ORIGINAL ARTICLE

The epidemiology of aseptic meningitis in New Zealand children from 1991 to 2020

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Aim: Aseptic meningitis, including culture negative and viral meningitis, contributes a significant health-care burden, including unnecessary antibiotic use and hospitalisation to treat possible bacterial meningitis. This study analysed aseptic meningitis hospitalisations in New Zealand (NZ) children over 29 years.

Methods: In this population-based study, aseptic meningitis hospitalisations in NZ children <15 years old were analysed from 1991 to 2020. Incident rate ratios were calculated using Poisson regression models. Variations in hospitalisations by age, year, sex, ethnicity, geographical region and socio-economic deprivation were analysed.

Results: There were 5142 paediatric aseptic meningitis hospitalisations from 1991 to 2020. Most were unspecified viral meningitis (64%), followed by enterovirus (29%). Hospitalisation rates varied annually with a median of 18.4/100 000 children including a peak in 2001 of 56.4/100 000 (51.7–61.6). From 2002 to 2019, rates increased by 8.4%/year (7.2–9.5%) in infants <90 days old but decreased in all other age groups. In 2020, a reduction in hospitalisations to 9.6/100 000 (7.9–11.8) occurred, and in infants <90 days old were 0.37 times expected. Hospitalisations were 1.50 times (1.49–1.68) higher in males than females; higher in children of Māori (*P* < 0.001) and Pacific (*P* < 0.001) versus European ethnicity; and higher for children living in the most (2.44 times, (2.16–2.75)) versus least deprived households; and in northern versus southern NZ.

Conclusions: Aseptic meningitis hospitalisations increased in young infants during 29 years of surveillance, apart from 2020 when admissions reduced during the COVID-19 pandemic. In contrast, hospitalisations decreased in children aged >1 year. Further investigation into reasons for higher admissions by ethnic group, geographical location and increased deprivation are required.

Key words: aseptic meningitis; enterovirus; epidemiology; viral meningitis.

What is already known on this topic	**What this paper adds**
1 Most meningitis in countries with similar immunisation schedules to New Zealand is aseptic (non-bacterial). 2 Most aseptic meningitis is presumed to be caused by viruses, although specific aetiologies are often not identified.	1 Aseptic meningitis hospitalisations in New Zealand children from 1991 to 2020 were highest in young infants, and were higher in Pacific and Māori children, and children living in socioeconomically deprived areas suggesting inequities in disease burden.

3 Aseptic meningitis contributes a large health-care burden although it is usually a self-limiting disease and for most children only supportive management is required.

2 Aseptic meningitis hospitalisations in New Zealand children aged >1 year decreased over time, whereas infant hospitalisations increased from 2004 to 2019.

3 There was a reduction in childhood aseptic meningitis hospitalisations in 2020 during the COVD-19 pandemic.

Aseptic meningitis is defined as all non-bacterial meningitis, including cases with no identifiable cause.[1] Viruses are identified as the causative organism in most aseptic meningitis.[1] In populations with comparable immunisation schedules to New Zealand (NZ), like the United Kingdom (UK), most meningitis is presumed to be aseptic.[2] The introduction of protein conjugate vaccines against *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* into the NZ immunisation schedule has reduced bacterial meningitis rates in NZ over the past 25 years.[3] Meningococcal conjugate vaccines are also part of routine vaccination schedules in many countries.[4] Although NZ introduced a strain-specific outer membrane vesicle vaccine from 2004 to 2008 during a meningococcal type B epidemic,[5] meningococcal vaccines are not currently included in the national NZ immunisation schedule.

Many viruses cause meningitis including enterovirus (EV), parechovirus, herpes viruses, respiratory viruses (adenovirus, influenza virus, coronaviruses), mumps virus, measles virus, rotavirus, parvovirus B19, lymphocytic choriomeningitis virus and human immunodeficiency virus.[6,7] Viral meningitis is usually a self-limiting disease and for most children only supportive management is required. Although improvements in diagnostic capabilities, including widespread use of polymerase chain reaction (PCR), have reduced the duration of hospital stay and antibiotic treatment for viral meningitis, aseptic meningitis still contributes a large health-care burden.[8] The long-term outcomes in children following viral meningitis are still poorly defined, with studies reporting conflicting results.[9]

Long-term epidemiological trends in childhood viral or aseptic meningitis in NZ have not been previously reported. Defining these trends is important to inform clinical practice and the national vaccination program, to establish future research priorities and improve understanding of ethnic disparities in disease and populations at risk of poorer health outcomes. The aim of this study was to analyse trends, over 29 years, in hospitalisations of children with aseptic meningitis.

Methods

Data sets

In this population-based study, a national cohort of hospital admissions for meningitis was identified from the National Minimum Dataset (NMDS), accessed via the Integrated Data Infrastructure (IDI) at StatsNZ.[10] Children were included if aged <15 years upon admission with viral or aseptic meningitis, identified by any relevant *International Classification of Disease* (ICD) code (Table 1), between 1 January 1991 and 31 December 2020.

The NMDS is the national data set of routinely collected hospital discharge information which includes data for both inpatients and emergency department presentations.[11] The current NMDS was introduced in 1999, but data have been submitted in an agreed format by public hospitals since 1993 and retrospectively

loaded with hospital discharge information from 1988.[11] The IDI is a large collection of national data sets which links de-identified data for individuals from a variety of governmental and non-governmental organisations. These data sets are linked by common variables including the National Health Index number, name, birthdate, sex and country of birth, with individuals than being de-identified.[10]

Data extracted from the IDI included the following individual-level and hospital event-level variables: birth year and month, sex, StatsNZ level 1 prioritised ethnic group, meshblock of residential address at time of admission (a small geographical area defined by StatsNZ comprising less than 120 dwellings),[12] date of admission, admitting hospital, ICD-9 and ICD-10 codes.

At StatsNZ level 1, ethnicity is categorised into one of six ethnic groups: European; Māori; Pacific Peoples; Asian; Middle Eastern, Latin American, African (MELAA); and Other. Individuals identifying more than one ethnic group were prioritised according to NZ Ministry of Health ethnicity protocols.[12] Meshblock geographic code was used to determine the District Health Board (DHB) of domicile and NZ deprivation index (NZDep).[13] The geographical region of NZ is divided into 20 DHBs. The NZDep is a small-area measure of neighbourhood deprivation that groups the population into deciles from 1 (least deprived) to 10 (most deprived). It is constructed from variables collected in national censuses including income, transport, living space, home ownership, employment, qualifications and government financial support.[13]

Data analysis

Data were analysed using the statistical software 'R' (version 3.4.1). Multiple admissions for an individual were excluded if less than 364 days apart. If multiple diagnoses were listed during an admission, any diagnosis specifying an organism was chosen preferentially.

Numbers of hospitalisations were cross-tabulated by ICD code, year, age at admission, sex, ethnic group, DHB, seasonality and NZDep categorised into quintiles. During the ICD-10 era, each case was also coded by an equivalent ICD-9 code. Therefore, ICD-9 coding was used in this analysis. Following StatsNZ confidentiality rules, all counts were randomly rounded to base 3 and raw counts less than 6 were suppressed.

Group-specific incidence rates with 95% binomial confidence intervals were calculated by dividing cases with the associated estimated resident population at 30th June each year, derived from NZ Census data from StatsNZ. Trends over time in annual age-specific incidence rates, and changes in the direction of trends, were identified using Joinpoint Trend Analysis Software (version 4.7.0.0), results of which were used to inform more complex models.[14] A multivariable generalised linear regression

Table 1 Cases of aseptic meningitis in New Zealand children from 1991 to 2020 defined by ICD-9 code and age

Aseptic meningitis diagnosis, as defined by ICD-9 coding	ICD-9 codes	ICD-10 codes	Age 0–14 years % (n)	<1 years % (n)	1–4 years % (n)	5–9 years % (n)	10–14 years % (n)
Viral meningitis unspecified	047.9	A879	64.1% (3294)	45.1% (1011)	78.6% (519)	79.0% (948)	78.6% (816)
Enterovirus specified	047.0 047.1	A870	29.1% (1497)	47.5% (1065)	13.2% (87)	15.8% (189)	15.0% (156)
Other viral meningitis, not elsewhere classified	047.8	A878	2.6% (132)	4.7% (105)	0.9% (6)	0.8% (9)	1.4% (15)
Aseptic meningitis unspecified	322.0	G030	2.2% (114)	2.0% (45)	4.1% (27)	1.5% (18)	2.0% (21)
Mumps virus	072.1	B261	0.8% (39)	NA‡	1.4% (9)	2.0% (24)	NA‡
Varicella zoster virus	053.0	B010 B021	0.5% (27)	NA‡	NA‡	NA‡	1.4% (15)
Herpes simplex virus	054.72	B003	0.4% (18)	NA‡	NA‡	NA‡	NA‡
Other† specified viral meningitis including adenovirus, measles, infectious mononucleosis	049.1 321.2	A871 B051 B278 G020	0.2% (12)	NA‡	NA‡	NA‡	NA‡
Lymphocytic choriomeningitis virus	049.0	A872	0.2% (9)	NA‡	NA‡	NA‡	NA‡
Total			5142	2244	660	1200	1038

† Includes diagnostic coding with numbers <6 for each code, which are not permitted to be reported separately in the Integrated Data Infrastructure.
‡ NA also includes cells where counts have been suppressed due to small numbers (usually <6).

model (Poisson) was constructed to assess change in incidence by year, sex and age group. Year was entered into the model as a linear spline with knots located in 1995, 2000 and 2002. In addition, an indicator variable was used to compensate for spikes in cases that occurred in 2000 and 2001, and a drop that occurred in 2020. All two-way and three-way interaction terms were investigated; age by sex and age by year interactions were included in the final model.

In the analysis by ethnic group; cases were aggregated to the closest census year (1996, 2001, 2006, 2013 and 2018), age groups <1 year were combined, and MELAA and Other ethnicities were excluded, due to small case numbers and availability of denominator data. Rates were not age-standardised due to the limited age range and relative uniformity of the age structure.

Poisson regression models were used to investigate ethnic differences in incident rate ratios and included the following parameters: census year, age, sex, prioritised ethnicity, and two-way interactions for age by ethnicity, and year by age, sex and ethnicity.

Ethics approval

This study received ethical approval from the NZ Ministry of Health, Northern B Health and Disability Ethics Committee Ref 18/NTB/226.

Results

During the 29-year period from 1991 to 2020, there were 5142 hospitalisations (63% male) due to aseptic meningitis. Unspecified viral meningitis was the most frequently coded accounting for 64% (3294/5142) of hospitalisations. Enterovirus was the most common specified cause accounting for 29%

(1497/5142) of hospitalisations. There were smaller numbers of cases caused by herpes simplex virus, mumps, varicella zoster virus and lymphocytic choriomeningitis virus (Tables 1 and 2).

Time trends by age and sex

Aseptic meningitis hospitalisation rates varied annually with a median of 18.4 (interquartile range 13.8, 21.9) admissions/100 000 children aged <15 years (Fig. 1). Rates were highest in 2001 at 56.4/100 000 (51.7–61.6) children <15 years, with smaller peaks in 1995, 2000 and 2004. In 2020, rates were approximately half of those observed in 2016–2019 (Fig. 2). The aseptic meningitis hospitalisation rate reduced in 2020 during the COVID-19 pandemic, to 9.6/100 000 (7.9–11.8) children <15 years.

Hospitalisation rates varied with age with an interaction effect with time. Overall rates were highest in infants aged <90 days and lowest in children aged 1–4 years. From 2002 until 2019, annual hospitalisations increased by, on average, 8.4%/year (7.2–9.5%) in infants aged <90 days, but decreased in all other age groups including by 4.9%/year in children aged 1–4 years and by 2.4%/year in children aged 10–14 years (Fig. 2). In 2020, the hospitalisation rate in young infants <90 days decreased to 0.37 (95% confidence interval (CI) 0.28–0.50) of expected if the trend from previous years had continued. Overall, rates for males were 1.58 times (1.49–1.68) higher than for females adjusting for age and year of admission (Fig. 3).

Ethnic group

From 1994 to 2020, aseptic meningitis hospitalisation rates in children were consistently highest, across time and age groups, for children of Pacific followed by those of Māori ethnicity (both

Table 2 Rates of aseptic meningitis per 100 000 person-years (with 95% binomial confidence intervals) in New Zealand children from 1991 to 2020 defined by ICD-9 code and age

Aseptic meningitis diagnosis, as defined by ICD-9 coding	ICD-9 codes	ICD-10 codes	0–14 year rate per 100 000 (CI)	<1 years rate per 100 000 (CI)	1–4 years rate per 100 000 (CI)	5–9 years rate per 100 000 (CI)	10–14 years rate per 100 000 (CI)
Viral meningitis unspecified	047.9	A879	12.3 (11.9–12.8)	57.0 (53.6–60.6)	7.3 (6.7–7.9)	10.6 (10.0–11.3)	9.2 (8.6–9.9)
Enterovirus specified	047.0 047.1	A870	5.6 (5.3–5.9)	60.0 (56.5–63.7)	1.2 (1.0–1.5)	2.1 (1.8–2.4)	1.8 (1.5–2.1)
Other viral meningitis, not elsewhere classified	047.8	A878	0.5 (0.4–0.6)	5.9 (4.9–7.2)	0.1 (0.0–0.2)	0.1 (0.1–0.2)	0.2 (0.1–0.3)
Aseptic meningitis unspecified	322.0	G030	0.4 (0.4–0.5)	2.5 (1.9–3.4)	0.4 (0.3–0.6)	0.2 (0.1–0.3)	0.2 (0.2–0.4)
Mumps virus	072.1	B261	0.1 (0.1–0.2)	NA‡	0.1 (0.1–0.2)	0.3 (0.2–0.4)	NA‡
Varicella zoster virus	053.0	B010 B021	0.1 (0.1–0.1)	NA‡	NA‡	NA‡	0.2 (0.1–0.3)
Herpes simplex virus	054.72	B003	0.1 (0.0–0.1)	NA‡	NA‡	NA‡	NA‡
Other[†] specified viral meningitis including adenovirus, measles, infectious mononucleosis	049.1 321.2	A871 B051 B278 G020	0.0 (0.0–0.1)	NA‡	NA‡	NA‡	NA‡
Lymphocytic choriomeningitis virus	049.0	A872	0.0 (0.0–0.1)	NA‡	NA‡	NA‡	NA‡
Total			19.3 (18.7–19.8)	126.5 (121.3–131.8)	9.2 (8.6–10.0)	13.4 (12.7–14.2)	11.7 (11.0–12.5)

[†] Includes diagnostic coding with numbers <6 for each code, which are not permitted to be reported separately in the Integrated Data Infrastructure.
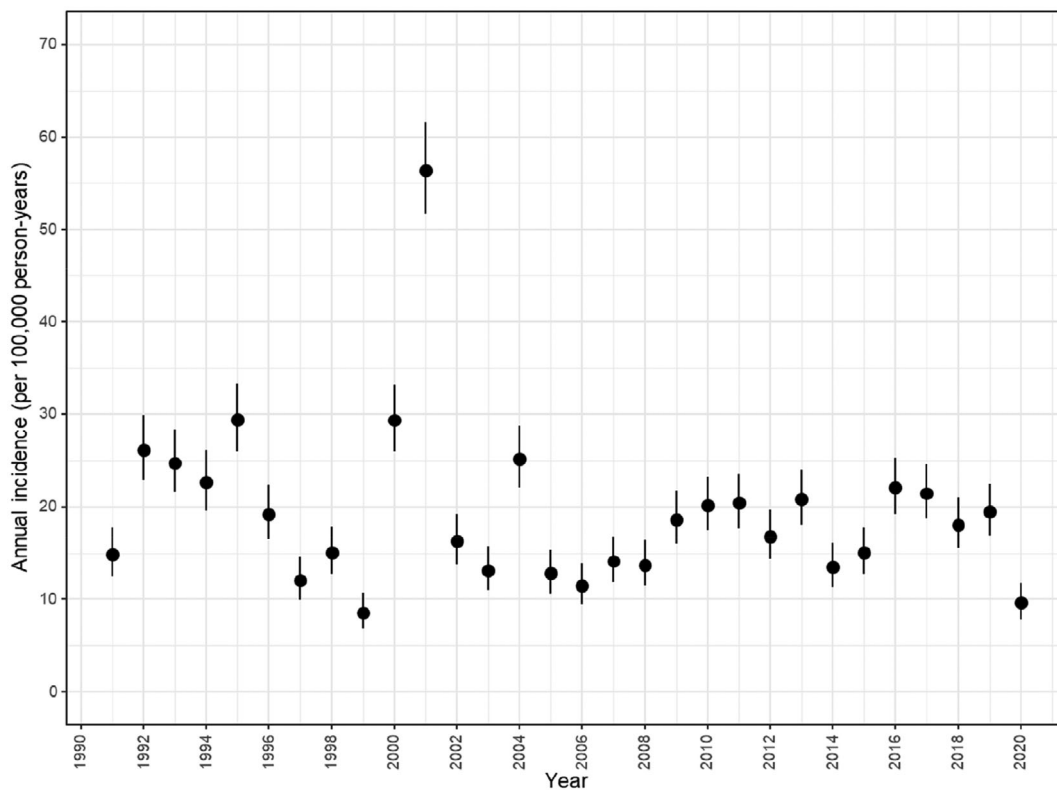‡ NA also includes cells where counts have been suppressed due to small numbers (usually <6).

Fig. 1 Observed annual aseptic meningitis hospitalisation rates in New Zealand children aged <15 years from 1991 to 2020 with 95% binomial confidence intervals.
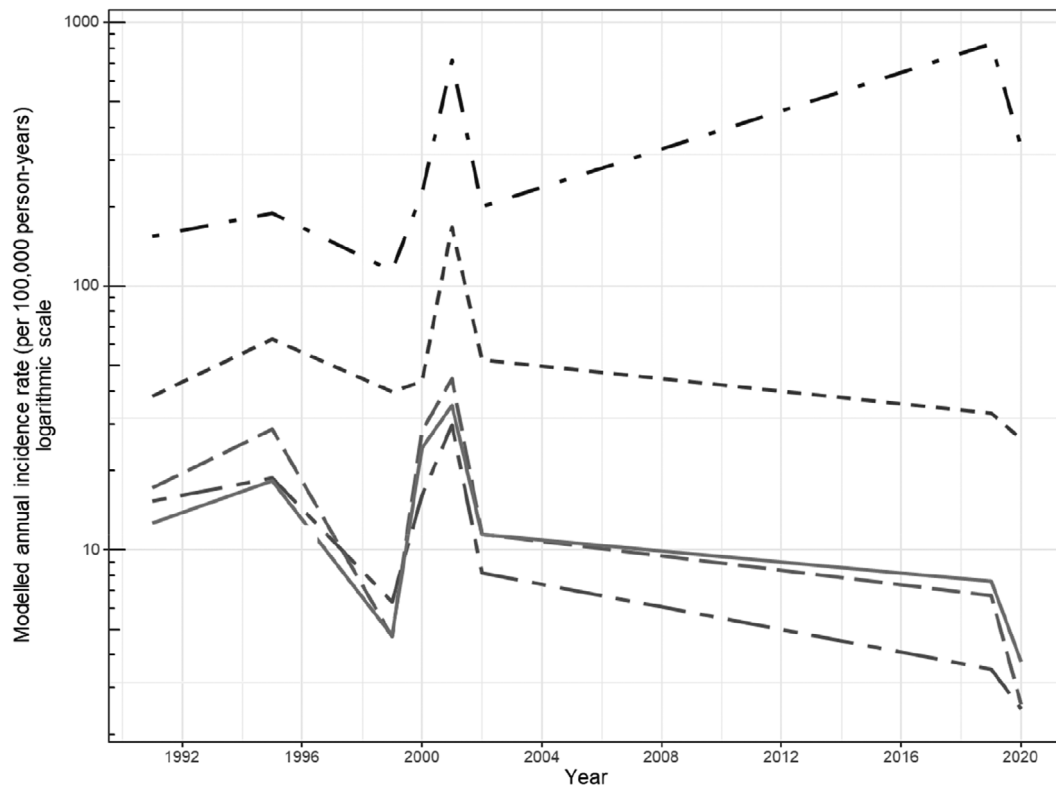
Fig. 2 Modelled annual aseptic meningitis hospitalisation rates in New Zealand children aged <15 years from 1991 to 2020, by age at admission. (────)
<90 days, (┈┈┈) 90–365 days, (─ ─ ─) 1–4 years, (─·─·─) 5–9 years, (───) 10–14 years.

P < 0.001 vs. European ethnicity). There was no evidence that rates in children of Asian ethnicity were ever higher than in children of European ethnicity. The differences in rates between Māori and NZ European children reduced between 2006 and 2013, partially due to decreased rates in Māori children aged >1 year and increased rates in European infants.

Deprivation, geographic location and seasonality

A larger proportion of the children aged <15 years hospitalised with aseptic meningitis lived in more deprived neighbourhoods. This trend was fairly constant over time (Fig. 4). Children living in NZDep quintile 5 (most deprived) had a hospitalisation rate 2.44 times (95% CI 2.16–2.75) higher than those living in NZDep quintile 1 (least deprived).

Analysis of aseptic meningitis hospitalisations by DHB showed higher rates in the north of NZ compared with the south (Fig. 5). Both enterovirus specified and viral meningitis unspecified hospitalisations peaked in the NZ summer months (Fig. 6).

Discussion

In NZ, from 1991 to 2019, aseptic meningitis hospitalisations have increased in infants, particularly since 2002 in young infants aged <90 days. In contrast, over 29 years, aseptic meningitis hospitalisation rates decreased in children aged >1 year. However, in 2020, there was a substantial reduction in aseptic

meningitis hospitalisations at the time of the COVID-19 pandemic, with widespread implementation of non-pharmaceutical interventions. Most aseptic meningitis hospitalisations were not defined by specific viral or other aetiology, with 64% coded as unspecified viral meningitis. Inequities in aseptic meningitis hospital admissions were evident by both ethnicity and deprivation, with higher hospitalisation rates in Māori and Pacific children and in children living in more deprived areas.

The epidemiology of paediatric viral and aseptic meningitis in NZ has not been previously defined. Strain-specific isolated enteroviral outbreaks have been described, for example, coxsackie B4 infections in neonates in 1999, echovirus type 33 in 2000 and more recently, coxsackie virus A6 in 2012–2013.[17–19] During 29 years of surveillance, there was a substantial peak in childhood aseptic meningitis cases in 2001. This was due to increased numbers of unspecified enterovirus meningitis, and was consistent with enteroviral outbreaks in both adults and children reported by the Institute of Environmental Science and Research Ltd. (ESR) in NZ.[19] In 2000, 203 cases of enterovirus were reported to ESR.[19] The main contributing type was echovirus 33, with 70 confirmed cases, mostly meningitis.[19] There were also increases in enteroviral types E30, CB2 and E7 compared with 1999.[19] There were 381 enteroviral cases reported by ESR in 2001 including 105 echovirus type 13 cases, a type associated with aseptic meningitis and not isolated in NZ since 1975, echovirus types 30 and 15, and coxsackie B.[19] This was the largest recorded echovirus outbreak in NZ.
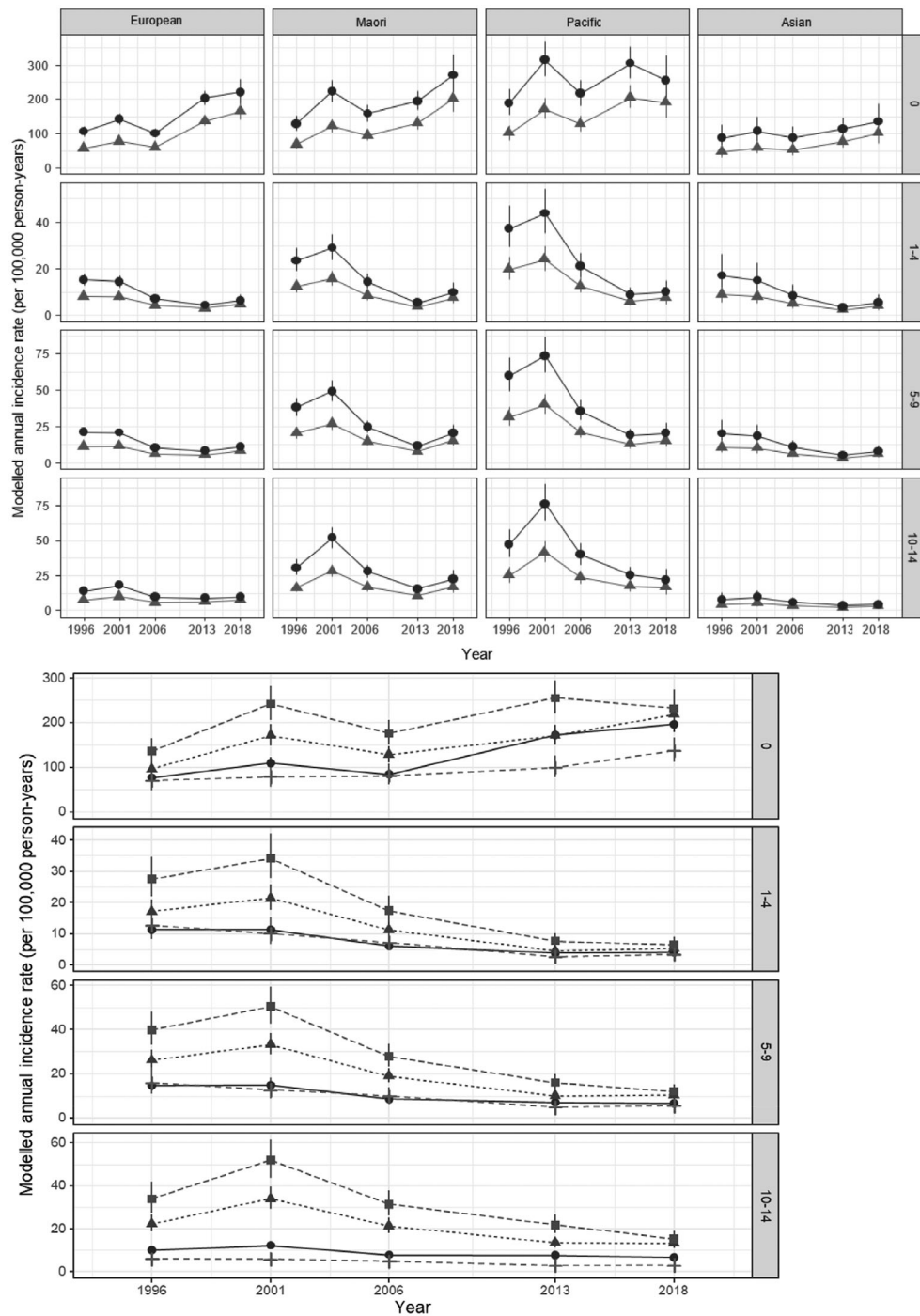
Fig. 3 Aseptic meningitis hospitalisation rates per 100 000 children aged <15 years by census year, ethnic group, age category and sex. (•) European, (▲) Maori, (■) Pacific and (+) Asian.

The peak in aseptic meningitis cases in 2001 could also have been influenced by increased cerebrospinal fluid testing due to the meningococcal capsular group B (MenB) epidemic in NZ from 1991 to 2003.[5] A potential contribution from culture-negative possible MenB cases may also have occurred. In response to the MenB epidemic, a strain-specific Outer Membrane Vesicle vaccine was introduced for children and young people aged <20 years in NZ from 2004 to 2006 and was phased out by March 2011.[5] A reduction in aseptic meningitis cases that may have been caused by pre-treated bacterial meningitis, was not seen following the introduction of childhood pneumococcal conjugate vaccination in NZ from June 2008.[3]
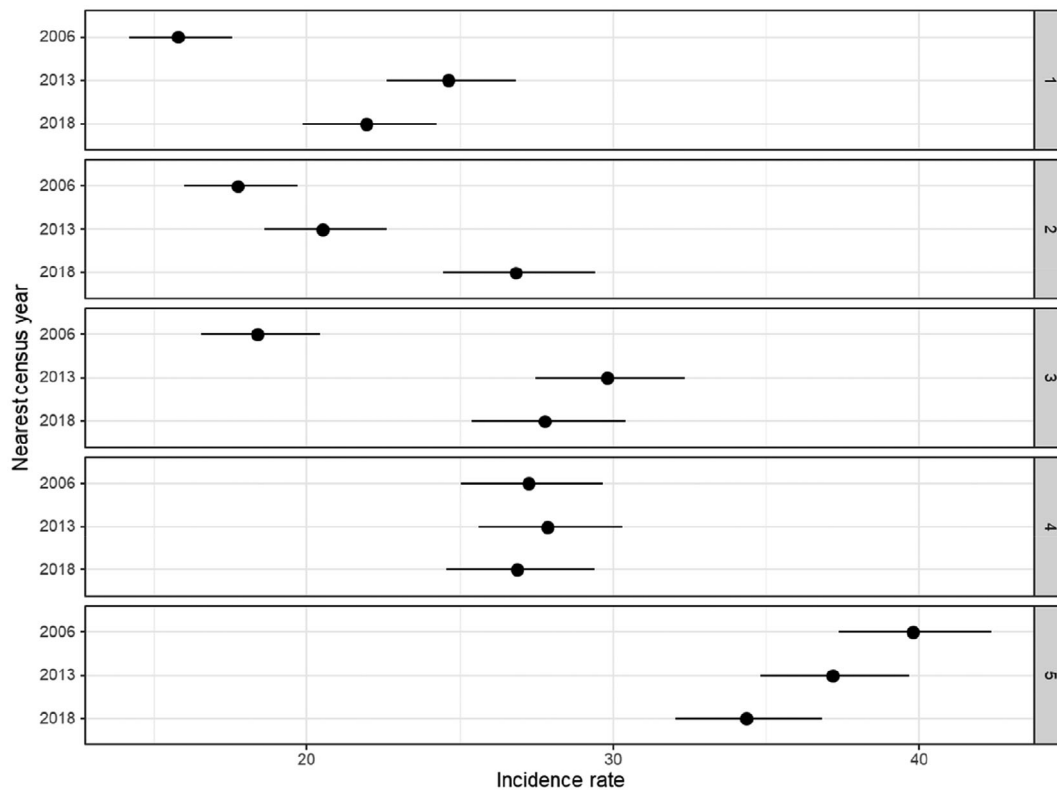
Fig. 4 Aseptic meningitis hospitalisation rates per 100 000 children by deprivation quintile (1 = least deprived, 5 = most deprived), in children aged <15 years from 2004 to 2020.[15,16]

The reduction in aseptic meningitis admissions in 2020 is consistent with world-wide reports of changes in the epidemiology of viral illnesses, respiratory illnesses and invasive bacterial disease during the COVID-19 pandemic, contributed to by non-pharmaceutical interventions (NPIs) including increased hand hygiene, mask use, isolation and closed international borders.[20] A recent English national study found a reduction of over 50% in both childhood meningitis and vaccine-preventable infections due to NPIs.[21] Interestingly, a study in South Auckland, NZ found that enterovirus and rhinovirus infections did not appear to reduce during 2020,[22] which supports the assumption that some aseptic meningitis diagnoses may comprise partially treated bacterial meningitis. It will be important to monitor aseptic meningitis cases with ongoing surveillance as these non-pharmaceutical interventions decrease.

Improvements in molecular diagnostic capabilities with the use of PCR testing since the 1990s are likely to have contributed to increased identification of viral meningitis in NZ infants.[23] PCR reduces time to diagnosis and has much greater sensitivity compared with viral culture.[24–26] Viral PCR is available throughout NZ and widely applied to CSF samples.[15,16,27–30] Studies from the UK have also reported an increase in viral meningoencephalitis cases associated with increased use of molecular diagnostics, with highest incidence in infants aged <3 months.[23,31] NZ ESR reports and laboratory isolates indicate increased numbers of any enteroviral infections being identified in children or adults from 2011 to 2017 compared with earlier time intervals.[32] Higher rates of

enteroviral meningitis in young infants may also be driven by hospital guideline recommendations for obtaining lumbar punctures in young infants who present to hospital with fever. Sepsis screening protocol for infants within the NICE guidelines (2013 fever, 2017 sepsis guidelines) recommend lumbar punctures for febrile infants (<3 months old), while lumbar punctures are performed based on clinical suspicion in older children, which may lead to diagnoses of aseptic meningitis being missed.[8,33–35] The Starship Clinical Guidelines are the main source of guidance for NZ paediatric practice.[36] Updates to the Meningitis guideline were reviewed and there were no major changes in practice that would influence the number of lumbar punctures undertaken.[37]

The inequities in Māori and Pacific disease burden from viral meningitis evident in this study are consistent with other studies of infectious diseases in NZ, including a study from 2004 to 2008 which found the age-standardised rate ratio for all infectious diseases was 2.15 (95% CI 2.14–2.16) higher for Māori and 2.35 (2.34–2.37) higher for Pacific peoples compared with people of European and other ethnicity.[38] Exposure to overcrowding may be a contributor to infectious diseases. Overcrowding is not uniform between ethnic groups with increased incidence in Māori and Pasifika populations, both in urban and rural areas.[38,39] There are long-standing differences in immunisation coverage between ethnic groups in NZ. In early 2020 lower childhood vaccination rates were observed in Māori and Pasifika populations compared to NZ European, with the lowest uptake in Māori (at age 6 months, 65.3% of Māori infants were fully vaccinated,
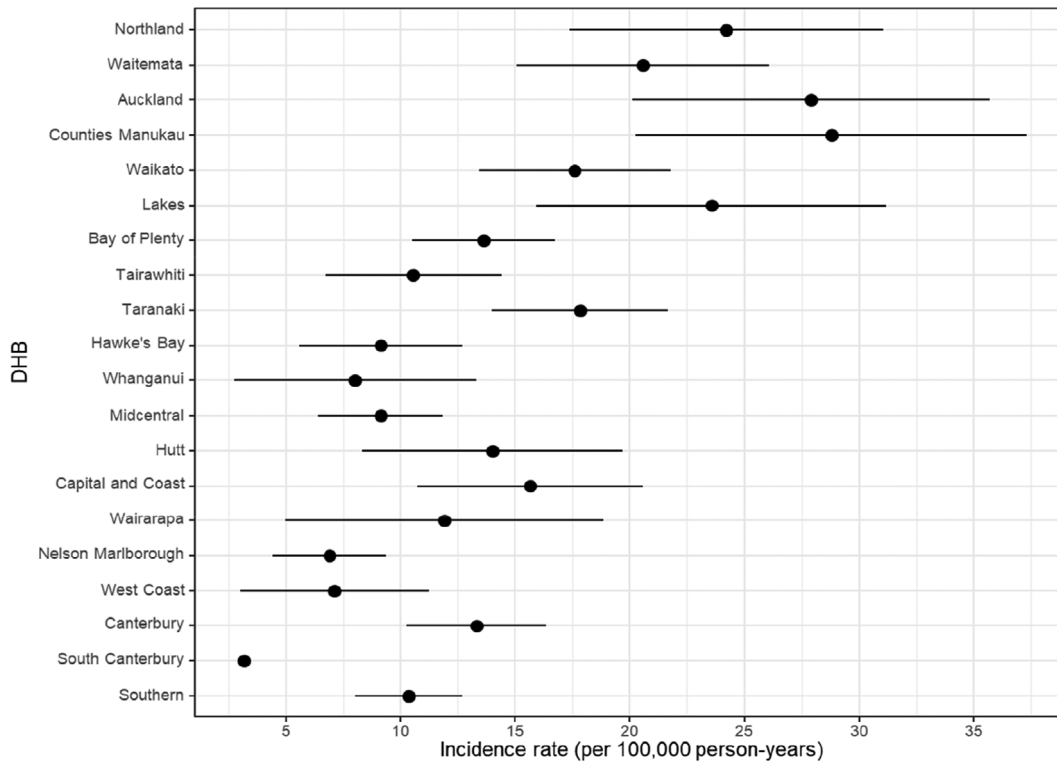
Fig. 5 Comparison of aseptic meningitis hospitalisation rates in NZ children aged <15 years by District Health Board region from 1997–2020. *District Health Boards listed in order from northern to southern New Zealand regions.

compared with 84.7% of NZ European infants from Jan-March 2020, an observation that is unchanged from 2005 when National Immunisation Register was started).[40] This may have contributed to higher rates of lumbar puncture, due to clinician decision-making about obtaining more investigations in unvaccinated children, and hence increased identification of aseptic meningitis in these populations. The NZ government has created a Māori health action plan 'Whakamaua' to address inequities across the health sector and seek to improve health-care delivery to and health of Māori.[41] Children living in households in the most socioeconomically deprived quintile of NZ had higher aseptic meningitis hospitalisation rates. This association is also consistent with a previous NZ study, which reported a rate ratio of 2.81 (2.80–2.83) for all infectious disease admissions at any age in people living in the most versus least socioeconomically deprived quintile.[38] Children living in the more northern regions of NZ had higher aseptic meningitis hospitalisation rates than those living in southern regions, which is likely contributed to by
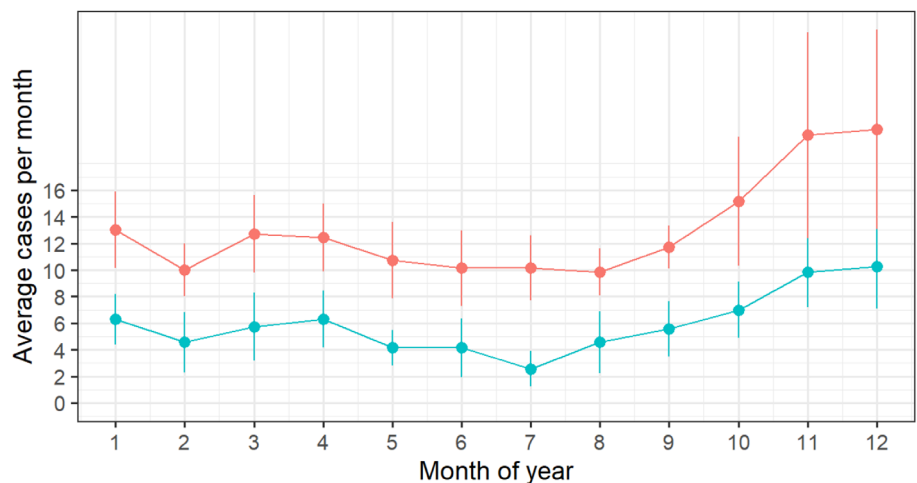

Fig. 6 Comparison of enterovirus specified and viral meningitis unspecified hospitalisation rates in NZ children aged <15 years by month from 1997 to 2020. (•) viral meningitis unspecified, (•) enterovirus specified.

regional variations in population demographics. It is important to note that ethnicity, deprivation and geographic location are all associated and the interrelationships between these were not controlled for in our analysis. Seasonality patterns of viral meningitis hospitalisations were consistent with international trends with a peak evident during summer.[42]

This study included a long period of surveillance. Additionally, linkage of data within national NZ data sets allowed a comprehensive analysis of ethnicity, deprivation and geographic factors in childhood aseptic meningitis hospitalisations. This study had several limitations. In NZ, all admissions to public hospitals are recorded, with data held and collated nationally in the NMDS. The NMDS data may under-report disease incidence, as non-admitted cases are not included. Additionally, viral meningitis cases and specific viral aetiologies are likely to be under-reported, because clinicians do not always obtain specimens for microbiological diagnostic testing for viral pathogens or obtain lumbar punctures. Denominator data for total number of lumbar punctures performed are not available. However notably, in NZ, there have been no significant changes in national clinical guidelines for obtaining lumbar punctures in febrile infants during the years included in this study.[37] Changes in diagnostic platforms and increased availability of PCR may have caused an increase in specific viral meningitis diagnoses; however, information about changes in PCR or molecular testing across NZ were not available. Prioritised ethnicity was used for the rate calculations, where people who identified as having multiple ethnicities were prioritised to one ethnic group: Māori first, then Pacific, Asian and European. Total response ethnicity, where subjects may be counted more than once would have allowed for more accurate descriptions of rates for each ethnic group, but make ethnic rate ratio comparisons more difficult. The impact of the prioritised ethnicity analytical approach is that Pacific and European disease rates may be underestimated.

Conclusions

The burden of disease due to aseptic meningitis in NZ children is highest in young infants, children of Pacific and Māori ethnicity, children living in more socioeconomically deprived areas and those living in more northern regions of NZ. Overall, during 29 years of surveillance in NZ, aseptic meningitis hospitalisation rates in children aged >1 year have reduced over time, in contrast to aseptic meningitis hospitalisation rates in infants which increased from 2004 to 2019 and then decreased in 2020 during the COVID-19 pandemic. The causes of ethnic, socio-economic and geographical inequities in aseptic meningitis hospitalisations require further investigation.

Acknowledgements

Data Availability Statement

The data that support the findings of this study are available from the NZ Ministry of Health through Statistics New Zealand (Stats NZ) but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Data is however available from the authors upon reasonable request and with permission of the NZ Ministry of Health and Stats NZ Tatauranga Aotearoa.

References

1 Tapiainen T, Prevots R, Izurieta HS *et al*. Aseptic meningitis: Case definition and guidelines for collection, analysis and presentation of immunization safety data. *Vaccine* 2007; **25**: 5793–802.

2 Sadarangani M, Willis L, Kadambari S *et al*. Childhood meningitis in the conjugate vaccine era: A prospective cohort study. *Arch. Dis. Child.* 2015; **100**: 292–4.

3 Walls T, Cho V, Martin N, Williman J, Brunton C. Vaccine impact on long-term trends in invasive bacterial disease in New Zealand children. *Pediatr. Infect. Dis. J.* 2018; **37**: 1041–7.

4 Dretler AW, Rouphael NG, Stephens DS. Progress toward the global control of Neisseria meningitidis: 21st century vaccines, current guidelines, and challenges for future vaccine development. *Hum. Vaccin. Immunother.* 2018; **14**: 1146–60.

5 Loring BJ, Turner N, Petousis-Harris H. MeNZB vaccine and epidemic control: When do you stop vaccinating? *Vaccine* 2008; **26**: 5899–904.

6 Lee BEA, Davies HDB. Aseptic meningitis. *Curr. Opin. Infect. Dis.* 2007; **20**: 272–7.

7 Koralnik IJ, Tyler KL. COVID-19: A global threat to the nervous system. *Ann. Neurol.* 2020; **88**: 1–11.

8 Nigrovic LE, Fine AM, Monuteaux MC, Shah SS, Neuman MI. Trends in the management of viral meningitis at United States children's hospitals. *Pediatrics* 2013; **131**: 670–6.

9 Hudson JA, Broad J, Martin NG *et al*. Outcomes beyond hospital discharge in infants and children with viral meningitis: A systematic review. *Rev. Med. Virol.* 2020; **30**: e2083.

10 Intergrated Data Infrastructure. Available from: https://www.stats.govt.nz/integrated-data/integrated-data-infrastructure/ [accessed 14 June 2021].

11 Ministry of Health. National Minimum Dataset (Hospital Events); 29 May 2019. Available from: https://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/national-minimum-dataset-hospital-events [accessed 29 January 2020].

12 HISO 10001:2017. Ethnicity Data Protocols. Wellington: Ministry of Health; 2017. Available from: https://www.health.govt.nz/publication/hiso-100012017-ethnicity-data-protocols

13 Salmond C, Crampton P, Sutton F. NZDep91: A New Zealand index of deprivation. *Aust. N. Z. J. Public Health* 1998; **22**: 835–7.

14 Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat. Med.* 2000; **19**: 335–51.

15 Southern Community LaboratoriesOtago and Southland Specimen Collection Guide. Available from: https://sclabs.co.nz/wp-content/uploads/sites/5/2020/05/Otago-Southland-Collection-Guide.pdf [accessed 5 May 2022].

16 Northland Pathology. Enterovirus PCR (Plasma). Available from: https://scg.aphg.co.nz/#!/NTH/details/EPC [accessed 11 May 2022].

17 Hayman R, Shepherd M, Tarring C, Best E. Outbreak of variant hand-foot-and-mouth disease caused by coxsackievirus A6 in Auckland, New Zealand. *J. Paediatr. Child Health* 2014; **50**: 751–5.

18 Austin BJ, Croxson MC, Powell KF, Gunn TR. The successful containment of coxsackie B4 infection in a neonatal unit. *J. Paediatr. Child Health* 1999; **35**: 102–4.

19 The Institute of Environmental Science and Research. Annual Summaries – 2000-2002. ESR Lablink 2001-2003; 8-10(1773-1591).

20 Brueggemann AB, Jansen van Rensburg MJ, Shaw D *et al*. Changes in the incidence of invasive disease due to *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* during the COVID-19 pandemic in 26 countries and territories in the invasive respiratory infection surveillance initiative: A prospective analysis of surveillance data. *Lancet Digit Health* 2021; **3**: e360–e70.

21 Kadambari S, Goldacre R, Morris E, Goldacre MJ, Pollard AJ. Indirect effects of the covid-19 pandemic on childhood infection in England: Population based observational study. *BMJ* 2022; **376**: e067519.

22 Trenholme A, Webb R, Lawrence S *et al*. COVID-19 and infant hospitalizations for seasonal respiratory virus infections, New Zealand, 2020. *Emerg. Infect. Dis.* 2021; **27**: 641–3.

23 Kadambari S, Bukasa A, Okike IO *et al*. Enterovirus infections in England and Wales, 2000-2011: The impact of increased molecular diagnostics. *Clin. Microbiol. Infect.* 2014; **20**: 1289–96.

24 Rotbart H. Enteroviral infections of the central nervous system. *Clin. Infect. Dis.* 1995; **20**: 971–81.

25 Jeffery K, Read S, Peto T, Mayon-White R, Bangham C. Diagnosis of viral infections of the central nervous system: Clinical interpretation of PCR results. *Lancet* 1997; **349**: 313–7.

26 Robinson C, Willis M, Meagher A, Gieseker K, Rotbart H, Glode M. Impact of rapid polymerase chain reaction results on management of pediatric patients with enteroviral meningitis. *J. Pediatr. Infect. Dis.* 2002; **21**: 283–6.

27 Auckland District Health Board. Enterovirus PCR. Available from: https://testguide.adhb.govt.nz/EGuide/?elv=1&name=Enterovirus%20PCR&pn=1324&mn=663&sd=3&ts=15a40172405 [accessed 11 May 2022].

28 Medlab Central. Enterovirus – PCR Swab. Available from: https://cdr.medlabcentral.co.nz/handbook/ [accessed 7 May 2022].

29 Canterbury Health Laboratories. CSF CNS PCR Infectious Screen. Available from: https://www.labnet.health.nz/testmanager/index.php?fuseaction=main.DisplayTest&testid=1359 [accessed 7 May 2022].

30 Wellington SCL. 3DHB Funded and Unfunded Laboratory Tests. Available from: https://www.wellingtonscl.co.nz/wp-content/uploads/sites/3/2020/05/3DHB-Funded-and-Unfunded-Test-List-WSCL-June-2019_1-1.pdf [accessed 6 May 2022].

31 Kadambari S, Okike I, Ribeiro S *et al*. Seven-fold increase in viral meningo-encephalitis reports in England and Wales during 2004-2013. *J. Infect.* 2014; **69**: 326–32.

32 The Institute of Environmental Science and Research. Virology Annual Reports 2011-2017. Public Health Surveillance; 2011–2017.

33 Davis T. NICE guideline: Feverish illness in children – Assessment and initial management in children younger than 5 years. *Arch. Dis. Child. Educ. Pract. Ed.* 2013; **98**: 232–5.

34 National Institute for Health and Care Excellence (NICE). Fever in under 5s: Assessment and Initial Management; November 2021. Available from: https://www.nice.org.uk/guidance/ng143/chapter/Recommendations#clinical-assessment-of-children-with-fever [accessed 7 May 2022].

35 National Institute for Health and Care Excellence (NICE). Sepsis: Recognition, Diagnosis and Early Management; September 2017. Available from: https://www.nice.org.uk/guidance/ng51/chapter/Recommendations [accessed 7 May 2022].

36 Hee Gan KD, Stuart, Voss L, Williams G. Fever in under 2 month olds; March 2022. Available from: https://starship.org.nz/guidelines/fever-in-under-2-month-olds/ [accessed 17 May 2022].

37 Meningitis, Starship Clinical Guidelines. Available from: www.starship.org.nz/guidelines Archive available 2005, 2009, 2016, 2018 editions [accessed 13 June 2022].

38 Baker MG, Barnard LT, Kvalsvig A *et al*. Increasing incidence of serious infectious diseases and inequalities in New Zealand: A national epidemiological study. *Lancet* 2012; **379**: 1112–9.

39 Statistics New Zealand. Crowding Measures By Ethnic Group. Available from: https://nzdotstat.stats.govt.nz/wbos/Index.aspx [accessed 8 May 2022].

40 Ministry of Health. National and DHB immunisation data. Available from: https://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-coverage/national-and-dhb-immunisation-data [accessed 8 May 2022].

41 Ministry of Health. *Whakamaua: Māori Health Action Plan 2020–2025*. Wellington: Ministry of Health; 2020.

42 Abedi GR, Watson JT, Nix WA, Oberste MS, Gerber SI. Enterovirus and parechovirus surveillance – United States, 2014-2016. *Morb. Mortal. Wkly. Rep. Surveill. Summ.* 2018; **67**: 515–8.