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Title: Rates and Correlates of Relapse Following Emergency Department Discharge for Acute Asthma: A Canadian 20-Site Prospective Cohort Study.

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Conflicts of Interest: Within the past three years, Dr. Rowe has received research funding from the following respiratory companies: GSK (Mississauga, ON, Canada) and ElectroCore (Morristown, NJ, USA). No other conflicts of interest were declared.

Running Head: Asthma Relapses

Key words: Asthma, emergency department, corticosteroids, relapse.

Document details: Abstract: 251 words; Text: **2831** words; References: 27; Tables: 3; Figures: 4.

Abstract

Background: Acute asthma is a common emergency department (ED) presentation. In a prospective multicenter cohort study we determined the frequency and factors associated with asthma relapse following discharge from the ED.

Methods: Adults aged 18-55 years who were treated for acute asthma and discharged from 20 Canadian EDs underwent a structured ED interview and follow-up telephone interview four weeks later. Standardized anti-inflammatory treatment was offered at discharge. Multivariable analyses were performed.

Results: Of 807 enrolled patients, 58% were female and the median age was 30 years. Relapse occurred in 144 patients (18%) within four weeks of ED discharge. Factors independently associated with relapse occurrence were: female sex (22% vs 12% males, adjusted odds ratio [aOR] = 1.9, 95% confidence interval [CI]: 1.2, 3.0), symptom duration of ≥ 24 hours prior to ED visit (19% vs 13% short duration, aOR = 1.7, 95% CI: 1.3, 2.3), ever using oral corticosteroids (21% vs 12% for never use, aOR = 1.5, 95% CI: 1.1, 2.0), current use of an inhaled corticosteroids[ICS]/long-acting β -agonist combination product (25% vs 15% for ICS monotherapy, aOR = 1.9, 95% CI: 1.1, 3.2), and owning a spacer device (24% vs 15% not owning one aOR = 1.6, 95% CI: 1.3, 1.9).

Conclusions: Despite receiving guideline-concordant anti-inflammatory treatments at ED discharge, almost one-in-five patients relapsed within four weeks. Female sex, prolonged symptoms, treatment-related factors and markers of prior asthma severity were significantly associated with relapse. These results may help clinicians target more aggressive interventions for patients at high risk of relapse.

Abbreviation List

aOR	adjusted odds ratio
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CTAS	Canadian Triage and Acuity Scale
ED	emergency department
FEV ₁	Forced expiratory volume in 1 second
GEE	generalized estimating equation
ICS	Inhaled corticosteroids
LABA	long-acting beta-agonists
LOS	length of stay
OCS	oral corticosteroids
PCP	primary care provider
PEF	peak expiratory flow

Introduction

Asthma is a serious chronic lung disease affecting between 7 and 10% of the adult population; in 2012, approximately 2.4 million (8.1%) Canadians aged 12 and older, reported being diagnosed with asthma by a health professional.[1, 2] It is estimated that nearly two million emergency department (ED) asthma visits occur annually in the US alone[3] and 80-90% of the patients with acute asthma who present to the ED will be discharged.[4] Clinical studies indicate that between 5 and 25% of patients discharged from the ED will relapse within the first week, and 21 to 35% will relapse within three weeks.[5, 6]

Asthma relapses represent important adverse health outcomes for the patient and result in important costs to the health care system.[7, 8] A variety of demographic, historical and treatment factors have been associated with relapse after ED discharge for acute asthma but previous studies have been limited because they did not account for disease severity at presentation; were not performed in a setting of universal health care access;[9-11] failed to standardize treatment after discharge; and/or involved patients with other co-morbidities or chronic obstructive pulmonary disease (COPD).[9, 10]

In an effort to enhance the interpretation and translation of research findings into practice, we undertook a prospective multicenter cohort study to document relapse events and factors associated with relapse in the month following discharge from Canadian EDs for patients with acute asthma prescribed evidence-based anti-inflammatory treatments.

Materials and Methods

Study design and setting: This prospective cohort study, enrolled patients treated for acute asthma in 20 EDs across Canada between 11/2003 and 03/2007. The study sites were all members of the Canadian Association of Emergency Physicians Research Consortium (CAEP RC; <https://www.caep.ca/rc>). Sixteen of the EDs were urban teaching sites and 4 were community based EDs. The median ED census of the study sites was 50,000 patients per year. Institutional Research Ethics Board approval was obtained from each site, University of Alberta, approval number 4884, and written informed consent was obtained from all participants.

Study population: All patients aged 18-55 years presenting with acute asthma were eligible. Asthma diagnosis was made by the treating emergency physician using clinical criteria (e.g., past history, response to β -agonists, and symptoms of shortness of breath, wheezing, cough or chest tightness). For pragmatic purposes, we included all patients with the above criteria with a history of < 30 pack years of smoking. Patients with exacerbations of COPD, mild obstruction (> 80% predicted peak expiratory flow [PEF] at presentation), chronic (daily) use or contraindications to oral corticosteroids (OCS), and serious or unstable comorbidities were excluded. Subjects with pneumonia, requiring admission, clinically unstable or those with documented pregnancy were not enrolled. Inability to communicate in English and to provide informed consent; cognitive impairment, and refusal to take OCS were additional exclusion criteria. Refusals, missed patients and other reasons for non-enrollment were documented.

Anti-inflammatory treatment: ED management was left to the discretion of the treating emergency physician; however, this usually included inhaled β -agonists, short-

acting anticholinergics and a systemic corticosteroid. At discharge, emergency physicians prescribed medications as deemed appropriate and provided patients with a personalized discharge plan regarding medication use, follow-up and criteria for return for reassessment in the event of symptom worsening. A short course of prednisone (50mg daily for 5-7 days) was provided by the study nurse; physicians were also strongly advised to maintain any inhaled corticosteroid (ICS) or ICS/long-acting β -agonist (LABA) treatment or **add** an ICS to patients not already taking one.

Baseline Data Collection: We collected sociodemographic data including age, sex, race (by visual assessment), marital status, level of education and employment, and availability of primary care provider (PCP) in a structured interview. Asthma history, use of preventive actions, and medications were ascertained by patient recall **while they were in the ED**. Smoking status was coded as never, previous, or current smoker. Insurance status related to medication coverage, percentage of medication costs usually paid by patients and any self-reported reduction in medication use in the previous 12 months were recorded.

Information on ED course, management and the discharge plan were obtained through medical record review following standard guidelines that include the need for explicit criteria and inter-rater reliability assessment. Severity at presentation was assessed through the Canadian Triage and Acuity Scale (CTAS). The CTAS score is the national standard for Canadian ED patients and has been shown to be valid and reliable.[12] Peak expiratory flow was performed before or after the first ED treatment and standardized as the percentage of the patient's predicted value according to age, sex, race and height[13]; spirometry was performed before discharge.

Study outcomes: Relapse was defined as an unscheduled visit to any ED, clinic or

physician office for worsening asthma (e.g., cough, dyspnea),[9, 14] and was assessed by telephone at three days, two weeks and four weeks after discharge. For any relapses identified at follow-up, objective confirmation was sought from the medical records. All relapses were adjudicated by an external review committee without knowledge of the patients or the treatments received.

Other measurements: Typical ICS side effects (e.g., insomnia, hoarseness, swelling, sore throat and nausea) were collected at time of follow-up. Scheduled follow-up visits to a PCP or clinic were documented with the exception of routine asthma checkups, which were not considered relapses. Adherence to the post ED short course of OCS was assessed at the three-day and two-week follow-up phone calls by asking whether the patient had taken the prednisone pills as prescribed and instructed. The use of ICS (mono-therapy or in combination with long-acting β -agonist agents) was also assessed.

Statistical analysis: Descriptive data included numbers and proportions or medians with interquartile range (IQR; 25th and 75th percentiles) as appropriate. The agreement between the two relapse adjudicators was measured using the Kappa (κ) statistic. Baseline comparisons based on relapse status four weeks following discharge were performed using generalized estimating equations (GEE) to adjust for the clustering of patients within the study sites. Multiple logistic regression analyses with GEE were performed and we used purposeful variable selection methods. First, variables identified at $p < 0.10$ significance in the univariate comparison and those deemed to be of clinical importance (e.g., age, sex) were selected. A final model was obtained after assessing the confounding effects of variables that could be removed ($\geq 15\%$ change in the study estimates between the models including/not including them) and categorizing those variables that didn't fulfill the

assumption of linearity (age and ED length of stay [LOS]). Adjusted odds ratio (aOR) and 95% confidence intervals (CI) for the variables included in the final multiple logistic regression are reported in the results. No statistically significant ($p < 0.05$) first order interaction terms were found and none were included in final models. All analyses were performed using StataCorp. 2009. *Stata Statistical Software: Release 11*. College Station, TX: StataCorp LP.

Results

Patients: Over the study period, 4598 ED patients were screened for enrollment and 3248 (71%) were *potentially* eligible (**Figure 1**). Of these, 2241 patients were ineligible due to one or more exclusion criteria, and 807 were enrolled in the cohort.

Patient Characteristics: Overall, 57% patients were female, the median age was 30 (IQR: 23, 39) years and most (85%) were white. **Tables 1** and **2** present sociodemographic and clinical data, ED treatments, and asthma severity stratified by asthma relapse within 4 weeks. In general, other than sex and symptom duration, most correlates of relapse were related to “intensity” of asthma management. Based on initial assessments using various criteria, most patients were classified as having severe acute asthma.

Prior to initial ED visit 25% of patients were steroid naïve, 29% were receiving ICS mono-therapy and 46% were receiving ICS/LABA agents (**Table 1**). Treatment for both groups was similar in the ED (**Table 2**). Treatment at discharge did vary slightly. For example, most patients (50%) were instructed to continue on their pre-existing anti-inflammatory, and 38% were prescribed a new ICS; however, 11% were not prescribed inhaled ICS agents at discharge (**Table 2; Figure 3**).

Patient Relapse: The two reviewers demonstrated high agreement relapse adjudication ($\kappa = 0.97$). Follow-ups 3 days (89%), 2 weeks (82%) and 1 month (80%) after ED discharge were high. Those patients who were and were not followed up at 1 month had a similar socio-demographic profile (e.g., age, sex, marital status, education), asthma history and indicators of severity at presentation (data not shown).

Early relapse (≤ 7 days) occurred in 86 (11%) patients; relapse within 2-weeks occurred in 112 (14%) patients; and relapse within four weeks occurred in 144 (18%)

patients (cumulative data). Of all patients who relapsed within four weeks of the ED visit, 130 (90%) relapsed once, 13 (9%) relapsed twice and 1 (<1%) relapsed three times during the follow up period. **Females relapsed more than males ($P = 0.003$; Figure 4).** Self-reported adherence to short course of OCS prescribed at discharge were high at day three (98%) and at completion of treatment (95%) follow-ups. Most of the patients who relapsed (79%) sought ED care during the four week follow up period, resulting in 18 (16% of all relapses; 2% of sample) hospitalizations. One death (unrelated to asthma) occurred in the group of patients who didn't relapse.

Factors Independently Associated with Relapse: Multivariable analyses indicated the following factors were independently associated with relapse: female sex (22% [102 of 465] vs 12% males [42 of 342], aOR = 1.9; 95% CI: 1.2, 3.0), ≥ 24 hours of symptoms prior to the ED visit (19% [116 of 595] vs 13% [26 of 201] short duration, aOR = 1.7; 95% CI: 1.3, 2.3), ever receiving OCS for asthma (21% [107 of 508] vs 12% [37 of 299] for never use, aOR = 1.5; 95% CI: 1.1, 2.0), use of ICS/LABA combination agents (with or without extra ICS) at the time of ED presentation (25% [66 of 263] vs 15% [42 of 285] ICS monotherapy aOR = 1.9; 95% CI: 1.1, 3.2) and owning a spacer device (24% [65 of 272] vs 15% [79 of 535] not owning one aOR = 1.6; 95% CI: 1.3, 1.9) (**Table 3**).

Discussion

This multicenter prospective study examined factors associated with relapse for patients **with moderate to severe asthma exacerbations** discharged from Canadian EDs following treatment with standard and evidence-based anti-inflammatory care for acute asthma. **This target population not only represents the majority of the asthmatics seen in the ED, but also includes a significant number of patients who will re-visit the ED within the next three weeks.** Most importantly, even with reasonably guideline-concordant discharge management, we observed that almost one-in-five patients experienced a relapse within 4 weeks of the ED visit. These results are consistent with a previous prospective study where anti-inflammatory treatment offered at discharge were not standardized,[9] suggesting both treatment and non-treatment factors contribute to relapse.

The following factors were independently and significantly associated with relapse: female sex, prolonged exacerbation symptoms prior to the ED visit, ever receiving OCS for asthma, the use of ICS/LABA combination agents at the time of ED presentation, and owning spacer devices. Other studies have explored factors associated with relapse in asthma; however, use shorter follow-up, do not provide all patients with OCS, and have lower proportion of patients discharged on recommended preventer inhaled medications.[9, 10]

Despite efforts to maximize the evidence-based medical treatment at discharge the proportion of study patients who received maximal medical care following discharge was lower than desired. For example, while approximately 98% received OCS for 5-7 days as recommended[15] 11% still received no ICS agents.[16] Nonetheless, these treatment

approaches are far more aggressive than those utilized in other studies evaluating factors associated with asthma relapse.[17] Since this study arguably provides the highest proportion of evidence-based anti-inflammatory treatments outside clinical trials, it is appropriate to focus on the non-medication management issues associated with relapse after discharge.

Women were far more likely to relapse than men (**Figure 4**). Our results are consistent with findings from other studies indicating that women with asthma experience more severe symptoms, which may result in more frequent relapses.[18] Moreover, it has been suggested that women have a phenotype of asthma that is more resistant to ICS agents.[19] While future mechanistic research will likely contribute to our understanding of these differences, women discharged from the ED should be considered at higher risk for relapse.

Prolonged symptoms prior to the ED visit was associated with a higher risk of relapse and this is consistent with previous findings.[9] Our results also suggest that patients who report ever having received OCS for asthma and those using an ICS/LABA combination agent at presentation were more likely to experience a relapse. These observations may reflect past poor control and current severe disease status, respectively. Demonstration of an association does not prove causation. It is likely that use of these medications is confounded by severity; sicker patients with more severe chronic asthma are treated with more aggressive therapy.

Finally, a failure to identify associations between relapse and several widely cited factors was important.[9, 10, 11] Most notably, the role of pulmonary flow measures has been a controversial area in the literature.[20-23] It appears that once the physicians decide

on patient discharge, the patient's change in PEF (delta between pre-post treatment measures) or the % predicted FEV₁ at discharge from the ED were not helpful in predicting future relapse.

Limitations

Some important limitations must be considered when interpreting our results. First, our sample was restricted to a specific group of patients with asthma recruited in mostly academic centres and during research coverage hours (08:00-24:00 M-F; 10:00-18:00 S&S); these findings may not be representative of all asthmatics presenting to Canadian EDs nor generalizable to those discharged from EDs after presenting with an extremely severe asthma-related condition, with mild disease, pneumonia and mixed entities (including, for example, COPD exacerbations). Second, despite the fact we used a common definition of asthma in ED settings, some may feel this is a less valid approach than using a specific set of international criteria.[24] We selected this approach because it has been used elsewhere, is clinically sensible, and is valid within the ED setting.[25-27] Third, **while patients may have been more inclined to respond to the research staff questions due to their acute condition, most of the information collected in the ED would not have changed if asked in a different time frame. Information on asthma history, prevention actions and medications could have been assessed more accurately; however, the risk of misclassification is minimal as the information collected through this ED interview didn't influence the definition of the primary study outcome. Fourth,** the definition of relapse did not include telephone contact with physicians for medication adjustment; as this practice is rare in Canada, this approach is unlikely to influence our results. Furthermore,

we collected objective evidence of worsening asthma and adjudicated outcomes by an external committee to minimize bias. **Fifth**, initial PEF and FEV₁, as well as, % predicted PEF and FEV₁ measurements were not obtained on all patients, which could have influenced our results. On the other hand, we elected to reflect the real ED-practice which under-utilizes pulmonary function measures, include a more generalizable sample and ensure a high proportion of patients with discharge pulmonary function measures. **Sixth**, **self-reported** non-adherence to **OCS** **was** extremely low in the entire cohort; therefore, non-adherence could not be examined as a relapse factor. **Adherence to the completion of the treatment prescribed in the ED was only measured through self-report as this study didn't include an in-person assessment after the ED visit; inhaler techniques were not assessed or the same reason.** Similarly, 89% of patients were prescribed an ICS at discharge, so our study did not have the power to determine the influence of ICS agents on relapse in the 4-week post-ED period. **Seventh, the generalizability of the study results may be limited due to the fact that all patients received OCS and a high proportion received inhaled anti-inflammatory agents; however, since these are evidence-based and recommended treatments, these results would reflect the best case scenario.** Finally, our four-week follow-up could be deemed by some to be insufficiently long for identifying all relapse events; however, this period has been used in similar studies and RCTs.[15, 22] Moreover, longer observation can be biased by re-exposure to other asthma precipitants, and thus may be a reflection of a new exacerbation rather than a relapse event.

Conclusions

This study identified a practical set of factors which could be used by clinicians to identify patients at risk for relapse after discharge from an ED and guide health providers in the development of evidence-based clinical decision rules, educational strategies and optimal follow-up plans for the prevention of relapses. We found female sex, prolonged exacerbation symptoms prior to the ED visit, and some markers of asthma treatment intensity prior to ED visit were significantly associated with relapse. Although some further work is required to validate our **specific** findings, we believe that the presence of one or more of these risk factors identifies patients at high risk of relapse who might benefit from more intensive ED management, **disposition decisions (e.g., early admissions) and discharge plans (e.g., closer follow-up by a primary care provider or specialist after discharge).**

Acknowledgements

The authors would like to thank the Canadian Institutes of Health Research (CIHR; Ottawa, ON) and the Medical Services Incorporated Foundation (MSI; Edmonton, AB) who provided research funding for this study; and the Department of Emergency Medicine Research Group (EMeRG®) at the University of Alberta for their in-kind support of this project.

The research team would like to thank Sandra Blitz for her assistance during the study design; the Epidemiology Coordinating and Research Center (EPICORE; Edmonton, AB) for their support in data collection and coordination; Diane Milette for her secretarial support; and the following AIR investigators (in order of recruitment numbers): Duncan Mackey (Lethbridge, AB), Brian Rowe (Edmonton, AB), Alan Walker (Edmonton, AB), Scott Ross (St. Albert, AB), Ian Stiell (Ottawa, ON), Bryan Young (Calgary, AB), Sam Campbell (Halifax, NS), Marco Sivilotti (Kingston, ON), Bjug Borgundvaag (Toronto, ON), Chris Boule (Mississauga, ON), Robert Stenstrom (Vancouver, BC), Andrew Worster (Hamilton, ON), Shaun Visser (Thunder Bay, ON), Eddy Lang/Marc Afilalo (Montreal, PQ), Riyadh Abu-Laban (Vancouver, BC), Jhon Froh (Saskatoon, SK), Marcel Emond (Quebec, QC), Jacques Lee (Toronto, ON), and Chantal Guimont (Ste-Foy, Quebec).

The authors would also like to express their gratitude to the following research staff for their assistance in site coordination (in order of recruitment): Marlene Myles, Ginny Willis, Leslie Tyler, Debbie Boyko, Michelle Pachal, Cathy Clement, Renee Vineff, Agnieszka Grabowski-Comeau, kathy Bowes, Michelle Loftus, Sharon Oliveros, Crystal-Anne Smith, Barbara Boychuck, Christina Brean, Sandra Stoger, Cristina Ciolofan, Jan

Buchanan, Tricia Pearson, Cynthia Reich, Patricia Chabot, Shana Huntly and Annie-Claude D'Anjou.

Dr. Rowe is supported by CIHR through a Tier I Canada Research Chair in Evidence-based Emergency Medicine from the Government of Canada (Ottawa, Ontario). Dr. Villa-Roel is supported by CIHR in partnership with the Knowledge Translation branch. Dr. Majumdar is a Health Scholar of the Alberta Heritage Foundation and Alberta Innovates Health Solutions (AIHS) and holds the Endowed Chair in Patient Health Management of the Faculties of Medicine and Dentistry and Pharmacy and Pharmaceutical Sciences, University of Alberta (Edmonton, Alberta, Canada). Dr. Johnson is a Senior Health Scholar with AIHS and Centennial Professor at University of Alberta.

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Table 1: Characteristics of patients with acute asthma discharged from the emergency department categorized by relapse status.

	Relapse (n=144)	No Relapse (n=663)			
Demographic and clinical factors	Number (%), Median (IQR)		Unadjusted OR	95% CI	p-value
Age (years)	30 (24, 39)	29 (23, 39)	1.0	(0.9, 1.0)	0.126
Female (Reference: male)	102 (70.8%)	363 (54.8%)	2.0	(1.3, 3.0)	0.001
White race (Reference: other races)	123 (85.4%)	559 (84.3%)	1.1	(0.6, 1.9)	0.736
High school graduate (Reference: no high school graduate)	32 (22.2%)	129 (19.5%)	1.2	(0.9, 1.6)	0.270
Marital status (single; (Reference: not single)	57 (39.6%)	299 (45.1%)	0.8	(0.5, 1.2)	0.270
Working for pay or profit during the last year (Reference: not working for pay or profit during the last year)	80 (55.6%)	353 (53.2%)	1.1	(0.7, 1.6)	0.625
Most common co-morbidity (hypertension)	12 (8.3%)	31 (4.7%)	1.8	(0.8, 4.1)	0.131
Most common concurrent medication (oral contraceptives)	16 (11.1%)	53 (8.0%)	1.4	(0.9, 2.2)	0.104
Preventive factors					
Have a Family Physician (Reference: not having a family physician)	22 (15.3%)	132 (19.9%)	0.7	(0.4, 1.1)	0.119
Have an "action plan" (Reference: not having an action plan)	74 (51.4%)	256 (38.7%)	1.7	(1.2, 2.3)	0.001
Use asthma diary/ peak flow meters (Reference: not using asthma diary/ peak flow meters)	50 (34.7%)	176 (26.5%)	1.4	(1.0, 2.1)	0.037
Own a spacer device (Reference: not owning a spacer device)	65 (45.1%)	207 (31.2%)	1.8	(1.4, 2.2)	<0.001
Have Influenza immunization (Reference: not having Influenza immunization)	69 (47.9%)	252 (38.0%)	1.5	(1.1, 2.1)	0.021
Smoking status					0.928
Never (Reference)	52 (36.1%)	243 (36.7%)	1.0		
Current	47 (32.6%)	222 (33.6%)	1.1	(0.7, 1.8)	
Previous	45 (31.2%)	196 (29.6%)	1.0	(0.7, 1.5)	
Resource Utilization					
Family physician most frequently treats his/her asthma (Reference: family physician does not treat his/her asthma)	96 (66.7%)	411 (61.9%)	1.2	(0.8, 1.8)	0.304
ED is the usual site for asthma care	98 (68.1%)	435 (65.6%)	1.1	(0.7, 1.7)	0.708

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(Reference: ED is not the usual site for asthma care)					
ED usual source of asthma prescriptions (Reference: ED is not the usual site for asthma prescriptions)	27 (18.7%)	114 (17.2%)	1.1	(0.6, 1.9)	0.763
Insurance status					
Have medication coverage (Reference: not having medication coverage)	71 (49.3%)	329 (49.6%)	0.8	(0.6, 1.2)	0.341
Percentage of medication costs usually paid by patients	20 (0, 20)	20 (0, 20)	1.0	(1.0, 1.0)	0.290
Reported less medication use (Reference: not reporting less medication use)	30 (20.8%)	110 (16.6%)	1.5	(0.9, 1.8)	0.138
Chronic asthma factors					
Asthma history (years)	16 (9, 24)	17 (10, 23)	0.9	(0.9, 1.0)	0.679
No. of ED visits in past 2 years	2 (0, 4)	1 (0, 3)	1.1	(1.0, 1.2)	<0.001
Hospitalizations for asthma in past 2 years (Reference: not being hospitalized for asthma in the past 2 years)	39 (27.1%)	151 (23.3%)	1.2	(0.8, 1.9)	0.309
Ever intubated for asthma (Reference: have never been intubated for asthma)	11 (7.6%)	46 (6.9%)	1.1	(0.7, 1.8)	0.633
Ever taken oral corticosteroids for asthma (Reference: have never taken oral corticosteroids for asthma)	107 (74.3%)	401 (60.5%)	1.9	(1.4, 2.5)	<0.001
Medication at presentation to the ED					
Inhaled short-acting β -agonists (SABA) (Reference: not on SABA)	133 (92.4%)	581 (87.8%)	1.7	(0.9, 3.0)	0.075
Inhaled long-acting β -agonists (LABA) (Reference: not on LABA)	5 (3.5%)	18 (2.7%)	1.3	(0.6, 2.6)	0.519
Inhaled corticosteroids (ICS)					<0.001
ICS monotherapy (Reference)	42 (29.2%)	243 (36.6%)	1.0		
ICS/LABA (with or without extra ICS)	66 (45.8%)	197 (29.7%)	1.9	(1.1, 3.2)	
None	36 (25.0%)	223 (33.6%)	0.9	(0.6, 1.4)	
Leukotriene modifier/antagonist (Reference: not on leukotriene modifier/antagonist)	13 (9.0%)	35 (5.3%)	1.7	(1.0, 3.2)	0.056
Prednisone (Reference: not on Prednisone)	4 (2.8%)	15 (2.3%)	0.8	(0.3, 2.3)	0.690
Anticholinergics (Reference: not on anticholinergics)	6 (4.2%)	18 (2.7%)	0.7	(0.3, 1.5)	0.313
Combined SABA + anticholinergics (Reference: not on SABA +	2 (1.7%)	19 (2.9%)	2.0	(0.5, 8.3)	0.313

anticholinergics)					
Theophylline	0	8 (1.2%)			
Antibiotics	0	2 (0.3%)			
ED, Emergency Department; GEE, Generalized Estimating Equations. OR, odds ratio; CI, confidence intervals. Interquartile range (IQR) is presented as 25 th and 75 th percentiles; OR, 95% CI and p-values are adjusted estimates from GEE.					

Table 2: Acute asthma presentation and ED course categorized by relapse status.

		Relapse (n=144)	No Relapse (n=663)			
Demographic factors		Number (%), Mean ($\pm$ SD) Median (IQR)		Unadjusted OR	95% CI	p-value
CTAS Score						0.335
	2 (Reference)	33 (22.9%)	136 (20.5%)	1.0		
	3	66 (45.8%)	319 (48.1%)	0.9	(0.6, 1.3)	
	4,5	22 (15.3%)	132 (19.9%)	0.8	(0.5, 1.2)	
	Not Documented	23 (16%)	76 (11.5%)			
Duration of Symptoms						0.001
	< 24 hours (Reference)	26 (18.3%)	175 (26.8%)	1.0		
	$\geq$ 24 hours	116 (81.7%)	479 (73.2%)	1.6	(1.2, 2.2)	
	Not Documented	2 (1.4%)	9 (1.4%)			
Days with activity limitation due to asthma		2 (1, 4)	2 (1, 4)	1.0	(0.9, 1.0)	0.938
No. of inhaled β -agonist puffs within 24 hours of ED		9 (4, 20)	8 (2, 16)	1.0	(0.9, 1.0)	0.338
Vital signs						
Pulse		99 (87, 110)	99 (87, 111)	0.9	(0.9, 1.0)	0.855
Respiratory rate		22 (20, 26)	22 (18, 24)	1.0	(1.0, 1.0)	0.017
SaO ₂ (On room air)		96 (94, 98)	96 (94, 98)	1.0	(0.9, 1.0)	0.823
Temperature		36.6 (36.3, 37.1)	36.6 (36.2, 37)	1.1	(0.8, 1.4)	0.426
ED Course						
Received inhaled β -agonists in the ED (Reference: not receiving inhaled β -agonists in the ED)		139 (96.5%)	652 (98.3%)	2.7	(0.7, 10.4)	0.148
No. of treatments in the first hour		1 (0, 2)	1 (0, 2)	1.0	(0.9, 1.1)	0.798
No. of treatments over ED stay		3 (1, 4)	3 (1, 4)	0.9	(0.9, 1.0)	0.421
Given any corticosteroid treatment (Reference: not receiving corticosteroid treatment in the ED)		141 (97.9%)	652 (98.3%)	0.7	(0.2, 2.6)	0.705
Received inhaled anticholinergics (Reference: not receiving inhaled anticholinergics in the ED)		122 (84.7%)	571 (86.1%)	1.1	(0.8, 1.6)	0.403
No. of treatments in the first hour		1 (0, 2)	1 (0, 2)	1.0	(0.9, 1.1)	0.535
No. of treatments over ED stay		2 (1, 3)	2 (1, 3)	0.9	(0.9, 1.0)	0.771
MgSO ₄ medication in the ED		2 (1.4%)	9 (1.4%)	1.0	(0.2, 4.4)	0.981

(Reference: not receiving MgSO ₄ medication in the ED)					
ED length-of-stay (hours)	4 (3, 5)	4 (3, 5)	0.9	(0.9, 1.0)	0.164
ED length-of-stay $\geq$ 6 hours (Reference: ED length-of-stay $\leq$ 6 hours)	26 (18.0%)	125 (18.8%)	0.9	(0.6, 1.5)	0.821
Lung Function					
Earliest PEF (n=630)	250 (200, 320)	250 (200, 320)	0.9	(0.9, 1.0)	0.355
Final PEF (n=764)	343 ($\pm$ 131)	329 ($\pm$ 119)	0.9	(0.9, 1.0)	0.306
Change in PEF (n=599)	80 (7, 148)	83 (20, 164)	0.9	(0.9, 1.0)	0.779
Earliest %Predicted PEF (n=626)	55 (40, 65)	52 (39, 65)	1.0	(0.9, 1.0)	0.692
Final %Predicted PEF (n=735)	77 (60, 91)	74 (55, 92)	1.0	(0.9, 1.0)	0.470
Change in %Predicted PEF (n=573)	21 (7, 41)	22 (7, 41)	1.0	(0.9, 1.0)	0.162
FEV ₁ % Predicted at discharge (n=709)	71 (59, 86)	71 (55, 89)	0.9	(0.9, 1.0)	0.980
FEV ₁ /FVC % (n=707)	77 (67, 89)	78 (67, 89)	0.9	(0.9, 1.0)	0.665
Discharge medication					0.064
No ICS prescribed by EP (Reference)	16 (16.1%)	76 (11.5%)			
New inhaled corticosteroids prescription by EP	44 (30.5%)	263 (39.7%)	1.2	(0.7, 2.1)	
Instructed to continue on ICS by EP	84 (58.3%)	320 (48.3%)	0.8	(0.4, 1.6)	
Not Documented		4 (0.6%)			
CTAS, Canadian Triage and Acuity Scale; ED, Emergency Department; PEF, Peak expiratory flow; FEV ₁ , Forced expiratory volume in 1 second; FVC, Forced vital capacity; ICS; inhaled corticosteroids; EP, Emergency physician; GEE, Generalized Estimating Equations. OR, odds ratio; CI, confidence intervals. Interquartile range (IQR) is presented as 25 th and 75 th percentiles; OR, 95% CI and p-values are adjusted estimates from GEE.					

Figures (4)

Figure 1: Study patient flow.

Legend: Exclusions included not being treated in the Emergency department for acute asthma (23%), admissions (18%), unclear clinical diagnosis of asthma (10%), suspected pneumonia (8%) and refusal to follow up (8%). Other reasons for exclusions (33%) were age outside the study range, >80% peak expiratory flow at presentation, antibiotic treatment for pneumonia, previous participation in the study, chronic use of oral corticosteroids, chronic obstructive disease exacerbation or ≥ 30 pack years of smoking, pregnancy, cognitive impairment, severe co-morbidities, refusal to take oral prednisone and patients who needed immediate resuscitation.

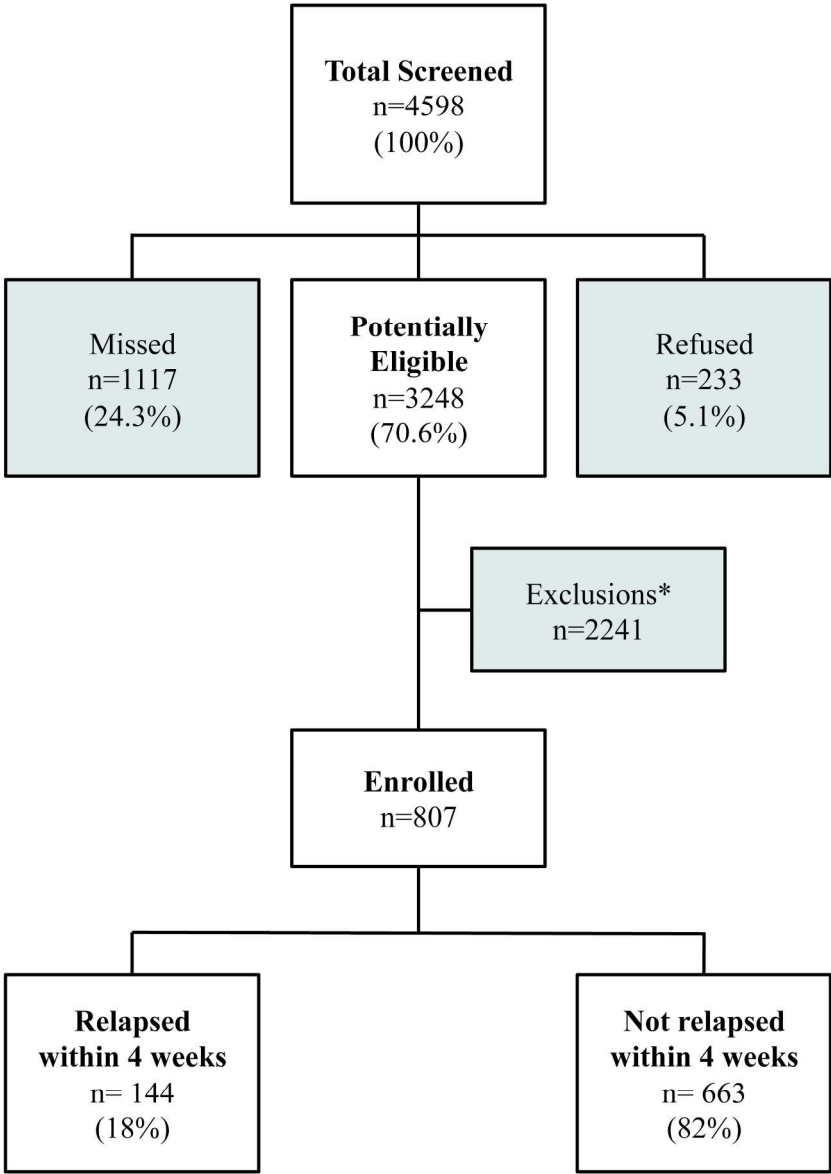
Figure 2: Medication at ED presentation.

Legend: SABA denotes inhaled short-acting b-agonists; ICS= inhaled corticosteroids; LABA= inhaled long-acting b-agonists; ICS+LABA= combination therapy; OCS= oral corticosteroids; LEUK= leukotriene modifier/antagonist.

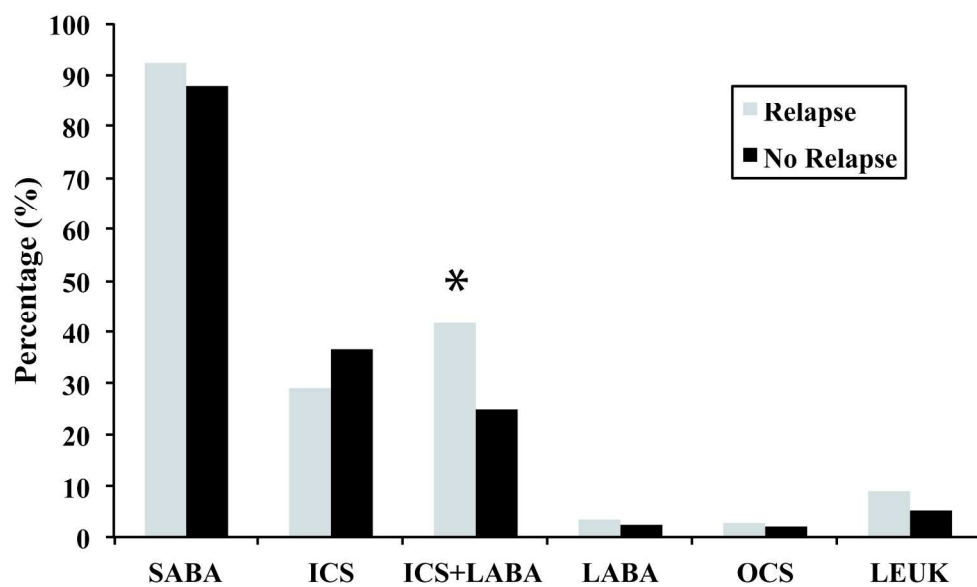
Figure 3: Medication at presentation and discharge.

Legend: ICS denotes inhaled corticosteroids; LABA= inhaled long-acting b-agonists; ICS+LABA= combination therapy; OCS= oral corticosteroids; LEUK= leukotriene modifier/antagonist.

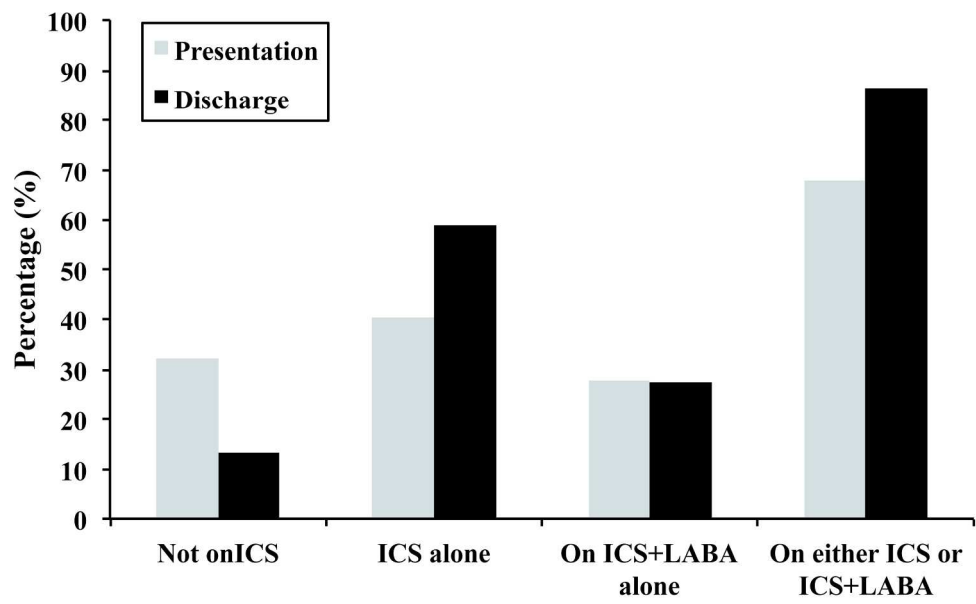
Figure 4: Relapse timing based on patient sex.



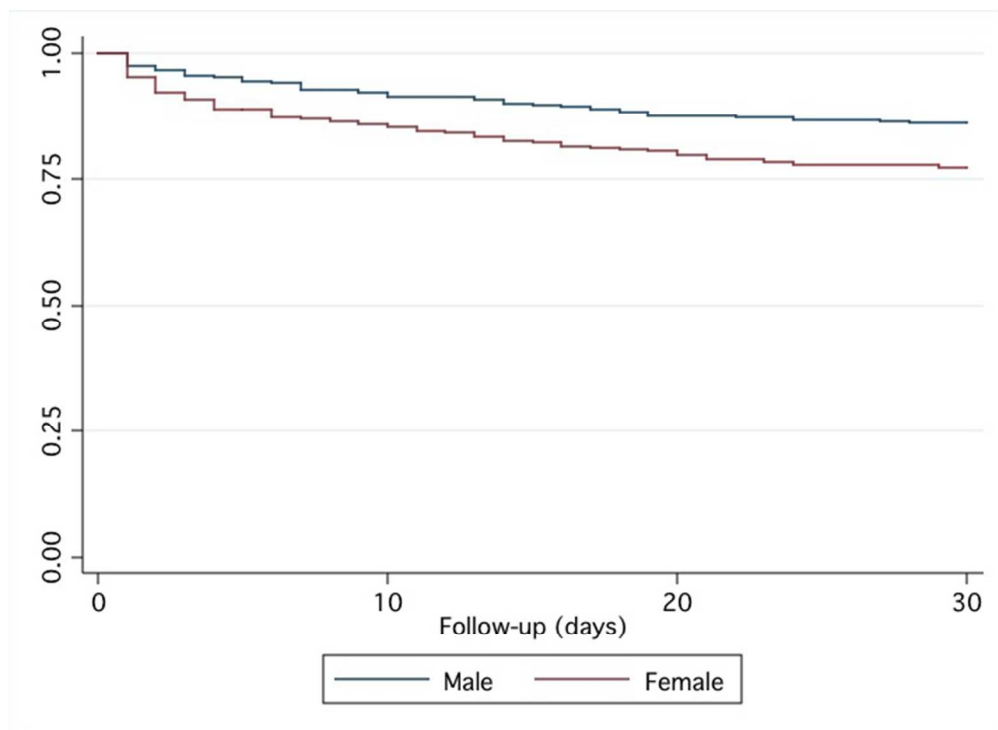
Study patient flow.
190x254mm (300 x 300 DPI)



Medication at ED presentation.
202x128mm (300 x 300 DPI)



Medication at presentation and discharge.
209x128mm (300 x 300 DPI)



Relapse timing based on patient sex.
252x183mm (72 x 72 DPI)