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Australian Meningococcal Surveillance Programme annual report, 2019

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Australian Meningococcal Surveillance Programme annual report, 2019

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Abstract

Invasive meningococcal disease (IMD) is a notifiable disease in Australia, and both probable and laboratory-confirmed cases of IMD are reported to the National Notifiable Diseases Surveillance System (NNDSS). In 2019, there were 206 notifications of IMD. Of these, 202 were laboratory-confirmed cases analysed by the reference laboratories of the Australian National Neisseria Network (NNN). Of the 202 laboratory-confirmed cases of IMD, 167 were confirmed by bacterial culture and 35 by nucleic acid amplification testing, and all had the serogroup determined. Fine typing was available on 146 samples (146/202, 72%). *Neisseria meningitidis* serogroup B (MenB) infections accounted for 50.0% (101/202); MenW for 26.2% (53/202); MenY for 20.8% (42/202) and MenC for 3.0% of cases (6/202). Of the MenW cases, 88% were PorA antigen type P1.5,2, and 65% of these (24/37) were sequence type 11, the hypervirulent strain reported in recent outbreaks in Australia and overseas.

The primary peaks of IMD notifications in Australia in 2019 were observed in infants less than 1 year of age (36/202, 18%) and in adults aged 65 years or older (39/202, 19%). MenB infections predominated in those aged less than 5 years and those aged 15–19 years, whereas MenW and MenY infections predominated in those aged 45 years or more.

All 167 IMD isolates were tested for antimicrobial susceptibility. One isolate out of these 167 (0.6%) was resistant to penicillin with an MIC \geq 1mg/L; 154/167 isolates (92%) had decreased susceptibility to penicillin. All isolates were susceptible to ceftriaxone and ciprofloxacin, and one isolate was resistant to rifampicin.

Keywords: antibiotic resistance; disease surveillance; meningococcal disease; *Neisseria meningitidis*

Introduction

Australia's National Neisseria Network (NNN) was established in 1979 as a collaborative network of reference laboratories in each state and territory which contribute to the laboratory surveillance of the pathogenic *Neisseria*: *N. meningitidis* and *N. gonorrhoeae*. The NNN has coordinated laboratory data from cases of invasive meningococcal disease (IMD) for the Australian Meningococcal Surveillance Programme (AMSP) since 1994, and is supported by the Australian Government Department of Health and the jurisdictions.¹ The NNN laboratories supply phenotypic and genotypic data to sup-

plement the notification data from the National Notifiable Diseases Surveillance System (NNDSS), which includes cases of probable and laboratory-confirmed IMD.

Notifications of IMD in Australia peaked in 2002 at 3.5 cases per 100,000,² with the majority of disease at that time caused by MenB and MenC. In 2003, the introduction of the conjugate serogroup C meningococcal vaccine to the National Immunisation Program was followed by significant and sustained reductions, in the 10 years that followed, of both the number of serogroup C IMD cases and the overall notifications of IMD, to a rate of only 0.6 cases per 100,000 in 2013.^{3,4}

After 2013, however, there followed increases both in IMD notifications and in the proportion of IMD caused by the MenW and MenY serogroups in Australia. The IMD notification rate increased to 1.5 cases per 100,000 in 2017,² when MenACWY immunisation programmes were implemented across jurisdictions in targeted age groups. This was followed by a change in the national immunisation programme in 2018 substituting monovalent MenC vaccine with the 4-valent MenACWY vaccine. In 2018 IMD notifications declined to 1.1 per 100,000, then to 0.8 per 100,000 in 2019.

IMD is a rare disease in Australia, but one of public health concern. Continued monitoring of phenotypic and genotypic features of IMD strains is critical to plan and inform clinical management of cases, case clusters and outbreaks of IMD locally and nationally, and to inform and monitor public health interventions.

Methods

Case confirmation of invasive meningococcal disease

Case confirmation is based on isolation of *N. meningitidis*, or on a positive nucleic acid amplification testing (NAAT) from a normally sterile site, defined as laboratory-definitive evidence of IMD according to the national case definition.⁵ Information regarding the site of infection, age and sex of the patients is collated by the NNN for the AMSP.

IMD cases are categorised on the basis of the site from which *N. meningitidis* was isolated, or from which meningococcal DNA was detected (blood, joint fluid, vitreous fluid). When *N. meningitidis* is detected from both blood and cerebrospinal fluid (CSF) from the same patient, the case is classified as one of meningitis.

Phenotyping and genotyping of *Neisseria meningitidis*

Phenotyping is limited to the determination of the serogroup by detection of soluble polysaccharide antigens. Genotyping of both isolates and DNA extracts is performed by sequencing of products derived from amplification of the porin genes *porA* and *porB* and the outer membrane protein, *fetA*.

Antibiotic susceptibility testing

Meningococcal isolates are tested to determine their minimum inhibitory concentration (MIC) values to antibiotics used for therapeutic and prophylactic purposes: ceftriaxone, ciprofloxacin, penicillin and rifampicin. This program has historically reported penicillin testing categories as: sensitive (MIC \leq 0.03 mg/L); less sensitive (MIC 0.06–0.5 mg/L); and resistant (MIC \geq 1 mg/L). However, to monitor across antimicrobial susceptibility testing methods, a distribution of penicillin MIC values is now reported.

Results

In 2019, there were 202 laboratory-confirmed cases of IMD analysed by the NNN, and 206 cases notified to the NNDSS.² The numbers of notifications has continued to decline following the recent MenACWY vaccination interventions in Australia – from 380 in 2017 to 281 in 2018 and 206 in 2019. Laboratory data were available for 98% of notified cases of IMD in Australia in 2019 (Figure 1). In 2019, the peak incidence for IMD occurred in midwinter and early spring (1 July to 30 September) (Table 1).

In 2019 there was a decrease in notifications of IMD across jurisdictions compared to 2018. While New South Wales reported the highest number of cases (58 cases), this was a decrease from 70 cases in 2018. Queensland had the second highest number of notifications (45 cases), a decrease from 58 cases in 2018. The number of cases from each jurisdiction for 2019 is shown in Table 2.

Figure 1: Number of invasive meningococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with laboratory-confirmed data from the Australian Meningococcal Surveillance Programme, Australia, 1991–2019

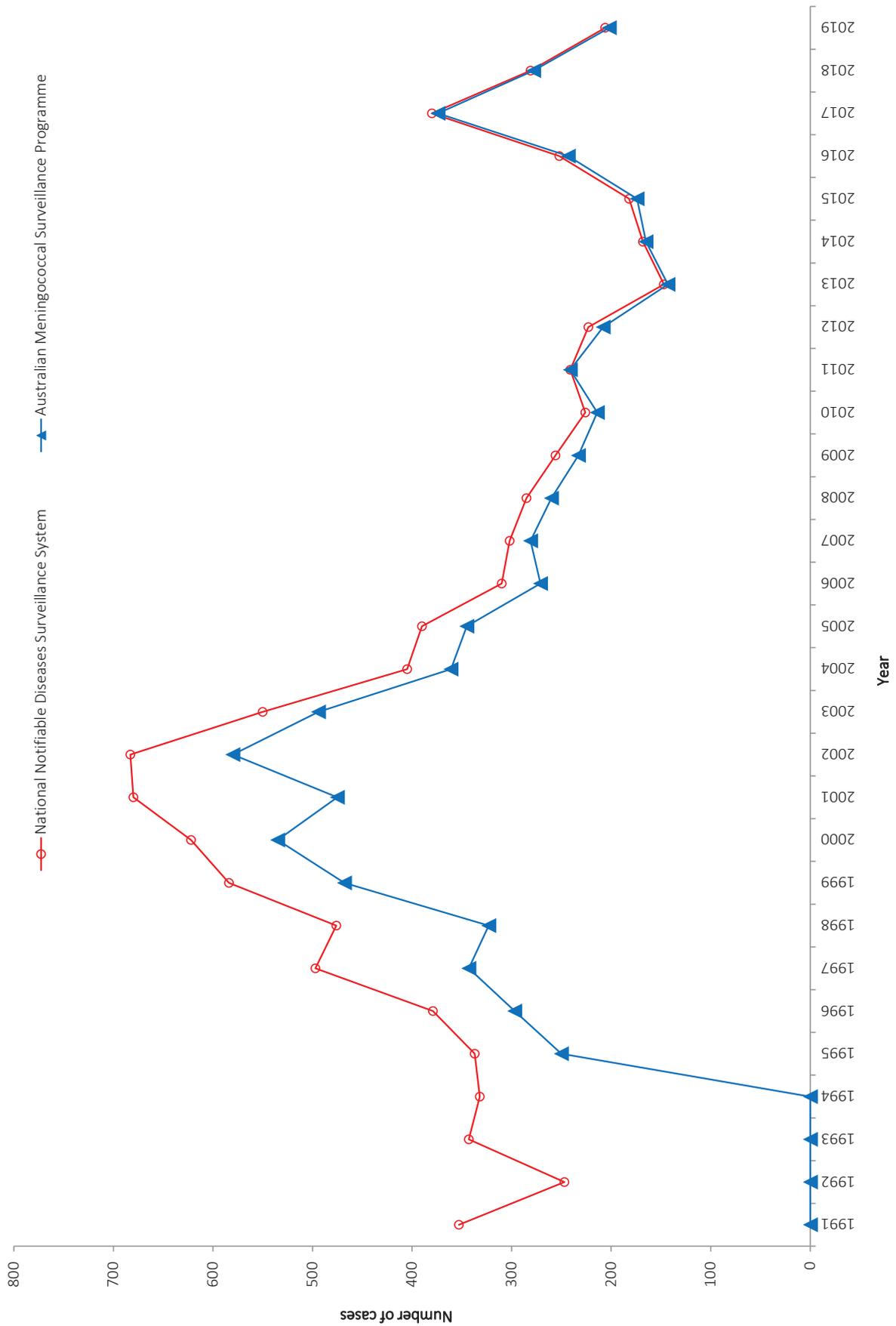


Table 1: Laboratory-confirmed cases of invasive meningococcal disease, Australia 2019

IMD serogroup 2019	1 January – 31 March	1 April – 30 June	1 July – 30 September	1 October – 31 December	Total
B	19	25	37	20	101
C	3	2	0	1	6
Y	4	8	21	9	42
W	11	13	19	10	53
Total	37	48	77	40	202

Table 2: Number of laboratory-confirmed cases of invasive meningococcal disease, Australia, 2019, by state or territory and serogroup

State/ territory	Serogroups				Total
	B	C	Y	W	
ACT	1	0	0	0	1
NSW	34	0	14	10	58
NT	1	0	0	6	7
Qld	18	0	18	9	45
SA	18	0	4	3	25
Tas	5	0	0	2	7
Vic	16	0	4	14	34
WA	8	6	2	9	25
Australia	101	6	42	53	202
	50.0	3.0	20.8	26.2	%

Table 3: Laboratory-confirmed cases of invasive meningococcal disease, by age and serogroup; and the proportion of IMD attributable to MenB Australia, 2019

Serogroup	Age group									Total
	<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	
B	20	13	3	6	21	10	12	12	4	101
C	1	0	1	0	0	0	3	1	0	6
Y	4	0	0	1	3	9	0	9	16	42
W	11	1	2	0	2	2	9	7	19	53
Total	36	14	6	7	26	21	24	29	39	202
%B of within age group	55.6	92.9	50.0	85.7	80.8	47.6	50.0	41.4	10.3	

Table 4: Number of laboratory-confirmed cases of invasive meningococcal disease, Australia, 2019, by specimen type and method of confirmation

Specimen	Bacterial culture	Nucleic Acid Amplification Test	Total
Blood	150	14	164
CSF +/- Blood	13	20	33
Other specimens ^a	4	1	5
Total	167	35	202

a Other specimens: joint aspirates (3); ascitic fluid (1); and unspecified (1).

Age distribution

The peak incidence of IMD in 2019 occurred in the extremes of age: in infants of less than one year (18% of cases, 36/202); and adults aged over 65 years or more, comprising 19% of IMD cases (38/202) in 2019 (Table 3). We note also that 25% of IMD occurred in children less than 5 years of age (50/202). Between 2003 and 2014, the proportion of IMD that occurred in children aged less than 5 years ranged from 28% to 36% of cases. Since 2015, in Australia the proportion of IMD in children less than 5 years of age has ranged from 21% to 27%.

Samples from laboratory-confirmed cases

In 2019, diagnosis was confirmed by a positive bacterial culture in 83% of cases of IMD (167/202); for 17% (35/202) of cases, IMD was confirmed by NAAT testing alone (Table 4). There were 33 diagnoses of meningitis and 164 diagnoses of septicaemia (Table 4). Additionally, there were 5 IMD diagnoses confirmed from other sites comprising joint fluid aspirates (n = 3), ascitic fluid (n = 1), and an unspecified site (n = 1).

Notifications and proportion of MenB, MenC, MenY and MenW

The serogroup was determined for all 202 laboratory-confirmed cases of IMD (Tables 2 and 3). In 2019, MenB accounted for 50% of all IMD in Australia. With respect to serogroup infections by age group, as shown in Table 3, in children aged 1–4 years (13/14, 92.9%) and in older chil-

dren and adolescents (10–19 years) (27/33, 81.8%) MenB predominated. MenB accounted for the largest proportion of disease in all age groups (range 41.4–92.9%) excepting 65 years and older where MenW and MenY were in the majority.

New South Wales reported the largest number of notifications of MenB IMD (n = 34), accounting for 59% of IMD in this state (34/58) in 2019. South Australia was again the state with the highest proportion of MenB, 72% of statewide IMD cases (18/25). In the years 2006–2012 the proportion of IMD cases caused by MenB was 84–88%, before falling in successive years: in 2013–2014 to 75–80%, in 2015 to 64%, and to 36% in 2016–2017. There was an increase in its attributable proportion in 2018 to 44% and again in 2019 to 50% of IMD cases reported (Figure 2).

There were 6 notifications of IMD caused by MenC in 2019; this is higher than the number reported in 2018 (n = 4), but similar to annual national case numbers for the period 2014–2016. All MenC IMD cases in 2019 were reported from Western Australia (Table 3, Figure 3).

The rise in IMD notifications in Australia since 2014 is due to a rise in the number of infections of both MenW and MenY, as shown in Figure 1 and Figure 2. Prior to 2015 the proportion of cases of IMD caused by MenW was low, ranging from 1.1–4.8% in 1997–2012, then increasing to 8.4–9.7% in 2013–2014. In 2015 it was 21%, in 2016 it was 44%, in 2017–2018 it was 36–38%, as shown in Figure 2. In 2019 there were 53/202 MenW infections, accounting for 26% of IMD.

Figure 2: Proportion of serogroups of laboratory-confirmed invasive meningococcal disease, Australia, by year

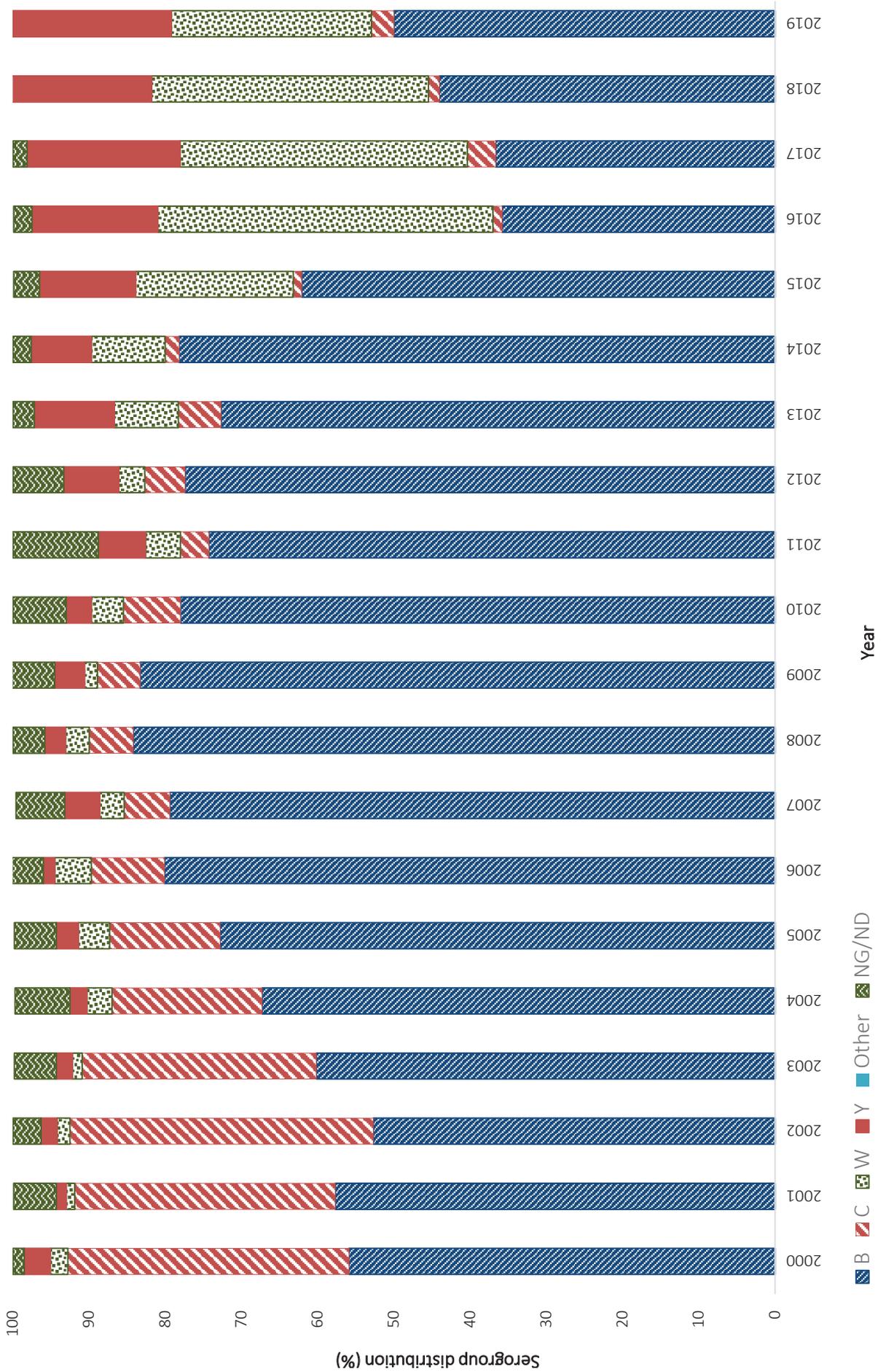


Figure 3: Number of serogroup B, C, Y and W cases of laboratory-confirmed invasive meningococcal disease, Australia, 2019, by age

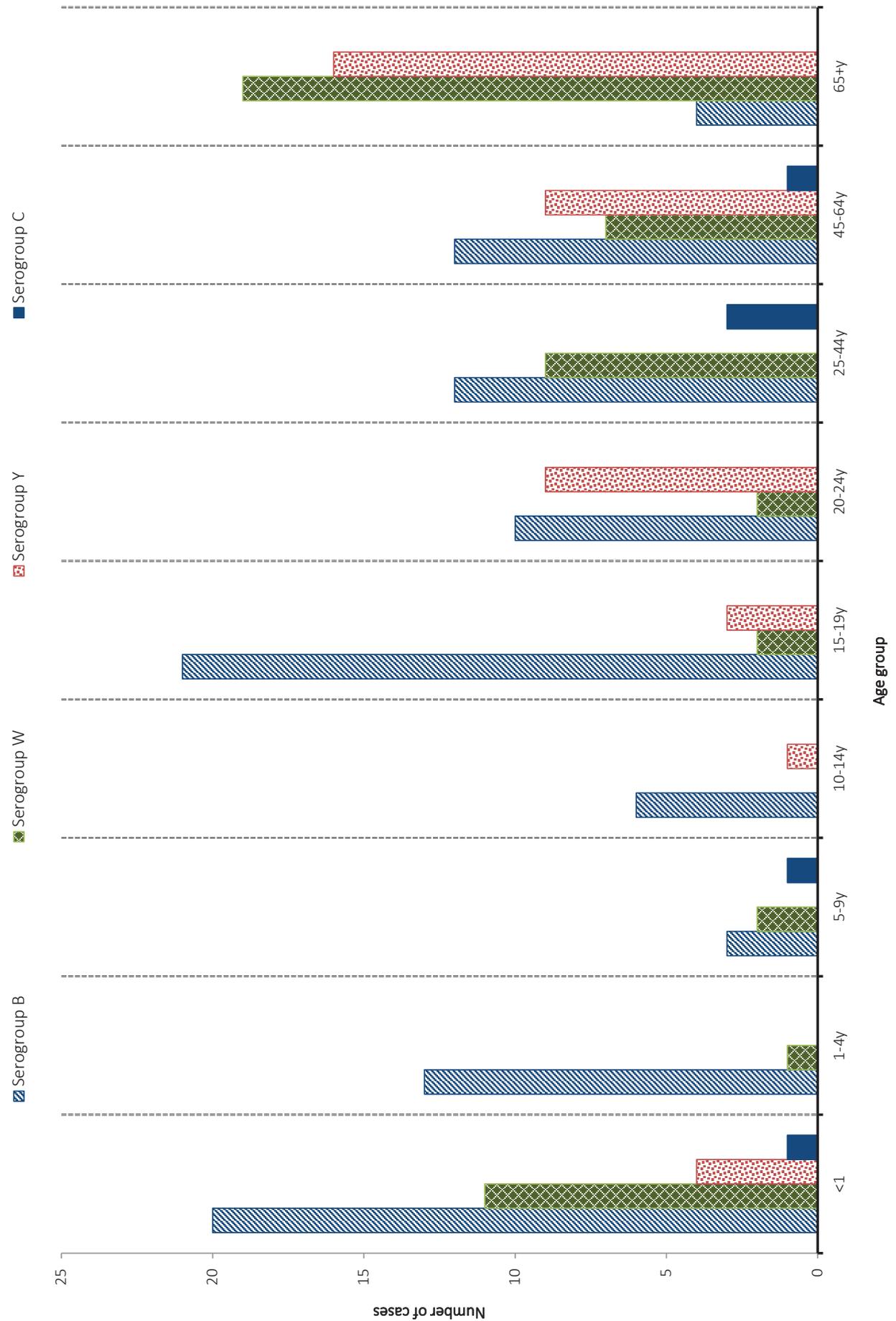


Figure 4: Number of *porA* genotypes for MenB in laboratory-confirmed cases of invasive meningococcal disease Australia, 2019

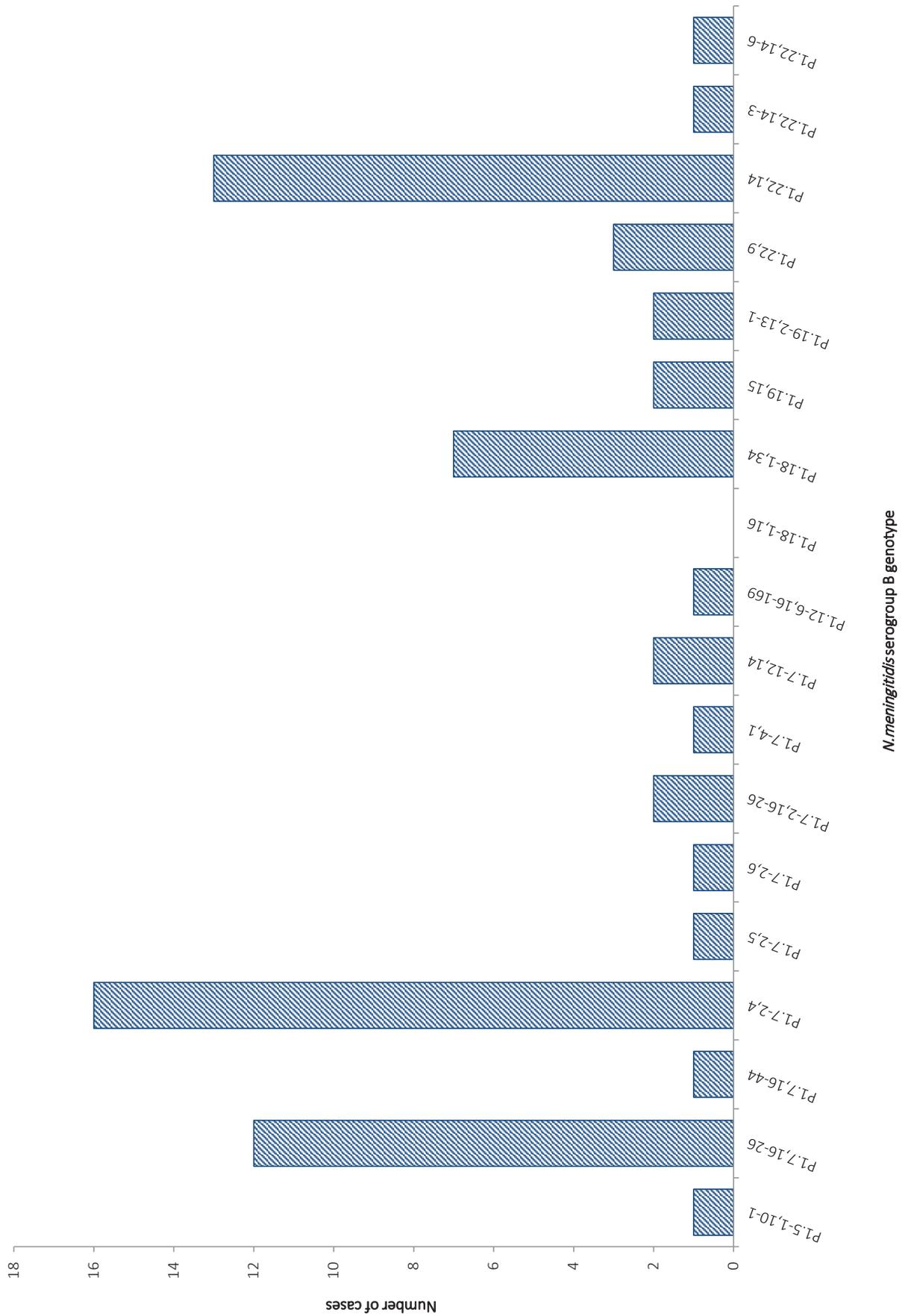


Figure 5: Number of *porA* genotypes for MenW in laboratory-confirmed cases of invasive meningococcal disease Australia, 2019

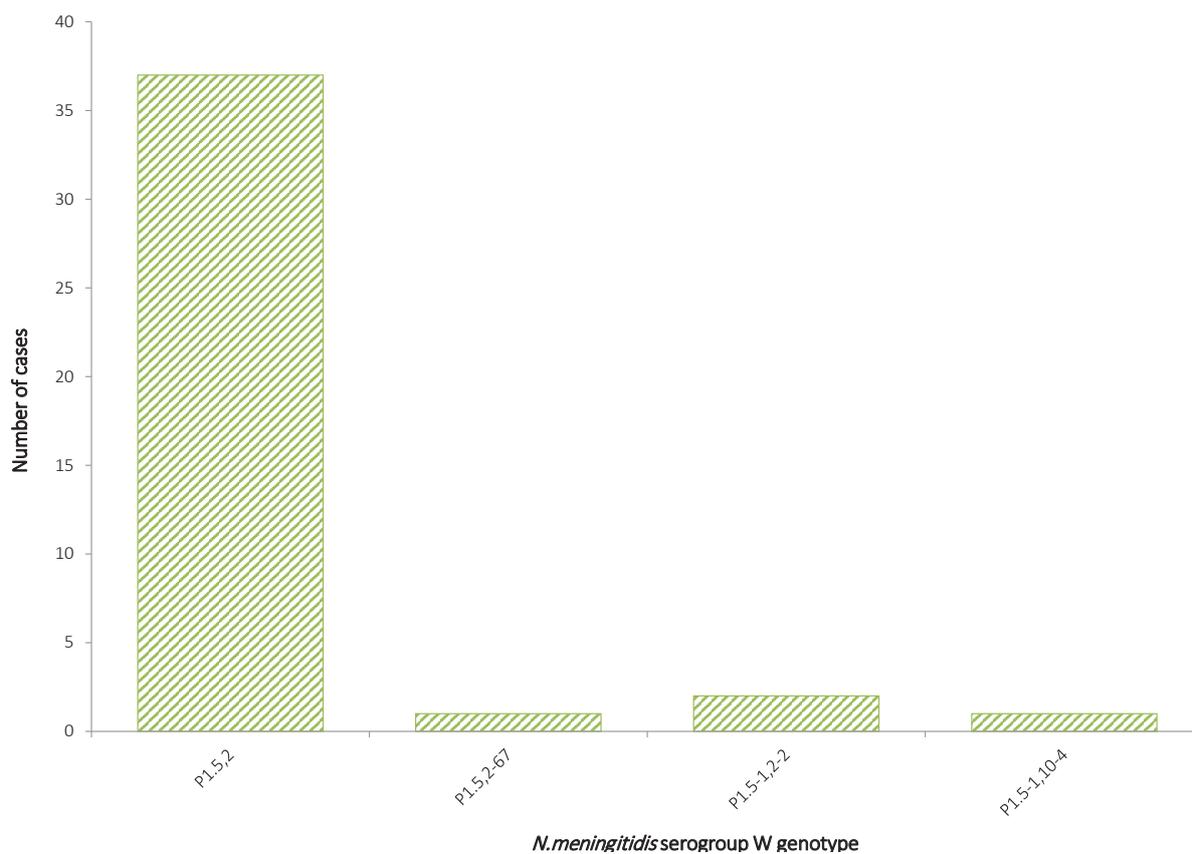


Figure 6: Number of *porA* genotypes for MenY in laboratory-confirmed cases of invasive meningococcal disease Australia, 2019

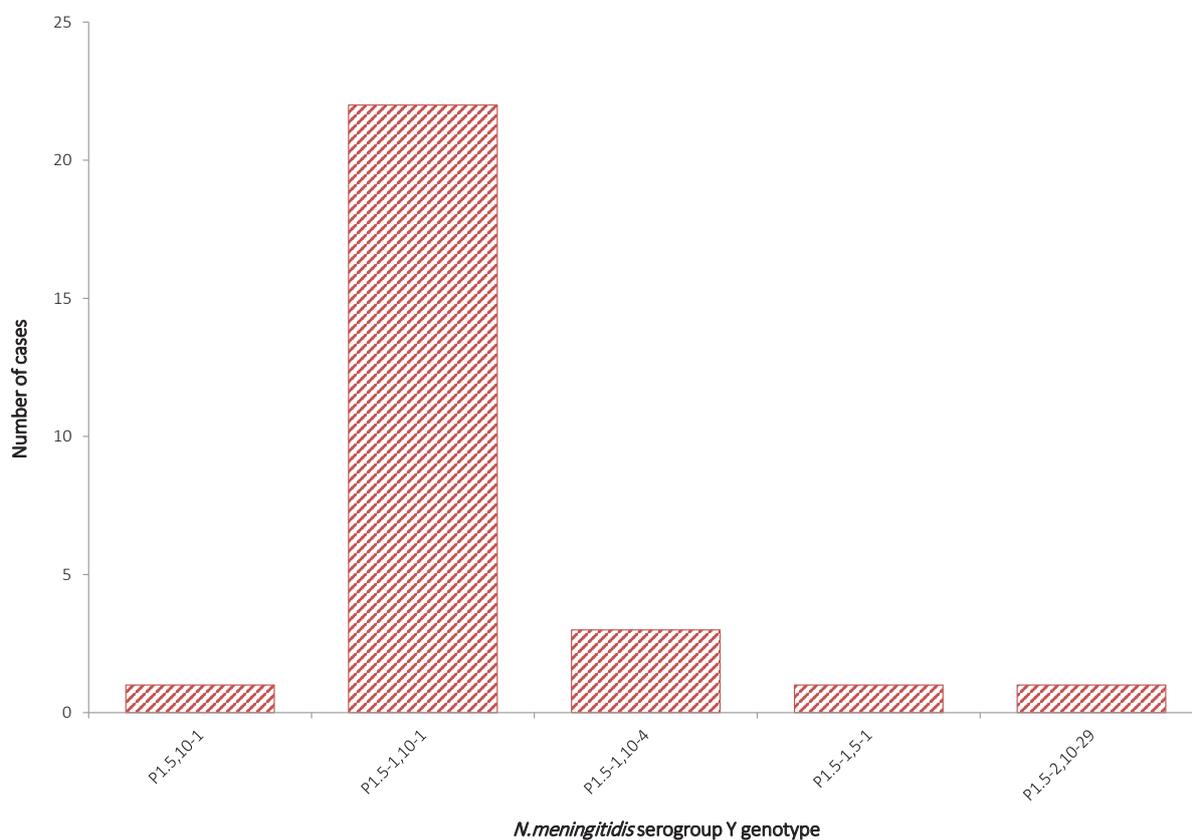


Table 5: Distribution of *porA* genotype laboratory-confirmed cases of invasive meningococcal disease, Australia, 2019, by state or territory

<i>porA</i> genotype	Number per serogroup per state / territory							
	NSW	Qld	Vic	SA	WA	ACT	Tas	NT
P1.5,2	3W	9W	11W	2W	7W, 5C	0	2W	3W
P1.5,2-67	0	0	0	0	1W	0	0	0
P1.5,10-1	0	1Y	0	0	0	0	0	0
P1.5-1,2-2	0	0	2W	0	0	0	0	0
P1.5-1,5-1	0	1Y	0	0	0	0	0	0
P1.5-1,10-1	1Y	14Y	3Y, 1B	2Y	2Y	0	0	0
P1.5-1,10-4	0	2Y	1Y, 1W	0	0	0	0	0
P1.5-2,10-29	1Y	0	0	0	0	0	0	0
P1.7,16-26	3B	3B	4B	1B	1B	0	0	0
P1.7,16-29	0	0	0	0	1C	0	0	0
P1.7, 16-44	1B	0	0	0	0	0	0	0
P1.7-2,4	3B	1B	3B	8B	1B	0	0	0
P1.7-2,5	0	0	0	1B	0	0	0	0
P1.7-2,6	0	0	0	1B	0	0	0	0
P1.7-2,16-26	1B	0	0	1B	0	0	0	0
P1.7-4,1	0	1B	0	0	0	0	0	0
P1.7-12,14	0	2B	0	0	0	0	0	0
P1.12-1,16	2B	0	0	0	0	0	0	0
P1.12-6,16-169	0	1B	0	0	0	0	0	0
P1.18-1,16	1W	0	0	0	0	0	0	0
P1.18-1,34	0	1B	3B	0	2B	0	1B	0
P1.19,15	0	0	1B	0	0	0	1B	0
P1.19-2,13-1	0	1B	0	1B	0	0	0	0
P1.22,9	0	0	1B	1B	1B	0	0	0
P1.22,14	1B	7B	3B	0	0	1B	1B	0
P1.22,14-3	0	1B	0	0	0	0	0	0
P1.22,14-6	0	0	0	0	1B	0	0	0
P1.22-1, 14	0	0	0	1B	0	0	0	0

Table 6: Laboratory-confirmed cases of MenW invasive meningococcal disease, Australia, 2019, by sequence type (ST)

Sequence type	MenW genotype					Total
	P1.5,2	P1.5,2-67	P1.5-1,2-2	P1.5-1,10-4	P1.18-1,16	
ST-11	24	1	0	1	0	26
ST-22	0	0	2	0	0	2
ST574	0	0	0	0	0	0
ST1158	0	0	0	0	0	0
ST1287	0	0	0	0	0	0
ST1655	0	0	0	0	0	0
ST2780	0	0	0	0	0	0
ST12351	0	0	0	0	0	0
ST13135	0	0	0	0	0	0
Not determined	13	0	0	0	1	14
Total	37	1	2	1	1	42

IMD caused by MenW was seen in all age groups in 2019 except those aged between 10 to 14 years. We note that this age group has historically had low numbers of IMD cases; in 2019, only 7 cases (6 MenB and 1 MenY) were reported. For those aged less than 5 years, the number and proportion of IMD cases caused by MenW (12 cases, 24%) was lower than that reported in 2018. For those aged over 65 years, MenW was the predominant cause of IMD.

A similar pattern and trend was seen in the number and proportion of IMD caused by MenY in 2019 (n = 42, 21% of total IMD). Prior to 2015, the proportion of cases of IMD caused by MenY ranged from 1.3–4.6% in the period 1997–2010 to 6.2–10.5% in 2011–2014. In 2015 the proportion rose to 12.6%, increasing to 16.5% in 2016 and again to 20% in 2017. The proportion was lower in 2018, at 15.8% (Figure 2).

Of the 42 cases of IMD caused by MenY in 2019, Queensland reported the largest number (18/45 statewide notifications in 2019). MenY was reported in all jurisdictions except the Australian Capital Territory, Northern Territory and Tasmania (Table 2). MenY IMD was reported in all age groups in 2019 except in

those aged between 1 to 9 years and 25 to 44 years, with the highest number and proportion seen in those aged 45 or more years (25/68 of the total IMD notifications for this age group), as in previous years (Table 3, Figure 3).

Genotyping

In 2019, genotyping was possible for 72% of IMD notifications (146/202). Results are shown in Figures 4–6 and Table 5. There were 70 MenB cases typed: the predominant *porA* type in 2019 continues to be P1.7-2,4 (16/70, 23%). Other prevalent MenB genotypes were P1.22,14 (13 cases, 19%), and P1.7,16-26 (12 cases, 17%), similar to previous years (Table 5). All MenC IMD in 2019 were from Western Australia, and investigation revealed that 5/6 were type P1.5,2 (Table 5). For serogroup W IMD, the predominant genotype remains P1.5,2 (37 cases, 88%) (Figures 4–6 and Table 5). Of these, 24 cases (65%) were clonal complex 11, the same strain type as the hyper-virulent serogroup W strain also reported in the UK and South America since 2009 (Table 6).^{6,7} For MenY IMD, the predominant genotype was P1.5-1,10-1 (22 cases, 79%), as has been reported since 2014, when the increase in serogroup Y IMD was first noted in Australia (Figure 6).

Antibiotic susceptibility testing

Isolates of *N meningitidis* are tested against both treatment (ceftriaxone and penicillin) and clearance antibiotics (rifampicin and ciprofloxacin). In 2019, 167/202 of laboratory-confirmed IMD had *Neisseria meningitidis* cultured, and it was therefore possible for antimicrobial susceptibility testing (AST) to be performed. All 167 *N. meningitidis* isolates had AST performed by the NNN.

Regarding antimicrobial susceptibility to the treatment antibiotics, ceftriaxone susceptibility testing was performed on all 167 isolates in 2019, and all isolates were susceptible. With regards to penicillin, the distribution of penicillin MIC values is shown in Table 7. There were 12/167 strains (7.2%) fully susceptible to penicillin ($\text{MIC} \leq 0.03 \text{ mg/L}$).

There were 154/167 isolates that were categorised as less susceptible to penicillin (MIC value 0.064–0.5 mg/L). Of these, 34 had a penicillin MIC of 0.5mg/L, which is close to the MIC breakpoint for resistance; 26/34 (76%) with this penicillin MIC were Men W. In recent years MenW has demonstrated higher penicillin MIC values and higher proportions of resistance. In 2019, one of 167 IMD isolates (0.6%) was resistant to penicillin ($\text{MIC} \geq 1 \text{ mg/L}$): this isolate was a MenW IMD, diagnosed in Victoria. The proportion of IMD isolates resistant to penicillin was lower than reported in 2018 (1.4%) and continues to decline from 2016 (5.8%) and 2017 (5.1%) as shown in Figure 7. Regarding the clearance antibiotics for IMD, all 167 isolates were susceptible to ciprofloxacin; one MenW isolate from Victoria was resistant to rifampicin with a MIC value $\geq 32 \text{ mg/L}$.

Discussion

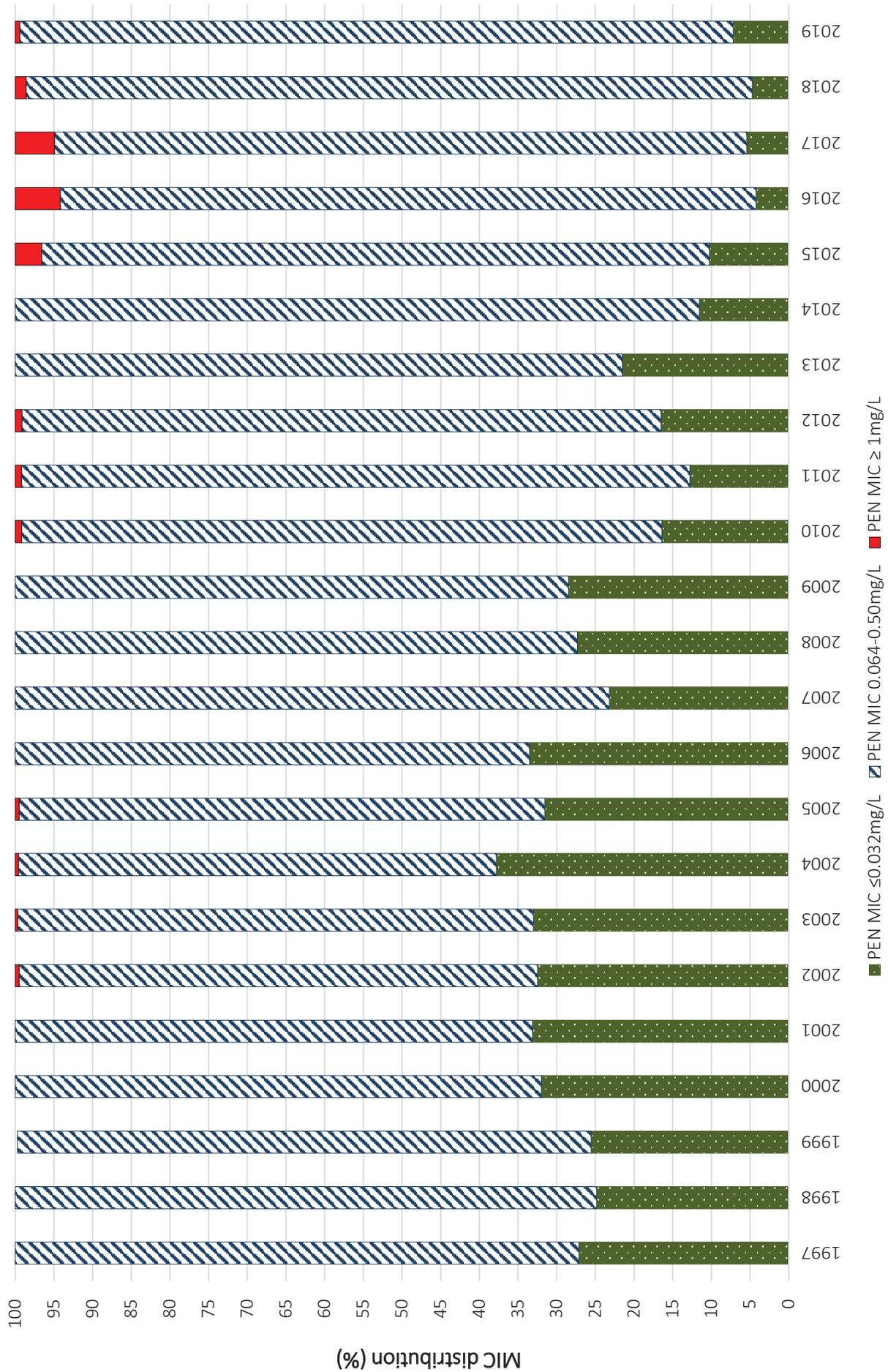
In 2019, 98% of IMD notifications (202/206) were laboratory confirmed.³ Overall there was a 27% decrease in notifications of IMD in Australia in 2019 compared to 2018. Following the increases in MenW and MenY disease in Australia during 2016–2017, there were jurisdictional, time-limited MenACWY vaccination programs for target age groups in 2017 and 2018.⁸ From 1 July 2018, a change to the National Immunisation Program (NIP) was implemented, where MenC vaccine at 12 months of age was replaced with a quadrivalent ACWY vaccine. This change in the NIP in 2018 has been followed by a decrease in both notifications and proportion of MenW and MenY disease, and also an increase in the proportion of disease caused by MenB from 36% in 2016–2017 to 50% in 2019. We note that, following the introduction of the MenC vaccine in 2003 in Australia, the proportion of MenB IMD was 84–88% in the years 2006–2012 then declining, along with disease notifications until the emergence of MenW and MenY disease since 2014 in Australia.⁸ In 2019 MenB accounted for 66% of IMD (33/50) notifications in those less than 5 years of age; 81% of IMD (21/26) in 15–19 year olds; 48% of IMD (10/21) in 20–24 year olds; 50% of IMD (12/24) in 25–44 year olds; and 41% of IMD (12/29) in 45–64 year olds. A recombinant multi-component meningococcal B vaccine has been available in Australia since 2014,⁹ however this vaccine is not currently on the NIP.

In 2019, with regards to serogroup infections by age group, as shown in Table 3, MenB predominated in children aged 1–4 years of age (13/14, 92.9%) and in older children and adolescents (10–19 years) (27/33, 81.8%). MenB accounted for

Table 7: Penicillin MIC distribution of laboratory-confirmed invasive meningococcal disease isolates, Australia, 2019

Penicillin MIC distribution									
MIC mg/L	≤ 0.032	0.064	0.125	0.25	0.5	1	2	≥ 4	Total
Number	12	35	25	60	34	1	0	0	167
%	7.2	21.0	15.0	35.9	20.4	0.6	0	0	100

Figure 7: Proportion of penicillin-susceptible, less susceptible and resistant invasive meningococcal disease isolates, Australia, by year



the greatest proportion of IMD in all age groups (range 41.4–92.9%) excepting 65 years and older where MenW and MenY were predominant.

MenW caused 26.1% of IMD (53/202) in Australia, a decrease from 36% in 2018. MenW IMD was reported in all age groups, except those between 10 to 14 years. MenW infections accounted for 30.6% of IMD in babies less than one year of age (11/36 notifications), and 49% of IMD notifications in those aged over 65 years (19/39 notifications). MenY IMD in 2019 (n = 42/202) accounted for 20.8% of IMD nationally; it was reported in babies less than one year of age (4/42, 9.5%); in 15–19 year olds (3/26, 11.5%); in 20–24 year olds (9/21, 43%); in 45–64 year olds (9/29, 31%); and in those aged 65 and older (16/39, 41%).

The primary peaks of IMD notifications were observed in infants less than 1 year of age (36/202, 18%) and in adults aged 65 years or older (39/202, 19%). In infants, IMD was predominately caused by MenB (20/36) and MenW (11/36), whereas in those aged 65 and older, IMD was attributable to MenW and MenY predominantly (35/39 notifications amongst those aged 65 and older were MenW or MenY). Secondary disease peaks were observed in adolescents 15–19 years of age, due primarily to MenB (81%).

With regards to the prevailing IMD serogroups and genotypes, the number of IMD cases caused by MenB in 2019 was less than in 2018, but the proportion was higher (101/202, 50% in 2019 compared with 123/278, 44% in 2018). New South Wales reported the largest number of MenB notifications. However, South Australia continues to report the highest proportion of MenB. The predominant genotypes of Men B in Australia continue to be P1.7-2,4 (16/70), followed by genotype P1.22,14 (13/70) and genotype P1.7,16-26 (12/70).

The predominant circulating strain of MenW continues to be genotype P1.5,2 sequence type (ST)-11. This MenW strain emerged in the United Kingdom and South America in 2009; it has spread to account for 25% of IMD in the

UK in 2014/15 and 59% of all cases in Chile in 2012.^{6,7} MenW ST11 is hypervirulent and associated with atypical clinical presentations, more severe disease, and a higher case fatality rate.⁷ The initial increase in MenW overseas, and in Australia, was seen in older adults; it was subsequently reported in all age groups, particularly in adolescents and infants.¹⁰

The predominant MenY genotype since 2014 continues to be P1.5-1,10-1; previously, MenY genotype distribution was more heterogeneous. The emergence of MenY IMD has also been reported recently in Europe.¹¹ The phenotypic and genotypic characterization of the MenY isolates is ongoing by the NNN.

Antimicrobial susceptibility testing of IMD isolates in 2019 showed that penicillin resistance has reduced compared with recent years (one isolate, 0.6%). The incidence of penicillin resistance in *N. meningitidis* in Australia was less than 1% annually among IMD isolates tested in 1996–2014, rising to 3.4% in 2015 and 5.8% in 2016; it has fallen from 5.1% in 2017 through 1.4% in 2018. However the proportion of IMD isolates less sensitive to penicillin has been increasing from 62–75% in 1996–2006; 67–79% in 2007–2009; 78–88% in 2010–2015; to 90–94% in 2016–2019. The majority of penicillin-resistant meningococcal isolates are MenW. All IMD isolates tested in 2019 were susceptible to ceftriaxone and ciprofloxacin, while one isolate was resistant to rifampicin.

There has been a year-on-year decrease in IMD notifications from 1.5 cases per 100,000 in 2017; to 1.1 per 100,000 in 2018; to 0.8 cases per 100,000 in 2019. There has also been a decrease in the proportion of isolates attributable to MenW and MenY following changes in the National Immunisation Programme. The NNN is continuing to lead further investigations with the Commonwealth Department of Health and is closely monitoring the phenotypic and genotypic features of *N. meningitidis* causing IMD in Australia. Additional investigations including whole genome sequencing are in place to enhance IMD surveillance. The AMSP data

are used for informing treatment guidelines and disease prevention strategies; and to monitor the effect of interventions.

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