

# Outcomes following admission to intensive care for asthma

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## ABSTRACT

**Objective** Acute severe asthma in children is a common cause of admission to intensive care units (ICU), but there are few reports on long-term outcomes. This study describes outcomes for children with asthma admitted to an ICU.

**Methods** All children with asthma aged 2–18 years admitted to the ICU at the Royal Children's Hospital Melbourne between 1990 and 2004 were eligible for the study. Data were collected by reviewing medical records and through telephone interviews.

**Results** Complete data were obtained for 410 (61%) of 684 eligible patients. The mean duration of follow-up was  $10.3 \pm 4.6$  years. After the index admission, 67% were readmitted to hospital for asthma and 17% to the ICU. Eighty-eight per cent continued to have asthma: 46% had episodic asthma and 42% persistent asthma. Twelve patients (1.8%) subsequently died from asthma. Five per cent of those who required ventilation at their index admission died within 10 years. Risk factors for ICU readmission were admission for asthma in the preceding year (AOR 4.7; 95% CI 2.4 to 9.3) and ventilation at admission (AOR 2.4; 95% CI 1.0 to 5.3). Risk factors for subsequent mortality were multiple ICU admissions (AOR 5.0; 95% CI 1.3 to 19), persistent asthma (AOR 5.8; 95% CI 1.2 to 28.5) and ventilation at admission (AOR 4.5; 95% CI 1.3 to 15.7).

**Conclusion** Admission to the ICU for asthma is a predictor of hospital readmission. Those with persistent asthma or requiring ventilation are at significant risk of mortality in subsequent years and require close follow-up.

## INTRODUCTION

After a consistent increase throughout the second half of the 20th century, the prevalence of asthma in children has been declining in recent years in Australia and other countries where it was previously high.<sup>1–2</sup> Admission rates for asthma in children aged 0–4 years and 5–14 years are seven times and twice as high, respectively, as that for adults, yet the proportion of children admitted with asthma who require invasive ventilation is similar.<sup>3</sup>

In published series, the proportion of children with asthma admitted to an intensive care unit (ICU) ranges from 1% to 15% of all hospital admission for asthma, with 8–33% requiring mechanical ventilation support.<sup>4–7</sup> This group of children is more likely to have recurrent emergency department presentations and admissions to hospital, and are at risk for subsequent near fatal asthma and death.<sup>8–13</sup>

While a number of studies have been conducted to determine the risk factors for ICU admission for asthma, few have evaluated long-term outcome

## What is already known on this topic

Children with asthma who have been admitted to the intensive care unit (ICU) are more likely to be readmitted to the hospital/ICU.

## What this study adds

- ▶ Readmission rate, mortality and pattern of asthma within 10 years of discharge from the ICU for asthma are reported.
- ▶ 1.8% of children died from asthma within 10 years of ICU discharge.
- ▶ 5% of children who required mechanical ventilation in the ICU died from asthma within 10 years of discharge.

following discharge from an ICU. These data are important for decisions on subsequent admissions and long-term management following discharge from the ICU.

This study aims to describe outcome in children following discharge from the ICU for asthma and to identify risk factors for readmission and mortality.

## METHODS

### Setting

The Royal Children's Hospital (RCH) Melbourne is a major teaching and tertiary referral hospital. It serves a population of more than 4 million and has 35 000 inpatients and 65 000 emergency department presentations each year. The paediatric ICU is one of two in the state of Victoria, with 1200 intensive care admissions annually. During the time of this study more than 90% of paediatric ICU admissions in Victoria were to the RCH.

### Subjects

All patients between 2 and 18 years of age admitted to the ICU at the RCH with a final diagnosis of asthma, between 1 January 1990 and 31 December 2004 were included in this study. Patients with underlying cardiovascular diseases, other chronic lung diseases (eg, cystic fibrosis, neonatal chronic lung disease) or neuromuscular diseases or those who had relocated outside Australia were excluded from the study. The index admission was the first ICU admission for asthma to the RCH during that period.

At the RCH, the criteria for admission to the ICU for asthma include impending respiratory failure,

severe hypoxaemia, requirement for continuous nebulised salbutamol for more than 1 h or salbutamol inhalation more frequently than every 30 min after 2 h. Standard treatment for severe asthma includes salbutamol inhalation, prednisolone (oral or intravenous), ipratropium and intravenous aminophylline.<sup>14</sup>

### Data collection

The study was conducted between June 2006 and October 2007. Approval was obtained from the RCH Human Research Ethics Committee. Information from the National Death Index at the Australian Institute of Health and Welfare was sought to identify further patients who had died following discharge from the index admission and to confirm the cause of death. Demographic and clinical data prior to the index admission were obtained from the patients' hospital records and telephone interview with patients and/or their parents. Data on hospital and ICU readmissions for asthma were obtained mainly from the telephone interview, and were confirmed with the data in RCH hospital records or, where appropriate, from the health information services of other hospitals identified in the telephone interview. Other data collected included history of prematurity, atopy (reported to have either eczema, hay fever or allergic rhinitis), family history of asthma (history of asthma in siblings or parents), age at diagnosis (age of the subject reported to have doctor-confirmed asthma), length of hospital stay, length of ICU stay, and whether the child received mechanical ventilation (via an endotracheal tube). The baseline asthma pattern (the pattern in the 12 months prior to the index admission) was classified as follows: (1) first diagnosis, the child had not previously been diagnosed with asthma by a doctor or had not used asthma medication prior to the index admission; (2) episodic asthma, the child remained symptom free between attacks and did not require preventive medication; (3) persistent asthma, the child had frequent symptoms between attacks, including daytime symptoms on more than 2 days per week and night symptoms more than one night a week; or had been prescribed preventive medication to control the symptoms. A telephone interview was not carried out with the parents or family of children who were known to have died following the index admission.

### Outcomes

The primary outcomes of the study were (1) hospital readmission for asthma, (2) mortality following the index admission and (3) current asthma pattern. Hospital readmission included all presentations for asthma to the emergency department, admissions to general wards and admissions to the ICU. Current asthma pattern, which was the pattern in the 12 months preceding the telephone interview, was classified as: (1) episodic asthma, (2) persistent asthma or (3) remission/no asthma (the child had no asthma symptoms and had not used asthma medication during the preceding 12 months).

### Statistical analysis

Agreement between the data obtained from the telephone interview and those from medical records was tested with the  $\kappa$  statistic. Univariate associations of variables with the outcomes were evaluated by logistic regression. Multiple logistic regression was performed for risk factors which were significant in the univariate analysis. Variables which were on the causal pathway between the exposure of interest and the outcome were not included in the multivariate analysis. All

statistical analyses were performed using STATA software, release 10 (StataCorp, College Station, Texas, USA).

### RESULTS

Between 1 January 1990 and 31 December 2004 a total of 12 857 children between 2 and 18 years of age were admitted for asthma, for a total of 15 168 admissions. Of those children, 718 (5.6%) were admitted to the ICU for a total of 954 ICU admissions (6.3% of hospital admissions for asthma).

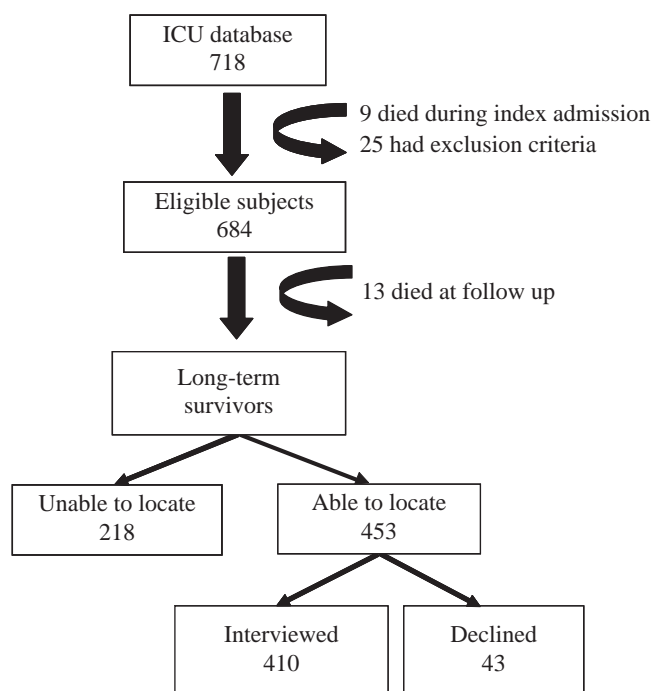
Thirty four patients were excluded from the study: nine had chronic lung disease, four had heart disease, five had severe scoliosis, seven moved overseas and nine died during the index admission. Of the remaining 684 eligible patients, 12 (1.8%) died from asthma and one died from cardiomyopathy secondary to clozapine following discharge from the index admission. Among the 671 long-term survivors, 410 (61%) were interviewed (figure 1). There was a poor agreement between the data obtained from the medical record and the telephone interview regarding age at diagnosis ( $\kappa=0.42$ ) and baseline asthma pattern ( $\kappa=0.56$ ). Therefore, data obtained from the medical record were used for further analysis of age at diagnosis and previous asthma pattern. As there was good agreement in the data on atopy ( $\kappa=0.68$ ), prematurity ( $\kappa=0.82$ ) and family history of asthma ( $\kappa=0.81$ ), information from the interview was used for further analysis due to the lack of completeness of these data in some medical records.

### Subject characteristics

The characteristics of the children and the index admission are shown in table 1. Forty (6%) children had been admitted to the ICU for asthma before 1990, 25 at the RCH and 15 at other hospitals. Therefore, the index admission was the first ICU admission for the majority of children.

### Hospital and ICU readmissions for asthma

Of 410 children interviewed, 276 (67%) were readmitted to the hospital following discharge from the index admission and 68 (16.6%) were readmitted to the ICU (table 2). The median



**Figure 1** Subject recruitment and participation. ICU, intensive care unit.

number of hospital readmissions within 1 year after discharge from the ICU was 2 (range: 1–9), while the median number of readmissions beyond the first 12 months of follow-up was 4.3 (range: 1–37).

The median length of time between discharge from the index admission and the first hospital readmission for asthma was 5.6 months (range: 3 days to 7.1 years), while for the first ICU readmission it was 18.7 months (range: 7 days to 15.3 years). Figure 2 shows a Kaplan–Meier graph of the timing of the first hospital readmission. At the end of the follow-up period, only 33% of the patients had not been readmitted to hospital. In comparison with the children who were not readmitted, those who were readmitted to the hospital more commonly had a hospital admission for asthma prior to the index admission, were younger at diagnosis and at admission, stayed longer in the ICU and had persistent asthma prior to the index admission. The proportion of children who required mechanical ventilation at the index admission was similar between the two groups (table 3). After adjusting for significant risk factors, hospital admission for asthma in the preceding year was the strongest risk factor for hospital readmission. Persistent asthma prior to the index admission and age at admission of 6 years or less were also identified

**Table 1** Characteristic of the subjects (n=684) and the index admission

Variable	
Sex, male (%)	403 (59)
Preterm birth (%)	98 (14.3)
Family history of asthma (%)	462 (67.6)
Age at diagnosis (years)*	2.0 (1.1–3.0)
Age at admission (years)*	7.0 (3.6–11.1)
Previous asthma pattern	
First diagnosis (%)	45 (6.46)
Episodic (%)	358 (52.3)
Persistent (%)	281 (41.1)
Previous hospital admission (%)	491 (71.8)
Previous ICU admission (%)	40 (5.8)
Previous intubation (%)	13 (1.9)
Duration of asthma (years)*	4.1 (1.6–8.3)
LOS in ICU (h)*	13.5 (8.5–22.5)
Duration of ventilation (h)*	10.1 (3.3–20.3)
Ventilated (%)	102 (14.9)
Current age (years)†	17.1 (4.5–32.7)
Duration of follow-up (years)†	10.3 (0.1–18.0)

\*Data presented as median (IQR).

†Data presented as mean (range).

ICU, intensive care unit; LOS, length of stay.

**Table 2** Hospital presentation for asthma following the index ICU admission

	Readmission at any time during follow-up (%)	Readmission within 1 year of the index ICU admission (%)	Readmission at least 12 months after the index ICU admission (%)
Total hospital readmission	67.0	46.0	54.0
Represented to the ED	36.1	14.9	28.0
Readmitted to the wards	59.3	38.8	43.7
Readmitted to the ICU	16.6	5.9	13.9

ED, emergency department; ICU, intensive care unit.

as significant risk factors for hospital readmission. For ICU readmission, the significant risk factors were hospital admission for asthma within 1 year prior to the index admission and mechanical ventilation during the index admission (table 4).

### Mortality

Nine children (1.3%) died during the index admission. All of these children had experienced cardiorespiratory arrest prior to their arrival in the RCH: six children had cardiorespiratory arrest at home, one developed an arrest during transport from home to the hospital, and two had cardiorespiratory arrest at other hospitals prior to transfer to the RCH.

Thirteen children died following discharge from the index admission; 12 deaths (1.8%) of these deaths were attributable to asthma. The mortality among children who had been ventilated during the index admission was 5% (5/102) compared to 1.2% (7/582) in those who had not been ventilated. The time from the index admission to death from asthma varied from 1 month to 13.3 years, with a median of 2.6 years. Four (33%) children died within 1 year and eight (67%) died more than 1 year after the index admission. The median age at death was 12.4 (8.3–18.4) years.

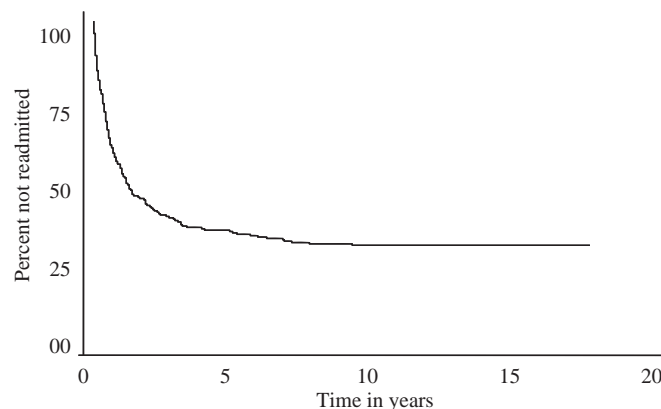
Children who died due to asthma following discharge more commonly had a history of persistent asthma, had previous ICU admission, stayed >24 h in the ICU and required mechanical ventilation during the index admission (table 4). After adjusting for significant risk factors, a history of persistent asthma, previous ICU admission and length of stay in the ICU >24 h remained significant risk factors.

### Current asthma pattern at follow-up

Of the 410 surviving children who were interviewed, the majority (87.6%) continued to have asthma symptoms up to and including the 12 months preceding the telephone interview: 46% had episodic asthma and 42% had persistent asthma. The current asthma pattern according to the pattern before the index admission is presented in figure 3.

### DISCUSSION

This study shows that readmission was common among children who survived their first ICU admission for asthma, and most children continued to have asthma symptoms at follow-up. The strengths of this study are the length of the follow-up period (an average of 10.3 years) and the large number of children involved (648 survivors). Earlier studies reported outcomes over 1–5 years among 22–78 children who experienced



**Figure 2** Kaplan–Meier estimate graph of first hospital readmission for asthma.

**Table 3** Demographic and clinical characteristics of patients readmitted to the hospital or ICU for asthma and of those who died following discharge from the index admission

	Hospital		ICU		Mortality	
	Readmitted (n=276)	Not readmitted (n=134)	Readmitted (n=68)	Not readmitted (n=342)	Died	Survived
Sex (male, %)	59.1	55.9	57.9	58.2	50.0	59.0
Previous asthma pattern						
First diagnosis (%)	5.0	9.8	1.6*	7.5	0.0*	7.0
Episodic (%)	49.2	54.4	41.9	52.7	18.0	53.0
Persistent (%)	45.8	35.8	56.5	39.8	82.0	40.0
Previous admission (%)	78.6**	56.1	97.1***	66.2	92.0	71.0
Previous admission within 12 months (%)	51.8***	15.6	73.5***	33.7	58.3	36.4
Previous ICU admission (%)	6.0	3.3	14.7***	3.5	33.0***	5.0
Age at diagnosis (years) <sup>†</sup>	2.0 (1.2–3.0)	2.0 (1.5–4.0)	1.5 (1.0–2.0)**	2.0 (1.5–3.3)	1.7 (0.7–2.0)	2.0 (1.2–3.0)
<1 year (%)	23.1	19.6	34.9	19.2		
>1–3 years (%)	56.7	49.5	55.6	54.2		
>3–6 years (%)	16.8	17.8	739.0	19.2		
>6 years (%)	3.4	13.1	1.6	7.4		
Age at admission <sup>†</sup>	6.0 (3.5–10.2)**	8.6 (3.8–12.2)	5.8 (3.4–10.2)	7.1 (3.6–11.6)	6.9 (4.0–12.10)	7.0 (3.6–11.0)
<3 years (%)	20.0	14.9	19.1	18.1		
>3–6 years (%)	29.7	22.4	33.8	26.0		
> 6–14 years (%)	42.0	53.0	39.7	46.8		
>14 years (%)	8.3	9.7	7.4	9.1		
LOS in hospital (days) <sup>†</sup>	3.1 (2.3–4.4)**	3.6 (2.7–4.9)	3.3 (2.5–4.3)	3.3 (2.4–4.6)	4.2 (3.5–6.6)	3.3 (2.5–4.5)
LOS in ICU (h) <sup>†</sup>	12.8 (8.0–1.0)***	16.0 (10.8–29.0)	14.3 (10.0–22.4)	14 (8.4–23.5)	21.8 (11.3–51.0)	13.5 (8.4–22.3)
Ventilated (%)	13.0	17.9	2.1	13.2	41.7**	14.5
Duration of ventilation (h) <sup>†</sup>	7.5 (2.2–19.8)	12.2 (5.1–22.5)	5.0 (2.3–16.0)	11.8 (2.8–22.3)	12.7 (10.8–13.2)	9.8 (3.0–21.7)

\*p&lt;0.05; \*\* p&lt;0.01; \*\*\* p&lt; 0.001.

<sup>†</sup>Data presented as median (IQR).

ICU, intensive care unit; LOS, length of stay.

**Table 4** Risk factors for readmission to hospital or the ICU and mortality following discharge from the ICU

Variable	Hospital readmission		ICU readmission		Mortality	
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
Previous hospital admission	3.3 (2.1 to 5.3)		16.9 (4.1 to 70.4)			
Admission within 1 year before the index admission	5.8 (3.4 to 10.0)	4.5 (2.5 to 8.4)	5.5 (3.0 to 9.8)	4.7 (2.4 to 9.3)		
Multiple previous hospital admissions	2.4 (1.3 to 4.2)		3.2 (1.6 to 6.7)			
Previous ICU admission			4.7 (2.0 to 11.4)	2.4 (0.8 to 6.7)	8.8 (2.5 to 30.7)	5.0 (1.3 to 19.0)
Previous mechanical ventilation			8.9 (2.1 to 38.4)		12.0 (2.3 to 61.3)	
Persistent asthma prior to index admission	1.6 (1.0 to 2.6)	1.8 (1.0 to 3.2)	2.0 (1.1 to 3.4)	1.5 (0.8 to 2.9)	6.7 (1.4 to 31.1)	5.8 (1.2 to 28.5)
Age at diagnosis (≤3 years)			3.5 (1.4 to 8.4)	2.0 (0.8 to 5.1)		
Age at diagnosis (≤6 years)	4.8 (2.0 to 12.0)	2.8 (0.9 to 8.3)				
Age at admission (<6 years)	1.8 (1.2 to 2.8)	1.9 (1.0 to 3.4)				
Ventilated at index admission			1.9 (1.0 to 3.6)	2.4 (1.0 to 5.3)	4.2 (1.3 to 13.6)	
LOS in ICU (≥24 h)					3.6 (1.1 to 11.3)	4.5 (1.3 to 15.7)
LOS in ICU (≥48 h)					5.9 (1.5 to 22.6)	

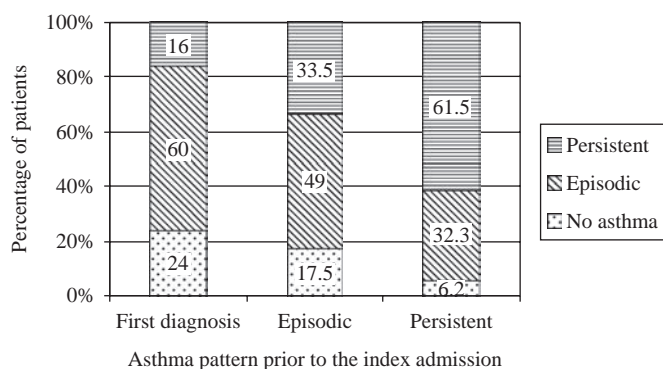
AOR, adjusted OR; ICU, intensive care unit; LOS, length of stay.

severe exacerbations.<sup>5 7 15</sup> The majority (67%) of the subjects in this study were readmitted to the hospital for asthma, confirming earlier reports that children with asthma who have had one episode of severe asthma exacerbation are at high risk for subsequent hospital admissions.<sup>5 7 16 17</sup> Wever-Hess and co-workers reported a hospital readmission rate of 26% among children 0–4 years of age,<sup>18</sup> Macarthur and colleagues found a hospital readmission rate of 47% among children above 6 months of age,<sup>19</sup> and To *et al* reported a hospital readmission rate of 31.3% among children below 18 years of age.<sup>20</sup>

Different populations, degrees of asthma severity and admission thresholds may explain these differences. Readmissions reported in some of the studies did not specifically refer to readmission following discharge from the ICU.<sup>19–22</sup>

Newcomb and Akhter in Chicago reported that 76% of 78 children with respiratory failure from asthma (defined as arterial hypoxaemia, hypercapnia or use of mechanical ventilation support or intravenous isoproterenol hydrochloride) had subsequent respiratory failure within 2 years following discharge from the ICU.<sup>15</sup> In Finland, this occurred in one third of 59





**Figure 3** Current asthma pattern according to the pattern of asthma before the index admission.

patients requiring mechanical ventilation for asthma.<sup>5</sup> Our rate was lower, which may be because our subjects consisted of children who required and did not require mechanical ventilation. Among mechanically ventilated patients, the proportion requiring ICU readmission in our cohort was 26.2%, which is still lower than in previous reports.

The high cumulative incidence of mortality (5%) over 10 years in those who received mechanical ventilation in our study corresponds to an annual incidence of 5 per 1000 children ventilated for asthma. A previous survey of paediatric asthma deaths in Victoria found that 22% of those who died had a previous admission to the ICU for asthma.<sup>23</sup> Patients with a prior history of near fatal asthma but who are in remission were shown to have reduced chemosensitivity to hypoxia and diminished perception of dyspnoea or gas exchange abnormalities.<sup>24</sup> This has been suggested as an underlying mechanism of the high risk of respiratory failure leading to death among patients with prior asthma exacerbation requiring mechanical ventilation and prior admission to the ICU for asthma.

Clinical remission for asthma occurred in a small subset of the cohort. However, this proportion might actually be smaller as defining remission for asthma by only assessing symptoms and asthma medication use will have overlooked subjects with subclinical disease.<sup>25</sup> Vonk *et al* reported that 57% of subjects with clinical remission (defined as absence of wheeze and asthma attacks and no use of inhaled corticosteroids) had bronchial hyper-responsiveness and/or low lung function.<sup>25</sup>

Belessis and co-workers reported that children who had three or more emergency department presentations in the previous year, an elevated IgE level, longer asthma duration or low oxygen saturation were more likely to have ICU admission for asthma.<sup>26</sup> Due to the lack of data obtained from medical record review in our study, not all of those important factors could be analysed. Our study showed that mechanical ventilation requirement at the index admission and hospitalisation for asthma within 1 year before the index admission were predictive for subsequent ICU admission. This is in line with a systematic review of 27 studies in adults and children which showed that a history of hospital admission for asthma was predictive for near fatal asthma.<sup>8</sup>

Our study is limited by its retrospective design, with recall bias being one of the drawbacks when obtaining information retrospectively through interview. Different admission policies over time and between different hospitals are another important issue that should be taken into account when evaluating admissions and readmissions for asthma. The difficulties in retrospectively establishing asthma severity prior to

the index admission should also be noted. While the information obtained from the telephone interview is subject to recall bias, the data obtained from the medical records are based on the history obtained by different physicians who had varied experience in gathering information related to asthma severity. Misclassification of asthma severity is also possible as hospital staff tend to focus on obtaining a history that relates to the acute events prior to admission rather than the long-term history of asthma symptoms.<sup>27</sup>

Our study recommends that following discharge from the ICU, children with multiple ICU admissions for asthma, particularly those who have persistent asthma and required invasive ventilation, should be followed closely in a specialist clinic.

**Competing interest** None.

**Ethics approval** This study was conducted with the approval of the Human Research Ethics Committee of the Royal Children Hospital Melbourne, Australia.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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