

Title:

Clinical manifestations of invasive meningococcal disease in Victoria with the emergence of serogroup W and serogroup Y *Neisseria meningitidis*

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Introduction

Invasive meningococcal disease (IMD) is a major cause of morbidity and mortality worldwide¹⁻³. It has long been recognised as a significant public health threat due to its capacity to cause outbreaks, a predilection to affect otherwise well young children and adolescents, as well as its ability to cause rapid sepsis and death¹. Whilst there are thirteen serogroups of *Neisseria meningitidis* (*N. meningitidis*), almost all human cases are due to six (A, B, C, W, X, Y).⁴

In Victoria, the incidence of IMD has decreased significantly over the last twenty years following the introduction of a meningococcal C conjugate vaccine in 2003, from 2.5 cases/100,000 population in 2003 to 0.6 cases per 100,000 population in 2014.⁵ Since the late 1990s the predominant meningococcal serogroup causing illness in both Victoria⁵ and Australia⁶ was serogroup B (MenB), however this has also been decreasing in frequency in recent years.⁶

Since 2015, a significant increase in *N. meningitidis* serogroup W (MenW) and serogroup Y (MenY) has been noted in Victoria⁵ and Australia.⁷ This follows increased rates of MenW in the United Kingdom, Europe, South America and the United States.^{2,8} The most common manifestations of IMD are meningitis or septicaemia,⁹ however a higher proportion of cases of IMD due to MenW have been described with altered clinical presentations, with atypical features such as pneumonia, septic arthritis and myocarditis.^{7,8,10} It is not clear how the overall clinical presentation of IMD has been affected by this change in circulating serogroups.

This study was undertaken to assess the clinical characteristics of IMD over a time period encompassing the emergence of MenW and MenY, and to demonstrate the impact of the change in circulating meningococcal strains on the overall clinical manifestations of IMD.

Materials and Methods

Study design

We performed a retrospective cohort series analysis of reported cases of IMD in Victoria, Australia between 1st January 2013 and 31st December 2017. For the purposes of this study we compared the time period between 1st January 2013 and 30th June 2015 (defined as P1) immediately before the increase in MenW and MenY was noted, with the equal time period of 1st July 2015 to 31st December 2017 (P2) when this increase was observed. Only confirmed cases of IMD using the definitions of the Communicable Diseases Network Australia¹¹ were included, which required either laboratory detection of *N. meningitidis* by culture or nucleic acid amplification testing (NAAT) from a usually sterile site, or suggestive laboratory evidence, for example Gram-negative diplococci on microscopy of a usually sterile site sample (e.g. cerebrospinal fluid), in the setting of a compatible clinical illness. Probable cases of IMD without laboratory evidence were excluded.

Data collection

Cases were identified through mandatory notifications to the Victorian Department of Health and Human Services (DHHS), as part of the National Notifiable Diseases Surveillance System. Demographic, clinical, laboratory and outcome data were collected prospectively at the time of notification using a standardised case report form through interviews with the treating clinicians and patient or next-of-kin as part of each case investigation by public health officers, and further supplemented by the hospital discharge summary from the index admission.

Clinical samples for meningococcal NAAT testing as well as isolates of *Neisseria meningitidis* were forwarded by diagnostic laboratories to the Microbiological Diagnostic Unit Public Health Laboratory (MDU), the *Neisseria* reference laboratory for the state of Victoria, where isolates underwent susceptibility testing. Susceptibility testing was performed according to the methods of the Australian Meningococcal Surveillance Programme,⁷ using a standardised agar plate dilution technique¹². Using this method, penicillin categories were defined as susceptible (MIC \leq 0.03 mg/L), less susceptible (MIC 0.06-0.5 mg/L) and resistant (MIC \geq 1 mg/L).⁷ Serotyping was performed on isolates by agglutination with meningococcal A, B, C, W and Y antisera (Remel, Thermo Fisher Scientific, Waltham, Mass, USA). DNA from clinical samples was serotyped using real-time polymerase chain reaction.¹³

Statistical Analysis

Descriptive statistics for continuous variables were represented as median +/- inter-quartile range. Mann-Whitney U test was used to compare continuous variables.

Categorical variables were compared by the use of Fisher's exact test. Differences were considered to be statistically significant at a p -value of <0.05 .

All data in this study were obtained and reported under the legislative authority of the Public Health and Wellbeing Act 2008 and separate ethics approval was not required.

Results

During the study period, 282 cases of IMD were notified to DHHS. Ten cases who were diagnosed when outside Victoria were excluded from further analysis. A further five cases considered probable without laboratory confirmation were also excluded. Serogroup data were available for 263 of the remaining 267 cases, with MenB (116 cases) and MenW (103 cases) making up the majority (Table 1). The serogroup was not able to be determined in 4 cases. There were 13 deaths (4.8% of cases) and 108 cases required intensive care admission (40.4%).

For P1, 80 cases of IMD were noted (32 cases per year; 0.53 cases per 100,000 population in Victoria), compared to 187 cases in P2 (74.8 cases per year; 1.24 cases per 100,000 population in Victoria). Whereas the most common serogroup in P1 was MenB (62/80; 77.5%), the most common circulating strain in P2 was MenW (92/187;

49.2%), although cases of MenB occurred at a similar frequency as during P1. [Figure 1]

As demonstrated in Table 1, the time period July 2015 – December 2017 was associated with a change in the age of cases affected by IMD, with the median age higher in P2 than P1 (46 years vs 19 years, $p < 0.001$), and a much higher proportion of cases aged 50 years or older (46.0% vs 18.8%, $p < 0.001$) [Figure 2]. No significant differences in the rates of in-hospital mortality or intensive care unit admission were observed.

Clinical manifestations of meningococcal disease differed during the two time periods (Table 1). P2 had a lower rate of meningitis (36.4% vs 51.3%, $p = 0.03$), but a higher rate of bacteraemia (80.7% vs 68.8%, $p = 0.04$) and pneumonia (13.4% vs 1.3%, $p = 0.001$) than P1. In addition, patients were less likely to present with any rash (35.9% vs 51.3%, $p = 0.002$), myalgia (55.4% vs 78.0%, $p = 0.003$) or headache (62.4% vs 93.7%, $p = 0.02$). The diagnosis of IMD was more likely to be based on a positive culture (81.3% vs 63.8%, $p = 0.003$) rather than NAAT testing.

A difference in penicillin susceptibility was also observed (Table 2), with overall higher MIC values for penicillin seen in P2 compared to P1 ($p < 0.001$). Susceptibility towards ceftriaxone, rifampicin and ciprofloxacin was not found to be significantly different.

When directly comparing cases due to the established serogroups of MenB and MenC with those due to the emerging serogroups of MenW and MenY similar findings were

observed, with a higher rate of bacteraemia due to the emerging serogroups (89.1% vs 64.0%, $p < 0.0001$) but less meningitis (21.7% vs 62.4%, $p < 0.0001$) [Table 3]. Cases due to the emerging serogroups were also more likely to be discharged home from an emergency department before the diagnosis was made, compared to those cases due to the established serogroups (9.4% vs 2.4%, $p = 0.02$). Penicillin MIC values were seen to be higher overall for the emerging serogroups of MenW and MenY compared to MenB and MenC ($p = 0.003$) [Table 4].

Discussion

This study demonstrates significant differences in the clinical features of cases of IMD that developed following the emergence of MenW and MenY, compared to those cases that occurred before this change. The incidence has significantly increased, many cases were significantly older, and had less signs and symptoms classically associated with IMD. These changes possibly presented difficulties for clinicians in recognising this condition, as we found a higher proportion of cases with IMD due to MenW or MenY were initially discharged from an emergency department, and this may have led to a delay in time critical interventions such as appropriate antibiotic therapy, potentially leading to significant patient harm and complications.^{14,15}

This change in the clinical presentation of IMD in the setting of different circulating serogroups has only been briefly described in overseas settings previously. Previous

epidemiological studies have found a higher rate of meningococcaemia for MenW compared to other serogroups,^{16,17} however there has only been limited data comparing MenW and MenY to MenB and MenC as seen in this study.^{17,18} Previously reported data identified the predominant circulating MenW strain in Australia was of the same genotype as the hypervirulent strain that previously emerged in the UK.⁷ This strain has been previously reported to have a high case fatality rate¹⁹, and MenW has been observed to have a higher overall case fatality rate compared to MenB.²⁰ No statistically significant difference in mortality between serogroups was observed in our cohort, although our study's overall mortality rate was lower than that seen in previous cohorts.²⁰ In addition, our analysis combined MenB with MenC, and compared this to MenW combined with MenY, and so any difference between individual serogroups may have been diluted. MenW has also been previously associated with higher rates of meningococcal pneumonia and septic arthritis.²¹ This increase in atypical manifestations of MenW may relate to the higher rate of bacteraemia^{16,21} however further studies are needed to investigate this phenomenon.

Previous data have shown that the introduction of new circulating strains of *N. meningitidis* leads to an increase in the incidence of older adults being affected.^{22,23} This has been seen in our study, with increased incidence in older patients, and a higher proportion of meningococcaemia and pneumonia; these differences may reflect a lack of pre-existing herd immunity within the community towards the new circulating strains of MenW and MenY. This phenomenon has previously been

described in other parts of the world^{16,24} and indicates a large proportion of the population remains vulnerable to IMD. These data could be used as part of a public health message to raise awareness about the disease in older adults. The role of vaccination in older adults is yet to be explored, with data for effectiveness of the MenACWY vaccines licensed in Australia in this population lacking.²⁵ The MenACWY vaccine has recently been introduced to the Australian immunisation schedule for 14-19 year olds;²⁶ this follows a similar vaccination program introduced in the United Kingdom targeting the adolescent group as the highest carriers of *N. meningitidis*, in an attempt to decrease the incidence of IMD across all age groups.²⁷ The impact of this vaccination strategy has not yet been thoroughly evaluated in the UK or Australia.

This study establishes that a wider range of individuals are at risk of IMD, with an increasing incidence of infection particularly noted in those aged fifty years or older. This has implications on the use of vaccination such as the conjugate MenACWY vaccine, which to date is not part of a routine vaccination program for or promoted towards older adults. The vaccine may need to be considered for those at highest risk, such as the immunocompromised.

Our data have also found altered trends in the method of diagnosis, with higher proportions of IMD being diagnosed via culture rather than NAAT. Factors contributing to this change may include the decreasing proportion of meningitis, which most often occurred due to MenB, as antibiotics are often given before a

lumbar puncture is performed and may lead to a negative culture result,²⁸ as well as the increase in bacteraemia and disseminated infection seen in particular with MenW. The comparatively low rate of MenW and MenY cases detected by molecular methods may mean a number of culture negative cases of IMD are never diagnosed due to insufficient clinical suspicion to order a *N. meningitidis* NAAT. The change in susceptibility results seen in relation to penicillin, which is consistent with national surveillance data,⁷ may also reflect different circulating strains of *N. meningitidis* in the community, although the clinical implications of this change require further consideration.

Strengths of this study include the significant patient numbers, standardised antimicrobial susceptibility testing by a reference laboratory, and patient data collection over several years. Mandatory notification of IMD to DHHS ensures all diagnosed cases of meningococcal disease in the state should be included, allowing for a complete representation of the burden of infection.

There are some caveats and limitations in drawing conclusions from this data. Whilst information was recorded prospectively, it was analysed retrospectively and it is possible that both the patient interviews conducted by public health officers and the testing patterns of clinicians evolved over time as more was learnt about the differing presentations of MenW and MenY. The interviews were designed for routine IMD surveillance rather than in response to an emerging serogroup; as such additional clinical data could not be collected. Secondly, a patient selection bias and under-

reporting may exist as some cases of MenW may have been empirically treated without an aetiologic diagnosis e.g. pneumonia, as the atypical manifestations may mean the diagnosis was not suspected, and so the overall true results may differ. The implementation of sepsis pathways, particularly in recent years, may have led to earlier or more frequent blood culture collection and hence more detection of *N. meningitidis* in cultures. Some information was incomplete, primarily in babies and young children unable to describe symptoms. This may have affected the reported differences in symptoms between time periods, though this limitation would be consistent across both time periods and the numbers of children less than five years old were small. Ideally we would have liked to perform a multivariate analysis to further assess the outcomes of ICU admission and death, however our sample size and number of events were insufficient to do this. Finally, the generalizability of these results to other jurisdictions that may have different circulating serogroups to Victoria may be limited.

Conclusion

This study demonstrates the evolving clinical presentation of IMD. Since the proliferation of MenW and MenY strains in Victoria, a significantly older population is being affected. In addition, more cases are identified due to bacteraemia, but there is a decrease in the observation of rash as well as other typical symptoms. The

combination of these findings illustrates the greater difficulty in early identification of cases of IMD, which could affect the timeliness of appropriate empiric therapy.

Ongoing surveillance will indicate if the introduction of the MenACWY vaccine in adolescents will impact the incidence of IMD in all age groups.

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Figure 1 - Invasive meningococcal disease incidence in Victoria per quarter 2013 - 2017; a) overall and b) stratified by serogroup (including not grouped [NG])

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Figure 2 - Invasive meningococcal disease in Victoria - Age group and Serogroup (including not grouped [NG]) stratified by P1 (January 2013 – June 2015) and P2 (July 2015 – December 2017)

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Table 1 – Major findings for comparison of P1 (Jan 2013 – Jun 2015) and P2 (Jul 2015 – Dec 2017)

	P1 (Jan 2013-Jun 2015)	P2 (Jul 2015 – Dec 2017)	<i>p</i> value
No. of cases	80	187	
Cases per yr	32	74.8	
Cases per 100,000 popn	0.53	1.24	<i>p</i> < 0.001*
Serogroup [number, (% of total)]			
B	62 (77.5%)	54 (28.9%)	<i>p</i> < 0.001*
C	1 (1.3%)	8 (4.3%)	<i>p</i> = 0.29
W	11 (13.8%)	92 (49.2%)	<i>p</i> < 0.001*
Y	4 (5.0%)	31 (16.6%)	<i>p</i> = 0.01*
Not specified	2 (2.5%)	2 (1.1%)	
Age [years, (interquartile range)]			
Median	19 (13.5-34.5)	46 (19-68)	<i>p</i> < 0.001*
Key Findings [number, (% of total)]			
Female	39 (48.8%)	96 (51.3%)	<i>p</i> = 0.70
ICU Admit	28 (35.0%)	80 (42.8%)	<i>p</i> = 0.22

Death	3 (3.8%)	10 (5.3%)	p = 0.60
Manifestation [% of total]			
Bacteraemia	55 (68.8%)	151 (80.7%)	p = 0.04*
Meningitis	41 (51.3%)	68 (36.4%)	p = 0.03*
Pneumonia	1 (1.3%)	25 (13.4%)	p = 0.001*
Septic Arthritis	5 (6.3%)	16 (8.6%)	p = 0.63
Epiglottitis/Pharyngitis	4 (5.0%)	14 (7.5%)	p = 0.60
Gastroenteritis	4 (5.0%)	10 (5.3%)	p = 1.00
Other	1 (1.3%) [†]	7 (3.7%) [‡]	
Presenting Symptoms [% of cases interviewed, (no. cases reporting this/ total cases interviewed)][§]			
Abdominal Pain	25.9% (15/58)	20.8% (32/154)	p = 0.46
Arthralgia	58.6% (34/58)	38.4% (58/151)	p = 0.01*
Ataxia	21.4% (12/56)	10.7% (16/150)	p = 0.07
Diarrhoea	22.4% (15/67)	18.8% (32/170)	p = 0.59
Fever	96.1% (74/77)	95.6% (175/183)	p = 1.00
Headache	93.7% (59/63)	62.4% (98/157)	p = 0.02*
Myalgia	78.0% (46/59)	55.4% (87/157)	p = 0.003*
Neck Stiffness	54.1% (33/61)	33.5% (55/164)	p = 0.006*
Photophobia	36.4% (24/66)	19.4% (31/160)	p = 0.01*
Rash	57.7% (45/78)	35.9% (65/181)	p = 0.002*

Vomiting	51.3% (39/76)	53.1% (94/177)	p = 0.89
Diagnostic Modality [number, (% of total)]			
Culture positive	51 (63.8%)	152 (81.3%)	p = 0.003*
Culture negative, NAAT positive	29 (36.2%)	35 (18.7%)	

† pericarditis x1

‡ myocarditis/pericarditis x3, cellulitis x2, conjunctivitis x2

§ Not all cases could report all symptoms, e.g. babies, or information was not recorded.

Where the presence or absence of a symptom could not be determined, the case was removed from this analysis only

Table 2 – Antimicrobial Susceptibility Testing results for P1 (Jan 2013 – Jun 2015) and P2 (Jul 2015 – Dec 2017)

	P1 (Jan 2013-Jun 2015)	P2 (Jul 2015 – Dec 2017)
No. of cases	80	187
No. of cases with susceptibility testing available (% of total cases in time period) [†]	49 (61.3%)	152 (81.3%)
Penicillin		
Interpretation (% of isolates tested)		
Susceptible (MIC ≤ 0.03 mg/L)	3/49 (6.1%)	2/147 (1.4%)
Less Susceptible (MIC 0.06 - 0.5 mg/L)	46/49 (93.9%)	131/147 (89.1%)
Resistant (MIC ≥ 1 mg/L)	0/49 (0.0%)	14/147 (9.5%)
MIC (mg/L) ^{‡*} [number, (% of isolates tested)]		
≤ 0.03	3/49 (6.1%)	2/147 (1.4%)
0.06	14/49 (28.6%)	20/147 (13.6%)
0.125	9/49 (18.4%)	12/147 (8.2%)
0.25	16/49 (32.7%)	17/147 (11.6%)
0.5	7/49 (14.3%)	82/147 (55.8%)
≥ 1	0/49 (0.0%)	14/147 (9.5%)

Ceftriaxone		
Interpretation (% of isolates tested)		
Susceptible	51/51 (100%)	151/151 (100%)
Resistant	0/51 (0%)	0/151 (0%)
Rifampicin		
Interpretation (% of isolates tested)		
Susceptible	47/47 (100.00%)	142/143 (99.3%)
Resistant	0/47 (0%)	1/143 (0.7%)
Ciprofloxacin		
Interpretation (% of isolates tested)		
Susceptible	51/51 (100.00%)	144/146 (98.6%)
Less Susceptible	0/51 (0.00%)	2/146 (1.4%)
Resistant	0/51 (0%)	0/146 (0%)

[†] Susceptibility testing only able to be performed on cases with a positive culture for *N. meningitidis*. A minority of specimens were not tested for all antimicrobials.

[‡] Higher overall MIC values seen for P2 compared to P1, $p < 0.001$

Table 3 – Major findings for comparison of MenB & MenC (established serogroups) and MenW & MenY (emerging serogroups) between 2013-2017.

	MenB & MenC		MenW & MenY		<i>p</i> value
No. of cases	125		138		
Age [years, (interquartile range)]					
Median	19 (16-35)		57 (22-71)		<i>p</i> < 0.001*
Key Findings [number of cases, (% of total)]					
Female	58	(46.4%)	77	(55.8%)	<i>p</i> = 0.14
Initially discharged home from ED	3	(2.4%)	13	(9.4%)	<i>p</i> = 0.02*
ICU Admit	51	(40.8%)	56	(40.6%)	<i>p</i> = 1
Death	2	(1.6%)	7	(5.1%)	<i>p</i> = 0.18
Manifestation [% of total]					
Bacteraemia	80	(64.0%)	123	(89.1%)	<i>p</i> < 0.0001*
Meningitis	78	(62.4%)	30	(21.7%)	<i>p</i> < 0.0001*
Pneumonia	3	(2.4%)	23	(16.7%)	<i>p</i> < 0.0001*
Septic Arthritis	3	(2.4%)	18	(13.0%)	<i>p</i> = 0.0001*
Epiglottitis/Pharyngitis	3	(2.4%)	15	(10.9%)	<i>p</i> = 0.007*
Gastroenteritis	4	(3.2%)	9	(6.5%)	<i>p</i> = 0.26
Other	1	(0.8%) [†]	6	(4.3%) [‡]	

Presenting Symptoms [% of cases interviewed, (no. cases reporting this/ total cases interviewed)][§]			
Abdominal Pain	21/93 (22.6%)	17/107 (15.9%)	p = 0.28
Arthralgia	46/92 (50.0%)	44/114 (38.6%)	p = 0.12
Ataxia	17/90 (18.9%)	11/103 (9.7%)	p = 0.07
Diarrhoea	27/107 (25.2%)	19/127 (15.0%)	p = 0.07
Fever	118/121 (97.5%)	128/136 (94.1%)	p = 0.23
Headache	85/102 (83.3%)	61/115 (53.0%)	p < 0.0001*
Myalgia	68/97 (70.1%)	63/116 (54.3%)	p = 0.02*
Neck Stiffness	56/100 (56.0%)	31/122 (25.4%)	p < 0.0001*
Photophobia	40/104 (38.5%)	15/109 (12.6%)	p < 0.0001*
Rash	80/123 (65.0%)	28/133 (21.1%)	p < 0.0001*
Vomiting	74/119 (62.2%)	57/131 (43.5%)	p = 0.004*
Diagnostic Modality [number of cases, (% of total)]			
Culture positive	74 (59.2%)	128 (92.8%)	p < 0.0001*
Culture negative, NAAT positive	51 (40.8%)	10 (7.2%)	

[†]pericarditis x1

[‡]myocarditis/pericarditis x3, cellulitis x2, conjunctivitis x1

[§] Not all cases could report all symptoms, e.g. babies, or information was not recorded.

Where the presence or absence of a symptom could not be determined, the case was removed from this analysis only

Table 4 – Antimicrobial Susceptibility Testing results for comparison of MenB & MenC (established serogroups) and MenW & MenY (emerging serogroups) between 2013-2017.

	MenB & MenC		MenW & MenY	
No. of cases	125		138	
No. of cases with susceptibility testing available (% of total cases in time period) [†]	73	(58.4%)	127	(92.0%)
Penicillin				
Interpretation (% of isolates tested)				
Susceptible (MIC ≤ 0.03 mg/L)	3/72	(41.7%)	2/123	(1.6%)
Less Susceptible (MIC 0.06 - 0.5 mg/L)	67/72	(93.1%)	109/123	(88.6%)
Resistant (MIC ≥ 1 mg/L)	2/72	(2.8%)	12/123	(9.8%)
MIC (mg/L) ^{‡*} [number, (% of isolates tested)]				
≤ 0.03	3/72	(4.2%)	2/123	(1.6%)
0.06	13/72	(18.1%)	21/123	(17.1%)
0.125	9/72	(12.5%)	12/123	(9.8%)
0.25	23/72	(31.9%)	10/123	(8.1%)
0.5	22/72	(30.6%)	66/123	(53.7%)
≥ 1	2/72	(2.8%)	12/123	(9.8%)
Ceftriaxone				

Interpretation (% of isolates tested)				
Susceptible	74/74	(100%)	127/127	(100%)
Resistant	0/0	(0%)	0/0	(0%)
Rifampicin				
Interpretation (% of isolates tested)				
Susceptible	69/69	(100%)	120/121	(99.2%)
Resistant	0/69	(0%)	1/121	(0.8%)
Ciprofloxacin				
Interpretation (% of isolates tested)				
Susceptible	72/73	(98.6%)	122/123	(99.2%)
Less Susceptible	1/73	(1.4%)	1/123	(0.8%)
Resistant	0/73	(0%)	0/123	(0%)

[†] Susceptibility testing only able to be performed on cases with a positive culture for *N. meningitidis*. A minority of specimens were not tested for all antimicrobials.

[‡] Higher overall MIC values seen for MenW & MenY compared to MenB & MenC, $p = 0.003$

Abstract:

Background:

Historically, Australian cases of invasive meningococcal disease (IMD) have been most frequently caused by *Neisseria meningitidis* serogroup-B, but recently an increase in cases due to serogroup-W (MenW) and serogroup-Y (MenY) has occurred.

Aims:

To determine whether clinical manifestations of IMD have changed due to increased incidence of MenW and MenY.

Methods:

We performed a retrospective review of IMD cases notified to the Department of Health and Human Services in Victoria, Australia. We compared the period between January 2013 and June 2015 (defined as P1) immediately before the increase in MenW and MenY was noted, with the equal time period of July 2015 to December 2017 (P2), when this increase was observed.

Results:

IMD was notified more frequently in P2 than P1 (1.24 vs 0.53 per 100,000 person-years; $p < 0.001$). IMD cases in P2 were older (46 vs 19 years; $p < 0.001$), and more likely due to MenW (92/187, 49.2% vs 11/80, 13.8%, $p < 0.001$) or MenY (31/187, 16.6% vs 4/80, 5.0%, $p = 0.01$). IMD cases from P2 were more likely bacteraemic (151/187, 80.7% vs 55/80, 68.8%, $p = 0.04$), while meningitis (68/187, 36.4% vs 41/80, 51.3%, $p = 0.03$) and rash (65/181, 35.9% vs 45/78, 57.7%, $p = 0.002$) were less frequent. ICU admission rates and in-hospital mortality were unchanged.

Conclusion:

Alongside an increase in IMD in Victoria, the proliferation of cases of MenW and MenY occurred in older patients, and were more often identified through bacteraemia rather than meningitis or purpura fulminans. Clinicians should be aware of these changes to facilitate earlier identification and treatment of IMD.

Key Words:

Bacteria; invasive meningococcal disease; epidemiology; Victoria; *Neisseria meningitidis* ; meningococcal serogroup W disease

Category: Original Article

Title:

Clinical manifestations of invasive meningococcal disease in Victoria with the emergence of serogroup W and serogroup Y *Neisseria meningitidis*

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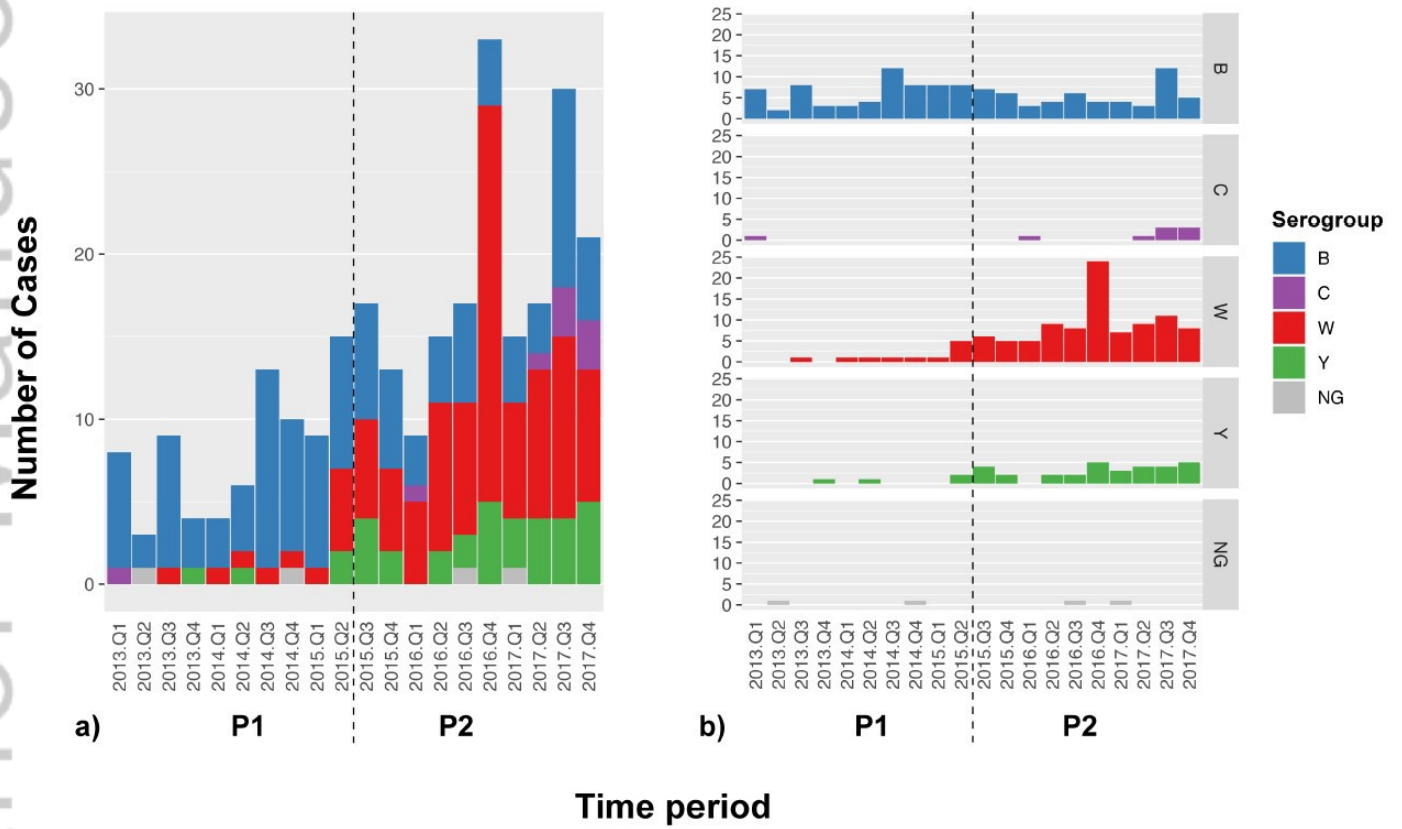
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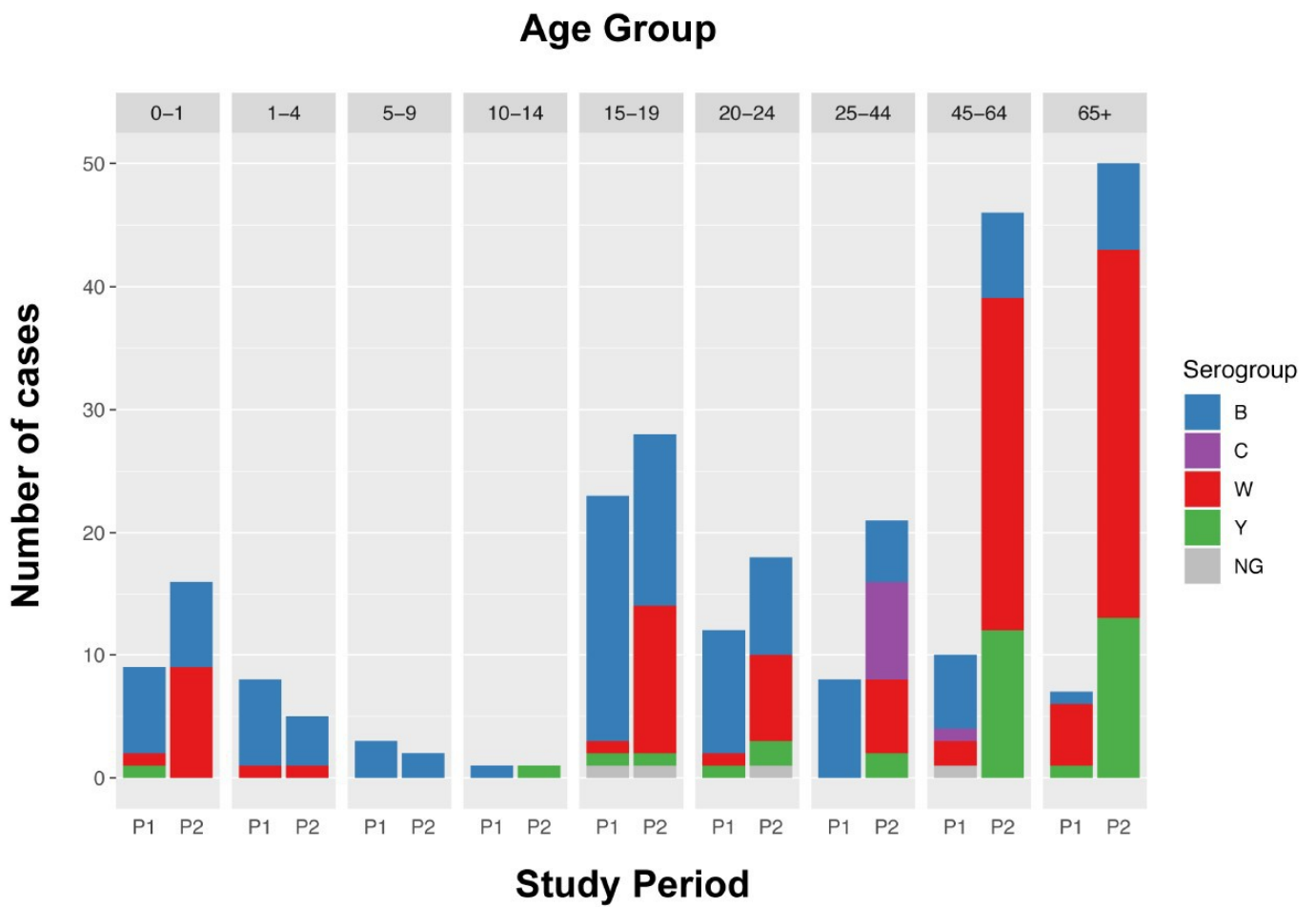
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Abstract	-	250 words
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IMJ_14771_Figure 2.jpg