the basic epidemiology of IPD, and the serotypes and antimicrobial susceptibility of invasive isolates. Information from this laboratory-based surveillance was published periodically.[1-5] In addition, between 2002 and 2007, annual reports on the antimicrobial susceptibility of isolates from IPD cases have been published on ESR's surveillance website at http://www.surv.esr.cri.nz/antimicrobial/streptococcus_pneumoniae.php.

The first of this series of annual reports on IPD in New Zealand covered IPD in 2008 and was based on data available from ESR's national laboratory-based surveillance.[6] On 1 June 2008, the 7-valent pneumococcal conjugate vaccine (PCV-7), Prevenar®, was added to the New Zealand childhood immunisation schedule and IPD became a notifiable disease on 17 October 2008. The 2009 IPD annual report was the first to be based on IPD notifications, supplemented with serotype and antimicrobial susceptibility data from ESR's laboratory-based surveillance of invasive *S. pneumoniae* isolates.[7]

Data on the IPD cases notified in 2010 is presented in this report, along with trend data for recent years.

2. METHODS

2.1 Surveillance methods

In this report, data for 2009 and 2010 is based on IPD case notifications supplemented with serotype and antimicrobial susceptibility data from the laboratory-based surveillance of invasive *S. pneumoniae* isolates. Data for earlier years is from ESR's national laboratory-based surveillance of IPD.

Since 17 October 2008, IPD has been notifiable to medical officers of health under the Health Act 1956. Data on each case is entered at public health units (PHUs), via a secure web-based portal, onto a computerised database (EpiSurv). The notification data is collated and analysed on behalf of the Ministry of Health by ESR.

For the national laboratory-based surveillance of IPD, diagnostic microbiology laboratories in New Zealand are requested to refer all invasive isolates of *S. pneumoniae* [ie, isolates from cerebrospinal fluid (CSF), blood or other normally sterile site] to ESR. In addition and less frequently, laboratories refer sterile site specimens to ESR to test for the presence of pneumococcal DNA by PCR. At ESR all invasive isolates are serotyped and tested for susceptibility to a range of antibiotics (see Section 2.2).

The notification data in this report is based on the information recorded on EpiSurv as at 17 February 2011. Any changes made to EpiSurv data by PHU staff after this date are not reflected in this report. Serotype and antimicrobial susceptibility data for invasive isolates was matched with the relevant case notification.

Except for disease rates by ethnicity and deprivation index, mid-year New Zealand population estimates were used to calculate incidence rates. The 2006 census population data was used to calculate ethnicity-specific IPD rates, and a prioritised approach was used with the order of prioritisation as: Māori, Pacific Peoples, Other (other groups except European), and European.[8] Incidence rates are not presented for categories where there were <5 cases.

A deprivation index, which ranges from 1 (least deprived) to 10 (most deprived), is calculated for each geographical mesh block in New Zealand. Approximately equal numbers of people reside in areas associated with each of the ten deprivation levels. The deprivation index analysis was confined to those cases for which the accuracy of index designation was recorded as exact or nearest. The IPD rates by deprivation index were calculated using the NZDep2006 classification.

In this report, any cases for which *S. pneumoniae* was identified in CSF (by culture, PCR or antigen test) and which were not notified as meningitis cases were considered to be cases of pneumococcal meningitis.

The immunisation status of cases born after 1 January 2008 is based on data in the national immunisation register (NIR), rather than the immunisation data reported with the case notification. IPD notifications were matched with relevant data in the NIR for cases born after 1 January 2008 only. The immunisation status of asplenic cases is based on the immunisation data reported with the case notification.

Data analyses were performed with SAS software v.9.1.3 (SAS Institute Inc, Cary, NC, USA). The chi-square test or Fisher's exact test, as appropriate, were used to determine the significance of any observed differences. Linear regression was used to calculate the significance and direction of time trends. An associated P value of ≤0.05 was used to identify whether a difference or trend was significant.

2.2 Laboratory methods

Detection of pneumococcal DNA in clinical specimens: The presence of pneumococcal DNA in clinical specimens is detected by polymerase chain reaction (PCR).

Strain typing: *S. pneumoniae* isolates are serotyped by the capsular antigen reaction (Neufeld test) using the Danish system of nomenclature and sera obtained from the Statens Serum Institut.[9] Methods have not been established at ESR to identify the strain type when only pneumococcal DNA, rather than an isolate, is available. Therefore, the serotype can only be determined for culture-positive IPD cases.

Antimicrobial susceptibility testing: The penicillin and cefotaxime susceptibilities of *S. pneumoniae* isolates are determined by Etest (BioMerieux, France), using Mueller-Hinton agar with 5% sheep blood and incubation for 20-24 hours in 5% CO_2. Chloramphenicol, clindamycin, co-trimoxazole, erythromycin, moxifloxacin, rifampicin, tetracycline and vancomycin susceptibilities are determined by the Clinical and Laboratory Standards Institute's (CLSI's) disc susceptibility testing method.[10] Inducible clindamycin resistance is detected by the D-zone test.[11] All minimum inhibitory concentrations (MICs) and zone of inhibition diameters were interpreted according to the 2010 CLSI standards.[11]

In this report, the penicillin interpretive standards, which were redefined in 2008, have been retrospectively applied to historical MIC data so that time trends are comparable. Also, in this report, when associations between penicillin or cefotaxime resistance and patient demographics, geographical distribution or serotypes are made, the meningitis interpretive standards have been used.

Multidrug resistance is defined as resistance to three antibiotics in addition to penicillin. For the purposes of this definition, the meningitis interpretive standards were used for both penicillin and cefotaxime.

2.3 Case definition

A case of IPD is defined as:

1 the isolation of *S. pneumoniae* from CSF, blood or other normally sterile site; or
2 the detection by nucleic acid amplification test of pneumococcal DNA in CSF, blood or other normally sterile site; or
3 a positive newer-generation *S. pneumoniae* antigen test (ie, Binax NOW) on CSF.

2.4 Abbreviations

PCV-7: 7-valent pneumococcal conjugate vaccine with serotypes 4, 6B, 9V, 14, 18C, 19F and 23F.
PCV-10: 10-valent pneumococcal conjugate vaccine with serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.
PCV-13: 13-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.
PPV-23: 23-valent pneumococcal polysaccharide vaccine with serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F.

3. RESULTS

In 2010, 535 IPD cases were notified. *S. pneumoniae* isolates from an invasive site were received at ESR for serotyping and susceptibility testing for 514 (96.1%) of these cases.

3.1 Laboratory criteria upon which diagnosis based

According to the case definition, IPD must be confirmed by the isolation of *S. pneumoniae* from CSF, blood or other normally sterile site; the detection of pneumococcal DNA in CSF, blood or other normally sterile site specimen; or a positive newer-generation pneumococcal antigen test on CSF. More than one method of laboratory confirmation was recorded for some cases in 2010. When only one method of laboratory confirmation was counted for each case and prioritised in the following order: pneumococcal culture from CSF, pneumococcal culture from blood, positive antigen test on CSF, pneumococcal culture from pleural fluid, pneumococcal culture from joint fluid, and pneumococcal culture from another normally sterile site, the majority (89.3%) of cases were confirmed on the basis of a positive blood culture (Appendix 1). No cases were notified as being confirmed on the basis of identification of pneumococcal DNA in CSF, blood or other normally sterile site. All cases notified as being diagnosed on the basis of a positive antigen test on CSF also had a positive CSF or blood culture.

3.2 Disease incidence by age

The age and sex distribution of the 2010 cases is presented in Table 1, along with the incidence rate for each age group. The highest rates of disease were in the elderly ≥75 years of age. There was an overall excess of males among cases. This excess was greatest in cases 1 year of age, with a male to female ratio of 2.8:1 in this age group.

A further breakdown of the age distribution of the cases <2 years of age is shown in Appendix 2.

Table 1. Numbers and rates of invasive pneumococcal disease cases by age group and sex, 2010

Age group (years)	Female		Male		All cases		
	Number	Rate[1]	Number	Rate[1]	Number	Percent	Rate[1]
<1	9	28.9	13	39.9	22	4.1	34.5
1	4	-	11	33.7	15	2.8	23.8
2-4	16	17.7	12	12.7	28	5.2	15.1
5-14	7	2.5	16	5.4	23	4.3	3.9
15-24	14	4.5	11	3.4	25	4.7	3.9
25-34	13	4.6	12	4.4	25	4.7	4.5
35-44	20	6.2	19	6.5	39	7.3	6.4
45-54	27	8.6	32	10.7	59	11.0	9.6
55-64	31	12.6	44	18.6	75	14.0	15.6
65-74	38	23.5	42	27.7	80	15.0	25.5
75-84	48	47.0	39	46.6	87	16.3	46.8
≥85	29	62.8	28	117.2	57	10.7	81.3
Aggregated age groups (years)[2]							
<2	13	21.1	24	36.8	37	6.9	29.2
<5	29	19.1	36	22.5	65	12.2	20.8
5-64	112	6.4	134	7.8	246	46.0	7.1
≥65	115	37.1	109	42.1	224	41.9	39.4
All ages	**256**	**11.5**	**279**	**13.0**	**535**		**12.2**

1 Annual incidence rate per 100 000. A rate is not presented where there are <5 cases.
2 Shaded rows indicate aggregated age groups.

The all-age rate of IPD in 2010 (12.2 cases per 100 000) was the lowest recorded in the last 5 years, 2006-2010 (Table 2). The rates in children <2 years and <5 years of age have decreased significantly since the addition of PCV-7 to the childhood immunisation schedule in 2008.

Table 2. Rates of invasive pneumococcal disease by age group, 2006-2010[1]

Age group (years)	Annual incidence rate per 100 000				
	2006	**2007**	**2008**	**2009**	**2010**
<1	122.0	78.0	57.7	53.9	34.5
1	86.8	115.4	68.2	39.1	23.8
2-4	18.9	23.3	20.1	23.0	15.1
5-14	3.3	4.9	5.9	9.9	3.9
15-24	2.5	3.1	4.7	8.4	3.9
25-34	2.9	4.4	5.9	9.6	4.5
35-44	8.5	6.3	8.5	11.0	6.4
45-54	7.4	6.3	9.2	9.1	9.6
55-64	13.0	14.3	19.1	14.7	15.6
65-74	24.3	30.5	29.8	31.1	25.5
75-84	38.3	40.5	48.3	51.1	46.8
≥85	58.6	42.7	80.0	79.6	81.3
Aggregated age groups (years)[2]					
<2	104.6	96.2	62.9	46.4	29.2
<5	53.8	53.4	38.0	32.7	20.8
5-64	6.0	6.2	8.5	10.3	7.1
≥65	33.0	35.3	42.0	43.6	39.4
All ages	12.6	13.1	14.8	16.1	12.2

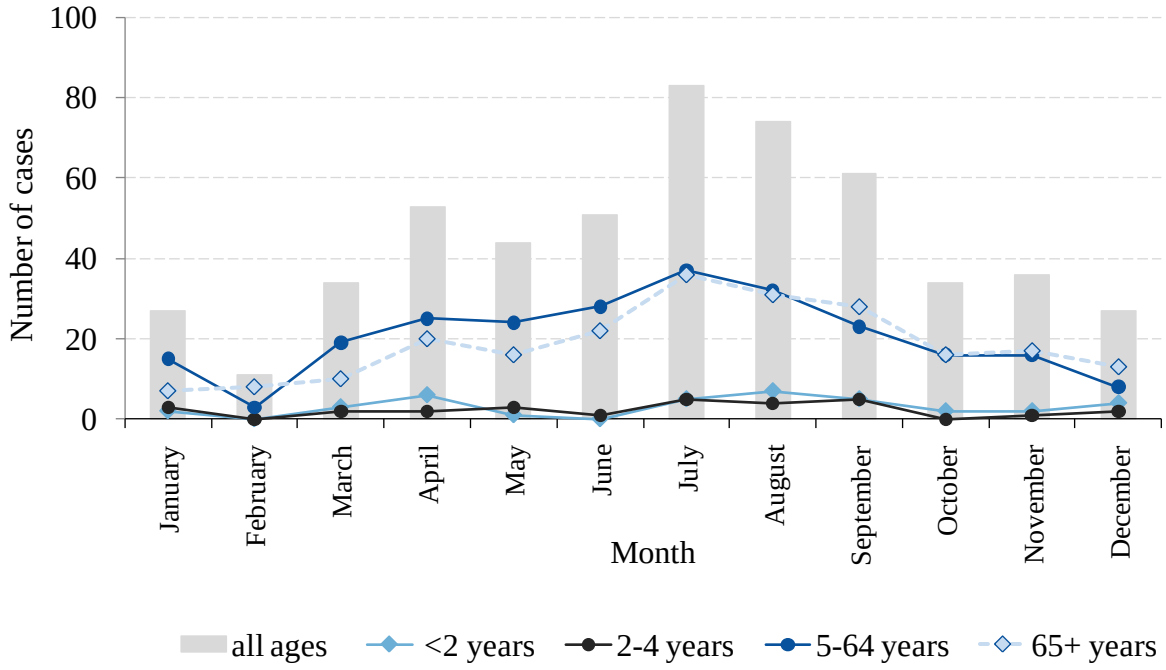
1 Data for 2006-2008 based on national laboratory-based surveillance. Data for 2009 and 2010 based on IPD notifications

2 Shaded rows indicate aggregated age groups.

3.3 Disease incidence by season

IPD showed the usual seasonality in 2010, with a marked peak of cases in the winter months, although this peak was less evident in the younger age groups (Figure 1).

Figure 1. Seasonality of invasive pneumococcal disease by age group, 2010



3.4 Disease incidence by ethnicity

The age-standardised rates of IPD were highest among Pacific Peoples (53.1 cases per 100 000) and Māori (32.0). The rates in these two ethnic groups were 5.9 and 3.6 times, respectively, the rate among Europeans (9.0) (Table 3).

Among cases <2 years of age, the rates were also highest in Pacific Peoples and Māori, with rates in these two ethnic groups being 3.3 and 5.0 times, respectively, that in Europeans. However, these rates are based on relatively small numbers of cases in this age group.

Between 2009 and 2010, the age-standardised IPD rates decreased 30.8% in Europeans, 22.3% in Māori, and 29.5% in Asians, but increased 6.2% in Pacific Peoples (Appendix 3). Among cases <2 years of age, rates decreased 52.6% in Europeans, 27.6% in Māori, and 37.4% in Pacific Peoples (Appendix 3). These decreases among <2 year olds in these ethnic groups were not significant. There was only one IPD case in Asian infants <2 years of age in both 2009 and 2010.

Table 3. Numbers and rates of invasive pneumococcal disease cases by ethnicity and age group, 2010

Age group (years)	European		Māori		Pacific Peoples		Asian		Other	Unknown
	No.	Rate[1]	No.	Rate[1]	No.	Rate[1]	No.	Rate[1]	No.	No.
<1	4	-	12	85.5	4	-	1	-	0	1
1	5	17.2	9	66.8	1	-	0	-	0	0
2-4	7	7.9	10	25.7	5	33.1	6	48.7	0	0
5-14	8	2.4	6	4.5	6	11.9	2	-	1	0
15-24	5	1.6	11	10.9	8	19.7	0	-	0	1
25-34	7	2.2	9	11.6	7	21.0	0	-	1	1
35-44	12	2.9	14	18.5	8	24.9	2	-	0	3
45-54	30	7.5	15	26.7	10	46.2	2	-	0	2
55-64	35	10.6	18	57.2	17	132.0	2	-	1	2
65-74	48	21.8	13	78.0	12	173.7	0	-	0	7
75-84	68	43.9	10	179.4	3	-	3	-	0	3
≥85	56	107.0	0	-	1	-	0	-	0	0
Aggregated age groups (years)[2]										
<2	9	15.3	21	76.3	5	49.8	1	-	0	1
<5	16	10.8	31	46.7	10	39.7	7	32.9	0	1
5-64	97	4.6	73	15.3	56	29.3	8	2.6	3	9
≥65	172	40.3	23	99.5	16	161.0	3	-	0	10
All ages[3]	285	9.0	127	32.0	82	53.1	18	8.6	3	20

1 Annual incidence rate per 100 000, based on prioritised ethnicity. A rate is not presented where there are <5 cases.
2 Shaded rows indicate aggregated age groups.
3 The rates for all ages are direct-standardised to the age distribution of the total NZ population.

3.5 Disease incidence by deprivation

Accurate NZ deprivation (NZDep) index data was available for 496 (92.7%) of the 535 IPD cases in 2010. With the exception of the 2-4 year age group, the highest numbers of cases were in the most deprived NZDep quintile (ie, NZDep indices 9-10) (Table 4). Rates of IPD within NZDep quintiles could only be calculated for all ages, as population data by NZDep index and age groups was not available. The all-age rate of IPD increased in each NZDep quintile from the least deprived (NZDep indices 1-2) to the most deprived quintile. The rate in the most deprived quintile (21.7 cases per 100 000) was 3.1 times that in the least deprived quintile (7.0 per 100 000).

Table 4. Number and percentage of invasive pneumococcal disease cases by 2006 NZ deprivation index and age group, 2010

2006 NZ deprivation index quintile	Age group (years)					
	Number (% within the age group) in each quintile[1]					Rate[2]
	<2	2-4	5-64	≥65	All ages	
1-2	3 (8.8)	5 (18.5)	13 (5.7)	37 (18.0)	58 (11.7)	7.0
3-4	3 (8.8)	2 (7.4)	26 (11.4)	32 (15.5)	63 (12.7)	7.8
5-6	6 (17.7)	7 (25.9)	31 (13.5)	43 (20.9)	87 (17.5)	10.9
7-8	6 (17.7)	6 (22.2)	60 (26.2)	43 (20.9)	115 (23.2)	14.5
9-10	16 (47.1)	7 (25.9)	99 (43.2)	51 (24.8)	173 (34.9)	21.7
Total	34	27	229	206	496	

1 Data available for 91.9% (34/37) of cases <2 years of age, 96.4% (27/28) of cases 2-4 years of age, 93.1% (229/246) of cases 5-64 years of age, and 92.0% (206/224) of cases ≥65 years of age.

2 Annual incidence rate per 100 000.

3.6 Disease presentation, fatalities and hospitalisation

Information on clinical presentation was available for 511 (95.5%) of the 535 IPD cases in 2010 (Table 5).

The rate of pneumococcal meningitis was 0.7 cases per 100 000 for all ages, 7.8 per 100 000 for the <1 year age group, 3.9 per 100 000 for the <2 year age group, and 2.6 per 100 000 for the <5 year age group.

Of the five cases of meningitis in infants <1 year of age, four were Māori (which equates to a rate of 28.5 cases per 100 000), and the fifth was a European infant.

Table 5. Clinical presentation of invasive pneumococcal disease cases by age group, 2010[1]

Age group (years)	Number of cases (% within the age group)					Number of cases for whom presentation information reported[2]
	Meningitis	Bacteraemia without focus	Empyema	Pneumonia	Other	
<1	5 (25.0)	4 (20.0)	2 (10.0)	5 (25.0)	4 (20.0)	20
1	0	2 (13.3)	0	9 (60.0)	4 (26.7)	15
2-4	3 (11.5)	1 (3.8)	0	17 (65.4)	5 (19.2)	26
5-14	2 (9.1)	3 (13.6)	1 (4.5)	11 (50.0)	5 (22.7)	22
15-64	16 (7.5)	26 (12.2)	4 (1.9)	149 (70.0)	18 (8.5)	213
≥65	6 (2.8)	37 (17.2)	5 (2.3)	149 (69.3)	18 (8.4)	215
Aggregated age groups (years)[3]						
<2	5 (14.3)	6 (17.1)	2 (5.6)	14 (40.0)	8 (22.9)	35
<5	8 (13.1)	7 (11.5)	2 (3.3)	31 (50.8)	13 (21.3)	61
All ages	32 (6.3)	73 (14.3)	12 (2.3)	340 (66.5)	54 (10.6)	511

1 In this analysis, only one presentation was counted for each case, with presentations prioritised in the following order: meningitis, bacteraemia, empyema, pneumonia and 'Other'.

2 Data available for 90.9% (20/22) of cases <1 year of age, all cases 1 year of age, 92.9% (26/28) of cases 2-4 years of age, 95.7% (22/23) of cases 5-14 years of age, 95.5% (213/223) of cases 15-64 years of age, and 96.0% (215/224) of cases ≥65 years of age.

3 Shaded rows indicate aggregated age groups.

Information on whether the patient survived or died was reported for 514 (96.1%) of the total 535 cases. Among the 45 cases who died, 27 were reported as dying from IPD, giving a case-fatality rate of 5.3% among the cases for whom this information was reported. The case-fatality rates for the different age groups are presented in Appendix 4.

Information on whether the patient was hospitalised was reported for 523 (97.8%) of the total 535 cases, and 96.0% (502) of these 523 cases were hospitalised. The case-fatality rate among hospitalised cases (5.1%, 25/491) was not significantly different to that among non-hospitalised cases (9.5%, 2/21).

3.7 Risk factors among IPD cases

The risk factors reported among IPD cases in 2010 are recorded in Table 6. Risk factors for the subset of 37 cases <2 years of age are presented in Appendix 5. The most common risk factor among all cases was chronic illness (52.8% of cases).

Table 6. Risk factors among invasive pneumococcal disease cases, 2010

Risk factor	Number of cases for whom information on the risk reported	Number (%[1]) of cases with the risk
Premature <37 weeks gestation (cases <1 year of age)	11	2 (18.2)
Congenital or chromosomal abnormality	487	6 (1.2)
Chronic lung disease or cystic fibrosis	490	83 (16.9)
Anatomical or functional asplenia	461	4 (0.9)
Immunocompromised[2]	466	87 (18.7)
Chronic illness[3]	481	254 (52.8)
Cochlear implants	462	1 (0.2)
Current smoker[4]	302	90 (29.8)
Smoking in household (cases <5 years of age)	21	9 (42.9)
In childcare (cases <5 years of age)	19	10 (52.6)
Resident in long-term or other chronic-care facility[5]	491	34 (6.9)
Other risk factors	NA[6]	118 (22.1[7])

1 Percentage based on only those cases for whom information reported for each particular risk factor, except for 'Other' risk factors (see footnote 7).
2 Includes HIV/AIDS, lymphoma, organ transplant, multiple myeloma, nephrotic syndrome, chronic drug therapy, dysgammaglobulinaemia and sickle cell anaemia.
3 Includes CSF leak, intracranial shunts, diabetes, cardiac disease, pulmonary disease, chronic liver disease, renal impairment and alcohol-related disease.
4 Only cases ≥18 years of age included in this analysis of current smokers
5 Among cases ≥75 years of age, 21.2% (28 of 132 for whom the information was reported) were residents in a long-term or other chronic-care facility.
6 Not applicable, as only reportable when case has 'Other' risk factors.
7 Percentage of all 535 IPD cases.

3.8 Immunisation status of cases

Among the 40 cases that were vaccine eligible, that is, those born after 1 January 2008, 35 were recorded as having ≥1 dose of PCV-7 before the onset of their disease (Table 7). Among the 34 cases who had had ≥1 dose of PCV-7, and for whom the serotype causing disease was known, 27 (79.4%) had IPD due to a non-PCV-7 type. Of the seven cases who had received ≥1 dose of PCV-7 and had disease due to a PCV-7 type, five had serotype 19F disease, one had type 6B disease and one had type 14 disease.

The immunisation status of three of the four asplenic cases was recorded. The ages of these cases ranged from 48-97 years, and none was reported to be immunised with a pneumococcal vaccine.

Table 7. PCV-7 immunisation status of the 2010 invasive pneumococcal disease cases who were born after 1 January 2008[1]

Number of doses received prior to onset of IPD[2]	Number (%) of cases		
	Cases due to a PCV-7 type n=10	Cases due to a non-PCV-7 type n=29	All cases n=40[3]
0	3 (30.0)	2 (6.9)	5 (12.5)
1	3 (30.0)[4]	2 (6.9)	5 (12.5)
2	1 (10.0)[5]	4 (13.8)	5 (12.5)
3	3 (30.0)[6]	14 (48.3)	18[3] (45.0)
4	0	7 (24.1)	7 (10.0)

1 All infants born after 1 January 2008 are eligible for PCV-7 immunisation.
2 If onset date not reported, notification date used.
3 The serotype of one case is not known.
4 All three cases were due to serotype 19F.
5 Case due to serotype 6B.
6 Two cases due to serotype 19F and one to serotype 14.

3.9 Incidence by district health board

Table 8 shows the number of cases by age group and the incidence rates in each region and district health board (DHB). Care should be taken with comparing the DHB rates, as some DHBs had relatively small numbers of cases. There were no significant differences in rates between the four regions. Within the Northern region, the rate of IPD in Counties Manukau DHB was significantly higher that the rates in the other three DHBs in the region.

Table 8. Invasive pneumococcal disease cases by region, district health board (DHB) and age group, 2010

	Number of cases by age group (years)					Rate[1]
Region and DHB	**<2**	**<5**	**5-64**	**≥65**	**All ages**	**(all ages)**
Northern region	**17**	**33**	**118**	**78**	**229**	**14.0**
Northland	3	4	6	7	17	10.8
Waitemata	3	5	33	24	62	11.5
Auckland	2	6	19	20	45	10.0
Counties Manukau	9	18	60	27	105	21.4
Midland region	**9**	**15**	**49**	**45**	**109**	**13.1**
Waikato	4	7	19	21	47	12.9
Lakes	3	4	8	6	18	17.5
Bay of Plenty	0	2	19	12	33	15.7
Tairawhiti	1	1	0	0	1	-
Taranaki	1	1	3	6	10	9.2
Central region	**8**	**13**	**44**	**47**	**104**	**10.4**
Hawke's Bay	5	6	11	7	24	15.5
Whanganui	0	0	6	3	9	14.2
MidCentral	0	0	5	13	18	10.8
Hutt	2	3	10	8	21	14.6
Capital and Coast	1	4	9	10	23	7.9
Wairarapa	0	0	1	4	5	12.4
Nelson Marlborough	0	0	2	2	4	-
Southern region	**3**	**1**	**35**	**54**	**93**	**10.3**
West Coast	0	0	0	1	1	-
Canterbury	3	3	19	20	42	8.3
South Canterbury	0	0	2	1	3	-
Southern	0	1	14	32	47	15.5
New Zealand total	**37**	**65**	**246**	**224**	**535**	**12.2**

1 Annual incidence rate per 100 000. A rate is not presented where there are <5 cases.

3.10 Serotype distribution

Table 9. Serotypes among invasive pneumococcal disease cases and vaccine coverage by age group, 2010

Serotype	Proportion (%) of IPD cases within the age group (years) due to the serotype:					
	<2 (n=36)	**2-4** (n=27)	**<5**[1] (n=63)	**5-64** (n=234)	**≥65** (n=217)[2]	**All ages** (n=514)
Serotypes in PCV-7:						
4	0.0	7.4	3.2	11.1	8.3	9.0
6B	2.8	3.7	3.2	1.7	6.9	4.1
9V	0.0	7.4	3.2	5.6	7.4	6.0
14	8.3	14.8	11.1	6.4	8.3	7.8
18C	0.0	0.0	0.0	1.7	2.3	1.8
19F	16.7	11.1	14.3	5.1	6.9	7.0
23F	0.0	7.4	3.2	3.9	6.5	4.9
Total for PCV-7 serotypes	**27.8**	**51.9**	**38.1**	**35.5**	**46.5**	**40.5**
Additional serotypes in PCV-10:						
1	5.6	25.9	14.3	24.8	4.6	15.0
5	0.0	0.0	0.0	0.0	0.5	0.2
7F	5.6	0.0	3.2	1.7	1.4	1.8
Total for PCV-10 serotypes	**38.9**	**77.8**	**55.6**	**62.0**	**53.0**	**57.4**
Additional serotypes in PCV-13:						
3	5.6	7.4	6.4	3.9	3.7	4.1
6A	0.0	0.0	0.0	1.3	3.2	2.0
19A	19.4	11.1	15.9	9.8	9.7	10.5
Total for PCV-13 serotypes	**63.9**	**96.3**	**77.8**	**76.9**	**69.6**	**73.9**
Non-PCV serotypes[3]						
6C	5.6	0.0	3.2	1.3	2.8	2.1
8	0.0	0.0	0.0	3.0	0.0	1.4
9N	0.0	0.0	0.0	3.0	3.7	2.9
10A	2.8	0.0	1.6	0.9	1.4	1.2
11A	0.0	0.0	0.0	3.4	2.3	2.5
20	0.0	0.0	0.0	0.9	2.3	1.4
22F	2.8	0.0	1.6	1.7	8.3	4.5
23A	0.0	0.0	0.0	1.7	1.8	1.6
33F	11.1	0.0	6.4	2.1	1.8	2.5
other types	13.9	3.7	9.5	5.1	6.0	6.0

1 Shaded column indicates an aggregated age group.

2 86.6% of the isolates from cases ≥65 years of age were due to one of the serotypes included in PPV-23. Vaccination with PPV-23 is recommended for people in this age group.

3 The specific serotypes listed are those that accounted for ≥1% of all cases. See Appendix 6 for a full list of all serotypes.

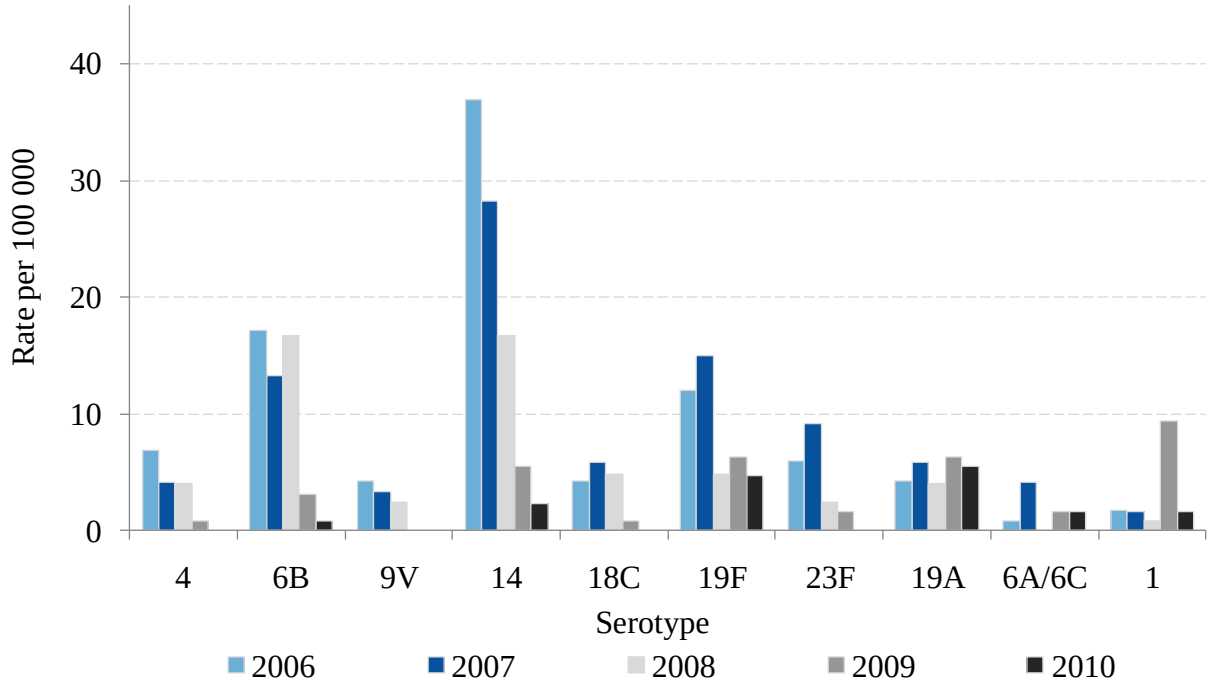
Table 9 shows, for the different age groups, the proportion of the 514 culture-positive IPD cases in 2010 caused by each of the serotypes included in the 7, 10 and 13-valent pneumococcal conjugate vaccines and any other serotypes that accounted for ≥1% of cases. A full list of the serotypes of all culture-positive cases is presented in Appendix 6.

The serotypes causing IPD during the 2 years before the introduction of PCV-7 to the childhood immunisation programme (2006 and 2007), and the 2 years after (2009 and 2010), are shown in Appendix 7. The proportion of IPD among <2 year olds caused by PCV-7 serotypes decreased from 83.8% in the 2006-7 period to 27.8% in 2010.

Figure 2 shows the trends since 2006 in the rates of disease, among infants <2 years of age, due to each of the serotypes included in PCV-7, and the other common serotypes in this age group (serotypes 19A, 6A/6C and 1). In these infants, there have been decreases in the rates of disease caused by all of the PCV-7 serotypes since the introduction of PCV-7 into the childhood immunisation schedule in 2008. Of note in 2010, there was no disease due to PCV-7 types 4, 9V, 18C and 23F in the <2 year age group.

While the proportion of disease in the <2 year olds caused by the non-PCV-7 serotype 19A has increased as total case numbers have decreased following the introduction of PCV-7 (Appendix 7), there has been no change in the rate of disease due to type 19A in this age group (Figure 2 and Appendix 8). There was, however, a notable but not significant increase in the rate of type 19A disease in the ≥65 year age group in 2010, with a rate of 3.7 cases per 100 000 compared with annual rates between 0.8-2.3 per 100 000 during the 2004-2009 period (Appendix 8).

Figure 2. Rates of invasive pneumococcal disease for PCV-7 serotypes, and types 19A, 6A/6C and 1, among <2 years olds each year 2006-2010



Serotypes 6A and 6C only distinguished since 2010; therefore they have been combined for this analysis.

The rate of disease among <2 year olds caused collectively by PCV-7 serotypes decreased from an annual average of 83.2 cases per 100 000 during the two years immediately prior to the introduction of PCV-7 (2006 and 2007) to 7.9 per 100 000 in 2010 (Figure 3). Of the ten cases due to PCV-7 serotypes in infants <2 years old in 2010, six were Māori infants, which equates to a rate of 21.8 per 100 000, three were European infants and one was Asian. In both 2009 and 2010, there were no cases of IPD due to a PCV-7 serotype among Pacific infants.

There was significant decrease in 2010 in the rate of IPD due to PCV-7 serotypes in the ≥65 year age group, with the rate decreasing from 26.4 cases per 100 000 in 2009 to 17.7 in 2010. There was also a decrease in rate of IPD due to PCV-7 serotypes in the 2-4 year age group (from 15.1 per 100 000 in 2009 to 7.6 in 2010), however, this decrease was not significant (Figure 3).

Figure 3. Rates of invasive pneumococcal disease caused by PCV-7 serotypes, by age group each year 2006-2010

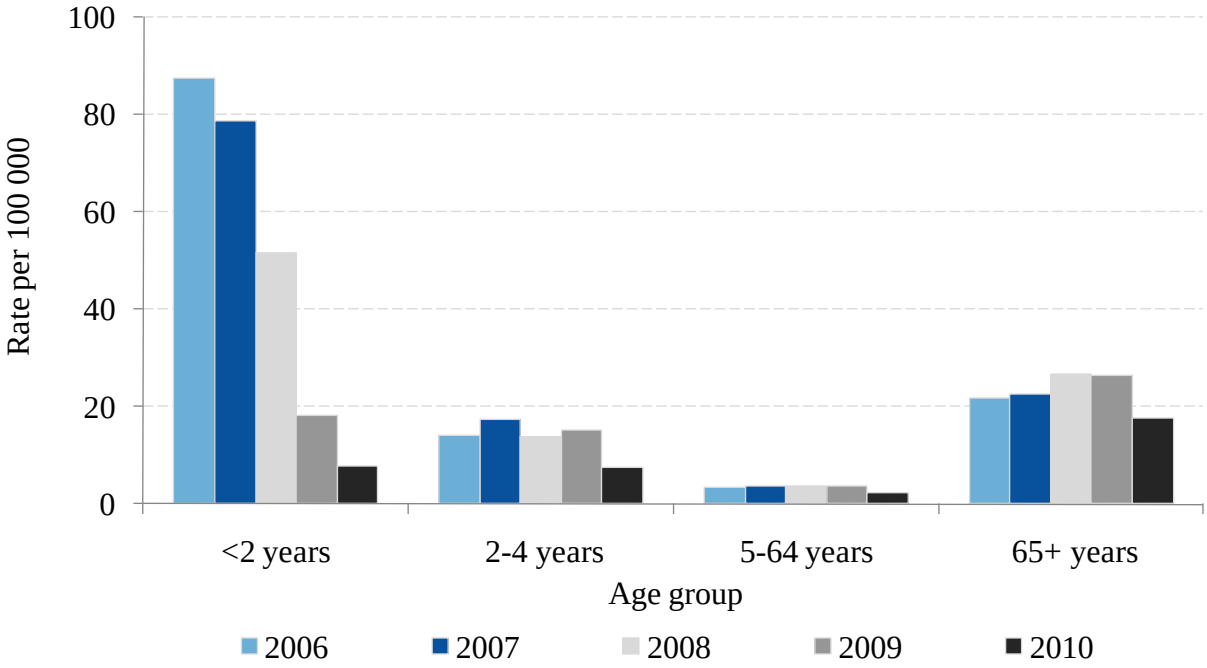
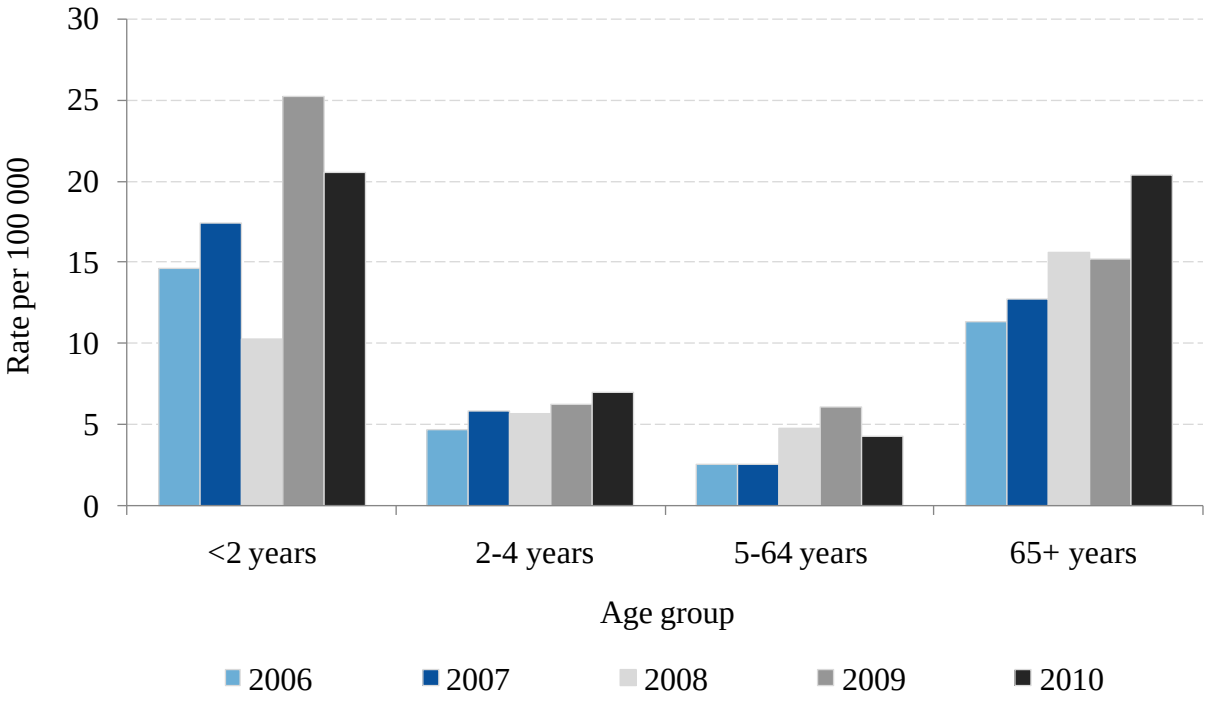


Figure 4 shows the trends since 2006 in the rates of disease due to serotypes not included in PCV-7. Any changes in rates of disease due to non-PCV-7 serotypes in recent years have been predominantly due to changes in the incidence of serotype 1 disease (Appendix 9).

An increase in serotype 1 disease was first noted in 2007 (Appendix 9). This serotype accounted for 2.9, 6.3, 11.1, 23.0 and 15.0% of culture-positive IPD cases in 2006, 2007, 2008, 2009 and 2010, respectively. In 2007 and 2008, most of the serotype 1 disease was in cases 5-34 years of age. But in 2009, this type also became common (21.8%, 12/55) among infants <2 years old, although this did not continue into 2010 when the type only accounted for 5.6% (2) of the cases in this age group (Table 9). With ethnicity data available for IPD cases for the first time in 2009, it was also clear that this type was associated with IPD in Māori and Pacific Peoples. While in 2010 the overall proportion of cases due to serotype 1 decreased, this serotype still accounted for 29.5% and 23.1%, respectively, of all IPD cases in Māori and Pacific Peoples, and 64.0% and 63.2%, respectively, of Māori and Pacific People cases 5-34 years of age.

Figure 4. Rates of invasive pneumococcal disease caused by non-PCV-7 serotypes, by age group each year 2006-2010



3.11 Antimicrobial susceptibility

Table 10 shows the antimicrobial susceptibility of the 514 culture-positive IPD cases in 2010. The penicillin and cefotaxime MICs displayed the typical bimodal distribution (Appendix 10).

6.0% of isolates had combined penicillin (meningitis interpretation) and erythromycin resistance, and 1.0% had combined penicillin-intermediate resistance (non-meningitis interpretation) and erythromycin resistance. Among the penicillin-resistant isolates (meningitis interpretation), 30.1% (28/93) were multiresistant to ≥3 additional antibiotics, commonly co-trimoxazole, erythromycin and tetracycline with or without cefotaxime resistance.

Table 10. Antimicrobial susceptibility among isolates from invasive pneumococcal disease cases, 2010

	Interpretive standards			Percent		
	S[1]	I[1]	R[1]			
	MIC (mg/L)			S	I	R
penicillin						
meningitis	≤0.06	-	≥0.12	81.9	-	18.1
non-meningitis	≤2	4	≥8	99.0	1.0	0.0
oral treatment	≤0.06	0.12-1	≥2	81.9	12.1	6.0
cefotaxime						
meningitis	≤0.5	1	≥2	91.8	6.2	1.9
non-meningitis	≤1	2	≥4	98.1	0.4	1.6
	Zone diameter (mm)					
chloramphenicol	≥21	-	≤20	98.1	-	2.0
clindamycin[2]	≥19	16-18	≤15	94.8	0.2	5.1
co-trimoxazole	≥19	16-18	≤15	73.5	2.1	24.3
erythromycin	≥21	16-20	≤15	91.1	0.0	9.0
moxifloxacin	≥18	15-17	≤14	99.8	0.2	0.0
rifampicin	≥19	17-18	≤16	100.0	0.0	0.0
tetracycline	≥23	19-22	≤18	91.6	0.8	7.6
vancomycin	≥17	-	-	100.0	-	-

1 S, susceptible; I, intermediate; R, resistant.
2 The percentage resistant given is for constitutive clindamycin resistance. One further isolate (0.2%) had inducible clindamycin resistance.

Trends in penicillin and cefotaxime resistance and multidrug resistance for the last 10 years (2001-2010) are shown in Appendix 11. Both penicillin and cefotaxime resistance, based on the meningitis interpretive standards, decreased between 2008 and 2009 after the introduction of PCV-7 in 2008, but there was no further decrease in resistance to either antibiotic between 2009 and 2010.

Trends in resistance to the non-β-lactam antibiotics for the last 10 years are shown in Appendix 12. All isolates remain susceptible to vancomycin. Moxifloxacin susceptibility has been tested since 2005, with no resistance identified and a maximum of one isolate per annum with intermediate resistance. Chloramphenicol resistance is uncommon and has varied between 1.2 and 3.4% over the last 10 years.

Penicillin and cefotaxime resistance in each region and DHB is shown in Appendix 13. There were no significant differences in resistance between the four regions.

Penicillin and cefotaxime resistance among isolates from the different age groups is shown in Table 11. There were no significant differences in resistance between the age groups.

Table 11. Penicillin and cefotaxime resistance among isolates from invasive pneumococcal disease cases by patient age, 2010

Age group (years)	Number (%[1]) isolates		
	Penicillin	Cefotaxime	
	resistant[2] MIC ≥0.12 mg/L	intermediate[2] MIC 1 mg/L	resistant[2] MIC ≥2 mg/L
<2 (n=36)	6 (16.7)	5 (13.9)	0
2-4 (n=27)	8 (29.6)	3 (11.1)	0
5-64 (n=234)	38 (16.2)	13 (5.6)	4 (1.7)
≥65 (n=217)	41 (18.9)	11 (5.1)	6 (2.8)
All ages (n=514)	**93 (18.1)**	**32 (6.2)**	**10 (1.9)**

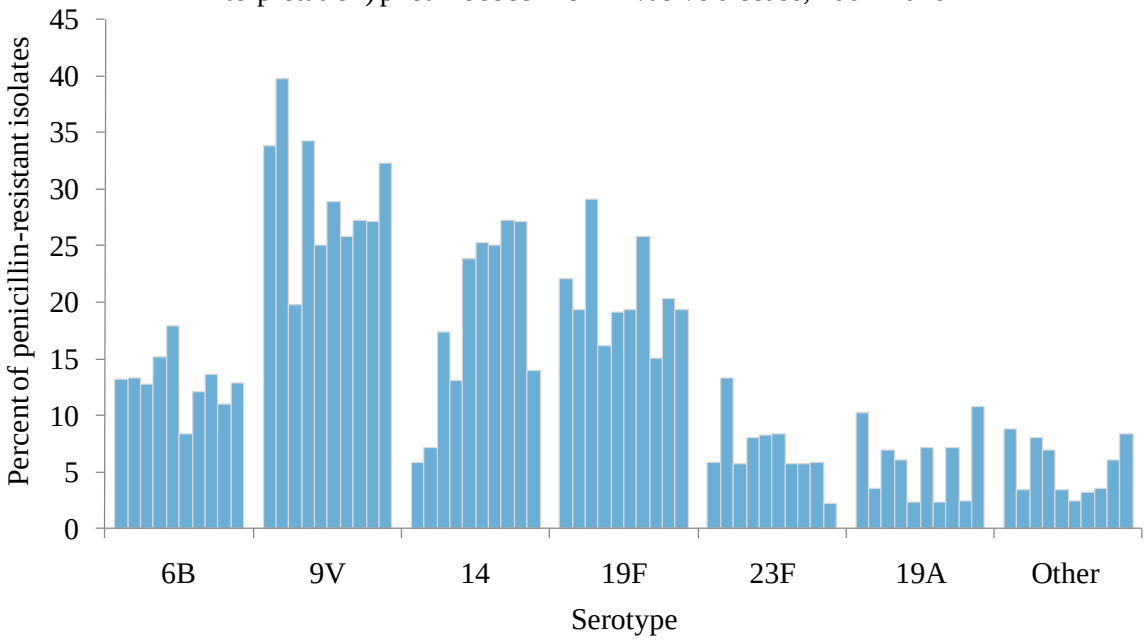
1 Percentage of the isolates from the cases within the age group.
2 Meningitis interpretations; no intermediate category for penicillin.

The majority of the penicillin-resistant (meningitis interpretation) invasive pneumococci were one of the serotypes usually associated with penicillin resistance. 80.7% of the penicillin-resistant isolates and all cefotaxime-resistant isolates were serotypes included in PCV-7 (Appendix 14).

Serotype 19F was the most common multiresistant serotype (Appendix 14). In recent years, the multiresistant type 19F isolates from IPD cases have most commonly been resistant to penicillin, cefotaxime, co-trimoxazole, erythromycin and tetracycline, and, in 2010, 64.3% (9/14) of the multiresistant type 19F isolates had this resistance pattern.

Over the last 10 years, serotype 9V has been the prevalent serotype among penicillin-resistant invasive pneumococci. Serotype 19F and, in more recent years, serotype 14 are the other two prevalent serotypes (Figure 5). In 2010, serotype 19A accounted for 10.8% of the penicillin-resistant invasive isolates. There have been no significant changes in penicillin, cefotaxime or multidrug resistance among invasive type 19A isolates over the last 10 years (Appendix 15).

Figure 5. Serotype distribution among penicillin-resistant (meningitis interpretation) pneumococci from invasive disease, 2001-2010



The series of bars for each serotype represent the individual years 2001 to 2010 from left to right.

4. DISCUSSION

A 4-dose schedule of PCV-7 (3-dose primary series plus booster) was added to the New Zealand childhood immunisation schedule in June 2008, with a catch-up programme for all children born on or after 1 January 2008. The impact of the vaccine is clearly evident among children eligible for vaccination. The incidence of IPD in infants <2 years old has reduced 71% since the introduction of PCV-7: from an average annual incidence of 100.4 cases per 100 000 in 2006 and 2007 to 29.2 per 100 000 in 2010. The reduction in IPD caused by PCV-7 serotypes in this age group is even more striking than the reduction in all IPD, with a 91% decrease from an average annual incidence of 83.2 per 100 000 in 2006 and 2007 to 7.9 per 100 000 in 2010. The actual reductions in disease rates may be greater than these figures indicate, as the 2010 rates are based on IPD notifications whereas the rates for 2006 and 2007 are based on case numbers captured by laboratory-based surveillance, which, compared with notifications, is likely to underestimate the burden of IPD.[7]

In 2010, IPD also decreased in the 2-4 year age group: from a rate of 23.0 cases per 100 000 in 2009 to 15.1 per 100 000. This is as expected, as some vaccine-eligible children would have been in this age group in 2010 (ie, the 2 year olds born throughout 2008).

The dramatic reductions in the incidence of IPD in the vaccine-eligible age groups in New Zealand mirror the global experience following the introduction of infant PCV immunisation. Global experience has also shown that, within a year or two of the introduction of infant PCV immunisation, the incidence of pneumococcal disease in non-vaccinated children and adults also begins to fall due to indirect herd immunity.[12,13] In 2010, there was evidence of this indirect effect in New Zealand for the first time, with a significant decrease in the rate of IPD due to PCV-7 serotypes in the ≥65 year age group between 2009 and 2010 with the rate falling 33% from 26.4 to 17.7 cases per 100 000. However, there was no corresponding significant decrease in the overall rate of IPD in this age group, due to PCV-7 serotypes constituting a smaller proportion of the disease in this age group than the age groups directly targeted for vaccination.

In 2010, the highest rate of pneumococcal meningitis was among the <1 year age group. Equal with pneumonia, meningitis was the most common IPD presentation in this age group. The rate of pneumococcal meningitis among <1 year olds almost halved between 2009 and 2010 from 14.3 cases per 100 000 (9 cases) to 7.8 per 100 000 (5 cases). However, this decrease was not significant. There were no cases of pneumococcal meningitis in the 1-2 year age group in either 2009 or 2010.[7]

Data on IPD among the different ethnic groups is only available for 2009 and 2010, that is, since IPD became a notifiable disease. In 2010, as was observed in 2009, the age-standardised rates of IPD in Māori and Pacific Peoples were at least 3 times that in Europeans. However, between 2009 and 2010, there were decreases, albeit non-significant, in IPD rates in European (53% decrease), Māori (28%) and Pacific (37%) infants in the <2 year age group.

As with all vaccines that target only specific types, there is concern that pneumococcal serotypes not included in PCV-7 will increase and essentially 'replace' vaccine types as the principal cause of IPD. This appears to have happened to some extent in several countries, although any increases in disease due to non-vaccine types have usually been somewhat smaller than the reductions in disease due to vaccine types. Serotype 19A is the non-PCV-7

type most frequently reported to have increased.[12,14] Increases in type 19A disease have been of particular concern as this serotype is often associated with antibiotic resistance.[14,15] There have been recent reports of increasing rates of resistance among invasive serotype 19A isolates associated with shifts in the genetic structure of the isolates and the expansion of particular resistant clonal complexes.[16] As yet there have not been any significant increases in rates of type 19A IPD in New Zealand since the introduction of PCV-7 but there was a non-significant increase in the rate of 19A disease in those ≥65 years old between 2009 and 2010: from 1.6 to 3.7 cases per 100 000. In addition, to date, invasive serotype 19A isolates in this country are not especially associated with resistance and there have been no significant changes in resistance among this type over the last 10 years.

IPD cases due to the non-PCV-7 serotype 1 have increased since 2007, but appear to have peaked in 2009 with the case numbers in 2010 (77) being less than half those in 2009 (153). These serotype 1 cases have been strongly associated with IPD in Māori and Pacific school-age children and young adults. However, this increase in serotype 1 disease is unlikely to be a result of serotype replacement following the introduction of PCV-7 since the increase in this type commenced before the introduction of the vaccine and appears to now be waning. In addition, it has mainly been associated with age-groups who are not eligible for PCV-7 vaccination. This pattern of serotype 1 disease fits with that observed globally for this serotype, that is, outbreaks that occurring cyclically every few years.[17]

Pneumococcal serotype 6C was first described in 2007.[18] Until 2010, the serotyping methods used at ESR resulted in both serotypes 6A and 6C being designated as type 6A. Retrospective work has commenced on re-typing invasive pneumococcal isolates designated as 6A prior to 2010 to differentiate types 6A and 6C. Correct categorisation of these isolates will enable more precise monitoring of any cross-serogroup protection conferred by the serotype 6B antigen included in PCV-7 and PCV-10. The epidemiology of IPD in other countries suggests that PCV-7 use has resulted in a reduction in type 6A, but not 6C, IPD.[19]

In 2010, most (79.4%) of the IPD cases in infants who had received ≥1 dose of PCV-7 were due to a non-PCV-7 type. Among the seven cases who had received ≥1 dose of PCV-7 and had disease due to a PCV-7 type, five had serotype 19F disease, one had type 6B disease and one had type 14 disease. Serotypes 19F and 6B were found to be the most common types associated with vaccine breakthrough cases in a United States study.[20]

As most resistant invasive pneumococci belong to one of the serotypes included in PCV-7, a decrease in IPD caused by vaccine types would be expected, and has been observed in other countries, to have the concomitant effect of reducing the incidence of IPD caused by resistant pneumococci.[21] Although there was a decrease in penicillin and cefotaxime resistance between 2008 and 2009, there was no further decrease between 2009 and 2010. However, there is no indication that resistance is increasing in non-PCV-7 serotypes in this country, with PCV-7 types still accounting for over 80% of the penicillin and cefotaxime resistance in 2010.

We noted last year that nearly one-tenth (59/697) of the IPD cases notified in 2009 did not include evidence that they met the case definition.[7] This improved considerably in 2010 with no cases notified on the basis of pneumococci or pneumococcal DNA isolated from or detected in a site that was unequivocally not a normally sterile site.

In late 2011, PCV-7 will be replaced with PCV-10 (Synflorix®) on the childhood immunisation schedule. PCV-10 will give additional coverage for serotypes 1, 5 and 7F. Hopefully, the serotype 1 coverage will prevent future outbreaks of this type such as that we have recently experienced in New Zealand. As the main protein carrier in Synflorix is protein D, an immunogenic protein on the surface of non-typable *Haemophilus influenzae*, this vaccine also provides protection against non-typable *H. influenzae* infections.

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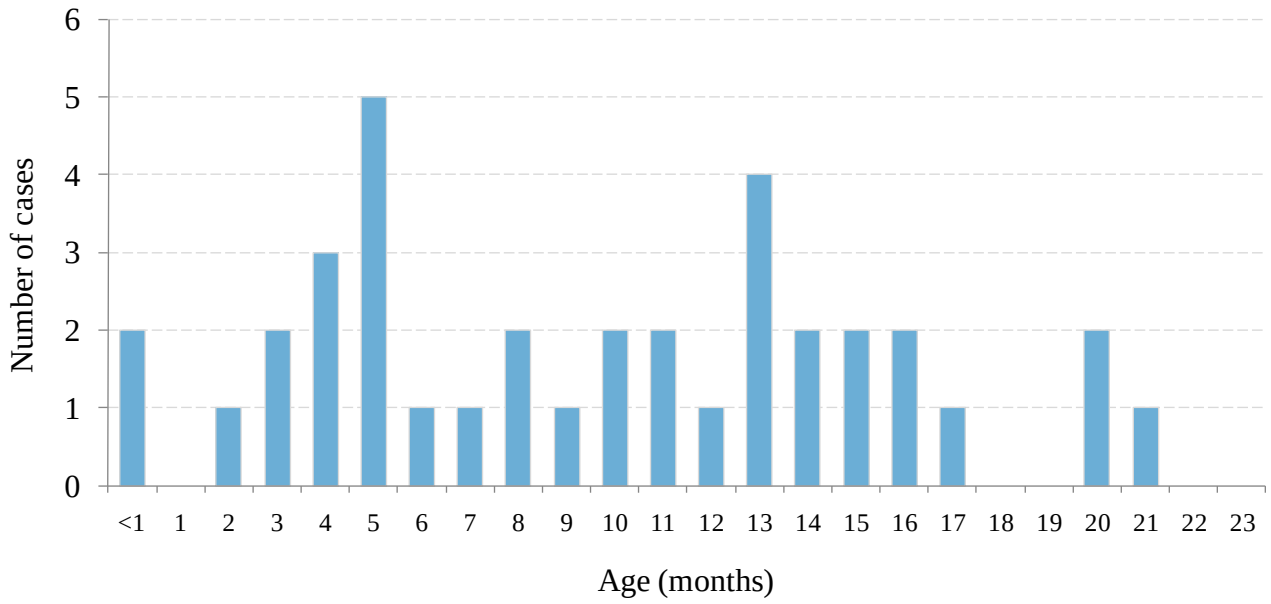
Appendix 1. Laboratory criteria upon which invasive pneumococcal disease diagnosis based, as recorded in the case notification, 2010

Basis of diagnosis[1,2]	Number of cases	Percent of total cases (n=535)	Percent of cases notified as culture positive for which an isolate was received at ESR
Culture of *Streptococcus pneumoniae* from:			
CSF	20	3.7	65.0
blood	478	89.3	99.0
pleural fluid	12	2.2	100.0
joint fluid	11	2.1	90.9
other sites	14	2.6	42.9

1 For several cases, more than one method of laboratory confirmation was recorded. In this analysis, only one method of laboratory confirmation was counted for each case, with methods prioritised in the following order: pneumococcal culture from CSF, pneumococcal culture from blood, positive antigen test on CSF, pneumococcal culture from pleural fluid, pneumococcal culture from joint fluid, and pneumococcal culture from another normally sterile site.

2 No cases were notified as being diagnosed on the basis of identification of pneumococcal DNA in a normally sterile site. All cases notified as being diagnosed on the basis of a positive antigen test on CSF also had a positive CSF or blood culture.

Appendix 2. Age distribution among invasive pneumococcal disease cases <2 years old, 2010 (n=37)



Appendix 3. Rates of invasive pneumococcal disease cases by ethnicity and age group, 2009 and 2010

Age group (years)	Rate per 100 000[1]							
	European		Māori		Pacific Peoples		Asian[2]	
	2009 n=385	2010 n=285	2009 n=179	2010 n=127	2009 n=90	2010 n=82	2009 n=24	2010 n=18
<2	32.3	15.3	105.4	76.3	79.6	49.8	-	-
<5	26.4	10.8	58.7	46.7	59.6	39.7	23.5	32.9
5-64	7.6	4.6	23.8	15.3	32.4	29.3	4.3	2.6
≥65	43.1	40.3	116.8	99.5	130.8	161.0	38.0	-
All ages[3]	13.0	9.0	41.2	32.0	50.0	53.1	12.2	8.6

1 Annual incidence rate per 100 000, based on prioritised ethnicity. A rate is not presented where there are <5 cases.

2 There was only one case among Asian infants <2 years old in both 2009 and 2010, and three cases in Asians ≥65 years in 2010.

3 The rates for all ages are direct-standardised to the age distribution of the total NZ population.

Appendix 4. Case-fatality rates for invasive pneumococcal disease cases by age group, 2010

Age group (years)	Number of cases who died[1]	Case-fatality rate (%[2])	Number of cases for whom information on whether they survived or died was reported[3]
<1	0	-	22
1	0	-	15
2-4	0	-	25
5-14	0	-	23
15-64	8	3.7	216
≥65	19	8.9	213
All ages	27	5.3	514

1 Only includes cases for whom IPD was recorded as the primary cause of death.
2 Calculated on the basis of the number of cases for whom information on outcome was reported.
3 Outcome information available for all cases <1 year of age, all cases 1 year of age, 89.3% (25/28) of cases 2-4 years of age, all cases 5-14 years of age, 96.9% (216/223) of cases 15-64 years of age, and 95.1% (213/224) of cases ≥65 years of age.

Appendix 5. Risk factors among invasive pneumococcal disease cases <2 years of age, 2010

Risk factor	Number of cases for whom information on the risk reported	Number (%[1]) of cases with the risk
Premature <37 weeks gestation (cases <1 year of age)	11	2 (18.2)
Congenital or chromosomal abnormality	34	3 (8.8)
Chronic lung disease or cystic fibrosis	35	1 (2.9)
Anatomical or functional asplenia	33	0
Immunocompromised[2]	34	1 (2.9)
Chronic illness[3]	34	6 (17.6)
Cochlear implants	36	0
Smoking in household	12	6 (50.0)
In childcare	13	5 (38.5)
Resident in long-term or other chronic-care facility	37	0
Other risk factors	NA[4]	1 (2.7[5])

1 Percentage based on only those cases for whom information reported for each particular risk factor, except for 'Other' risk factors (see footnote 5).
2 Includes HIV/AIDS, lymphoma, organ transplant, multiple myeloma, nephrotic syndrome, chronic drug therapy, dysgammaglobulinaemia and sickle cell anaemia.
3 Includes CSF leak, intracranial shunts, diabetes, cardiac disease, pulmonary disease, chronic liver disease, renal impairment and alcohol-related disease.
4 Not applicable, as only reportable when case has 'Other' risk factors.
5 Percentage of all 37 IPD cases ≤2 years of age.

Appendix 6. Serotypes among invasive pneumococcal disease cases by age group, 2010

Serotype	Number (% within age group) of IPD cases due to each serotype:									
	<2 years (n=36)		2-4 years (n=27)		5-64 years (n=234)		≥65 years (n=217)		All ages (n=514)	
1	2	(5.6)	7	(25.9)	58	(24.8)	10	(4.6)	77	(15.0)
3	2	(5.6)	2	(7.4)	9	(3.9)	8	(3.7)	21	(4.1)
4	0		2	(7.4)	26	(11.1)	18	(8.3)	46	(9.0)
5	0		0		0		1	(0.5)	1	(0.2)
6A	0		0		3	(1.3)	7	(3.2)	10	(2.0)
6B	1	(2.8)	1	(3.7)	4	(1.7)	15	(6.9)	21	(4.1)
6C	2	(5.6)	0		3	(1.3)	6	(2.8)	11	(2.1)
7A	0		0		1	(0.4)	1	(0.5)	2	(0.4)
7F	2	(5.6)	0		4	(1.7)	3	(1.4)	9	(1.8)
8	0		0		7	(3.0)	0		7	(1.4)
9N	0		0		7	(3.0)	8	(3.7)	15	(2.9)
9V	0		2	(7.4)	13	(5.6)	16	(7.4)	31	(6.0)
9 nt[1]	0		0		1	(0.4)	0		1	(0.2)
10A	1	(2.8)	0		2	(0.9)	3	(1.4)	6	(1.2)
11A	0		0		8	(3.4)	5	(2.3)	13	(2.5)
12F	0		0		1	(0.4)	0		1	(0.2)
14	3	(8.3)	4	(14.8)	15	(6.4)	18	(8.3)	40	(7.8)
16 nfs[2]	0		0		0		2	(0.9)	2	(0.4)
17F	0		0		3	(1.3)	1	(0.5)	4	(0.8)
17 nt	0		0		1	(0.4)	0		1	(0.2)
18B	0		0		1	(0.4)	0		1	(0.2)
18C	0		0		4	(1.7)	5	(2.3)	9	(1.8)
18F	0		0		0		1	(0.5)	1	(0.2)
19A	7	(19.4)	3	(11.1)	23	(9.8)	21	(9.7)	54	(10.5)
19F	6	(16.7)	3	(11.1)	12	(5.1)	15	(6.9)	36	(7.0)
20	0		0		2	(0.9)	5	(2.3)	7	(1.4)
22F	1	(2.8)	0		4	(1.7)	18	(8.3)	23	(4.5)
22 nt	1	(2.8)	0		0		3	(1.4)	4	(0.8)
23A	0		0		4	(1.7)	4	(1.8)	8	(1.6)
23B	0		0		1	(0.4)	1	(0.5)	2	(0.4)
23F	0		2	(7.4)	9	(3.9)	14	(6.5)	25	(4.9)
33F	4	(11.1)	0		5	(2.1)	4	(1.8)	13	(2.5)
33 nt	1	(2.8)	0		0		0		1	(0.2)
35 nfs	1	(2.8)	0		0		1	(0.5)	2	(0.4)
38	0		1	(3.7)	2	(0.9)	1	(0.5)	4	(0.8)
non-typable	2	(5.6)	0		1	(0.4)	2	(0.9)	5	(1.0)

1 nt, not serotypable with factorised antisera held.
2 nfs, factorised sera not held for serogroup.

Appendix 7. Serotypes among invasive pneumococcal disease cases and vaccine coverage by age group, 2006-07 compared with 2009-10

Serotype	Proportion (%) of IPD cases within the age group (years) due to the serotype:									
	<2		<5		5-64		≥65		All ages	
	06-07 n=235	09-10 n=91	06-07 n=307	09-10 n=156	06-07 n=415	09-10 n=576	06-07 n=355	09-10 n=447	06-07 n=1077	09-10 n=1179
Serotypes in PCV-7:										
4	5.5	1.1	5.2	2.6	18.3	10.1	11.0	9.2	12.2	8.7
6B	15.3	5.5	15.3	6.4	5.5	2.1	6.2	7.2	8.5	4.6
9V	3.8	0.0	4.6	1.9	5.3	4.9	8.2	7.8	6.0	5.6
14	32.8	11.0	30.9	15.4	14.9	6.6	20.0	11.9	21.2	9.8
18C	5.1	1.1	6.8	2.6	2.7	2.4	1.7	2.5	3.5	2.5
19F	13.6	15.4	12.7	14.1	5.8	6.6	9.3	7.6	8.9	8.0
23F	7.7	2.2	6.2	4.5	5.8	4.3	8.5	9.2	6.8	6.2
Total for PCV-7 serotypes	**83.8**	**36.3**	**81.8**	**47.4**	**58.3**	**37.0**	**64.8**	**55.3**	**67.1**	**45.3**
Additional serotypes in PCV-10:										
1	1.7	15.4	1.6	15.4	9.2	31.6	2.0	5.4	4.6	19.5
5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.1
7F	0.4	3.3	0.3	1.9	2.9	3.0	2.0	1.6	1.9	2.3
Total for PCV-10 serotypes	**86.0**	**55.0**	**83.7**	**64.7**	**70.4**	**71.5**	**68.7**	**62.4**	**73.6**	**67.2**
Additional serotypes in PCV-13:										
3	0.9	5.5	0.7	4.5	4.1	3.7	7.0	4.3	4.1	4.0
6A&6C[1]	2.6	4.4	2.9	3.2	2.4	1.9	1.4	4.0	2.2	2.9
19A	5.1	16.5	6.8	14.1	4.8	6.8	4.5	6.7	5.3	7.7
Total for PCV-13 serotypes	**94.5**	**81.3**	**94.1**	**86.5**	**81.7**	**83.9**	**81.7**	**77.4**	**85.2**	**81.8**
Non-PCV serotypes[2]:										
8	0.0	0.0	0.0	0.0	5.8	2.6	2.0	0.9	2.9	1.6
9N	0.0	0.0	0.0	1.3	1.9	1.9	2.3	2.2	1.5	2.0
10A	0.4	1.1	0.7	0.6	1.5	0.7	1.1	1.1	1.1	0.9
11A	0.4	1.1	0.3	0.6	1.7	1.7	2.0	1.8	1.4	1.6
20	0.0	0.0	0.0	0.0	0.5	0.9	1.4	1.8	0.7	1.1
22F	0.9	2.2	0.7	1.3	2.4	2.6	2.5	6.3	2.0	3.8
23A	0.0	1.1	0.3	0.6	0.2	0.9	0.6	1.3	0.4	1.0
33F	0.4	4.4	0.7	2.6	0.0	1.0	0.9	1.6	0.5	1.4

1 Serotypes 6A and 6C only distinguished since 2010; therefore they have been combined for this analysis.

2 The specific serotypes listed are those that accounted for ≥1% of all cases in either of the two 2-year periods.

Appendix 8. Serotype 19A invasive pneumococcal disease case numbers and rates, by age group, 2004-2010

Year	Age group (years)									
	<2		<5		5-64		≥65		All ages	
	Total number of cases	Number (rate[1]) serotype 19A cases	Total number of cases	Number (rate[1]) serotype 19A cases	Total number of cases	Number (rate[1]) serotype 19A cases	Total number of cases	Number (rate[1]) serotype 19A cases	Total number of cases	Number (rate[1]) serotype 19A cases
2004	128	8 (7.1)	161	10 (3.5)	193	5 (0.2)	190	8 (1.6)	545	23 (0.6)
2005	113	6 (5.2)	152	8 (2.8)	177	10 (0.3)	163	9 (1.8)	492	27 (0.7)
2006	119	5 (4.3)	151	10 (3.5)	202	13 (0.4)	169	4 (0.8)	522	27 (0.6)
2007	116	7 (5.8)	156	11 (3.8)	213	7 (0.2)	186	12 (2.3)	555	30 (0.7)
2008	78	5 (4.0)	112	7 (2.3)	291	22 (0.6)	227	11 (2.0)	630	40 (0.9)
2009	55	8 (6.3)	93	12 (3.9)	342	16 (0.5)	230	9 (1.6)	665	37 (0.9)
2010	36	7 (5.5)	63	10 (3.2)	234	23 (0.7)	217	21 (3.7)	514	54 (1.2)

1 Rate per 100 000 population

Appendix 9. Serotype 1 invasive pneumococcal disease case numbers and rates, by age group, 2004-2010

Year	Age group (years)									
	<2		<5		5-64		≥65		All ages	
	Total number of cases	Number (rate[1]) serotype 1 cases	Total number of cases	Number (rate[1]) serotype 1 cases	Total number of cases	Number (rate[1]) serotype 1 cases	Total number of cases	Number (rate[1]) serotype 1 cases	Total number of cases	Number (rate[1]) serotype 1 cases
2004	128	0	161	0	193	2 (0.1)	190	0	545	2 (0.1)
2005	113	0	152	0	177	0	163	0	492	0
2006	119	2 (1.7)	151	2 (0.7)	202	10 (0.3)	169	3 (0.6)	522	15 (0.4)
2007	116	2 (1.7)	156	3 (1.0)	213	28 (0.8)	186	4 (0.8)	555	35 (0.8)
2008	78	1 (0.8)	112	5 (1.7)	291	56 (1.6)	227	9 (1.7)	630	70 (1.6)
2009	55	12 (9.4)	93	15 (4.9)	342	124 (3.6)	230	14 (2.5)	665	153 (3.5)
2010	36	2 (1.6)	63	9 (2.9)	234	58 (1.7)	217	10 (1.8)	514	77 (1.8)

1 Rate per 100 000 population.

Appendix 10. Penicillin and cefotaxime MIC distribution of pneumococci from invasive disease, 2010

	Percent of isolates with an MIC (mg/L) of:[1]											
	0.008	**0.016**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**
penicillin	1.4	47.9	30.9	1.8	1.6	1.0	3.1	6.4	5.1	1.0		
cefotaxime	1.8	65.0	13.0	1.9	1.8	1.8	6.6	6.2	0.4	1.0	0.4	0.2

1 Shaded cells represent MICs that are categorised as penicillin resistant or cefotaxime non-susceptible (intermediate and resistant), based on the meningitis interpretations: penicillin resistant, MIC ≥0.12 mg/L; cefotaxime intermediate, MIC 1 mg/L; and cefotaxime resistant, MIC ≥2 mg/L.

Appendix 11. Trends in penicillin resistance, cefotaxime resistance and multidrug resistance among pneumococci from invasive disease, 2001-2010

Year	Number of isolates	Penicillin								Cefotaxime						MDR[6]
		Meningitis[1]		Non-meningitis[2]			Oral[3]			Meningitis[4]			Non-meningitis[5]			
		%S	%R	%S	%I	%R	%S	%I	%R	%S	%I	%R	%S	%I	%R	
2001	537	87.3	12.7	99.1	0.9	0.0	87.3	8.8	3.9	95.2	3.4	1.5	98.5	0.6	0.9	3.5
2002	490	83.1	16.9	99.6	0.4	0.0	83.1	13.5	3.5	94.9	3.1	2.0	98.0	0.4	1.6	5.1
2003	523	83.6	16.4	98.9	1.2	0.0	83.6	9.0	7.5	88.0	8.4	3.6	96.4	1.9	1.7	7.1
2004	545	81.8	18.2	98.5	1.5	0.0	81.8	8.1	10.1	87.2	9.7	3.1	96.9	2.4	0.7	5.3
2005	492	82.9	17.1	98.6	1.4	0.0	82.9	10.0	7.1	90.5	6.5	3.1	97.0	1.7	1.4	6.7
2006	522	84.1	15.9	98.9	1.0	0.2	84.1	8.1	7.9	90.0	7.3	2.7	97.3	1.7	1.0	4.4
2007	555	77.7	22.3	99.1	0.7	0.2	77.7	16.0	6.3	86.0	11.4	2.7	97.3	1.1	1.6	6.1
2008	630	77.9	22.1	99.5	0.5	0.0	77.9	14.6	7.5	84.9	10.0	5.1	94.9	3.0	2.1	5.9
2009	665	82.3	17.7	99.7	0.3	0.0	82.3	12.3	5.4	91.1	6.9	2.0	98.1	1.4	0.6	5.3
2010	514	81.9	18.1	99.0	1.0	0.0	81.9	12.1	6.0	91.8	6.2	1.9	98.1	0.4	1.6	5.4

1 Penicillin meningitis interpretations: susceptible (S), MIC ≤0.06 mg/L; resistant (R), MIC ≥0.12 mg/L; no intermediate category.
2 Penicillin non-meningitis (parenteral treatment) interpretations: susceptible (S), MIC ≤2 mg/L; intermediate (I), MIC 4 mg/L; resistant (R), MIC ≥8 mg/L.
3 Penicillin non-meningitis (oral treatment) interpretations: susceptible (S), MIC ≤0.06 mg/L; intermediate (I), MIC 0.12-1 mg/L; resistant (R), MIC ≥2 mg/L.
4 Cefotaxime meningitis interpretations: susceptible (S), MIC ≤0.5 mg/L; intermediate (I), MIC 1 mg/L; resistant (R), MIC ≥2 mg/L.
5 Cefotaxime non-meningitis interpretations: susceptible (S), MIC ≤1 mg/L; intermediate (I), MIC 2 mg/L; resistant (R), MIC ≥4 mg/L.
6 Multidrug resistant, that is, resistant to penicillin (meningitis interpretation) and three additional antibiotics.

Appendix 12. Trends in resistance to non-β-lactam antibiotics, among pneumococci from invasive disease, 2001-2010[1]

Year	Number of isolates	Chloramphenicol		Clindamycin[2]			Co-trimoxazole			Erythromycin			Tetracycline		
		%S[3]	%R[3]	%S	%I[3]	%R[4]	%S	%I	%R	%S	%I	%R	%S	%I	%R
2001	537	98.7	1.3				62.8	6.0	31.3	94.2	0.4	5.4	94.8	0.2	5.0
2002	490	97.6	2.5				62.5	1.4	36.1	90.6	0.4	9.0	93.1	0.0	6.9
2003	523	96.6	3.4				64.4	1.7	33.8	90.1	0.6	9.4	91.0	0.4	8.6
2004	545	97.3	2.8				61.1	0.2	38.7	91.4	0.2	8.4	91.9	0.2	7.9
2005	492	96.8	3.3				67.3	0.6	32.1	87.8	0.0	12.2	90.9	0.6	8.5
2006	522	98.5	1.5				65.7	1.5	32.8	88.7	0.2	11.1	92.5	0.4	7.1
2007	555	97.7	2.3	93.7	0.0	6.3	63.2	1.8	35.0	86.0	0.4	13.7	90.8	0.7	8.5
2008	630	97.6	2.4	94.6	0.0	5.4	67.6	2.2	30.2	87.8	0.3	11.9	91.9	0.5	7.6
2009	665	98.8	1.2	95.3	0.2	4.5	72.6	2.1	25.3	90.2	0.2	9.6	92.5	0.3	7.2
2010	514	98.1	2.0	94.7	0.0	5.3	73.5	2.1	24.3	91.1	0.0	9.0	91.6	0.8	7.6

1 All isolates susceptible to vancomycin. Moxifloxacin susceptibility tested since 2005, with no resistance identified and a maximum of one isolate per annum with intermediate resistance. Rifampicin susceptibility tested in 2010 only, with no resistance identified.
2 Clindamycin susceptibility tested since 2007.
3 S, susceptible; I, intermediate; R, resistant.
4 Includes isolates with inducible clindamycin resistance.

Appendix 13. Penicillin and cefotaxime resistance among isolates from invasive pneumococcal disease by region and district health board (DHB), 2010

Region and DHB	Number of isolates	Penicillin	Cefotaxime	
		% resistant[1] MIC ≥0.12 mg/L	% intermediate[1] MIC 1 mg/L	% resistant[1] MIC ≥2 mg/L
Northland region	**214**	**19.2**	**6.1**	**1.9**
Northland	17	11.8	5.9	0.0
Waitemata	56	28.6	8.9	1.8
Auckland	43	20.9	2.3	0.0
Counties Manukau	98	14.3	6.1	3.1
Midland region	**107**	**15.9**	**3.7**	**2.8**
Waikato	47	21.3	8.5	4.3
Lakes	18	5.6	0.0	0.0
Bay of Plenty	31	12.9	0.0	3.2
Tairawhiti	1	0.0	0.0	0.0
Taranaki	10	20.0	0.0	0.0
Central region	**102**	**17.7**	**5.9**	**2.0**
Hawke's Bay	22	13.6	9.1	0.0
Whanganui	9	33.3	0.0	0.0
MidCentral	18	22.2	5.6	5.6
Hutt	21	14.3	9.5	0.0
Capital and Coast	23	21.7	4.4	4.4
Wairarapa	5	0.0	0.0	0.0
Nelson Marlborough	4	0.0	0.0	0.0
Southern region	**91**	**18.7**	**9.9**	**1.1**
West Coast	1	0.0	0.0	0.0
Canterbury	40	22.5	7.5	2.5
South Canterbury	3	33.3	0.0	0.0
Southern	7	14.9	12.8	0.0
New Zealand total	**514**	**18.1**	**6.2**	**2.0**

1 Meningitis interpretations; no intermediate category for penicillin.

Appendix 14. Serotypes among penicillin resistant, cefotaxime resistant and intermediate, and multiresistant isolates from invasive pneumococcal disease cases, 2010

Serotype	Number (%[1]) isolates			
	Penicillin	Cefotaxime		Multi-resistant[3] (n=28)
	resistant[2] MIC ≥0.12 mg/L (n=93)	intermediate[2] MIC 1 mg/L (n=32)	resistant[2] MIC ≥2 mg/L (n=10)	
Serotypes in PCV-7:				
4	0	0	0	0
6B	12 (12.9)	4 (12.5)	0	5 (17.9)
9V	30 (32.3)	11 (34.4)	0	0
14	13 (14.0)	9 (28.1)	1 (10.0)	2 (7.1)
18C	0	0	0	0
19F	18 (19.4)	4 (12.5)	9 (90.0)	14 (50.0)
23F	2 (2.2)	0	0	1 (3.6)
Total for PCV-7 serotypes	**75 (80.7)**	**28 (87.5)**	**10 (100.0)**	**22 (78.6)**
Additional serotypes in PCV-10:				
1	1 (1.1)	0	0	0
5	0	0	0	0
7F	0	0	0	0
Total for PCV-10 serotypes	**76 (81.7)**	**28 (87.5)**	**10 (100.0)**	**22 (78.6)**
Additional serotypes in PCV-13:				
3		0	0	0
6A	1 (1.1)	1 (3.1)	0	1 (3.6)
19A	10 (10.8)	3 (9.4)	0	4 (14.3)
Total for PCV-13 serotypes	**87 (93.6)**	**32 (100.0)**	**10 (100.0)**	**27 (96.4)**
Non-PCV serotypes:				
6C	1 (1.1)	0	0	0
9 non-typable	1 (1.1)	0	0	0
11A	1 (1.1)	0	0	0
Non-typable	3 (3.2)	0	0	1 (3.6)

1 Percentage of the intermediate or resistant isolates.
2 Meningitis interpretations; no intermediate category for penicillin.
3 Resistant to penicillin (meningitis interpretation) and three additional antibiotics.

Appendix 15. Trends in penicillin resistance, cefotaxime resistance and multidrug resistance among serotype 19A pneumococci from invasive disease, 2001-2010[1]

Year	Number of isolates	Penicillin resistant[2]		Cefotaxime resistant[3]		Multiresistant[4]	
		Number	Percent (95% CIs)	Number	Percent (95% CIs)	Number	Percent (95% CIs)
2001	23	7	30.4 (13.2-52.9)	0	0.0 (0.0-14.8)	0	0.0 (0.0-14.8)
2002	18	3	16.7 (3.6-41.4)	0	0.0 (0.0-18.5)	0	0.0 (0.0-18.5)
2003	22	6	27.3 (10.7-50.2)	1	4.6 (0.1-22.8)	1	4.6 (0.1-22.8)
2004	23	6	26.1 (10.2-48.4)	1	4.4 (0.1-21.9)	1	4.4 (0.1-21.9)
2005	27	2	7.4 (0.9-24.3)	0	0.0 (0.0-12.7)	0	0.0 (0.0-12.7)
2006	27	6	22.2 (8.6-42.3)	0	0.0 (0.0-12.7)	0	0.0 (0.0-12.7)
2007	30	3	10.0 (2.1-26.5)	0	0.0 (0.0-11.6)	1	3.3 (0.1-17.2)
2008	40	10	25.0 (12.7-41.2)	1	2.5 (0.1-13.2)	3	7.5 (1.6-20.4)
2009	37	3	8.1 (1.7-21.9)	0	0.0 (0.0-9.5)	0	0.0 (0.0-9.5)
2010	54	10	18.5 (9.3-31.4)	0	0.0 (0.0-6.6)	4	7.4 (2.1-17.9)

1 There were no significant differences ($P \leq 0.05$) in penicillin, cefotaxime or multidrug resistance over the 10 year period.
2 Penicillin resistant using meningitis interpretations, that is, MIC ≥ 0.12 mg/L.
3 Cefotaxime resistant using meningitis interpretations, that is, MIC ≥ 2 mg/L.
4 Resistant to penicillin (meningitis interpretation) and three additional antibiotics.