Queensland Family and Child Commission | Queensland Paediatric Sepsis Program

Queensland paediatric sepsis mortality study

Incidence of, and factors associated with, sepsis-related child deaths, Queensland 2004–2021

FEBRUARY 2024

Key findings

- Sepsis in children is the biggest single cause of preventable death in childhood in Queensland.
- A total of 748 sepsis-related infant and child deaths occurred in Queensland between 2004 and 2021.
- Rates of sepsis were higher than other causes including transport incidents, suicide and childhood cancer. Encouragingly, rates have declined significantly over time.
- Aboriginal and Torres Strait Islander children, children living in remote and socio-economically disadvantaged areas, and infants, toddlers and pre school-aged children are over-represented.
- A large proportion of sepsis-related deaths occurred among medically complex children, while hospitalised. These children have higher sepsis risk and severity.
- Nearly thirty per cent of sepsis-related deaths occurred in the community, predominately unexpectedly, among infants and younger children without underlying medical conditions known to increase sepsis risk. Most of these deaths were likely preventable with timely sepsis recognition and treatment.
- The methodological complexities involved in reliably identifying the incidence of paediatric sepsis deaths have highlighted inefficiencies in death certification practice, which can be remedied at very low cost, via education and practice change.
- Gaps in our understanding of the large proportion of sepsis and other infection-related deaths occurring in the community present opportunities for improvements in the investigation and systemic oversight of sepsis-related deaths.
- Public awareness, community and the primary care sector should be priority areas for quality improvement and research initiatives.

Queensland Family & Child Commission
Queensland Paediatric Sepsis Program
Reducing the burden of sepsis on Queensland children and families
Children's Health Queensland Hospital and Health Service
Queensland Government

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Overview

Sepsis—a life threatening condition that occurs when the body's response to an infection damages the organs and tissues—is a notable contributor to preventable childhood morbidity and mortality worldwide. According to the most current available estimates, approximately 49 million cases of sepsis and 11 million sepsis-related deaths occurred worldwide in 2017.[1] Over 40 per cent (20.3 million) of all sepsis cases, and nearly 27 per cent (2.9 million) of deaths were among children under five years of age.[2]

Internationally, sepsis is reported to be among the top ten leading causes of death in children and adolescents.[3] Where children survive, the long-term morbidity is substantial. One-third of paediatric sepsis survivors will experience long-term morbidity and/or disability, resulting in life-long impacts for affected children, their families, and communities.[4]

Sepsis places a substantial burden on the health system and society. The direct hospital cost of sepsis (both children and adults) to the Australian healthcare system is estimated to be close to $700 million per annum. The indirect costs due to sepsis-related deaths far exceed the immediate, direct costs, approaching $5 billion annually (for both adult and paediatric patients).[5]

Recognition of the enormity of the sepsis burden in both children and adults resulted in the World Health Organization declaring it a global health threat, and recommending the prioritisation of efforts to quantify, document, prevent and treat sepsis.[6] Reducing death and disability from sepsis has also been recognised as both a national[7] and a Queensland[8] health priority. The Australian Commission on Safety and Quality in Health Care (ACSQHC) developed a Sepsis National Standard, released in June 2022.*

Understanding sepsis and its magnitude is challenging. Our current knowledge of paediatric sepsis mortality remains limited, hampered by inconsistent definitions and poor administrative data quality.[9,10] There is also a paucity of population-based studies of sepsis mortality in children,[11] with no such studies in Australia to date. ACSQHC performed an epidemiological study of adult and paediatric sepsis incidence and mortality in Australian public hospitals from 2013–2018. They found the incidence of sepsis was highest in infants (under 1 year), higher in Aboriginal and Torres Strait Islander populations and in populations in more remote regions or with socio-economic disadvantage. They reported difficulties in identifying sepsis cases due to challenges in clinical coding with under-recording being likely. They noted that mortality from sepsis in the Australian population seemed stable.

Accurate surveillance of child deaths from sepsis has important implications for the development of paediatric sepsis recognition, treatment, and management initiatives. Improved surveillance has been identified as a research priority by the Surviving Sepsis Campaign.[12] Reliably tracking trends in paediatric sepsis mortality is essential to evaluate the impact of quality improvement initiatives.

In 2022, the Queensland Family and Child Commission (QFCC) partnered with the Queensland Paediatric Sepsis Program (QPSP) at Children's Health Queensland, with the objective of determining the true incidence of paediatric sepsis deaths in Queensland. This is the first population-based study of paediatric sepsis mortality in Queensland and Australia to date. This information paper reports the findings of the Queensland Paediatric Sepsis Mortality Study. It uses information from the Queensland Child Death Register, linked with perinatal, hospital admission and emergency presentation data, to identify the incidence of, and consider trends and patterns in, sepsis-related child deaths in Queensland.

Background

What is sepsis?

Clinically, sepsis is defined as a dysregulated immune response to an infection resulting in new organ dysfunction.[13,14] Explained in lay terms, sepsis is the body's overwhelming and life-threatening response to an infection.

A person's immune system works to fight infection. For reasons that are not well understood, sometimes the immune system's response is abnormal, causing extensive inflammation throughout the body, resulting in organ dysfunction. Without urgent treatment, sepsis can lead to tissue damage, organ failure, septic shock and death.

* The National Clinical Care Standards, developed by the Australian Commission for Safety and Quality in Health Care, are nationally agreed statements describing the key elements of care health professionals and health services should offer to patients for a specific condition. They apply to health conditions that benefit from a national, coordinated approach. The Sepsis Clinical Care Standard was developed to address the need for guidance related to the entire patient journey, from symptom onset to discharge and survivorship care.

Children with sepsis can deteriorate rapidly.[15] Early detection and treatment are essential for survival and limiting long term morbidity and disability.[16,17] Unfortunately, in its early stages, while potentially reversible, sepsis is difficult to recognise and therefore is frequently under-diagnosed, particularly in paediatric patients. This is in part because sepsis often presents with non-specific symptoms such as fast heart or respiratory rates (particularly in younger age groups), which also occur in children with less serious illness.[18] The early recognition, diagnosis and management of sepsis is acknowledged to be one of the most significant challenges in paediatric critical care medicine.[19,20]

Which children are most at risk?

Any child can develop sepsis and it can be caused by most types of infectious agents (bacterial, viral, fungal, parasitical) at any time. There are reasons why a child may have an increased risk of developing sepsis from an infection, that include 'host factors' such as genetic make-up, immune function or age for example, or pathogen-related factors such as virulence.

Age is an important risk factor for sepsis, with newborns and infants particularly susceptible because their immune systems are immature. Full immunologic maturity is reached in adolescence.[21] Children with comorbid chronic and complex medical conditions, children with medical devices in their body (such as central venous access devices), and those with a weakened or impaired immune system, including children receiving chemotherapy, are at increased risk for developing sepsis. These conditions also increase the risk of healthcare associated sepsis,[†] due to these children's frequent interactions with the healthcare system.[22] Children who are unimmunised or who have not yet completed the full immunisation schedule are also at increased sepsis risk.

What do parents know about sepsis?

The George Institute for Global Health performed national polls of Australians' understanding of sepsis in 2016 and 2020. Fifty-nine per cent of Australians had heard of sepsis as a medical condition in 2020, however this was lower in Australians of parenting age (45 per cent) than in the older age groups.[23] This study, and a recent Child Health Poll in Victoria,[24] showed that Queenslanders were more likely to have heard of sepsis. The Queensland Paediatric Sepsis Program was acknowledged to have an active, consumer-based approach to paediatric sepsis awareness that may have contributed to this improvement.

Study scope

This is a census study of paediatric sepsis deaths in Queensland. It aimed to identify every sepsis-related child death that occurred between 2004 and 2021, both in-hospital and at home or in the community, by using linked datasets.

Sepsis criteria

The sepsis deaths reported in this study include infection-related deaths in which sepsis was identified through:

- cause of death information contained in the Queensland Child Death Register,
- linked hospital admission data for in-patient child deaths, and
- coronial records (including autopsy reports and coronial findings).

Sepsis was identified using coded cause of death data and hospital diagnosis data. These included explicit sepsis codes and implicit sepsis codes (a combination of an infection code and an organ failure code). Autopsy and coronial findings were also used. A complete description of the study's methods is provided in Appendix 1.

Study cohort

The focus of this study is paediatric sepsis. Sepsis in newborn babies with very low birth weight or gestation, which occurs while in hospital following birth, is thought to be a distinct disease from sepsis in a term newborn, young infant, child, or adolescent.[25] For clarity, the following terms have been used to distinguish these two groups:

Paediatric sepsis—deaths of infants and children (0–17 years) who have been discharged from hospital following birth; paediatric sepsis may develop in the community or be acquired during a subsequent hospital admission.

Neonatal sepsis—deaths of newborn infants that occur in hospital following birth; neonatal sepsis is acquired from the mother before or during delivery or contracted during an extended hospital stay.

[†] Healthcare associated infections, also referred to as nosocomial infections, are infections acquired during the process of receiving healthcare that were not present at the time of admission.

In this report, cases of neonatal sepsis have been included only in the discussion of the total burden of sepsis mortality and trends over time. The more detailed findings and analyses focus on paediatric sepsis.

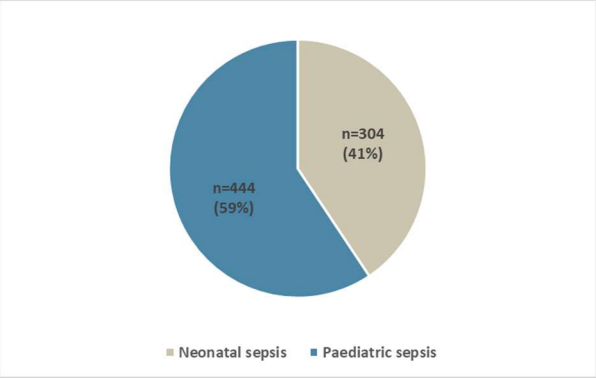
Results

Deaths due to sepsis, 2004–2021

Our analysis shows that between 1 January 2004 and 31 December 2021, there were 8002 child deaths from all causes in Queensland, with 5787 (72.3 per cent) due to natural causes (diseases and morbid conditions). Of these, 748 (12.9 per cent) were sepsis-related deaths of infants and children aged 0–17 years, a rate of 3.8 deaths per 100,000 children. Mortality rates from sepsis were similar to transport incidents (3.0 per 100,000) and substantially higher than other more widely reported causes of death in childhood, such as drowning (1.3 per 100,000), youth suicide (2.0 per 100,000), and childhood cancers (2.5 per 100,000)[‡].

Paediatric sepsis deaths accounted for 59 per cent of the total burden of sepsis mortality in Queensland children (see Figure 1), with 444 deaths, a rate of 2.3 per 100,000.

Figure 1: Paediatric and neonatal sepsis as a proportion of total burden of childhood sepsis deaths, 2004–2021



Trends over time

Between 2004 and 2021, rates for all sepsis-related child deaths in Queensland (including neonatal sepsis) declined significantly (see Figure 2). These decreases retained significance with the exclusion of the years 2020 and 2021. World- and nation-wide, deaths from infectious diseases reduced in the first two years of the COVID-19 pandemic.[26] This was likely due to public health measures (such as wearing masks, frequent handwashing, and physical distancing) aimed at reducing infection and transmission.

Between the two nine-year periods 2004–2012 and 2013–2021, sepsis mortality rates for all children decreased 16.7 per cent, from 4.2 to 3.5 deaths per 100,000 children aged 0–17 years. When cases of neonatal sepsis were excluded, greater reductions were observed in paediatric sepsis mortality rates, with rates decreasing 23.1 per cent, from 2.6 to 2.0 per 100,000 between the two periods.

These are encouraging trends. The Australian Commission for Safety and Quality in Health Care[27] reported an unchanged sepsis mortality in Australian public hospitals between 2013–14 and 2017–18, despite an increase in hospitalised sepsis incidence. In Queensland, an approximate 12.0 per cent decrease was observed in childhood sepsis mortality (including neonatal sepsis) during the same period.

The decreases in paediatric sepsis in Queensland may be in part explained by the introduction of the Paediatric Sepsis Pathway in 2019–20,[8] following which paediatric sepsis deaths decreased by over a third (compared to the prior three years). This evidence-based, co-designed clinical decision-making support tool has been implemented in 16 tertiary and secondary emergency departments and over 80 rural and remote sites across Queensland. It provides guidance to support early sepsis recognition and treatment as well as empiric[§] antibiotic choice, dose, and administration. Longitudinal data will be needed to disentangle the impact of the Paediatric Sepsis Pathway from the potentially confounding effect of the non-pharmaceutical COVID-19 interventions during 2020–2021, which saw reductions in the prevalence of common respiratory virus and certain bacterial infections,[26] as well as lower than expected all-cause mortality at both national and state levels.[28]

Reductions in rates of paediatric sepsis mortality have not been shared equally by all population groups. Rather, overall decreases have been predominantly driven by declines in non-Indigenous sepsis death rates, rates among infants, and rates among children living in areas with high accessibility to goods and services.

[‡] Queensland Child Death Register, 2004–2021.
[§] Empiric antimicrobial therapy refers to the use of broad-spectrum antimicrobials directed against an *anticipated* and *likely* cause of disease. This term is used when antimicrobials are given to a person before the specific organism causing an infection is known.

Figure 2: Total sepsis and paediatric sepsis (excluding neonatal sepsis) mortality rates, 2004–2021

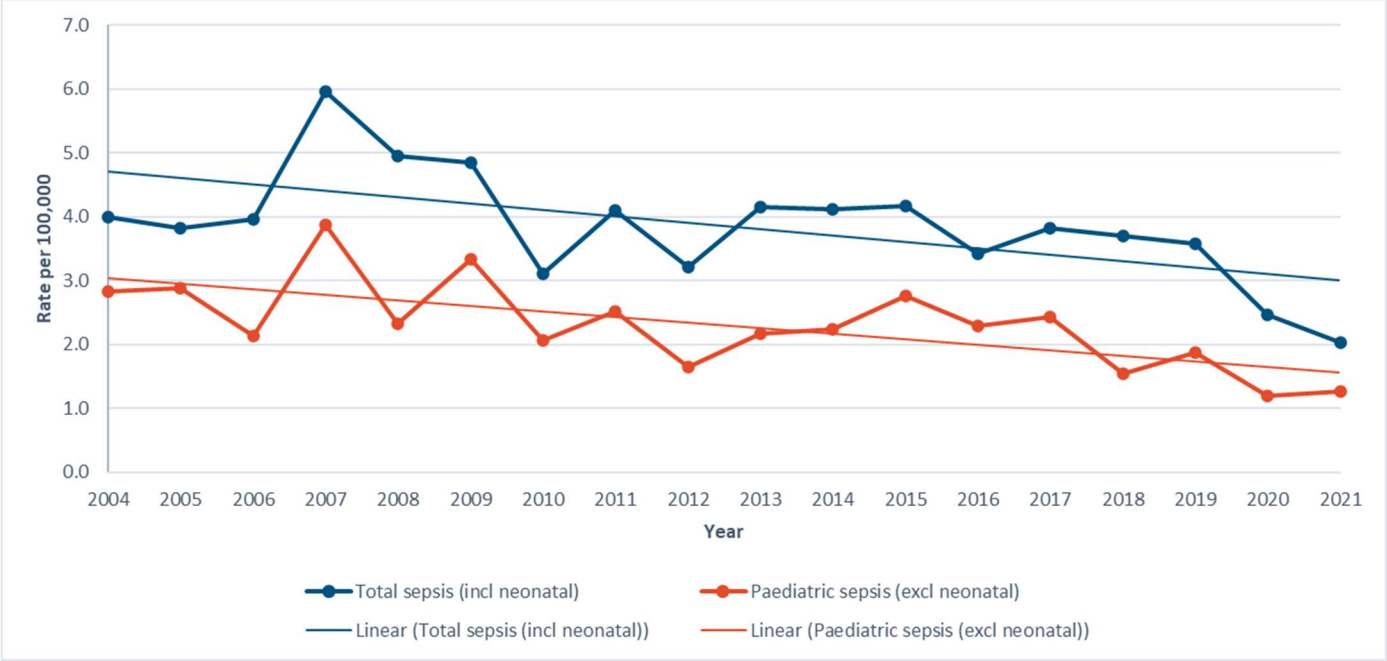


Figure 3: Indigenous and non-Indigenous paediatric sepsis (excluding neonatal) mortality rates, 2004–2021

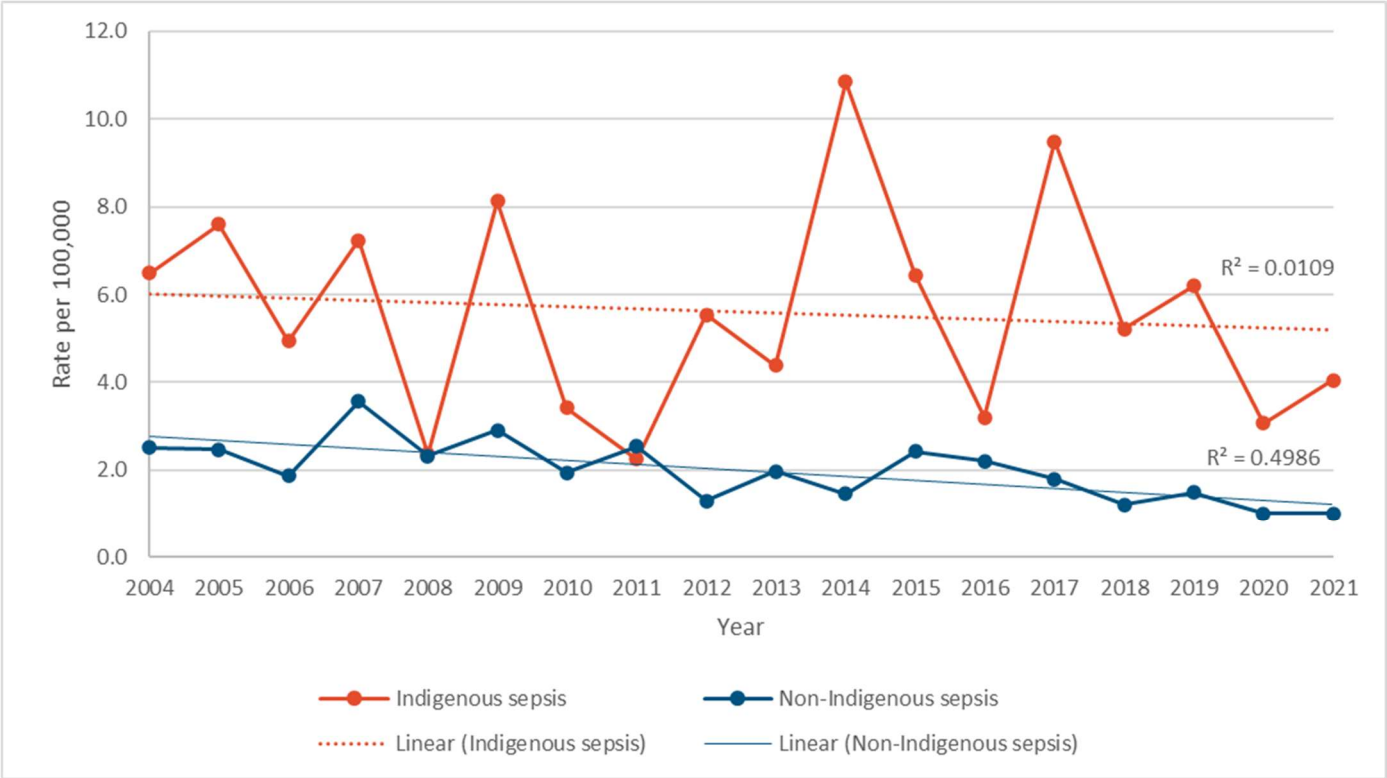
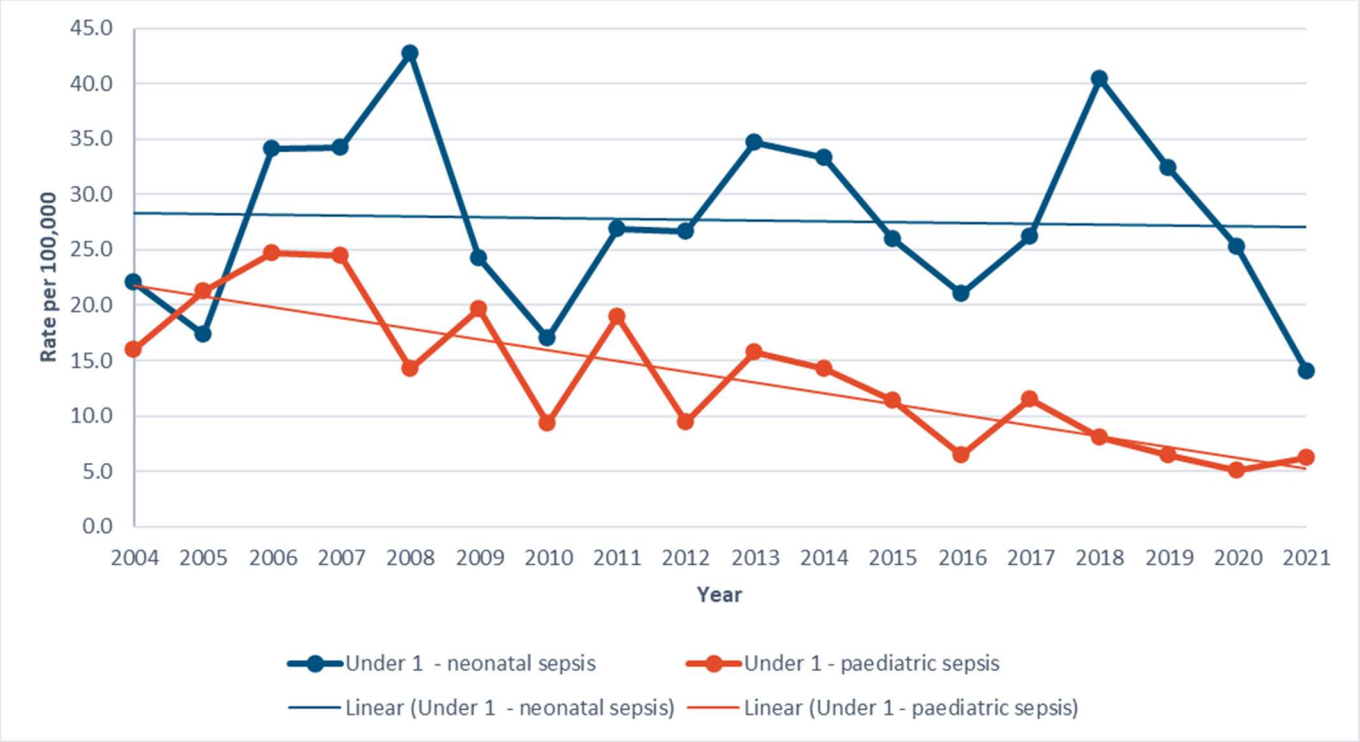


Figure 4: Neonatal sepsis and community acquired sepsis in infants aged under 1 year, 2004–2021



*rate per 100,000 live births

Figure 5: Sepsis in toddlers and pre school-aged, primary and high school children, 2004–2021

Since 2004, there has been a significant reduction in non-Indigenous paediatric sepsis mortality, with rates decreasing by 33.0 per cent between 2004–2012 and 2013–2021. There has been no comparable reduction in mortality for Queensland's Aboriginal and Torres Strait Islander children. Rather Aboriginal and Torres Strait Islander sepsis death rates have fluctuated substantially (due to small population sizes), with no discernible rate decrease evident (see Figure 3). This increased the disparity for Aboriginal and Torres Strait Islander children by over 63 per cent, with the rate ratio widening from 2.2 to 3.6 times that of non-Indigenous children.

While there has been little change in neonatal sepsis rates over time, significant reductions have occurred in paediatric sepsis among infants under 1 year of age, as shown in Figure 4. Paediatric sepsis deaths in infants declined by approximately 45 per cent between 2004–2012 and 2013–2021, from 17.3 deaths per 100,000 live births to 9.5 per 100,000. Decreases were also seen in primary school (aged 5–11 years) and high school children (aged 12–17 years) however these were not significant (see Figure 5).

Between the two periods, declines of around 30 per cent were also observed among children living in major cities and inner regional areas. Children living in these areas have relatively unrestricted or only some restrictions in accessibility to a wide range of goods and services, including specialist tertiary healthcare. While decreases were also observed in outer regional and remote and very remote areas, these were smaller and did not reach statistical significance.

Demographics

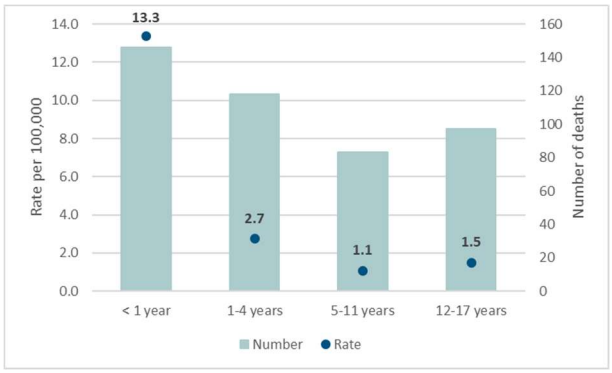
Sex

Rates of sepsis-related deaths for male children were 13.3 per cent higher than rates for female children, with a rate of 2.4 per 100,000 males aged 0–17, compared with 2.1 per 100,000 female children. Male children were over-represented in all age categories although the largest disparities were in infants (under 1 year) and primary school aged children (5–11 years). Previous research has identified gender disparities in the incidence of sepsis, with males more likely to develop sepsis than females.[27,29]

Age

The incidence of sepsis and sepsis mortality is known to be significantly higher in the younger age groups (particularly among infants less than 1 year of age).[30] Figure 6 compares the rate of paediatric sepsis deaths by age group. It shows that infants (under 1 year) and toddlers and young children (aged 1–4 years) are at greatest risk of death from sepsis. Infants died from sepsis at over 12 times the rate of primary school aged children (5–11 years), who had the lowest rate of sepsis. Toddlers and young children were also significantly more likely to die from sepsis than primary school children (rate ratio 2.5).

Figure 6: Number and rate of sepsis deaths by age group, 2004–2021



Notes: rates for <1 year calculated per 100,000 live births.

Babies born pre-term have an increased risk of sepsis that persists beyond the neonatal period because their immune systems are immature. Linked perinatal data was available for 123 of the 146 infant deaths in the paediatric sepsis group (84.2 per cent). Birth before 37 weeks gestation was significantly associated with later paediatric sepsis mortality, with infants born before 37 weeks gestation dying at nearly four times the rate of infants born at term (34.7 per 100,000 pre-term births compared to 9.0 per 100,000 term births).

Remoteness and accessibility

In Queensland, the all-cause child mortality rate is consistently higher in remote and very remote and outer regional areas.[31] Sepsis incidence in Australia is also reported to be highest in remote areas.[27] Consistent with these findings, rates of paediatric sepsis mortality were significantly higher in remote and very remote areas, with 6.1 deaths per 100,000 children living in remote and very remote areas compared to 1.8 per 100,000 in major cities (see Figure 7). Interestingly, rates were lowest in outer regional areas, with rates in these areas significantly lower than rates in major cities. While these findings are consistent with findings regarding sepsis incidence in Australian public hospitals,[27] they are less consistent with general patterns in all-cause childhood mortality, in which rates of death increasing with remoteness are observed.[31]

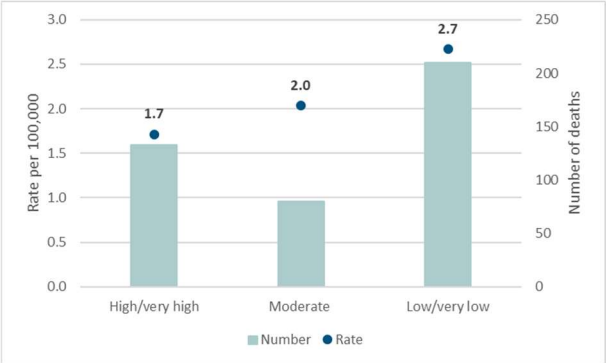
Figure 7: Number and rate of sepsis deaths by remoteness, 2004–2021

Notes: excludes the deaths of 21 children whose usual place of residence was outside Queensland or could not be coded.

Socio-economic disadvantage

Living in an area with socio-economic disadvantage was associated with higher paediatric sepsis mortality rates. Rates of death from sepsis were 1.6 times higher for those living in the lowest socio-economic areas compared with the highest socio-economic areas (see Figure 8). These findings align with national findings regarding sepsis incidence, where sepsis incidence was reported at 1.2 times higher in low and very low socio-economic areas, compared to high and very high areas.

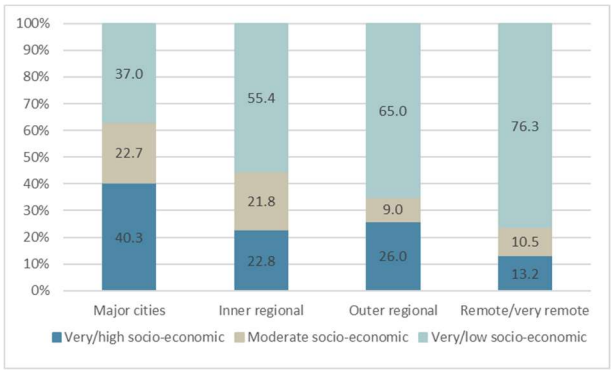
Figure 8: Number and rate of sepsis deaths by socio-economic area, 2004–2021



Notes: excludes the deaths of 21 children whose usual place of residence was outside Queensland or could not be coded.

Census data demonstrate that there is a relatively higher concentration of disadvantage in regional and remote communities.[32] Poor sepsis outcomes for children experiencing socio-economic disadvantage are likely to be compounded by a lack of access to services where these children also reside in regional or remote areas. In the study period, there were significant differences in socio-economic status in rural and remote areas, with 65.0 per cent of children living in outer regional areas and 76.3 per cent of children living in remote and very remote areas also residing in areas of socio-economic disadvantage, as shown in Figure 9.

Figure 9: Sepsis deaths by geographic remoteness and socio-economic disadvantage, 2004–2021



Notes: excludes the deaths of 21 children whose usual place of residence was outside Queensland or could not be coded.

Aboriginal and Torres Strait Islander children

In Australia, as in other high resource countries such as Canada, the United States, and New Zealand, Indigenous status is a risk factor for death during childhood due to a complex interplay of multiple factors. These include remoteness, access to culturally safe healthcare, and socio-economic and educational resources.[33] The historical and continued marginalisation of First Nations peoples, knowledge systems and culture, forced child removals, and intergenerational trauma contribute to higher rates of social risk factors for current generations including those relevant to ill-health, injury, and death.

In Queensland, Aboriginal and Torres Strait Islander children are consistently and significantly over-represented in child mortality statistics, with rates of death approximately twice that of non-Indigenous children.[34] Aboriginal and Torres Strait Islander children have a higher risk of invasive infections, including bloodstream infections and pneumonia, with reported rates comparable with those in low- and middle-income countries.[33]

Between 2004 and 2021, Aboriginal and Torres Strait Islander children accounted for 20 per cent of sepsis-related deaths (90 deaths). Aboriginal and Torres Strait Islander children were significantly over-represented in deaths due to sepsis, dying at nearly three times the rate of non-Indigenous children, with 5.6 deaths per 100,000 First Nations children, compared to 2.0 per 100,000 non-Indigenous children.

Table 1: Number and per cent or median and univariable odds ratios of socio-demographic and clinical factors by Indigenous status, 2004–2021

Variable	Indigenous n (%) Median[a] (IQR)	Non-Indigenous n (%) Median[a] (IQR)	Univariable OR 95% CI	Total Sepsis n (%) Mediana (IQR)
Indigenous status	90 (20.3)	354 (79.7)		444 (100.0)
Age in years	1.4[a] (0.4, 5.5)	3.6[a] (0.7, 11.5)	*p* = 0.0016*	2.9 (0.7, 10.4)
Age category				
Under 1 year	38 (42.2)	108 (30.5)	2.27 (1.14, 4.54)	146 (32.9)
1–4 years	27 (30.0)	91 (25.7)	1.92 (0.93, 3.96)	118 (26.6)
5–11 years	12 (13.3)	71 (20.1)	1.09 (0.47, 2.55)	83 (18.7)
12–14 years	13 (14.4)	84 (23.7)	Reference	97 (21.7)
Remoteness and accessibility (missing =21)				
Major cities	22 (25.3)	194 (57.7)	Reference	216 (51.1)
Inner regional	17 (19.5)	75 (22.3)	2.00 (1.01, 4.00)	92 (21.8)
Outer regional	24 (27.6)	53 (15.8)	4.00 (2.08, 7.68)	77 (18.2)
Remote/very remote	24 (27.6)	14 (4.2)	15.12 (6.84, 33.41)	38 (9.0)
Socio-economic status (missing = 21)				
High/very high socio-economic area	12 (13.8)	121 (36.0)	Reference	133 (31.4)
Moderate socio-economic area	10 (11.5)	70 (20.8)	1.44 (0.59, 3.50)	80 (18.9)
Low/very low socio-economic area	65 (74.7)	145 (43.2)	4.52 (2.33, 8.76)	210 (49.6)
Medical complexity				
Complex chronic condition	29 (32.2)	199 (56.2)	Reference	228 (51.4)
Non-complex chronic condition	4 (4.4)	18 (5.1)	1.53 (0.48, 4.82)	22 (5.0)
No chronic disease	57 (63.3)	137 (38.7)	2.82 (1.74, 4.65)	194 (43.7)
Death location				
Home/community	39 (43.3)	92 (26.0)	2.18 (1.35, 3.52)	131 (29.5)
Hospital	51 (56.7)	262 (74.0)	Reference	313 (70.5)
Sudden and unexpected death				
Reportable	48 (53.3)	105 (29.7)	2.71 (1.69, 4.35)	153 (34.5)
Non-reportable	42 (46.7)	249 (70.3)	Reference	291 (65.5)

Significant at the 5% level

*Wilcoxson test

Several socio-demographic, environmental and clinical factors were found in univariable analysis to have a higher prevalence among Aboriginal and Torres Strait Islander children who died from sepsis compared with non-Indigenous children (Table 1).

Aboriginal and Torres Strait Islander children were significantly younger than non-Indigenous children, with a median age of 1.4 years compared with 3.6 years for non-Indigenous children. Aboriginal and Torres Strait Islander children were significantly more likely to be aged under 1 year than non-Indigenous children. They were also more likely to be aged 1–4 years, however, these differences did not reach the threshold for statistical significance, likely due to small numbers.

Aboriginal and Torres Strait Islander children were significantly more likely to live in regional, remote, and socio-economically disadvantaged areas of Queensland. Compared to non-Indigenous children, Aboriginal and Torres Strait Islander children were 2.0 times more likely to live in inner regional areas, 4.0 times more likely to live in outer regional areas and 15.1 times more likely to live in remote and very remote areas. They were also 4.5 times more likely to live in socio-economically disadvantaged areas.

Importantly, Aboriginal and Torres Strait Islander children were significantly less likely to have an underlying complex chronic medical condition that would increase the risk of both the initial infection and developing sepsis. However, the deaths of Aboriginal and Torres Strait Islander children were significantly more likely to occur at home[**] than in hospital and were more likely to occur unexpectedly (and therefore be reportable to a coroner).

Together, these factors indicate that, overall, sepsis-related deaths in Aboriginal and Torres Strait children are more likely to occur unexpectedly in previously healthy young children and may be preventable through early recognition and appropriate treatment. The presence of racial disparities in the management of sepsis is well established in the research literature.[35–37] A considerable body of research (mostly from the United States where racial disparities in sepsis have been most extensively studied) demonstrates that the factors contributing to racial differences in sepsis incidence and mortality largely map to indicators of colonial practices.[35,38] These include residential segregation (here reflected in Aboriginal and Torres Strait Islander children being more than 15 times more likely than non-Indigenous children to live remotely), economic marginalisation, social stress, and limited access to and/or denial of care.[35,38] Help-seeking and healthcare access and utilisation by Queensland children who die from sepsis has not been studied in detail here or elsewhere; it is a neglected area of research. However, residence in a medically under-served area,[††] as was the case for over half the Aboriginal and Torres Strait Islander children in this study, has been found to be associated with significantly higher sepsis mortality rates compared with appropriately served areas.[39] Racial differences in the provision of healthcare have also been observed in emergency department settings, with black patients (in the United States) receiving lower acuity ratings and experiencing significantly longer wait times post triage than white patients. Such findings support the hypothesis that race may affect the triage and treatment process in children presenting with symptoms of sepsis.[40] There is a need to explore the patient, community, and hospital-based factors contributing to the overrepresentation of Aboriginal and Torres Strait Islander children in sepsis mortality.

Clinical factors

A fundamental first step in devising and improving sepsis prevention strategies is to identify the characteristics of individuals at increased risk of developing and dying from sepsis. Data on the underlying health conditions, types of infections, and pathogens most associated with sepsis-related child deaths may be used to guide development of programs to inform clinicians, patients, and families about prevention and management of infections that can lead to sepsis, particularly in at-risk cohorts of children.

Medical complexity

Children with special healthcare needs due to complex and chronic pre-existing medical conditions are known to be at increased risk of developing sepsis and sepsis mortality.[15,29,41] Over half of the children who died from sepsis had complex chronic disease (228 children, 51.4 per cent) that increased the risk of both infection and progression to invasive disease. Importantly however, nearly 44 per cent of children were previously healthy, without pre-existing complex chronic disease that would have increased their healthcare need or sepsis risk. A very small number of children had a single, chronic condition that may have marginally increased sepsis risk (5.0 per cent).

[**] Deaths categorised as occurring at home or in the community include cases in which a child arrived at hospital moribund or under resuscitation.
[††] This is a defining feature of being categorised as residing in an ‘outer regional’ or ‘remote’ location.

Despite being over-represented in sepsis mortality, Aboriginal and Torres Strait Islander children were nearly 3 times less likely to have pre-existing complex chronic medical conditions known to increase sepsis risk [OR = 2.82 (1.74, 4.65)]. Just under a third of Aboriginal and Torres Strait Islander children (32.2 per cent) exhibited medical complexity, compared with 56.2 per cent of non-Indigenous children. This finding highlights a pressing need to explore the clinical, environmental, and socio-demographic reasons for Aboriginal and Torres Strait Islander children's over-representation in paediatric sepsis mortality.

Similarly, despite having the highest incidence of sepsis mortality, infants (under 1 year) and toddlers and young children (1–4 years) were also significantly less likely to be medically complex than school-aged children (5–17 years). Only 28.8 per cent of infants and 44.8 per cent of toddlers and young children had a complex chronic underlying condition, while approximately 73 per cent of both primary and secondary school-aged children were medically complex. Early sepsis recognition in young children can be particularly challenging, with infants and toddlers often presenting with non-specific symptoms and signs that mirror those seen in common illnesses.[18]

Children with complex chronic conditions face unique challenges that make their medical care highly complex. These children were significantly more likely to be hospitalised at the time of death (87.7 per cent of children with medical complexity were hospitalised at the time of death, compared to 52.1 per cent of children with no chronic underlying disease). Consequently, the deaths of children with medical complexity were significantly more likely to have been anticipated (and therefore non-reportable)[‡‡] than those without underlying complex comorbidities (86.0 per cent and 41.8 per cent respectively).

Types of complex chronic conditions

Table 2 shows the types of underlying complex chronic condition present in children with complex chronic comorbidities.

Table 2: Type of underlying complex chronic conditions in paediatric sepsis deaths, 2004–2021

Complex chronic condition (CCC)	Number	Per cent*
Cardiovascular	37	16.2
Gastrointestinal	15	6.6
Haematological & immunological	19	8.3
Malignancy	56	24.6
Metabolic	24	10.5
Neurological & neuromuscular	100	43.9
Renal and urological	9	3.9
Respiratory	31	13.6
Congenital and genetic	113	49.6
Transplantation	29	12.7
Total CCC	429	n/a
Total children with CCC	**228**	**100**

**Proportion of distinct children with complex chronic conditions. Notes: total exceeds number of sepsis cases due to some cases having more than one type of condition identified. Percentages may not add to 100 due to rounding. CCC = Complex chronic (medical) conditions.*

A substantial proportion of children had conditions that spanned more than one complex chronic condition category (63.4 per cent), with 15.0 per cent having conditions that spanned three or more categories. Children with more than one complex chronic condition category have significant, multisystem comorbidities that result in a higher risk of hospitalisation and death.[42]

The most common types of conditions were congenital and genetic, neurological and neuromuscular, malignancy, and cardiovascular. Congenital and genetic conditions refer to diseases present from birth (congenital) or caused by an altered gene or set of genes (genetic). Many of the conditions in other complexity categories have a congenital or genetic basis. As such, 92.0 per cent of children with congenital and genetic conditions—the most common type of complex chronic condition—had conditions which were classified in at least one other category.

[‡‡]Deaths that are reportable to a coroner are discussed in more detail under the section 'Unexpected deaths' on page 12.

Complex chronic condition categories

Cardiovascular: includes heart and great vessel malformations, cardiomyopathies, conduction disorders and dysrhythmias.

Gastrointestinal: includes chronic diseases and certain congenital abnormalities of the stomach, intestines, liver gallbladder and pancreas.

Haematological and immunological: disorders of the separate but interrelated body systems that provide all blood cell lineages including those involved in the provision of immunity to fight infection, such as blood cells, platelets, bone marrow, lymph nodes and spleen.

Malignancy: neoplasms (cancerous tumours).

Metabolic: disorders negatively altering the body's processing and distribution of macronutrients, such as proteins, fats, and carbohydrates.

Neurological and neuromuscular: disorders affecting the brain, spinal cord and nerves, including intellectual disabilities, neural tube defects, central nervous system degeneration and disease, cerebral palsy, epilepsy syndromes and muscular dystrophies and myopathies.

Renal and urological: includes chronic kidney failure, chronic bladder diseases, and certain congenital malformations involving the urinary system.

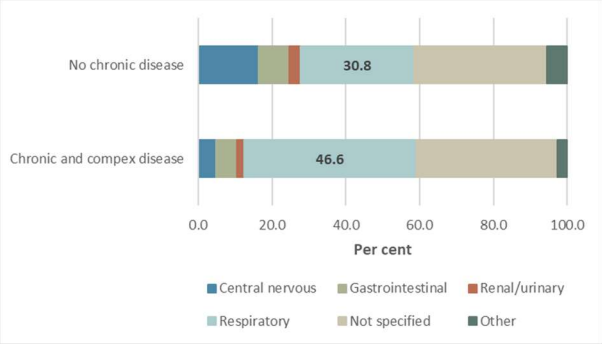
Respiratory: includes malformations of the respiratory system, cystic fibrosis, and chronic respiratory diseases.

Other congenital and genetic: includes chromosomal abnormalities such as Down syndrome and other trisomies, Edwards syndrome, Patau syndrome, Turner syndrome as well as certain other congenital abnormalities.

Transplantation: organ and tissue transplantation including bone, kidney, and liver transplants.

Children with neurological and neuromuscular conditions such as severe cerebral palsy, spina bifida, and muscular dystrophy typically are vulnerable to respiratory complications, including aspiration and pneumonia and reduced respiratory function with scoliosis development. This is because these conditions cause difficulties with movement, muscle tone and posture, eating, swallowing, and airway clearance, all of which compromise respiratory health. Respiratory illnesses are a common cause of death in this cohort of children. For example, studies of cerebral palsy mortality have found that death is frequently attributed to respiratory problems.[43,44] Consistent with these findings, respiratory illnesses were the source of infection in 63.0 per cent of sepsis-related deaths in children with complex chronic neurologic and neuromuscular conditions in Queensland. Indeed, as demonstrated in Figure 10, all medically complex children were significantly more likely to succumb to a respiratory infection than those without underlying chronic conditions.

Figure 10: Sepsis source by medical complexity, 2004–2021



Recent research indicates that inhaled antibiotic therapy may offer a promising approach to the prevention of respiratory infections in patients with severe neurological and neuromuscular conditions, who have chronic microbial airway colonisation and recurrent respiratory tract infections.[45] Nevertheless, the high proportion of respiratory infections as the final causal pathway in sepsis-related deaths of medically complex children underscores the importance of opening discussions with families about care and treatment options, particularly for children with severe neurological and neuromuscular conditions, life limiting diagnoses,[§§] and/or prognostic uncertainty. Prior research has demonstrated that in this group of children there is often little discussion about whether and in what circumstances it is appropriate for invasive interventions aimed at prolonging life.[46,47] Optimal care for children with life-limiting conditions encompasses parallel planning to achieve the health goals of the family, involving paediatric palliative care services and the wider multidisciplinary team.[48]

Source of infection

Sepsis can occur from specific and consistent sources; but it is also recognised that these infectious sources can be difficult to define when children present with shock or toxic shock without a pre-existing site of infection. A possible source of the underlying infection leading to sepsis was identified in 279 of the 444 sepsis-related deaths (62.8 per cent). Lower respiratory

[§§] Life-limiting conditions are those for which there is no reasonable hope of cure and from which a child may die.

infections were the most common source, with upper and lower respiratory infections together the source of sepsis in nearly 40 per cent of cases (Table 2). This is consistent with the findings of a previous all-age sepsis study as well as an international study of sepsis in paediatric intensive care. These show respiratory infections to be the most common source of sepsis and septic shock, accounting for around half of all cases of sepsis.[4,22]

The primary source of sepsis may not always be apparent,[49,50] reflected in the source of sepsis not being able to be identified and/or being unspecified in 37.2 per cent of cases.

Table 3: Source of underlying infection in sepsis-related child deaths, 2004–2021

Source of infection	n	%
Cardiovascular system	7	1.6
Central venous device	2	0.5
Central nervous system	44	9.9
Gastrointestinal system	30	6.8
Renal/urinary system	11	2.5
Respiratory system—lower	168	37.8
Respiratory system—upper	8	1.8
Skin and cellulitis, skeletal or soft tissue	9	2.0
Source not identified/specified	165	37.2
Total	**444**	**100**

Notes: percentages may not add to 100 due to rounding.

Responsible pathogen

One or more responsible pathogens were identified in 315 of the 444 cases of sepsis (70.0 per cent). Bacterial organisms were the most common cause of sepsis deaths (43.4 per cent). *Staphylococcus aureus*, *Streptococcus pyogenes* (Group A streptococcus), *Streptococcus pneumoniae*, and *Neisseria meningitidis* were the most common bacterial pathogens, together accounting for 51.2 per cent of infections (Table 4).

Staphylococcus aureus (*S. aureus*) infections are reported to be the most common cause of sepsis requiring paediatric intensive care unit admission in Australia and New Zealand,[51,52] with First Nations children, children from disadvantaged socio-economic areas and infants over-represented.[52] Consistent with these findings, 15 of the 41 children who died of sepsis due to *S. aureus* (36.6 per cent) were under 1 year, 10 were Indigenous (29.3 per cent) and 20 lived in socio-economically disadvantaged areas (48.9 per cent). *S. aureus* is a bacterium of notable concern as it is reported to increasingly account for paediatric hospitalisation for invasive disease and because of the rising incidence of methicillin-resistant (MRSA) strains, impacting both empiric antibiotic selection and long-term management strategies.[53]

Invasive *Streptococcus pyogenes*, also termed Group A streptococcus or GAS, is a ubiquitous pathogen that causes a wide range of infections in several areas of the body including, commonly, the oropharynx, lungs, skin, soft tissue, and endometrium.[54] Despite its common nature, Group A streptococcus infection has been shown to lead to severe necrotising pneumonias accompanied by septic shock, causing rapid mortality in otherwise healthy children.[53,54] Infants and young children (less than 2 years) as well as individuals with concurrent acute viral infections, pre-existing skin/soft tissue lesions, diabetes mellitus, heart disease, underlying malignancy or other immune suppression have been shown to be associated with increased risk of both infection and progression to invasive disease.[54] Aligning with these findings, 83.3 per cent of children who died of sepsis due to Group A streptococcus were under 5 years of age. In our study medical complexity was not associated with a higher incidence of sepsis from Group A streptococcus, with 91.7 per cent of these deaths occurring in non-medically complex children. In more recent years, Queensland has observed a progressive increase in the incidence of invasive Group A streptococcus infection in both paediatric and adult populations. Since 2016, the incidence of invasive Group A streptococcus infection in children and young people aged 0-19 years*** has increased by nearly 5 percent annually, on average. *Staphylococcus aureus* and Group A streptococcus are important causes of toxic shock syndrome in children.

Vaccines are available for many strains of *Streptococcus pneumoniae* and *Neisseria meningitis*. Pneumococcal disease refers to infection caused by the bacterium *Streptococcus pneumoniae* (*S. pneumoniae*), also called pneumococcus. These bacteria commonly colonise the nose and throat of many people, most of whom remain healthy. However, pneumococcus can cause severe invasive disease, including meningitis, pneumonia, and sepsis.[55] It remains the leading cause of hospitalisation for pneumonia in childhood,[53] with infants having the highest pneumococcal disease burden.

***Data on children and young people up to 19 years of age is reported, as data on invasive paediatric Group A streptococcus infections is published in five year age groups only.

Table 4: Pathogens in children with sepsis, 2004–2021

Pathogen	n	%
Bacterial	**207**	**43.4**
Bordetella pertussis*	4	0.8
Burkholderia pseudomallei	4	0.8
Escherichia coli	14	2.9
Haemophilus influenzae*	2	0.4
Klebsiella pneumoniae	9	1.9
Mycobacterium tuberculosis	2	0.4
Neisseria meningitidis (meningococcus)*	20	4.2
Pseudomonas	17	3.6
Salmonella	4	0.8
Staphylococcus aureus (MSSA and MRSA)	41	8.6
Streptococcus agalactiae (Group B streptococcus)	14	2.9
Streptococcus pneumoniae (pneumococcus)*	21	4.4
Streptococcus pyogenes (Group A streptococcus)	24	5.0
Streptococcus, other and unspecified	6	1.3
Other and unspecified bacteria	25	5.2
Viral	**111**	**23.3**
Adenovirus	16	3.4
CMV, EBV, HSV, VZV*	26	5.5
Enterovirus	3	0.6
Human metapneumovirus	3	0.6
Influenza*	13	2.7
Norovirus	2	0.4
Parainfluenza	5	1.0
Respiratory syncytial virus	17	3.6
Rhinovirus	3	0.6
Rotavirus*	2	0.4
Other and unspecified viruses	21	4.4
Fungal	**30**	**6.3**
Fungi	26	5.5
Parasite	4	0.8
Unascertained and unspecified	**129**	**27.0**
Not specified	105	22.0
Unascertained	24	5.0
Total	**477**	**100**

** Vaccine preventable*
Notes: Cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus 1 and 2 (HSV) and varicella-zoster virus (VZV) are herpesviruses comprising five of the 8 members of the Herpesviridae family, a large family of DNA viruses that cause infections.
Total exceeds number of sepsis cases due to some cases having more than one responsible pathogen identified. Per centages may not add to 100 due to rounding.
MSSA = Methicillin sensitive Staphylococcus aureus, MRSA = Methicillin resistant Staphylococcus aureus.

Pneumococcal vaccination for a number of *S. pneumoniae* strains is available in the Australian National Immunisation Program (NIP) for infants and young children, recommended in a three-dose schedule at 2, 4 and 12 months of age.[56] Twelve of the 21 children who died from pneumococcal sepsis (57.1 per cent) were aged less than 1 year, and as such, did not have the opportunity to complete the full vaccination schedule.

Meningococcal disease is a rare but serious bacterial disease caused by *Neisseria meningitidis*, also termed meningococcus. Like pneumococcus, these bacteria are found in the nose and throat of many people who remain healthy. Invasive meningococcal disease most commonly presents as sepsis and/or meningitis.[57] Meningococcal disease tends to occur in a bimodal age distribution, affecting young children and adolescents.[30] There are 13 known meningococcal serogroups, of which serogroups A, B, C, W and Y are the most common causes of the disease worldwide.[56] The NIP has provided vaccination against meningococcal serogroup C since 2003, and serogroups A, C, W and Y since July 2018. Meningococcal ACWY vaccination is recommended for all children aged 12 months, all adolescents aged 14–16 years, and infants with certain medical conditions from 2 months of age. Meningococcal B vaccination is recommended for Aboriginal and Torres Strait Islander children and children with certain underlying medical conditions from 2 months.[56] Sixteen of the twenty children who died with *Neisseria meningitidis* were 2 years or younger (80.0 per cent). Nine were under 1 year (45.0 per cent) and did not have the opportunity to receive the Meningococcal ACWY vaccine prior to death.

Invasive Group A streptococcal disease, pneumococcal disease and meningococcal disease are notifiable diseases in Australia, which means that diagnosed cases are reported to state or territory health departments. Overall, vaccine preventable diseases (both bacterial and viral) accounted for 18.7 per cent of identified pathogens. Vaccine preventable diseases are indicated by use of an asterisk in Table 4.

Viral infections were the cause of 23.3 per cent of sepsis-related deaths. As demonstrated in Table 4, the most common causes of viral-induced sepsis were Herpesviruses, Respiratory syncytial virus (RSV) and Adenovirus. Influenza was the fourth most common virus causing death, and a vaccine preventable disease. There were no COVID–19 related sepsis deaths in children recorded during the period of this study.

Infants (particularly neonates) and immunocompromised children have been shown to be most at risk of developing overwhelming viral sepsis from Adenovirus and Herpesviruses.[53] Similarly, while RSV is the most common infectious agent causing acute bronchiolitis in children,[58] few die if given supportive care.[53] Risk factors for life-threatening bronchiolitis

include premature birth and background medical complexity including, chronic lung disease, congenital cardiac abnormalities and immunodeficiency. Consistent with these findings, 76.3 per cent of children who died from sepsis from *Herpesviruses*, *Adenovirus*, and RSV had background complex chronic medical conditions. Infants under 1 year accounted for 35.6 per cent of sepsis from *Herpesviruses*, *Adenovirus*, and RSV.

Overall, children who died from viral-induced sepsis were significantly more likely to have background complex chronic medical conditions than children who died of bacterial infections (66.4 per cent of children with viral sepsis had complex comorbidities, compared to 22.2 per cent of children who died from bacterial sepsis). Older children and adolescents with healthy immune and cardiorespiratory systems are infrequently hospitalised and rarely die from viral sepsis.[53]

Trends over time and differences between population subgroups

There were no significant changes in the prevalence of bacterial and viral organisms over time; notably there were no COVID-related paediatric sepsis deaths in this time. The incidence of fungal and parasitic infections more than halved between 2004–2012 and 2013–2021, however this reduction did not reach the threshold for statistical significance, likely due to small numbers.

Significant differences in the prevalence of bacterial, viral, fungal and parasitic organisms were observed according to age; with infants (under 1 year) and young children (1–4 years) significantly more likely to have bacterial infections than older children. Previous research has shown that the pathogens typically causing sepsis in children differ by age, medical co-morbidities and geographical location/local geography.[53] Aligning with previous research,[37] there was no significant difference in the causative organisms between Aboriginal and Torres Strait Islander and non-Indigenous children.

Unexpected paediatric sepsis deaths in the community

Most sepsis studies worldwide (both adult and paediatric) have focused on in-hospital sepsis deaths.[4,50] Those that do consider out-of-hospital sepsis mortality largely report on deaths occurring in community settings post-discharge following a sepsis episode.[59] A few isolated studies have sought to quantify the extent to which septic patient outcomes can be improved by increased sepsis recognition within pre-hospital emergency service settings.[60,61] There have been no studies to date investigating deaths from sepsis in paediatric patients who die or become moribund at home.

The care of critically unwell children frequently begins in pre-hospital, primary-care settings. Unfortunately, the lack of research into out-of-hospital sepsis and sepsis mortality means there is limited evidence regarding predictors and interventions specific to sepsis in the primary-care arena. Understanding differences in in-hospital and out-of-hospital paediatric sepsis deaths is vital for comprehensive, coordinated and population-wide efforts to reduce paediatric sepsis mortality.

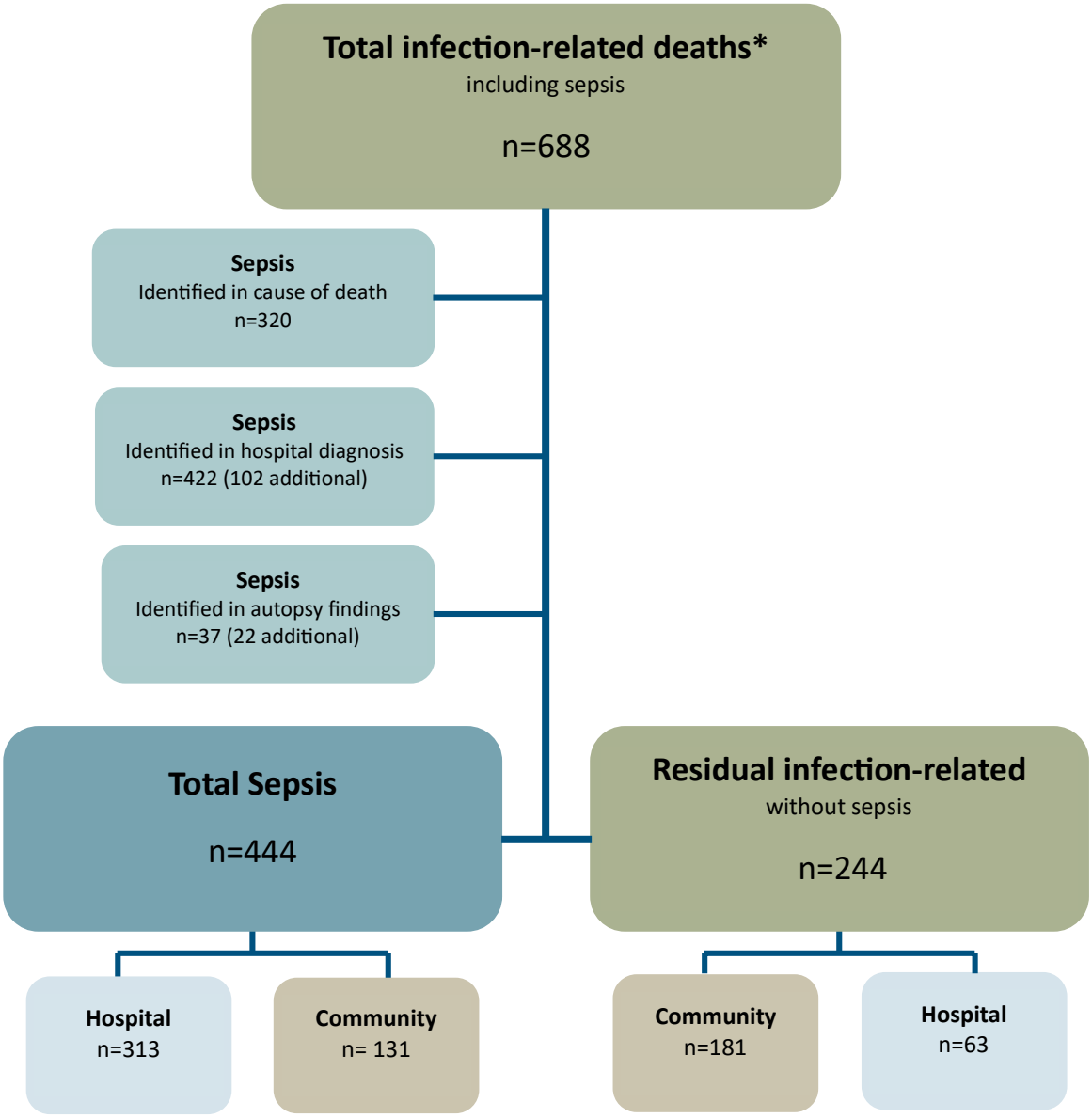
While the majority of sepsis-related deaths occurred in-hospital (70.5 per cent, 313 deaths), nearly 30 per cent occurred at home or in community settings (131 deaths).[†††]

Once the study investigators had completed screening all infection-related child deaths to identify sepsis cases, they noticed a large residual pool of deaths involving infection but without evidence of sepsis. As shown in Figure 11, most of these residual, non-sepsis but infection-related child deaths occurred in the community (74.2 per cent of infection-related child deaths where sepsis was not identified occurred in the community). For deaths occurring in the community, the infection was significantly more likely to be the underlying cause of death than in in-hospital infection-related child deaths. In 64.6 per cent of deaths in the community the underlying cause of death was attributed to infection without sepsis compared with only 27.0 per of cent deaths in hospital. Moreover, infection-related child deaths in the community were more likely to occur in children without underlying complex chronic medical conditions (69.1 per cent), while deaths that occurred in hospital were more likely to occur in medically complex children (73.0 per cent).

Stated simply, we can infer that, in general, children in the community were previously healthy children who died *from* infection, whereas children who died in hospital tended to be medically complex children who may have died *with* infection, from conditions related to their underlying complex chronic condition.

[†††] Deaths were classified as occurring either in hospital or community settings (such as at home or during transport to a medical facility). Children who arrived at hospital moribund were classified as having died in a community setting as this is the environment the deterioration and/or initial collapse occurred.

Figure 11: Screening process to identify sepsis in death records, diagnosis data and autopsy findings, 2004–2021



*Of children having left hospital after birth

These findings give rise to a suspicion that a proportion of the infection-related deaths in the community may involve sepsis. Difficulties concerning the diagnosis of sepsis in hospital settings are extensively documented in the literature.[18] These challenges are compounded where death occurs in community settings, particularly where antecedent clinical data may be scant (i.e. relevant physical checks may not have been undertaken or documented) and/or laboratory tests not conducted.[62]

In reviewing autopsy reports for all infection-related child deaths reported to a coroner in the study period for evidence of sepsis, study investigators also observed inconsistencies in the attribution of sepsis. It is possible therefore, that the out-of-hospital sepsis deaths reported in this study could represent the tip of the iceberg in community-based sepsis mortality, with a number of child deaths recorded as infection-related but without recognition or documentation of associated organ dysfunction representing undiagnosed sepsis.

Sepsis-related deaths of Aboriginal and Torres Strait Islander children were significantly more likely to occur at home or in the community than the deaths of non-Indigenous children, with 43.3 per cent of First Nations children occurring in community settings, compared with 26.0 per cent of non-Indigenous children.

Children who died at home or in the community were significantly younger than children who died in hospital. Approximately 68 per cent of children who died at home were less than 3 years of age, compared with 44.1 per cent of children who died in hospital.

Of the identified sepsis-related infant deaths (under 1 year) that occurred at home or in the community, 66.7 per cent occurred suddenly and unexpectedly, meeting the definition of Sudden Unexpected Death in Infancy (SUDI).[‡‡‡] Unsafe sleep factors were present in many cases, presenting a threat to breathing. The role of infection in SUDI has long been debated, however there is some evidence that infection and the inflammatory response to infection may play a role in these deaths,[63,64] with respiratory tract infections a well-documented risk factor for SUDI. The peak incidence of SUDI has been reported to occur during the developmental period in which infants have low levels of specific antibody protection, either maternal or actively acquired immunity.[65] Sepsis in infants and young children can progress rapidly from minor clinical signs and symptoms to severe illness. Certain infectious diseases are also known to advance so rapidly that they may initially be considered a sudden death.[66] However, even the most fulminant infections produce signs and symptoms that precede death, pointing to the importance of collecting a complete clinical history, including carer recollections, as part of the death investigation process.

Children who died at home were also significantly less likely to have a pre-existing complex chronic medical condition, with nearly 80 per cent of the children who died unexpectedly at home having no underlying medical complexity that may have accounted for the development of sepsis. The families of children with medical complexities may have altered thresholds for health seeking behaviours as well as potentially improved access to healthcare.

Mirroring these findings, sepsis-related child deaths that occurred in the community were also significantly less likely to have been anticipated, and as such, while nearly two-thirds of all sepsis-related child deaths were non-reportable (65.5 per cent), most sepsis deaths that occurred in the community were reported to a coroner (85.5 per cent) (See Figure 12). In the context of paediatric sepsis and other infection-related deaths, reportable deaths principally comprise deaths that were sudden and unexpected (such that it was not possible to form a medical opinion about the cause of death).[§§§] Occasionally, sepsis-related deaths may be reportable because the child was in care or because the provision of, or a failure to provide, healthcare contributed to the death. Between 2004 and 2021, less than 3 per cent of sepsis-related deaths occurred in care, suggesting that reportable deaths can be used as an effective proxy indicating that the deaths were not anticipated by clinical history.

‡‡‡ The SUDI classification groups together the deaths of apparently health (or only mildly unwell) infants who die suddenly and unexpectedly with no immediately obvious causes. These deaths may be later identified as being due to a previously unrecognised disease or morbid condition such as congenital birth defects or infection. In some cases, an external cause (such as a sleep accident) is identified. In many cases no potential cause can be identified; these are classified as due to Sudden Infant Death Syndrome (SIDS) or undetermined causes.

§§§ Under s. 8(3) of the *Coroners Act 2003*, a death is reportable if: (a) the identity of the person is unknown (b) the death was violent or otherwise unnatural (c) the death happened in suspicious circumstances (d) the death was health care related (e) a cause of death certificate was not issued and is unlikely to be issued (f) the death occurred in care (g) the death occurred in custody (h) the death occurred in the course of police operations.

Figure 12: Sepsis death location (and all sepsis) by reportable status

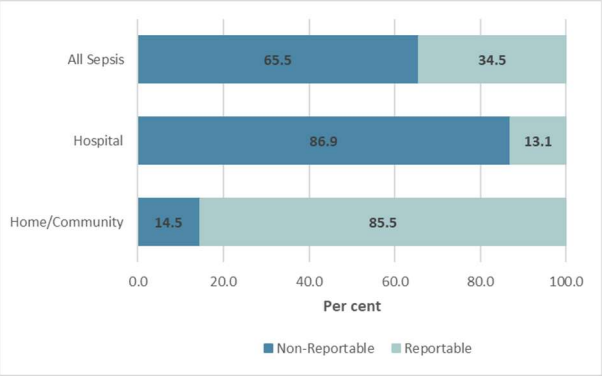
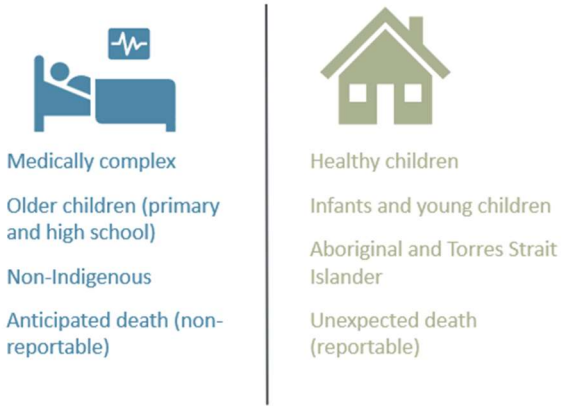


Figure 13 shows the key differences between sepsis-related child deaths occurring in the community compared with in-hospital deaths.

Figure 13: Depiction of key differences between in- and out-of-hospital paediatric sepsis deaths



These findings indicate that paediatric sepsis-related deaths occurring in the community may be preventable with timely sepsis recognition and treatment. Most sepsis arises in the community. Therefore, primary care, and in particular general practitioners (GPs), are often an acutely unwell child's first point of contact with the healthcare system. Unfortunately, sepsis-recognition in prehospital settings is known to be both challenging and poor.[67,68] Research on sepsis in primary care is scarce, and the role of families (public awareness of sepsis), general practitioners, and paramedics in managing paediatric sepsis remains a neglected area in current literature.[67,69]

In-depth analysis of the interactions children and their families had with healthcare professionals prior to death was outside the scope of this study. However, information collected during coronial investigations provided some high-level information on health status and recent contact with health services for the 112 reportable child deaths that occurred in the community.

In nearly 84 per cent of reportable child deaths that occurred in the community, the children were known to be unwell in the preceding days, with nearly half symptomatic for 48 hours or less, highlighting the rapid progression from infection to severe sepsis in children. Infants (under 1 year) were the least likely to be observably unwell in the hours leading to death, with 26.8 per cent of infants reported to appear well prior to being placed to sleep before death. Serious illness in infants may be confused with tiredness, as persistent irritability and crying, poor feeding, and difficulty settling may be symptoms of both a tired, over-stimulated baby and a seriously unwell child.

Of the reportable child deaths where children were known to be unwell in the lead up to death, 47.9 per cent had one or more contacts with a healthcare professional in relation to their illness prior to death (most commonly a general practitioner or hospital emergency department). In 64.4 per cent of cases, children had one contact with a healthcare professional in relation to their illness prior to death, 26.7 per cent of children had between two and three healthcare contacts, and a further 8.9 per cent had four or more contacts with a healthcare professional in relation to their illness prior to death. Research exploring parental experiences of paediatric sepsis indicate that parents can be reassured by initial consultations and may be reluctant to re-present to a general practitioner or emergency department even though their child is deteriorating.[****]

In 73.3 per cent of cases the most recent contact with a health professional prior to death occurred on the day of, or within 24-hours prior to death. In most of these cases, the child was not identified as being seriously ill.

The proportion of children who were recognised by parents as being unwell and the number of visits to a health care professional prior to death were broadly similar for Aboriginal and Torres Strait and non-Indigenous children. The time between last presentation to a health professional and death was shorter for Aboriginal and Torres Strait Islander children. Approximately 82 per cent of Aboriginal and Torres Strait Islander children presented to a healthcare professional on the day of, or within 24-hours of death compared to 67.7 per cent of non-Indigenous children.

Some early clinical signs of sepsis may be more difficult to detect in children with dark skin. Abnormal skin

[****] Unpublished data and personal communication with Queensland Paediatric Sepsis Program.

colour and perfusion (capillary refill time) have been documented to be some of the first clinical signs that develop in children with sepsis.[70] Blue, grey, pale or mottled skin or lips are more difficult to detect in brown or black skin, where these signs may be only apparent on the hands or soles of the feet. It is also more difficult to detect abnormal capillary refill time in patients with dark skin.

In 60.0 per cent of cases where the child had one or more recent presentations to a healthcare professional, the coronial findings did not consider the adequacy of healthcare provided. Critical examination of the healthcare service provided was frequently triggered by parental concerns or root cause analyses undertaken by the health system after an unexpected death following discharge from a Queensland public hospital (including emergency department).

Opportunities for practice improvement

This study revealed several areas in which information gaps present opportunities for improved practice.

Better identification of sepsis in death records

Information from death certificates is used to measure the relative contributions of different diseases to mortality.[71] Statistical information on deaths by cause is important for monitoring the health of the population, designing and evaluating public health interventions, planning and assessing the effectiveness of health services, and determining research priorities. Death certificate data are extensively used in research of infectious diseases (including those which result in sepsis) and the most virulent pathogens causing morbidity and mortality.

Unfortunately, the identification of sepsis in cause of death records is not straightforward, hampering these efforts. In 2014, the National Confidential Enquiry into Patient Outcomes and Death (United Kingdom) conducted a prospective study of adult patients diagnosed with sepsis in a two-week study period.[71] For those patients who died, sepsis was only mentioned on the death certificate in 40 per cent of cases. However, upon review, investigators were of the view that sepsis should have been included as a cause of death in 81.4 per cent of those cases for which sepsis was not mentioned on the death certificate.

To understand the methodological complexities involved in identifying sepsis in cause of death records, it is necessary to consider how causes of death are coded and reported in the vast majority of publications identifying leading causes of death.

Coding and reporting causes of death

In Australia, and internationally, all diseases, morbid conditions, or injuries that either resulted in or contributed to death are entered on the cause of death certificate.

Cause of death records provide details of:

- the immediate cause of death (the final disease or condition resulting in death)
- the intermediate or main contributing causes
- a single underlying cause of death (the disease or injury that initiated the chain of events leading to death), and
- any significant conditions that were present at the time of death but did not directly contribute to death.

Clinical coders[††††] code this information to an international standard, using the tenth revision of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10). Coding causes of death enables them to be categorised into disease groupings, which provide a meaningful way of examining trends and patterns in causes of death.

In coding causes of death, the underlying cause of death is selected from the conditions reported on the death certificate. The intermediate and immediate causes (also termed associated or chain causes) may also be coded, although in publications analysing causes of death, it is the underlying cause of death that is reported. This is because from a public health perspective, preventing this first disease or injury will usually result in the greatest health gain.

Identifying sepsis in cause of death data

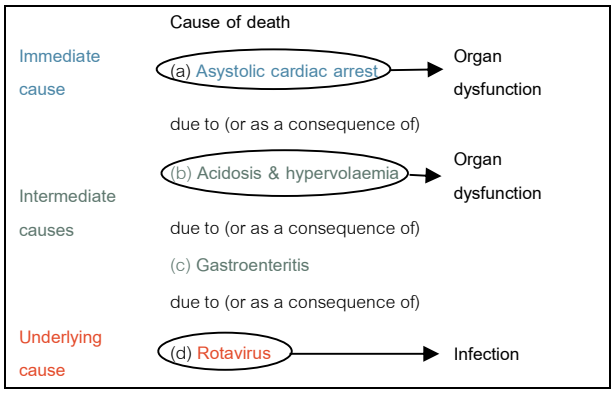
Identifying sepsis in cause of death records is complex. Sepsis is rarely the underlying cause of death. In most sepsis-related deaths, the underlying cause is attributed to the underlying infection, or in cases with pre-existing medical complexity, the background chronic condition. In this study, sepsis was the underlying cause of death

[††††]A Clinical Coder is a health information management professional who assigns codes to narrative descriptions of patients' diseases, operations, and procedures in accordance with recognised classification systems to allow for easy storage, retrieval, and analysis of health data.

in only 25.5 per cent of cases where sepsis was recorded on the death certificate.

Additionally, sepsis may not be explicitly documented on the cause of death certificate. Rather, both an acute infection and consequential organ dysfunction (the clinical definition of sepsis) may be recorded in the underlying and chain causes. As demonstrated in Figure 12, in these cases sepsis is implied by the combination of infection and organ dysfunction.

Figure 12: Implied sepsis in cause of death certification



Due to these factors, accurate identification of sepsis-related deaths requires individual level data using both underlying and chain causes of death (termed multiple cause of death analysis).

The internationally agreed best practice method for identifying sepsis in cause of death data,[11,72,73] used in this study, involves identifying sepsis via two mutually exclusive groups:[‡‡‡‡]

Explicit sepsis—cases with an ICD-10 code referencing sepsis explicitly, listed as either the underlying, chain or contributing cause of death.

Implicit sepsis—cases with an ICD-10 code referencing severe infection listed as either the underlying or chain cause of death and an ICD-10 code referencing organ dysfunction listed as a chain cause of death.

Increased sepsis identification through data linkage

Cause of death data has limitations; it relies on accurate determination and documentation of sepsis and/or organ dysfunction in the underlying and chain causes of death, which is subject to variability between certifiers. To produce robust estimates of sepsis mortality, these current limitations can be reduced through data linkage. For children who died in hospital, linked diagnosis data from the final admission resulting in death can supplement cause of death data to increase sepsis identification.

Recording sepsis on the cause of death certificate

We found that sepsis was explicitly documented on the cause of death certificate provided by the certifying medical practitioner or pathologist in 224 of the 444[§§§§] sepsis-related deaths (50.5 per cent). In a further 96 cases sepsis was implied from the presence of infection and organ dysfunction, resulting in 320 cases of sepsis being identified from death certificate data alone. Diagnosis codes from linked hospital admission data were used to identify further sepsis cases. An additional seventy-six cases of explicit sepsis and 53 cases of implied sepsis were identified, resulting in 102 additional sepsis cases being incorporated,[*****] a near 32 per cent increase in sepsis deaths.

The findings described in autopsy reports, particularly histological findings, were also used to increase sepsis identification in reportable infection-related deaths. An additional 37 cases of explicit sepsis, which had not been documented on the cause of death certificate, were identified through the autopsy findings.[†††††] Most of these deaths occurred out-of-hospital, in the community.

In total, the use of linked hospital admission data and autopsy findings resulted in a 38.75 per cent increase in the identification of sepsis (124 additional cases).[‡‡‡‡‡] These are cases in which sepsis was diagnosed prior to death or was identified through postmortem examination and testing. Such cases shine a light on the under-recording of sepsis in the chain of causes reported on the death certificate, occurring in one-third

[‡‡‡‡] The ICD-10 codes and key terms used to identify explicit and implicit sepsis[11,73] are listed in Appendix 2.
[§§§§] The 444 sepsis-related deaths comprised 330 explicit sepsis cases (i.e. the term sepsis included in the medical cause of death, autopsy report, or diagnosis codes from linked hospital admission data) and 114 implicit sepsis cases (i.e. infection and new organ dysfunction documented in medical cause of death or diagnosis codes from linked hospital admission data).
[*****] The number of additional distinct sepsis cases identified (102) is less than the sum of additional explicit and implied sepsis cases identified in hospital diagnosis codes (129). This is because there were 27 cases of implied sepsis identified in cause of death data that were 'up coded' from implied to explicit sepsis, using linked hospital admission data, however this did not affect overall sepsis numbers.
[†††††] Fifteen of the 37 explicit sepsis cases identified in the autopsy findings were also identified as either explicit or implied sepsis in hospital admissions data.
[‡‡‡‡‡] Numbers sum to more than the total (444) sepsis cases as there were cases identified in both autopsy reports and diagnosis data.

of cases in this study. This was not an unusual finding, as the experience in the United Kingdom was similar.[71]

Accurate mortality data are important in the surveillance of infectious diseases as well as monitoring the effectiveness of immunisation and other prevention programs. In Queensland, the current under-recording of sepsis on death certificates means that currently sepsis-related deaths cannot be identified using death registration records alone, with accurate identification requiring linked hospital admission and coronial data (via the hand screening of autopsy findings). This is methodologically complex, with large scale, linked-data studies needed to quantify the burden of sepsis mortality, making interjurisdictional comparisons challenging.

Despite being a national health priority, sepsis mortality is neither routinely nor accurately reported in population health statistics. Research and epidemiological analyses and resultant health and preventative care efforts are also hampered by the under-documentation of sepsis on death certificates. Specification of the causal pathway leading to death in Part I of the cause of death certificate is important. Best practice in certification requires that all conditions contributing to death and their duration be included, with certifiers recording as much detail as possible. Death certifiers (clinicians and pathologists) should explicitly document sepsis on the death certificate and in the cause of death as provided in an autopsy report, to facilitate the reliable identification of sepsis-related deaths in vital statistics.

Practice improvement recommendation

Where sepsis is known to have caused or contributed to death, this should be documented in the causes of death on the death certificate.

Documenting the responsible pathogen on death certificates

A responsible pathogen was identified in 315 of the 444 cases (70 per cent) but only explicitly documented in the cause of death in 256 cases, fewer than 60 per cent of cases.

In those cases where an autopsy was conducted (i.e. in unexpected deaths that were reported to a coroner) deficits in the documentation of known pathogens in the cause of death can be highlighted. A responsible pathogen was documented on the Medical Certificate Cause of Death in 93 of the 153 cases in which an autopsy was conducted (60.8 per cent). In a further 35 cases a responsible pathogen was documented in the histopathology and/or microbiology findings at autopsy, but not included as part of the chain of causes reported by the pathologist. Together, this resulted in a responsible pathogen being identified in 83.7 per cent of sepsis cases in which an autopsy was conducted.

At autopsy, some infections may be obscured by prior antimicrobial therapy (which can render microbial cultures negative) or by postmortem artefacts,§§§§§ making the identification of a responsible pathogen difficult, if not impossible.[66] Previous studies have shown that in approximately 30 to 40 per cent of sepsis cases, microbiological testing at autopsy is negative, due to antibiotic therapy prior to death.[74] This likely accounts for the 16.3 per cent of cases in which the autopsy was unable to identify a responsible pathogen.

For deaths that occur in hospital, antemortem testing should be used to identify and document a responsible pathogen. If a responsible pathogen cannot be identified via antemortem findings, the cause of death is arguably incompletely understood, and an autopsy should be recommended.

Recent Queensland coronial guidance for medical practitioners around issuing a cause of death certificate for apparent natural cause deaths,[75] enables a cause of death certificate to be issued if an opinion about the medical cause of death can be formed, based on a review of the clinical history and without examination of the person's body in situations where the person has not been seen by a medical practitioner in some months. While such guidance may be reasonable in a death of an elderly person from apparent heart failure against background of known congestive heart disease, it is arguably less appropriate in deaths due to apparent infectious causes, and less appropriate still in children, a cohort in which many deaths may be preventable. It also has the unintended consequence of increasing the likelihood of imprecise and vague certification of probable causes rather than accurate identification of causes and contributing pathogens. Such an approach to the certification of natural cause deaths hampers public health or preventive care efforts to reduce premature mortality.

It is important for public health surveillance to have information on the pathogens responsible for death on a national basis; for example, to know how many infection-related deaths are due to Group A

§§§§§ A post-mortem artefact is a change in the body after death (introduced in the period between death and autopsy or during autopsy), including decomposition changes and sample contamination.

streptococcus, or to other bacterial infections. Currently, no Australian burden estimates exist for many common bacterial pathogens, making establishment of public health priorities difficult.[76] At a state-wide level, identification of childhood mortality from common pathogens in the Queensland Child Death Register is largely reliant on this important information being recorded on the death certificate. Research and epidemiological analyses are also hampered by missed cases due to the under-reporting of the pathogens responsible for death in the medical cause of death.

Current best practice recommendations for death certifiers (including pathologists and other medical practitioners) specify that where the organism that caused the infection is known, death certifiers should:

- accurately record organisms responsible for infections on the cause of death certificate if they directly led or contributed to death,
- where the infection caused or significantly contributed to death and the organism was resistant to antimicrobials record this on the cause of death certificate,
- where it is possible to identify whether the infection was hospital-associated or community-associated record this on the cause of death certificate.[77]

Practice improvement recommendation

Death certifiers should document the pathogen responsible for death on the medical cause of death certificate where known.

If a responsible pathogen cannot be identified via antemortem testing, the cause of death is arguably incompletely understood, and an autopsy should be recommended.

To reduce paediatric sepsis, it is necessary to better understand its epidemiology.****** Large scale, population-based studies of paediatric sepsis mortality, and some of the most important microbial agents contributing to sepsis, frequently rely on cause of death information in vital statistics.[78] Not documenting these on the death certificate results in an underestimation of the burden of, and factors contributing to, paediatric sepsis mortality. Both the documentation of sepsis in the chain of causes, and the identification and documentation of a responsible pathogen on the cause of death certificate represent simple, low-cost, upstream changes that will have an indirect impact on sepsis rates long term.

Understanding and reducing out-of-hospital paediatric sepsis mortality

The findings of this study show that out-of-hospital paediatric sepsis deaths are not uncommon; they occur largely unexpectedly, in healthy children without background medical conditions, who have mostly been in recent contact with health services. Aboriginal and Torres Strait Islander children are over-represented in this cohort.

Children who have presented to healthcare services such as general practitioners (GPs) and hospital emergency departments prior to dying in the community or arriving at hospital moribund are an important group of sepsis- and infection-related deaths. This cohort could benefit from preventative strategies to improve the early recognition of sepsis by families, primary health services and emergency departments allowing early treatment and improved outcomes.

Public awareness of sepsis is poor in Australians of parenting age in comparison to other medical conditions.[23] Improving parental and family awareness of the signs and symptoms of sepsis will encourage health seeking behaviour, particularly when there is deterioration after an earlier presentation.

Media campaigns can be a useful tool to expose high proportions of large populations to health messages and produce positive changes in health-related behaviours.[79] In other areas of preventable child deaths, most notably SUDI, large reductions in mortality have been attributed to national campaigns with strong mass media components, aimed at members of the public and medical practitioners.[80] There may be benefit in developing a targeted media campaign to improve caregiver and community awareness of sepsis and its symptoms. Culturally safe campaigns aimed at Aboriginal and Torres Strait Islander communities should also be developed.

Practice improvement recommendation

Media campaigns designed to increase caregiver and community awareness of sepsis and its symptoms should be developed, including culturally safe campaigns aimed at Aboriginal and Torres Strait Islander communities.

A range of sepsis tool kits have been developed to improve sepsis care in emergency department and in-patient settings. In Queensland, the Paediatric Sepsis Clinical Guideline and Sepsis Pathway[81] represent a

****** The determinants, occurrence and distribution of health and disease in a defined population.

comprehensive initiative to increase the screening, recognition, care, and management of children with acute and severe illness presenting to Emergency Departments. The pathway includes culturally appropriate checklists of the signs and symptoms of sepsis for families.

There is limited sepsis recognition and treatment guidance aimed at general practitioners and the primary care sector more generally. HealthPathways are evidence-based guides containing information on the assessment and management of common clinical conditions, including local referral options. The pathways are designed primarily for general practice teams but are also available to other health professionals in each region. The Queensland Paediatric Sepsis Program (QPSP) has adapted existing HealthPathways used by primary health practitioners to include references to paediatric sepsis in a few, but not all, Queensland Primary Health Network (PHN) regions. There would be benefit in embedding sepsis red flags into the infection HealthPathways of all seven Primary Health Network (PHN) regions in Queensland.

Encouragingly, the QPSP has worked with 13-HEALTH and the Queensland Ambulance Service to embed paediatric sepsis education into their programs. The QPSP has also embedded paediatric sepsis into the primary health care manual (PHCM) which is reviewed every two years.

Practice improvement recommendation

Sepsis red flags should be embedded into the infection HealthPathways of all seven Primary Health Network (PHN) regions in Queensland.

The National Sepsis Clinical Standard requires that all sepsis cases are monitored and reviewed by a governing body within a healthcare facility to enable monitoring of compliance with guidelines as well as sepsis incidence and outcomes. The Sepsis Clinical Standard recommends that deaths due to sepsis, particularly if not expected, should be reviewed to identify areas for improving care. A recent multi-incident analysis of adverse clinical events related to paediatric sepsis by the Queensland Paediatric Quality Council—a gazetted Quality Assurance Committee established for the purpose of improving the safety and quality of paediatric health services—reported that reviewing events such as delayed diagnosis of sepsis may result in improved sepsis recognition and treatment.[20]

The Sepsis Clinical Standard does not require a review of sepsis-related deaths shortly after an episode of care. This means deaths of children who have presented or had multiple presentations to health services (including primary care services such as general practitioners and acute care services such as hospital emergency departments) prior to dying in the community are not required to be subject to routine clinical review. As such, the interactions children who die from sepsis in the community had with health services remains largely hidden. While deaths in this group are, in the main, reported to a coroner, the majority appear investigated only until a medical cause of death is ascertained, with limited discussion of the healthcare received or its adequacy reported in the majority of coronial findings.

Coronial investigations of unexpected infection-related child deaths predominantly rely on partial medical histories, collected by police who have limited clinical knowledge. Unfortunately, this also means that important information about the oftentimes subtle signs and symptoms indicating the progression of disease (from infection to sepsis) as well as information about caregiver awareness of the same is seldom collected as part of the routine investigation of these deaths.

Optimally, forensic death investigation should involve a paediatric healthcare professional, to gather and record a detailed clinical history. This should include:

- interviews with parents and caregivers designed to elucidate information on parental sepsis awareness and the subtle signs of clinical deterioration that may have been present but perhaps not recognised by parents and caregivers or health professionals,
- comprehensive information on previous underlying conditions that increase infection and sepsis risk,
- vaccination history, and
- previous touchpoints with healthcare practitioners or services, including any relevant laboratory test and culture results.

This is consistent with best practice guidelines pertaining to the investigation of other sudden and unexpected child deaths.[82]

Collecting a comprehensive clinical history would also better enable coroners to assess whether sepsis and other infection-related deaths occurring in the community shortly after presentation to a health service may be ‘health care related deaths’ (under the

Coroners Act 2003), for the purpose of improving out-of-hospital sepsis recognition and treatment.[††††††]

Practice improvement recommendation

Coronial investigations of unexpected infection-related child deaths should involve a paediatric healthcare professional, to gather and record a detailed clinical history, including underlying medical conditions, vaccination history, and touchpoints with health services in the lead up to death.

General practitioner and other health service records, including any laboratory test and culture results should be obtained and reviewed.

Preventing sepsis—opportunities for future research

The results of this study suggest that sepsis may be under-diagnosed in out-of-hospital infection-related child deaths. A recent systematic review of the current methods used to identify sepsis in forensic contexts has identified the main investigations and combination of markers needed to achieve a confident post-mortem diagnosis of sepsis.[62] A study is needed to evaluate autopsy reports in unexpected infection-related child deaths against these evidence-based markers, to accurately estimate the incidence of out-of-hospital paediatric sepsis mortality.

Community-based sepsis and the primary care sector should be priority areas for new quality improvement and research initiatives. There is a pressing need for further research into this hitherto largely neglected cohort of sepsis deaths. There is a need to better understand children's health status at the time of death and their interactions with health services in the preceding days and hours, including children's clinical presentation, assessment, testing, prescription, and monitoring.

Our understanding of parental experiences of out-of-hospital sepsis mortality remains limited. While a range of studies have assessed sepsis recognition in hospital settings, little is known about sepsis recognition in the community. Most commonly, sepsis starts in the community and the decision and timing of parents in seeking medical care for children is likely to contribute to severity upon presentation and sepsis-related outcomes. Parental concern has also been proposed as a valuable tool to assist in the recognition of sepsis.[83] However, little is known about how parents assess the severity of illness in their child and make decisions regarding the timing of presentation and/or representation. In other areas of child death prevention, understanding decision-making processes in families with children at risk has supported the development of more targeted and effective interventions.[84]

Further research into out-of-hospital paediatric sepsis deaths may improve the information provided to both families and health practitioners regarding the recognition of, and referral pathways for, paediatric sepsis in community settings.

Lastly, further research to understand the social determinants of sepsis-related mortality in children is needed. Our study has shown that socio-economic disadvantage, regional and remote living and Indigenous status are associated with poorer outcomes for paediatric sepsis. Understanding the drivers for these impacts is key to developing effective preventative initiatives.

[††††††] Health care related deaths are defined under the *Coroners Act 2003*. A death is considered a health care related death if the health care or a failure to provide health care caused or contributed to the death and the death was an unexpected outcome of the health care being provided.

Appendix 1: Methods

This population-based retrospective cohort study (the Queensland Paediatric Sepsis Mortality Study) included all deaths of infants and children (0–17 years) due to sepsis that met the inclusion criteria and occurred in Queensland between 1 January 2004 and 31 December 2021. The source population for this study was all infant and child deaths that occurred in Queensland during this period.

Data sources

The Queensland Child Death Register was the primary source of information for this study, as it captures information on both in- and out-of-hospital child deaths. The Queensland Family and Child Commission (QFCC) is the data custodian of the register. The QFCC has a statutory obligation under Part 3, sections 25–29 of the *Family and Child Commission Act 2014* to maintain a register of all deaths of children and young people under the age of 18 years in Queensland. The Child Death Register is based on notifications from the Registry of Births, Deaths and Marriages as well as details of the circumstances and factors associated with all reportable deaths under Section 8 of the *Coroners Act 2003*. Information in the register is classified according to cause of death, demographic information and other relevant factors. Cause of death information is coded according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (ICD-10).

Data quality in the Child Death Register is impacted by the quality and completeness of the data in the source documents and datasets that comprise the register. However, the QFCC have established rigorous quality assurance and data cleaning processes and in general, data quality and completeness are of a high standard.

Data linkage

Data for child deaths due to sepsis and deaths where infectious disease with the possibility of resulting in sepsis played a causal or contributory role in the death (without an accompanying organ dysfunction code) were linked to the Perinatal Data Collection (hereafter perinatal), the Queensland Hospital Admitted Patient Data Collection (inpatient hospitalisations), the Emergency Department Collection (emergency presentations), and the Congenital Abnormalities Linked File (congenital abnormalities).

Linked perinatal, inpatient hospitalisations, emergency presentations and congenital abnormalities data for infants and children were obtained from Queensland Health's Master Linkage File. The Master Linkage File contains linked references to multiple health-related data collections and registries in Queensland.

These datasets contain diagnostic and demographic data. Morbidities, including congenital anomalies, diseases, injuries and related health problems are coded according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification* (ICD-10-AM). The Australian Classification of Health Interventions (ACHI) is used to classify surgeries, therapies and health interventions.

Due to the time span of the 18-year study period, certain records in the cohort predated available linked data. The earliest linked data available for the listed data collections was as follows:

- Public inpatient hospitalisations were available for the entire study period.
- Private inpatient hospitalisations were available from 1 July 2007.
- Perinatal data were available from 1 July 2007. Where the birth occurred in a Queensland public hospital, after the year 2000 and had an associated admission, additional links to the Perinatal Data Collection were able to be made deterministically. However, perinatal data linkage for the period 1 January 2004 to 30 June 2007 is incomplete and does not include births in private facilities.
- Congenital abnormalities data were available from 1 July 2007.
- Emergency presentations were available from 1 July 2008.

As a result, there may be some sepsis-related deaths occurring pre 2007 that the study was unable to identify.

Study cases and screening

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[13] Since sepsis results from underlying infection, it is inherently an intermediate cause of death. In some cases, another condition might contribute to the infection (e.g. diabetes mellitus).

All infant and child deaths where infectious disease with the possibility of resulting in sepsis played a causal or contributory role in the death (without an accompanying organ dysfunction code) were identified. From this large cohort (1204 deaths), two mutually exclusive sepsis groups were identified, based on mortality and morbidity codes.

Explicit sepsis—cases with an ICD-10 code referencing sepsis explicitly, listed as either the underlying, chain (immediate or intermediate) cause of death or an ICD-10AM principal or other diagnosis code refencing sepsis explicitly, in the final hospital admission resulting in death.

Implicit sepsis—cases with an ICD-10 code referencing infection listed as either the underlying, chain or contributing cause of death and at least one ICD-10 code or a key term for which an ICD-10 code does not exist (e.g., multiple organ failure) referencing organ dysfunction listed as a chain cause of death OR an ICD-10AM principal or other diagnosis code referencing organ dysfunction, in the final hospital admission resulting in death.

For children who experienced multiple transfers and/or changes in care status in one continuous episode of care, morbidity data for the entire episode of care was used.

The number of sepsis deaths reported in this study is based on both explicit and implicit cases, identified through either cause of death information contained in the Queensland Child Death Register or linked hospital admission data obtained from the Queensland Hospital Admitted Patient Data Collection.

Explicit and implicit sepsis codes

To identify explicit and implicit sepsis we used ICD-10 codes identified as comprising explicit and implied sepsis in previous studies by the Global Burden of Disease (GBD) Study collaborators[11] as well as the modified GBD codes list used in Thompson and colleagues'[73] study of sepsis hospitalisations in older adults in Australia. These codes were independently reviewed by study investigators with clinical expertise in the management of critical illness in paediatric patients and clinical coding. Additional advice was provided by a clinical coding specialist. Inclusion or exclusion was determined by discussion and consensus.

Upon review, the GBD Study explicit sepsis codes were found to include a number of non-specific infection codes, which, in isolation from evidence of organ dysfunction may or may not represent sepsis (e.g. A02.9, Salmonella infection, unspecified). Such codes are more appropriately included as implied sepsis (if an organ dysfunction code was also present). A small number of explicit codes were excluded as they represented conditions that either do not present clinically as sepsis (e.g. O91.0, Infection of nipple associated with childbirth) or do not relate to paediatric patients (e.g., N98.0, Infection associated with artificial insemination). Likewise, several implicit codes produced by the GBD Study were excluded due to representing non-infectious conditions (e.g. N15.0, Balkan nephropathy) or being more appropriately included as an organ dysfunction code (e.g. I74, Arterial embolism and thrombosis).

The GBD study organ dysfunction codes were found to include a number of codes related to chronic rather than acute dysfunction (e.g., J96.1, Chronic respiratory failure), as well as codes used for specific conditions unrelated to sepsis (e.g., N00.6, Acute nephritic syndrome). In addition, GBD Study organ dysfunction codes were found to be insufficient to capture some of the most common terms related to organ dysfunction used in cause of death certification. For example, there is no specific ICD-10 code for multiple organ failure, with this terminal dysfunction receiving the codes R99, Other ill-defined and unspecified causes of mortality, R68.8, Other specified general symptoms and signs, or in infants aged less than 28 days, P96.8, Other unspecified conditions.

Agreement testing was undertaken to determine the degree of concordance between the modified GBD Study codes lists developed by Thompson and colleagues[73] and those proposed for use in this study. As the study populations were markedly different, with Thompson et al focusing on older adults and the present study to focus on infants and children, perinatal codes were removed from this analysis to enable comparability of results. Overall, there was 89.4 per cent agreement, comprising 95.6 per cent agreement as between explicit sepsis codes lists, 89.2 per cent agreement between implied sepsis codes lists and 82.5. per cent agreement between organ dysfunction codes lists. This suggests that modification to the GBD Study explicit and implied sepsis codes lists is appropriate in the Australian context specifically, and developed countries more generally, where underestimation of the disease burden is less common due to the use of specialist clinical coders. Coded data quality has been shown to be impacted by physician documentation and clinical coder training, both of which are known to be more limited in developing countries.[85] However, the lower levels of agreement in organ dysfunctions codes points to the problematic nature of coding terminal organ dysfunction.

The ICD-10 codes and key terms to be used for the identification of explicit sepsis and the source of infection and organ dysfunction (implied sepsis) are listed in Appendix 2.

Identifying additional cases of sepsis

Autopsy reports for reportable child deaths under the *Coroners Act 2003* were individually reviewed to

identify additional cases where sepsis was noted in the autopsy findings, but not recorded in the chain causes of death.

Inclusion and exclusion criteria

The study cohort included infants and children aged birth to 17 years who died from a sepsis in Queensland. Cases of sepsis (explicit and implied) were identified based on the presence of ICD-10 codes or key terms as listed in Appendix 2.

Deaths were further distinguished as either 'neonatal' or 'paediatric' sepsis.

Neonatal sepsis—deaths of newborn infants that occur in hospital following birth.

Paediatric sepsis—deaths of infants and children (0–17 years) who have been discharged from hospital following birth.

Cases of neonatal sepsis were only included in analysis of the total burden of child deaths due to sepsis, and trends over time.

Explanatory variables

The study investigated socio-demographic factors, location of death, factors related to the child's health status and the clinical presentation of the deceased. Specific details about a number of variables that are not straightforward in definition are provided below.

Indigenous status

Historically, the identification of Indigenous status on death registration forms was often incomplete or inaccurate, leading to an undercount of the numbers of deaths of Aboriginal and Torres Strait Islander people. The identification of the deaths of Indigenous people has improved considerably in recent years; however, the extent of any continued under-reporting is unknown, and it is likely some undercount of the number of deaths registered as Aboriginal and Torres Strait Islander continues.

The Child Death Register records Aboriginal and Torres Strait Islander status as noted in the derived birth registration and death registration data, in coronial data and in other official records. There are instances of inconsistent reporting of Aboriginal and Torres Strait Islander status across official records. The QFCC uses a guideline to determine which status will be recorded within the Register.

The Queensland Paediatric Sepsis Mortality Study dataset also contained variables recording Indigenous status from the linked data sources used in the study. The multistage algorithm proposed by the 'Getting our Story Right' cross agency data linkage project (GOSR algorithm)[86] was applied to the linked data. This combined a child's Indigenous statuses within and between collections to determine their overall Indigenous status. The application of this algorithm has been used in previous studies of infant and child mortality in Queensland,[87,88] and has been shown to identify Aboriginal and Torres Strait Islander child deaths more accurately.[87]

Geographic location

The Accessibility/Remoteness Index of Australia (ARIA+) which divides Australia into classes of remoteness based on relative access to goods and services, including healthcare, was used to assess and report a child's geographic location.[89] For the purposes of analysis, geographic location was grouped into four areas: major cities, inner regional areas, outer regional areas, and remote and very remote areas.

Socio-economic status

The socio-economic status of the area in which a child was living at the time of death was classified using the Socio-Economic Indexes for Areas (SEIFA)–Index of Relative Socioeconomic Advantage and Disadvantage.[90] For analysis, areas were grouped as high and very high, moderate, and low and very low socio-economic status.

Medical complexity

A modified version of the Paediatric Medical Complexity Algorithm (PMCA), version 3.0[91,92] was applied to the coded morbidity and mortality data from the linked data sources used in this study. The PMCA classifies children into three levels of medical complexity.

Children with chronic complex disease—includes children with significant chronic conditions in two or more body systems OR a progressive condition that is associated with deteriorating health with a decreased life expectancy in adulthood OR continuous dependence on technology for at least 6 months OR progressive or metastatic malignancies that affect life function.

Children with non-complex chronic disease—includes persistent conditions involving a single body system, that are not progressive.

Children without chronic disease—includes children with acute non-chronic conditions and healthy children with no acute or chronic health conditions.

The paediatric complex chronic conditions (CCC) classification system,[42] was used to classify children with complex chronic conditions into ten categories: neurological/neuromuscular, cardiovascular, respiratory, renal, gastrointestinal, hematologic/immunologic, metabolic, other congenital or genetic defect (chromosomal abnormalities, bone/joint abnormalities, diaphragm/abdominal abnormalities, other abnormalities), malignancy, and transplantation.

Death location

Deaths were classified as occurring either in hospital or community settings (such as at home or during transport to a medical facility). Children who arrived at hospital moribund were classified as having died in a community setting as this is the environment the deterioration and/or initial collapse occurred.

Ethics approval

Ethical approval for this study was provided by the Children's Health Queensland Hospital and Health Service Human Research Ethics Committee (HREC/22/QCHQ/90900).

Data analysis

Univariable analysis was undertaken to examine the relationships between variables. Associations were assessed using chi-square for categorical, and t tests or Wilcoxon tests for continuous variables according to the normality of the distribution of the continuous variables. Quantification of the association between factors and Indigenous status was estimated by odds ratios determined by carrying out logistic regression. Statistical significance was defined at the 5 per cent level. Analyses were carried out in SAS (version 9.4; SAS Institute). Mortality rates were calculated using the number of live births in Queensland for infants (under 1 year) and estimated resident population data (ERP) for children aged 1–17 years.

Appendix 2: Codes list

ICD-10 Code	ICD-10 Descriptor
Explicit Sepsis	
A02.1	Salmonella sepsis
A20.7	Septicaemic plague
A21.7	Generalized tularaemia (incl. tularemia sepsis)
A22.7	Anthrax sepsis
A24.1	Acute and fulminating melioidosis
A26.7	Erysipelothrix sepsis
A32.7	Listerial sepsis
A39.1	Waterhouse-Friderichsen syndrome
A39.2	Acute meningococcaemia
A39.4	Meningococcaemia, unspecified
A40.0	Sepsis due to streptococcus, group A
A40.1	Sepsis due to streptococcus, group B
A40.2	Sepsis due to streptococcus, group D and enterococcus
A40.3	Sepsis due to Streptococcus pneumoniae
A40.8	Other streptococcal sepsis
A40.9	Streptococcal sepsis, unspecified
A41.0	Sepsis due to Staphylococcus aureus
A41.1	Sepsis due to other specified staphylococcus
A41.2	Sepsis due to unspecified staphylococcus
A41.3	Sepsis due to Haemophilus influenzae
A41.4	Sepsis due to anaerobes
A41.5	Sepsis due to other Gram-negative organisms
A41.8	Other specified sepsis
A41.9	Sepsis, unspecified
A42.7	Actinomycotic sepsis
A48.0	Gas gangrene
A48.3	Toxic shock syndrome
A48.4	Brazilian purpuric fever
A98.4	Ebola virus disease
A98.5	Haemorrhagic fever with renal syndrome
B00.7	Disseminated herpesviral disease
B33.4	Hantavirus (cardio-)pulmonary syndrome [HPS] [HCPS]
B37.7	Candidal sepsis
B50.0	Plasmodium falciparum malaria with cerebral complications
B50.8	Other severe and complicated Plasmodium falciparum malaria
O85	Puerperal sepsis
O88.3	Obstetric pyaemic and septic embolism
P36.0	Sepsis of newborn due to streptococcus, group B
P36.1	Sepsis of newborn due to other and unspecified streptococci
P36.2	Sepsis of newborn due to Staphylococcus aureus
P36.3	Sepsis of newborn due to other and unspecified staphylococci
P36.4	Sepsis of newborn due to Escherichia coli
P36.5	Sepsis of newborn due to anaerobes
P36.8	Other bacterial sepsis of newborn
P36.9	Bacterial sepsis of newborn, unspecified
R57.2	Septic shock
R65.1	Systemic Inflammatory Response Syndrome of infectious origin with organ failure (severe sepsis)
Implied sepsis	
A00.0	Cholera due to Vibrio cholerae 01, biovar cholerae
A00.1	Cholera due to Vibrio cholerae 01, biovar eltor
A00.9	Cholera, unspecified
A01.0	Typhoid fever
A01.1	Paratyphoid fever A
A01.2	Paratyphoid fever B
A01.3	Paratyphoid fever C
A01.4	Paratyphoid fever, unspecified
A02.0	Salmonella enteritis
A02.2	Localised salmonella infections
A02.8	Other specified salmonella infections
A02.9	Salmonella infection, unspecified
A03.0	Shigellosis due to Shigella dysenteriae
A03.1	Shigellosis due to Shigella flexneri
A03.2	Shigellosis due to Shigella boydii
A03.3	Shigellosis due to Shigella sonnei
A03.8	Other shigellosis
A03.9	Shigellosis, unspecified
A04.0	Enteropathogenic Escherichia coli infection
A04.1	Enterotoxigenic Escherichia coli infection
A04.2	Enteroinvasive Escherichia coli infection
A04.3	Enterohaemorrhagic Escherichia coli infection
A04.4	Other intestinal Escherichia coli infections
A04.5	Campylobacter enteritis
A04.6	Enteritis due to Yersinia enterocolitica
A04.7	Enterocolitis due to Clostridium difficile
A04.8	Other specified bacterial intestinal infections
A04.9	Bacterial intestinal infection, unspecified
A05.0	Foodborne staphylococcal intoxication
A05.1	Botulism
A05.2	Foodborne Clostridium perfringens [Clostridium welchii] intoxication
A05.3	Foodborne Vibrio parahaemolyticus intoxication
A05.4	Foodborne Bacillus cereus intoxication
A05.8	Other specified bacterial foodborne intoxications
A05.9	Bacterial foodborne intoxication, unspecified
A06.0	Acute amoebic dysentery
A06.1	Chronic intestinal amoebiasis
A06.2	Amoebic nondysenteric colitis
A06.3	Amoeboma of intestine
A06.4	Amoebic liver abscess
A06.5	Amoebic lung abscess
A06.6	Amoebic brain abscess
A06.7	Cutaneous amoebiasis
A06.8	Amoebic infection of other sites
A06.9	Amoebiasis, unspecified
A07.0	Balantidiasis
A07.1	Giardiasis [lambliasis]
A07.2	Cryptosporidiosis
A07.3	Isosporiasis
A07.8	Other specified protozoal intestinal diseases
A07.9	Protozoal intestinal disease, unspecified
A08.0	Rotaviral enteritis
A08.1	Acute gastroenteropathy due to Norovirus
A08.2	Adenoviral enteritis
A08.3	Other viral enteritis
A08.4	Viral intestinal infection, unspecified
A08.5	Other specified intestinal infections
A09.0	Other and unspecified gastroenteritis and colitis of infectious origin
A09.9	Gastroenteritis and colitis of unspecified origin
A19.0	Acute miliary tuberculosis of a single specified site

ICD-10 Code	ICD-10 Descriptor
A19.1	Acute miliary tuberculosis of multiple sites
A19.2	Acute miliary tuberculosis, unspecified
A19.8	Other miliary tuberculosis
A19.9	Miliary tuberculosis, unspecified
A20.0	Bubonic plague
A20.1	Cellulocutaneous plague
A20.2	Pneumonic plague
A20.3	Plague meningitis
A20.8	Other forms of plague
A20.9	Plague, unspecified
A21.0	Ulceroglandular tularaemia
A21.1	Oculoglandular tularaemia
A21.2	Pulmonary tularaemia
A21.3	Gastrointestinal tularaemia
A21.8	Other forms of tularaemia
A21.9	Tularaemia, unspecified
A22.0	Cutaneous anthrax
A22.1	Pulmonary anthrax
A22.2	Gastrointestinal anthrax
A22.8	Other forms of anthrax
A22.9	Anthrax, unspecified
A23.0	Brucellosis due to Brucella melitensis
A23.1	Brucellosis due to Brucella abortus
A23.2	Brucellosis due to Brucella suis
A23.3	Brucellosis due to Brucella canis
A23.8	Other brucellosis
A23.9	Brucellosis, unspecified
A24.0	Glanders
A24.2	Subacute and chronic melioidosis
A24.3	Other melioidosis
A24.4	Melioidosis, unspecified
A25.0	Spirillosis
A25.1	Streptobacillosis
A25.9	Rat-bite fever, unspecified
A26.0	Cutaneous erysipeloid
A26.8	Other forms of erysipeloid
A26.9	Erysipeloid, unspecified
A27.0	Leptospirosis icterohaemorrhagica
A27.8	Other forms of leptospirosis
A27.9	Leptospirosis, unspecified
A28.0	Pasteurellosis
A28.1	Cat-scratch disease
A28.2	Extraintestinal yersiniosis
A28.8	Other specified zoonotic bacterial diseases, not elsewhere classified
A28.9	Zoonotic bacterial disease, unspecified
A31.0	Pulmonary mycobacterial infection
A31.1	Cutaneous mycobacterial infection
A31.8	Other mycobacterial infections
A31.9	Mycobacterial infection, unspecified
A32.0	Cutaneous listeriosis
A32.1	Listerial meningitis and meningoencephalitis
A32.8	Other forms of listeriosis
A32.9	Listeriosis, unspecified
A36.0	Pharyngeal diphtheria
A36.1	Nasopharyngeal diphtheria
A36.2	Laryngeal diphtheria
A36.3	Cutaneous diphtheria
A36.8	Other diphtheria
A36.9	Diphtheria, unspecified
A37.0	Whooping cough due to Bordetella pertussis
A37.1	Whooping cough due to Bordetella parapertussis
A37.8	Whooping cough due to other Bordetella species
A37.9	Whooping cough, unspecified
A38	Scarlet fever

ICD-10 Code	ICD-10 Descriptor
A39.0	Meningococcal meningitis
A39.5	Meningococcal heart disease
A39.8	Other meningococcal infections
A39.9	Meningococcal infection, unspecified
A43.0	Pulmonary nocardiosis
A43.1	Cutaneous nocardiosis
A43.8	Other forms of nocardiosis
A43.9	Nocardiosis, unspecified
A44.0	Systemic bartonellosis
A44.1	Cutaneous and mucocutaneous bartonellosis
A44.8	Other forms of bartonellosis
A44.9	Bartonellosis, unspecified
A46	Erysipelas
A48.1	Legionnaires disease
A48.2	Nonpneumonic Legionnaires disease [Pontiac fever]
A48.8	Other specified bacterial diseases
A49.0	Staphylococcal infection, unspecified site
A49.1	Streptococcal infection and enterococcal infection, unspecified site
A49.2	Haemophilus influenzae infection, unspecified site
A49.3	Mycoplasma infection, unspecified site
A49.8	Other bacterial infections of unspecified site
A49.9	Bacterial infection, unspecified
A50.0	Early congenital syphilis, symptomatic
A50.1	Early congenital syphilis, latent
A50.2	Early congenital syphilis, unspecified
A50.9	Congenital syphilis, unspecified
A54.8	Other gonococcal infections
A65	Nonvenereal syphilis
A69.0	Necrotizing ulcerative stomatitis
A69.1	Other Vincent infections
A69.9	Spirochaetal infection, unspecified
A74.8	Other chlamydial diseases
A74.9	Chlamydial infection, unspecified
A75.0	Epidemic louse-borne typhus fever due to Rickettsia prowazekii
A75.1	Recrudescent typhus [Brill disease]
A75.2	Typhus fever due to Rickettsia typhi
A75.3	Typhus fever due to Rickettsia tsutsugamushi
A75.9	Typhus fever, unspecified
A77.0	Spotted fever due to Rickettsia rickettsii
A77.1	Spotted fever due to Rickettsia conorii
A77.2	Spotted fever due to Rickettsia sibirica
A77.3	Spotted fever due to Rickettsia australis
A77.8	Other spotted fevers
A77.9	Spotted fever, unspecified
A78	Q fever
A79.0	Trench fever
A79.1	Rickettsialpox due to Rickettsia akari
A79.8	Other specified rickettsioses
A79.9	Rickettsiosis, unspecified
A80.0	Acute paralytic poliomyelitis, vaccine-associated
A80.1	Acute paralytic poliomyelitis, wild virus, imported
A80.2	Acute paralytic poliomyelitis, wild virus, indigenous
A80.3	Acute paralytic poliomyelitis, other and unspecified
A80.4	Acute nonparalytic poliomyelitis
A80.9	Acute poliomyelitis, unspecified
A81.0	Creutzfeldt-Jakob disease
A81.2	Progressive multifocal leukoencephalopathy
A81.8	Other atypical virus infections of central nervous system
A81.9	Atypical virus infection of central nervous system, unspecified
A83.0	Japanese encephalitis
A83.1	Western equine encephalitis

ICD-10 Code	ICD-10 Descriptor
A83.2	Eastern equine encephalitis
A83.3	St Louis encephalitis
A83.4	Australian encephalitis
A83.5	California encephalitis
A83.6	Rocio virus disease
A83.8	Other mosquito-borne viral encephalitis
A83.9	Mosquito-borne viral encephalitis, unspecified
A84.0	Far Eastern tick-borne encephalitis [Russian spring-summer encephalitis]
A84.1	Central European tick-borne encephalitis
A84.8	Other tick-borne viral encephalitis
A84.9	Tick-borne viral encephalitis, unspecified
A85.0	Enteroviral encephalitis
A85.1	Adenoviral encephalitis
A85.2	Arthropod-borne viral encephalitis, unspecified
A85.8	Other specified viral encephalitis
A86	Unspecified viral encephalitis
A87.0	Enteroviral meningitis
A87.1	Adenoviral meningitis
A87.2	Lymphocytic choriomeningitis
A87.8	Other viral meningitis
A87.9	Viral meningitis, unspecified
A88.8	Other specified viral infections of central nervous system
A89	Unspecified viral infection of central nervous system
A92.0	Chikungunya virus disease
A92.1	O'nyong-nyong fever
A92.2	Venezuelan equine fever
A92.3	West Nile virus infection
A92.4	Rift Valley fever
A92.5	Zika virus disease
A92.8	Other specified mosquito-borne viral fevers
A92.9	Mosquito-borne viral fever, unspecified
A93.0	Oropouche virus disease
A93.1	Sandfly fever
A93.2	Colorado tick fever
A93.8	Other specified arthropod-borne viral fevers
A94	Unspecified arthropod-borne viral fever
A95.0	Sylvatic yellow fever
A95.1	Urban yellow fever
A95.9	Yellow fever, unspecified
A96.0	Junin haemorrhagic fever
A96.1	Machupo haemorrhagic fever
A96.2	Lassa fever
A96.8	Other arenaviral haemorrhagic fevers
A96.9	Arenaviral haemorrhagic fever, unspecified
A97.0	Dengue without warning signs
A97.1	Dengue with warning signs
A97.2	Severe Dengue
A97.9	Dengue, unspecified
A98.0	Crimean-Congo haemorrhagic fever
A98.1	Omsk haemorrhagic fever
A98.2	Kyasanur Forest disease
A98.3	Marburg virus disease
A98.8	Other specified viral haemorrhagic fevers
A99	Unspecified viral haemorrhagic fever
B00.0	Eczema herpeticum
B00.1	Herpesviral vesicular dermatitis
B00.2	Herpesviral gingivostomatitis and pharyngotonsillitis
B00.3	Herpesviral meningitis
B00.4	Herpesviral encephalitis
B00.5	Herpesviral ocular disease
B00.8	Other forms of herpesviral infection
B00.9	Herpesviral infection, unspecified
B01.0	Varicella meningitis

ICD-10 Code	ICD-10 Descriptor
B01.1	Varicella encephalitis
B01.2	Varicella pneumonia
B01.8	Varicella with other complications
B01.9	Varicella without complication
B02.0	Zoster encephalitis
B02.1	Zoster meningitis
B02.2	Zoster with other nervous system involvement
B02.3	Zoster ocular disease
B02.7	Disseminated zoster
B02.8	Zoster with other complications
B02.9	Zoster without complication
B03	Smallpox
B04	Monkeypox
B05.0	Measles complicated by encephalitis
B05.1	Measles complicated by meningitis
B05.2	Measles complicated by pneumonia
B05.3	Measles complicated by otitis media
B05.4	Measles with intestinal complications
B05.8	Measles with other complications
B05.9	Measles without complication
B06.0	Rubella with neurological complications
B06.8	Rubella with other complications
B06.9	Rubella without complication
B08.0	Other orthopoxvirus infections
B08.2	Exanthema subitum [sixth disease]
B08.3	Erythema infectiosum [fifth disease]
B08.4	Enteroviral vesicular stomatitis with exanthem
B08.5	Enteroviral vesicular pharyngitis
B08.8	Other specified viral infections characterized by skin and mucous membrane lesions
B09	Unspecified viral infection characterized by skin and mucous membrane lesions
B25.0	Cytomegaloviral pneumonitis
B25.1	Cytomegaloviral hepatitis
B25.2	Cytomegaloviral pancreatitis
B25.8	Other cytomegaloviral diseases
B25.9	Cytomegaloviral disease, unspecified
B26.0	Mumps orchitis
B26.1	Mumps meningitis
B26.2	Mumps encephalitis
B26.3	Mumps pancreatitis
B26.8	Mumps with other complications
B27.0	Gammaherpesviral mononucleosis
B27.1	Cytomegaloviral mononucleosis
B27.8	Other infectious mononucleosis
B27.9	Infectious mononucleosis, unspecified
B33.0	Epidemic myalgia
B33.1	Ross River disease
B33.2	Viral carditis
B33.3	Retrovirus infections, not elsewhere classified
B33.8	Other specified viral diseases
B34.0	Adenovirus infection, unspecified site
B34.1	Enterovirus infection, unspecified site
B34.2	Coronavirus infection, unspecified site
B34.3	Parvovirus infection, unspecified site
B34.4	Papovavirus infection, unspecified site
B34.8	Other viral infections of unspecified site
B34.9	Viral infection, unspecified
B37.0	Candidal stomatitis
B37.1	Pulmonary candidiasis
B37.2	Candidiasis of skin and nail
B37.3	Candidiasis of vulva and vagina
B37.4	Candidiasis of other urogenital sites
B37.5	Candidal meningitis
B37.6	Candidal endocarditis

ICD-10 Code	ICD-10 Descriptor
B37.8	Candidiasis of other sites
B37.9	Candidiasis, unspecified
B38.0	Acute pulmonary coccidioidomycosis
B38.2	Pulmonary coccidioidomycosis, unspecified
B38.3	Cutaneous coccidioidomycosis
B38.4	Coccidioidomycosis meningitis
B38.7	Disseminated coccidioidomycosis
B38.8	Other forms of coccidioidomycosis
B38.9	Coccidioidomycosis, unspecified
B39.0	Acute pulmonary histoplasmosis capsulati
B39.2	Pulmonary histoplasmosis capsulati, unspecified
B39.3	Disseminated histoplasmosis capsulati
B39.4	Histoplasmosis capsulati, unspecified
B39.5	Histoplasmosis duboisii
B39.9	Histoplasmosis, unspecified
B40.0	Acute pulmonary blastomycosis
B40.2	Pulmonary blastomycosis, unspecified
B40.3	Cutaneous blastomycosis
B40.7	Disseminated blastomycosis
B40.8	Other forms of blastomycosis
B40.9	Blastomycosis, unspecified
B41.0	Pulmonary paracoccidioidomycosis
B41.7	Disseminated paracoccidioidomycosis
B41.8	Other forms of paracoccidioidomycosis
B41.9	Paracoccidioidomycosis, unspecified
B42.0	Pulmonary sporotrichosis
B42.1	Lymphocutaneous sporotrichosis
B42.7	Disseminated sporotrichosis
B42.8	Other forms of sporotrichosis
B42.9	Sporotrichosis, unspecified
B43.0	Cutaneous chromomycosis
B43.1	Phaeomycotic brain abscess
B43.2	Subcutaneous phaeomycotic abscess and cyst
B43.8	Other forms of chromomycosis
B43.9	Chromomycosis, unspecified
B44.0	Invasive pulmonary aspergillosis
B44.1	Other pulmonary aspergillosis
B44.2	Tonsillar aspergillosis
B44.7	Disseminated aspergillosis
B44.8	Other forms of aspergillosis
B44.9	Aspergillosis, unspecified
B45.0	Pulmonary cryptococcosis
B45.1	Cerebral cryptococcosis
B45.2	Cutaneous cryptococcosis
B45.3	Osseous cryptococcosis
B45.7	Disseminated cryptococcosis
B45.8	Other forms of cryptococcosis
B45.9	Cryptococcosis, unspecified
B46.0	Pulmonary mucormycosis
B46.1	Rhinocerebral mucormycosis
B46.2	Gastrointestinal mucormycosis
B46.3	Cutaneous mucormycosis
B46.4	Disseminated mucormycosis
B46.5	Mucormycosis, unspecified
B46.8	Other zygomycoses
B46.9	Zygomycosis, unspecified
B48.0	Lobomycosis
B48.1	Rhinosporidiosis
B48.2	Allescheriasis
B48.3	Geotrichosis
B48.4	Penicillosis
B48.7	Opportunistic mycoses
B48.8	Other specified mycoses
B49	Unspecified mycosis
B50.9	Plasmodium falciparum malaria, unspecified

ICD-10 Code	ICD-10 Descriptor
B54	Unspecified malaria
B55.0	Visceral leishmaniasis
B55.1	Cutaneous leishmaniasis
B55.2	Mucocutaneous leishmaniasis
B55.9	Leishmaniasis, unspecified
B58.0	Toxoplasma oculopathy
B58.1	Toxoplasma hepatitis
B58.2	Toxoplasma meningoencephalitis
B58.3	Pulmonary toxoplasmosis
B58.8	Toxoplasmosis with other organ involvement
B58.9	Toxoplasmosis, unspecified
B60.0	Babesiosis
B60.1	Acanthamoebiasis
B60.2	Naegleriasis
B60.8	Other specified protozoal diseases
B64	Unspecified protozoal disease
B95.0	Streptococcus, group A, as the cause of diseases classified to other chapters
B95.1	Streptococcus, group B, as the cause of diseases classified to other chapters
B95.2	Streptococcus, group D, as the cause of diseases classified to other chapters
B95.3	Streptococcus pneumoniae as the cause of diseases classified to other chapters
B95.4	Other streptococcus as the cause of diseases classified to other chapters
B95.5	Unspecified streptococcus as the cause of diseases classified to other chapters
B95.6	Staphylococcus aureus as the cause of diseases classified to other chapters
B95.7	Other staphylococcus as the cause of diseases classified to other chapters
B95.8	Unspecified staphylococcus as the cause of diseases classified to other chapters
B96.0	Mycoplasma pneumoniae [M. pneumoniae] as the cause of diseases classified to other chapters
B96.1	Klebsiella pneumoniae [K. pneumoniae] as the cause of diseases classified to other chapters
B96.2	Escherichia coli [E. coli] as the cause of diseases classified to other chapters
B96.3	Haemophilus influenzae [H. influenzae] as the cause of diseases classified to other chapters
B96.4	Proteus (mirabilis)(morganii) as the cause of diseases classified to other chapters
B96.5	Pseudomonas (aeruginosa) as the cause of diseases classified to other chapters
B96.6	Bacillus fragilis [B. fragilis] as the cause of diseases classified to other chapters
B96.7	Clostridium perfringens [C. perfringens] as the cause of diseases classified to other chapters
B96.8	Other specified bacterial agents as the cause of diseases classified to other chapters
B97.0	Adenovirus as the cause of diseases classified to other chapters
B97.1	Enterovirus as the cause of diseases classified to other chapters
B97.2	Coronavirus as the cause of diseases classified to other chapters
B97.3	Retrovirus as the cause of diseases classified to other chapters
B97.4	Respiratory syncytial virus as the cause of diseases classified to other chapters
B97.5	Reovirus as the cause of diseases classified to other chapters
B97.6	Parvovirus as the cause of diseases classified to other chapters

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ICD-10 Code	ICD-10 Descriptor
B97.7	Papillomavirus as the cause of diseases classified to other chapters
B97.8	Other viral agents as the cause of diseases classified to other chapters
B98.0	Helicobacter pylori [H.pylori] as the cause of diseases classified to other chapters
B98.1	Vibrio vulnificus as the cause of diseases classified to other chapters
B99	Other and unspecified infectious diseases
G00.0	Haemophilus meningitis
G00.1	Pneumococcal meningitis
G00.2	Streptococcal meningitis
G00.3	Staphylococcal meningitis
G00.8	Other bacterial meningitis
G00.9	Bacterial meningitis, unspecified
G01	Meningitis in bacterial diseases classified elsewhere
G02.0	Meningitis in viral diseases classified elsewhere
G02.1	Meningitis in mycoses
G02.8	Meningitis in other specified infectious and parasitic diseases classified elsewhere
G03.0	Nonpyogenic meningitis
G03.1	Chronic meningitis
G03.8	Meningitis due to other specified causes
G03.9	Meningitis, unspecified
G04.0	Acute disseminated encephalitis
G04.1	Human T-cell lymphotropic virus associated myelopathy
G04.2	Bacterial meningoencephalitis and meningomyelitis, not elsewhere classified
G04.8	Other encephalitis, myelitis and encephalomyelitis
G04.9	Encephalitis, myelitis and encephalomyelitis, unspecified
G05.0	Encephalitis, myelitis and encephalomyelitis in bacterial diseases classified elsewhere
G05.1	Encephalitis, myelitis and encephalomyelitis in viral diseases classified elsewhere
G05.2	Encephalitis, myelitis and encephalomyelitis in other infectious and parasitic diseases classified elsewhere
G05.8	Encephalitis, myelitis and encephalomyelitis in other diseases classified elsewhere
G06.0	Intracranial abscess and granuloma
G06.1	Intraspinal abscess and granuloma
G06.2	Extradural and subdural abscess, unspecified
G07	Intracranial and intraspinal abscess and granuloma in diseases classified elsewhere
G08	Intracranial and intraspinal phlebitis and thrombophlebitis
H05.0	Acute inflammation of orbit
H60.2	Malignant otitis externa
H70.0	Acute mastoiditis
I00	Rheumatic fever without mention of heart involvement
I01.1	Acute rheumatic endocarditis
I26.0	Pulmonary embolism with mention of acute cor pulmonale
I33.0	Acute and subacute infective endocarditis
I33.9	Acute endocarditis, unspecified
I38	Endocarditis, valve unspecified
I39.0	Mitral valve disorders in diseases classified elsewhere
I39.1	Aortic valve disorders in diseases classified elsewhere
I39.2	Tricuspid valve disorders in diseases classified elsewhere
I39.3	Pulmonary valve disorders in diseases classified elsewhere
I39.4	Multiple valve disorders in diseases classified elsewhere
I39.8	Endocarditis, valve unspecified, in diseases classified elsewhere
I40.0	Infective myocarditis
I40.1	Isolated myocarditis
I40.8	Other acute myocarditis
I40.9	Acute myocarditis, unspecified
I98.1	Cardiovascular disorders in other infectious and parasitic diseases classified elsewhere
J01.0	Acute maxillary sinusitis
J01.1	Acute frontal sinusitis
J01.2	Acute ethmoidal sinusitis
J01.3	Acute sphenoidal sinusitis
J01.4	Acute pansinusitis
J01.8	Other acute sinusitis
J01.9	Acute sinusitis, unspecified
J02.0	Streptococcal pharyngitis
J02.8	Acute pharyngitis due to other specified organisms
J02.9	Acute pharyngitis, unspecified
J03.0	Streptococcal tonsillitis
J03.8	Acute tonsillitis due to other specified organisms
J03.9	Acute tonsillitis, unspecified
J04.0	Acute laryngitis
J04.1	Acute tracheitis
J04.2	Acute laryngotracheitis
J05.0	Acute obstructive laryngitis [croup]
J05.1	Acute epiglottitis
J06.0	Acute laryngopharyngitis
J06.8	Other acute upper respiratory infections of multiple sites
J06.9	Acute upper respiratory infection, unspecified
J09	Influenza due to identified zoonotic or pandemic influenza virus
J10.0	Influenza with pneumonia, seasonal influenza virus identified
J10.1	Influenza with other respiratory manifestations, seasonal influenza virus identified
J10.8	Influenza with other manifestations, seasonal influenza virus identified
J11.0	Influenza with pneumonia, virus not identified
J11.1	Influenza with other respiratory manifestations, virus not identified
J11.8	Influenza with other manifestations, virus not identified
J12.0	Adenoviral pneumonia
J12.1	Respiratory syncytial virus pneumonia
J12.2	Parainfluenza virus pneumonia
J12.3	Human metapneumovirus pneumonia
J12.8	Other viral pneumonia
J12.9	Viral pneumonia, unspecified
J13	Pneumonia due to Streptococcus pneumoniae
J14	Pneumonia due to Haemophilus influenzae
J15.0	Pneumonia due to Klebsiella pneumoniae
J15.1	Pneumonia due to Pseudomonas
J15.2	Pneumonia due to staphylococcus
J15.3	Pneumonia due to streptococcus, group B
J15.4	Pneumonia due to other streptococci
J15.5	Pneumonia due to Escherichia coli
J15.6	Pneumonia due to other Gram-negative bacteria
J15.7	Pneumonia due to Mycoplasma pneumoniae
J15.8	Other bacterial pneumonia
J15.9	Bacterial pneumonia, unspecified
J16.0	Chlamydial pneumonia

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J16.8	Pneumonia due to other specified infectious organisms
J17.0	Pneumonia in bacterial diseases classified elsewhere
J17.1	Pneumonia in viral diseases classified elsewhere
J17.2	Pneumonia in mycoses
J17.3	Pneumonia in parasitic diseases
J17.8	Pneumonia in other diseases classified elsewhere
J18.0	Bronchopneumonia, unspecified
J18.1	Lobar pneumonia, unspecified
J18.2	Hypostatic pneumonia, unspecified
J18.8	Other pneumonia, organism unspecified
J18.9	Pneumonia, unspecified
J20.0	Acute bronchitis due to Mycoplasma pneumoniae
J20.1	Acute bronchitis due to Haemophilus influenzae
J20.2	Acute bronchitis due to streptococcus
J20.3	Acute bronchitis due to coxsackievirus
J20.4	Acute bronchitis due to parainfluenza virus
J20.5	Acute bronchitis due to respiratory syncytial virus
J20.6	Acute bronchitis due to rhinovirus
J20.7	Acute bronchitis due to echovirus
J20.8	Acute bronchitis due to other specified organisms
J20.9	Acute bronchitis, unspecified
J21.0	Acute bronchiolitis due to respiratory syncytial virus
J21.1	Acute bronchiolitis due to human metapneumovirus
J21.8	Acute bronchiolitis due to other specified organisms
J21.9	Acute bronchiolitis, unspecified
J22	Unspecified acute lower respiratory infection
J36	Peritonsillar abscess
J39.0	Retropharyngeal and parapharyngeal abscess
J39.1	Other abscess of pharynx
J85.0	Gangrene and necrosis of lung
J85.1	Abscess of lung with pneumonia
J85.2	Abscess of lung without pneumonia
J85.3	Abscess of mediastinum
J86.0	Pyothorax with fistula
J86.9	Pyothorax without fistula
K35.2	Acute appendicitis with generalized peritonitis
K35.3	Acute appendicitis with localized peritonitis
K35.8	Acute appendicitis, other and unspecified
K36	Other appendicitis
K37	Unspecified appendicitis
K57.0	Diverticular disease of small intestine with perforation and abscess
K57.1	Diverticular disease of small intestine without perforation or abscess
K57.2	Diverticular disease of large intestine with perforation and abscess
K57.3	Diverticular disease of large intestine without perforation or abscess
K57.4	Diverticular disease of both small and large intestine with perforation and abscess
K57.5	Diverticular disease of both small and large intestine without perforation or abscess
K57.8	Diverticular disease of intestine, part unspecified, with perforation and abscess
K57.9	Diverticular disease of intestine, part unspecified, without perforation or abscess
K61.0	Anal abscess
K61.1	Rectal abscess
K61.2	Anorectal abscess
K61.3	Ischiorectal abscess
K61.4	Intrasphincteric abscess
K63.0	Abscess of intestine
K63.1	Perforation of intestine (nontraumatic)
K65.0	Acute peritonitis

ICD-10 Code	ICD-10 Descriptor
K65.8	Other peritonitis
K65.9	Peritonitis, unspecified
K67.8	Other disorders of peritoneum in infectious diseases classified elsewhere
K75.0	Abscess of liver
K75.1	Phlebitis of portal vein
K75.3	Granulomatous hepatitis, not elsewhere classified
K77.0	Liver disorders in infectious and parasitic diseases classified elsewhere
K81.0	Acute cholecystitis
K83.0	Cholangitis
L02.0	Cutaneous abscess, furuncle and carbuncle of face
L02.1	Cutaneous abscess, furuncle and carbuncle of neck
L02.2	Cutaneous abscess, furuncle and carbuncle of trunk
L02.3	Cutaneous abscess, furuncle and carbuncle of buttock
L02.4	Cutaneous abscess, furuncle and carbuncle of limb
L02.8	Cutaneous abscess, furuncle and carbuncle of other sites
L02.9	Cutaneous abscess, furuncle and carbuncle, unspecified
L03.0	Cellulitis of finger and toe
L03.1	Cellulitis of other parts of limb
L03.2	Cellulitis of face
L03.3	Cellulitis of trunk
L03.8	Cellulitis of other sites
L03.9	Cellulitis, unspecified
L04.0	Acute lymphadenitis of face, head and neck
L04.1	Acute lymphadenitis of trunk
L04.2	Acute lymphadenitis of upper limb
L04.3	Acute lymphadenitis of lower limb
L04.8	Acute lymphadenitis of other sites
L04.9	Acute lymphadenitis, unspecified
L05.0	Pilonidal cyst with abscess
L05.9	Pilonidal cyst without abscess
L08.0	Other local infections of skin and subcutaneous tissue
L08.1	Erythrasma
L08.8	Other specified local infections of skin and subcutaneous tissue
L08.9	Local infection of skin and subcutaneous tissue, unspecified
M00.0	Staphylococcal arthritis and polyarthritis
M00.1	Pneumococcal arthritis and polyarthritis
M00.2	Other streptococcal arthritis and polyarthritis
M00.8	Arthritis and polyarthritis due to other specified bacterial agents
M00.9	Pyogenic arthritis, unspecified
M01.0	Meningococcal arthritis
M01.1	Tuberculous arthritis
M01.2	Arthritis in Lyme disease
M01.3	Arthritis in other bacterial diseases classified elsewhere
M01.4	Rubella arthritis
M01.5	Arthritis in other viral diseases classified elsewhere
M01.6	Arthritis in mycoses
M01.8	Arthritis in other infectious and parasitic diseases classified elsewhere
M86.0	Acute haematogenous osteomyelitis
M86.1	Other acute osteomyelitis
M86.2	Subacute osteomyelitis
M86.3	Chronic multifocal osteomyelitis
M86.4	Chronic osteomyelitis with draining sinus
M86.5	Other chronic haematogenous osteomyelitis
M86.6	Other chronic osteomyelitis

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ICD-10 Code	ICD-10 Descriptor
M86.8	Other osteomyelitis
M86.9	Osteomyelitis, unspecified
N15.1	Renal and perinephric abscess
N30.0	Acute cystitis
N30.8	Other cystitis
N30.9	Cystitis, unspecified
N39.0	Urinary tract infection, site not specified
N41.0	Acute prostatitis
N41.2	Abscess of prostate
N41.3	Prostatocystitis
N45.0	Orchitis, epididymitis and epididymo-orchitis with abscess
N45.9	Orchitis, epididymitis and epididymo-orchitis without abscess
N70.0	Acute salpingitis and oophoritis
N70.1	Chronic salpingitis and oophoritis
N70.9	Salpingitis and oophoritis, unspecified
N71.0	Acute inflammatory disease of uterus
N71.1	Chronic inflammatory disease of uterus
N71.9	Inflammatory disease of uterus, unspecified
N72	Inflammatory disease of cervix uteri
N73.0	Acute parametritis and pelvic cellulitis
N73.1	Chronic parametritis and pelvic cellulitis
N73.2	Unspecified parametritis and pelvic cellulitis
N73.3	Female acute pelvic peritonitis
N73.4	Female chronic pelvic peritonitis
N73.5	Female pelvic peritonitis, unspecified
N73.6	Female pelvic peritoneal adhesions
N73.8	Other specified female pelvic inflammatory diseases
N73.9	Female pelvic inflammatory disease, unspecified
N74.0	Tuberculous infection of cervix uteri
N74.1	Female tuberculous pelvic inflammatory disease
N74.2	Female syphilitic pelvic inflammatory disease
N74.3	Female gonococcal pelvic inflammatory disease
N74.4	Female chlamydial pelvic inflammatory disease
N74.8	Female pelvic inflammatory disorders in other diseases classified elsewhere
N75.0	Cyst of Bartholin gland
N75.1	Abscess of Bartholin gland
N75.8	Other diseases of Bartholin gland
N75.9	Disease of Bartholin's gland, unspecified
N76.0	Acute vaginitis
N76.1	Subacute and chronic vaginitis
N76.2	Acute vulvitis
N76.3	Subacute and chronic vulvitis
N76.4	Abscess of vulva
N76.5	Ulceration of vagina
N76.6	Ulceration of vulva
N76.8	Other specified inflammation of vagina and vulva
N77.0	Ulceration of vulva in infectious and parasitic diseases classified elsewhere
N77.1	Vaginitis, vulvitis and vulvovaginitis in infectious and parasitic diseases classified elsewhere
N77.8	Vulvovaginal ulceration and inflammation in other diseases classified elsewhere
O03.0	Spontaneous abortion: Incomplete, complicated by genital tract and pelvic infection
O03.5	Spontaneous abortion: Complete or unspecified, complicated by genital tract and pelvic infection
O04.5	Medical abortion: Complete or unspecified, complicated by genital tract and pelvic infection
O08.0	Genital tract and pelvic infection following abortion and ectopic and molar pregnancy
O23.0	Infections of kidney in pregnancy
O23.1	Infections of bladder in pregnancy

ICD-10 Code	ICD-10 Descriptor
O23.2	Infections of urethra in pregnancy
O23.3	Infections of other parts of urinary tract in pregnancy
O23.4	Unspecified infection of urinary tract in pregnancy
O23.5	Infections of the genital tract in pregnancy
O23.9	Other and unspecified genitourinary tract infection in pregnancy
O75.3	Other infection during labour
O86.0	Infection of obstetric surgical wound
O86.1	Other infection of genital tract following delivery
O86.2	Urinary tract infection following delivery
O86.3	Other genitourinary tract infections following delivery
O86.4	Pyrexia of unknown origin following delivery
O86.8	Other specified puerperal infections
O91.1	Abscess of breast associated with childbirth
O98.0	Tuberculosis complicating pregnancy, childbirth and the puerperium
O98.1	Syphilis complicating pregnancy, childbirth and the puerperium
O98.2	Gonorrhoea complicating pregnancy, childbirth and the puerperium
O98.3	Other infections with a predominantly sexual mode of transmission complicating pregnancy, childbirth and the puerperium
O98.4	Viral hepatitis complicating pregnancy, childbirth and the puerperium
O98.5	Other viral diseases complicating pregnancy, childbirth and the puerperium
O98.6	Protozoal diseases complicating pregnancy, childbirth and the puerperium
O98.7	Human immunodeficiency virus [HIV] disease complicating pregnancy, childbirth and the puerperium
O98.8	Other maternal infectious and parasitic diseases complicating pregnancy, childbirth and the puerperium
O98.9	Unspecified maternal infectious or parasitic disease complicating pregnancy, childbirth and the puerperium
P00.2	Fetus and newborn affected by maternal infectious and parasitic diseases
P23.0	Congenital pneumonia due to viral agent
P23.1	Congenital pneumonia due to Chlamydia
P23.2	Congenital pneumonia due to staphylococcus
P23.3	Congenital pneumonia due to streptococcus, group B
P23.4	Congenital pneumonia due to Escherichia coli
P23.5	Congenital pneumonia due to Pseudomonas
P23.6	Congenital pneumonia due to other bacterial agents
P23.8	Congenital pneumonia due to other organisms
P23.9	Congenital pneumonia, unspecified
P35.0	Congenital rubella syndrome
P35.1	Congenital cytomegalovirus infection
P35.2	Congenital herpesviral [herpes simplex] infection
P35.3	Congenital viral hepatitis
P35.4	Congenital Zika virus disease
P35.8	Other congenital viral diseases
P35.9	Congenital viral disease, unspecified
P37.0	Congenital tuberculosis
P37.1	Congenital toxoplasmosis
P37.2	Neonatal (disseminated) listeriosis
P37.3	Congenital falciparum malaria
P37.4	Other congenital malaria
P37.5	Neonatal candidiasis
P37.8	Other specified congenital infectious and parasitic diseases

ICD-10 Code	ICD-10 Descriptor
P37.9	Congenital infectious and parasitic disease, unspecified
P38	Omphalitis of newborn with or without mild haemorrhage
P39.0	Neonatal infective mastitis
P39.1	Neonatal conjunctivitis and dacryocystitis
P39.2	Intra-amniotic infection of fetus, not elsewhere classified
P39.3	Neonatal urinary tract infection
P39.4	Neonatal skin infection
P39.8	Other specified infections specific to the perinatal period
P39.9	Infection specific to the perinatal period, unspecified
R02	Gangrene, not elsewhere classified
T80.2	Infections following infusion, transfusion and therapeutic injection
T81.4	Infection following a procedure, not elsewhere classified.
T82.6	Infection and inflammatory reaction due to cardiac valve prosthesis
T82.7	Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts
T83.5	Infection and inflammatory reaction due to prosthetic device, implant and graft in urinary system
T83.6	Infection and inflammatory reaction due to prosthetic device, implant and graft in genital tract
T84.5	Infection and inflammatory reaction due to internal joint prosthesis
T84.6	Infection and inflammatory reaction due to internal fixation device [any site]
T84.7	Infection and inflammatory reaction due to other internal orthopaedic prosthetic devices, implants and grafts
T85.7	Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts
T88.0	Infection following immunization
U04.9	Severe acute respiratory syndrome [SARS], unspecified
U07.1	COVID-19, virus identified
U07.2	COVID-19, virus not identified
Organ dysfunction	
D65	Disseminated intravascular coagulation [defibrination syndrome]
D69.5	Secondary thrombocytopenia
E87.2	Acidosis
G93.4	Encephalopathy, unspecified
I42.4	Endocardial fibroelastosis
I46.0	Cardiac arrest with successful resuscitation
I46.1	Sudden cardiac death, so described
I46.9	Cardiac arrest, unspecified
I74.0	Embolism and thrombosis of abdominal aorta
I74.1	Embolism and thrombosis of other and unspecified parts of aorta
I74.2	Embolism and thrombosis of arteries of upper extremities
I74.3	Embolism and thrombosis of arteries of lower extremities
I74.4	Embolism and thrombosis of arteries of extremities, unspecified
I74.5	Embolism and thrombosis of iliac artery
I74.8	Embolism and thrombosis of other arteries
I74.9	Embolism and thrombosis of unspecified artery
I95.2	Hypotension due to drugs
I95.8	Other hypotension
I95.9	Hypotension, unspecified
J80	Adult respiratory distress syndrome
J95.2	Acute pulmonary insufficiency following nonthoracic surgery
J96.0	Acute respiratory failure
J96.9	Respiratory failure, unspecified
K72.0	Acute and subacute hepatic failure
K72.9	Hepatic failure, unspecified
K76.3	Infarction of liver
N00.8	Acute nephritic syndrome: Other
N00.9	Acute nephritic syndrome: Unspecified
N10	Acute tubulo-interstitial nephritis
N15.8	Other specified renal tubulo-interstitial diseases
N15.9	Renal tubulo-interstitial disease, unspecified
N17.0	Acute renal failure with tubular necrosis
N17.1	Acute renal failure with acute cortical necrosis
N17.2	Acute renal failure with medullary necrosis
N17.8	Other acute renal failure
N17.9	Acute renal failure, unspecified
N19	Unspecified renal failure
P22.0	Respiratory distress syndrome of newborn
P22.8	Other respiratory distress of newborn
P22.9	Respiratory distress of newborn, unspecified
P28.5	Respiratory failure of newborn
P29.1	Neonatal cardiac dysrhythmia
P60	Disseminated intravascular coagulation of fetus and newborn
R09.0	Asphyxia
R09.2	Respiratory arrest
R40.0	Somnolence
R40.1	Stupor
R40.2	Coma, unspecified
R41.8	Other and unspecified symptoms and signs involving cognitive functions and awareness
R55	Syncope and collapse
R57.0	Cardiogenic shock
R57.1	Hypovolaemic shock
R57.8	Other shock
R57.9	Shock, unspecified
Additional key terms for identifying organ dysfunction	
• Multiple organ dysfunction syndrome (MODS) • Multiple organ failure	

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