Clinical management practices of life-threatening asthma: An audit of practices in intensive care

Author

Secombe, P, Stewart, P, Singh, S, Campbell, L, Stephens, D, Tran, K, White, H, Sheehy, R, Gibson, J, Cooke, R, Townsend, S, Apte, Y, Winearls, J, Ferry, OR, Pradhan, R, Ziegenfuss, M, Fong, KM, Yang, IA, McGinnity, P, Meyer, J, Walsham, J, Boots, R, Clement, P, Bandeshe, H, Gracie, C, Jarret, P, Collins, S, Coulston, C, Ng, M, Howells, V, Chatterjee, I, Visser, A, Smith, J, Trout, M

Published

2019

Journal Title

Critical Care and Resuscitation

Version

Accepted Manuscript (AM)

Clinical Management Practices of Life-Threatening Asthma: An Audit of Practices in Intensive Care

The Critical Care Asthma Investigators

Abstract

Objective: Lack of management guidelines for life-threatening asthma (LTA) risks practice variation. This study aims to elucidate management practices of LTA in the intensive care unit (ICU).

Design: A retrospective cohort study.

Setting: 13 participating ICUs between July 2010 to June 2013

Participants: Patients with the principal diagnosis of LTA.

Main Outcome Measures: Clinical history, ICU management, patient outcomes, ward education and discharge plans.

Results: 270 ICU admissions (267 patients) were 69% female with a median age of 39 years (IQR 26-53). 119 (44%) were current smokers. 89 (29%) previously required ICU admission of whom 23 (25%) were intubated. Median ICU stay was 2 days (IQR 2-4). Three patients (1%) died. 79 patients (29%) received non-invasive ventilation with 11 (14%) needing subsequent invasive ventilation. 68 patients (25%) were intubated with the majority of patients receiving volume-cycled ventilation (N=63 SIMV-VC, 93%). Drug use included beta2-agonist by intravenous infusion (N=69, 26%), inhaled adrenaline (N=15, 6%) or an adrenaline intravenous infusion (N=23, 9%), inhaled anticholinergics (N= 238, 90%), systemic corticosteroids (N= 232, 88%), antibiotics (N= 126 48%) and antivirals (N= 22, 8%). Where suitable, 105 (N=200, 53%) had an asthma management plan and 122 (N=202, 60%) had asthma education upon hospital discharge. Myopathy was associated with hyperglycaemia requiring treatment (OR 31.6, 95%CI 2.1-474). Asthma education was more common under specialist thoracic medicine care (OR 3.0, 95% CI 1.61-5.54).

Conclusions: In life threatening asthma, practice variation is common, with opportunities to improve discharge management plans and asthma education.

Abstract Word Length: 244

Word length excluding abstract, tables and references: 3434

Discussion word length: 1220

Keywords: asthma, intensive care, mechanical ventilation, non-invasive ventilation, practice audit

With fond and sincere memory of our friend Dr Sunil Singh

Corresponding Author: Associate Professor Rob Boots
Department of Thoracic Medicine
Royal Brisbane and Women's Hospital
Butterfield Street, Herston.
Queensland. AUSTRALIA. 4029

The Critical Care Asthma Investigators

Alice Springs Hospital. Northern Territory, Australia
Dr Paul Secombe, Senior Staff Specialist
Dr Penny Stewart, Director of Intensive Care

Bundaberg Hospital, Queensland Australia
Dr Sunil Singh, Previous Director of Intensive Care

Royal Darwin Hospital. Northern Territory, Australia
Dr Lewis Campbell. Staff Specialist Intensive Care Unit, Adjunct Lecturer - Flinders University
Associate Professor Dianne Stephens, Director National Critical Care and Trauma Response Centre

Logan Hospital. Queensland, Australia.
Dr Khoa Tran, Director of Respiratory Medicine, Senior Staff Specialist Intensive Care
Dr Hayden White, Associate Professor and Deputy Director ICU
Dr Robert Sheehy, previous Respiratory Registrar (now Staff Specialist, Respiratory Medicine, Princess Alexandra Hospital)
Dr Justine Gibson, previous Respiratory Registrar (now Sleep Medicine Registrar, Greenslopes Private Hospital)

Mater Adult Hospital, Queensland. Australia
Dr Robyn Cooke, Staff Specialist
Dr Shane Townsend, Previous Director of Adult Intensive Care Services

Robina Hospital. Queensland, Australia
Dr Yogesh Apte, Staff Specialist

The Gold Coast University Hospital. Queensland. Australia.
Dr James Winearls, Staff Specialist

The Prince Charles Hospital. Queensland, Australia
Olivia R Ferry, Medical Student. The University of Queensland
Rahul Pradhan, Medical Student. The University of Queensland
Dr Marc Ziegenfuss, Director of Intensive Care
Professor Kwun M Fong, Department of Thoracic Medicine and UQ Thoracic Research Centre, Faculty of Medicine, The University of Queensland
Professor Ian A Yang, Department of Thoracic Medicine and UQ Thoracic Research Centre, Faculty of Medicine, The University of Queensland

The Princess Alexandra Hospital. Queensland, Australia.
Dr Paul McGinnity, Staff Specialist. Intensive Care Unit
Jason Meyer. Research Coordinator. Intensive Care Unit
Dr James Walsham. Director of Research Intensive Care Unit

The Royal Brisbane Hospital. Queensland. Australia
Associate Professor Rob Boots, Department of Thoracic Medicine and Previous Deputy Director of Intensive Care. Faculty of Medicine, The University of Queensland
Pierre Clement, Clinical Information System Manager. Intensive Care Unit
Hiran Bandeshe, Previous Data Manager. Intensive Care Unit
Christopher Gracie, Nurse Manager Materials Management. Intensive Care Unit
Paul Jarret, Previous Research Coordinator. Intensive Care Unit
Dr Stephenie Collins, Medical Officer
Caitlin Coulston, Previous Medical Student. The University of Queensland
Melisa Ng, Previous Medical Student. The University of Queensland
Valerie Howells, RN. Data Manager. Royal Brisbane and Women's Hospital

Toowoomba Base Hospital. Queensland. Australia.
Dr Indranil Chatterjee, Senior Specialist Intensive Care
Dr Adam Visser, Director of Intensive Care Unit
Judy Smith, Data Collection and Research Coordination

The Townsville Hospital. Queensland, Australia.
Dr Melita Trout, Staff Specialist

Introduction:

Asthma requiring management in the intensive care unit (ICU) is a serious but potentially reversible condition. Recent reviews of life threatening asthma (LTA) in Australia and New Zealand are more than 10 years old and lack detail on clinical management.[1] Although asthma prevalence is increasing, rates of presentation requiring ICU admission have been decreasing since the 1990s despite an increasing severity of illness.[2,3,4] The need for mechanical ventilation is accepted as an indicator of LTA with an associated mortality of 2.8%.[1,5]

Variation in both clinical practice guidelines and physician practices for asthma are well documented,[6,7] contributing to recurrent admissions, patient morbidity, costs of care, interval symptoms and mortality.[8,] Currently there are limited data examining these trends in adult LTA. Clinical audits allows current practices to be evaluated and provides insight into the efficacy of various treatments as well as drive further research. The current study aimed to elucidate contemporary physician practices and treatment modalities for LTA and compare these practices with current guidelines.

Methodology

A multicentre retrospective cohort study was conducted using ICU and patient clinical charts from July 2010 to June 2013. All 15 intensive care units in Queensland and the Northern Territory in Australia were invited to participate. Patients for inclusion were identified from local unit datasets of the Australia and New Zealand Intensive Care Outcomes and Resource Evaluation Database (ANZICS CORE) for adult patients and the Australian and New Zealand Paediatric Intensive Care (ANZPIC) Registry where a primary diagnosis of asthma was the primary reason for admission. Medical charts were audited using a written proforma to collect de-identified data. Data collection included patient demographics, Acute Physiology and Chronic Health Evaluation (APACHE II) score[9], past clinical history of asthma including exacerbations, atopy, smoking history, outpatient management, intensive care pharmacological and mechanical ventilation management and discharge outcomes including discharge destination, the presence of a documented asthma management plan and follow-up arrangements. Children were defined as being less than 16 years at the time of admission. Where there were multiple admissions for one patient during the study period, the details of the most severe episode (requiring invasive mechanical ventilation or with the longest length of ICU stay if not invasively

ventilated), was used to record demographic data. Data from presentations were included in the study of clinical practice. It was not possible to identify patients presenting to different hospitals within the methodology of the blinded data collection. For NIV, the terms bilevel, BiPap™ and pressure support ventilation were combined as B-PS due to a common use of these terms interchangeably. Two units without a research assistant used an abbreviated survey form collecting information largely related to ICU management. Physiologic data were collected from the ICU flowsheet. Managements were compared to contemporary published guidelines for LTA including the British Thoracic Society[10], National Heart Lung and Blood Institute Expert Panel 3 Guidelines for the Diagnosis and Management of Asthma (EPR-3)[11] and the Global Initiative for Asthma (GINA) guidelines.[12,13]

Sample Sizing and Statistical Methods

For the time period of the study it was estimated that 300 cases including children would be available for review. This would provide the potential to build a multivariate linear regression model from an anticipated 30 variables for asthma management predictors or outcomes.[14] Univariate data was described using medians with interquartile ranges (IQR) and 95% confidence intervals (95%CI) unless otherwise specified. Actual data ranges [Range] were used to reflect the spread of a broad distribution where clinically relevant. Logistic models included variables where associations in univariate analysis has $P \leq 0.2$ with goodness of fit and calibration assessed by the Hosmer-Lemeshow statistic and area under the receiver-operator curve respectively. Analysis used Stata 15.1 statistical software (College Station, Texas. United States of America).

Ethical Considerations

Low risk ethical approval was granted from the Royal Brisbane and Women's Hospitals HREC (HREC/13/QRBW/310). De-identified data were collected and stored using secure password protected computer encryption.

Results

Study Cohort

Over the three-year study period there were 270 ICU admissions representing 267 patients. Demographic patient characteristics are summarised in Table 1. The majority of presentations were female (N=183, 69%) of a median age of 39 years (IQR 26-53) with only 8 children (3%) included in the dataset. Most patients presented to hospital from their home (N=205, 76%) with the source of ICU admission being the emergency department (N=218, 81%) and 22 (7%) admitted to ICU from ward based or specialised high dependency care. 156 (58%) had one or more comorbid conditions, the most common being mood and psychiatric disorders (N=72, 27%). There was no history of atopy in 58 (22%) patients. Only 59 patients (22%) had never smoked while 119 (44%) were current smokers. 134 patients (50%) had no previous asthma presentations. From the recorded 356 previous presentations for asthma in the cohort, 74 (27%) had two or more presentations. Of those with previous admissions 89 (29%) required an ICU admission with 23 (25%) needing intubation.

Information on usual maintenance therapy was available for 255 patients. Only a little over half the patients were receiving regular inhaled long acting beta$_2$-agonists (LABA) (N=144, 56%) and inhaled corticosteroids (ICS) (N=151, 59%). Anticholinergics (AC) were used by 47 patients (18%) with systemic corticosteroids (SC) used regularly in 43 patients (17%). Emergency parenteral adrenaline prescription was only identified in 3 patients (1%). There was rescue therapy information recorded for 209 patients in the days prior to the acute hospital presentation. In contrast to the records of routine maintenance therapy, most patients were taking additional short-acting beta$_2$-agonists (SABA) (N=191, 91%), however only 64 (31%) were taking ICS and 89 (43%) were receiving a SC. Table S1 of the supplementary material summarises the relationship between maintenance therapy use and asthma control.

Acute Asthma Presentation

In the month prior to presentation, 61 patients (26%) had few or no symptoms, 58 (21%) were short of breath on two or fewer occasions a week, 44 (42%) were waking from sleep weekly or less frequently or needed to use rescue medications less frequently than weekly 45 (17%). Overall asthma symptoms were assessed as well controlled in only 52 (19%). The majority of presentations were precipitated by upper respiratory tract infections (N=171, 63%) however 52 patients (18%) had no recognised precipitant. The details of the acute asthma presentation are summarised in Supplementary Materials Tables S2 and S3.

Intensive Care Admission

Patients on admission to ICU were moderately ill with a median APACHE II score of 12 (IQR 8-15) with a $PaCO_2$ of 41 mmHg (N=103, Range 22-118 mmHg) and a median SpO_2 of 92% (Range 40-100%).

Non-Invasive Ventilation

Of the 270 admissions to the ICU, 79 (29%) received NIV, with rescue invasive ventilation required in 11 (14%). Three needed ongoing NIV following invasive ventilation. On commencing NIV, the median $PaCO_2$ was 44 mmHg (N=97, IQR 37-49, Range 21-119). The median total time spent receiving NIV was 8 hours (IQR 4-17, Range 0.2-62) representing a median of 62% (IQR 21-100, Range 2-100) of the hours spent in ICU. B-PS was used as the sole NIV mode in 64 patients (81%) and continuous positive airway pressure (CPAP) in 11 (14%). B-PS used a median inspiratory positive airway pressure (IPAP) of 12 cm H_2O (IQR 10-14, Range 7-40) and a positive end-expiratory pressure (PEEP or EPAP) of 5 cm H_2O, (IQR 5-7, Range 1-15). In those patients only receiving CPAP, the median airway pressure was 5 cm H_2O (IQR 5-6, Range 3-15).

Invasive Ventilation

Of the 68 patients (25%) who received invasive ventilation, 63 received volume cycled synchronised intermittent mechanical ventilation (SIMV-VC, 93% being the initial mode used in ICU in 80%). The ventilation mode initiated in the emergency department was not recorded in our survey. A pressure-based strategy was used in 29 patients (43%), SIMV-Pressure Control (PC) in 9 (13%), bilevel in 15 (22%), assist control (AC-PC) in 2 (3%) with one patient (1%) each receiving either airway pressure release ventilation (APRV), adaptive support ventilation (ASV) or pressure regulated volume control (PRVC). Only one ventilation mode was used in 47 patients (64%). Some patients received multiple modes during the admission with two modes used in 18 (24%) and three modes in three patients (4%) exclusive of spontaneous weaning modes. Invasive ventilation continued for a median of 2.6 days (IQR 1.0-5.2, Range 0.17-19.5). The median minimum respiratory rate used was 10 breaths/min (IQR 8-12, Range 4-18) with a median tidal volume of 0.61 litres (IQR 0.55-0.70, Range 0.32-1.85). There were 21 patients with tidal volumes greater than 0.8 litres while receiving a mandatory rate of mechanical ventilation. Twelve of these patients (57%) were ventilated with a pressure targeted strategy while the remainder were all receiving SIMV-VC. In only 23 patients (31%) were measurements of auto-PEEP

available in the clinical record. The median highest auto-PEEP recorded was 10 cm H_2O (IQR 7-13, Range 13-24).

During invasive ventilation the median highest value of $PaCO_2$ was 53 mmHg (IQR 44-67, Range 21-130). The median percentage of the total invasive ventilation time where the patient remained hypercapnic ($PaCO_2$> 45 mmHg) was 50% (IQR 21-71, Range 0-100), with 8 patients remaining hypercapnic following cessation of invasive ventilation. These patients only had mild hypercapnia with a median $PaCO_2$ at the time of weaning of 49 mmHg (IQR 48.5-52, Range 46-58). The median maximal I:E was 1:4.3 (IQR 1:3.6-1:7, Range 1:1.7-1:19) where the most prolonged I:E ratios were associated with low mandatory respiratory rates. The minimal setting of PEEP was a median of 5 cm H_2O (IQR 0-9, Range 0-20) with the highest recorded median peak inspiratory pressure being 38 cm H_2O (IQR 27-48, Range 15-85). Plateau pressures were inconsistently recorded to be available for analysis. PaO_2 was recorded for patients receiving any form of ventilation. The highest median PaO_2 was 317 mmHg (IQR 220-427, Range 55-650).

Pharmacological Management

The pharmacologic details of management were available for 265 episodes of ICU care (Table 2). All patients received some form of adrenergic agonist via a SABA (263, 99%), $beta_2$-agonist intravenous infusion (69, 26%), inhaled adrenaline (15, 6%) or an adrenaline intravenous infusion (23, 9%). There were 20 patients (8%) who received both intravenous infusions of catecholamines and nebulised SABA, 12 (5%) received both inhaled SABA and non-selective catecholamines while one patient received inhaled and intravenous catecholamines in addition to short-term nebulised SABA on the same day. AC were used in 238 patients (90%). SC were used in 232 patients (88%), the formulations predominantly being hydrocortisone and prednisolone (median prednisiolone equivalent dose 75mg/day). Three patients received dexamethasone. ICS were given to 56 patients (21%). Antibiotics were used in 126 patients (48%), antivirals in 22 (8%). Inhaled or nebulised and systemic corticosteroids were received concurrently in 43 patients (16 %) where SC dose remained greater than 15 mg in prednisolone equivalents.

Clinical Outcomes

Clinical outcomes are summarised in Table 3. Although most patients (N=296, 91%) were able to be discharged home and independent, three patients (1%) died in hospital (two while within ICU), nine (3%) were able to be discharged home but were not independent and seven (3%) needed to be transferred to another hospital. The median length of ICU stay was 2 days (IQR 2-4, Range 1-24). Common electrolyte disturbances were hypokalaemia (75, 28%), hyperglycaemia needing treatment (63, 23%) and hypophosphataemia (13, 5%). Additional common complications included lactic acidosis (21, 8%), myopathy (10, 4%), nosocomial pneumonia (14, 5%) with hypoxic brain injury occurring in three patients (1%).

In univariate modelling, the development of myopathy was associated with APACHE II score, antibiotic use, time hypercapnic, cumulative dose of prednisolone while in ICU, ventilation hours and hyperglycaemia needing treatment with ventilation hours and hyperglycaemia being independent predictors (Table 4). All patients with myopathy had been invasively ventilated.

Where patients remained in their original hospital and with a documented discharge to ward based care (N=254), 135 (53%) were cared for most commonly by general medical physicians (102, 40%). In patients where a discharge management plan was considered applicable, 105 (N=200, 53%) received a documented asthma management plan and 122 (N=202, 60%) had documentation of asthma education prior to discharge. We could not find any predictors for documentation of an asthma management plan at discharge (Supplementary Material Table S4). However, the only predictor of documentation of asthma education occurring during the admission was when care was under specialist thoracic medicine following ICU discharge (Table 5).

We were unable to find specific predictors of NIV failure. Patients needing both NIV and invasive ventilation were not predicted by APACHE II score (P=0.10), currently smoking (P=0.74), asthma control in the month prior to presentation (P=0.81), weight (P=0.94), age (P=0.88), the number of comorbidities (P=0.2), the number of previous admissions (P=0.41), worst SpO2 prior to ICU admission (P=0.88), worst $PaCO_2$ prior to ICU admission (P=0.78), history of OSA (P=0.74) nor a mood disorder (P=0.58) or antibiotic use (P=0.71). No patients with a history of diabetes mellitus needed to receive invasive ventilation after NIV.

Discussion:

Our study found a low overall mortality of LTA, consistent with previous findings.[3,4] Previous studies have noted that most mortality occurs prior to hospital admission[15] and within hospital mortality largely attributed to inadequate observation, limited recognition of respiratory failure or deficient treatment.[16] Most patients did not meet current guidelines for recommended maintenance or acute exacerbation therapy [17,18] with smoking common and many struggling with asthma symptoms for some time before hospital presentation.[15]

Treatment options in LTA are mainly extrapolated from severe presentations.[19] There was variability in use of intravenous beta$_2$-agonists and catecholamines. With no documented advantage of parenteral administration of bronchodilators, prescription may relate to a clinical assessment of the efficacy of nebulisation therapy with drug delivery better assured parenterally.[20] Nebulised therapy was more common than metred dose aerosol despite lack of documented efficacy. Drug delivery varies with nebuliser type, ventilator mode and gas flow parameters with the optimal method of aerosolised drug delivery in ventilated patients remaining unclear.[21] There does not seem to be a difference in aerosolised drug delivery efficacy with NIV compared to spontaneous breathing [22] although studies in patients with significant airflow obstruction are lacking. Not all patients received inhaled anticholinergic agents although their safety and beneficial adjunct to beta$_2$-agonists has been demonstrated.[23-25] Some 18% of patients were receiving antibiotics prior to hospital presentation which increased to 48% during their ICU admission despite not generally being needed in LTA.[19] Data was not collected for microbiologically confirmation of infection. In a life-threatening situation where pulmonary infiltrates are present on X-rays, it would be a difficult decision to withhold antibiotics while awaiting culture confirmation. Clearly appropriate early de-escalation as part of ward-based care is important.

Not all patients received systemic corticosteroids while in the ICU, perhaps reflecting the speed of recovery and administration prior to ICU admission. The median dose of systemic corticosteroids in equivalents of prednisolone was 75 mg and is consistent with guidelines for adults.[17] Prescription of larger doses (8 patients), largely pulse methylprednisolone[26-28] was in the absence of evidence-based support. The individual response to systemic corticosteroids is variable and is related to the degree of obstruction.[29] Although for mild to moderate asthma, ICS may be used as an alternative to systemic administration,[30] the addition of ICS to

systemic corticosteroids does not improve clinical outcome and the effects are unknown in ventilated patients.[31] Parenteral and enteral corticosteroids would appear equivalent except in patients thought to have systemic absorption issues.[32-34]

The use of adjunctive agents was variable in our cohort with a limited evidence base.[35] No patient received inhaled helium-oxygen admixtures with limited evidence to support its use and limited availability.[19] Parenteral administration of magnesium was consistent with guidelines. Lack of use as a continuous infusion to target a particular serum level would be in keeping with maintenance of a normal serum concentration.[17] Guideline recommendations for aminophylline remain confusing with continued support in children[18] but not in adults, [17] hampered by a lack of pharmacokinetic and pharmacodynamic data in the critically ill.[36] Ketamine was rarely used in our cohort. It has limited clinical efficacy as a bronchodilator salvage therapy. The propensity for increased airway secretions may also be undesirable. It has usually been reserved for patients receiving mechanical ventilation due to its anaesthetic properties.[37] However, nebulised ketamine has been reported and awaits further efficacy evaluation.[38] Inhalational anaesthetics were also rarely used. The literature supporting their use is based on the pharmacological potential for adrenergic receptor stimulation, direct bronchodilation, histamine antagonism and interference with hypercapnic bronchoconstriction[39] and physiologic before-after studies.[40] Hypotension is common with inotropic support required with prolonged administration and associations with neuropathy, renal impairment and hepatotoxicity. [40]

NIV is commonly used in LTA with low complication and similar deterioration rates (4.5-12 %) as found in our study [41] despite inconclusive benefits[42] and higher mortality rates in those deteriorating on NIV as is the case for most other respiratory conditions.[43] The need for invasive ventilation in patients receiving NIV is largely predicted by the severity of respiratory failure,[42-44] concomitant diagnosis of pneumonia, the number of prior asthma admissions and comorbid diabetes mellitus.[45] We could not confirm these associations using antibiotic therapy and worst SpO_2 as a surrogate for a pneumonia diagnosis.

In our study, although both pressure and volume strategies were employed, preference was for volume cycled ventilation. There is no recommended consensus on the mode of invasive ventilation that should be used and perhaps consistent institutional preference is most important.[44] Most strategies aim for controlled

hypercarbia, avoiding air trapping and heterogenous ventilation.[44] No significant gains in lung emptying beyond an expiratory time of 4 seconds and no PEEP,[46] although there may be some improvement in dynamic airway closure by small amounts of PEEP between 1-3 cm H_2O.[47] Measures of auto-PEEP, persisting expiratory flow when the next breath is delivered or dynamic trapped volume may be used when making ventilation changes to ensure lung emptying, but are not commonly recorded in the chart. Our study suggests that there were patients with mixed disease needing higher PEEP than would be recommended for severe asthma. Some tidal volumes were large suggesting improved monitoring of this parameter is required, especially when using a pressure mode. I:E ratios were generally managed to facilitate prolonged expiration. The use of high-flow oxygen therapy (HFO_2) was not able to be determined accurately in our study. Some publications have suggested that HFO_2 in severe asthma may prolong length of stay due to a delay in instituting positive pressure ventilation[48] but further specific study is needed for benefit over conventional oxygen therapy.[49]

Myopathy potentially delays ventilator weaning and prolongs hospital length of stay. We found that myopathy was associated with the duration of mechanical ventilation and hyperglycaemia. Hyperglycaemia, oxidative stress and depletion of troponin-T has been shown to weaken diaphragm strength[50] and more generally is recognised as a risk for post-critical illness weakness.[51]

National and international guidelines support referral of LTA patients to specialists with expertise in ambulatory management and asthma education. A structured approach and management of co-morbidities which may not be readily available outside larger centres. [52] Our cohort had poor documentation of an asthma management plan or having received asthma education, also observed by others.[53] A designated patient education role held by clinical staff may improve readmission rates by ensuring education occurs. [54] This is an important issue as the one year post discharge mortality in LTA is 10%, with women, smokers and patients over the age of 40 years disproportionately represented.[55] The mortality remains high for 10 years post discharge particularly in those requiring mechanical ventilation.[56] A “recollection” of the case history while during post-ICUward care would be a variable addition to improve the detail of clinical notes and could be part of an asthma education prior to discharge.

This study represents a contemporary summary of intensive care asthma management within two of Australia's states and territories. It is important because the detail of clinical care in LTA is under-reported.[57] Variation in practice is recognised in ambulatory care but has not been characterised previously for LTA.[58] The study is limited by its retrospective nature and surety of data such as interval symptoms, auto-PEEP documentation, asthma education and discharge planning. Modelling for predictors of mortality was not performed due to its rarity. Although the time frame for the study was prolonged due to significant staff movement, the data is reflective of current practice.

Conclusions

There is a significant variability in the management of critically severe asthma within intensive care units, particularly related to the use of second-line therapies. Many modes of mechanical ventilation are used with an overall successful outcome suggesting that familiarity with ventilatory approaches may be more important than any particular technique. Avoiding hyperglycaemia may be important to avoid the development of myopathy. We need to ensure that LTA patients have a well-documented history particularly in relation to preventable risks and receive recommended ambulatory care and education.

References

1. Stow PJ, Pilcher D, Wilson J, et al. Improved outcomes from acute severe asthma in Australian intensive care units (1996 2003). Thorax 2007;62:842-7.

2. Han P, Cole RP. Evolving differences in the presentation of severe asthma requiring intensive care unit admission. Respiration 2004;71:458-62.

3. Peters JI, Stupka JE, Singh H, et al. Status asthmaticus in the medical intensive care unit: a 30-year experience. Respir Med 2012;106:344-8.

4. Gupta D, Keogh B, Chung KF, et al. Characteristics and outcome for admissions to adult, general critical care units with acute severe asthma: a secondary analysis of the ICNARC Case Mix Programme Database. Crit Care 2004;8:R112-21.

5. Kearney SE, Graham DR, Atherton ST. Acute severe asthma treated by mechanical ventilation: a comparison of the changing characteristics over a 17 yr period. Respiratory medicine 1998;92:716-21.

6. Bratton SL, Newth CJ, Zuppa AF, et al. Critical care for pediatric asthma: wide care variability and challenges for study. Pediatr Crit Care Med 2012;13:407-14.

7. Bratton SL, Odetola FO, McCollegan J, Cabana MD, Levy FH, Keenan HT. Regional variation in ICU care for pediatric patients with asthma. J Pediatr 2005;147:355-61.

8. D'Amato M, Baiardini I, Solidoro P, Braido F. Adherence to treatment and monitoring tools: what's new? Minerva Med 2016;107:5-8.

9. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818-29.

10. British guideline on the management of asthma. Thorax 2014;69 Suppl 1:1-192.

11. National Heart L, and Blood Institute (NHLBI),. Guidelines for the Diagnosis and Management of Asthma (EPR-3). 2007.

12. Reddel HK, Bateman ED, Becker A, et al. A summary of the new GINA strategy: a roadmap to asthma control. Eur Respir J 2015;46:622-39.

13. Reddy AP, Gupta MR. Management of asthma: the current US and European guidelines. Adv Exp Med Biol 2014;795:81-103.

14. Dawson B TR. Statistical Methods for Multiple Variables. Basic and clinical biostatistics: McGraw-Hill Companies; 2004.

15. Goeman DP, Abramson MJ, McCarthy EA, Zubrinich CM, Douglass JA. Asthma mortality in Australia in the 21st century: a case series analysis. BMJ Open 2013;3.

16. Phipps P, Garrard CS. The pulmonary physician in critical care . 12: Acute severe asthma in the intensive care unit. Thorax 2003;58:81-8.

17. Global Initiative for Asthma (GINA) 2017,. 2017. 2018, at http://ginasthma.org.)

18. James DR, Lyttle MD. British guideline on the management of asthma: SIGN Clinical Guideline 141, 2014. Arch Dis Child Educ Pract Ed 2016;101:319-22.

19. Rodrigo G. Asthma in adults (acute). BMJ Clin Evid 2011;2011.

20. Travers AH, Milan SJ, Jones AP, Camargo CA, Jr., Rowe BH. Addition of intravenous beta(2)-agonists to inhaled beta(2)-agonists for acute asthma. Cochrane Database Syst Rev 2012;12:CD010179.

21. Moustafa IOF, ElHansy MHE, Al Hallag M, et al. Clinical outcome associated with the use of different inhalation method with and without humidification in asthmatic mechanically ventilated patients. Pulm Pharmacol Ther 2017;45:40-6.

22. Maccari JG, Teixeira C, Savi A, et al. Nebulization during spontaneous breathing, CPAP, and bi-level positive-pressure ventilation: a randomized analysis of pulmonary radioaerosol deposition. Respir Care 2014;59:479-84.

23. Rodrigo GJ, Castro-Rodriguez JA. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. Thorax 2005;60:740-6.

24. Aaron SD. The use of ipratropium bromide for the management of acute asthma exacerbation in adults and children: a systematic review. J Asthma 2001;38:521-30.

25. Salo D, Tuel M, Lavery RF, Reischel U, Lebowitz J, Moore T. A randomized, clinical trial comparing the efficacy of continuous nebulized albuterol (15 mg) versus continuous nebulized albuterol (15 mg) plus ipratropium bromide (2 mg) for the treatment of acute asthma. J Emerg Med 2006;31:371-6.

26. Marquette CH, Stach B, Cardot E, et al. High-dose and low-dose systemic corticosteroids are equally efficient in acute severe asthma. Eur Respir J 1995;8:22-7.

27. Manser R, Reid D, Abramson M. Corticosteroids for acute severe asthma in hospitalised patients. Cochrane Database Syst Rev 2001:CD001740.

28. Smith M, Iqbal S, Elliott TM, Everard M, Rowe BH. Corticosteroids for hospitalised children with acute asthma. Cochrane Database Syst Rev 2003:CD002886.

29. Klaustermeyer WB, Choi SH. A perspective on systemic corticosteroid therapy in severe bronchial asthma in adults. Allergy Asthma Proc 2016;37:192-8.

30. Edmonds ML, Camargo CA, Jr., Brenner BE, Rowe BH. Replacement of oral corticosteroids with inhaled corticosteroids in the treatment of acute asthma following emergency department discharge: a meta-analysis. Chest 2002;121:1798-805.

31. Edmonds ML, Milan SJ, Brenner BE, Camargo CA, Jr., Rowe BH. Inhaled steroids for acute asthma following emergency department discharge. Cochrane Database Syst Rev 2012;12:CD002316.

32. Harrison BD, Stokes TC, Hart GJ, Vaughan DA, Ali NJ, Robinson AA. Need for intravenous hydrocortisone in addition to oral prednisolone in patients admitted to hospital with severe asthma without ventilatory failure. Lancet 1986;1:181-4.

33. Ratto D, Alfaro C, Sipsey J, Glovsky MM, Sharma OP. Are intravenous corticosteroids required in status asthmaticus? JAMA 1988;260:527-9.

34. Agrawal M, French L, Becker JM, et al. Oral versus i.v. steroids for children hospitalized with asthma. J Fam Pract 1999;48:578-9.

35. DeSanti RL, Agasthya N, Hunter K, Hussain MJ. The effectiveness of magnesium sulfate for status asthmaticus outside the intensive care setting. Pediatr Pulmonol 2018.

36. Saint GL, Semple MG, Sinha I, Hawcutt DB. Optimizing the Dosing of Intravenous Theophylline in Acute Severe Asthma in Children. Paediatr Drugs 2018;20:209-14.

37. Goyal S, Agrawal A. Ketamine in status asthmaticus: A review. Indian J Crit Care Med 2013;17:154-61.

38. Elkoundi A, Bentalha A, El Koraichi A, El Kettani SE. Nebulized ketamine to avoid mechanical ventilation in a pediatric patient with severe asthma exacerbation. Am J Emerg Med 2018;36:734 e3- e4.

39. Tobias JD. Inhalational anesthesia: basic pharmacology, end organ effects, and applications in the treatment of status asthmaticus. J Intensive Care Med 2009;24:361-71.

40. Vaschetto R, Bellotti E, Turucz E, Gregoretti C, Corte FD, Navalesi P. Inhalational anesthetics in acute severe asthma. Curr Drug Targets 2009;10:826-32.

41. Nanchal R, Kumar G, Majumdar T, et al. Utilization of mechanical ventilation for asthma exacerbations: analysis of a national database. Respir Care 2014;59:644-53.

42. Green E, Jain P, Bernoth M. Noninvasive ventilation for acute exacerbations of asthma: A systematic review of the literature. Aust Crit Care 2017;30:289-97.

43. Nicolini A, Piroddi IM, Barlascini C, Senarega R. Predictors of non-invasive ventilation failure in severe respiratory failure due to community acquired pneumonia. Tanaffos 2014;13:20-8.

44. Medoff BD. Invasive and noninvasive ventilation in patients with asthma. Respir Care 2008;53:740-48; discussion 9-50.

45. Bahloul M, Chtara K, Gargouri R, Majdoub A, Chaari A, Bouaziz M. Failure of noninvasive ventilation in adult patients with acute asthma exacerbation. J Thorac Dis 2016;8:744-7.

46. Leatherman JW, McArthur C, Shapiro RS. Effect of prolongation of expiratory time on dynamic hyperinflation in mechanically ventilated patients with severe asthma. Crit Care Med 2004;32:1542-5.

47. Caramez MP, Borges JB, Tucci MR, et al. Paradoxical responses to positive end-expiratory pressure in patients with airway obstruction during controlled ventilation. Crit Care Med 2005;33:1519-28.

48. Pilar J, Modesto IAV, Lopez-Fernandez YM, Lopez-Macias O, Garcia-Urabayen D, Amores-Hernandez I. High-flow nasal cannula therapy versus non-invasive ventilation in children with severe acute asthma exacerbation: An observational cohort study. Med Intensiva 2017;41:418-24.

49. Ballestero Y, De Pedro J, Portillo N, Martinez-Mugica O, Arana-Arri E, Benito J. Pilot Clinical Trial of High-Flow Oxygen Therapy in Children with Asthma in the Emergency Service. J Pediatr 2018;194:204-10 e3.

50. Callahan LA, Supinski GS. Hyperglycemia-induced diaphragm weakness is mediated by oxidative stress. Crit Care 2014;18:R88.

51. Hafner S, Radermacher P, Frick M, Dietl P, Calzia E. Hyperglycemia, oxidative stress, and the diaphragm: a link between chronic co-morbidity and acute stress? Crit Care 2014;18:149.

52. Becker AB, Abrams EM. Asthma guidelines: the Global Initiative for Asthma in relation to national guidelines. Curr Opin Allergy Clin Immunol 2017;17:99-103.

53. Hasegawa K, Ahn J, Brown MA, et al. Underuse of guideline-recommended long-term asthma management in children hospitalized to the intensive care unit: a multicenter observational study. Ann Allergy Asthma Immunol 2015;115:10-6 e1.

54. Polster D. Preventing readmissions with discharge education. Nurs Manage 2015;46:30-7; quiz 7-8.

55. Marquette CH, Saulnier F, Leroy O, et al. Long-term prognosis of near-fatal asthma. A 6-year follow-up study of 145 asthmatic patients who underwent mechanical ventilation for a near-fatal attack of asthma. Am Rev Respir Dis 1992;146:76-81.

56. Triasih R, Duke T, Robertson CF. Outcomes following admission to intensive care for asthma. Arch Dis Child 2011;96:729-34.

57. Boeschoten SA, Buysse CMP, Merkus P, et al. Children with severe acute asthma admitted to Dutch PICUs: A changing landscape. Pediatr Pulmonol 2018.

58. Garbutt JM, Yan Y, Strunk RC. Practice Variation in Management of Childhood Asthma Is Associated with Outcome Differences. J Allergy Clin Immunol Pract 2016;4:474-80.

Table 1. Demographic characteristics of ICU asthma admissions

Parameter		Asthma Episodes N=270 (%) Median (IQR)[Range]
Patients		267
Gender (female) N=267		183 (69)
Unit Recruitment	1	20 (7)
	2	21 (8)
	3	9 (3)
	4	35 (13)
	5	10 (4)
	6	21 (8)
	7	35 (13)
	8	34 (13)
	9	32 (12)
	10	15 (6)
	11	38 (14)
Age (years) N=267		39 (26-53)
Children < 16 years (N=267)		8 (3)
Onset Asthma (N=267)	Child	101 (38)
	Adult (>15 years)	66 (25)
	Unknown	100 (37)
Smoking History	Current smoker	119 (44)
	Life-long non-smoker	59 (22)
	Previous smoker	49 (18)
	Unknown	43 (16)
Current Smoking Use	Pack Years (N=55)	15 (5-20) [0.25-57]
	Present Packs Per Day (N=74)	0.75 (0.5-1) [0.07-3]
Previous Smoking Use	Years Ceased (N=38)	7 (0.25-40) [0.25-40]
	Pack Years (N=21)	15 (8-20) [2-70]
Previously Known Asthma Triggers	Allergen	55 (20)
	Upper Respiratory Tract Infection	106 (39)
	Weather	47 (17)
	Exercise	17 (6)
	Other	19 (7)
	Unknown	65 (24)
Comorbidities (N=267)	Diabetes mellitus	31(12)
	Hypertension	47 (18)
	Ischaemic Heart Disease	10 (4)
	Congestive Cardiac Failure	4 (1)
	Gastro-oesophageal reflux	34 (13)
	Obstructive Sleep Apnoea	29 (11)
	Mood or Psychiatric Disorder	72 (27)
Number of comorbidities (N=267)	0	111 (42)
	1	83 (31)
	2	40 (15)
	3	19 (7)
	4	8 (3)
	≥ 5	6 (2)
Associates of Asthma (N=267)	Rhinosinusitis or conjunctivitis	39 (15)
	Elevated IgE	19 (7)
	Atopic dermatitis/eczema	11 (4)
	Allergies	78 (29)
	Known +ve skin prick tests	10 (4)
	No associates	58 (22)
	Unknown	108 (40)
Previous Hospital Admissions in previous 5 years (N=216)	0	104 (48)
	1	53 (24)
	2	17 (8)
	3	18 (8)
	4	9 (4)
	≥ 5	15 (7)

Table 2. Summary of Drug Use During ICU admission

	N=270 (%) Median (IQR)[Range]	Proportion of ICU Admission Time of Medication Use Median (IQR) [Range]
Systemic corticosteroids		1 (1-1) [0.08-1]
Total	232 (88)	
Enteral	131 (49)	
Parenteral	192 (72)	
Dexamethasone	3 (1)	
Hydrocortisone	181 (67)	
Methylprednisolone	14 (5)	
Prednisolone	131 (49)	
Dose (Prednisone Equivalent mg)	75 (5-100) [10-625]	
Greater than 150 mg/day	4 (2)	
SABA*		1 (1-1) [0.06-1]
Total	263 (99)	
MDI	28 (11)	
Nebuliser	245 (92)	
Intravenous Infusion	69 (26)	
Inhaled Anticholinergic		1 (0.5-1) [0.08-1]
Total	238 (90)	
MDI	27 (10)	
Nebuliser	228 (86)	
ICS*		0.73 (0.5-1) [0.08-1]
Total	56 (21)	
MDI	33 (12)	
Nebuliser	24 (9)	
Magnesium	91 (35)	0.5 (0.33-0.66) [0.08-1]
Antibiotics	126 (48)	1 (0.5-1) [0.08-1]
Antivirals	22 (8)	
Non-selective catecholamines		
Total	38 (14)	
Nebuliser	15 (6)	0.5 (0.33-0.73) [0.08-1)
Intravenous Infusion	23 (9)	0.41 (0.25-0.6) [0.14-1)
Emergency Parenteral Adrenaline	3 (1)	0.42 (0.29-0.75) [0.25-1)
Methylxanthines		0.68 (0.4-1) [0.125-1)
Total	38 (14)	
Enteral	9 (3)	
Intravenous Infusion	33 (12)	
Long acting beta agonist	32 (12)	1 (0.5-1) [0.2-1]
Ketamine infusion	12 (5)	0.4 (0.17-0.60) [0.125-1]
Inhalational anaesthetic	2 (1)	0.14 (0.09-0.18) [0.09-0.18]

* SABA – short acting beta$_2$-agonist, ICS – inhaled corticosteroids

Table 3. Principle Outcomes

	N=265 (%) *Median (IQR)[Range]
Days in ICU (days)	2 (2-4) [1-24]
Complications in ICU	
All Electrolyte Disturbances	91 (33)
Hypokalaemia	75 (28)
Hypophosphataemia	13 (5)
Hyperkalaemia	2 (1)
Hypomagnesaemia	3 (1)
Hyponatraemia	3 (1)
Hypocalcaemia	4 (1)
Hyperglycaemia needing treatment	63 (23)
Lactic acidosis	21 (8)
Pneumonia	14 (5)
Myopathy	10(4)
Atelectasis	8(3)
Pneumomediastinum	3 (1)
Pneumothorax	2 (1)
Diaphragm paralysis	1(<1)
Cardiac arrhythmia needing treatment	8 (3)
Myocardial infarction	8 (3)
Hypoxic brain injury	3(1)
Discharge Management plan documented where deemed applicable (N=200)	105 (53)
Asthma Education where deemed applicable (N =202)	122 (60)
Hospital Outcome	
Died in hospital	3 (1)
Home and independent	246 (91)
Home and ***not*** independent	9 (3)
Transfer to another hospital	7 (3)
Not documented	5 (2)

Table 4. Associations of Myopathy Present at ICU Discharge

Univariate Models	OR (95% CI)	P
Lactic Acidosis	1.49 (0.2-12.5)	0.72
APACHE II	1.11 (1.03-1.20)	0.01
Number Comorbidities	0.77 (0.41-1.42)	0.36
Gender	2.23 (0.63-7.89)	0.22
Non-invasive ventilation	0.34 (0.04-2.73)	0.25
Antibiotic Use	5.20 (1.08-25.0)	0.02
Hypercapnia (hours)	1.07 (1.04-1.11)	<0.001
Prednisone Cumulative Dose in ICU (mg)	1.001 (1.0003-1.002)	0.06
Ventilation Hours	1.02 (1.01-1.02)	<0.001
Hyperglycaemia needing treatment	35.15 (4.35-283.60)	<0.001
Electrolyte Disturbance	0.49 (0.10-2.35)	0.34
Hypokalaemia	0.30 (0.04-2.42)	0.19
Hypomagnesaemia	7.11 (0.72-70.20)	0.16
Hypophosphataemia	2.30 (0.27-19.63)	0.49
Multiple Regression Model		
Ventilation Hours	1.02 (1.01-1.02)	<0.001
Hyperglycaemia needing treatment	31.56 (2.10-474.11)	0.01
Calibration of Model: Hosmer Lemeshow Good of Fit Chi2=0.54 P=0.91 Discrimination of Model: Area under ROC curve 0.97		

Table 5. Associations of Documentation of Asthma Education

Univariate Models	OR (95% CI)	P
Age	0.99 (0.98-1.01)	0.17
APACHE II	1.00 (0.95-1.04)	0.87
Number comorbidities	0.81 (0.63-1.03)	0.09
Myopathy	5.45 (0.67-44.42)	0.11
Number of previous admissions	0.97 (0.84-1.12)	0.66
Non-invasive ventilation	1.10 (0.55-2.16)	0.80
Invasive ventilation	0.83 (0.44-1.57)	0.58
Smoking (compared to current smoking) Non-smoker Previous smoker	 0.58 (0.27-1.24) 0.53 (0.25-1.14)	0.17
Asthma Control (Compared to well controlled) Somewhat controlled Poorly controlled	 1.87 (0.74-4.69) 1.16 (0.53-2.55)	0.34
Corticosteroid Accumulated Dose in ICU (Prednisone equivalent mg)	0.99 (0.99-0.99)	0.01
Ventilation Hours	0.99 (0.99-1.02)	0.48
Non-invasive ventilation	1.09 (0.55-2.16)	0.80
Invasive ventilation	0.84 (0.44-1.57)	0.58
ICU discharge care (Compared with general medical care) Shared Specialist/General Care Specialist Thoracic Care	 1.49 (0.48-4.65) 3.18 (1.72-5.86)	0.001
Multiple Regression		0.0002
Corticosteroid Accumulated Dose in ICU (Prednisone equivalent mg)	0.99 (0.99-0.99)	0.05
ICU discharge care (Compared with general medical care) Shared Specialist/General Care Specialist Thoracic Care	 1.59 (0.49-5.14) 3.0 (1.61-5.54)	0.001
Calibration of Model: Hosmer Lemeshow Good of Fit Chi2=9.88 P=0.27 Discrimination of Model: Area under ROC curve 0.67		

Supplementary Material

Table S1. Use of Maintenance Medications Related to Interval Symptoms

Parameter	N (%) *OR (95% CI)* *ICS**	P
Impression Asthma Control (N=223)		0.19
Asthma well controlled (N=52)	25 (48)	
Asthma not well controlled (N=171)	100 (80)	
Use of rescue medications (N=137)		0.52
≤ Once per week (N=45)	19 (42)	
> Once per week (N=92)	56 (61)	
Waking with Asthma symptoms (N=102)		0.77
≤ Once/week (N=42)	24 (40)	
> Once/week (N=60)	36 (60)	
Shortness of Breath (N=131)		0.06
≤ Once or twice a week (N=57)	26 (46)	
> Twice a week (N=74)	46 (62)	
Asthma Affecting Activities of Daily Living (N=135)		0.91
≤ A Little of the Time (N=61)	34 (56)	
> A Little of the Time (N=74)	42 (57)	
Previous Number of Asthma Presentations	*OR 0.97 (0.82-1.15)*	0.75
	*Inhaled LABA**	
Impression Asthma Control (N=223)		0.04
Asthma well controlled (N=52)	25 (48)	
Asthma not well controlled (N=171)	92 (53)	
Use of rescue medications (N=137)		0.02
≤ Once per week (N=45)	17 (38)	
> Once per week (N=92)	53 (57)	
Waking with Asthma symptoms (N=102)	24 (45)	0.38
≤ Once/week (N=42)	29 (55)	
> Once/week (N=60)		
Shortness of Breath (N=131)		0.11
≤ Once or twice a week (N=57)	25 (43)	
> Twice a week (N=74)	43 (58)	
Asthma Affecting Activities of Daily Living (N=135)		0.66
≤ A Little of the Time (N=61)	32 (52)	
> A Little of the Time (N=74)	36 (49)	
Previous Number of Asthma Presentations	*OR 0.96 (0.80-1.14)*	0.61
	Inhaled Anticholinergics	
Impression Asthma Control (N=223)		0.27
Asthma well controlled (N=52)	5 (10)	
Asthma not well controlled (N=171)	27 (16)	
Use of rescue medications (N=137)		0.09
≤ Once per week (N=45)	3 (7)	
> Once per week (N=92)	16 (17)	
Waking with Asthma symptoms (N=102)		0.34
≤ Once/week (N=42)	6 (14)	
> Once/week (N=60)	5 (8)	
Shortness of Breath (N=131)		0.02
≤ Once or twice a week (N=57)	5 (9)	
> Twice a week (N=74)	18 (24)	
Asthma Affecting Activities of Daily Living (N=135)		0.02
≤ A Little of the Time (N=61)	5 (8)	
> A Little of the Time (N=74)	17 (23)	
Previous Number of Asthma Presentations	*OR 0.99 (0.78-1.24)*	0.96

* LABA – long acting beta$_2$-agonist, ICS – inhaled corticosteroids

Table S2 Description of Current Episode of Asthma

	N=270 (%) Median (IQR) [Range]
Number of Presentations to ICU in study period	
1	267 (99)
2	3 (1)
Triggers for Current Episode of Asthma	
Allergen	22 (8)
Upper Respiratory Tract Infection	171 (63)
Weather	12 (4)
Exercise	1 (<1)
Other	32 (12)
Unknown	52 (19)
Asthma Affecting Activities of Daily Living in Last 4 weeks	
None of the Time	34 (13)
A little of the Time	27 (10)
Some of the Time	52 (19)
Most of the Time	20 (7)
All of the Time	4 (1)
Unknown	133 (49)
Shortness of breath in prior 4 weeks	
Not at all	21 (8)
Once or twice a week	37(14)
3 to 6 times/week	22 (8)
Once a day	15 (6)
More than once a day	38 (14)
Unknown	137 (51)
Frequency of awakening from asthma in prior 4 weeks	
4 or more night per week	16 (6)
2 or 3 nights per week	22 (8)
Once or twice a week	22 (8)
Once a week	15 (6)
Not at all	29 (11)
Unknown	166 (61)
Use of rescue medications in prior 4 weeks	
3 or more times per day	36 (13)
1-2 times per day	33 (12)
2-3 times per week	26 (10)
Once per week or less	24 (9)
Not at all	21 (7)
Unknown	130 (48)
Previous Presentations for Asthma last 5 yrs (N=356)	
0	134 (50)
1	63 (23)
2	22 (8)
3	16 (6)
4	11 (4)
≥ 5	25 (9)
Complexity of Care for previous admissions (N=307)	
Emergency Department Only	33 (11)
Ward Care Only	185 (60)
Required ICU admission	89 (29)

Table S3. Usual and acute therapy prior to current ICU presentation

	N=270 (%)
Usual Therapy (N=255)	
SABA*	247 (98)
LABA*	144 (56)
ICS*	151 (59)
Inhaled Anticholinergic	47 (18)
Systemic Corticosteroid	43 (17)
Methylxanthine	11 (4)
Emergency parental adrenaline	3 (1)
Leukotriene receptor antagonist	8 (3)
Methotrexate	1 (<1)
Sodium chromoglycolate	1 (<1)
Acute Home Therapy for this Episode (N=209)	
Inhaled B2 agonists	191 (91)
Inhaled corticosteroids	64 (31)
Inhaled anticholinergics	51 (24)
Systemic steroids	89 (43)
Methylxanthines	11 (5)
Antibiotics	38 (18)

*SABA – short acting beta$_2$-agonist, LABA – long acting beta$_2$-agonist, ICS – inhaled corticosteroids

Table S4. Associations of Discharge Plan

Univariate Models	OR (95% CI)	P
Number of comorbidities	0.99 (0.81-1.21)	0.93
Age	0.99 (0.98-1.01)	0.27
Smoking		0.13
(compared to current smoking)		
Non-smoker	0.83 (0.44-1.59)	
Previous smoker	0.50 (0.25-0.98)	
APACHE II	1.01 (0.97-1.10)	0.66
Corticosteroid Accumulated Dose in ICU (Prednisone equivalent mg)	1.00 (0.99-1.00)	0.07
Ventilation Hours	1.00 (1.00-1.00)	0.95
Invasive ventilation	0.87 (0.50-1.5)	0.62
Non-invasive ventilation	1.00 (0.57-1.77)	1.00
Myopathy	2.74 (0.57-13.14)	0.17
Number of previous admissions	0.97 (0.86-1.10)	0.65
Asthma Control		0.21
(Compared to well controlled)		
Somewhat controlled	0.98 (0.44-2.16)	
Poorly controlled	0.53 (0.26-1.07)	
ICU discharge care		0.21
(Compared with general medical care)		
Shared Specialist/General Care	0.38(0.13-1.13	
Specialist Thoracic Care	0.85 (0.51-1.42)	