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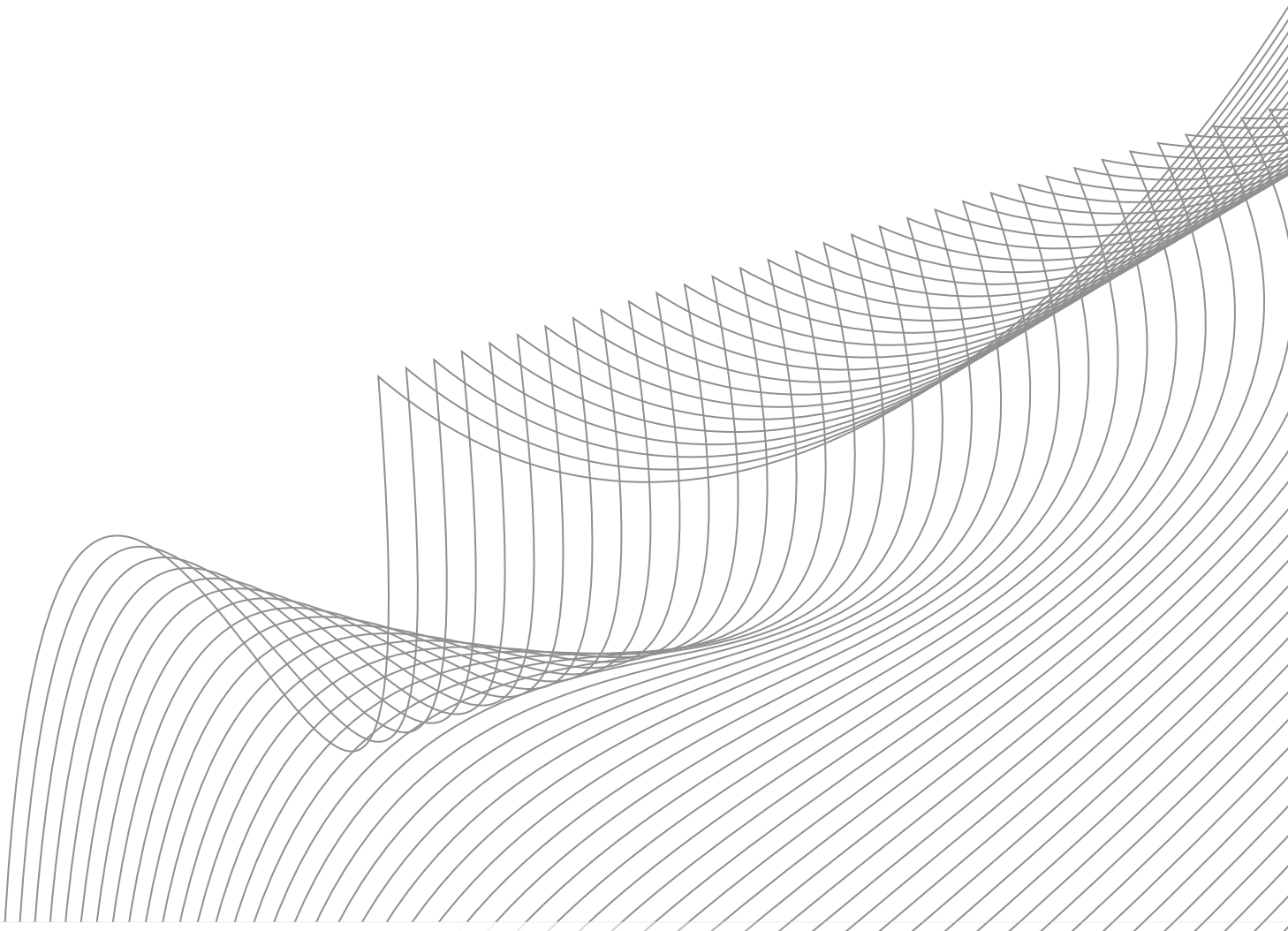

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Original article

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Abstract

Invasive Group A Streptococcal infection (iGAS) is an uncommon but serious infection with *Streptococcus pyogenes* in a normally sterile body site. Manifestations include bacteraemia, necrotising fasciitis and toxic shock syndrome with attendant serious morbidity and mortality. An increasing incidence of iGAS has been observed in some regions of Australia. iGAS became a nationally notifiable condition from 1 July 2021.

To determine if regional incidence has increased, and to identify priority populations, we undertook a retrospective data analysis of Group A Streptococcal (GAS) bacteraemia cases in Hunter New England Local Health District (HNELHD), New South Wales, Australia, from 1 January 2008 to 31 December 2019, as identified by NSW Health Pathology, John Hunter Hospital.

A total of 486 cases were identified (age-standardised rate: 4.05 cases per 100,000 population per year). Incidence in HNELHD gradually increased over the study period (adjusted incidence rate ratio: 1.04; 95% confidence interval: 1.01–1.07) and was significantly higher in children under 5 years of age; in adults over 70 years of age; in males; and in First Nations peoples. A significant peak occurred in 2017 (9.00 cases per 100,000 population), the cause of which remains unclear.

GAS bacteraemia is uncommon but severe, and incidence in HNELHD has slowly increased. Public health and clinical guidelines must address the needs of priority populations, which include young children, older adults and First Nations peoples. Routine surveillance and genomic analysis will help improve our understanding of iGAS and inform best public health management.

Keywords: group A *Streptococcus*; *Streptococcus pyogenes*; iGAS; GAS; invasive; bacteraemia; sepsis; notifiable condition; infectious disease; epidemiology

Introduction

Streptococcus pyogenes, or Group A Streptococcus (GAS), is a gram-positive bacterium that colonises the skin and pharynx and can cause a range of illness in humans.[1,2] Group A streptococci possess surface M-proteins, encoded by different *emm* genes, which are essential for virulence and for survival of the bacteria in human tissues.[3,4]

Invasive Group A Streptococcal infection (iGAS) is a serious infection in a normally sterile body site.[5] Manifestations of iGAS include bacteraemia; septic arthritis; pneumonia; puerperal sepsis; necrotising fasciitis; and streptococcal toxic shock syndrome (STSS).[6] Treatment requires prompt administration of antibiotics and cases often need invasive therapies, including ventilation, dialysis and/or surgery.[7] iGAS carries a case fatality ratio (CFR) of up to 15% in

high-income countries and may result in long-term sequelae.[8,9] Factors associated with mortality include older age, comorbidities, clinical manifestation and *emm*-types 1 and 3.[10–13]

The incidence of iGAS varies by population, climate and country, and disproportionately impacts First Nations peoples across the globe.[9,14–16] iGAS rates appear to be increasing internationally[17,18] and within Australia.[9,19] Clustering of cases within households and residential care facilities has been documented.[12,20–23] The household attack rate of iGAS within 30 days of a primary case has been estimated at 0.66 to 3.22 cases per 1000 people,[12,22] which equates to an approximately 2000-fold increased risk depending on background community incidence.[23]

Previously, iGAS was only notifiable in two Australian states/territories: Northern Territory and Queensland;[5,24] however, it became a nationally notifiable condition from 1 July 2021.[25] At time of writing this paper, state and territory public health guidelines for iGAS varied, particularly regarding antibiotic prophylaxis for household contacts, and national guidelines were in development.[5,24,26] Routine genomic surveillance of iGAS was not available.

Hunter New England Local Health District (HNELHD) is situated in north-eastern New South Wales and encompasses an area of 131,785 square kilometres.[27] It has an estimated population of 920,370 and consists of metropolitan, regional and rural communities.[28] In HNELHD, 7.1% of the population identify as Aboriginal and/or Torres Strait Islander,[i] compared to 3.3% across Australia.[29]

An increase in GAS bacteraemia cases in HNELHD was observed through a scoping review of public hospital laboratory data, including an increase in admissions from GAS pneumonia in two major HNELHD hospitals during the 2017 influenza season.[30]

The purposes of this study were:

1. to determine if the incidence of GAS bacteraemia in HNELHD has increased; and

2. to identify priority populations and influencing factors for prevention and diagnosis of GAS bacteraemia in HNELHD.

A broader aim of this study was to help inform local and national guidelines relating to iGAS.

Methods

Study population

Retrospective data analysis was performed on GAS bacteraemia cases that occurred in HNELHD from 1 January 2008 to 31 December 2019. Cases of GAS bacteraemia were defined as patients with Group A *Streptococcus* (*S. pyogenes*) isolated from a blood culture specimen collected at an HNELHD hospital, as identified by NSW Health Pathology, John Hunter Hospital (hereafter NSW HP JHH). NSW HP JHH is a public hospital pathology provider that services 34 of 38 hospitals in HNELHD; however, general practices, private hospitals and some rural public hospitals are serviced by other laboratories. Given the severity of GAS bacteraemia, it was anticipated that most cases would present to public emergency departments rather than to practices.[16] Therefore the NSW HP JHH dataset should capture the majority of cases.

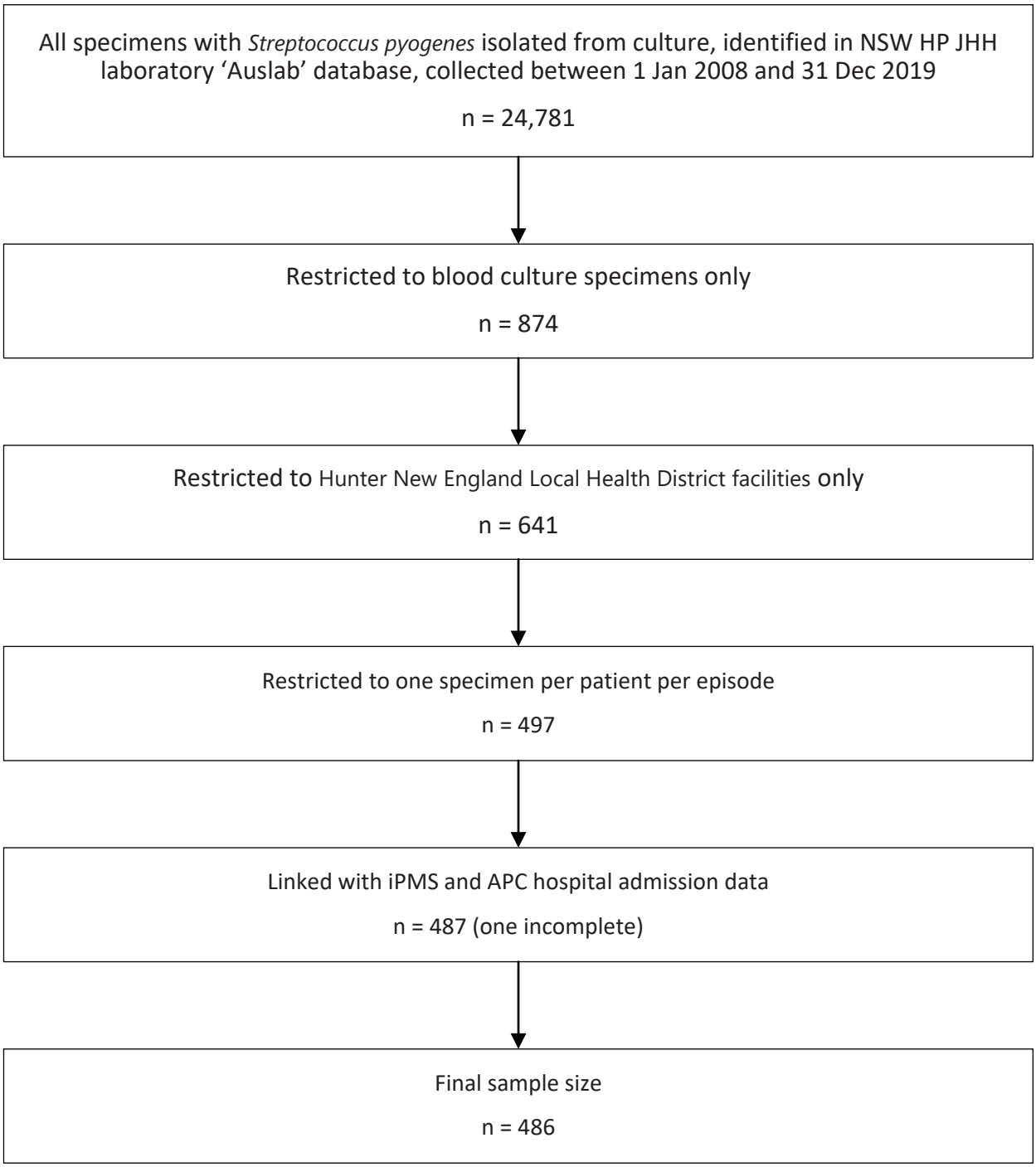
Data collection

Cases were identified from 'Auslab', the NSW HP JHH laboratory database. Data were linked using laboratory specimen number, medical record number and collection date with data from HNELHD patient information system (iSoft Patient Manager [iPMS]) to obtain demographic details and the Admitted Patient

i Hereafter, Aboriginal and/or Torres Strait Islander peoples are respectfully referred to as First Nations peoples of Australia, acknowledging that there are more than 500 First Nations across the country, each with its own diverse customs, culture and lore.

Collection (APC) to obtain outcomes. (Figure 1) Annual influenza notification data was obtained from the New South Wales Notifiable Conditions Information Management System to compare trends in GAS bacteraemia and influenza cases over time, given an anecdotal increase in iGAS cases noted by local clinicians during the 2017 influenza season.

Figure 1: Data extraction and cleaning steps to identify GAS bacteraemia cases in HNELHD that occurred from 1 January 2008 to 31 December 2019[a]



a NSW HP JHH = NSW Health Pathology, John Hunter Hospital; iPMS = iSoft Patient Manager patient information system; APC = Admitted Patient Collection.

Definitions

Date of infection was based on cases' earliest positive specimen collection date. Geographic sectors were based on cases' residential postcodes and 2016 local government areas (LGA). A potential cluster was defined as two or more GAS bacteraemia cases that occurred in the same household or residential care facility within 90 days.

First Nations status was extracted from iPMS records. Completeness of this field is largely dependent on healthcare staff asking and recording the Aboriginal and Torres Strait Islander status of patients during their presentation to the health service.[31]

Critical care was defined as admission to an intensive care unit (ICU) or high dependency unit (HDU) at any time during the admission episode. Death related to GAS bacteraemia was defined as death within 30 days of a case's earliest positive specimen collection.

Data analysis

Data were extracted from the Auslab and iPMS databases to Excel spreadsheets (Microsoft Office 2013; USA) and datasets linked using SAS Enterprise Guide 7.1 (SAS Institute Inc. 2017; USA). Analyses were performed using Stata 14.0 (StataCorp 2018; USA). Denominators were based on the mid-year estimated resident populations (ERP) and projected populations for each year of the study period (ABS 2006, 2011, 2016).[28] Denominators for First Nations peoples involved ERP for 2008 to 2016; the 2016 population was repeated for 2017–2019 rather than using projections.

Age-standardised rates were calculated by the direct method using the 2001 Standard Australian Population.[32] Incidence rate ratios were calculated using Poisson distribution. Chi-square test for trend and post-hoc goodness-of-fit analysis were used to assess incidence over time and Poisson regression to examine seasonality. Logistic regression was used to identify factors associated with outcomes. Multivariate analysis was performed using Poisson regression to estimate adjusted incidence rate ratios. Variables were included in the model if $p < 0.25$ in the initial univariate analyses.[33] Post-hoc analysis was performed using Pearson Chi-squared goodness-of-fit test.

Assessing the impact of GAS bacteraemia on First Nations peoples in HNELHD

Other GAS illnesses disproportionately impact First Nations peoples in Australia;[9,16] therefore, it was considered important to assess the impact of GAS bacteraemia on First Nations peoples in HNELHD. Many studies describe the health of First Nations peoples in relation to non-First Nations populations, which can stigmatise, and which fails to acknowledge the strengths of First Nations peoples in Australia and the significant impact of colonisation and systemic racism on health.[34] Therefore, an in-depth, within-population analysis of GAS bacteraemia in First Nations peoples in HNELHD was performed rather than a between-populations comparison. However, there are circumstances where comparisons are useful to influence policy;[34,35] and with the endorsement of the First Nations researchers, First Nations status was included in the multivariate analysis. Age-standardisation for First Nations peoples was not performed as small numbers within age groups can result in imprecise estimates.[36]

Ethical considerations and cultural governance

Ethical approval was obtained from the Hunter New England Local Health District (Ref: 2019/ETH12208), Aboriginal Health & Medical Research Council of New South Wales (Ref: 1641/20) and Australian National University (Ref: 2019/778) Human Research Ethics Committees. Aboriginal research team members provided cultural governance throughout and an Aboriginal research advisory group contributed to the interpretation of results and study recommendations.

Results

Between 1 January 2008 and 31 December 2019, a total of 486 GAS bacteraemia cases were identified in HNELHD across 24 public healthcare facilities (Figure 1). Of these, 467 (96.1%) had *S. pyogenes* only, six (1.2%) had *S. pyogenes* plus a likely contaminant, and thirteen (2.7%) had co-infection with another bacterium (e.g. *Staphylococcus aureus*).

The mean number of cases per year was 40.5 (standard deviation, SD: 15.8; range: 22–83 cases), with crude and age-standardised incidence rates of 4.53 cases and 4.05 cases per 100,000 population per year, respectively. The median age was 61 years (inter-quartile range, IQR: 39–78 years) and 57.2% of cases were male (Table 1).

Incidence in HNELHD over time

The incidence of GAS bacteraemia in HNELHD gradually increased over the study period, with a peak incidence in 2017 of 9.00 cases per 100,000 population. This peak was more than double the previous five-year average (4.18 cases per 100,000 population per year for 2012–2016; IRR: 2.15 [95% CI: 1.64–2.80]) (Figure 2).

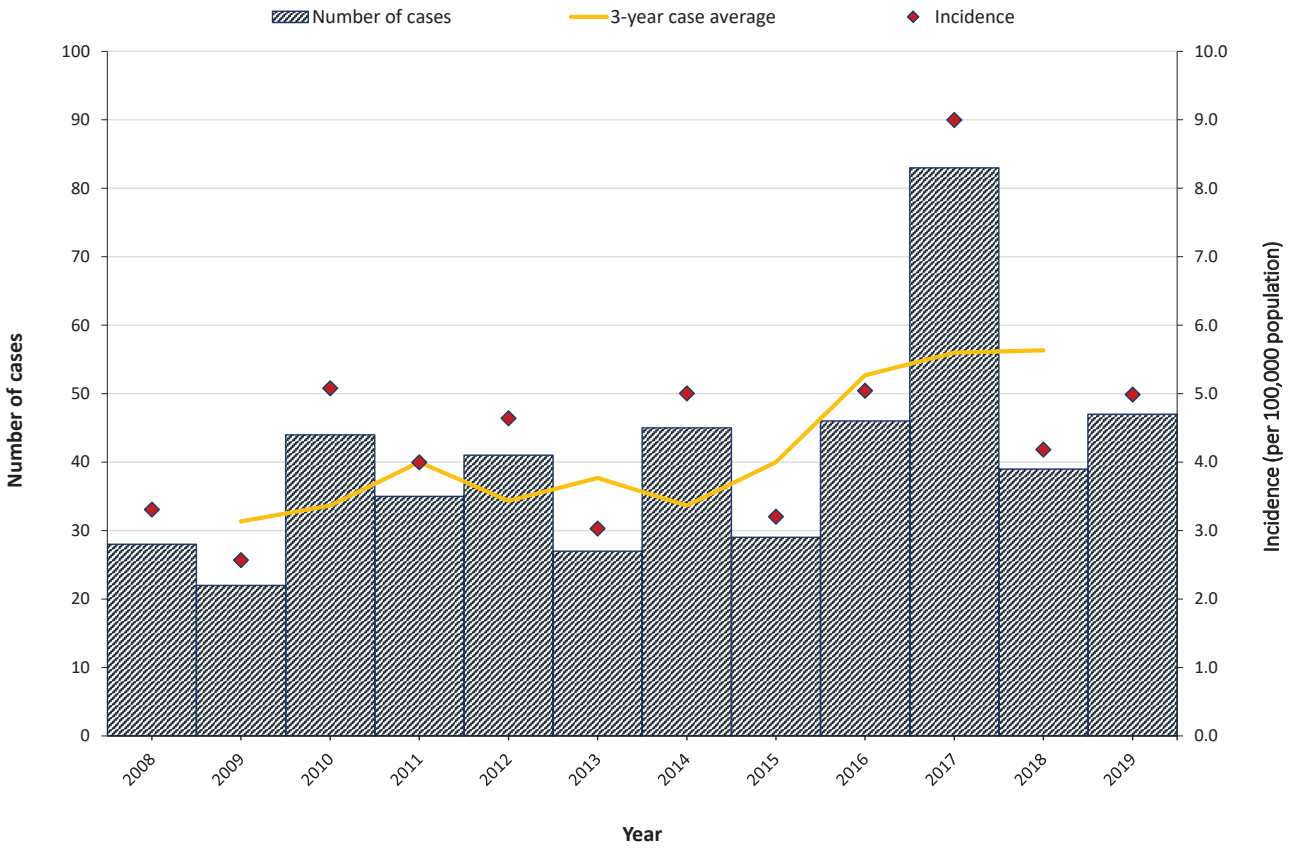
The mean incidence rate was 39% higher in the latter half of the study period (2014–2019) than in the earlier half (2008–2013): 5.24 vs. 3.77 cases per 100,000 population per year,

Table 1: Number of cases, incidence rates and incidence rate ratios (IRR) of GAS bacteraemia cases by sex and age groups in HNELHD, 1 January 2008 to 31 December 2019

Characteristic	Value or range	Number of cases (%)	Incidence rate (per 100,000 per year)	IRR [95% CI][a]
Total cases		486 (100.0)	4.53	—
Sex	Female	208 (42.8)	3.84	Reference group
	Male	278 (57.2)	5.22	*1.36 [1.03–1.80]*
Age group (years)	0–9	46 (9.5)	3.34	*3.04 [1.73–5.36]*
	10–19	15 (3.1)	1.10	Reference group
	20–29	23 (4.7)	1.72	1.56 [0.88–2.79]
	30–39	42 (8.6)	3.29	*2.99 [1.60–5.57]*
	40–49	38 (7.8)	2.76	*2.51 [1.44–4.40]*
	50–59	70 (14.4)	4.96	*4.51 [2.66–7.64]*
	60–69	62 (12.8)	4.96	*4.51 [2.46–8.29]*
	70–79	87 (17.9)	10.52	*9.57 [5.57–16.47]*
	80+	103 (21.2)	20.03	*18.23 [10.58–31.40]*
Paediatric groups (years)	0–4	29 (6.0)	4.22	*4.76 [1.98–11.48]*
	5–9	17 (3.5)	2.47	*2.78 [1.10–7.06]*
	10–14	6 (1.2)	0.89	Reference group
	15–17	7 (1.4)	1.70	1.91 [0.64–5.70]
	Total paediatric	**59 (12.1)**	**2.39**	**—**

a IRR: incidence rate ratio; 95% CI: 95% confidence interval. Significant IRR values ($p < 0.05$) are shown in italics.

Figure 2: Annual case numbers, three-year case average and incidence of GAS bacteraemia cases in HNELHD, 1 January 2008 to 31 December 2019



respectively; IRR: 1.39 [95% CI: 1.15–1.67]. Poisson regression showed a small increase in incidence each year (IRR: 1.05; 95% CI: 1.01–1.10). Chi-square test for trend showed a slight but significant upward trend (slope = 2.2×10^{-6}; standard error, SE: 6.0×10^{-7}; $p < 0.001$); however, post-hoc analysis showed deviation from linear trend, likely due to the 2017 peak. When 2017 data was replaced with the median annual case count for 2014–2019 (45.5 cases), incidence remained 21% higher in the latter half of the study period (2014–2019) than in the earlier half (2008–2013): (4.56 vs. 3.77 cases per 100,000 population per year, respectively; IRR: 1.21 [95% CI: 1.00–1.47].

Incidence by age and sex

Incidence was higher in older age groups, particularly from 70 years upwards (≥ 10.52 cases per 100,000 population per year). Figure 3 shows that the highest age-specific incidence was in adults 80 years and over (20.0 cases per 100,000 population per year), particularly in males in this age group (30.6 cases per 100,000 population per year).

Overall, the incidence was higher in males than females (5.22 vs. 3.84 cases per 100,000 population per year; IRR: 1.36; 95% CI: 1.13–1.63) (Table 2). When stratified by ten-year age group, incidence was significantly higher in males than females aged 60 years and over. Incidence was slightly higher in females than males aged 20–29 years and 30–39 years; however, this was not statistically significant.

Seasonality and influenza

No statistically significant seasonal trend was found when examining aggregated data by quarters ($p = 0.147$). However, there was a notable increase in cases in late winter/early spring, particularly in 2017 (Appendix A, Figure A.1).

Table 2: Adjusted incidence rate ratios of GAS bacteraemia cases in HNELHD during 2008–2019 by year, ten-year age group, sex, and Indigenous status using multivariable analysis

Characteristic	Value or range	Adjusted IRR [95% CI][a]
Year (average annual change)		*1.04 [1.01–1.07]*
Age group (years)	0–9	*2.99 [1.72–5.18]*
	10–19	Reference group
	20–29	1.63 [0.90–2.94]
	30–39	*3.22 [1.73–6.01]*
	40–49	*2.75 [1.59–4.75]*
	50–59	*5.00 [2.96–8.44]*
	60–69	*5.07 [2.82–9.11]*
	70–79	*10.90 [6.40–18.56]*
	80+	*21.87 [12.96–36.93]*
Sex	Female	Reference group
	Male	*1.48 [1.21–1.82]*
Indigenous status	First Nations people	*2.73 [1.98–3.76]*
	non-First Nations people	Reference group

a IRR: incidence rate ratio; 95% CI: 95% confidence interval. Significant adjusted IRR values ($p < 0.05$) are shown in italics.

The number of GAS bacteraemia cases were compared with the number of influenza notifications in HNELHD over time. There appeared to be some visual association between GAS bacteraemia and influenza in later years, particularly in 2017 where high levels of both Influenza A and B were circulating (Figure 4). This was not seen in the earlier years of the study, notably in 2009, the year of the H1N1 'swine flu' pandemic. Closer examination of years 2017 to 2019 demonstrated that the peak of GAS bacteraemia cases in 2017 mostly occurred in winter at a similar time to the peak in influenza notifications. GAS bacteraemia cases were less substantial in 2019, when Influenza A notifications were high but Influenza B notifications were not.

Clustering of cases and repeated episodes

There were only three separate instances where two cases occurred within the same residential care facilities. Two such case-pairs occurred within 30 days of each other, and one pair occurred within 90 days of each other.

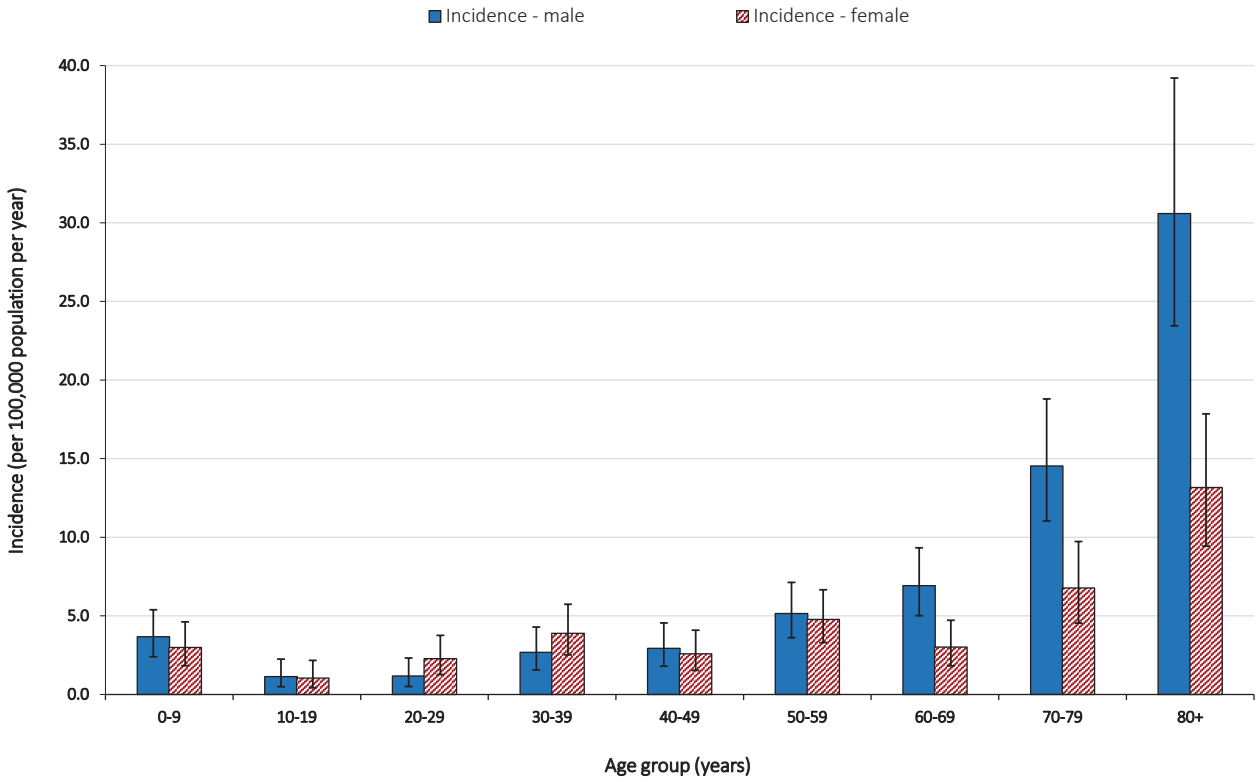
Four patients each had two discrete episodes of GAS bacteraemia greater than 30 days apart with apparent recovery between episodes.

Severity and outcomes

Overall, 27.8% of cases (135/486) were admitted to a critical care unit and 12.6% of cases (61/486) died. There was no significant difference between females and males in outcomes of critical care admission or death ($p = 0.96$ and $p = 0.81$, respectively).

Mortality was significantly associated with older age (odds ratio, OR: 1.04; 95% CI: 1.02–1.05, for each year of age) ($p < 0.001$). Death occurred in approximately one-third of cases aged 80 years and over (31/103 [30.1%]); in approximately one-tenth of cases aged 40–59 year and 60–79

Figure 3: Incidence of GAS bacteraemia (and 95% confidence intervals) by sex and ten-year age groups in HNELHD, 1 January 2008 to 31 December 2019



years (11/108 [10.2%] and 15/149 [10.1%] respectively); and in less than 4% of cases aged under 40 years.

Critical care admission was also significantly associated with age ($p < 0.01$). Approximately one-third of cases aged 40–59 year and 60–79 years (38/108 [35.2%] and 48/149 [32.2%] respectively), and one-quarter of cases aged 20–39 years and 80 years and over (17/65 [26.2%] and 26/103 [25.2%] respectively) were admitted to critical care. The proportion admitted was lowest in cases under 20 years but still substantial (6/61 [9.8%]).

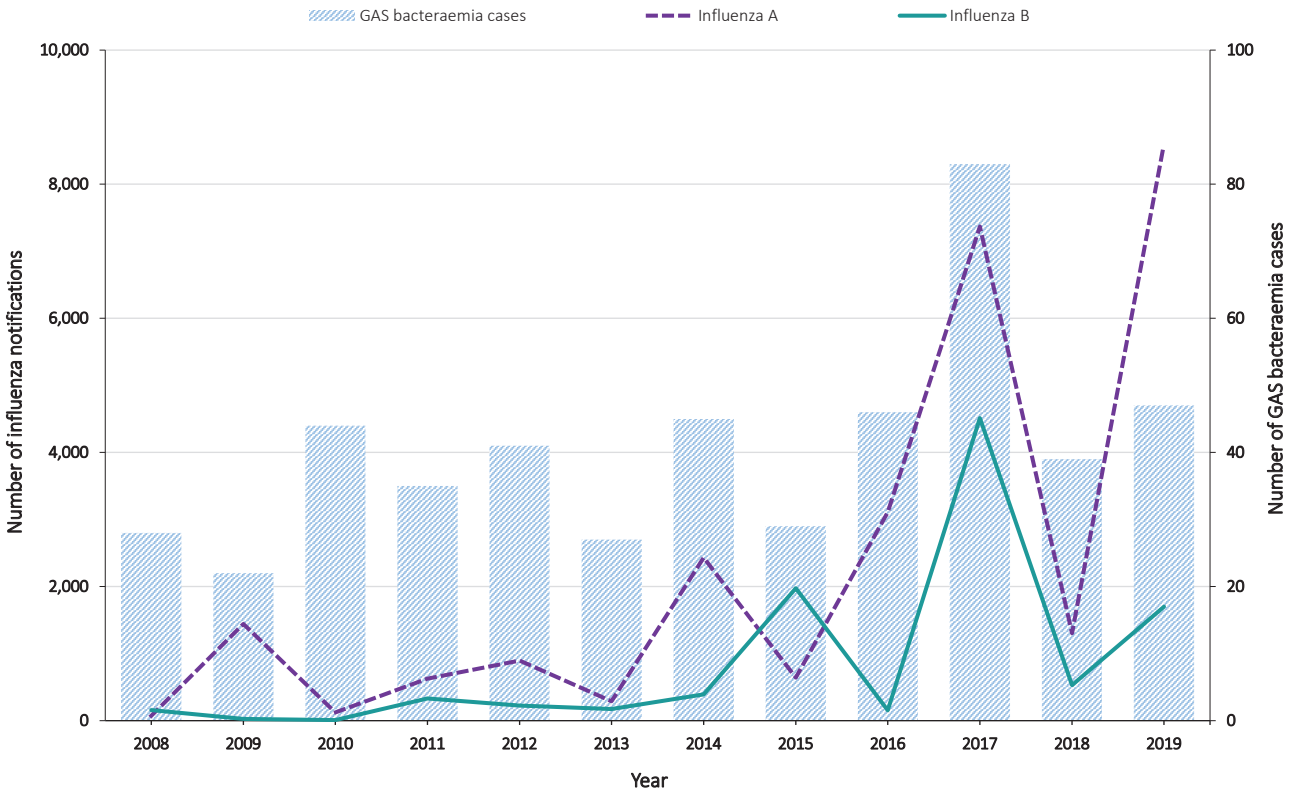
When examined over time, the proportion of critical cases each year ranged from 11.4% to 37.9%, but was not significantly different ($p = 0.23$). The CFR was notably higher in 2010 (27.3%) but did not reach statistical significance ($p = 0.11$) (Figure 5).

Impact of GAS bacteraemia on First Nations peoples in HNELHD

Of the 486 GAS bacteraemia cases in HNELHD between 1 January 2008 and 31 December 2019, forty-three cases (8.8%) identified as First Nations peoples. This gave a crude incidence rate of 7.25 cases per 100,000 population per year, with a peak of 18.9 cases per 100,000 population in 2017.

The median age was 36 years [IQR: 6–49 years]; 56% of cases were female. Incidence was not significantly different between females and males (8.09 vs 6.42 cases per 100,000 population per year; IRR: 0.79 [95% CI: 0.44–1.44]). Incidence was substantial across all age groups (≥ 4.98 cases per 100,000 population per year), with the highest age-specific incidence in children under 5 years old (12.02 cases per 100,000 population per year) and in adults 40 years and over (11.19 cases per 100,000 population per year) (Appendix A, Table A.1).

Figure 4: Number of annual influenza notifications and GAS bacteraemia cases in HNELHD, 1 January 2008 to 31 December 2019



Twenty-one percent of cases were admitted to a critical care unit and 7% died. There were no significant differences in critical care admission or death by sex (p = 0.48 and p = 0.41, respectively) or age groups (p = 0.65 and p = 0.60, respectively). There was no statistically significant difference in outcomes of critical care admission (p = 0.62) or death (p = 0.66) between First Nations peoples and non-First Nations peoples when adjusted for age and sex; however, analysis was limited by small numbers.

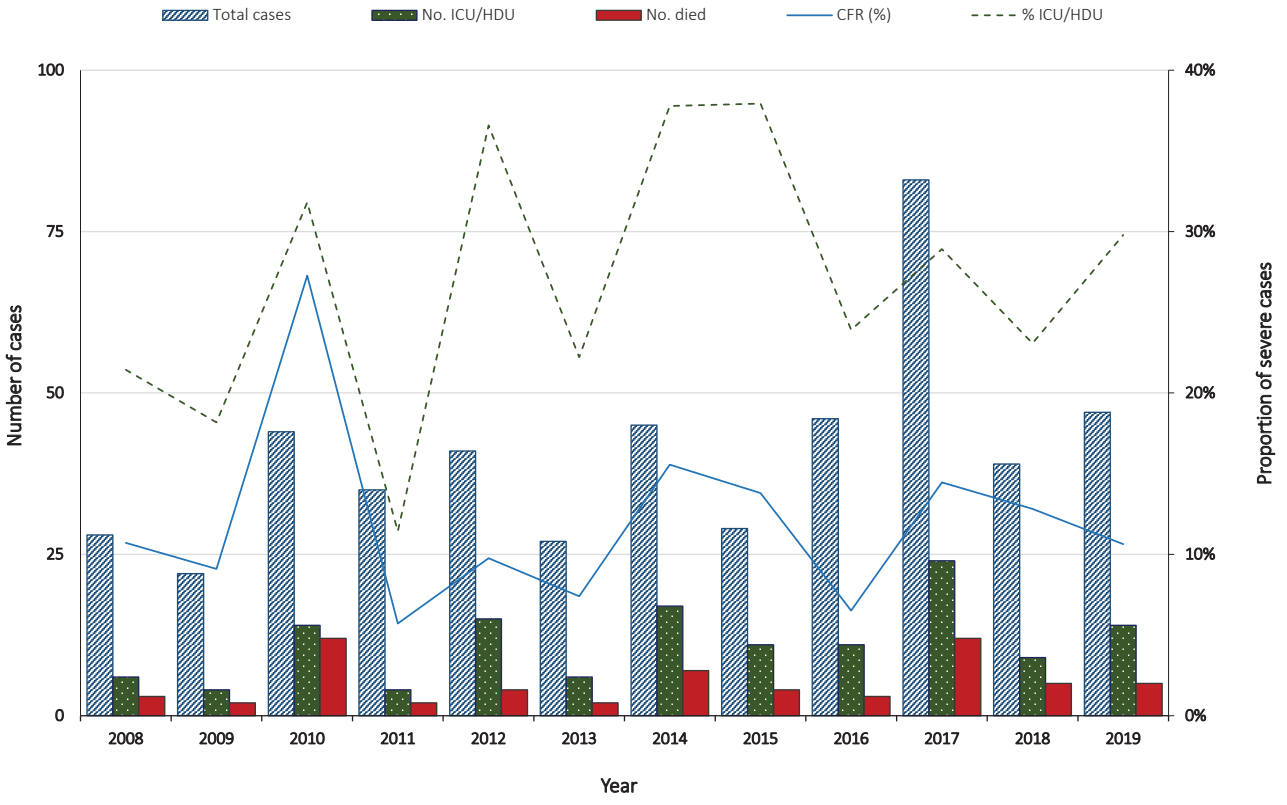
Multivariate analysis for whole-of-study population

Year of infection, sex, age group, and First Nations status were included in the multivariate analysis and all were found to be significant predictors of incidence. Incidence gradually increased with each calendar year (adjusted IRR, aIRR: 1.04; 95% CI: 1.01–1.07). Incidence was higher in males than females (aIRR: 1.48; 95% CI: 1.21–1.82). Age overall was a significant predictor of incidence (p < 0.001). Incidence was significantly higher in the under 10 year age group, and in people aged 30 years and over, than in the 10–19 year age group. Incidence was highest in those aged 80 years and over, who were twenty times more likely to be diagnosed with GAS bacteraemia than 10–19 year olds (aIRR: 21.87; 95% CI: 12.96–36.93). First Nations peoples were more than two-and-a-half times as likely as non-First Nations peoples in HNELHD to be diagnosed with GAS bacteraemia (aIRR: 2.73; 95% CI: 1.98–3.76) (Table 2).

Discussion

The incidence of GAS bacteraemia in HNELHD gradually increased over the study period. Similar increases in iGAS have been seen in other Australian states and high-income countries.[9,17–19] Where genotyping was available, it appeared that increases in other jurisdictions were not driven by a single *emm*-type.[17,19] Further investigation is required to determine the cause of the HNELHD increase, and a follow-up genomic study of iGAS isolates in HNELHD is

Figure 5: Number and proportion of GAS bacteraemia cases who required critical care admission (ICU/HDU) or died in HNELHD, 1 January 2008 to 31 December 2019, by year



currently being conducted to explore potential virulence factors and to identify any genomic clustering.

The overall incidence rate of GAS bacteraemia in HNELHD (4.5 cases per 100,000 population per year) was higher than GAS bacteraemia and meningitis rates seen in Victoria (2.1 cases per 100,000 population per year),[19] lower than GAS bacteraemia rates in the Northern Territory (15.2 cases per 100,000 population per year),[9] and similar to iGAS notification rates in Queensland (4.5 cases per 100,000 population per year) and in other high-income countries.[17,18,37] To ensure a consistent case definition, our study looked at blood culture specimens only; therefore, cases involving iGAS infections of other sterile sites (e.g. joint, deep tissue) without a concurrent bacteraemia were not captured. In a Canadian surveillance study, one-third of iGAS cases did not have bacteraemia, thus the incidence of *all* iGAS in HNELHD is likely to be higher than our estimate.[12]

Our study showed a significant peak in incidence in 2017, particularly over winter. A similar peak in 2017 was seen in Victoria and in a number of paediatric hospitals across Australia,[19,38] and in the 2017/2018 winter in England.[39] While notification data suggested a possible association with influenza in HNELHD, this was unable to be fully explored.[40] This does support the consideration of promoting influenza vaccination to reduce the potential burden of iGAS.[41] However, no obvious increase in GAS bacteraemia occurred in HNELHD in 2009, which was also a significant influenza year. A possible contributor may be the interaction between different GAS emm-types and influenza strains. Both influenza A (predominantly H3N2) and influenza B circulated at very high levels throughout the 2017 influenza season, while H1N1 was the major circulating strain during the 2009 'swine flu' pandemic.[42–44]

The overall proportion of cases admitted to critical care in HNELHD (27.8%) was similar to that reported in a study of GAS bacteraemia

in the Northern Territory.[9] The overall CFR of 12.6% in our study, and the association with age, were similar to findings in other studies in high-income countries.[8–10,12] However, our study may have missed GAS bacteraemia cases who died before reaching hospital care and who did not have ante-mortem specimens available to confirm the diagnosis.[45] Also, our study did not capture non-bloodstream specimens from other sterile sites. Necrotising fasciitis, which carries a high mortality risk, is often diagnosed on deep tissue specimens obtained during surgical debridement while blood cultures may be negative.[11,12]

The risk of GAS bacteraemia in HNELHD was higher in children under 5 years old, and in adults over 70 years old, particularly males, which is consistent with other studies.[9,10,17,19,38] Similar age and sex distribution is also seen in sepsis from all causes in Australia.[46] While there are multiple reasons for increased susceptibility to serious bacterial infections at extremes of age,[47,48] the reasons for the increased risk of GAS bacteraemia in males remain unclear.[17-19]

In HNELHD, First Nations peoples were significantly more likely to be affected by GAS bacteraemia. These findings were consistent with other Australian studies.[9,16] Comparing First Nations peoples with a non-First Nations "reference group" is problematic, as discussed in the methods.[36] However, if policy-makers were to look at whole-of-population results alone, decisions regarding iGAS may prioritise older age groups only. Given the younger age distribution of First Nations populations in Australia generally, and the higher incidence of GAS bacteraemia across all ages within those populations, it is imperative that First Nations peoples of all ages are considered in guidelines and are not disempowered by policies that aim to reduce the impact of iGAS. Given the disproportionate impacts, a within-population focus is required to gain a better understanding of the epidemiology, and to guide the development of holistic models of care and implementation for First Nations peoples in Australia, led by First Nations peoples.

Prompt diagnosis and treatment is critical for improving outcomes from iGAS. Public health guidelines for the prevention, control and management of iGAS need to consider the priority populations identified in this study, and should be co-developed with First Nations peoples to ensure those guidelines serve their needs and priorities. Health services need to be culturally safe to ensure timely and appropriate care, and best outcomes. Culturally appropriate programs and approaches, determined by First Nations peoples, are needed to increase awareness of iGAS amongst community.

Currently, management of close contacts varies widely in Australia. Oliver et al. showed that the proportion of iGAS cases whose household contacts were offered prophylaxis, in selected paediatric hospitals, ranged from 0 to 81%.[38] National guidelines would improve the data needed to inform prophylaxis strategies and ensure consistent practice. Mandatory notification and routine genomic analysis should improve data; enable identification and investigation of outbreaks; and increase understanding of potential risk and virulence factors.

This study did not capture iGAS cases without concurrent bacteraemia nor those detected by private laboratories. Thus the true incidence and severity of iGAS in HNELHD is likely underestimated. The impact of GAS bacteraemia in First Nations peoples in HNELHD was also likely underestimated, as the study relied upon First Nations status completeness within public hospital admissions databases. Generally, inaccurate and incomplete recording of First Nations status is due to staff not asking the question, or asking inappropriately, or if patients do not wish to identify.[29,31] Because GAS bacteraemia is uncommon, small case numbers meant that some differences between groups may not have been detected statistically. Data limitations restricted the exploration of other potential risk factors, such as comorbidities and influenza. Without typing of bacterial isolates, the clustering of cases could not be fully investigated.

Conclusions

GAS bacteraemia is uncommon but severe, and incidence in HNELHD has slowly increased. Risk of iGAS was higher in children under 5 years, adults over 70 years (particularly males), and First Nations peoples. Public health and clinical guidelines must address the physical, social and cultural needs of these priority populations. Routine surveillance and genomic analysis will help improve our understanding of iGAS and inform best public health management.

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Nil conflicts of interest to declare.

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Appendix A: Supplementary materials

Figure A.1: Number of GAS bacteraemia cases in HNELHD, 1 January 2008 to 31 December 2019, by month and year

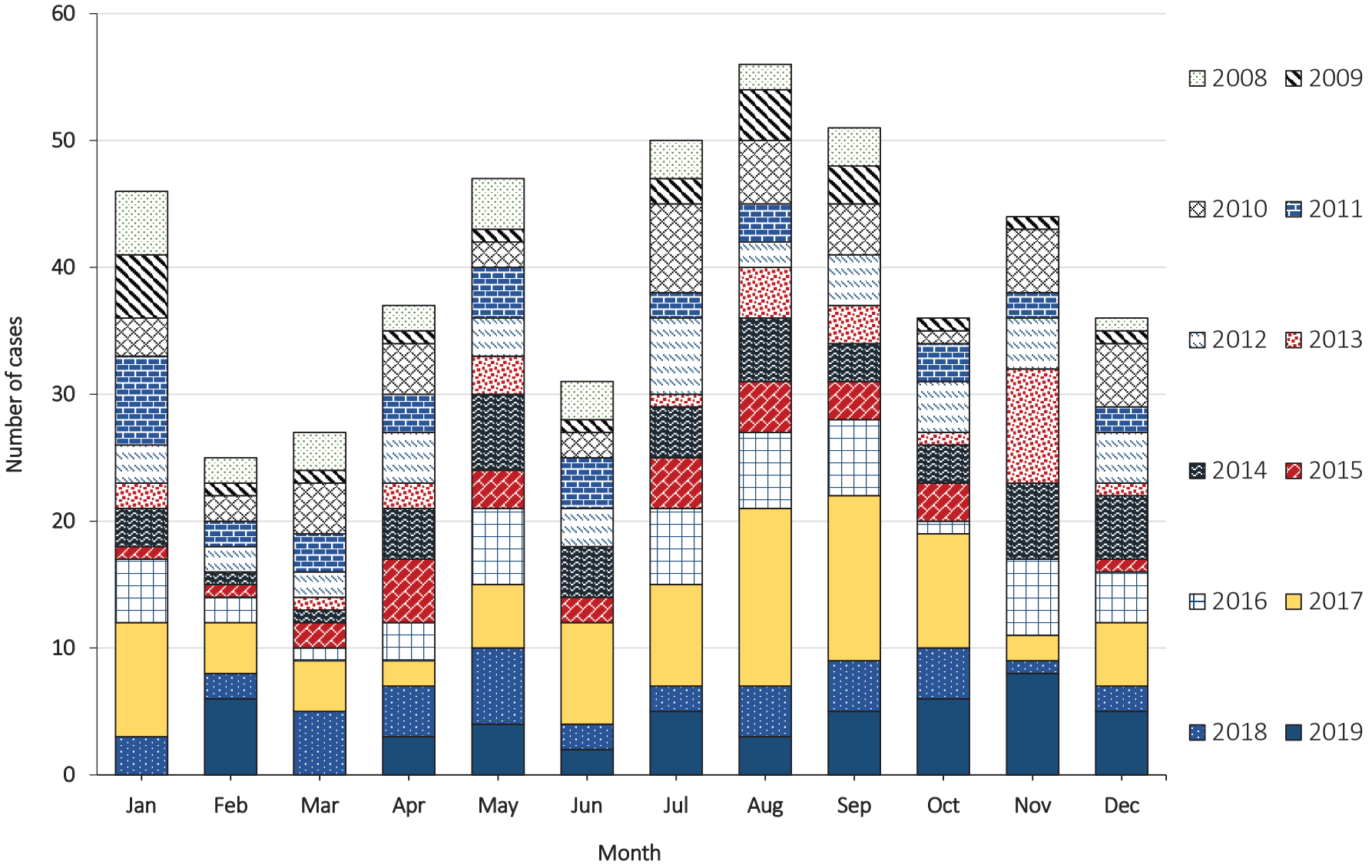

Table A.1: Number of cases, incidence rates and incidence rate ratios of GAS bacteraemia in First Nations peoples in HNELHD, 1 January 2008 to 31 December 2019, by sex and age group

Characteristic	Value or range	Number of cases (%)	Incidence rate (per 100,000 per year)	IRR [95% CI][a]
Total cases		43 (100.0)	7.25	—
Sex	Female	24 (55.8)	8.09	Reference group
	Male	19 (44.2)	6.42	0.79 [0.44–1.44]
Age group (years)[b]	0–19	14 (32.6)	4.98	Reference group
	20–49	19 (44.2)	8.55	1.72 [0.86–3.42]
	50+	10 (23.3)	11.22	2.25 [1.00–5.08]

a IRR: incidence rate ratio; 95% CI: 95% confidence interval. Significant IRR values ($p < 0.05$) are shown in italics.

b Age groups have been aggregated to minimise identification.