MENINGOCOCCAL DISEASE

Introduction

Neisseria meningitidis is a gram-negative diplococcus and the only known natural reservoir of this bacterium is the human nasopharyngeal mucosa [151]. Asymptomatic carriage of the bacterium is common. Most cases of the disease are acquired through contact with the respiratory droplets of asymptomatic carriers [152]. The onset of symptoms of meningitis is often sudden and death can follow within hours, therefore prompt treatment with appropriate antibiotics is vital. Survivors of the disease may be left with severe disabilities including deafness, loss of limbs, mental retardation and paralysis. The initial symptoms are often non-specific and may be difficult to distinguish from those of common viral infections. They include fever, nausea and vomiting, irritability, refusing food or drink, headache and muscle or joint aches. More specific symptoms include a non-blanching petechial rash, neck stiffness, a bulging fontanelle in babies, altered mental state and photophobia [153].

There are a number of different pathogenic strains of *Neisseria meningitidis*. An epidemic of meningococcal disease due to a specific Group B strain began in New Zealand in 1991. A strain-specific vaccine was developed and introduced into the immunisation schedule in 2004. While the epidemic was already waning by this time, the number of cases due to the epidemic strain fell significantly after the vaccine was introduced [154]. The vaccine was withdrawn in 2008 [155].

Currently there are two types of meningococcal vaccine available in New Zealand. Quadrivalent polysaccharide vaccines are effective against strains A, C, Y and W135 (and are approved for use in adults and children over the age of two, funded for those who have had or are about to have a splenectomy, and recommended, but not funded, for other high risk groups such as young adults in their first year of hostel accommodation, close contacts of disease cases and laboratory workers). Meningococcal C conjugate vaccines can be used in infants as well as in other age groups. Both types of vaccine may be funded to control an outbreak [148].

The following section explores meningococcal disease rates in children and young people using information from the National Minimum Dataset and Mortality Collection. The section concludes with a brief overview of policy and evidence-based review documents which consider interventions to address meningococcal disease at the population level.

Data Sources and Methods

Indicator

1. *Acute and Semi Acute Hospital Admissions for Meningococcal Disease in Children and Young People Aged 0–24 Years*

Numerator: National Minimum Dataset: Acute and semi-acute hospital admissions for children and young people aged 0–24 years with an ICD-10-AM primary diagnosis of Meningococcal Disease, including meningococcal meningitis (A39).

Denominator: Statistics NZ Estimated Resident Population (with linear extrapolation being used to calculate denominators between Census years).

2. Mortality from Meningococcal Disease in Children and Young People Aged 0–24 Years

Numerator: National Mortality Collection; Deaths in children and young people aged 0–24 years where the main underlying cause of death was Meningococcal Disease, including meningococcal meningitis (A39).

Denominator: Statistics NZ Estimated Resident Population (with linear extrapolation being used to calculate denominators between Census years).

Notes on Interpretation

Note 1: An acute admission is an unplanned admission occurring on the day of presentation, while a semi-acute admission (referred to in the NMDS as an arranged admission) is a non-acute admission with an admission date <7 days after the date the decision was made that the admission was necessary.

Note 2: **Appendix 3** outlines the limitations of the hospital admission data used. The reader is urged to review this Appendix before interpreting any trends based on hospital admission data.

Note 3: 95% confidence intervals have been provided for the rate ratios in this section and where appropriate, the terms *significant* or not *significant* have been used to communicate the significance of the observed associations. Tests of statistical significance have not been applied to other data in this section, and thus (unless the terms *significant* or non-*significant* are specifically used) the associations described do not imply statistical significance or non-significance (see **Appendix 2** for further discussion of this issue).

New Zealand Distribution and Trends

New Zealand Trends

In New Zealand, hospital admissions for meningococcal disease in children and young people declined rapidly during the early-mid 2000s, but became more static after 2006–07. Similar patterns were seen for mortality during 2000–2008, although the number of deaths in 2008 (n=7) was higher than in the previous four years (average n=3.5) (**Figure 78**).

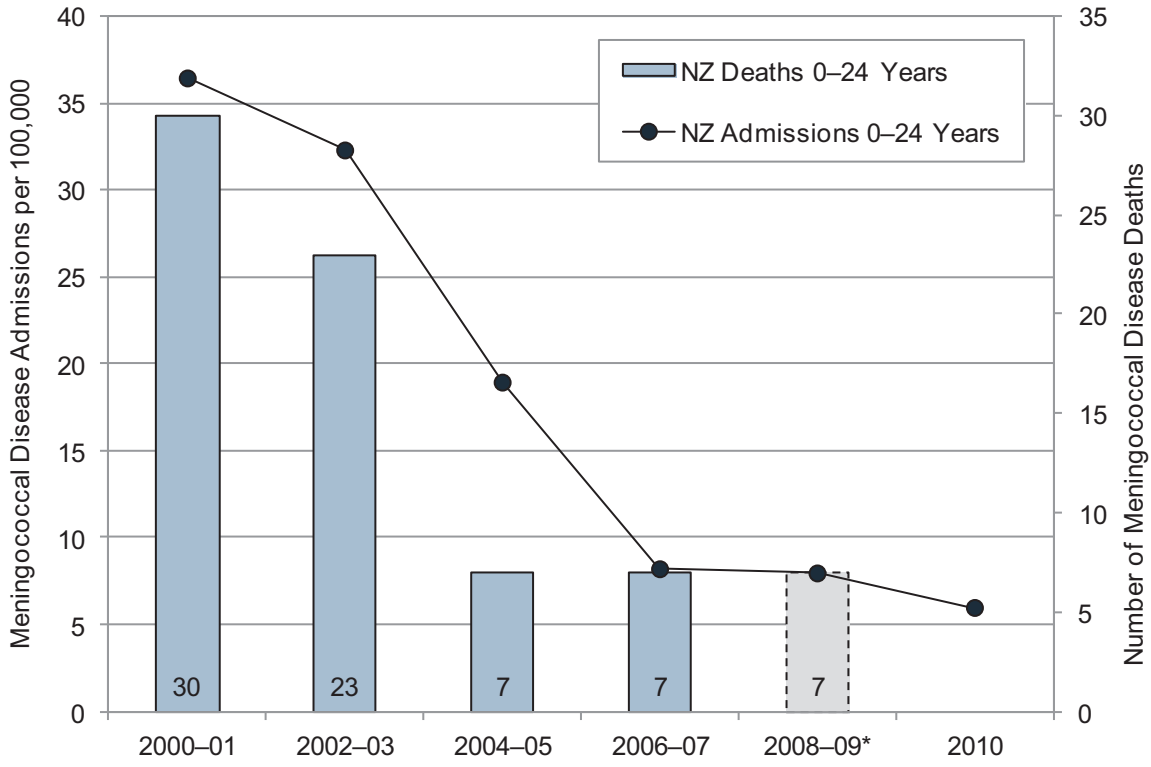
New Zealand Distribution by Age

In New Zealand during 2006–2010, hospital admissions for meningococcal disease were highest in infants <1 year, followed by those <5 years of age. Mortality during 2004–2008 was also highest in infants, followed by those <3 years of age, although a small number of deaths also occurred amongst those in their late teens and early twenties (**Figure 79**).

New Zealand Distribution by Ethnicity, NZDep Index Decile and Gender

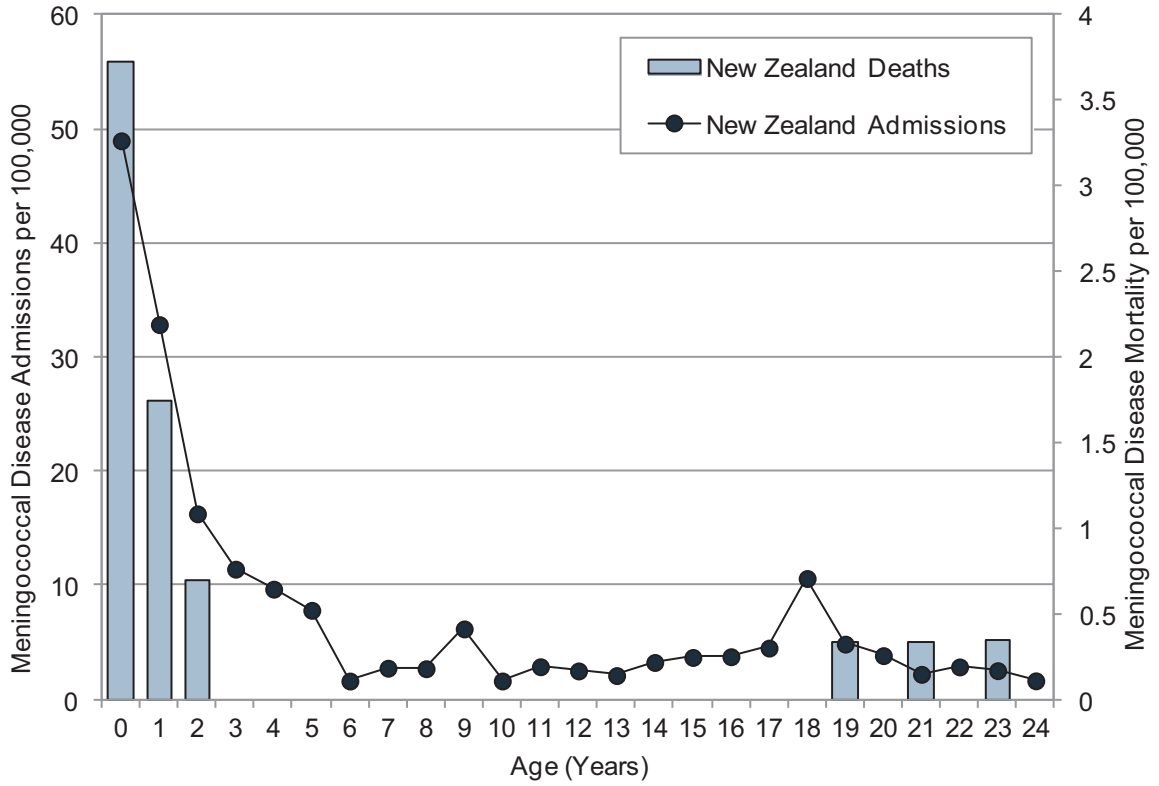
In New Zealand during 2006–2010, hospital admissions for meningococcal disease were *significantly* higher for males, Pacific and Māori > European > Asian/Indian children and young people and those living in more deprived (NZDep decile 5–10) areas (**Table 83**). Similar ethnic differences were seen during 2000–2010, with the largest absolute decreases in admissions during this period being amongst Pacific and Māori children and young people (**Figure 80**).

Figure 78. Acute and Semi-Acute Hospital Admissions (2000−2010) and Deaths (2000−2008) from Meningococcal Disease in New Zealand Children and Young People Aged 0−24 Years



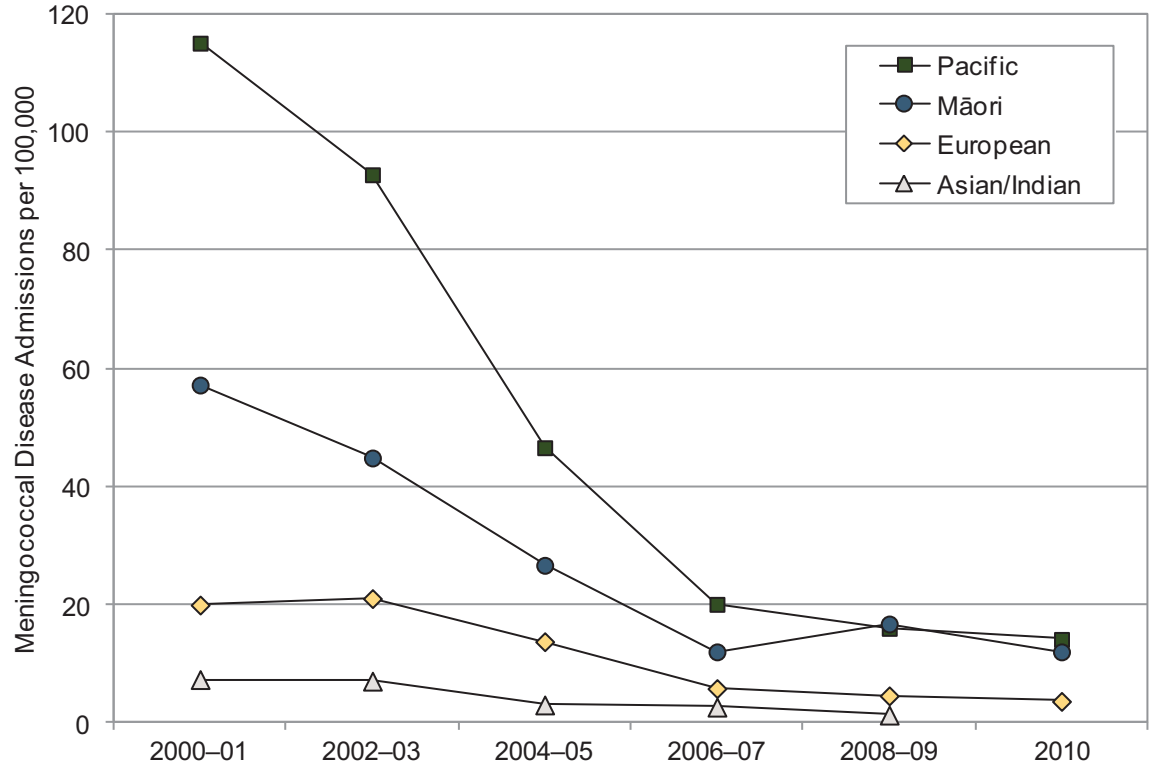
Source: Numerators: National Minimum Dataset (Acute and semi-acute admissions only) and National Mortality Collection; Denominator: Statistics NZ Estimated Resident Population. *Note: Number of Deaths is per 2 year period, with the exception of 2008–09, which is for a single year (2008) only.

Figure 79. Acute and Semi-Acute Hospital Admissions (2006−2010) and Deaths (2004−2008) from Meningococcal Disease in New Zealand Children and Young People by Age



Source: Numerators: National Minimum Dataset (Acute and semi-acute admissions only) and National Mortality Collection; Denominator: Statistics NZ Estimated Resident Population

Figure 80. Acute and Semi-Acute Hospital Admissions for Meningococcal Disease in Children and Young People Aged 0−24 Years by Ethnicity, New Zealand 2000−2010



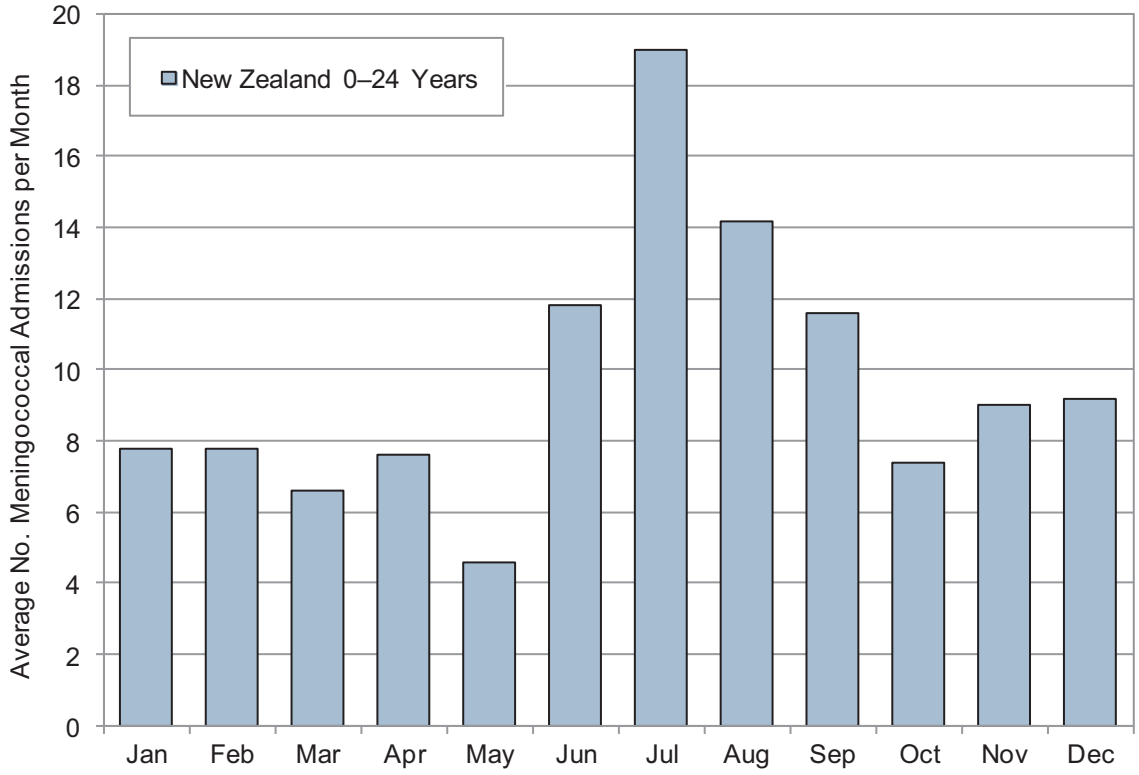
Source: Numerator: National Minimum Dataset (Acute and semi-acute admissions only); Denominator: Statistics NZ Estimated Resident Population. Note: Ethnicity is Level 1 Prioritised.

Table 83. Acute and Semi-Acute Hospital Admissions for Meningococcal Disease in Children and Young People Aged 0−24 Years by Ethnicity, NZ Deprivation Index Decile and Gender, New Zealand 2006−2010

Variable	Rate	Rate Ratio	95% CI	Variable	Rate	Rate Ratio	95% CI
Meningococcal Disease 0–24 Years							
NZ Deprivation Index Quintile				Prioritised Ethnicity			
Decile 1–2	2.92	1.00		European	4.88	1.00	
Decile 3–4	3.59	1.23	0.81–1.86	Māori	13.9	2.85	2.37–3.44
Decile 5–6	5.52	1.89	1.29–2.76	Pacific	17.2	3.52	2.81–4.42
Decile 7–8	8.41	2.88	2.03–4.09	Asian/Indian	1.52	0.31	0.18–0.54
Decile 9–10	14.9	5.09	3.67–7.07				
Gender							
Female	6.94	1.00		Male	8.32	1.20	1.02–1.41

Source: Numerator: National Minimum Dataset (Acute and semi-acute admissions only); Denominator: Statistics NZ Estimated Resident Population. Note: Rate per 100,000; Ethnicity is Level 1 Prioritised; Decile is NZDep2001

Figure 81. Average Number of Acute and Semi-Acute Hospital Admissions for Meningococcal Disease in Children and Young People Aged 0−24 Years by Month, New Zealand 2006−2010



Source: National Minimum Dataset (Acute and semi-acute admissions only)

New Zealand Distribution by Season

In New Zealand during 2006–2010, hospital admissions for meningococcal disease were highest during the winter months **(Figure 81**).

South Island Distribution and Trends

South Island DHBs vs. New Zealand

In Nelson Marlborough and Canterbury during 2006–2010, hospital admissions for meningococcal disease were *significantly* lower than the New Zealand rate, while in Southland rates were *significantly* higher. In the West Coast, South Canterbury and Otago rates were not *significantly* different from the New Zealand rate (**Table 84**).

Table 84. Acute and Semi-Acute Hospital Admissions for Meningococcal Disease in Children and Young People 0−24 Years, South Island DHBs vs. New Zealand 2006−2010

DHB	Number: Total 2006–2010	Number: Annual Average	Rate per 100,000	Rate Ratio	95% CI
Meningococcal Disease 0–24 Years					
Nelson Marlborough	7	1.4	3.37	0.44	0.21–0.93
West Coast	6	1.2	12.0	1.58	0.71–3.52
Canterbury	41	8.2	4.85	0.64	0.46–0.87
South Canterbury	3	0.6	3.61	0.47	0.15–1.47
Otago	26	5.2	7.87	1.03	0.70–1.53
Southland	24	4.8	13.2	1.73	1.15–2.60
New Zealand	583	116.6	7.64	1.00	

Source: Numerator: National Minimum Dataset (Acute and semi-acute admissions only); Denominator: Statistics NZ Estimated Resident Population

South Island Trends

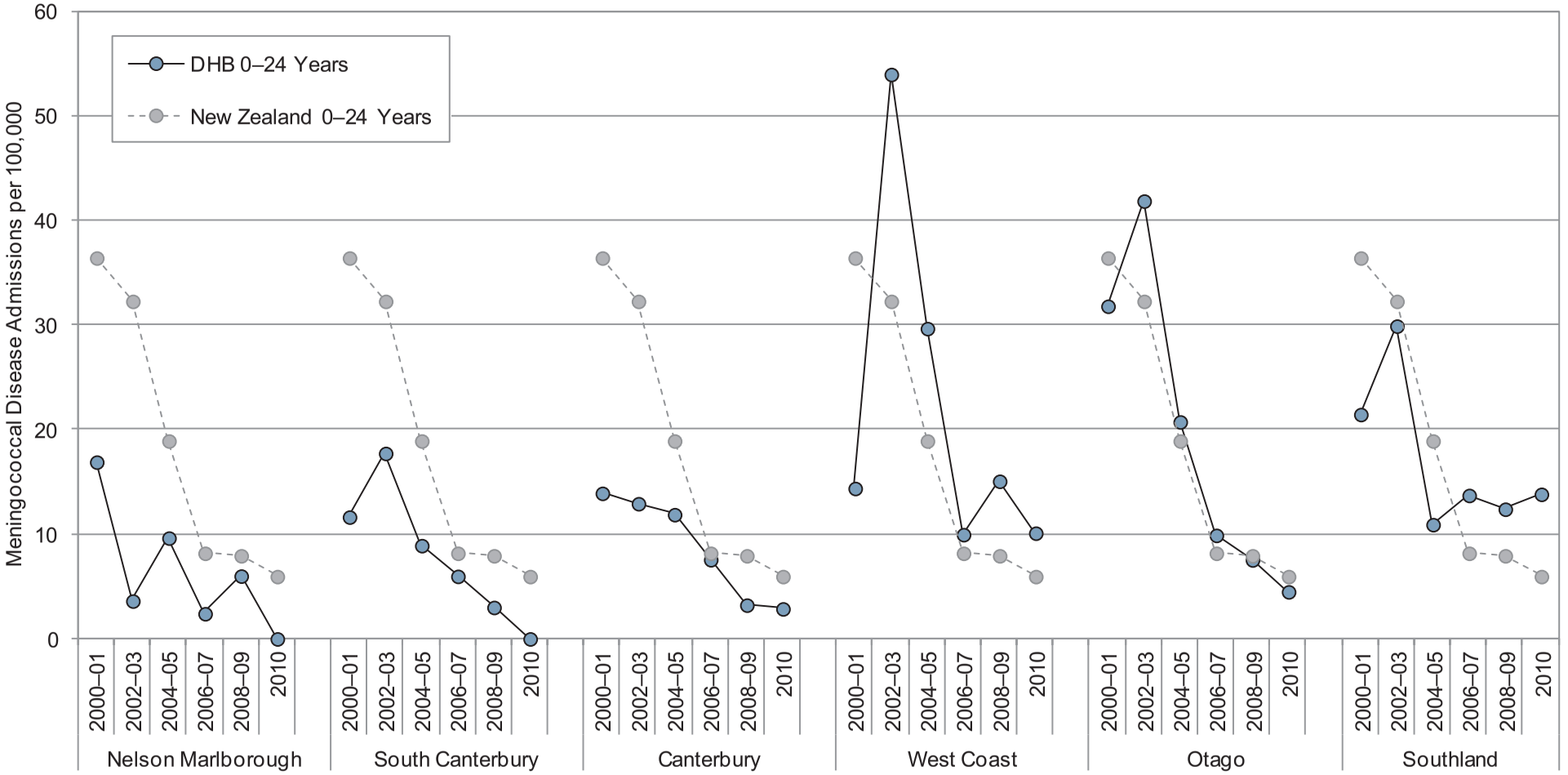
In the South Island during 2000–2010, hospital admissions for meningococcal disease in children and young people decreased in all DHBs (**Figure 82**).

Summary

In New Zealand, hospital admissions for meningococcal disease in children and young people declined rapidly during the early-mid 2000s, but became more static after 2006–07. Similar patterns were seen for mortality during 2000–2008, although the number of deaths in 2008 was higher than in the previous four years. Admissions and mortality were both highest for infants <1 year, followed by those <5 years. During 2006–2010, admissions were also *significantly* higher for males, Pacific and Māori > European > Asian/Indian children and young people and those from more deprived (NZDep decile 5–10) areas.

In the South Island during 2000–2010, hospital admissions for meningococcal disease in children and young people decreased in all DHBs. During 2006–2010, admissions were *significantly* lower than the New Zealand rate in Nelson Marlborough and Canterbury, while in Southland rates were *significantly* higher. In the West Coast, South Canterbury and Otago rates were not *significantly* different from the New Zealand rate.

Figure 82. Acute and Semi-Acute Hospital Admissions for Meningococcal Disease in Children and Young People Aged 0−24 Years, South Island DHBs vs. New Zealand 2000−2010



Source: Numerator: National Minimum Dataset (Acute and semi-acute admissions only); Denominator: Statistics NZ Estimated Resident Population

Local Policy Documents and Evidence-Based Reviews Relevant to the Prevention and Management of Meningococcal Disease

In New Zealand a number of policy documents consider the prevention and management of meningococcal disease, and these are considered in **Table 85**, along with a number of international reviews and guidelines which also consider these issues. In addition, a number of publications consider approaches to respiratory and infectious diseases more generally, and these are reviewed in other sections of this report:

1. **Generic Approaches to Infectious and Respiratory Disease:** Table 46 on Page 166
2. **The Prevention of Second Hand Smoke Exposure:** Table 47 on Page 168
3. **Interventions Aimed at Housing and Household Crowding:** Table 48 on Page 170
4. **Interventions to Improve Breastfeeding:** Breastfeeding Section on Page 100

Table 85. Local Policy Documents and Evidence-Based Reviews Relevant to the Prevention and Management of Meningococcal Disease

Ministry of Health Policy Documents
Ministry of Health. 2011. **Immunisation Handbook 2011**. Wellington: Ministry of Health. http://www.moh.govt.nz/moh.nsf/Files/immunise-handbook/$file/16MeningococcalInvDisease.pdf Chapter 16 of this handbook covers invasive meningococcal disease. It provides information on the available vaccines and the groups for which vaccination is funded (adults and children pre-and post-splenectomy, those living in areas where there is a community programme to control an outbreak) and recommended but not funded (young adults in their first year of hostel accommodation, close contacts of disease cases, and some other high risk groups).
Ministry of Health. 2011. **Targeted vaccinations: Meningococcal Disease**. http://www.moh.govt.nz/moh.nsf/indexmh/immunisation-diseasesandvaccines-meningococcaldisease This web page provides brief information on the two main types of meningococcal vaccine available in New Zealand, the quadrivalent polysaccharide vaccines, which protect against groups A, C, Y, and W135 and are approved for use in people over the age of two, and the separate conjugate meningococcal C vaccines which protect against group C meningococcal disease only and can be used in children under the age of two. Immunity from the quadrivalent vaccine lasts for about three years and the duration of immunity produced by the conjugate vaccines is currently unknown.
The Ministry of Health meningococcal disease web page http://www.moh.govt.nz/moh.nsf/wpg_index/Publications-Meningococcal+Disease+-+Publications contains links to a number of publications relating to the meningococcal B immunisation programme. These are not summarised in this table because they are now largely of historical interest.
International Guidelines
National Collaborating Centre for Women's and Children's Health. 2010. **Bacterial Meningitis and Meningococcal Septicaemia in Children**. London: Royal College of Obstetricians and Gynaecologists. **http://www.nice.org.uk/nicemedia/live/13027/49437/49437.pdf** These detailed evidence-based guidelines cover diagnosis of bacterial meningitis and meningococcal septicaemia, management of these conditions in primary and pre-hospital care settings and in secondary and tertiary care, investigations, long term management and giving information to parents and carers. It is intended that these guidelines be used in conjunction with NICE clinical guideline 84: "Diarrhoea and vomiting in children under 5" and NICE clinical guideline 47: "Feverish illness in children". Each section in the guideline includes a review of the published evidence and concludes with recommendations for clinical practice and for research. The appendices, some of which are not included in the guideline but can be downloaded from the NICE website: http://guidance.nice.org.uk/CG102/Guidance include the literature search strategies, the clinical questions which the research aimed to answer and details of the relevant studies and meta-analyses on which the guidelines are based, as well as cost-effectiveness analyses on various diagnostic and therapeutic options.
Scottish Intercollegiate Guidelines Network. 2008. **Management of invasive meningococcal disease in children and young people: A national clinical guideline**. Edinburgh: Scottish Intercollegiate Guidelines Network. http://www.sign.ac.uk/pdf/sign102.pdf This guideline provides evidence-based best practice recommendations on the recognition and management of meningococcal disease in children and young people. It covers the patient journey from pre-hospital care through referral, diagnostic testing, management in hospital, follow up care and rehabilitation and it also covers public health issues. Statements in the guideline which summarise the research literature are accompanied by a grade indicating the quality of the evidence. Recommendations in the guideline are accompanied by a grade (A–D) indicating the strength of the evidence on which they are based. Section 8 covers prevention of secondary transmission via prophylactic antibiotics, vaccination and infection control measures.

Systematic and Other Reviews from the International Literature
Fraser A, Gafter-Gvili A, Paul M, et al. 2011. **Antibiotics for preventing meningococcal infections**. Cochrane Database of Systematic Reviews 2011(8) Art. No.: CD004785. DOI: 10.1002/14651858.CD004785.pub4. Household contacts of people with meningococcal infection are at high risk of contracting the disease. This review of 24 studies (19 RCTs including 2531 participants and 5 cluster RCTs including 4354 participants) aimed to determine the effectiveness of different prophylactic antibiotics for a) preventing cases of meningococcal disease and b) eradicating naso-pharyngeal carriage of *Neisseria meningitides.* No trials reported any cases of meningococcal disease during the trials so it was not possible to assess directly the effectiveness of antibiotics in preventing disease. Regarding eradication of *N. meningitidis,* ciprofloxacin (RR 0.04, 95% CI 0.01 to 0.12), rifampin (rifampicin) (RR 0.17, 95% CI 0.13 to 0.24), minocycline (RR 0.28, 95% CI 0.21 to 0.37) and penicillin (RR 0.47, 95% CI 0.24 to 0.94) were all more effective than placebo up to one week after treatment and, after one to two weeks, rifampin (RR 0.20; 95% CI 0.14 to 0.29), ciprofloxacin (RR 0.03; 95% CI 0.00 to 0.42) and penicillin (RR 0.63; 95% CI 0.51 to 0.79) were more effective than placebo. Rifampin was more effective than placebo up to four weeks after treatment but resistant isolates were detected following treatment. No trials compared ceftriaxone with placebo but ceftriaxone was more effective than rifampin after one to two weeks of follow up in one study. Therefore the use of ciprofloxacin, ceftriaxone or penicillin should be considered however the use of rifampin during an outbreak may lead to the circulation of resistant isolates.
Khatami A, Pollard AJ. 2010. **The epidemiology of meningococcal disease and the impact of vaccines**. *Expert Review of Vaccines* 9(3) 285-98. This review provides an overview of meningococcal disease, its various serogroups and how vaccines have been developed over time. The success of particular vaccines in a number of different countries is also discussed. The review notes that conjugate vaccines were developed for meningococcal disease in the 1990s. They have been shown to be safe and effective in all age groups but there is still concern that antibody persistence is poor when vaccines are given in infancy. These vaccines also reduce naso-pharyngeal carriage of *N. meningitidis* which means that there are benefits from herd immunity and reduced transmission. A number of countries including the U.K., the Netherlands and Greece have introduced MenC conjugate vaccines and seen dramatic declines in incidence of disease. In January 2005, a MenACWY conjugate vaccine was licensed in the USA and was recommended for 11 to 18-year-olds, beginning with 12-year-old children, and supplemented by a catch-up program at high school entry. Since the vaccine became available, there have been 26 cases of Guillain–Barré syndrome reported as occurring within six weeks of vaccination. As a result a heightened surveillance system has been implemented but there has been no change in the recommendation for immunization. Epidemics of disease due to MenB have occurred in Norway and New Zealand and strain-specific outer membrane vesicle vaccines have been developed. The New Zealand MenB immunisation campaign ceased in 2008. Over time there are natural changes in the epidemiology of meningococcal antigens whereby a particular strain emerges and then declines to be replaced by a new strain, possibly due to herd immune responses. This makes vaccine prevention challenging.
Patel M, Lee CK. 2005. **Polysaccharide vaccines for preventing serogroup A meningococcal meningitis**. Cochrane Database of Systematic Reviews 2005(1) Art. No.: CD001093. DOI: 10.1002/14651858.CD001093.pub2. Updated after new search for studies with no change to conclusions and published in Issue 8, 2010. This review considered the effectiveness of polysaccharide serogroup A vaccine against serogroup A meningococcal meningitis, the age-specific effectiveness of the vaccine, the effectiveness of booster doses in children under five years of age, and the duration of protection in adults and children. Based on a review of eight RCTs (6 in Africa and 2 in Finland, 480,068 participants) the authors concluded that, in children over the age of five and adults the vaccine was strongly protective for the first year (summary vaccine efficacy 95%, 95% CI 87% - 99%). Data from two trials suggested that there was a protective effect in the second year and two trials suggested that the vaccine was protective in younger children but these results were not statistically significant. Only one study assessed the effect of a booster dose and it lacked the power to identify a statistically significant effect.
Sudarsanam T, Rupali P, Tharyan P, et al. 2008. **Pre-admission antibiotics for suspected cases of meningococcal disease**. Cochrane Database of Systematic Reviews 2008(1) Art. No.: CD005437. DOI: 10.1002/14651858.CD005437.pub2. Meningococcal disease can progress rapidly and lead to death or disability within hours of onset. Starting therapy with pre-admission antibiotics before confirmation of diagnosis aims to reduce the risk of death and disability. The authors of this review found no reliable evidence from RCTs for the benefit or otherwise of pre-admission antibiotics for suspected cases of non-severe meningococcal disease. For ethical reasons it is not likely such trials will be undertaken. One RCT of moderate quality indicated that single intramuscular injections of either ceftriaxone or long-acting chloramphenicol were equally effective, safe and economical in reducing serious outcomes. Local affordability, availability and patterns of antibiotic resistance should guide the choice between these antibiotics. The review authors state that “further RCTs comparing different pre-admission antibiotics, accompanied by intensive supportive measures, are ethically justifiable in participants with severe illness, and are needed to provide reliable evidence in different clinical settings”.

Other Relevant Publications
Lopez L, Sexton K, Carter P. 2011. **The Epidemiology of Meningococcal Disease in New Zealand in 2010**. Wellington: Institute of Environmental Science and Research Ltd (ESR). http://www.surv.esr.cri.nz/PDF_surveillance/MeningococcalDisease/2010/2010AnnualRpt.pdf This publication reports on the incidence and distribution of cases of meningococcal disease in New Zealand in 2010 and reviews the trends in disease patterns since the beginning of the epidemic in 1991 and since the MeNZB™ vaccination campaign began in 2004. In 2001, at the height of the epidemic, 80% of confirmed cases that could be strain typed were due to the epidemic strain (B:4:P1.7-2,4). In 2010, 31% were due to this strain indicating that the epidemic strain is still in circulation in the population. Almost 26% of cases in 2010 were due to other B strains and 27.2% to group C strains. In 2010, as in previous years, the highest age specific rates were in children aged less than one year and this was particularly noticeable for Māori and Pacific children who had rates five to six times higher than European children in this age group. Over the last ten years there has been a marked reduction in disparities in disease incidence by socio-economic status and by ethnicity. In 1991 disease rate differences in Māori and Pacific peoples compared to Europeans were 15.3 and 58.7 per 100,000 while in 2010 they were 3.5 and 4.1 per 100,000 respectively. Although the number of deaths was low the case fatality rate in 2010 was higher than in most years. Almost half of all hospitalised cases were seen in primary care before admission but only 30% of these received antibiotics in primary care. The report states that "Although it is difficult to determine the impact of pre-hospital antibiotics on disease severity and death due to small numbers and confounding factors, it would be prudent to increase this practice."
Galloway Y, Stehr-Green P, McNicholas A, et al. 2009. **Use of an observational cohort study to estimate the effectiveness of the New Zealand group B meningococcal vaccine in children aged under 5 years**. International Journal of Epidemiology 38(2) 413-8. This study was a cohort analysis of all children who were aged six months to <five years at the time the MeNZB™ vaccine became available in their DHB. It was found that, in the 24 months after they became eligible to receive a full vaccination series, fully vaccinated children were five to six times less likely than unvaccinated children to contract epidemic strain meningococcal disease. This corresponds to a vaccine effectiveness of 80.0% (95% CI 52.5–91.6) for children aged six months to <five years and 84.8% (95% CI 59.4–94.3) for children aged six months to <three years.
Kelly C, Arnold R, Galloway Y, et al. 2007. **A prospective study of the effectiveness of the New Zealand meningococcal B vaccine**. *American Journal of Epidemiology* 166(7) 817-23. This study used data from January 2001 to June 2006 to assess the effectiveness of the New Zealand meningococcal B vaccine, a strain-specific vaccine developed by Chiron vaccines (Siena, Italy) in collaboration with the Norwegian Institute of Public Health. It was estimated (using a generalised estimating equation rates model) that disease rates were 3.7 times higher in unvaccinated people (95% CI 2.1 - 6.8) and that the vaccine effectiveness was 73% (95% CI 52% - 85%). The model included allowances for region-specific disease rates, age, ethnicity, socioeconomic status, disease progression over time, and seasonality. The study authors found no statistically significant interactions between any demographic variable and the vaccine effect despite the crude rates suggesting that the vaccine was possibly less effective for children under the age of one year (2005 risk ratio for 0-1 years 0.9, risk ratio for children1-4 years 11.3 and risk ratio for children and youth 5-19 years 2.9). It was estimated that 54 epidemic strain cases had been prevented in the two years since the programme began (95% CI assuming a fixed population size 22-115).