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Complete List of Authors:	Craig, Simon; Monash Medical Centre Clayton, Paediatric Emergency Department; Monash University Department of Paediatrics Delardes, Belinda; Ambulance Victoria; Monash University Department of Paramedicine Nehme, Ziad; Ambulance Victoria, Research & Evaluation; Monash University School of Public Health and Preventive Medicine Wilson, Catherine; Murdoch Childrens Research Institute, Emergency Medicine Research Group; PREDICT, Research Group Dalziel, Stuart; Starship Children's Health, Emergency Department; The University of Auckland Faculty of Medical and Health Sciences, Paediatrics and Surgery Nixon, Gillian; Monash University Department of Paediatrics; Monash Children's Hospital, Respiratory Medicine Powell, Colin; Sidra Medical and Research Center, Department of Emergency Medicine; Cardiff School of Health Sciences Graudins, Andis; Monash Health, Dandenong Emergency Department; Monash University Babl, Franz; Royal Childrens Hospital, Emergency Department; The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Paediatrics
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Escalation of care for treatment of acute asthma in children is rare in the pre-hospital setting.

Simon Craig[1,2,3] MBBS FACEM MPH MHPE, **Belinda Delardes**[4,5] B Paramedic (Hons), **Ziad Nehme**[4,5,6] PhD, **Catherine L Wilson**[3] Dip App Sci Nurs MPH Ms Evaluation and Assessment, **Stuart R Dalziel**[7,8] MBChB FRACP PhD, **Gillian M Nixon**[1,9] MBChB MD FRACP, **Colin VE Powell**[10,11] MBChB DCH MRCP(UK) FRACP FRCPCH MD, **Andis Graudins**[12,13,14] MBBS PhD FACEM FACMT, **Franz E Babl**[3,15,16,17] MD MPH DMedSc FRACP FAAP FACEP on behalf of the PREDICT Network.

Affiliations

1. Department of Paediatrics, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.
2. Monash Emergency Program, Paediatric Emergency Department, Monash Medical Centre, Monash Health, Victoria, Australia.
3. Emergency Research, Clinical Sciences, Murdoch Children's Research Institute, Victoria, Australia
4. Ambulance Victoria, Blackburn North, Victoria, Australia
5. Department of Paramedicine, Monash University, Frankston, Victoria, Australia
6. School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
7. Departments of Surgery and Paediatrics: Child and Youth Health, The University of Auckland, New Zealand.

8. Children's Emergency Department, Starship Children's Hospital, Auckland, New Zealand
9. Department of Respiratory Medicine, Monash Children's Hospital, Melbourne, Victoria, Australia.
10. Division of Population Medicine, School of Medicine, Cardiff, United Kingdom.
11. Emergency Medicine, Sidra Medicine, Doha Qatar
12. Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.
13. Monash Emergency Program, Monash Health, Dandenong Hospital, Victoria, Australia.
14. Monash Health Clinical Toxicology and Addiction Medicine Service, Monash Health, Dandenong Hospital, Victoria, Australia.
15. Department of Emergency Medicine, The Royal Children's Hospital, Victoria, Australia.
16. Department of Paediatrics, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia.
17. Department of Critical Care, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia.

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Corresponding author

Prof Simon Craig

- Paediatric Emergency Department, Monash Medical Centre, Monash Health, Clayton, Victoria, Australia
- Department of Paediatrics, Monash University, Clayton, Victoria, Australia

Simon.Craig@monash.edu

Background

Asthma is a common reason for ambulance paramedic attendance for children, however, there are little data available on pre-hospital treatment patterns or outcomes. This study aimed to understand the incidence of and patterns of "escalated care" (care in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators).

Methods

We conducted a retrospective observational study of state-wide ambulance service data (Ambulance Victoria in Victoria, Australia, population 6.5 million). Children aged 1-17 years and given a final diagnosis of asthma by the treating paramedics and/or treated with inhaled bronchodilators from 1 July 2019 to 30 June 2020 were analysed for demographic and clinical features, and treatment administered. We classified "escalation of care" as parenteral administration of adrenaline, or provision of respiratory support. We compared clinical, demographic and treatment administered between those receiving and not receiving escalation of care.

Results

Paramedics attended 1,572 children with acute exacerbations of asthma during the 1 year study period. Of these, 22 (1.4%) had escalated care, all receiving parenteral adrenaline. Patients with escalated care were more likely to be older, had previously required hospital admission for asthma and had severe respiratory distress at initial assessment.

Of 1307 children with respiratory status data available, at arrival to hospital the respiratory status of children had improved overall (normal/mild respiratory distress at initial assessment 847 (64.8%), normal/mild respiratory distress at hospital arrival 1142 (87.4%), p<0.0001).

Conclusion

Most children with acute exacerbations of asthma did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital.

What is already known on this topic – An acute exacerbation of asthma is a common reason for ambulance paramedic attendance for children, however, there is little data available on treatment patterns or pre-hospital outcomes.

What this study adds – Most children with acute exacerbations of asthma do not receive escalated therapy (treatment beyond systemic corticosteroids and inhaled bronchodilators) during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital.

How this study might affect research, practice or policy – Due to the very low incidence of treatment escalation or clinical deterioration, any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

Introduction

Asthma is a frequent reason for children to attend the emergency department (ED),[1,2] and one of the most common reasons for paediatric hospitalization after an ED visit.[3] In the USA, the rate of paediatric ED visits for asthma increased by 13.3% between 2001 and 2010,[4] while in the United Kingdom, it is estimated that a child is admitted to hospital with an asthma attack every 20 minutes.[5]

Most children with asthma have mild or moderate exacerbations, and respond to first-line treatment with inhaled bronchodilator therapy and systemic steroids.[6-9] However, some children with severe asthma require more intensive therapies including intravenous (IV) medications, endotracheal intubation and/or admission to intensive care.[9-11] Management of acute severe asthma is complicated by a number of problems, including a large number of treatment options, wide variation in self-reported and actual physician practice,[12-15] and a weak evidence base.[16,17]

Early initiation of therapy in the pre-hospital setting may abort an asthma attack and prevent further escalation on arrival to the ED. This in turn may prevent the need for more invasive treatment and potential complications or side effects of medications used in escalation. The introduction of a new treatment protocol emphasizing early use of systemic corticosteroids in a large Emergency Medical Services system was associated with reduced rates of hospitalization, less need for critical care and shorted hospital length of stay.[18] Systemic corticosteroid administration has been the subject of successful improvement projects in the pre-hospital setting.[19] However, a separate study identified high rates of paramedic non-compliance with pre-hospital treatment protocols recommending parenteral adrenaline for children with high-severity respiratory distress.[20]

There are little data available on treatment patterns or pre-hospital outcomes for children with acute asthma in the Australian setting. This study aimed to extract information from the electronic medical records of Ambulance Victoria (AV), Australia, on all children treated for asthma to understand the incidence of and patterns of "escalated" care (care in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators).

Methods

Study design

This was a retrospective cohort study of all children who were either given a final diagnosis of asthma by the treating AV paramedics or treated with inhaled bronchodilators from 1 July 2019 to 30 June 2020. The project is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[21]

Study setting

AV is the single public emergency medical service for the state of Victoria, Australia (population of 6.5 million over 227,000 square kilometres).

AV clinical practice guidelines[22] provide recommendations for asthma management according to severity (Box 1), which include: inhaled salbutamol via a pressurised metered dose inhaler (pMDI) as initial treatment for mild / moderate asthma; nebulised salbutamol and ipratropium reserved for severe or critical illness, or failure of moderate asthma to respond to treatment after 20 minutes; corticosteroids (intravenous or oral dexamethasone) for critical asthma in children and for severe and critical asthma in adults; parenteral adrenaline (intramuscular, intravenous infusion or titrated boluses) for critical asthma; and assisted ventilation and/or intubation for unconsciousness or respiratory arrest. Children aged 12

years or more are managed according to an "adult" algorithm, which has a lower threshold for corticosteroids compared to the paediatric algorithm (recommended for all severe cases, rather than only in critical illness) .[22]

Selection of participants.

We searched the AV electronic patient care system for presentations of children aged more than one year and less than 18 years matching the following criteria: final primary assessment of asthma or cough or shortness of breath. We excluded children with a paramedic diagnosis of cough or shortness of breath if they were not administered any inhaled bronchodilator (salbutamol or ipratropium). Records of cases assessed by multiple ambulance teams during the same incident were unified as a single paramedic attendance. Interhospital transports and patients managed for cardiac arrest were excluded.

Data collection

Data were extracted directly from the AV medical record database into a purpose-designed spreadsheet and analysed.

We defined "respiratory support" as the use of continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), assisted ventilation, intubation and mechanical ventilation, or application of a bag-valve-mask device.

We defined "escalation" of care as parenteral administration of adrenaline, or provision of respiratory support. Although AV protocols recommend oral (or parenteral) corticosteroids for severe and critical asthma, corticosteroids are usually considered part of routine asthma care (rather than reserved for critical illness). We did not include nebulised adrenaline for suspected croup / upper airway obstruction. The case notes were reviewed and verified by a

second paramedic abstractor (BD) for all patients where escalation was identified through electronic medical record data.

Analysis

Descriptive statistics were used to summarise patient characteristics, clinical features and treatments administered. Non-parametric data is reported using median and interquartile range (IQR), while categorical data is presented as count and percentage. We did not impute any missing data.

Comparisons were made between those requiring escalation of care to those not requiring escalation of care. Categorical data is compared using Chi-square test or Fisher's exact test as appropriate. Non-parametric data is compared using Mann-Whitney U test.

All analyses were performed using SPSS for Windows (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.).

Patient and public involvement

Patients were not involved in the design of this study.

Results

Over the study period, the service responded to 633,950 on-road emergency cases,[23] mainly using advanced life support (ALS) or mobile intensive care ambulance (MICA) paramedics. We identified 3,587 children who had been assessed by AV with a primary assessment diagnosis of asthma, cough, or shortness of breath, 1,520 were excluded, leaving 1,572 children managed by AV with asthma (figure 1).

The median age of the cohort was 6 years (IQR 4-10 years) and 888 (56.5%) were male. Most (87.6%) patients had a documented past history of asthma, 115 (7.3%) had been hospitalised, 63 (4%) had required intensive care admission, and 19 (1.2%) had been intubated for a previous asthma exacerbation. The median initial respiratory rate was 32 breaths/minute (IQR 24 – 40 breaths/minute). Of the 1,460 patients who had initial work of breathing documented, 978 (67.0%) had normal or mild work of breathing, and 166 (7.7%) had severe work of breathing.

Ambulance response time was a median of 11.9 minutes (IQR 8.2 to 15.2 minutes); paramedics were on the scene with the patient for a median of 17 minutes (IQR 12.7 to 25.1 minutes). Patients were transported by ambulance in 90% (n=1419) of attendances.

Paramedics administered inhaled bronchodilators in 946 (60.2%) of cases. Of those, 493 (52.1%) received salbutamol alone, 13 (1.4%) received ipratropium alone, and 440 (46.5%) received salbutamol and ipratropium. For those receiving bronchodilators, a median (IQR) of 1 (1-2) doses was administered. Oxygen administration was documented in 306 (19.4%) patients, most commonly by nebuliser mask, nasal cannulae, or an oxygen mask; however, 514 (32.6%) received nebulised medication, driven by oxygen. Oral corticosteroids were administered to 141 (9.0%) patients.

Twenty-six records were reviewed for escalation of care; in four patients the electronic record was incorrectly coded, due to inadvertent selection of intravenous salbutamol (used by AV for pre-term labour) instead of nebulised salbutamol, leaving 22 (1.4%) patients with escalated care (figure 1). Patients with escalated care were more likely to be older, had previously required hospital admission for asthma and had severe respiratory distress at initial assessment (Table 1). Those receiving escalated care were more likely to be treated with inhaled bronchodilators, corticosteroids and oxygen (Table 2).

All patients who received escalated care received parenteral adrenaline. No patients received non-invasive ventilation, assisted ventilation or intubation. Four children (aged two, fourteen, sixteen and seventeen years) received an adrenaline infusion. One patient who received IM adrenaline also had a bag-valve-mask applied, however, did not receive positive pressure ventilation. They were a two-year-old child who had difficulty breathing and cough that was not improving with salbutamol administered at home. They became unresponsive after a coughing episode and bystander cardiopulmonary resuscitation was initiated. They were breathing spontaneously and responsive upon initial paramedic assessment.

Reports of respiratory status at initial assessment and hospital arrival were available for 1307 (85.5%) of the cohort. On arrival to hospital the respiratory status of children had improved overall (normal/mild respiratory distress at initial assessment 847 (64.8%), normal/mild respiratory distress at hospital arrival 1142 (87.4%), $p<0.0001$). One hundred and thirty-one (81.2%) of the 160 children with severe respiratory distress at initial assessment had improved. Of the 847 children with normal/mild respiratory distress at initial assessment, only 24 (2.8%) were documented as having moderate or severe respiratory distress at hospital arrival; and only 9 (0.8%) of the 1146 children with normal/mild/moderate respiratory distress at initial assessment were documented as having severe respiratory distress at hospital arrival (Figure 2).

Discussion.

This study provides a population-based state-wide assessment of pre-hospital asthma management in children. Most children with acute exacerbations of asthma in Victoria, Australia, did not receive escalated therapy during their pre-hospital treatment from

ambulance paramedics. Overall, the respiratory status of children improved from ambulance arrival to hospital arrival in all severity categories.

The overall rate of parenteral bronchodilator (adrenaline) administration was 1.6%. No patients received non-invasive ventilation, assisted ventilation or intubation, and most patients were treated with inhaled bronchodilators and clinically improved by the time they arrived in hospital. Those receiving escalated care were older, were more likely to have a history of asthma requiring hospital admission and/or intubation and have severe respiratory distress on ambulance arrival.

A recent large study described in-hospital management of acute asthma exacerbations in Australia and New Zealand. In 14,029 children, there was a higher overall rates of escalated therapy (7.3% overall, with 4.2% receiving parenteral bronchodilators and 4.3% respiratory support).[24] A common indication for escalation of care is failure to adequately respond to first-line therapy. The relatively low rates of treatment escalation in the pre-hospital setting (1.6%) suggests that a small proportion of children are seriously ill, while most are early in their treatment, and may not have had sufficient time to demonstrate improvement (or lack of improvement) prior to hospital arrival.

There is little evidence to guide escalated therapy for asthma. A recent Overview of Cochrane reviews of clinical trials on escalated therapy for asthma[16] assessed the evidence for parenteral bronchodilators, Heliox, respiratory support and inhaled magnesium. The review found that the majority of comparisons involved between one and three trials and fewer than 100 participants, making it difficult to assess the balance between benefits and potential harms. The authors were unable to make firm practice recommendations.[16]

There is little evidence to support intramuscular adrenaline as first-line treatment for seriously ill children with asthma,[25] although it has a number of advantages, including ease of

administration and paramedic familiarity. Parenteral adrenaline is also used for anaphylaxis, cardiac arrest, and management of hypotension, while nebulised adrenaline is used for severe upper airway obstruction in croup. In addition, it can be easily and rapidly administered as there is no need for dilution prior to administration, and no requirement for a prolonged infusion.[22]

Pre-hospital treatment of asthma rarely results in escalation of therapy beyond inhaled bronchodilators and systemic corticosteroids. In addition, the use of parenteral bronchodilators is often reserved for those who do not improve after initial inhaled bronchodilators, and is administered relatively late in the course of an ED visit.[15] Given that most children with asthma will improve with pre-hospital treatment, and/or will not have sufficient time to "fail to improve" with standard therapy, it appears that any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

Limitations

Inclusion in the study was based on a combination of paramedic diagnosis of asthma and administration of inhaled bronchodilators. While only 89% had a diagnosis of asthma recorded in the ambulance notes, it seems that the cohort is reflective of the asthma population as over 87% of cases had a previous diagnosis of asthma.

Due to state-wide data collection and large numbers of patients, our study is likely to be generalisable to other settings with similar pre-hospital care systems. However, most ambulance cases within Victoria are concentrated in the metropolitan area of Melbourne (the capital city), which may limit generalisability to rural and regional settings. Approximately 10%

of children were not transported to hospital; this is similar to the rate identified in a study of children with seizures from the same ambulance service.[26]

This study is a retrospective review of a comprehensive electronic database. We optimised data extraction and minimised bias through the collection of variables using a piloted data collection instrument, and application of pre-defined inclusion and exclusion criteria.[27,28] Due to the nature of record-keeping within the ambulance service (all cases are documented using the electronic system), it is unlikely that any cases of escalated care were missed. As we downloaded fields directly from the electronic medical record system, we did not independently abstract any variables. However, we verified all instances of documented escalation of care through consultation with a second (paramedic) reviewer and identified four cases of misclassification. It is possible that we missed some children who were not classified as asthma, were critically ill, not given inhaled bronchodilators and only given parenteral adrenaline. However, this is likely to be a very small number of cases.

Conclusions

Most children with acute exacerbations of asthma did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital. Due to the very low incidence of treatment escalation or clinical deterioration, any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

Figure 1. Flow chart – pre-hospital management of acute asthma in children.

AV, Ambulance Victoria.

Box 1. Asthma severity assessment according to Ambulance Victoria Clinical Practice Guidelines

Mild / Moderate: normal conscious state, some increased work of breathing, tachycardia, speaking in phrases / sentences
Severe: agitated / distressed, markedly increased work of breathing, including accessory muscle use / retraction, tachycardia, speaking in words.
Critical: altered conscious state, maximal work of breathing, marked tachycardia, unable to talk.

Table 1. Demographics and clinical characteristics of children treated or assessed for asthma by AV.

	Total (n=1572)	Escalation of care (n=22)	No escalation of care (n=1550)	P value (escalation vs no escalation)
Age, years, n (%)				
1-4	561 (36.3)	6 (27.3)	555 (35.8)	0.38
5-11	690 (43.9)	9 (40.9)	681 (43.9)	
12-17	321 (20.4)	7 (31.8)	314 (20.3)	
Median age, years (IQR)	6 (4-10)	10.5 (3.8 – 14.3)	6 (3.8 – 10)	0.045
Female sex, n (%)	684 (43.5)	11 (50)	877 (43.4)	0.54
Pre-existing conditions, n (%)				
Asthma	1377 (87.6)	20 (90.9)	1357 (87.5)	0.64
Requiring hospital admission	115 (7.3)	5 (22.7)	110 (7.1)	0.005
Requiring intensive care	63 (4)	1 (4.5)	62 (4)	0.89
Requiring intubation	19 (1.2)	1 (4.5)	18 (1.2)	0.15
With cardiac / respiratory arrest	5 (0.3)	0 (0)	5 (0.3)	0.79
Other respiratory illness				
Croup	94 (6)	1 (4.5)	93 (6)	0.78
Bronchiolitis	80 (5.1)	1 (4.5)	79 (5.1)	0.91
Pneumonia	44 (2.8)	1 (4.5)	43 (2.8)	0.62
Chest infection	32 (2)	1 (4.5)	31 (2)	0.40
Other	8 (0.5)	0 (0)	8 (0.5)	0.64
Initial physiological parameters				
Respiratory rate (breaths/minute), median (IQR)	32 (24 – 40)	35.5 (28 – 48.5)	32 (24 – 40)	0.09
Pulse rate (beats/minute), median (IQR)	130 (112 – 146)	134.5 (120 – 150.5)	130 (112 – 146)	0.24
Initial respiratory status, n (%)				
Normal	615 (39.1)	3 (13.6)	612 (39.5)	<0.001
Mild respiratory distress	363 (23.1)	1 (4.5)	362 (23.4)	
Moderate respiratory distress	315 (20)	2 (9.1)	313 (20.2)	
Severe respiratory distress	166 (10.6)	16 (72.7)	150 (9.7)	
Depressed respirations	1 (0.1)	0 (0)	1 (0.1)	

All P values calculated using Chi-Square tests, except for continuous variables where Mann-Whitney U tests* were used.

Table 2. Treatment provided by AV paramedics.

	Total (n=1572)	Escalation of care (n=22)	No escalation of care (n=1550)	P value (escalation vs no escalation)
Respiratory support, n(%)				
Bag-valve-mask applied	1 (0.1)	1 (4.5)	0 (0)	<0.001
Oxygen delivery				
Nasal cannulae	46 (2.9)	4 (18.2)	42 (2.7)	<0.001
Nebuliser mask	258 (16.4)	10 (45.5)	248 (16)	<0.001
Oxygen mask	48 (3.1)	0 (0)	48 (3.1)	0.40
Non-rebreather mask	8 (0.5)	0 (0)	8 (0.5)	0.74
Other oxygen therapy (not otherwise specified)	2 (0.1)	0 (0)	2 (0.1)	0.87
Parenteral bronchodilator				
Adrenaline IM injection	20 (1.3)	20 (90.9)	0 (0)	<0.001
Adrenaline infusion	4 (0.3)	4 (18.2)	0 (0)	<0.001
Dexamethasone				
IV injection	25 (1.6)	4 (18.2)	21 (1.4)	<0.001
Oral	141 (9)	11 (50)	130 (8.4)	<0.001
Inhaled bronchodilator				
Any inhaled bronchodilator	946 (60.2)	21 (95.5)	925 (59.7)	<0.001
Any Ipratropium bromide nebulisation	453 (28.8)	17 (77.3)	436 (28.1)	<0.001
Any Salbutamol pMDI	465 (29.6)	3 (13.6)	462 (29.8)	0.10
Any Salbutamol nebulisation	514 (32.6)	20 (90.9)	493 (31.8)	<0.001
Single dose of inhaled salbutamol	348 (22.1)	3 (13.6)	345 (22.3)	
Single dose of inhaled ipratropium bromide	13 (0.8)	1 (4.5)	12 (0.8)	
Single dose of inhaled salbutamol and single dose of inhaled iptratropium bromide	280 (17.8)	6 (27.3)	274 (17.7)	
Two doses of inhaled salbutamol alone	114 (7.3)	1 (4.5)	113 (7.3)	

Two doses of inhaled salbutamol and at least one dose of ipratropium bromide	112 (7.1)	3 (13.6)	109 (7)	
Three or more doses of inhaled salbutamol alone	31 (2.0)	0 (0)	31 (2)	
Three or more doses of inhaled salbutamol and at least one dose of ipratropium bromide	49 (3.1)	7 (31.8)	41 (2.6)	
Total instances of inhaled bronchodilator administration, median (IQR)	1 (0-2)	2 (1.8 – 4)	1 (0 – 2)	<0.001
Intravenous access				
Intravenous access attempt	39 (2.5)	7 (31.8)	32 (2.1)	<0.001
Successful IV attempt	34 (2.2)	7 (31.8)	27 (1.7)	<0.001

No patients received any of: BIPAP, manual ventilation, mechanical ventilation, IV salbutamol infusion, IM dexamethasone.

Figure 2. Initial and final respiratory status documented by AV paramedics.

Note: 111 patients missing initial respiratory status, and 265 missing final respiratory status.

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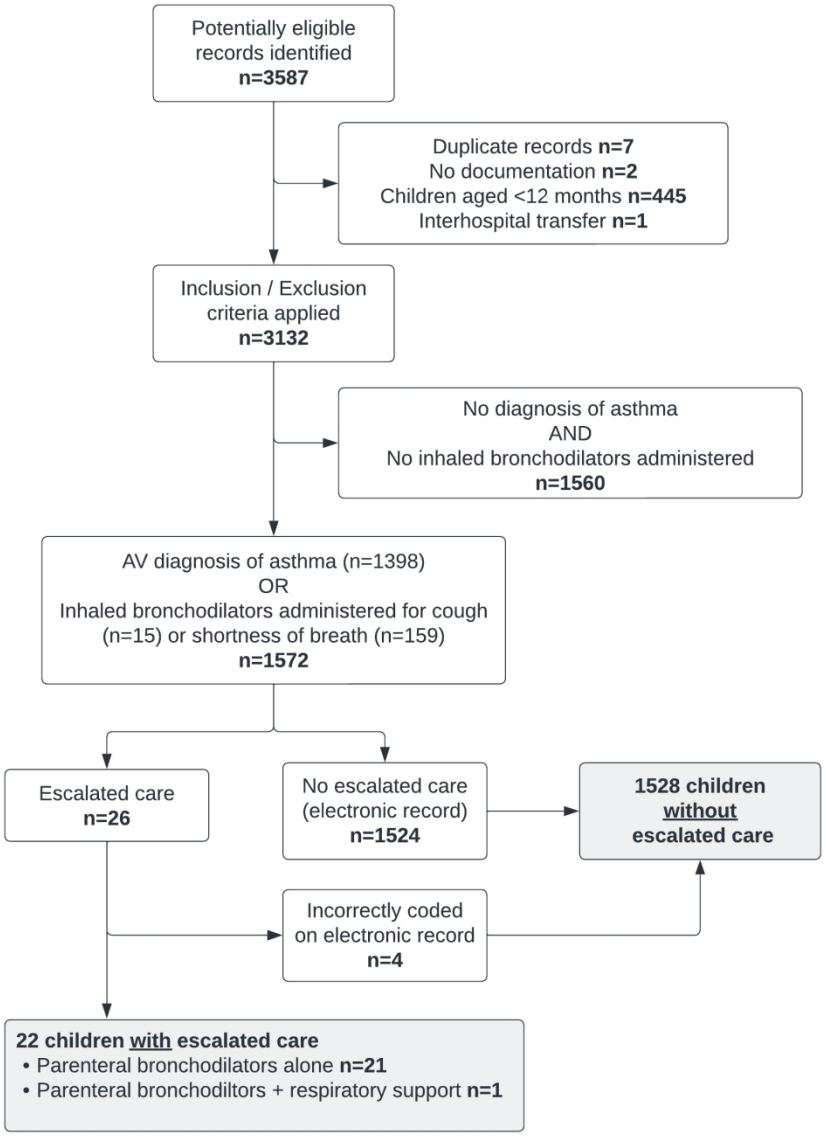

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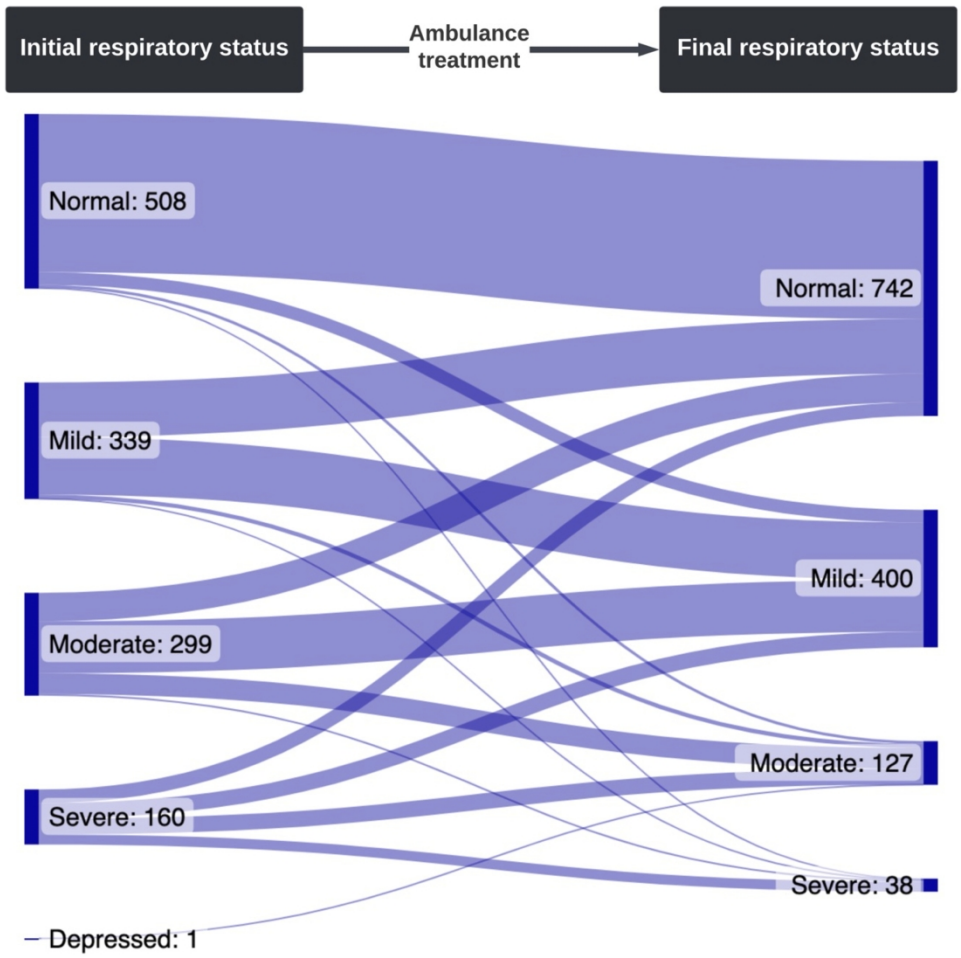

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract YES – see title.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Structured abstract provided
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 7
Objectives	3	State specific objectives, including any prespecified hypotheses Page 8
Methods		
Study design	4	Present key elements of study design early in the paper Page 8 – ("study design" section)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 8-9 ("study setting" section)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case Page 9 ("selection of participants" section)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 9-10 ("data collection" section)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 9-10 ("data collection" section)
Bias	9	Describe any efforts to address potential sources of bias Page 10 (end of "data collection" section)
Study size	10	Explain how the study size was arrived at Page 10 ("analysis" section)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Page 10 ("analysis" section)

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses Page 10 ("analysis" section)
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Page 10-11 ("results" section)
		(b) Give reasons for non-participation at each stage Page 10-11 ("results" section)
		(c) Consider use of a flow diagram – See figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page 10-11 ("results" section) and table 1
		(b) Indicate number of participants with missing data for each variable of interest Not applicable (no missing data)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) Not applicable (no patient follow-up)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures Table 2, Figure 2 and results (page 10-12)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Table 2, Figure 2 and results (page 10-12)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Not applicable. No subgroup analyses performed
Discussion		
Key results	18	Summarise key results with reference to study objectives Page 13-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 14-15

Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 13-15
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Funding disclosures provided

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Acute paediatric asthma treatment in the pre-hospital setting: a retrospective observational study.

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Acute paediatric asthma treatment in the pre-hospital setting: a retrospective observational study.

Simon Craig[1,2,3] MBBS FACEM MPH MHPE, **Belinda Delardes**[4,5] B Paramedic (Hons), **Ziad Nehme**[4,5,6] PhD, **Catherine L Wilson**[3] Dip App Sci Nurs MPH Ms Evaluation and Assessment, **Stuart R Dalziel**[7,8] MBChB FRACP PhD, **Gillian M Nixon**[1,9] MBChB MD FRACP, **Colin VE Powell**[10,11] MBChB DCH MRCP(UK) FRACP FRCPCH MD, **Andis Graudins**[12,13,14] MBBS PhD FACEM FACMT, **Franz E Babl**[3,15,16,17] MD MPH DMedSc FRACP FAAP FACEP on behalf of the PREDICT Network.

Affiliations

1. Department of Paediatrics, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.
2. Monash Emergency Program, Paediatric Emergency Department, Monash Medical Centre, Monash Health, Victoria, Australia.
3. Emergency Research, Clinical Sciences, Murdoch Children's Research Institute, Victoria, Australia
4. Ambulance Victoria, Blackburn North, Victoria, Australia
5. Department of Paramedicine, Monash University, Frankston, Victoria, Australia
6. School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
7. Departments of Surgery and Paediatrics: Child and Youth Health, The University of Auckland, New Zealand.

8. Children's Emergency Department, Starship Children's Hospital, Auckland, New Zealand
9. Department of Respiratory Medicine, Monash Children's Hospital, Melbourne, Victoria, Australia.
10. Division of Population Medicine, School of Medicine, Cardiff, United Kingdom.
11. Emergency Medicine, Sidra Medicine, Doha Qatar
12. Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.
13. Monash Emergency Program, Monash Health, Dandenong Hospital, Victoria, Australia.
14. Monash Health Clinical Toxicology and Addiction Medicine Service, Monash Health, Dandenong Hospital, Victoria, Australia.
15. Department of Emergency Medicine, The Royal Children's Hospital, Victoria, Australia.
16. Department of Paediatrics, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia.
17. Department of Critical Care, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia.

Abstract 238 words (max 300)

Main text 2398 words (max 3000)

27 references (max 30)

2 tables, 2 figures, 1 box (up to 6 total). One supplementary online table.

Corresponding author

Prof Simon Craig

- Paediatric Emergency Department, Monash Medical Centre, Monash Health, Clayton, Victoria, Australia
- Department of Paediatrics, Monash University, Clayton, Victoria, Australia

Simon.Craig@monash.edu

Objectives: To describe the incidence of and patterns of "escalated care" (care in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators) for children receiving pre-hospital treatment for asthma.

Design: Retrospective observational study

Setting: State-wide ambulance service data (Ambulance Victoria in Victoria, Australia, population 6.5 million)

Participants: Children aged 1-17 years and given a final diagnosis of asthma by the treating paramedics and/or treated with inhaled bronchodilators from 1 July 2019 to 30 June 2020.

Primary and secondary outcome measures: We classified "escalation of care" as parenteral administration of adrenaline, or provision of respiratory support. We compared clinical, demographic and treatments administered between those receiving and not receiving escalation of care.

Results: Paramedics attended 1,572 children with acute exacerbations of asthma during the 1-year study period. Of these, 22 (1.4%) had escalated care, all receiving parenteral adrenaline. Patients with escalated care were more likely to be older, had previously required hospital admission for asthma and had severe respiratory distress at initial assessment.
Of 1307 children with respiratory status data available, at arrival to hospital the respiratory status of children had improved overall (normal/mild respiratory distress at initial assessment 847 (64.8%), normal/mild respiratory distress at hospital arrival 1142 (87.4%), p<0.0001).

Conclusions: Most children with acute exacerbations of asthma did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital.

Strengths and limitations of this study

- Highly generalisable, with the use of a comprehensive electronic state-wide ambulance database.
- Most ambulance cases were concentrated in metropolitan regions; this may limit generalisability to rural and regional settings.
- Bias was minimised by direct download from electronic medical record, rather than abstraction by reviewers.
- It is possible that a small number of critically ill cases were misclassified due to an ambulance diagnosis other than asthma.

Introduction

Asthma is a frequent reason for children to attend the emergency department (ED),[1,2] and one of the most common reasons for paediatric hospitalization after an ED visit.[3] In the USA, the rate of paediatric ED visits for asthma increased by 13.3% between 2001 and 2010,[4] while in the United Kingdom, it is estimated that a child is admitted to hospital with an asthma attack every 20 minutes.[5]

Most children with asthma have mild or moderate exacerbations, and respond to first-line treatment with inhaled bronchodilator therapy and systemic steroids.[6-9] However, some children with severe asthma require more intensive therapies including intravenous (IV) medications, endotracheal intubation and/or admission to intensive care.[9-11] Management of acute severe asthma is complicated by a number of problems, including a large number of treatment options, wide variation in self-reported and actual physician practice,[12-15] and a weak evidence base.[16,17]

Early initiation of therapy in the pre-hospital setting may abort an asthma attack and prevent further escalation on arrival to the ED. This in turn may prevent the need for more invasive treatment and potential complications or side effects of medications used in escalation. The introduction of a new treatment protocol emphasizing early use of systemic corticosteroids in a large Emergency Medical Services system was associated with reduced rates of hospitalization, less need for critical care and shorted hospital length of stay.[18] Systemic corticosteroid administration has been the subject of successful improvement projects in the pre-hospital setting.[19] However, a separate study identified high rates of paramedic non-compliance with pre-hospital treatment protocols recommending parenteral adrenaline for children with high-severity respiratory distress.[20]

There are little data available on treatment patterns or pre-hospital outcomes for children with acute asthma in the Australian setting. This study aimed to extract information from the electronic medical records of Ambulance Victoria (AV), Australia, on all children treated for asthma to understand the incidence of and patterns of "escalated" care (care in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators).

Methods

Study design

This was a retrospective cohort study of all children who were either given a final diagnosis of asthma by the treating AV paramedics or treated with inhaled bronchodilators from 1 July 2019 to 30 June 2020. The project is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[21] The study was approved by the Royal Children's Hospital Research Ethics and Governance Office, Melbourne, Australia (60707) and the Ambulance Victoria Research Governance Committee, Melbourne, Australia.

Study setting

AV is the single public emergency medical service for the state of Victoria, Australia (population of 6.5 million over 227,000 square kilometres).

AV clinical practice guidelines[22] provide recommendations for asthma management according to severity (Box 1), which include: inhaled salbutamol via a pressurised metered dose inhaler (pMDI) as initial treatment for mild / moderate asthma; nebulised salbutamol and ipratropium reserved for severe or critical illness, or failure of moderate asthma to respond to treatment after 20 minutes; corticosteroids (intravenous or oral dexamethasone) for critical asthma in children and for severe and critical asthma in adults; parenteral adrenaline

(intramuscular, intravenous infusion or titrated boluses) for critical asthma; and assisted ventilation and/or intubation for unconsciousness or respiratory arrest. Children aged 12 years or more are managed according to an "adult" algorithm, which has a lower threshold for corticosteroids compared to the paediatric algorithm (recommended for all severe cases, rather than only in critical illness) .[22]

Selection of participants.

We searched the AV electronic patient care system for presentations of children aged more than one year and less than 18 years matching the following criteria: final primary assessment of asthma or cough or shortness of breath. We excluded children with a paramedic diagnosis of cough or shortness of breath if they were not administered any inhaled bronchodilator (salbutamol or ipratropium). Records of cases assessed by multiple ambulance teams during the same incident were unified as a single paramedic attendance. Interhospital transports and patients managed for cardiac arrest were excluded.

Data collection

Data were extracted directly from the AV medical record database into a purpose-designed spreadsheet and analysed. Exact medication doses were not extracted, as treatment is highly protocolised (Box 1).

We defined "respiratory support" as the use of continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), assisted ventilation, intubation and mechanical ventilation, or application of a bag-valve-mask device.

We defined "escalation" of care as parenteral administration of adrenaline, or provision of respiratory support. Although AV protocols recommend oral (or parenteral) corticosteroids

for severe and critical asthma, corticosteroids are usually considered part of routine asthma care (rather than reserved for critical illness). We did not include nebulised adrenaline for suspected croup / upper airway obstruction. The case notes were reviewed and verified by a second paramedic abstractor (BD) for all patients where escalation was identified through electronic medical record data.

Analysis

Descriptive statistics were used to summarise patient characteristics, clinical features and treatments administered. Non-parametric data is reported using median and interquartile range (IQR), while categorical data is presented as count and percentage. We did not impute any missing data.

Comparisons were made between those requiring escalation of care to those not requiring escalation of care. Categorical data is compared using Chi-square test or Fisher's exact test as appropriate. Non-parametric data is compared using Mann-Whitney U test.

All analyses were performed using SPSS for Windows (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.).

Patient and public involvement

Patients were not involved in the design of this study.

Results

Over the study period, the service responded to 633,950 on-road emergency cases,[23] mainly using advanced life support (ALS) or mobile intensive care ambulance (MICA) paramedics. We identified 3,587 children who had been assessed by AV with a primary assessment diagnosis

of asthma, cough, or shortness of breath, 1,520 were excluded, leaving 1,572 children managed by AV with asthma (figure 1).

The median age of the cohort was 6 years (IQR 4-10 years) and 888 (56.5%) were male. Most (87.6%) patients had a documented past history of asthma, 115 (7.3%) had been hospitalised, 63 (4%) had required intensive care admission, and 19 (1.2%) had been intubated for a previous asthma exacerbation. Information on usual asthma medications was not available. The median initial respiratory rate was 32 breaths/minute (IQR 24 – 40 breaths/minute). Of the 1,460 patients who had initial work of breathing documented, 978 (67.0%) had normal or mild work of breathing, and 166 (7.7%) had severe work of breathing.

Ambulance response time was a median of 11.9 minutes (IQR 8.2 to 15.2 minutes); paramedics were on the scene with the patient for a median of 17 minutes (IQR 12.7 to 25.1 minutes). Patients were transported by ambulance in 90% (n=1419) of attendances.

Paramedics administered inhaled bronchodilators in 946 (60.2%) of cases. Of those, 493 (52.1%) received salbutamol alone, 13 (1.4%) received ipratropium alone, and 440 (46.5%) received salbutamol and ipratropium. For those receiving bronchodilators, a median (IQR) of 1 (1-2) administrations were recorded. Oxygen administration was documented in 306 (19.4%) patients, most commonly by nebuliser mask, nasal cannulae, or an oxygen mask; however, 514 (32.6%) received nebulised medication, driven by oxygen. Oral corticosteroids were administered to 141 (9.0%) patients.

Twenty-six records were reviewed for escalation of care; in four patients the electronic record was incorrectly coded, due to inadvertent selection of intravenous salbutamol (used by AV for pre-term labour) instead of nebulised salbutamol, leaving 22 (1.4%) patients with escalated care (figure 1). Patients with escalated care were more likely to be older, had previously required hospital admission for asthma and had severe respiratory distress at

initial assessment (Table 1). Those receiving escalated care were more likely to be treated with inhaled bronchodilators, corticosteroids and oxygen (Table 2). With increasing severity of illness, children were more likely to be administered nebulised salbutamol, less likely to be administered salbutamol by a pMDI, more likely to receive ipratropium and more likely to receive systemic corticosteroids (Supplementary Online Table).

All patients who received escalated care received parenteral adrenaline. No patients received non-invasive ventilation, assisted ventilation or intubation. Four children (aged two, fourteen, sixteen and seventeen years) received an adrenaline infusion. One patient who received IM adrenaline also had a bag-valve-mask applied, however, did not receive positive pressure ventilation. They were a two-year-old child who had difficulty breathing and cough that was not improving with salbutamol administered at home. They became unresponsive after a coughing episode and bystander cardiopulmonary resuscitation was initiated. They were breathing spontaneously and responsive upon initial paramedic assessment.

Reports of respiratory status at initial assessment and hospital arrival were available for 1307 (85.5%) of the cohort. On arrival to hospital the respiratory status of children had improved overall (normal/mild respiratory distress at initial assessment 847 (64.8%), normal/mild respiratory distress at hospital arrival 1142 (87.4%), $p<0.0001$). One hundred and thirty-one (81.2%) of the 160 children with severe respiratory distress at initial assessment had improved. Of the 847 children with normal/mild respiratory distress at initial assessment, only 24 (2.8%) were documented as having moderate or severe respiratory distress at hospital arrival; and only 9 (0.8%) of the 1146 children with normal/mild/moderate respiratory distress at initial assessment were documented as having severe respiratory distress at hospital arrival (Figure 2).

Discussion.

This study provides a population-based state-wide assessment of pre-hospital asthma management in children. Most children with acute exacerbations of asthma in Victoria, Australia, did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Although more than 60% had either mild or no respiratory distress, over 90% of all patients were transported to hospital. Overall, the respiratory status of children improved from ambulance arrival to hospital arrival in all severity categories.

The overall rate of parenteral bronchodilator (adrenaline) administration was 1.6%. No patients received non-invasive ventilation, assisted ventilation or intubation, and most patients were treated with inhaled bronchodilators and clinically improved by the time they arrived in hospital. Those receiving escalated care were older, were more likely to have a history of asthma requiring hospital admission and/or intubation and have severe respiratory distress on ambulance arrival.

A recent large study described in-hospital management of acute asthma exacerbations in Australia and New Zealand. In 14,029 children, there was a higher overall rates of escalated therapy (7.3% overall, with 4.2% receiving parenteral bronchodilators and 4.3% respiratory support).[24] A common indication for escalation of care is failure to adequately respond to first-line therapy. The relatively low rates of treatment escalation in the pre-hospital setting (1.6%) suggests that a small proportion of children are seriously ill, while most are early in their treatment, and may not have had sufficient time to demonstrate improvement (or lack of improvement) prior to hospital arrival.

There is little evidence to guide escalated therapy for asthma. A recent Overview of Cochrane reviews of clinical trials on escalated therapy for asthma[16] assessed the evidence for parenteral bronchodilators, Heliox, respiratory support and inhaled magnesium. The review

found that the majority of comparisons involved between one and three trials and fewer than 100 participants, making it difficult to assess the balance between benefits and potential harms. The authors were unable to make firm practice recommendations.[16]

There is little evidence to support intramuscular adrenaline as first-line treatment for seriously ill children with asthma,[25] although it has a number of advantages, including ease of administration and paramedic familiarity. Parenteral adrenaline is also used for anaphylaxis, cardiac arrest, and management of hypotension, while nebulised adrenaline is used for severe upper airway obstruction in croup. In addition, it can be easily and rapidly administered as there is no need for dilution prior to administration, and no requirement for a prolonged infusion.[22]

Pre-hospital treatment of asthma rarely results in escalation of therapy beyond inhaled bronchodilators and systemic corticosteroids. In addition, the use of parenteral bronchodilators is often reserved for those who do not improve after initial inhaled bronchodilators, and is administered relatively late in the course of an ED visit.[15] Given that most children with asthma will improve with pre-hospital treatment, and/or will not have sufficient time to "fail to improve" with standard therapy, it appears that any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

Limitations

Inclusion in the study was based on a combination of paramedic diagnosis of asthma and administration of inhaled bronchodilators. While only 89% had a diagnosis of asthma recorded in the ambulance notes, it seems that the cohort is reflective of the asthma population as over 87% of cases had a previous diagnosis of asthma.

Due to state-wide data collection and large numbers of patients, our study is likely to be generalisable to other settings with similar pre-hospital care systems. However, most ambulance cases within Victoria are concentrated in the metropolitan area of Melbourne (the capital city), which may limit generalisability to rural and regional settings. Approximately 10% of children were not transported to hospital; this is similar to the rate identified in a study of children with seizures from the same ambulance service.[26]

This study is a retrospective review of a comprehensive electronic database. We optimised data extraction and minimised bias through the collection of variables using a piloted data collection instrument, and application of pre-defined inclusion and exclusion criteria.[27,28] Due to the nature of record-keeping within the ambulance service (all cases are documented using the electronic system), it is unlikely that any cases of escalated care were missed. As we downloaded fields directly from the electronic medical record system, we did not independently abstract any variables. However, we verified all instances of documented escalation of care through consultation with a second (paramedic) reviewer and identified four cases of misclassification. It is possible that we missed some children who were not classified as asthma, were critically ill, not given inhaled bronchodilators and only given parenteral adrenaline. However, this is likely to be a very small number of cases. There was some missing data on final observations on arrival to hospital, however, this was not a primary objective of our study.

Conclusions

Most children with acute exacerbations of asthma did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital. Due

to the very low incidence of treatment escalation or clinical deterioration, any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

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Figure 1. Flow chart – pre-hospital management of acute asthma in children.

AV, Ambulance Victoria.

Box 1. Asthma severity assessment and treatment according to Ambulance Victoria Clinical Practice Guidelines

Mild / Moderate: normal conscious state, some increased work of breathing, tachycardia, speaking in phrases / sentences

- Salbutamol pMDI and spacer:
  - 6 or more years: 4-12 doses
  - 2-5 years: 2-6 doses

Severe: agitated / distressed, markedly increased work of breathing, including accessory muscle use / retraction, tachycardia, speaking in words.

- Salbutamol nebulised (repeated at 20 minutes if required)
  - 2-4 years: 2.5 mg
  - 5-11 years: 2.5 - 5 mg
- Ipratropium bromide nebulised 250 mcg

Critical: altered conscious state, maximal work of breathing, marked tachycardia, unable to talk.

- Salbutamol nebulised 10 mg (repeated at 5 minutes if required)
- Ipratropium bromide nebulised 250 mcg
- Adrenaline 10 mcg/kg IM (repeated at 5 minutes if required)
- Dexamethasone 0.6 mg/kg IV or oral (max 12 mg)
- Adrenaline IV boluses and infusion (for Mobile Intensive Care Paramedics)

Table 1. Demographics and clinical characteristics of children treated or assessed for asthma by AV.

	Total (n=1572)	Escalation of care (n=22)	No escalation of care (n=1550)	P value (escalation vs no escalation)
Age, years, n (%)				
1-4	561 (36.3)	6 (27.3)	555 (35.8)	0.38
5-11	690 (43.9)	9 (40.9)	681 (43.9)	
12-17	321 (20.4)	7 (31.8)	314 (20.3)	
Median age, years (IQR)	6 (4-10)	10.5 (3.8 – 14.3)	6 (3.8 – 10)	0.045
Female sex, n (%)	684 (43.5)	11 (50)	877 (43.4)	0.54
Pre-existing conditions, n (%)				
Asthma	1377 (87.6)	20 (90.9)	1357 (87.5)	0.64
Requiring hospital admission	115 (7.3)	5 (22.7)	110 (7.1)	0.005
Requiring intensive care	63 (4)	1 (4.5)	62 (4)	0.89
Requiring intubation	19 (1.2)	1 (4.5)	18 (1.2)	0.15
With cardiac / respiratory arrest	5 (0.3)	0 (0)	5 (0.3)	0.79
Other respiratory illness				
Croup	94 (6)	1 (4.5)	93 (6)	0.78
Bronchiolitis	80 (5.1)	1 (4.5)	79 (5.1)	0.91
Pneumonia	44 (2.8)	1 (4.5)	43 (2.8)	0.62
Chest infection	32 (2)	1 (4.5)	31 (2)	0.40
Other	8 (0.5)	0 (0)	8 (0.5)	0.64
Initial physiological parameters				
Respiratory rate (breaths/minute), median (IQR)	32 (24 – 40)	35.5 (28 – 48.5)	32 (24 – 40)	0.09
Pulse rate (beats/minute), median (IQR)	130 (112 – 146)	134.5 (120 – 150.5)	130 (112 – 146)	0.24
Initial respiratory status, n (%)				
Normal	615 (39.1)	3 (13.6)	612 (39.5)	<0.001
Mild respiratory distress	363 (23.1)	1 (4.5)	362 (23.4)	
Moderate respiratory distress	315 (20)	2 (9.1)	313 (20.2)	
Severe respiratory distress	166 (10.6)	16 (72.7)	150 (9.7)	
Depressed respirations	1 (0.1)	0 (0)	1 (0.1)	
Final physiological parameters				

Respiratory rate (breaths/minute), median (IQR) †	28 (22 – 36)	28 (22 – 36)	30 (27 – 40)	0.06
Pulse rate (beats/minute), median (IQR) †	126 (108 – 142)	126 (108 – 142)	126 (112-162)	0.29
Final respiratory status, n (%)‡				
Normal	742 (56.8)	4 (18.2)	738 (57.4)	<0.001
Mild respiratory distress	400 (30.6)	4 (18.2)	396 (30.8)	
Moderate respiratory distress	127 (9.7)	6 (27.3)	121 (9.4)	
Severe respiratory distress	38 (2.9)	8 (36.4)	30 (2.4)	

All P values calculated using Chi-Square tests, except for continuous variables where Mann-Whitney U tests* were used.

† Data was not available for final pulse rate and respiratory rate for 54 patients in the "No escalation of care" group

‡ Data was not available for final respiratory status for 265 patients in the "No escalation of care" group

Table 2. Treatment provided by AV paramedics.

	Total (n=1572)	Escalation of care (n=22)	No escalation of care (n=1550)	P value (escalation vs no escalation)
Respiratory support, n(%)				
Bag-valve-mask applied	1 (0.1)	1 (4.5)	0 (0)	<0.001
Oxygen delivery				
Nasal cannulae	46 (2.9)	4 (18.2)	42 (2.7)	<0.001
Nebuliser mask	258 (16.4)	10 (45.5)	248 (16)	<0.001
Oxygen mask	48 (3.1)	0 (0)	48 (3.1)	0.40
Non-rebreather mask	8 (0.5)	0 (0)	8 (0.5)	0.74
Other oxygen therapy (not otherwise specified)	2 (0.1)	0 (0)	2 (0.1)	0.87
Parenteral bronchodilator				
Adrenaline IM injection	20 (1.3)	20 (90.9)	0 (0)	<0.001
Adrenaline infusion	4 (0.3)	4 (18.2)	0 (0)	<0.001
Dexamethasone				
IV injection	25 (1.6)	4 (18.2)	21 (1.4)	<0.001
Oral	141 (9)	11 (50)	130 (8.4)	<0.001
Inhaled bronchodilator				
Any inhaled bronchodilator	946 (60.2)	21 (95.5)	925 (59.7)	<0.001
Any Ipratropium bromide nebulisation	453 (28.8)	17 (77.3)	436 (28.1)	<0.001
Any Salbutamol pMDI	465 (29.6)	3 (13.6)	462 (29.8)	0.10
Any Salbutamol nebulisation	513 (32.6)	20 (90.9)	493 (31.8)	<0.001
Single administration of inhaled salbutamol	348 (22.1)	3 (13.6)	345 (22.3)	
Single administration of inhaled ipratropium bromide	13 (0.8)	1 (4.5)	12 (0.8)	
Single administration of inhaled salbutamol and single administration of inhaled iptratropium bromide	280 (17.8)	6 (27.3)	274 (17.7)	
Two adminitrations of inhaled salbutamol alone	114 (7.3)	1 (4.5)	113 (7.3)	
Two administrations of inhaled salbutamol and at	112 (7.1)	3 (13.6)	109 (7)	

least one administration of ipratropium bromide				
Three or more administations of inhaled salbutamol alone	31 (2.0)	0 (0)	31 (2)	
Three or more administrations of inhaled salbutamol and at least one administration of ipratropium bromide	48 (3.1)	7 (31.8)	41 (2.6)	
Total instances of inhaled bronchodilator administration, median (IQR)	1 (0-2)	2 (1.8 – 4)	1 (0 – 2)	<0.001
Intravenous access				
Intravenous access attempt	39 (2.5)	7 (31.8)	32 (2.1)	<0.001
Successful IV attempt	34 (2.2)	7 (31.8)	27 (1.7)	<0.001

No patients received any of: BIPAP, manual ventilation, mechanical ventilation, IV salbutamol infusion, IM dexamethasone.

Figure 2. Initial and final respiratory status documented by AV paramedics.

Note: 111 patients missing initial respiratory status, and 265 missing final respiratory status.

Contributorship statement

SC, CW and FEB identified the research question. SC and CLW were responsible for the study design and research protocol. BD and ZN obtained data and input into data cleaning and analysis. SC was responsible for statistical analysis. SC drafted the initial manuscript. SC, BD, ZN, CLW, SRD, GMN, CVEP, AG and FEB contributed equally to writing, reviewing and editing the manuscript.

All authors provided comments on the drafts and have read and approved the final version of the article. All authors has full access to all of the data (including statistical reports and tables) at the conclusion of the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

SC is the guarantor for the paper, accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish.

Competing interests

There are no competing interests for any author.

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FEB's time was part funded by a grant from the Royal Children's Hospital Foundation, Melbourne, Victoria, Australia; an NHMRC (National Health and Medical Research Council) Practitioner Fellowship; and an NHMRC Investigator Leadership Grant (GNT1171228).

ZN's time is part funded by a grant from the National Heart Foundation of Australia.

Data sharing statement

Data are available on reasonable request. De-identified participant data will be available for sharing from 1 July 2024. Any data access requests should be sent to SC (simon.craig@monash.edu), and should include a proposal from the individual or organisation regarding their plan for use of the data.

The study team will review the request and consider the scientific merit of the proposed use of the data, and the legal, regulatory and ethical issues pertinent to the request. Presuming all constraints are addressed, the data will be shared using a secure file transfer platform.

Ethical statement.

The project was approved by the Royal Children's Hospital Research Ethics and Governance Office, Melbourne, Australia (60707), and the Ambulance Victoria Research Governance Committee, Melbourne, Australia.

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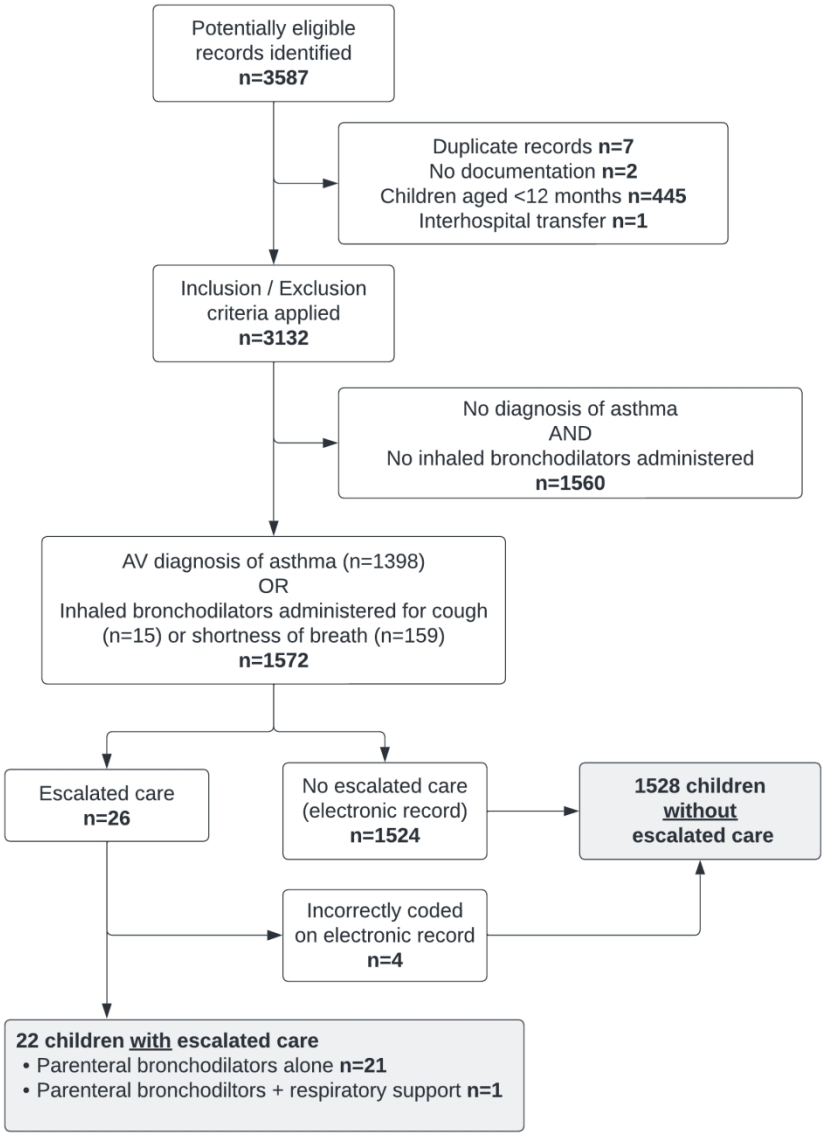
Supplementary Online Table

Administration of asthma treatment according to initial respiratory status

	Normal respiratory status or mild respiratory distress (n=978)	Moderate respiratory distress (n=315)	Severe respiratory distress or Depressed respirations (n=167)
Salbutamol (pMDI)			
n (%)	314 (32.1)	111 (35.2)	15 (9.0)
Median (IQR)	0 (0 – 1)	0 (0 – 1)	0 (0 – 0)
Salbutamol (nebuliser)			
n (%)	155 (15.8)	182 (57.8)	151 (90.4)
Median (IQR)	0 (0 – 0)	1 (0 – 1)	1 (1 – 2)
Any salbutamol			
n (%)	455 (46.5)	274 (87.0)	157 (94.0)
Median (IQR)	0 (0 – 0)	1 (0 – 1)	1 (1 – 2)
Ipratropium, n (%)			
n (%)	125 (12.8)	164 (52.1)	144 (86.2)
Median (IQR)	0 (0 – 0	1 (0 – 1)	1 (1 – 1)
Dexamethasone (any route)			
Any route, n (%)	41 (4.2)	56 (17.8)	58 (34.8)



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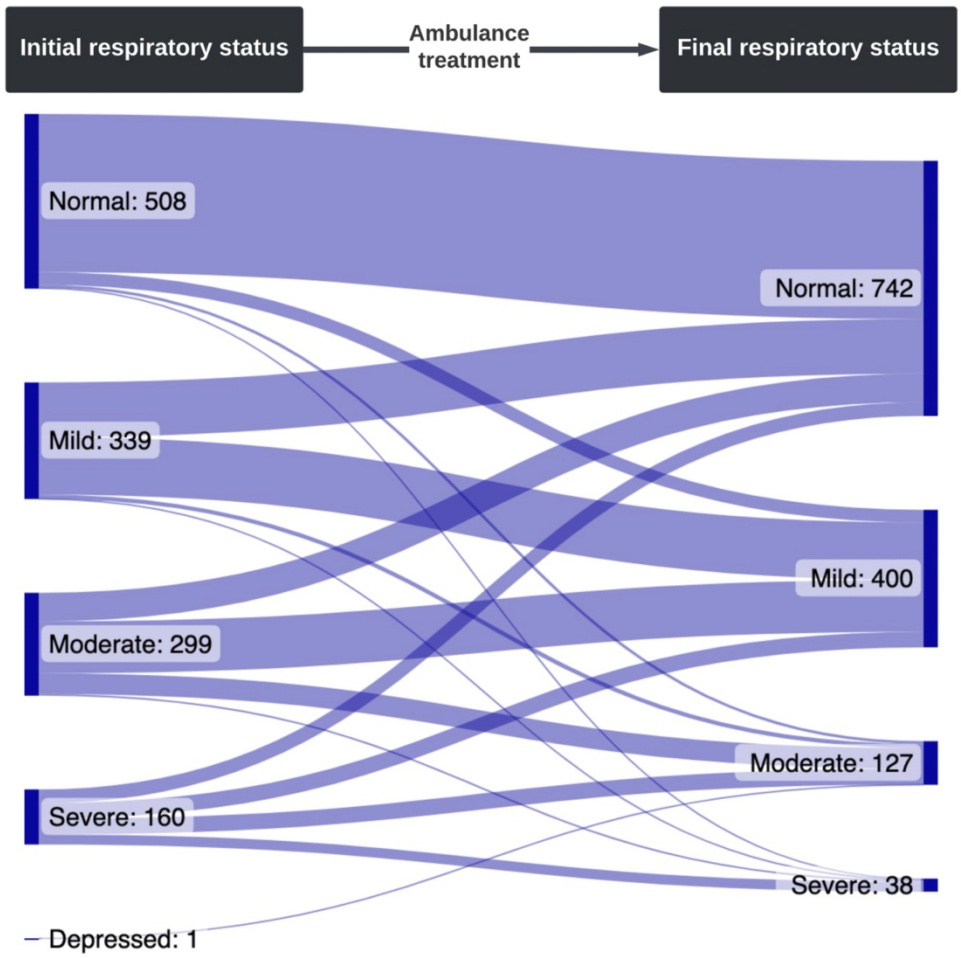

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract YES – see title.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Structured abstract provided
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 7
Objectives	3	State specific objectives, including any prespecified hypotheses Page 8
Methods		
Study design	4	Present key elements of study design early in the paper Page 8 – ("study design" section)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 8-9 ("study setting" section)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case Page 9 ("selection of participants" section)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 9-10 ("data collection" section)
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Bias	9	Describe any efforts to address potential sources of bias Page 10 (end of "data collection" section)
Study size	10	Explain how the study size was arrived at Page 10 ("analysis" section)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Page 10 ("analysis" section)

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
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		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) Not applicable (no patient follow-up)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
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Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
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		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Table 2, Figure 2 and results (page 10-12)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Not applicable. No subgroup analyses performed
Discussion		
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Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 14-15

Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 13-15
Other information		
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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BMJ Open

Acute paediatric asthma treatment in the pre-hospital setting: a retrospective observational study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-073029.R2
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Complete List of Authors:	Craig, Simon; Monash Medical Centre Clayton, Paediatric Emergency Department; Monash University Department of Paediatrics Delardes, Belinda; Ambulance Victoria; Monash University Department of Paramedicine Nehme, Ziad; Ambulance Victoria, Research & Evaluation; Monash University School of Public Health and Preventive Medicine Wilson, Catherine; Murdoch Childrens Research Institute, Emergency Medicine Research Group; PREDICT, Research Group Dalziel, Stuart; Starship Children's Health, Emergency Department; The University of Auckland Faculty of Medical and Health Sciences, Paediatrics and Surgery Nixon, Gillian; Monash University Department of Paediatrics; Monash Children's Hospital, Respiratory Medicine Powell, Colin; Sidra Medical and Research Center, Department of Emergency Medicine; Cardiff School of Health Sciences Graudins, Andis; Monash Health, Dandenong Emergency Department; Monash University Babl, Franz; Royal Childrens Hospital, Emergency Department; The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Paediatrics
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Acute paediatric asthma treatment in the pre-hospital setting: a retrospective observational study.

Simon Craig[1,2,3] MBBS FACEM MPH MHPE, **Belinda Delardes**[4,5] B Paramedic (Hons), **Ziad Nehme**[4,5,6] PhD, **Catherine L Wilson**[3] Dip App Sci Nurs MPH Ms Evaluation and Assessment, **Stuart R Dalziel**[7,8] MBChB FRACP PhD, **Gillian M Nixon**[1,9] MBChB MD FRACP, **Colin VE Powell**[10,11] MBChB DCH MRCP(UK) FRACP FRCPCH MD, **Andis Graudins**[12,13,14] MBBS PhD FACEM FACMT, **Franz E Babl**[3,15,16,17] MD MPH DMedSc FRACP FAAP FACEP on behalf of the PREDICT Network.

Affiliations

1. Department of Paediatrics, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.
2. Monash Emergency Program, Paediatric Emergency Department, Monash Medical Centre, Monash Health, Victoria, Australia.
3. Emergency Research, Clinical Sciences, Murdoch Children's Research Institute, Victoria, Australia
4. Ambulance Victoria, Blackburn North, Victoria, Australia
5. Department of Paramedicine, Monash University, Frankston, Victoria, Australia
6. School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
7. Departments of Surgery and Paediatrics: Child and Youth Health, The University of Auckland, New Zealand.

8. Children's Emergency Department, Starship Children's Hospital, Auckland, New Zealand
9. Department of Respiratory Medicine, Monash Children's Hospital, Melbourne, Victoria, Australia.
10. Division of Population Medicine, School of Medicine, Cardiff, United Kingdom.
11. Emergency Medicine, Sidra Medicine, Doha Qatar
12. Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.
13. Monash Emergency Program, Monash Health, Dandenong Hospital, Victoria, Australia.
14. Monash Health Clinical Toxicology and Addiction Medicine Service, Monash Health, Dandenong Hospital, Victoria, Australia.
15. Department of Emergency Medicine, The Royal Children's Hospital, Victoria, Australia.
16. Department of Paediatrics, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia.
17. Department of Critical Care, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia.

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Corresponding author

Prof Simon Craig

- Paediatric Emergency Department, Monash Medical Centre, Monash Health, Clayton, Victoria, Australia
- Department of Paediatrics, Monash University, Clayton, Victoria, Australia

Simon.Craig@monash.edu

Objectives: To describe the incidence of and patterns of "escalated care" (care in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators) for children receiving pre-hospital treatment for asthma.

Design: Retrospective observational study

Setting: State-wide ambulance service data (Ambulance Victoria in Victoria, Australia, population 6.5 million)

Participants: Children aged 1-17 years and given a final diagnosis of asthma by the treating paramedics and/or treated with inhaled bronchodilators from 1 July 2019 to 30 June 2020.

Primary and secondary outcome measures: We classified "escalation of care" as parenteral administration of adrenaline, or provision of respiratory support. We compared clinical, demographic and treatments administered between those receiving and not receiving escalation of care.

Results: Paramedics attended 1,572 children with acute exacerbations of asthma during the 1-year study period. Of these, 22 (1.4%) had escalated care, all receiving parenteral adrenaline. Patients with escalated care were more likely to be older, had previously required hospital admission for asthma and had severe respiratory distress at initial assessment.
Of 1307 children with respiratory status data available, at arrival to hospital the respiratory status of children had improved overall (normal/mild respiratory distress at initial assessment 847 (64.8%), normal/mild respiratory distress at hospital arrival 1142 (87.4%), p<0.0001).

Conclusions: Most children with acute exacerbations of asthma did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital.

Strengths and limitations of this study

- Highly generalisable, with the use of a comprehensive electronic state-wide ambulance database.
- Most ambulance cases were concentrated in metropolitan regions; this may limit generalisability to rural and regional settings.
- Bias was minimised by direct download from electronic medical record, rather than abstraction by reviewers.
- It is possible that a small number of critically ill cases were misclassified due to an ambulance diagnosis other than asthma.

Introduction

Asthma is a frequent reason for children to attend the emergency department (ED),[1,2] and one of the most common reasons for paediatric hospitalization after an ED visit.[3] In the USA, the rate of paediatric ED visits for asthma increased by 13.3% between 2001 and 2010,[4] while in the United Kingdom, it is estimated that a child is admitted to hospital with an asthma attack every 20 minutes.[5]

Most children with asthma have mild or moderate exacerbations, and respond to first-line treatment with inhaled bronchodilator therapy and systemic steroids.[6-9] However, some children with severe asthma require more intensive therapies including intravenous (IV) medications, endotracheal intubation and/or admission to intensive care.[9-11] Management of acute severe asthma is complicated by a number of problems, including a large number of treatment options, wide variation in self-reported and actual physician practice,[12-15] and a weak evidence base.[16,17]

Early initiation of therapy in the pre-hospital setting may abort an asthma attack and prevent further escalation on arrival to the ED. This in turn may prevent the need for more invasive treatment and potential complications or side effects of medications used in escalation. The introduction of a new treatment protocol emphasizing early use of systemic corticosteroids in a large Emergency Medical Services system was associated with reduced rates of hospitalization, less need for critical care and shorted hospital length of stay.[18] Systemic corticosteroid administration has been the subject of successful improvement projects in the pre-hospital setting.[19] However, a separate study identified high rates of paramedic non-compliance with pre-hospital treatment protocols recommending parenteral adrenaline for children with high-severity respiratory distress.[20]

There are little data available on treatment patterns or pre-hospital outcomes for children with acute asthma in the Australian setting. This study aimed to extract information from the electronic medical records of Ambulance Victoria (AV), Australia, on all children treated for asthma to understand the incidence of and patterns of "escalated" care (care in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators).

Methods

Study design

This was a retrospective cohort study of all children who were either given a final diagnosis of asthma by the treating AV paramedics or treated with inhaled bronchodilators from 1 July 2019 to 30 June 2020. The project is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[21] The study was approved by the Royal Children's Hospital Research Ethics and Governance Office, Melbourne, Australia (60707) and the Ambulance Victoria Research Governance Committee, Melbourne, Australia.

Study setting

AV is the single public emergency medical service for the state of Victoria, Australia (population of 6.5 million over 227,000 square kilometres).

AV clinical practice guidelines[22] provide recommendations for asthma management according to severity (Box 1), which include: inhaled salbutamol via a pressurised metered dose inhaler (pMDI) as initial treatment for mild / moderate asthma; nebulised salbutamol and ipratropium reserved for severe or critical illness, or failure of moderate asthma to respond to treatment after 20 minutes; corticosteroids (intravenous or oral dexamethasone) for critical asthma in children and for severe and critical asthma in adults; parenteral adrenaline

(intramuscular, intravenous infusion or titrated boluses) for critical asthma; and assisted ventilation and/or intubation for unconsciousness or respiratory arrest. Children aged 12 years or more are managed according to an "adult" algorithm, which has a lower threshold for corticosteroids compared to the paediatric algorithm (recommended for all severe cases, rather than only in critical illness) .[22]

Selection of participants.

We searched the AV electronic patient care system for presentations of children aged more than one year and less than 18 years matching the following criteria: final primary assessment of asthma or cough or shortness of breath. We excluded children with a paramedic diagnosis of cough or shortness of breath if they were not administered any inhaled bronchodilator (salbutamol or ipratropium). Records of cases assessed by multiple ambulance teams during the same incident were unified as a single paramedic attendance. Interhospital transports and patients managed for cardiac arrest were excluded.

Data collection

Data were extracted directly from the AV medical record database into a purpose-designed spreadsheet and analysed. Exact medication doses were not extracted, as treatment is highly protocolised (Box 1).

We defined "respiratory support" as the use of continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), assisted ventilation, intubation and mechanical ventilation, or application of a bag-valve-mask device.

We defined "escalation" of care as parenteral administration of adrenaline, or provision of respiratory support. Although AV protocols recommend oral (or parenteral) corticosteroids

for severe and critical asthma, corticosteroids are usually considered part of routine asthma care (rather than reserved for critical illness). We did not include nebulised adrenaline for suspected croup / upper airway obstruction. The case notes were reviewed and verified by a second paramedic abstractor (BD) for all patients where escalation was identified through electronic medical record data.

Analysis

Descriptive statistics were used to summarise patient characteristics, clinical features and treatments administered. Non-parametric data is reported using median and interquartile range (IQR), while categorical data is presented as count and percentage. We did not impute any missing data.

Comparisons were made between those requiring escalation of care to those not requiring escalation of care. Categorical data is compared using Chi-square test or Fisher's exact test as appropriate. Non-parametric data is compared using Mann-Whitney U test.

All analyses were performed using SPSS for Windows (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.).

Patient and public involvement

Patients were not involved in the design of this study.

Results

Over the study period, the service responded to 633,950 on-road emergency cases,[23] mainly using advanced life support (ALS) or mobile intensive care ambulance (MICA) paramedics. We identified 3,587 children who had been assessed by AV with a primary assessment diagnosis

of asthma, cough, or shortness of breath, 1,520 were excluded, leaving 1,572 children managed by AV with asthma (figure 1).

The median age of the cohort was 6 years (IQR 4-10 years) and 888 (56.5%) were male. Most (87.6%) patients had a documented past history of asthma, 115 (7.3%) had been hospitalised, 63 (4%) had required intensive care admission, and 19 (1.2%) had been intubated for a previous asthma exacerbation. Information on usual asthma medications was not available. The median initial respiratory rate was 32 breaths/minute (IQR 24 – 40 breaths/minute). Of the 1,460 patients who had initial work of breathing documented, 978 (67.0%) had normal or mild work of breathing, and 166 (7.7%) had severe work of breathing.

Ambulance response time was a median of 11.9 minutes (IQR 8.2 to 15.2 minutes); paramedics were on the scene with the patient for a median of 17 minutes (IQR 12.7 to 25.1 minutes). Patients were transported by ambulance in 90% (n=1419) of attendances.

Paramedics administered inhaled bronchodilators in 946 (60.2%) of cases. Of those, 493 (52.1%) received salbutamol alone, 13 (1.4%) received ipratropium alone, and 440 (46.5%) received salbutamol and ipratropium. For those receiving bronchodilators, a median (IQR) of 1 (1-2) administrations were recorded. Oxygen administration was documented in 306 (19.4%) patients, most commonly by nebuliser mask, nasal cannulae, or an oxygen mask; however, 514 (32.6%) received nebulised medication, driven by oxygen. Oral corticosteroids were administered to 141 (9.0%) patients.

Twenty-six records were reviewed for escalation of care; in four patients the electronic record was incorrectly coded, due to inadvertent selection of intravenous salbutamol (used by AV for pre-term labour) instead of nebulised salbutamol, leaving 22 (1.4%) patients with escalated care (figure 1). Patients with escalated care were more likely to be older, had previously required hospital admission for asthma and had severe respiratory distress at

initial assessment (Table 1). Those receiving escalated care were more likely to be treated with inhaled bronchodilators, corticosteroids and oxygen (Table 2). With increasing severity of illness, children were more likely to be administered nebulised salbutamol, less likely to be administered salbutamol by a pMDI, more likely to receive ipratropium and more likely to receive systemic corticosteroids (Supplementary Online Table).

All patients who received escalated care received parenteral adrenaline. No patients received non-invasive ventilation, assisted ventilation or intubation. Four children (aged two, fourteen, sixteen and seventeen years) received an adrenaline infusion. One patient who received IM adrenaline also had a bag-valve-mask applied, however, did not receive positive pressure ventilation. They were a two-year-old child who had difficulty breathing and cough that was not improving with salbutamol administered at home. They became unresponsive after a coughing episode and bystander cardiopulmonary resuscitation was initiated. They were breathing spontaneously and responsive upon initial paramedic assessment.

Reports of respiratory status at initial assessment and hospital arrival were available for 1307 (85.5%) of the cohort. On arrival to hospital the respiratory status of children had improved overall (normal/mild respiratory distress at initial assessment 847 (64.8%), normal/mild respiratory distress at hospital arrival 1142 (87.4%), $p<0.0001$). One hundred and thirty-one (81.2%) of the 160 children with severe respiratory distress at initial assessment had improved. Of the 847 children with normal/mild respiratory distress at initial assessment, only 24 (2.8%) were documented as having moderate or severe respiratory distress at hospital arrival; and only 9 (0.8%) of the 1146 children with normal/mild/moderate respiratory distress at initial assessment were documented as having severe respiratory distress at hospital arrival (Figure 2).

Discussion.

This study provides a population-based state-wide assessment of pre-hospital asthma management in children. Most children with acute exacerbations of asthma in Victoria, Australia, did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Although more than 60% had either mild or no respiratory distress, over 90% of all patients were transported to hospital. Overall, the respiratory status of children improved from ambulance arrival to hospital arrival in all severity categories.

The overall rate of parenteral bronchodilator (adrenaline) administration was 1.6%. No patients received non-invasive ventilation, assisted ventilation or intubation, and most patients were treated with inhaled bronchodilators and clinically improved by the time they arrived in hospital. Those receiving escalated care were older, were more likely to have a history of asthma requiring hospital admission and/or intubation and have severe respiratory distress on ambulance arrival.

A recent large study described in-hospital management of acute asthma exacerbations in Australia and New Zealand. In 14,029 children, there was a higher overall rates of escalated therapy (7.3% overall, with 4.2% receiving parenteral bronchodilators and 4.3% respiratory support).[24] A common indication for escalation of care is failure to adequately respond to first-line therapy. The relatively low rates of treatment escalation in the pre-hospital setting (1.6%) suggests that a small proportion of children are seriously ill, while most are early in their treatment, and may not have had sufficient time to demonstrate improvement (or lack of improvement) prior to hospital arrival.

There is little evidence to guide escalated therapy for asthma. A recent Overview of Cochrane reviews of clinical trials on escalated therapy for asthma[16] assessed the evidence for parenteral bronchodilators, Heliox, respiratory support and inhaled magnesium. The review

found that the majority of comparisons involved between one and three trials and fewer than 100 participants, making it difficult to assess the balance between benefits and potential harms. The authors were unable to make firm practice recommendations.[16]

There is little evidence to support intramuscular adrenaline as first-line treatment for seriously ill children with asthma,[25] although it has a number of advantages, including ease of administration and paramedic familiarity. Parenteral adrenaline is also used for anaphylaxis, cardiac arrest, and management of hypotension, while nebulised adrenaline is used for severe upper airway obstruction in croup. In addition, it can be easily and rapidly administered as there is no need for dilution prior to administration, and no requirement for a prolonged infusion.[22]

Pre-hospital treatment of asthma rarely results in escalation of therapy beyond inhaled bronchodilators and systemic corticosteroids. In addition, the use of parenteral bronchodilators is often reserved for those who do not improve after initial inhaled bronchodilators, and is administered relatively late in the course of an ED visit.[15] Given that most children with asthma will improve with pre-hospital treatment, and/or will not have sufficient time to "fail to improve" with standard therapy, it appears that any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

Limitations

Inclusion in the study was based on a combination of paramedic diagnosis of asthma and administration of inhaled bronchodilators. While only 89% had a diagnosis of asthma recorded in the ambulance notes, it seems that the cohort is reflective of the asthma population as over 87% of cases had a previous diagnosis of asthma.

Due to state-wide data collection and large numbers of patients, our study is likely to be generalisable to other settings with similar pre-hospital care systems. However, most ambulance cases within Victoria are concentrated in the metropolitan area of Melbourne (the capital city), which may limit generalisability to rural and regional settings. Approximately 10% of children were not transported to hospital; this is similar to the rate identified in a study of children with seizures from the same ambulance service.[26]

This study is a retrospective review of a comprehensive electronic database. We optimised data extraction and minimised bias through the collection of variables using a piloted data collection instrument, and application of pre-defined inclusion and exclusion criteria.[27,28] Due to the nature of record-keeping within the ambulance service (all cases are documented using the electronic system), it is unlikely that any cases of escalated care were missed. As we downloaded fields directly from the electronic medical record system, we did not independently abstract any variables. However, we verified all instances of documented escalation of care through consultation with a second (paramedic) reviewer and identified four cases of misclassification. It is possible that we missed some children who were not classified as asthma, were critically ill, not given inhaled bronchodilators and only given parenteral adrenaline. However, this is likely to be a very small number of cases. There was some missing data on final observations on arrival to hospital, however, this was not a primary objective of our study.

Conclusions

Most children with acute exacerbations of asthma did not receive escalated therapy during their pre-hospital treatment from ambulance paramedics. Most patients were treated with inhaled bronchodilators only and clinically improved by the time they arrived in hospital. Due

to the very low incidence of treatment escalation or clinical deterioration, any comparative clinical trials to determine the superiority of one parenteral bronchodilator over another should be reserved for the in-hospital rather than pre-hospital setting.

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Figure 1. Flow chart – pre-hospital management of acute asthma in children.

AV, Ambulance Victoria.

Box 1. Asthma severity assessment and treatment according to Ambulance Victoria Clinical Practice Guidelines

Mild / Moderate: normal conscious state, some increased work of breathing, tachycardia, speaking in phrases / sentences

- Salbutamol pMDI and spacer:
  - 6 or more years: 4-12 doses
  - 2-5 years: 2-6 doses

Severe: agitated / distressed, markedly increased work of breathing, including accessory muscle use / retraction, tachycardia, speaking in words.

- Salbutamol nebulised (repeated at 20 minutes if required)
  - 2-4 years: 2.5 mg
  - 5-11 years: 2.5 - 5 mg
- Ipratropium bromide nebulised 250 mcg

Critical: altered conscious state, maximal work of breathing, marked tachycardia, unable to talk.

- Salbutamol nebulised 10 mg (repeated at 5 minutes if required)
- Ipratropium bromide nebulised 250 mcg
- Adrenaline 10 mcg/kg IM (repeated at 5 minutes if required)
- Dexamethasone 0.6 mg/kg IV or oral (max 12 mg)
- Adrenaline IV boluses and infusion (for Mobile Intensive Care Paramedics)

Table 1. Demographics and clinical characteristics of children treated or assessed for asthma by AV.

	Total (n=1572)	Escalation of care (n=22)	No escalation of care (n=1550)	P value (escalation vs no escalation)
Age, years, n (%)				
1-4	561 (36.3)	6 (27.3)	555 (35.8)	0.38
5-11	690 (43.9)	9 (40.9)	681 (43.9)	
12-17	321 (20.4)	7 (31.8)	314 (20.3)	
Median age, years (IQR)	6 (4-10)	10.5 (3.8 – 14.3)	6 (3.8 – 10)	0.045
Female sex, n (%)	684 (43.5)	11 (50)	877 (43.4)	0.54
Pre-existing conditions, n (%)				
Asthma	1377 (87.6)	20 (90.9)	1357 (87.5)	0.64
Requiring hospital admission	115 (7.3)	5 (22.7)	110 (7.1)	0.005
Requiring intensive care	63 (4)	1 (4.5)	62 (4)	0.89
Requiring intubation	19 (1.2)	1 (4.5)	18 (1.2)	0.15
With cardiac / respiratory arrest	5 (0.3)	0 (0)	5 (0.3)	0.79
Other respiratory illness				
Croup	94 (6)	1 (4.5)	93 (6)	0.78
Bronchiolitis	80 (5.1)	1 (4.5)	79 (5.1)	0.91
Pneumonia	44 (2.8)	1 (4.5)	43 (2.8)	0.62
Chest infection	32 (2)	1 (4.5)	31 (2)	0.40
Other	8 (0.5)	0 (0)	8 (0.5)	0.64
Initial physiological parameters				
Respiratory rate (breaths/minute), median (IQR)	32 (24 – 40)	35.5 (28 – 48.5)	32 (24 – 40)	0.09
Pulse rate (beats/minute), median (IQR)	130 (112 – 146)	134.5 (120 – 150.5)	130 (112 – 146)	0.24
Initial respiratory status, n (%)				
Normal	615 (39.1)	3 (13.6)	612 (39.5)	<0.001
Mild respiratory distress	363 (23.1)	1 (4.5)	362 (23.4)	
Moderate respiratory distress	315 (20)	2 (9.1)	313 (20.2)	
Severe respiratory distress	166 (10.6)	16 (72.7)	150 (9.7)	
Depressed respirations	1 (0.1)	0 (0)	1 (0.1)	
Final physiological parameters				

Respiratory rate (breaths/minute), median (IQR) †	28 (22 – 36)	28 (22 – 36)	30 (27 – 40)	0.06
Pulse rate (beats/minute), median (IQR) †	126 (108 – 142)	126 (108 – 142)	126 (112-162)	0.29
Final respiratory status, n (%)‡				
Normal	742 (56.8)	4 (18.2)	738 (57.4)	<0.001
Mild respiratory distress	400 (30.6)	4 (18.2)	396 (30.8)	
Moderate respiratory distress	127 (9.7)	6 (27.3)	121 (9.4)	
Severe respiratory distress	38 (2.9)	8 (36.4)	30 (2.4)	

All P values calculated using Chi-Square tests, except for continuous variables where Mann-Whitney U tests* were used.

† Data was not available for final pulse rate and respiratory rate for 54 patients in the "No escalation of care" group

‡ Data was not available for final respiratory status for 265 patients in the "No escalation of care" group

Table 2. Treatment provided by AV paramedics.

	Total (n=1572)	Escalation of care (n=22)	No escalation of care (n=1550)	P value (escalation vs no escalation)
Respiratory support, n(%)				
Bag-valve-mask applied	1 (0.1)	1 (4.5)	0 (0)	<0.001
Oxygen delivery				
Nasal cannulae	46 (2.9)	4 (18.2)	42 (2.7)	<0.001
Nebuliser mask	258 (16.4)	10 (45.5)	248 (16)	<0.001
Oxygen mask	48 (3.1)	0 (0)	48 (3.1)	0.40
Non-rebreather mask	8 (0.5)	0 (0)	8 (0.5)	0.74
Other oxygen therapy (not otherwise specified)	2 (0.1)	0 (0)	2 (0.1)	0.87
Parenteral bronchodilator				
Adrenaline IM injection	20 (1.3)	20 (90.9)	0 (0)	<0.001
Adrenaline infusion	4 (0.3)	4 (18.2)	0 (0)	<0.001
Dexamethasone				
IV injection	25 (1.6)	4 (18.2)	21 (1.4)	<0.001
Oral	141 (9)	11 (50)	130 (8.4)	<0.001
Inhaled bronchodilator				
Any inhaled bronchodilator	946 (60.2)	21 (95.5)	925 (59.7)	<0.001
Any Ipratropium bromide nebulisation	453 (28.8)	17 (77.3)	436 (28.1)	<0.001
Any Salbutamol pMDI	465 (29.6)	3 (13.6)	462 (29.8)	0.10
Any Salbutamol nebulisation	513 (32.6)	20 (90.9)	493 (31.8)	<0.001
Single administration of inhaled salbutamol	348 (22.1)	3 (13.6)	345 (22.3)	
Single administration of inhaled ipratropium bromide	13 (0.8)	1 (4.5)	12 (0.8)	
Single administration of inhaled salbutamol and single administration of inhaled iptratropium bromide	280 (17.8)	6 (27.3)	274 (17.7)	
Two adminitrations of inhaled salbutamol alone	114 (7.3)	1 (4.5)	113 (7.3)	
Two administrations of inhaled salbutamol and at	112 (7.1)	3 (13.6)	109 (7)	

least one administration of ipratropium bromide				
Three or more administations of inhaled salbutamol alone	31 (2.0)	0 (0)	31 (2)	
Three or more administrations of inhaled salbutamol and at least one administration of ipratropium bromide	48 (3.1)	7 (31.8)	41 (2.6)	
Total instances of inhaled bronchodilator administration, median (IQR)	1 (0-2)	2 (1.8 – 4)	1 (0 – 2)	<0.001
Intravenous access				
Intravenous access attempt	39 (2.5)	7 (31.8)	32 (2.1)	<0.001
Successful IV attempt	34 (2.2)	7 (31.8)	27 (1.7)	<0.001

No patients received any of: BIPAP, manual ventilation, mechanical ventilation, IV salbutamol infusion, IM dexamethasone.

Figure 2. Initial and final respiratory status documented by AV paramedics.

Note: 111 patients missing initial respiratory status, and 265 missing final respiratory status.

Contributorship statement

SC, CW and FEB identified the research question. SC and CW were responsible for the study design and research protocol. BD and ZN obtained data and input into data cleaning and analysis. SC was responsible for statistical analysis. SC drafted the initial manuscript. SC, BD, ZN, CW, SRD, GMN, CVEP, AG and FEB contributed equally to writing, reviewing and editing the manuscript.

All authors provided comments on the drafts and have read and approved the final version of the article. All authors has full access to all of the data (including statistical reports and tables) at the conclusion of the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

SC is the guarantor for the paper, accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish.

Competing interests

There are no competing interests for any author.

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ZN's time is part funded by a grant from the National Heart Foundation of Australia.

Data sharing statement

Data are available on reasonable request. De-identified participant data will be available for sharing from 1 July 2024. Any data access requests should be sent to SC (simon.craig@monash.edu), and should include a proposal from the individual or organisation regarding their plan for use of the data.

The study team will review the request and consider the scientific merit of the proposed use of the data, and the legal, regulatory and ethical issues pertinent to the request. Presuming all constraints are addressed, the data will be shared using a secure file transfer platform.

Ethical statement.

The project was approved by the Royal Children's Hospital Research Ethics and Governance Office, Melbourne, Australia (60707), and the Ambulance Victoria Research Governance Committee, Melbourne, Australia.

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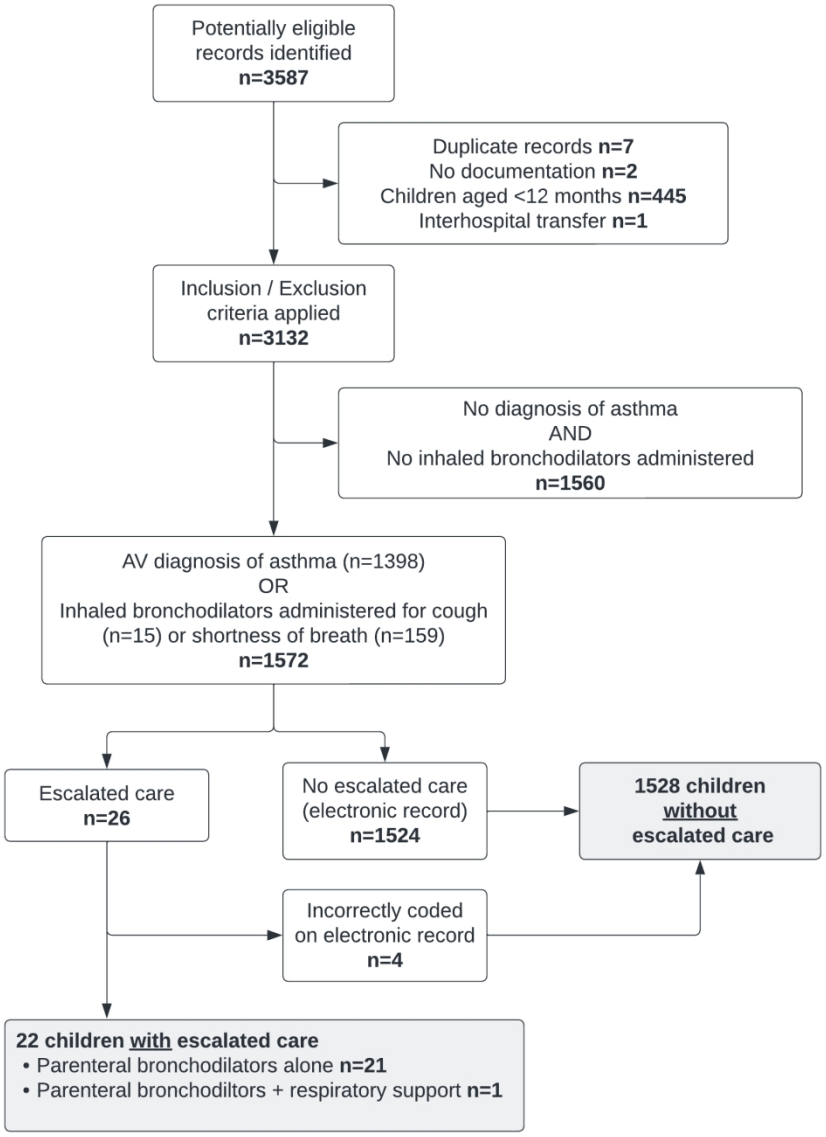

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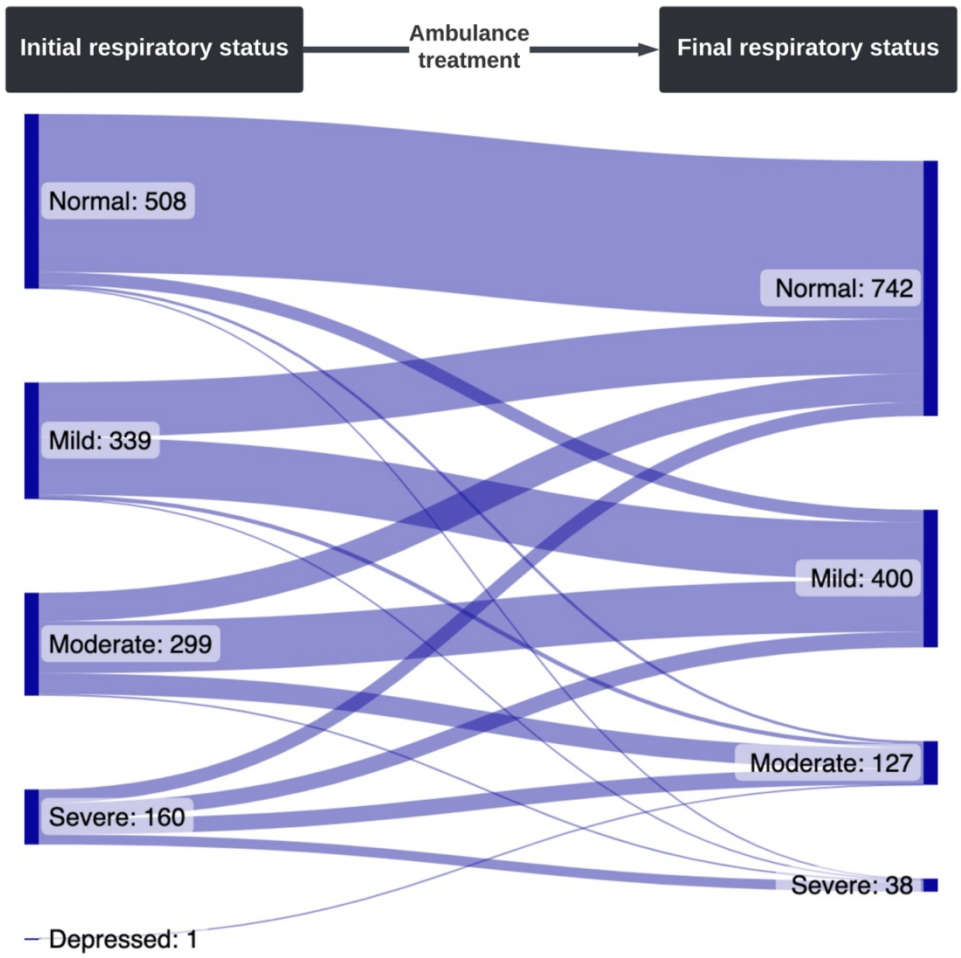

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Supplementary Online Table

Administration of asthma treatment according to initial respiratory status

	Normal respiratory status or mild respiratory distress (n=978)	Moderate respiratory distress (n=315)	Severe respiratory distress or Depressed respirations (n=167)
Salbutamol (pMDI)			
n (%)	314 (32.1)	111 (35.2)	15 (9.0)
Median (IQR)	0 (0 – 1)	0 (0 – 1)	0 (0 – 0)
Salbutamol (nebuliser)			
n (%)	155 (15.8)	182 (57.8)	151 (90.4)
Median (IQR)	0 (0 – 0)	1 (0 – 1)	1 (1 – 2)
Any salbutamol			
n (%)	455 (46.5)	274 (87.0)	157 (94.0)
Median (IQR)	0 (0 – 0)	1 (0 – 1)	1 (1 – 2)
Ipratropium, n (%)			
n (%)	125 (12.8)	164 (52.1)	144 (86.2)
Median (IQR)	0 (0 – 0	1 (0 – 1)	1 (1 – 1)
Dexamethasone (any route)			
Any route, n (%)	41 (4.2)	56 (17.8)	58 (34.8)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract YES – see title.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Structured abstract provided
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 7
Objectives	3	State specific objectives, including any prespecified hypotheses Page 8
Methods		
Study design	4	Present key elements of study design early in the paper Page 8 – ("study design" section)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 8-9 ("study setting" section)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case Page 9 ("selection of participants" section)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 9-10 ("data collection" section)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 9-10 ("data collection" section)
Bias	9	Describe any efforts to address potential sources of bias Page 10 (end of "data collection" section)
Study size	10	Explain how the study size was arrived at Page 10 ("analysis" section)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Page 10 ("analysis" section)

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses Page 10 ("analysis" section)
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Page 10-11 ("results" section)
		(b) Give reasons for non-participation at each stage Page 10-11 ("results" section)
		(c) Consider use of a flow diagram – See figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page 10-11 ("results" section) and table 1
		(b) Indicate number of participants with missing data for each variable of interest Missing data indicated in Table 1, and mentioned in limitations section
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) Not applicable (no patient follow-up)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
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Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
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Key results	18	Summarise key results with reference to study objectives Page 13-14
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Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 13-15
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Funding disclosures provided

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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