A Knowledge Translation Approach To Improve Outcomes After Asthma Exacerbations

by

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A thesis submitted
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

In

Epidemiology

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ABSTRACT

Background: A knowledge translation (KT) gap between evidence and action exists in asthma care and this gap may explain the suboptimal quality of care and poor health outcomes after asthma exacerbations. While recently published and widely disseminated asthma guidelines have highlighted the essential role of individualized patient-centered approaches, the following elements of high-quality care have not been well described or deployed: patient education components and key care partnerships; strategies targeting the sustained implementation of various recommendations; and methods to facilitate the transitions in care between the emergency department (ED) and community-based follow-up with primary care providers (PCPs).

Methods: The Graham and Straus knowledge to action (KTA) model was used to facilitate and accelerate the use of high-quality asthma evidence into practice settings. Seven steps were followed to support the design, evaluation and implementation of opinion leader (OL) and care manager (CM) -based interventions generated in the ED and directed at community-based PCP and patients, respectively.

Results: 1-2) Potential solutions that could help address a problem (Chest. 2015;147:140-9) were targeted through the following research question: In adult patients with acute asthma discharged from the ED, will ED-directed interventions reduce relapses and improve outcomes compared to usual care (UC)? 3) A systematic review of the literature provided conclusive evidence to support the consideration of ED-directed

educational interventions targeting either adult patients or providers as effective strategies to increase PCP follow-up visits after asthma exacerbations; 4) Surveys and focus groups involving patients and PCPs helped refine the study interventions to account for local context and identify potential barriers for implementation. 5) Using randomized controlled trial methods, patients were allocated to receive UC (including notification to their PCP of their ED visit), personalized OL-letters faxed to their PCPs (PF; identifying gaps in care and providing guidance on ambulatory management) or OL and patient education by an asthma CM within a week of being discharged from the ED, in an incremental approach. A significant increase in the proportion of PCP follow-up visits within 30 days occurred in the intervention arms when compared to UC; however, this effect was attenuated by 90 days. The interventions did not improve patient-oriented outcomes such as relapses, quality of life and hospitalization; results were counterintuitive and overtreatment was documented at the PCP follow-up visits. 6) Traditional and non-traditional dissemination methods helped make research results available and more useful to stakeholders. 7) Determinants and strategies for the sustained application of this new knowledge were identified and proposed.

Conclusions: The use of a KTA conceptual framework favored a reflective and synergistic research process with the engagement of potential end users and the use of high-quality research methods. The costs required to implement these multifaceted and tailored ED-directed

interventions would not be warranted given the negative effects on patient oriented health outcomes. Regardless of the results of the comparative effectiveness research, the interpretability of the overall conclusions were facilitated by the previous contact with the practice environment.

PREFACE

This thesis is an original work of M.I Cristina Villa-Roel. Two research projects involved in this thesis, received research ethics approval from the University of Alberta Health Research Ethics Board – Health Panel, Project Names “Tailoring Educational Interventions in Acute Asthma” No. Pro00023191; and “ED-directed interventions to improve outcomes after asthma exacerbations”, No. Pro00029699 (Appendices 4-1 and 5-1). M.I Cristina was a co-applicant in the successful submission of the Pro00023191-research project to Knowledge Translation Canada (SEED Grant) and of the Pro00029699-research project to the Canadian Institutes of Health Research (CIHR operating grant # RES0011584; CIHR Fellowship # 201002KPD).

Chapter 3 of this thesis has been published in the journal *Academic Emergency Medicine* (**Villa-Roel C**, Nikel T, Ospina M, Voaklander B, Campbell S, Rowe BH. Effectiveness of Educational Interventions to Increase Primary Care Follow-up for Adults Seen in the Emergency Department for Acute Asthma: A Systematic Review and Meta-analysis. *Acad Emerg Med*. 2016;23:5-13). Cristina Villa-Roel and Brian H. Rowe wrote the study protocol and were responsible for the general coordination of the study; Taylor Nikel and Britt Voaklander contributed to study selection, data abstraction and quality/fidelity assessment; Maria Ospina participated in the analysis/interpretation of data and Sandra Campbell designed the search strategy as well as conducted the literature search.

Cristina Villa-Roel drafted the final manuscript; all authors reviewed and approved the final version of the manuscript before its submission for publication.

Chapter 4 of this thesis has been prepared as a manuscript awaiting submission for publication (**Villa-Roel C**, Ospina M, Majumdar SR, Couperthwaite S, Rawe E, Nikel T, Rowe BH. Engaging Patients and Primary Care Providers in the Design of Novel Opinion Leader Based Interventions for Acute Asthma in the Emergency Department: A Mixed Methods Study). Cristina Villa-Roel and Brian H. Rowe wrote the study protocol and were responsible for the general coordination of the study;

Maria Ospina led the focus groups, their analysis and interpretation. Sumit R. Majumdar made substantial contributions to both the study protocol and the final manuscript. Stephanie Couperthwaite coordinated the study data management; Erin Rawe and Taylor Nikel contributed to the study data collection and analysis. Cristina Villa-Roel drafted the final manuscript; all authors will review and approve the final version of the manuscript before its submission for publication.

DEDICATION

To Chris, Federico and Amelia… the ones who teach me everyday the full significance of life.

ACKNOWLEDGEMENTS

With this thesis dissertation I conclude one of the most challenging yet incredibly gratifying chapters of my life. During the last six years I learned to formulate my own research questions and to find their answers using appropriate and feasible methods. I was able to confirm in my own mind that research success is not always about knowing everything but about being disciplined, committed and having a strong work ethic surrounded by supportive collaborators. This is perhaps the most important lesson I have learned from my mentor and PhD supervisor Brian H. Rowe. Brian, your guidance and support over the past six years of training were invaluable; my eternal gratitude for your trust and kindness.

Working with the Emergency Medicine Research Group while conducting my PhD has been an enormous pleasure and a great privilege. I would like to express special gratitude to Stephanie Couperthwaite, Natalie Runham, and Danielle DeVuyst; the asthma educators (Ginny Willis, Debbie Boyko and Janel Carley); the research staff in Edmonton (Francis Tenorio, Janette Leipntiz, Pamela Pang, Pamela Chow, Justin Lowes and Rajiv Chetram) and Calgary (Tiffany Junghans and Heidi Boyda); and the summer students (Erin, Elfriede, Kyla, Bryn, Taylor and Britt) who helped me complete the studies involved in my thesis. Your efforts and commitment allowed me to meet my PhD deadlines. Scott, Chris, Lynette and Lindsay, thanks for your assistance and support during the last 6 months of thesis writing.

I would like to thank the other members of my PhD supervisory committee (Drs. Bhutani, Majumdar, Leigh, Senthilselvan) for challenging me during all these years; your guidance and advice were important factors in the completion of the program of research. Special thanks to those who also supported the grant (Drs. Lang, Borgundvaag, Rosychuck and McCabe) and fellowship application (Dr. Rowe) that funded my research. There is a deep sense of appreciation for the organizations (the Department of Emergency Medicine at the University of Alberta and the Canadian Institutes of Health Research) and people who have contributed to my academic and personal accomplishments over these years.

To my many friends (Jude, Laura, Katharyn, Maria, and others), words cannot express my appreciation for all your support during these six years. You all witnessed my deep personal transformation while becoming a mom during my PhD training; thanks for your encouragement during my PhD journey.

Mami y papi, gracias por proveerme una excelente educación; soy quien soy gracias a ustedes. Manuel, Gabriel y Dianita, gracias por su apoyo y compañia en la distancia. Gracias a mi familia extendida por valorar mis intereses y a Maru por su apoyo incondicional mientras cumplí este sueño. Finally but not lastly, my heartfelt thanks to Chris, my husband and best friend. Chris, you encouraged me to pursue this PhD, allowed me to enjoy it and gave me the two most important reasons to complete it: Fede and Ame.

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1.1 Definition

Asthma is a chronic respiratory disorder characterized by intermittent episodes of shortness of breath, wheezing, chest tightness, sputum production and coughing, particularly at night or in the early morning. Chronic inflammation of the airways, hyper-responsiveness to endogenous or exogenous triggers and variable airflow limitation are the key pathophysiological features of asthma; which are often reversible either spontaneously or with treatment.[1, 2]

1.2 Epidemiology and costs

According to the 2014 Global Asthma Report, asthma affects more than 300 million people worldwide; the World Health Organization (WHO) estimates this number will increase by more than 100 million by 2025.[1, 2] Asthma is a serious public health problem in all countries regardless of their level of development; it represents a significant social and economic burden to individuals, families and health care systems.[3, 4] In North America, asthma affects 7-10% of the adult population; the prevalence of diagnosed asthma in Canada and the United States (US) is amongst the highest in the world both for adults and children.[2, 5] According to *Statistics Canada*, 8.1% of the population (aged 12 and over) reported they had been diagnosed as having asthma by a health professional in 2014, an estimate that differs between females and males (9.2% vs. 7.0%) and that

has generally increased over the last 20 years.[6] Asthma has been identified as one of the leading causes of work absenteeism.[3] Asthma costs have not been directly assessed across Canada since the nineties;[7] however, conservative estimates suggest that the annual medical and non-medical costs of asthma in Canada rose from Canadian(C)$504 million in 1990 to C$2.2 billion in 2010, and that this number could increase to C$4.2 billion by 2030.[8] Annually, 146,000 visits to emergency departments (EDs) are related to asthma exacerbations in Canada[9] and acute care costs represent about 25% of the annual estimated expenditures.[10] Asthma exacerbations and the level of asthma control have been associated with increased resource utilization and health care costs.[11]

1.3 Factors that influence the expression of asthma in adulthood

Asthma commonly presents during childhood; however, in some instances it starts later in life. Some clinical presentations (e.g., no-self-report of asthma in adult life with parent-report of childhood asthma or long-standing periods of time with no symptoms/medication in patients who have been diagnosed with asthma) have opened a debate about potential remissions of this respiratory condition;[12] however, several studies have demonstrated the presence of ongoing inflammation despite the absence of symptoms.[13, 14] The earlier the diagnosis of asthma is made and anti-inflammatory management is started, the better the long-term prognosis.[15] Although deaths occur from asthma, these events are

extremely rare in Canada and usually result from co-morbid conditions or poor chronic asthma control.[16-19]

Factors involved in the expression of asthma could be categorized into host factors (primarily genetic) and environmental factors (Table 1-1). Some of them are unavoidable and the mechanisms whereby they influence the expression of asthma are interactive.[20, 21] Regardless of their nature and complex role in the expression of asthma, their identification and avoidance is a critical component of successful asthma management.

1.4 Underlying mechanisms of asthma

Over the past two decades, the pathophysiology of asthma has advanced considerably. Asthma is now considered a chronic, immunologically mediated condition with disturbance of the normal airway repair mechanism.[22-24] The interactions between environmental factors and genetic susceptibility are key determinants in the development and propagation of pro-inflammatory, fibro-proliferative and remodeling responses in asthma. In addition, dynamic interactions between the innate and acquired immune systems have been clarified, proving new insights to the role that inflammatory cells (e.g., basophils, mast cells, dendritic cells, T lymphocytes, eosinophils and neutrophils) and structural elements of the airway (e.g., epithelium, smooth muscle and endothelium) play in the in the clinical manifestations of asthma, particularly in the development of exacerbations.[25, 26] Airway narrowing is the common pathway leading to asthma symptoms and hyper-responsiveness is the typical physiological

response. The understanding of the pathophysiology of asthma has had important implications on its treatment targets; the current goal of asthma management is mainly reduce exposure to antigenic triggers and control airway inflammation.

1.5 Diagnosis

The diagnosis of asthma relies on the combination of a compatible clinical history, physical examination, and objective measures of lung function.

1.5.1 Clinical history:

While there is no unique pattern, history of respiratory symptoms such as shortness of breath, wheezing, chest tightness, sputum production and cough (usually since childhood); personal/family history of atopy or allergies; exposure to triggers (e.g., aeroallergens, viral upper respiratory infections); and comorbid conditions (e.g., rhinitis, gastroesophageal reflux disease [GERD]) are helpful guides.

1.5.2 Physical examination:

When quiescent, routine physical examination of patients with asthma may be remarkably normal. When symptoms are persistent, physical examination (e.g., vital signs, observation and chest auscultation) may confirm the presence of airflow limitation; signs such as difficulty breathing and speaking, cyanosis, hyper-inflated chest and use of

accessory muscles and intercostal recession vary depending on asthma severity.

1.5.3 Lung function tests:

Spirometry and peak expiratory flow (PEF) measurements are the most readily available and useful tests for the diagnosis and monitoring of asthma.[27, 28] Spirometry measurements such as the forced vital capacity (FVC), the forced expiratory volume in the first second (FEV_1), their ratio (FEV_1 /FVC), and the PEF are particularly relevant either as baseline indicators or as pre/post bronchodilator indicators (e.g., administration of short-acting β_2- agonist [SABA] by meter-dose inhaler [MDI]) of reversibility of the airway obstruction.[1] These values can be reported as absolute measures or percentage of predicted. Predicted values of FEV_1, FVC and PEF based on age, sex, race and height have been obtained from population-based studies; these values help judging whether a given value is abnormal or not.

A reduced FEV_1/FVC (<70%) with 12% degree of reversibility in FEV_1 and/or >200 ml from the pre-bronchodilator PEF value, is generally accepted for the diagnosis of asthma (greater confidence if increase is >15% and >400 ml). Nevertheless, some patients won't exhibit reversibility of their airflow obstruction (especially those experiencing an acute severe episode, those who are controlled and receiving treatment, or those with airway remodeling) and repeated testing at different visits (e.g., diagnosis is confirmed if there is an increase in FEV_1 >12% and >200 ml from

baseline after four weeks of treatment, outside respiratory infections) or bronchial challenge testing (methacholine/histamine/mannitol challenge tests) may be required. Because race, age and co-morbid conditions may influence FEV_1 values, the FEV_1 /FVC ratio is usually preferred for the assessment of airflow limitation. The FEV_1 /FVC ratio is normally greater than 0.75 to 0.80; any value lower than these suggest asthma; however, alternative diagnoses should always be considered and ruled out (e.g., chronic obstructive pulmonary disease [COPD], asthma and COPD overlap syndrome [ACOS], pneumonia, viral upper respiratory infection [URI], etc).

While more practical, PEF measurements are not interchangeable with other airflow measures such as the FEV_1. Factors such as device-dependent variability and the wide range of predicting values limit their utility for “between-persons” comparison; measurements should preferably be compared to the patient’s own previous/best measurements (e.g., asymptomatic or on full treatment) using the same device. More than 10% average diurnal variation in twice-daily PEF over two weeks or ≥20% improvement after bronchodilator or repeated testing (e.g., baseline after four weeks of treatment, outside respiratory infections) suggests the diagnosis of asthma. Peak expiratory flow daily readings can help monitoring the effect of environmental triggers at home, at the workplace, during exercise and even during periods of no symptoms; which can help clarifying the role of such exposures.

Both spirometry and PEF are effort-dependent measures. Therefore, the quality and reliability of the information provided by these tests depends on the instructions given to patients such as how to perform the forced expiratory maneuvers and what to record (highest of three reproducible recordings [no more than 5% variation among them]).

For patients with symptoms compatible with asthma but no clear diagnosis with conventional spirometry or PEF, the bronchial challenge tests are useful; a positive methacholine/histamine/mannitol challenge (fall in FEV_1 from baseline ≥20% for the first two and ≥15% for the last one [with standard doses and procedures]) or exercise challenge (fall in FEV_1 from baseline 10-15%) may help establishing the diagnosis of asthma. The rationale behind these "challenges" is the airway responsiveness (usually a ≥20% fall in the FEV_1) that can be observed as the result of provocative concentrations (increased dosage) of these agonists. Due to the high sensitivity but limited specificity of these tests,[29] their results need to be analyzed carefully in the presence of co-morbid conditions.[30, 31]

1.5.4 Differential diagnosis:

As in many other entities, the differential diagnosis in adult patients with suspected asthma is very important. Conditions such as bronchitis, vocal cord dysfunction, cystic fibrosis, GERD, and the presence of foreign bodies in the upper airways should be ruled out in adolescents and young adults (<39 years old). Chronic obstructive pulmonary disease, parenchymal lung disease, pulmonary embolism, and cardiac failure are

some of the conditions that can co-exist in older patients (age > 40 years old). Additional tests such as electrocardiograms (ECG) and chest X-rays usually clarify these complex cases and help guiding their treatment.

Distinguishing asthma from COPD can be problematic in some instances (Table 1-2); both are chronic obstructive conditions with underlying airway inflammation. Long-standing asthma with remodeling and chronic irreversible airflow obstruction with reduced lung function,[32, 33] ACOS[1] and COPD patients with significant bronchodilator response[34] represent challenging diagnostic and therapeutic processes. They are alternative or co-existent diagnoses to consider when the clinical impression doesn't match the results of the diagnostics tests or the expected response to treatment. Finally, special populations such as subjects with occupational asthma, athletes, pregnant women and the elderly usually benefit from a specialized examination due to their physiological features, and diagnostic/treatment restrictions.

1.5.5 Other tests:

The evaluation of airway inflammation can also be examined through non-invasive markers; induced or not induced sputum samples (for the documentation of eosinophilic or neutrophilic inflammation), levels of exhaled nitric oxide (FeNO) and carbon monoxide (FeCO) have been evaluated for potential use in determining optimal asthma treatment.[35, 36] Metabolomic profiling has been proposed; however, its not widely applied outside a research environment. Finally, the role of allergy testing (e.g.,

skin tests and specific IgE serum levels) can help identifying factors associated with asthma symptoms in certain patients (e.g., those with an allergic profile). Unfortunately, many of these alternatives diagnostic aids are rarely available outside of research studies and settings, expensive, and not widely available to clinicians at the bedside.

1.6 Asthma classification

Asthma is often classified based on its etiology (e.g., allergic vs. non-allergic, occupational vs. non-occupational) and its underlying phenotype (e.g., exercise-induced asthma, aspirin-induced asthma). However, these classifications have limited clinical utility due to the existence of cases with unclear roots, heterogeneous manifestations and differential response to treatment.[37]

Levels of asthma control (Table 1-3) and levels of asthma severity (intermittent, mild-persistent, moderate persistent and severe persistent) are classifications commonly used to guide management and to follow patients' response.

According to the current guidelines the assessment of asthma control should reflect balance of the manifestations of disease and explore factors associated with future risk of undesired outcomes.[38, 39] Other standardized tools such as the Asthma Control Questionnaire (ACQ),[40] the Asthma Control Test (ACT),[41] the Asthma Therapy Assessment Questionnaire (ATAQ)[42] and the Asthma control Scoring System[43] have been used for research purposes; however, they have been promoted for

patient care as well. Its important to recognize that asthma severity is a dynamic feature on an individual's health, based on this, periodic assessments (e.g., weekly/monthly basis or during treatment) are recommended. The classification of asthma severity proposed by the National Asthma Education and Prevention Program (NAEPP)[44] is based on the level of symptoms, airflow limitation and lung function variability and it applies to patients not receiving corticosteroid treatment. Due to the poor predictive value of this method of classification regarding treatment requirements and response;[39] asthma is now classified on the basis of the intensity of treatment required to achieve control:

- Mild asthma: The patient who can be well-controlled with low intensity treatment such as low-dose inhaled corticosteroids (ICS), leukotriene receptor antagonists (LTRA) or theophylline.
- Moderate asthma: The patient who can be well-controlled with low intensity ICS/long-acting β_2-agonist (ICS/LABA) treatment.
- Severe asthma: The patient who requires high intensity treatment (e.g., med/high dose ICS/LABA ± anti-immunoglobulin E [anti-IgE]) to prevent "uncontrolled" asthma or the patient who remains uncontrolled despite high intensity treatment.

1.7 Asthma management

The long-term goals of asthma management are to achieve good symptom control, and to minimize future risk of exacerbations, decline in lung function and side effects of treatment. An effective partnership

between adult patients with asthma and their health care provider(s) is one of the key determinants of the success of any management strategy. Partnerships based on principles of mutual understanding, engagement and adapted interventions have been associated with improved outcomes.[45-49]

1.7.1 Pharmacologic management:

Once the diagnosis of asthma has been made, treatment decisions can be guided based on cycles of assessment, adjustment and review of the response (Figure 1-2).[1] The Global Initiative for Asthma (GINA) guidelines place an emphasis on the robust evidence behind control-based management options;[50-52] however, other alternatives have been evaluated for treatment adjustment in severe or non-conventional cases.[53, 54]

The pharmacologic options for long-term asthma treatment include:

- Controller medications (ICS, ICS/LABA): targeting the reduction of airway inflammation, the control of asthma symptoms and the reduction of future risks (e.g., exacerbations and decline in lung function);
- Reliever medications (e.g., SABA, short-acting anticholinergics [SAAC], LABA): targeting the relief of breakthrough symptoms during worsening or exacerbations. Also used for short-term prevention of exercise-induced bronchoconstriction.

- Add-on therapies (e.g., LTRA, anti-IgE, anti-IL5 agents): targeting the control of persistent asthma symptoms in patients with severe asthma who have optimal management (e.g., treatment with high-dose controller medications and control of modifiable environmental factors).

Figure 1-1 summarizes the general recommendations for asthma management from the 2012 update of the Canadian Respiratory Guidelines.[55]

The GINA adapted these recommendations into a step-based approach (Figure 1-2).[1] This step-based approach recommends early treatment with ICS (low dose) and SABA (as-needed) based on its positive impact on the reduction of asthma-related exacerbations, hospitalizations and death (STEPS 1 & 2).[56-59] For patients with persistent symptoms despite proper pharmacologic and non-pharmacologic management, the preferred step-up treatment is ICS/LABA (STEPS 3 & 4).[51, 60-63] STEP 5 recommendations involve referral to a specialist and add-on treatment (e.g., tiotropium, anti-IgE and oral corticosteroids [OCS]).[64-66]

The introduction of add-on treatments could be considered as early as STEP 2 or as late as STEP 5 based on particular considerations (e.g., ICS intolerance, persistent symptoms despite good adherence and proper inhaler techniques).[67-69]

Important considerations:

- At each treatment step, patient characteristics (e.g., response, restrictions), the clinical context (e.g., costs and available resources) and potential impact on outcomes should be considered.[70, 71]
- Regular medical monitoring offers the opportunity of making adjustments or changes to medication. The frequency of visits depends on individual factors such as the initial level of asthma control, treatment response and level of engagement in self-management. Patients should be seen one to three months after starting treatment and every three to twelve months thereafter.
- Before considering any step-up in treatment, a careful examination of non-pharmacologic factors such as incorrect diagnosis, inhaler techniques, adherence, exposure to asthma triggers and comorbidities should be completed. Sustained step-up (2-3 months) may be considered for those patients who fail to respond adequately to initial treatment. Short-term step-up (1-2 weeks) may be necessary during viral infections or seasonal allergen exposure. Day to day adjustments depends on the prescribed medication and on the control of symptoms.[1]
- Step-down should be individualized and only considered after achieving/maintaining good asthma control for about

three to four months. Patient should be on their minimum effective treatment (e.g., the one that favours good control of symptoms and exacerbations at the minimum cost and risk for potential side-effects).[1]

- Non-pharmacologic strategies aiming an improvement in asthma self-management (e.g., inhaler skills training, provision of written asthma action plans [AAPs], regular medical review) help encouraging medication adherence among other risk reduction-related benefits.[1]

1.7.2 Non-pharmacologic management:

Identifying and treating modifiable risk factors is as important as optimizing asthma medications for achieving the long-term goals of asthma management. The GINA guidelines recommend the following non-pharmacologic interventions in adults with asthma:[1]

Smoking cessation: Providing access to counselling and smoking cessation programs at every encounter with a health provider.

Promotion of physical activity: Encouraging patients with asthma to engage in regular physical activity and providing advice about prevention and management of exercise-induced bronchoconstriction.

Avoidance of agents that act as asthma triggers: Identifying and eliminating potential sensitizers (e.g., Non-steroidal anti-inflammatory drugs [NSAIDS], allergens and occupational exposures).

Promotion of healthy diet: Encouraging patients with asthma to consume a diet high in fruit and vegetables for its general health benefits.

Other interventions such as breathing exercises, weight reduction, immunizations, avoidance of indoor/outdoor pollutants and food chemicals are also recommended. Finally, current indications for referrals to specialist are considered in complex cases (e.g., difficult diagnoses, persistent uncontrolled asthma, any risk-factors for asthma-related death, suspected occupational asthma, side-effects).

Patient education is the most common non-pharmacologic intervention the current asthma guidelines support and encourage.[1] An important clarification in the current guidelines is that the provision of asthma education may be influenced by several factors (e.g., skills and training of both the provider and the learner). The provision of limited patient education (transfer of information about asthma, its causes and treatment) has shown no significant impact on the reduction of hospitalizations for asthma, emergency department (ED) visits, doctors visits, lung function and medication use.[72]

Asthma self-management is a type of asthma education that involves a collaborative partnership between the education provider and the patient and its essential components are:

- Skills training for the effective use of inhaler devices: Poor inhaler techniques are common among adults with asthma[73] and have been associated with poor asthma control,[74]

increased exacerbations and adverse effects. Standardized educational interventions provided by nurses and pharmacists have demonstrated to be highly effective in the reduction of undesired outcomes.[75, 76]

- Encouraging adherence with medications, appointments and other advice, within an agreed management strategy: Poor adherence to asthma management is a common care gap among adults with asthma.[77] The current guidelines emphasize the importance of understanding factors associated with patient behavior (e.g., low health literacy)[78] and the assistance that allied health professionals such as trained asthma educators, nurses/respiratory therapists, and pharmacists can provide in the delivery of targeted educational strategies.[79]
- Provision of asthma information (personalized education).
- Training in guided self-management with:

✓ Self-monitoring of symptoms or PEF: patients trained to keep track of their symptoms and/or their PEF benefit from taking action early and when necessary.[80]

✓ Provision or written AAPs: individualized written recommendations help patients identify 1) triggers to increase therapy (based on symptoms or PEF readings), 2) strategies to

increase therapy (including duration), and 3) the tipping point to seek additional medical help.[81]

- ✓ Regular review by a health care provider: Follow-up consultation taking place at regular intervals provide health practitioners with an opportunity to assess asthma control and management issues;[82] they also allow patients to raise questions and express concerns.

The effectiveness of different components of self-management educational interventions has been evaluated in a rigorous way. A systematic review (SR) that included 36 RCTs of self-management education for adults[83] found a significant reduction in hospitalizations (Relative Risk [RR] = 0.64; 95% Confidence Interval [CI]: 0.50 to 0.82), ED visits (RR = 0.82; 95% CI: 0.73 to 0.94), unscheduled doctor visits (RR = 0.68; 95% CI: 0.56 to 0.81), work/school absenteeism (RR = 0.79; 95% CI: 0.67 to 0.93), and nocturnal asthma symptoms (RR = 0.67; 95% CI: 0.56 to 0.79). While there was significant statistical heterogeneity (I^2=85%), there was a considerable improvement in health related quality of life (HRQoL) for those receiving the self-management interventions (standard mean difference [SMD] = 0.29; 95% CI: 0.11 to 0.47). If a written AAP was added to this program there was an even greater reduction in hospitalization (RR = 0.58; 95% CI: 0.43, 0.77).

1.8 Asthma exacerbations

1.8.1 Definition:

Asthma exacerbations are episodes characterized by a progressive increase in asthma symptoms and decrease in lung function.[84] Despite improved understanding of their treatment and prevention of asthma, exacerbations continue to result in visits to health professionals, school and work absenteeism, ED visits, hospitalizations and significant costs to the health care system throughout the developed world. The diagnosis of asthma exacerbations usually relies on compatible history and physical examination; objective measures of the severity of the exacerbation (e.g., decreased PEF or FEV_1 based on the patients' usual status) should be obtained when possible. Severe exacerbations are potentially life threatening, thus factors that increase the risk of asthma-related death should be identified and evidence-based care promptly provided.

Patients with asthma should be able to recognize and respond to their exacerbations if adequate guidance on asthma self-management has been provided (e.g., a written AAP appropriate for their level of asthma control and health literacy has been developed).

1.8.2 Management:

1.8.2.1 Management of asthma exacerbations in primary care:

The primary care setting can contribute to the management of asthma exacerbations by assessing the patients' severity, adjusting their

medication (e.g., increasing SABA/SAAC, stepping up the dose of existing controller medication and starting patients on systemic corticosteroids) and referring them to an acute care facility if needed. Before patients go home, a follow-up appointment is recommended within the next week (Figure 1-3).[85]

1.8.2.2 Management of asthma exacerbations in EDs:

Emergency departments (or equivalent acute care facilities) are the ideal settings to manage mild/moderate exacerbations that don't improve with the initial management provided in the primary care setting or at home, as well as, severe and/or potentially life-threatening exacerbations (Figure 1-3). A brief medical history, physical examination and objective measure of lung function (e.g., PEF or if possible full spirometry) should precede the prompt initiation of therapy (Figure 1-4). Patients' clinical condition and response to treatment should be re-assessed regularly during their ED stay. Current guidelines recommend lung function to be measured one hour after initial bronchodilator/corticosteroid treatment in order to document improvement or deterioration. Ordering additional tests (e.g., chest radiographs) is not routinely recommended in adults, unless other diagnoses need to be ruled out.[86]

1.8.2.2.1 Treatment in EDs:

The goals of treatment in acute care settings are to control symptoms and to stabilize patient conditions.

Oxygen: Significant hypoxemia is common in moderate to severe exacerbations and therapy should target physiological levels of oxygen. Oxygen saturation above 92% is not recommended; hyperoxia should be avoided in patients with asthma exacerbations due to its association with increased oxidative stress and free radical damage.[87] Oxygen therapy either by nasal cannulae or mask is recommended to all patients whose saturation is below this parameter (using oximetry when possible).[88]

Inhaled SABA: Inhaled SABA therapy should administered as early as possible to all patients presenting to the ED with asthma exacerbations in an attempt to reverse airflow obstruction. Nebulizer delivery products have not been associated with significantly better outcomes than metered-dose inhalers delivered by spacer.[89]

Systemic corticosteroids: Systemic corticosteroids (either oral or intravenous [IV]) speed the resolution of exacerbations, prevent admission and relapses, and are recommended to all but the mildest cases of acute asthma.[90] Systemic corticosteroids should be administered within the first hour of presentation when possible. Fifty (50) mg of prednisone or 200 mg of hydrocortisone for 5-7 days have shown to be effective in the resolution of exacerbations.[91, 92] No benefit has been associated with tapering the dose of OCS in the short-medium term;[93] in adults, very short courses have not replaced standard 7-10 day therapy.

Inhaled Corticosteroids: Although ICS agents are thought to improve asthma control over days to weeks; there is evidence that they

are effective in the acute setting. The administration of high doses of ICS within the first hour of ED presentation reduces the need for hospitalization in those patients receiving and not receiving systemic corticosteroids.[94] These observations are likely the result of local vasodilatation, membrane stabilization and inhibition of the inflammatory cascade.

Other treatments:

Short-acting anticholinergics: Anticholinergic agents are designated as weak bronchodilators and mucolytic agents. The combined use of SAAC/SABA has been associated with synergistic effects, especially in severe disease; fewer hospitalizations and greater improvement in lung function, specifically PEF and FEV_1 when compared to SABA administration alone.[95]

Aminophylline/theophylline: Methyl-xanthine agents are weak bronchodilators and respiratory muscle enhancers through their influence on cyclic adenosine monophosphate (cAMP). The IV administration of aminophylline is not routinely recommended in the ED management of asthma exacerbations due to non-additional bronchodilation effect and increased risk of adverse events when compared to standard inhaled bronchodilators and steroids.[96]

Magnesium sulphate ($MgSO_4$**):** Magnesium sulphate exhibits its effect on smooth muscles, including those in the respiratory system, and also is a weak anti-inflammatory agent. Administered intravenously (2 g infusion over 20 min), $MgSO_4$ is recommended in adults presenting with

severe exacerbations who have exhibited blunted response to inhaled bronchodilation therapy (e.g., initial FEV_1 <25-30% predicted, those who fail to respond to initial treatment and have persistent hypoxemia).[97, 98] This agent must be used in combination of systemic corticosteroids and bronchodilators and has a wide margin of safety.

Epinephrine: Epinephrine, a mixed α- and β-receptor agent, is most often used in allergic reactions, such as anaphylaxis. The intramuscular (IM) administration of this agent (adrenaline) is not routinely recommended in the ED management of asthma exacerbations; it is only indicated in acute asthma cases associated with anaphylaxis and allergic angioedema.

Leukotriene receptor antagonists: While these novel and important add-on therapeutic options are commonly recommended and used in chronic asthma, their administration is not routinely recommended in the ED management of asthma exacerbations.[99, 100]

Inhaled Corticosteroids/long-acting β_2-agonist combination agents: The administration of these agents is not routinely recommended in the ED management of asthma exacerbations.[101, 102]

Antibiotics: Despite the fact that most acute asthma episodes result from exposure to triggers such as upper respiratory infections from viral infections, antibiotics are commonly administered to patients who wheeze, in an attempt to treat any infection (or super-infection). The administration of these agents is only recommended for asthma

exacerbations in which there is strong evidence of lung infection or who have failed to respond to an initial trial of aggressive anti-inflammatory agents.

Sedatives: The use of sedatives should be strictly avoided due to their association with undesired outcomes including death.[103]

Non-invasive ventilation (NIV): The use of NIV for acute asthma is not supported by strong evidence.[104] For example, only one randomized controlled trial (RCT) exists, and while positive, the evidence is insufficient for most guidelines to recommend its use in all but the most extreme cases. Nonetheless, given its use in exacerbations for heart failure and COPD in the ED, familiarity and a willingness to avoid intubations in these patients, a trial may be considered. It should be avoided in agitated patients and concomitant sedation should not be attempted.

Heliox: The administration of heliox (helium/oxygen mixture in a ratio of 80:20 or 70:30) is not recommended for the routine ED care of adult asthma. It has been suggested as an alternative for patients not responding to standard therapy.[105]

Intravenous (IV) fluids: While many patients with acute asthma have increased insensible losses (e.g., fever, hyperventilation, nausea/vomiting) and decreased fluid intake, most patients are not clinically dehydrated. The administration of IV fluids is therefore not recommended in the ED management of all asthma exacerbations; some patients may need rehydration and correction of electrolyte imbalance.

1.8.2.2.2 Disposition:

Most patients with acute asthma respond to therapy and can be safely discharged from the ED with follow-up after several hours of therapy. Patients' clinical condition and lung function one hour after commencement of therapy have shown to predict the need for hospital admissions.[106, 107] Sociodemographic factors (e.g., female sex, older age and non-white race), asthma history (e.g., previous severe exacerbations), medication factors (e.g., previous use of OCS) and severity at presentation have also been associated with an increased likelihood of hospitalizations.[108, 109]

1.8.2.2.3 Post–ED management:

Management of asthma in the hospital is beyond the scope of this thesis project so emphasis is made on the evidence behind current discharge planning.

1.8.2.2.3.1 Medical management at ED discharge:

- **Systemic corticosteroids:** Systemic corticosteroids (oral or IM) use in the outpatient treatment of exacerbations has been associated with a reduction in relapses and the need for reassessment in the subsequent 7-10 days.[90] Since most patients have little to no interest in IM administration of these agents, short courses of corticosteroids are preferred. Ultra-short doses of agents such as dexamethasone, while used in

children,[110] have not proven to be effective in adults and should be avoided.

- **Inhaled Corticosteroids:** Inhaled corticosteroids are widely recommended as first line agents for mild-to moderate stable asthma.[111] The addition of ICS agents to OCS has been associated with a significant reduction in relapses, improvement in HRQoL, and reduction in SABA use, without significant adverse events.[112] Given that patients who have an exacerbation of asthma have demonstrated a failure of current management, the addition of ICS agents after an ED visit makes intuitive and guideline-recommended sense. The overall evidence in this field is based on three trials of variable quality and the pooled evidence fails to reach statistical significance (RR= 0.68; 0.46, 1.02); however, it is difficult to ignore a 25% reduction in relapse with a potential of up to a 50% decrease in relapses compared to a possible 2% increase in relapses. Overall, these agents are well tolerated and safe.[113]
- **Inhaled Corticosteroids/LABA combination agents:** Asthma guidelines in adults suggest a step-up to ICS/LABA agents in chronic stable asthma if the use of regular moderate dose ICS agents fails to achieve control. The addition of ICS/LABA agents after an ED discharge for acute

asthma has been studied infrequently. There is weak evidence to suggest that patients who experience an exacerbation while already receiving ICS may experience improved HRQoL and potentially less frequent relapses if ICS/LABA agents are combined with OCS at discharge.[102] Finally, patients already receiving these agents at ED presentation should not have them discontinued if discharged, since this represents a step-down in treatment.

- **Leukotriene receptor antagonists:** The use of these agents is not routinely recommended in the post-ED management of acute asthma. Patients already receiving these agents at ED presentation should not have them discontinued if discharged, since this represents a step-down in treatment.

1.8.2.2.3.2 Non-medical management at ED discharge:

Emergency department visits due to asthma exacerbations have been recognized as ideal scenarios for the identification of gaps in asthma care.[114, 115] Recent asthma guidelines have added content dedicated to the management of asthma exacerbations and highlighted the essential role of the discharge planning.[1] Follow-up 2-7 days after ED presentations for asthma exacerbations and strategies to promote self-management such as reviewing inhaler techniques, providing written AAPs and instruction on patient self-monitoring following discharge are

recommended.[1, 44, 116] However, no clear evidence supports the timing proposed for this visit and the overall effectiveness of this encounter.

A Cochrane SR examining the impact of ED-based educational strategies vs. standard care showed that re-visits to the ED were not significantly decreased in the group receiving education (RR = 0.72; 95% CI: 0.47 to 1.11); however, hospitalizations were reduced (RR = 0.50; 5% CI: 0.27 to 0.91).[117] A SR completed as part of this thesis revealed that ED-directed educational interventions targeting either patients or providers increase the chance of having office follow-up visits with Primary Care Providers (PCPs) after asthma exacerbations. Their impact on health-related outcomes (e.g., relapse and admissions) remains unclear (refer to Chapter 3 for more details).[118]

Despite these recommendations, many Canadian patients visiting EDs with acute asthma have limited or no access to PCPs[119], even when patients are linked to a PCP, some don't consider this follow-up necessary, and/or their post-ED visit follow-up is considerably delayed.[120] Moreover, some PCPs do not base their recommendations on current asthma guidelines and focus only on the pharmacologic treatments; patients often leave their offices without the revision of their written AAP and therapy adjustment.[121]

1.9 Summary and problem targeted by this thesis project

Asthma is a condition in which considerable change in practice has occurred over the last two decades (e.g., the pathophysiology is better

understood, evidence-based management has been clarified and promoted). Taking into account that a substantial proportion of adult patients presenting to EDs with acute asthma do relapse within two weeks of being discharged (even when receiving evidence-based treatment) and that PCP follow-up visits have shown to be delayed, the coordination of effective transitions in care between the ED and the primary care setting was identified as a critical area needing improvement and action. This program of research compared the effectiveness of ED-directed interventions to improve outcomes after asthma exacerbations; importantly, it engaged patients and PCPs' in the design of novel opinion leader (OL) based interventions for acute asthma directed from the ED, and targeted gaps in care and health-related outcomes relevant for knowledge implementation. Regardless of the results of this research program, patients and clinicians have benefited from the promotion of evidence-based practices; the research community has also benefited from the efforts to facilitate the interpretability, applicability and uptake of the overall conclusions.

1.10 General research (PICO-D) question

Using randomized controlled trial methods (**D**esign), in adult patients with acute asthma discharged from the ED (**P**opulation), will OL or care manager -based interventions directed from the ED (**I**ntervention) reduce relapses and improve outcomes (**O**utcomes) compared to usual care (**C**ontrol)?

1.11 Objectives

1) To examine the evidence of effectiveness of ED-directed educational interventions to improve PCP follow-up visits after asthma exacerbations;

2) To determine the ideal OL -based interventions directed from the ED to test in an experimental study by engaging patients and PCPs;

3) To determine if tailored OL or CM -based interventions directed from the ED (personalized recommendations for follow-up care/treatment options and self-management education), reduce relapses within 90 days for acute asthma (primary outcome) when compared to usual care.

Table 1-1 Factors influencing the expression of asthma.

Type	Factors
Host	Genetic Sex Obesity Physical activity Emotional stress
Environmental	Allergens (e.g., dust, mold, pollen, mice, cockroaches) Tobacco smoke (active or passive exposure) Air pollution (indoor/outdoor) Diet (e.g., sulfite compounds) Infections (predominantly viral) Medications (e.g., non-selective β-blockers, aspirin, non-steroidal anti-inflammatories) Occupational sensitizers (e.g., isocyanates, platinum salts)

Note: Adapted from the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2015.[1] Permission for reproduction has been granted.

Table 1-2 Factors that can assist in the differentiation of Asthma, COPD and ACOS exacerbations.

Factors		Asthma	ACOS	COPD
Pathophysiology	Inflammation	+++	+++	+++
	Infection		+/-	+++
Age of onset	Early	+++		
	Late (age > 40)		+++	+++
Sex	Female > male	+++		
	Male > female		+++	+++
Family history		+++		
Allergic conditions		+++		
Previous diagnosis of asthma		+++	+/-	
History of cigarette smoke exposure			+/-	+++
Co-morbidities		+/-	+++	+++
Symptoms	Wheeze	+++	+/-	+/-
	Dyspnea	+++	+++	+++
	Cough	+/-	+/-	+++
	Sputum production		+/-	+++
Course	Intermittent exacerbations	+++		
	Chronic progressive		+/-	+++
Response to treatment	Response to bronchodilators	+++	+/-	+/-
	Response to corticosteroids	+++	+/-	+/-
Post-bronchodilator flow measurement	FEV_1/FVC ratio> 0.7	+++		
	FEV_1/FVC ratio< 0.7		+++	+++
Recovery after exacerbation		+++	+/-	+/-

Note: ACOS = asthma/COPD overlap syndrome; COPD = chronic obstructive pulmonary disease; FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second.

Table 1-3 GINA assessment of asthma control in adults, adolescents and children 6-11 years.

<table>
<tr><td>A. Asthma symptom control</td><td colspan="3">Level of symptom asthma control</td></tr>
<tr><td>In the past 4 weeks, has the patient had:</td><td>Well controlled</td><td>Partly controlled</td><td>Uncontrolled</td></tr>
<tr><td>Daytime asthma symptoms* more than twice/week?</td><td rowspan="4">None of these</td><td rowspan="4">1-2 of these</td><td rowspan="4">3-4 of these</td></tr>
<tr><td>Any night walking due to asthma?</td></tr>
<tr><td>Reliever needed for symptoms more than twice/week?</td></tr>
<tr><td>Any activity limitation due to asthma?</td></tr>
<tr><td colspan="4">B. Risk factors for poor asthma outcomes</td></tr>
<tr><td colspan="4">Assess risk factors at diagnosis and periodically, particularly for patients experiencing exacerbations.
Measure FEV_1 at start of treatment, after 3–6 months of controller treatment to record the patient's personal best lung function, then periodically for ongoing risk assessment.</td></tr>
<tr><td colspan="3">Potentially modifiable independent risk factors for flare-ups (exacerbations)
• Uncontrolled asthma symptoms
• High SABA use (with increased mortality if >1 x 200-dose canister/ month)
• Inadequate ICS: not prescribed ICS; poor adherence; incorrect inhaler technique
• Low FEV_1, especially if <60% predicted
• Major psychological or socioeconomic problems
• Exposures: smoking; allergen exposure if sensitized
• Comorbidities: obesity; rhinosinusitis; confirmed food allergy
• Sputum or blood eosinophilia
• Pregnancy
Other major independent risk factors for flare-ups (exacerbations)
• Ever intubated or in intensive care unit for asthma
• >1 Severe exacerbation in the last 12 months</td><td>Having one or more of these risk factors increases the risk of exacerbations even if symptoms are well controlled.</td></tr>
<tr><td colspan="4">Risk factors for developing fixed airflow limitation
• Lack of ICS treatment
• Exposures: tobacco smoke; noxious chemicals; occupational exposures
• Low initial FEV_1; chronic mucus hyper-secretion; sputum or blood eosinophilia</td></tr>
<tr><td colspan="4">Risk factors for medication side-effects</td></tr>
</table>

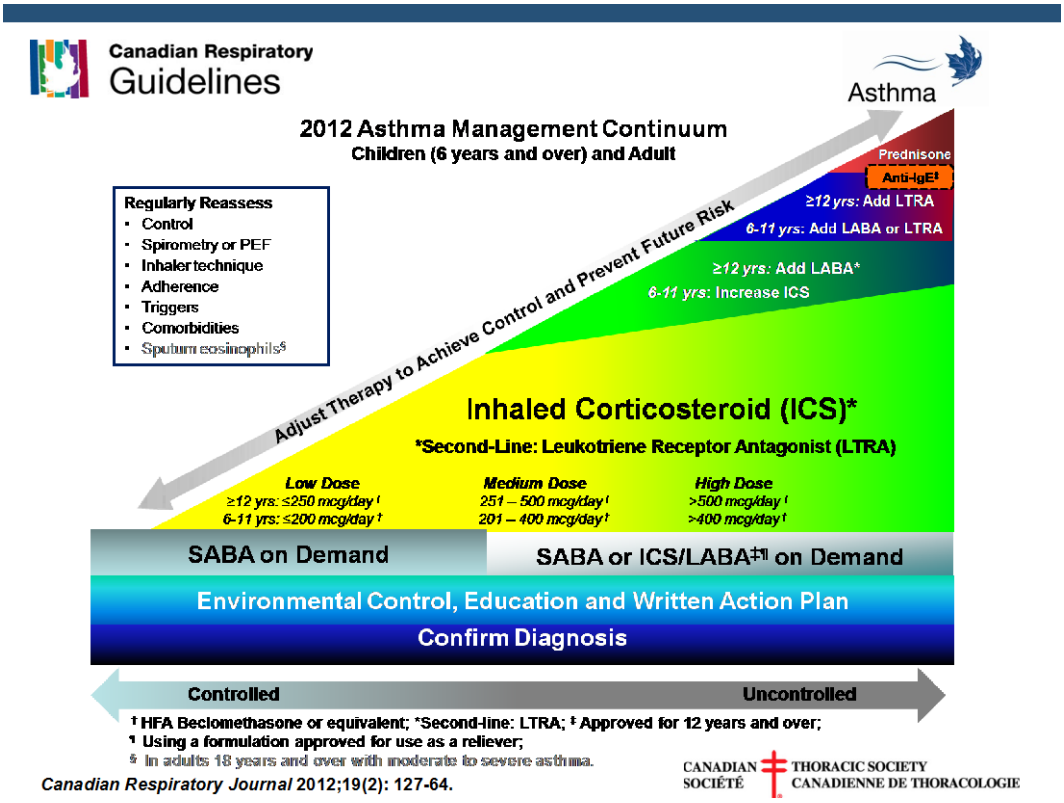
- *Systemic*: frequent OCS; long-term, high dose and/or potent ICS; also taking P450 inhibitors
- *Local*: high-dose or potent ICS; poor inhaler technique

Note: FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroid; OCS: oral corticosteroid; P450 inhibitors: cytochrome P450 inhibitors such as ritonavir, ketoconazole, itraconazole; SABA: short-acting β_2-agonist.

*Excludes reliever taken before exercise.

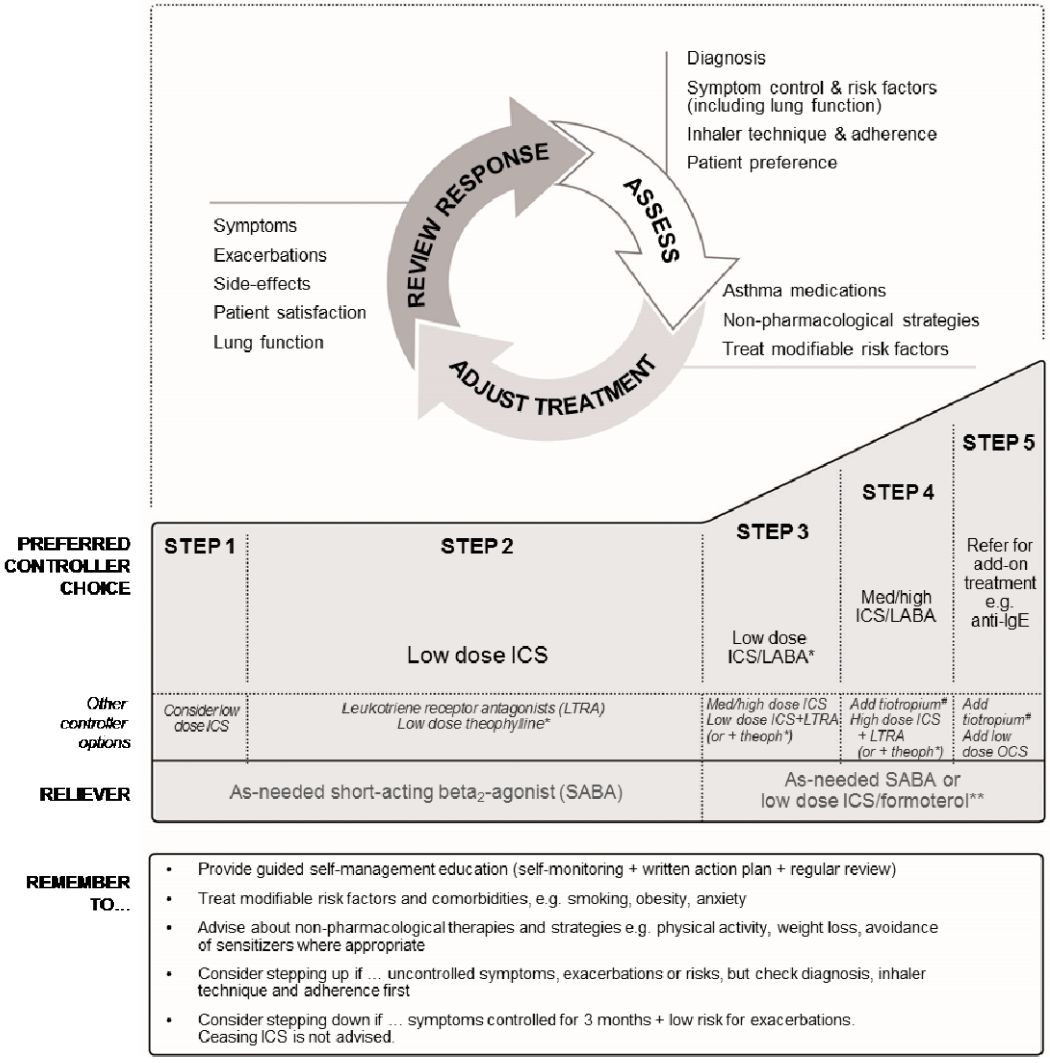
This table was adapted from the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2015.[1] Permission for reproduction has been granted.

Figure 1-1 Asthma management continuum (for children 6 years and over) and adults.



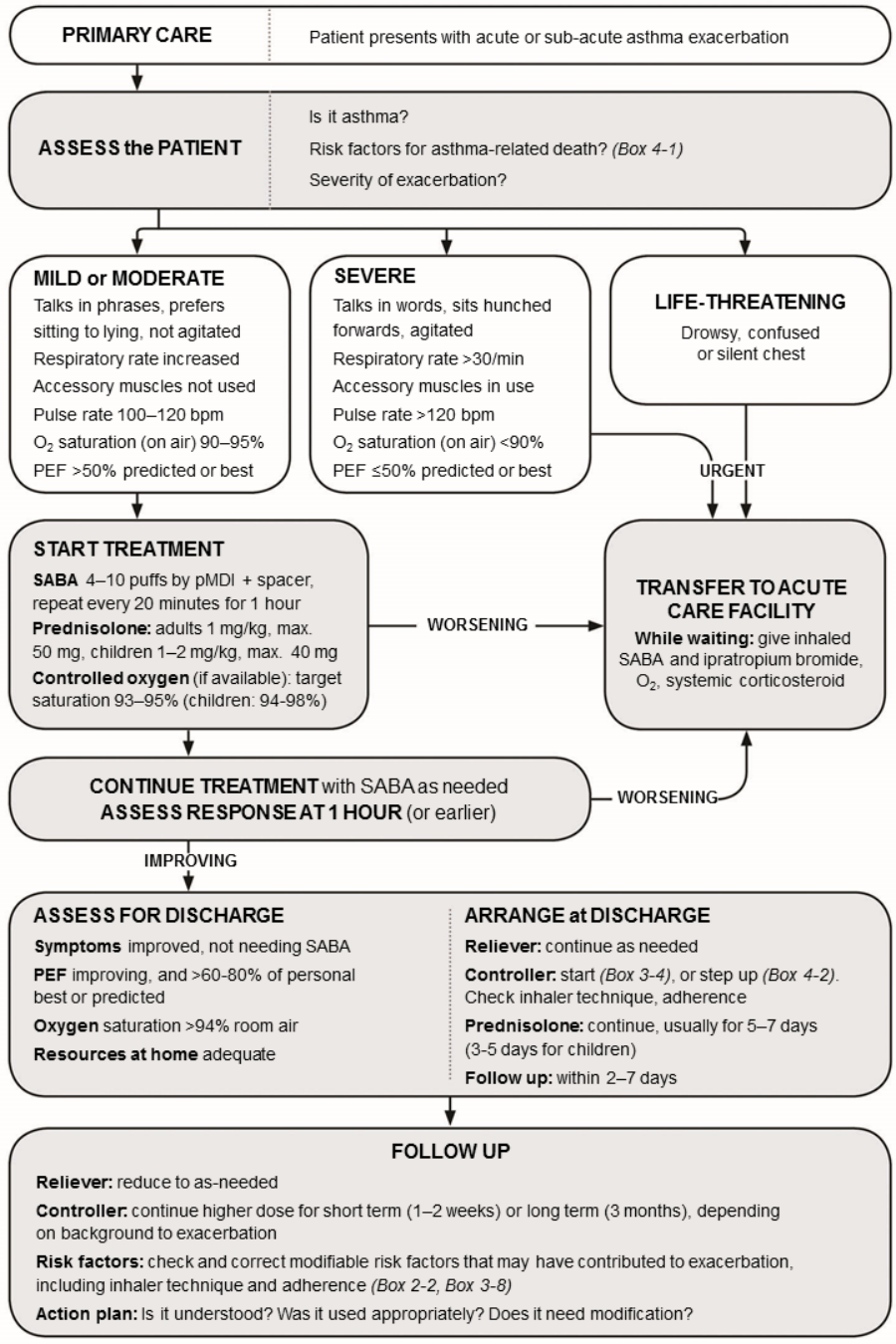
Note: Figure from the Canadian Thoracic Society 2012 guideline update: diagnosis and management of asthma in preschoolers, children and adults.[55] Permission for reproduction has been granted.

Figure 1-2 Stepwise approach to control asthma symptoms and minimize future risk.



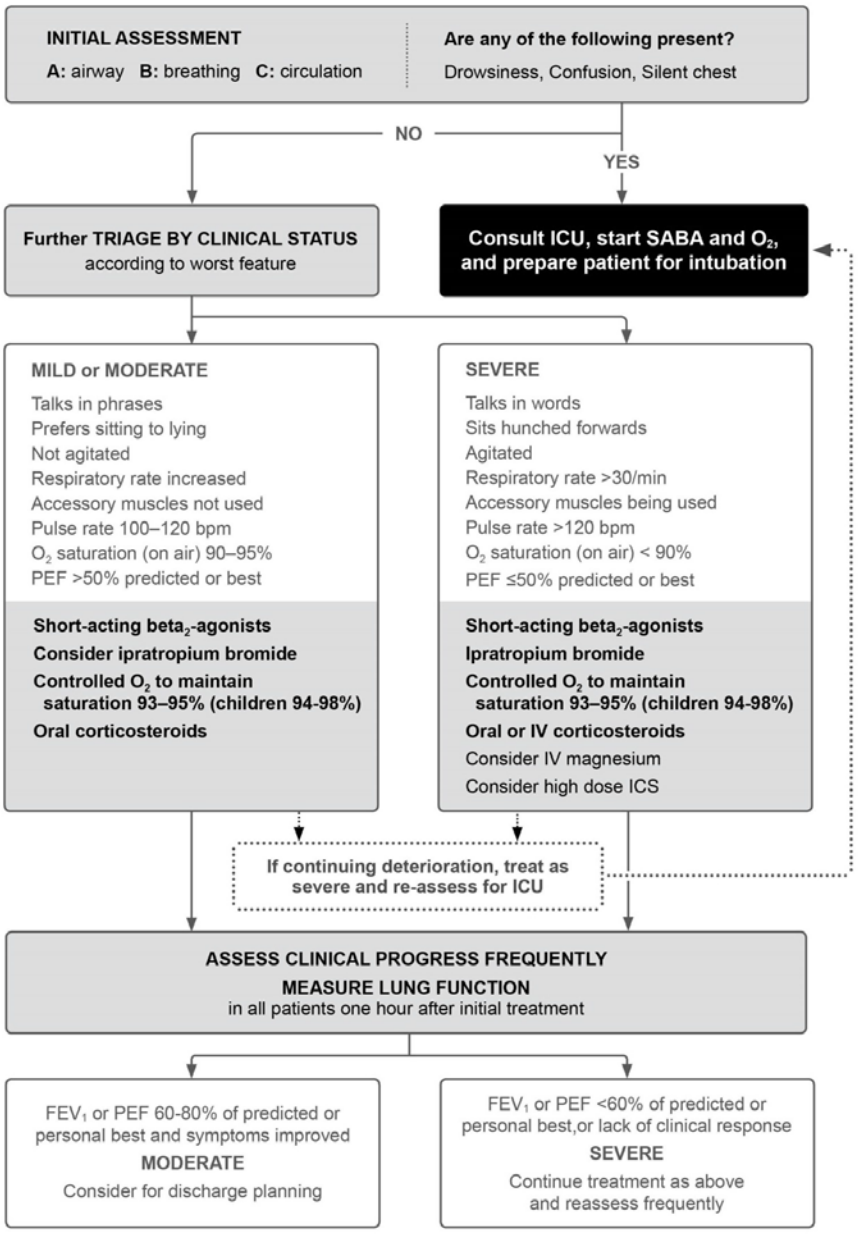
Note: Figure from the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2015.[1] Permission for reproduction has been granted.

Figure 1-3 Management of asthma exacerbations in primary care (adults, adolescents, children 6-11 years).



Note: Figure from the global strategy for asthma management and prevention, global initiative for asthma (GINA) 2015.[1] Permission for reproduction has been granted.

Figure 1-4 Management of asthma in acute care facilities (e.g., emergency departments).



ICS: inhaled corticosteroids; ICU: intensive care unit; IV: intravenous; O_2: oxygen; PEF; peak expiratory flow; FEV_1; forced expiratory volume in 1 second

Note: Figure from the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2015.[1] Permission for reproduction has been granted.

2 USING A KNOWLEDGE TRANSLATION CONCEPTUAL FRAMEWORK TO IMPROVE OUTCOMES AFTER ASTHMA EXACERBATIONS

2.1 Rationale

Despite improved understanding of the pathophysiology of asthma and the promotion of effective management through evidence-based guidelines, asthma control in Canada remains suboptimal and presentations to emergency departments (ED) are still considered high.[6, 122] A gap between evidence and action in asthma care is one of the challenges faced by the current health care systems.[123] The way data from different type of studies are interpreted and implemented in real-world practices may explain some of the discrepancies observed between the outcomes found in research environments and in day-to-day clinical management.[124]

Evolving practices and the wealth of scholarship bring different opportunities and challenges that have the potential to enrich research initiatives and facilitate the uptake of their results through different levels of stakeholder engagement.[125-127] Several strategies have been promoted to facilitate the movement of evidence into action. One of them is the incorporation of knowledge translation (KT) principles into research projects. The Canadian Institutes of Health Research (CIHR) defines KT as “a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically sound application of knowledge to

improve health, provide more effective health services and products and strengthen the health care system".[128] This definition clarifies a common misperception of this term limited to knowledge "dissemination" by giving prominence to the actual "use" of knowledge to improve decision-making. Two approaches to KT are recognized by CIHR: *integrated KT* (focused on the collaborative venture between researchers and knowledge users in the research process [iKT]) and *end-of grant KT* (focused on the dissemination activities once the research has been completed); *KT/implementation science* (focused on the determinants of knowledge use and effectives methods for knowledge uptake) is another approach that has been promoted and funded by this organization.

A number of KT theories suggest that knowledge is not used because there has been a failure to transfer it effectively to the intended users.[129] Other theories don't see this problem as a failure of knowledge dissemination, but as a failure of knowledge production. Proponents and supporters of *Engaged Scholarship*, understanding this concept as a form of collaborative inquiry between academics and practitioners that leverages their different perspectives to generate useful knowledge, advocate for the involvement of potential end users since early stages of research processes.[127, 130-132]

2.2 The Knowledge to Action Cycle

The *Knowledge to Action (KTA) Cycle* is a conceptual framework that was developed by Graham and Straus[133, 134] in an effort to facilitate

the use of research in practice settings (Figure 1). This model was adopted by CIHR for promoting the application of new knowledge derived from research.[135] The *KTA Cycle* illustrates the dynamic and interactive relations that can occur between sequential or simultaneous phases for *knowledge creation* (included in the funnel) and *knowledge* application/action (included in the cycle). While the funnel components can be interpreted in several ways, in the end, they symbolize the scientific filters through which new knowledge should pass in order to determine what is valid and useful.[136] The *knowledge application/action* part of the model, derived from the commonalities among more than 30 planned-action theories,[137, 138] highlights the following key activities and processes that may be needed for knowledge application:

1. Identifying a problem or issue that deserves attention and further search for knowledge or research.
2. Identifying a knowledge-practice gap that needs filling with new knowledge.
3. Adapting new knowledge to the local context or setting in which the knowledge is to be used. Aspects such as the involvement of potential adopters, the identification of potential barriers that may limit knowledge uptake, and the opportunity to tailor intervention strategies are important targets of this phase.

4. Disseminating or transferring new knowledge, which involves the execution of interventions that facilitate the promotion, awareness and implementation of new and ideally, tailored knowledge.
5. Monitoring the use or application of new knowledge. Changes in knowledge can be measured from conceptual (e.g., better understanding or attitudes), instrumental (e.g., changes in behaviour or practices), or strategic (e.g., use of new knowledge for specific purposes) perspectives. Changes in certain indicators (e.g., improved health outcomes) can also be the reflection of knowledge application.
6. Determining the impact of using the new knowledge in order to evaluate if the acquired knowledge influences individual (e.g., patient or health practitioner) and/or system outcomes.
7. Assessing the sustained application of new knowledge. The identification of barriers that may limit knowledge sustainability, and the evaluation of the impact of new knowledge on specific indicators are examples of the activities that could be included in this phase. The completion of this phase should set in motion an iterative feedback loop through the action phases.

2.3 Improving outcomes after asthma exacerbations through the use of a knowledge translation conceptual framework

The activities proposed in the KTA process developed by Graham and Strauss were the basis of the conceptual framework used for this research program (Figure 2).

2.3.1 Knowledge to action cycle followed in this thesis project

2.3.1.1 Identifying the problem and research that might help addressing it:

Despite the dissemination of effective pharmacologic interventions for the prevention of relapses after asthma exacerbations, these outcomes still occur, affect the quality of life of patients with asthma, and represent significant costs to the health care system (refer to Chapter 1 for more details).[139] Follow-up with a primary care provider (PCP) or asthma specialist after ED discharge is strongly recommended; however, this follow-up is often delayed or absent[119, 120] and when it occurs, the encounter may not address important gaps in care or be evidence-based.[121]

Since the first Canadian recommendations for the assessment and treatment of adult asthma were disseminated,[140-142] continuous revisions and updates have been released.[55, 143] While the most recently published asthma guidelines have highlighted non-pharmacologic interventions for the improvement of outcomes after asthma exacerbations (e.g.,

individualized asthma care, patient education and care partnerships), the following elements of high-quality care have not been well described: strategies targeting the sustained implementation of various recommendations, and methods to facilitate the transitions in care between the hospital care (either ED or in-patient) and community-based follow-up with PCPs.[1, 44, 116]

Emergency department visits due to asthma exacerbations are recognized as potential scenarios for the identification of gaps in asthma care and education.[114, 144-146] While a number of trials have been conducted in the ED setting to improve outcomes such as relapses after asthma exacerbations,[117] only a few have included strategies to facilitate the transitions in care between the ED and PCPs.[118] In addition, the proposed interventions have been identified as complex/impractical, costly and have not achieved the desired impact on health-related outcomes.[147]

The hypothesis behind this PhD project was that no follow-up by the PCP or poor PCP management review after an asthma exacerbation increases the risk of relapses. Multiple study designs and mixed-research methods were considered to support the design; evaluation and potential implementation of opinion leader (OL) and care manager (CM)-based interventions directed from the ED to improve outcomes after asthma exacerbations.

2.3.1.2 Identifying a knowledge-practice gap:

A synthesis of the evidence regarding ED-directed educational interventions to increase primary care follow-up after asthma exacerbations was completed: “Effectiveness of educational interventions to increase primary care follow-up for adults seen in the emergency department for acute asthma: a systematic review and meta-analysis”.[118]

Following the Cochrane approach,[148] the evidence was critically appraised to determine its internal and external validity; statistical pooling was performed when possible. A call for standardization in terms of the description and evaluation of intervention fidelity was made (refer to Chapter 3 for more details).

2.3.1.3 Adapting new knowledge to the local context and identifying determinants for implementation:

Patients and potential knowledge end-users (PCPs) were involved at earlier stages of the research process: “ Engaging patients and primary care providers in the design of novel OL-based interventions for acute asthma in the emergency department: a mixed-methods study”.

Perceptions and expectations of patients and PCPs from Edmonton were considered (using survey methods) for the design of ED-directed OL-based interventions in acute asthma.[149] Focus groups were conducted in order to identify potential facilitators and barriers for implementation (refer to Chapter 4 for more details).

2.3.1.4 Implementing interventions:

A prospective, randomized, open label, blinded endpoints ascertainment (PROBE) study to assess relapses within 90 days for acute asthma was completed: “Emergency-Department Directed Interventions to improve outcomes after asthma exacerbations”.

A structured evaluation of asthma care gaps at ED presentation was followed by the conduct of a three-armed trial to compare the effectiveness of tailored OL and CM -based interventions for acute asthma. Determinants of new knowledge implementation (e.g., intervention fidelity) were discussed (refer to Chapter 6 for more details).

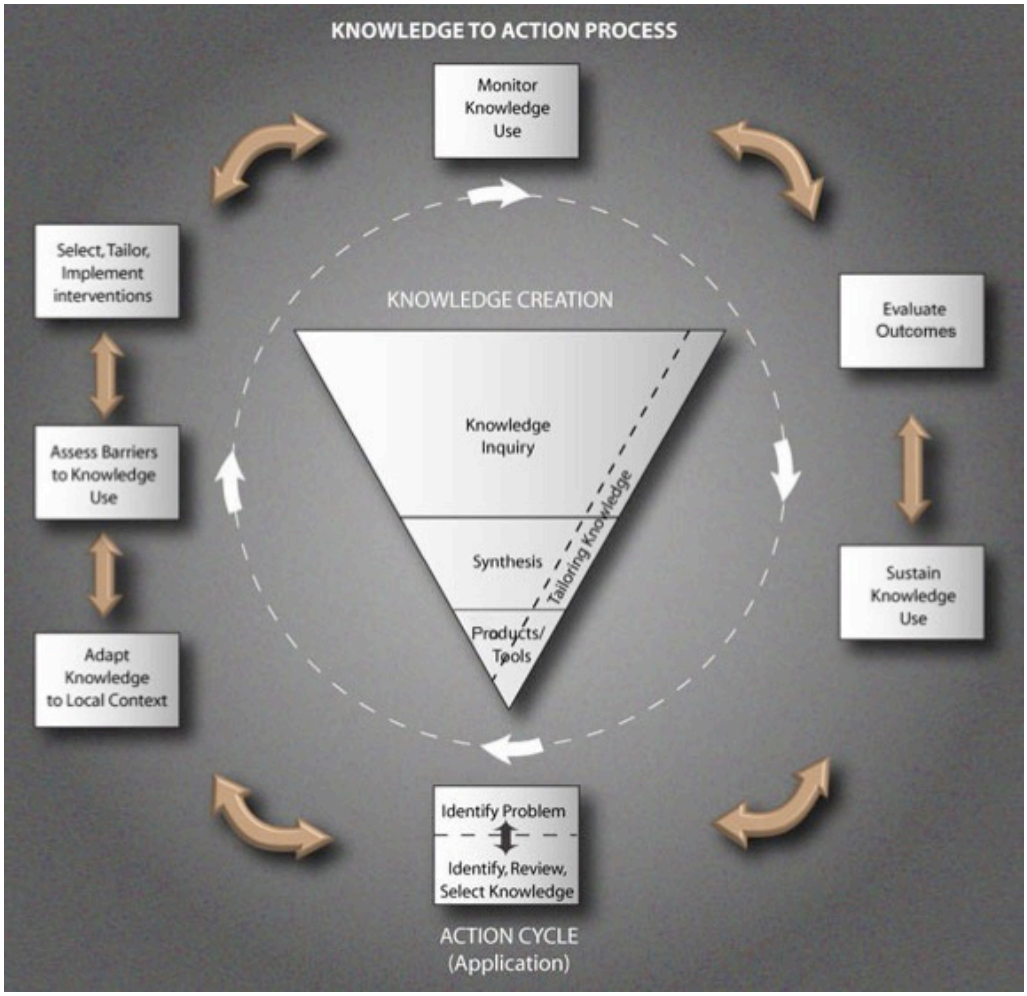
2.3.1.5 Disseminating knowledge:

Parallel to the dynamic activities immersed in the *knowledge application/action* components of the KTA cycle, traditional (e.g., scientific articles, conference presentations) and non-traditional (e.g., blogs, podcasts, social media postings) dissemination methods were used to make the research results available and more useful to stakeholders including patients, health providers and research/clinical networks.

While actions related to the monitoring of the proposed interventions were measured through the evaluation of the primary and secondary outcomes of the PROBE study, the assessment of the sustained use of the new knowledge generated by this research program (step 7 of the action part of the KTA process developed by Graham and

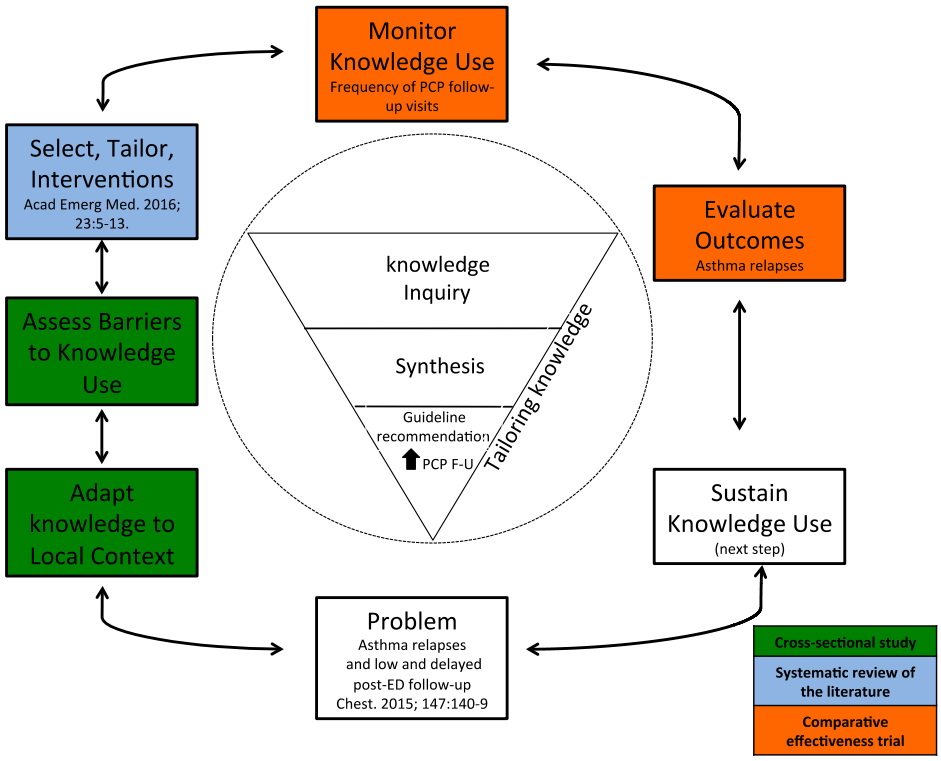
Strauss) was beyond the scope of this thesis project, future directions were given in this regard (refer to Chapter 7 for more details).

Figure 2-1 Knowledge to action cycle.



Note: Figure from the Canadian Institutes of Health Research (CIHR) website.[133, 135] Permission for reproduction has been requested.

Figure 2-2 Knowledge to action framework supporting this thesis project.



Note: Knowledge to action (KTA) cycle adapted from the KTA model proposed by Graham et al.[133]

3 EFFECTIVENESS OF EDUCATIONAL INTERVENTIONS TO INCREASE PRIMARY CARE FOLLOW-UP FOR ADULTS SEEN IN THE EMERGENCY DEPARTMENT FOR ACUTE ASTHMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

3.1 Introduction

Asthma exacerbations are common presentations to emergency departments (EDs), representing a significant burden to patients and their families and generating substantial costs for patients and the health care system.[7, 150, 151] In Canada, the majority of patients who present to the ED with acute asthma are treated and safely discharged.[108] Current asthma guidelines recommend scheduling a follow-up visit with a primary care provider (PCP) soon after ED discharge;[116, 152] however, studies have shown this linkage to be delayed or absent.[120, 153] Moreover, there is variation among guidelines with respect to the timing of this visit, and the evidence to support the effectiveness of the encounter. Guidelines also recommend that patients who have come to the ED with an asthma exacerbation should be targeted for educational interventions; nonetheless, no clear ED-directed strategies promoting return to routine primary care are proposed.

There is controversy regarding EDs being appropriate settings for the delivery of formal asthma education.[147] Despite the well-known challenges of these environments, ED visits have been identified as potential “teachable moments” during which patients are ready to accept

new information.[154] Most patients presenting to the ED with acute asthma have gaps in knowledge and asthma care and often have never received asthma education.[155] Particularly in those with inadequate primary care support, an ED visit may offer a unique opportunity to receive guidance on the chronic nature of their respiratory condition, tools for self-management, and other preventive strategies.[114, 145, 156]

Systematic reviews on educational interventions in adult patients with chronic asthma have identified positive outcomes associated with education components such as information only (limited asthma education)[157] and self-management coupled with regular medical review and written Asthma Action Plans (AAPs).[158] Positive outcomes include reduction in symptoms, hospitalizations, ED visits for asthma, unscheduled doctors' visits, work absenteeism, episodes of nocturnal asthma, indirect costs, and improvement of quality of life. While some of these interventions have been associated with reduction of future hospital admissions and improvement of outpatient follow-up in patients who attend the ED, their fidelity and effect on health-related outcomes, like relapses, are still unclear.[117]

The objective of this review is to assess and describe the evidence from randomized controlled trials (RCTs) on the effectiveness of ED-directed educational interventions to improve office follow-up visits with PCPs in adults who were discharged from the ED after being treated for acute asthma.

3.2 Methods

A study protocol was developed *a priori* to define the objectives, search strategy, eligibility criteria, outcomes of interest, the process for abstracting and synthesizing information from eligible studies, and the methods for data analysis. The systematic review conforms to PRISMA guidelines. No ethics approval was required.

3.2.1 Data sources and searches:

Comprehensive searches of seven electronic databases (Medline, EMBASE, Cochrane Library, CINAHL, SCOPUS, ERIC, and ProQuest Dissertations and Theses Database) were conducted from database inception to June 2014 (updated in June 2016). The search strategy was designed by an information specialist and comprised both controlled vocabulary and keywords adapted to each database (Appendix 1 includes the complete search strategy).

Google Scholar was also searched and references were manually selected from the first ten pages of Google Scholar results. Conference proceedings from 2004-2014 (updated in June 2016) Canadian (CAEP) and US (SAEM) Emergency Medicine conferences were hand-searched. No limits were applied on the basis of date, language or publication status.

3.2.2 Study selection:

Studies were included in the review if they were RCTs assessing any educational intervention directed from the ED targeting adults (or

adults and children with ≥80% of the study population being ≥16 years of age) discharged from the ED after an asthma exacerbation. Educational interventions were permitted to have taken place in any setting (e.g., hospital, community, home) and had to occur within a week of the ED visit. The control was the provision of usual or standard care following the ED presentation. The primary outcome was the percentage of PCP office follow-up visits after an asthma exacerbation. Primary care providers may have included family physicians, general practitioners, general internists and/or nurses. Secondary outcomes included the percentage of subsequent unscheduled visits to the doctor/EDs for asthma care (relapses), admissions, time to first PCP office follow-up visit and time to first relapse.

Two reviewers (*BV* and *TN*) independently screened the titles and abstracts of studies identified by the literature search. The full text of articles deemed relevant and those whose abstracts and titles provided insufficient information were retrieved and independently reviewed (*BV* and *TN*) to determine study eligibility. Disagreements were discussed and resolved with a third party (*CVR*).

3.2.3 Data extraction and quality assessment:

Information on patients, methods, interventions and outcomes was extracted from the original reports onto standardized data collection forms. The detailed data extraction process involved contact with authors to clarify study methods and to obtain non-published original data.

Two reviewers (*BV* and *TN*) independently assessed the internal validity of the studies that met our inclusion criteria using the Risk of bias (RoB) tool. Disagreements were discussed and resolved with a third party (*CVR*).[148]

Fidelity assessment refers to the methodological strategies used to monitor and enhance the reliability and validity of behavioral interventions.[159] In other words, how planned delivery was measured and reported in a trial. Intervention fidelity in individual studies was assessed using the five domains of the Treatment Fidelity Assessment Grid (*CVR*):[160] fidelity to theory (i.e., did the intervention include the relevant "active ingredients" based on theory?); provider training (i.e., were the treatment providers capable of delivering the intervention as designed?; treatment implementation (i.e., did the treatment providers actually implement the intervention as it was designed?); treatment receipt (i.e., did the participant receive the relevant "active ingredients" as intended?) and treatment enactment (i.e., did the participant put new skills or behaviours into practice?).

3.2.4 Data synthesis and analysis:

Abstracted data were entered and analyzed using Review Manager (RevMan) software (IMS Inc, Nordic Cochrane Centre, Copenhagen, Denmark), Version 5.2 and a recognized Cochrane-endorsed EBM Web Site (www.nntonline.net). For studies including more than one intervention arm, a combination of event data was considered for dichotomous

outcomes. Pooled estimates were calculated as risk ratios (RR) with a 95% confidence interval (CI) using a random effects model (anticipating variation in sample sizes and substantial *between-trial* heterogeneity). Statistical heterogeneity was tested using the I^2 statistic with I^2 values of 25, 50, and 75% representing low, moderate, and high degrees of heterogeneity, respectively.[161] Studies were pooled only if they had similar populations, interventions, controls, outcomes and study designs, while still allowing for variation among study protocols. Sub-group analyses were performed based on the time to relapse assessment (three weeks, three and 12 months); sensitivity analyses (random vs. fixed effects were also performed).

3.3 Results

3.3.1 Search results:

Figure 3-1 reflects the study selection process; five articles satisfied the eligibility criteria for the review.[162-166] Fifty-five manuscripts were excluded for the following reasons: not ED based studies (n=22), not primary research (n=8), not RCT study designs (n=6), studies included admitted patients (n=5) or improving linkages with PCPs was not the main purpose of the study interventions (n=4). Ten studies were excluded for "other reasons" (e.g., type of publication and nature of the intervention; Appendix 2).

3.3.2 Study characteristics:

Included studies were conducted in the United States (n=2) and Canada (n=3) and completed between 2001 and 2013. Two studies included a post-ED phone call to the patient to remind or help arrange a follow-up appointment with the PCP at his/her office;[165, 166] two studies provided a short course of oral corticosteroids (Prednisone 50mgs/day for 5 days) and transportation vouchers[164, 165]; two studies faxed letters with tailored recommendations to the patient's PCP office[162, 163] and one study provided AAP at ED discharge.[163] All studies evaluated the effectiveness of educational interventions compared to usual care. Usual care mostly involved discharge instructions and medication prescription at the discretion of the treating emergency physician; however, two studies had the provision of printed educational material about asthma, medication use and compliance as standard care.[162, 163] For more details see Table 3-1.

3.3.3 Quality assessment:

The overall risk of bias of all five included studies was rated as "unclear". Sequence generation and allocation concealment were judged to be at *low* risk of bias in all but one of the included studies.[166] This study reported the randomization of weeks following a "time-series method"; however, no details were provided with regards to the methods used to generate this allocation sequence or to prevent this sequence from being predicted in advance of enrolment. Four studies reported having outcome assessors blinded to the study interventions[162-165] and two were free of

incomplete reporting of outcome data.[164, 165] All studies were judged to be at *unclear* risk of bias for selective outcome reporting due to the lack of registered protocols or full-text publication. Finally, one study reported data to be analyzed on an "intention-to-treat' basis; however; it was unclear how missing information and drop outs were handled in the analyses.[166] The principal investigator of two studies provided details on study methods and original data;[162, 163] the RoB assessment of these studies was based on the information provided by the study author and the available publications (abstracts). Please see Figure 3-2.

3.3.4 Fidelity of the interventions:

None of the trials reported that the study intervention included "active ingredients" based on *theory*. While all studies reported who delivered the interventions (*providers*), the description of their skills and training protocols varied. *Treatment implementation* was described in all the included studies and the provision of standard delivery materials was the most common method to ensure that providers actually implemented the intervention as designed. *Treatment receipt* (methods to ensure that participants received the "active ingredients" as intended) was not reported in any of the included studies. Finally, steps taken to ensure/assess *treatment enactment* (participants put new skills or behaviours in practice) were not described (Table 3-2).

3.3.5 Primary outcome:

All the included studies (n=825 participants) reported the percentage of PCP office follow-up visits after an asthma exacerbation. Emergency department-directed educational interventions significantly increased the proportion of office follow-up visits after ED discharge for acute asthma (RR = 1.6; 95% CI: 1.31, 1.87); there was no statistical heterogeneity for this outcome (I^2 = 0%; Figure 3-3). The median time to outcome assessment was four weeks from the index ED presentation (interquartile range [IQR]: 4, 6). Based on an absolute increased risk of 0.19 (95% CI: 0.11, 0.26), the number needed to treat (NNT) for benefit was 6 (95% CI: 4, 11).

3.3.6 Secondary outcomes:

All the included studies reported the percentage of relapses. There was no statistically significant difference in the proportion of relapses between ED-directed educational interventions and usual care (RR = 1.3; 95% CI: 0.82, 1.98); statistical heterogeneity for this outcome was low (I^2 = 23%; Figure 3-4). The median time to outcome assessment was three months from the index ED presentation (IQR: 1, 3). Time to first PCP office follow-up visit and relapse was not consistently reported among the included studies. Non-published data from one of the studies revealed that the median time for a first PCP office follow-up visit was 18 days (IQR: 11, 45) in the educational intervention arm compared to a median time of 16 days (IQR: 3, 52) in the usual care arm. This study also found that the

median time to first relapse in the educational group was 45 days (IQR: 4, 65) compared to 28 days (IQR: 12, 45) in the usual care arm.[162] Three studies reported the percentage of admissions, assessed at two, three and 12 months, respectively.[162-164] No statistically significant difference in hospital admissions was observed between the groups that received ED-directed education interventions compared to usual care (RR =0.51; 95% CI: 0.24, 1.06); there was no statistical heterogeneity for this outcome (I^2=0%; Figure 3-5).

Self-management and quality-of-life metrics were poorly reported in the included studies. One study reported a higher proportion of patients having written AAPs (46% vs. 25%, p=0.02) and higher quality-of-life scores (5.7± 1.2 vs. 5.0± 1.3, p=0.01) in the educational intervention arm at the six-month follow-up; however these differences disappeared at 12 months.[166] Most of the studies reported no difference in medication compliance between their comparison groups (data not available).[162-166]

3.3.7 Subgroup and sensitivity analyses:

Sub-group analyses based on time to relapse (i.e., three weeks, three and 12 months) did not show a specific change in the direction of the effect or significant changes in the magnitude and precision of the pooled estimates. The results of the analyses using a fixed effects model were very similar (RR = 1.56; 95% CI: 1.31, 1.86).

3.4 Discussion

This systematic review revealed that ED-directed educational interventions targeting either adult asthma patients or their PCPs led to a greater likelihood of having follow-up with a clinician after ED discharge for an acute exacerbation. Approximately six patients would need to receive ED-directed education after being discharged in order to generate one office follow-up visit with a PCP. This conclusion arises from five RCTs involving 825 participants and usually measuring this outcome four weeks after the index ED presentation. These results add value to previous findings;[117] they clarify the benefit of ED-directed educational interventions on a specific subgroup of the asthma population.[167] They also point out, however, that early PCP visits don't necessarily impact patient-oriented outcomes. The contribution of having an effective ED-PCP linkage to improve the continuum of asthma care stills need to be clarified.[168]

The review failed to identify a significant reduction in the proportion of relapses after the index ED presentation resulting from educational interventions. Similarly to previous reviews, statistical imprecision and unclear RoB of the individual studies precluded a meaningful interpretation of their pooled estimate.[117] Differences in the direction of the effect could be explained by the specific population targeted in this review (only those asthmatics who were discharged from the ED); however, the lack of a significant reduction on relapses in this and a previous systematic review[117] may be interpreted in several ways. First, the low frequency of

events and the small samples in individual studies highlight the need of more research in this area. Second, increased proportions of both PCP office follow-up visits and relapses in those who attend the ED and are discharged may be related to issues outside the hospital (e.g., problems filling prescriptions and difficulties accessing counseling or educational programs). These post-ED issues may play an important role in specific subgroups of patients such as those with low income, minority groups, documented non-compliance and poor access to health care.[145] Third, different levels of interventions during these post-ED PCP office follow-up visits could be influencing these results; as it has been shown for medication adjustment,[169] the provision or revision of written AAPs, counseling on adequate inhaler techniques, smoking cessation, influenza vaccination and referral to asthma education could have a positive impact on such asthma-related outcomes. The difference between being seen by a PCP vs. being seen by a PCP with special interest and training in asthma education after and ED visit has not been formally assessed; however, skills and resources available to patients at the time of follow-up (e.g., development of a written AAP appropriate for their level of asthma control and health literacy) may influence the effectiveness of the educational interventions on health outcomes.[78] Finally, similarly to previous reviews, educational interventions were associated with a reduction in hospital admissions.[117] While the imprecision and lack of statistical significance in our review may be related to the low frequency of

these events and the small study samples; a 50% reduction in the proportion of hospital admissions (with a potential reduction of 76% and a 6% increase) is a clinically important finding that could be clarified with the addition of a small number of studies.

Similarities in the components of the educational interventions across the included studies may explain the low statistical heterogeneity observed for the two outcomes evaluated in the meta-analysis; co-interventions such as the provision of a short course of oral corticosteroids, transportation vouchers and letters faxed to the patient's PCP office were delivered in more than one study. The assessment of intervention fidelity confirmed that description of the objectives, methods and content of educational interventions targeting adults with asthma are quite variable.[170] The most common fidelity factors lacking in the included studies were a clear theoretical foundation and the use of measures of participants' acquisition of knowledge (e.g., better understanding) and implementation of new behaviors (e.g., development of new skills and change in practices).

Despite the positive impact on health-related outcomes, educational interventions in asthma have been strongly criticized due to difficulties in replication and limited applicability in busy and overcrowded environments like EDs.[171] Some of the factors that may limit the external validity of ED-directed educational trials are the absence of primary care coverage in many settings, the lack of asthma education training and/or dedicated time

to provide education among emergency physicians and PCPs; insufficient evidence on the cost-effectiveness of the assistance that health professional liaisons such as trained asthma educators, nurses, respiratory therapists and pharmacists are currently providing in transitions in care between the ED and the primary care setting[75, 76] can also explain the delay in incorporating evidence into practice.[123] While progress has been made on identifying what works and what does not work in adult asthma education,[117, 157, 158, 172-174] a call to standardize the description and evaluation of proposed interventions still needs to be made.[159, 170] Similarly to what exists for other study designs,[175] research on predictors of effectiveness such as intervention fidelity, can help researchers reach more robust conclusions on the information that should consistently be measured and reported. The overall goal of enhancing the fidelity and integrity of these interventions can be supported by demonstrating that changes in effect sizes are attributable to one or more independent variables (fidelity domains). Finally, the cost-effectiveness of educational interventions in asthma such as the ones included in this review is unknown. High costs and inadequate implementation fidelity have been proposed as important barriers to the dissemination of innovative and effective programs in other settings.[176]

3.4.1 Limitations

The strengths of this systematic review pertain to its rigor in searching the literature, the criteria-based selection of studies, the

approach to assessing study validity and implementation fidelity assessment, and the evidence-based inferences. The review has several limitations that should be noted. First, study inclusion was restricted to RCTs based on our interest in summarizing the highest quality evidence to provide support to current guideline recommendations. Six studies identified by our searches were excluded due to non-experimental (n=3)[177-179], before/after (n=2)[180, 181] and pilot (n=1)[182] designs. While some of these studies showed a positive effect on indicators such as asthma control, asthma knowledge, medication use, health-resources utilization and found relatively good acceptability among patients and ED staff, they consistently highlighted the need for evaluations of repeated-measures in a randomized trials before this evidence can be implemented in clinical practice. Second, due to the small number of studies for each comparison, we were unable to formally assess the potential for publication bias. Nonetheless, a comprehensive search of the published and grey literature was conducted without restrictions on publication status or language of publication. Consequently, the risk of publication bias should be low. There is also the possibility of study selection bias. To address this, at least two independent reviewers identified potentially relevant studies and the authors are confident that the studies that were excluded were done so for consistent and appropriate reasons.

There are other limitations in this review that are inherent to the characteristics of the individual studies. First, while statistically robust,

meta-analysis results are derived from studies rated as *unclear* in the RoB assessment (only moderate quality evidence). Second, inconsistent and incomplete outcome reporting precluded the statistical pooling of other outcomes such as time to first PCP office follow-up visit, time to first relapse, self-efficacy and self-management metrics. Third, despite similarities in the components of education interventions across the studies, variation in the reporting of their characteristics limited the assessment of intervention fidelity and the analysis of the relative effectiveness of specific domains. Consequently, it was difficult to determine which specific component(s) of the intervention were beneficial and under which circumstances. Fourth, the poor description of factors that could be influencing study outcomes (e.g., different levels of health literacy, multilingual populations) limited the interpretation of individual and pooled effects.

3.5 Conclusion

This review provides evidence supporting consideration of ED-directed educational interventions targeting either adult patients or providers as effective strategies to increase office follow-up visits with a PCP after asthma exacerbations. It does not provide conclusive evidence to suggest that these interventions are effective in improving other health-related outcomes such as relapses or admissions. The decision to implement ED-directed educational interventions should rely on more than an indicator of effectiveness and take into account factors limiting the

external validity of systematic review findings (e.g., providers' skills/training, targeted populations, ED setting/ health system characteristics of included studies). What exactly works, in whom, under which conditions and based on what cost should be further assessed and incorporated into evidence synthesis methods of behavioral trials. Future research should focus on standardizing the reporting of non-pharmacologic interventions among scientific journals and evaluating their costs. This will promote the sharing, comparison and synthesis of experience, and facilitate the translation of research results into clinical practice.[147]

Table 3-1 Characteristics of included studies.

Authors	Year	Country	Sample size	Age (years)	Outcomes	Follow-up period
Baren et al.	2001	United States	192	16-46	PCP follow-up visit after ED discharge	4 weeks
					Relapses	21 days
Sin et al.	2004	Canada	125	5-50	Quality of life Asthma control Use of anti-asthma medications and written asthma action plans PCP follow-up visit after ED discharge Relapses	1, 2, 3, 6 and 12 months
Baren et al.	2006	United States	384	2-54	PCP follow-up visit after ED discharge Relapses	30 days
					ED visits Hospitalizations for asthma Use of anti-asthma medications Symptoms Activity limitation	12 months
Rowe et al.	2006	Canada	104	8-60	PCP follow-up visit after ED discharge Relapses	3 and 6 weeks
Rowe et al.	2013	Canada	80	18-94	PCP follow-up visit after ED discharge Relapses	30 and 90 days

Note: PCP denotes primary care providers; ED= emergency department.

Table 3-2. Fidelity assessment of studies' interventions.

Study	Domains	Steps taken to ensure fidelity
		How was fidelity assessed?
Baren et al. 2001	Fidelity to Theory	No theoretical framework.
		N/A
	Provider Training	Trained research assistants.
		N/A
	Intervention Implementation	**Intervention:** Self-contained "fanny pack" including: 5-day course of oral prednisone (50 mgs/day) + 2 taxicab vouchers for transportation to the PCP office + asthma information card + written instructions for the use of medication and vouchers. Participants were contacted by phone within 48 hours of ED release and reminded to make an appointment with the PCP. **Control:** ED-discharge instructions and medication prescription at the discretion of the treating physician. All study participants with no PCP were referred to a hospital-based asthma clinic that had agreed to accept referrals.
		Standard delivery materials were used. The study personnel tracked utilization of transportation vouchers; no subgroups analyses were made. No measures of provider monitoring and no strategies to prevent contamination are described.
	Intervention Receipt	No
		N/A
	Intervention Enactment	No
		N/A
Sin et al. 2004	Fidelity to Theory	No theoretical framework.
		N/A
	Provider Training	A study coordinator.
		N/A
	Intervention Implementation	**Intervention:** A study coordinator made an appointment with the patient's PCP on behalf of the patient. Patients received a phone call 1-2 days before the scheduled follow-up visit. **Control:** Patients were encouraged to visit their regular PCP within 4 weeks of discharge.
		There is no mention that standard delivery materials were used. No measures of provider monitoring are described.

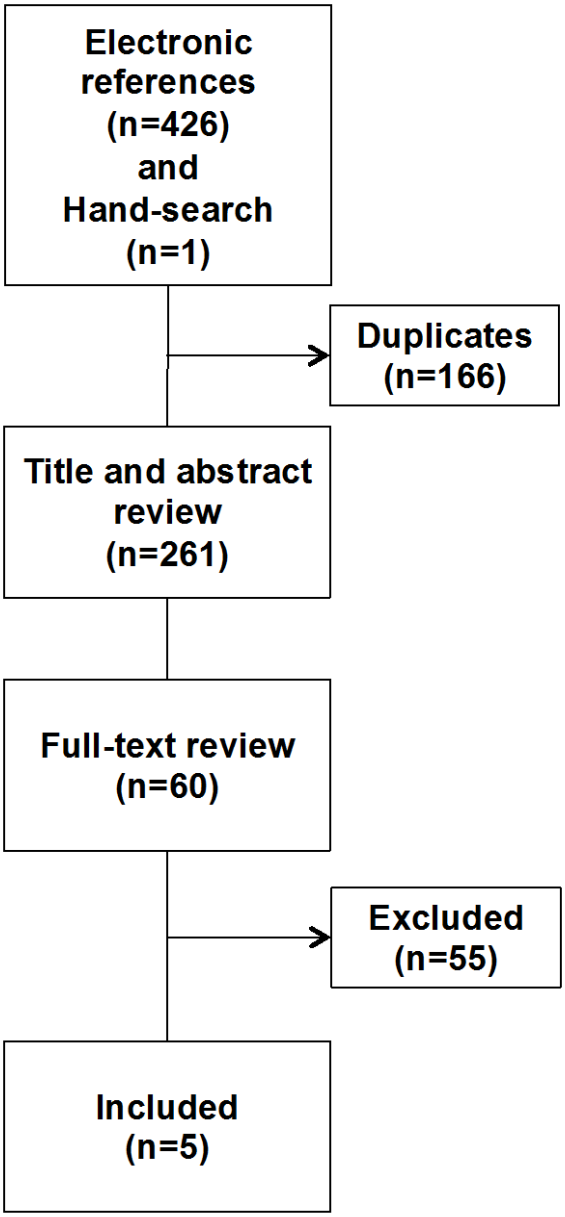
	Intervention Receipt	No
		N/A
	Intervention Enactment	No
		N/A
Baren et al. 2006	**Fidelity to Theory**	No theoretical framework.
		N/A
	Provider Training	Research assistants.
		N/A
	Intervention Implementation	**Intervention:** B: 5-day course of prednisone (2 mg/kg/day up to 50 mgs/day) + two taxicab transportation vouchers ($15.00 each) to travel to and from the PCP office (patients were instructed on how to use them); C: interventions stated above (B) + patients completed a preference-for-appointment form to assist in arranging their follow-up. **Control:** Usual discharge instructions from treating physician.
		Standard delivery materials were used. No subgroups analyses were made. No measures of provider monitoring and strategies to prevent contamination are described.
	Intervention Receipt	No
		N/A
	Intervention Enactment	No
		N/A
Rowe et al. 2006*	**Fidelity to Theory**	No theoretical framework.
		N/A
	Provider Training	Research nurses.
		N/A
	Intervention Implementation	**Intervention:** At discharge, patients were provided a written asthma action plan (AAP) from the Canadian Thoracic Society. They were also encouraged to visit their PCP and review the AAP in detail. A typed letter was faxed to the patients' PCP office outlining the need for a follow-up and the gaps in care identified during the interview. **Control:** Usual discharge instructions. All study patients received a package including a standardized discharge plan: web resources, information about asthma exacerbations, education on medication compliance.
		Standard delivery materials were used. No measures of provider monitoring are mentioned; strategies to prevent contamination are not described.

	Intervention Receipt	No
		N/A
	Intervention Enactment	No
		N/A
Rowe et al. 2013**	**Fidelity to Theory**	No theoretical framework.
		N/A
	Provider Training	Research nurses.
		N/A
	Intervention Implementation	**Intervention:** An individualized "Lung Attack Letter" was faxed to the patients' PCP. The Lung Attack Letter" summarized the following points: a) that the PCP's asthma/COPD patient has had a presentation to the ED for an exacerbation but did not require a prolonged hospital admission; b) description of the ED and discharge management plan; c) recommendation to the PCP to follow up with the patient within 1-2 weeks after discharge from the ED; d) care gaps identified in the patients chronic management of asthma/COPD based on the Canadian Thoracic Society guidelines. **Control:** Usual discharge instructions. Patients received a standardized outpatient protocol including printed asthma/COPD educational materials from the Canadian Lung Association; they were advised to follow up with their PCP.
		Standard delivery materials were used. No measures of provider monitoring are mentioned; strategies to prevent contamination are not described.
	Intervention Receipt	No
		N/A
	Intervention Enactment	No
		N/A

* Fidelity was assessed based upon a manuscript draft provided by the study authors;

** Fidelity was assessed based upon a study protocol provided by the study authors.

Figure 3-1 Literature search.



Reproduced from: Villa-Roel C, et al. *Acad Emerg Med*. 2016; 23:5-13

Figure 3-2 Risk of bias assessment of the included studies.

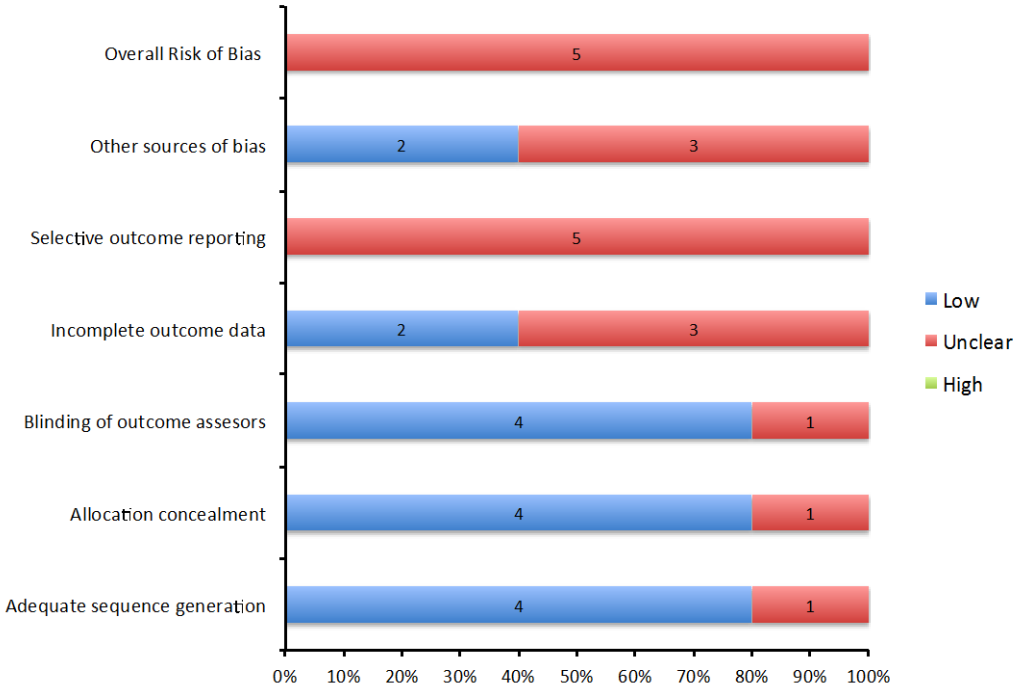
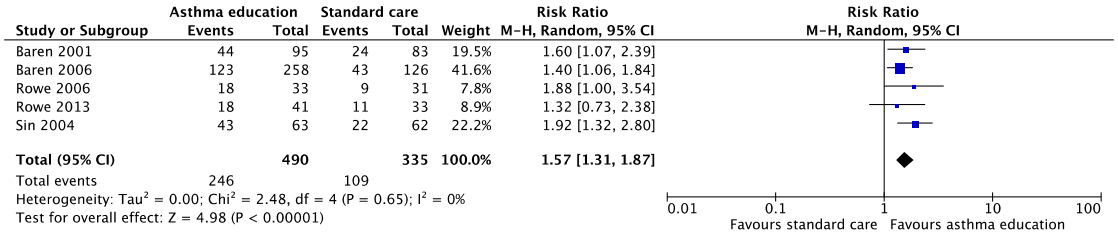


Figure 3-3 Effect of ED-directed educational interventions on percentage of primary care provider follow-up after an ED visit for acute asthma.



Reproduced from: Villa-Roel C, et al. *Acad Emerg Med*. 2016; 23:5-13

Figure 3-4 Effect of ED-directed educational interventions on percentage of relapses after an ED visit for acute asthma.

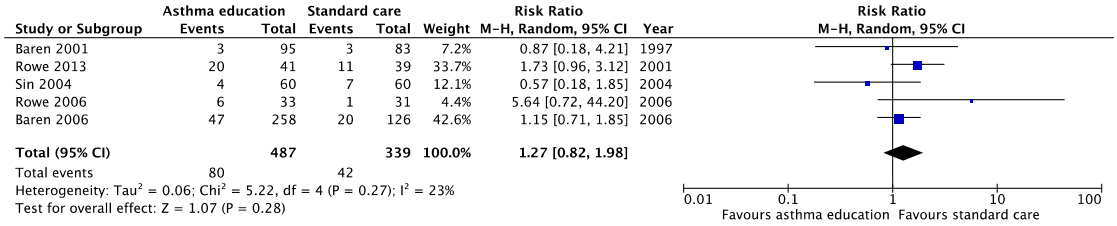


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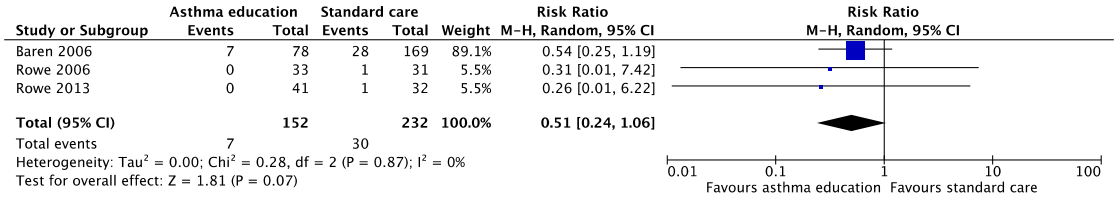
Figure 3-5 Effect of ED-directed educational interventions on percentage of hospital admissions after an ED visit for acute asthma.



Appendix 3-1 Search strategies.

1. Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present> (searched June 3, 2014)

1 asthma.mp. or exp Asthma/ (136623)
2 (emergen? adj2 (department* or doctor* or ward or wards or medic* or unit or units or care or room* or service* or physician or nurse*or resident*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (367)
3 exp Emergency Service, Hospital/ or exp Emergency Medical Services/ (95231)
4 2 or 3 (95492)
5 (Patient adj2 (educat* or instruct* or brochure* or teach* or train*)).mp. (83418)
6 exp Patient Education as Topic/ (70082)
7 random*.ti,ab. or rct.mp. (713824)
8 (workbook* or ((behaviour* or behavior*) adj2 (contract* or agreement*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1232)
9 (telephone adj2 (reminder* or call or reinforc*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (990)
10 5 or 6 or 8 or 9 (85493)
11 1 and 4 and 10 (219)
12 11 (219)
13 limit 12 to randomized controlled trial (40)
14 7 and 12 (51)
15 Emergency Treatment/ or Emergency Medicine/ or emergency medical services/ or emergency service, hospital/ or trauma centers/ or triage/ or exp Evidence-Based Emergency Medicine/ or exp Emergency Nursing/ or Emergencies/ or emergicent*.mp. or ((emergenc* or ED) adj1 (room* or accident or ward or wards or unit or units or department* or physician* or doctor* or nurs* or treatment*or visit*)).mp. or (triage or critical care or (trauma adj1 (cent* or care))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word,
protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (201348)
16 asthma*.mp. or exp Asthma/ [mp=title, abstract, original title, name of substance word, subject heading word,

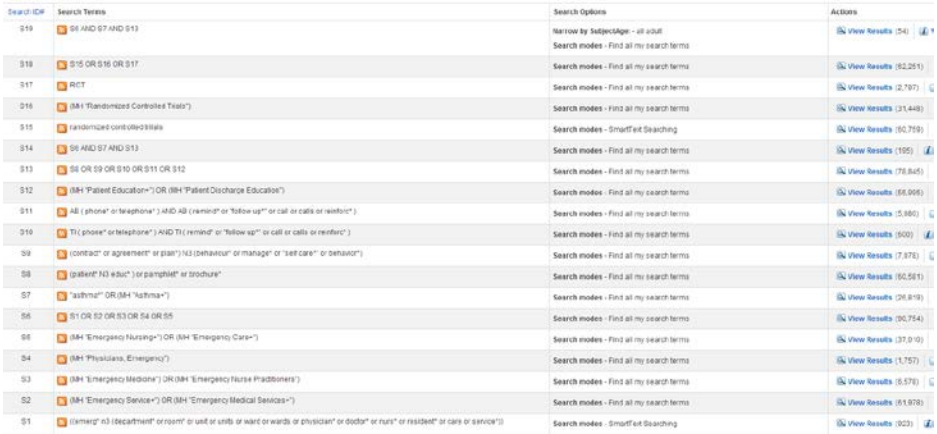
keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (139965)
17 10 and 15 and 16 (419)
18 exp child/ or exp congenital/ or exp infant/ or exp adolescence/ or exp infant, newborn/ or exp child, preschool/ or (pediatric* or paediatric* or child* or newborn$ or adolescen* or newborn* or congenital* or infan* or preschool* or pre-school* or teen$ or kindergarden$ or kindergarten* or elementary school$ or nursery school$ or youth$ or baby$ or babies or neonat$ or schoolchild* or toddler$ or boy or boys or girl* or pubescen* or juvenile* or adolesc*or pre-pubesc*).mp. or (child* or adolesc* or pediat* or paediat*).jn. (3511151)
19 17 not 18 (129)
20 17 (419)
21 exp Adult/ (5549596)
22 17 not 19 (290)
23 21 and 22 (107)
24 19 or 23 (236)
25 7 or 13 (713827)
26 24 and 25 (58)
27 14 or 26 (86)

2. Database: Embase <1974 to 2014 Week 22> (searched June 3, 2014)

1 asthma.mp. or exp Asthma/ (210713)
2 (emergen? adj2 (department* or doctor* or ward or wards or medic* or unit or units or care or room* or service* or physician or nurse*or resident*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (547)
3 exp Emergency Service, Hospital/ or exp Emergency Medical Services/ or exp emergency health service/ (65991)
4 2 or 3 (66447)
5 (Patient adj2 (educat* or instruct* or brochure* or teach* or train*)).mp. (129237)
6 exp Patient Education as Topic/ (85540)
7 random*.ti,ab. or rct.mp. (887500)
8 (workbook* or ((behaviour* or behavior*) adj2 (contract* or agreement*))).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1617)
9 (telephone adj2 (reminder* or call or reinforc*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1462)

10 5 or 6 or 8 or 9 (132093)
11 1 and 4 and 10 (96)
12 11 (96)
13 limit 12 to randomized controlled trial (5)
14 7 and 12 (15)
15 Emergency Treatment/ or Emergency Medicine/ or emergency medical services/ or emergency service, hospital/ or trauma centers/ or triage/ or exp Evidence-Based Emergency Medicine/ or exp Emergency Nursing/ or Emergencies/ or emergicent*.mp. or ((emergenc* or ED) adj1 (room* or accident or ward or wards or unit or units or department* or physician* or doctor* or nurs* or treatment*or visit*)).mp. or (triage or critical care or (trauma adj1 (cent* or care))).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (254696)
16 asthma*.mp. or exp Asthma/ [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (213020)
17 10 and 15 and 16 (640)
18 exp child/ or exp congenital/ or exp infant/ or exp adolescence/ or exp infant, newborn/ or exp child, preschool/ or (pediatric* or paediatric* or child* or newborn$ or adolescen* or newborn* or congenital* or infan* or preschool* or pre-school* or teen$ or kindergarden$ or kindergarten* or elementary school$ or nursery school$ or youth$ or baby$ or babies or neonat$ or schoolchild* or toddler$ or boy or boys or girl* or pubescen* or juvenile* or adolesc*or pre-pubesc*).mp. or (child* or adolesc* or pediat* or paediat*).jn. (3632986)
19 17 not 18 (289)
20 17 (640)
21 exp Adult/ (5332705)
22 17 not 19 (351)
23 21 and 22 (109)
24 19 or 23 (398)
25 7 or 13 (887502)
26 24 and 25 (69)
27 14 or 26 (78)

3. Database: CINAHL (searched June 3, 2014)



Search ID#	Search Terms	Search Options	Actions
S19	S6 AND S7 AND S13	Narrow by Subject/Age: - all adult Search modes - Find all my search terms	View Results (54)
S18	S15 OR S16 OR S17	Search modes - Find all my search terms	View Results (62,261)
S17	RCT	Search modes - Find all my search terms	View Results (2,797)
S16	(MH "Randomized Controlled Trials")	Search modes - Find all my search terms	View Results (31,448)
S15	randomized controlled trials	Search modes - SmartText Searching	View Results (60,759)
S14	S6 AND S7 AND S13	Search modes - Find all my search terms	View Results (195)
S13	S8 OR S9 OR S10 OR S11 OR S12	Search modes - Find all my search terms	View Results (76,845)
S12	(MH "Patient Education+") OR (MH "Patient Discharge Education")	Search modes - Find all my search terms	View Results (66,996)
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S9	(contract* or agreement* or plan*) N3 (behaviour* or manage* or "self care*" or behavior*)	Search modes - Find all my search terms	View Results (7,976)
S8	(patient* N3 educ*) or pamphlet* or brochure*	Search modes - Find all my search terms	View Results (60,561)
S7	"asthma*" OR (MH "Asthma+")	Search modes - Find all my search terms	View Results (26,819)
S6	S1 OR S2 OR S3 OR S4 OR S5	Search modes - Find all my search terms	View Results (90,754)
S5	(MH "Emergency Nursing+") OR (MH "Emergency Care+")	Search modes - Find all my search terms	View Results (37,010)
S4	(MH "Physicians, Emergency")	Search modes - Find all my search terms	View Results (1,757)
S3	(MH "Emergency Medicine") OR (MH "Emergency Nurse Practitioners")	Search modes - Find all my search terms	View Results (5,578)
S2	(MH "Emergency Service+") OR (MH "Emergency Medical Services+")	Search modes - Find all my search terms	View Results (61,978)
S1	((emerg* n3 (department* or room* or unit or units or ward or wards or physician* or doctor* or nurs* or resident* or care or service*))	Search modes - SmartText Searching	View Results (923)

4. Database: SCOPUS (searched June 3, 2014)

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NOT (TITLE(child* OR pediatric* OR adolesc* OR youth))

5. Database: ERIC (1965 to April 2014)

1 asthma.mp. (489)
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physician* or doctor* or nurs* or treatment*or visit*)) or (triage or critical care or (trauma adj1 (cent* or
care)))).mp. [mp=abstract, title, heading word, identifiers] (628)
3 1 and 2 (20)
4 exp Older Adults/ or adult.mp. or exp Adults/ or exp Young Adults/ (109526)
5 3 and 4 (2)

6. Database: Proquest Dissertations and Theses Full Text (searched June 3, 2014)

Search #1: all(emerg* W/3 (doctor* OR department* OR unit OR units OR ward OR wards OR nurse* OR resident* OR physician* OR service* OR room*)) AND all(asthma*) AND all(patient* W/3 (educate* OR train* OR

instruct* OR teach* OR pamphlet* OR brochure* OR workbook OR plan* OR "behav*contract*" OR "behav* agree*")) **= 16**

Search #2: all(emerg* W/3 (doctor* OR department* OR unit OR units OR ward OR wards OR nurs* OR resident* OR physician* OR service* OR room*)) AND all(asthma*) AND all((phone* or telephone*) w/3 (call* OR reinforc* OR remind* OR follow-up*)) = 3

7. Google Scholar (searched June 3, 2014)

First ten pages: emergency and "patient education" and asthma * and rct or random * * *

8. Database: OVID EBM All

Ovid Technologies, Inc. Email Service
Search for: 10 or 14
Results: Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to April 2014>, EBM Reviews - ACP Journal Club <1991 to May 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <2nd Quarter 2014>, EBM Reviews – Cochrane Central Register of Controlled Trials <April 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <2nd Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <2nd Quarter 2014>
Search Strategy:
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2 exp Patient Education as Topic/ (5731)
3 (workbook* or ((behaviour* or behavior*) adj2 (contract* or agreement*))).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
(256)
4 (telephone adj2 (reminder* or call or reinforc*)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw] (660)
5 1 or 2 or 3 or 4 (9515)
6 Emergency Treatment/ or Emergency Medicine/ or emergency medical services/ or emergency service, hospital/ or
trauma centers/ or triage/ or exp Evidence-Based Emergency Medicine/ or exp Emergency Nursing/ or Emergencies/ or
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(20540)

8 5 and 6 and 7 (115)
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14 12 and 13 (26)
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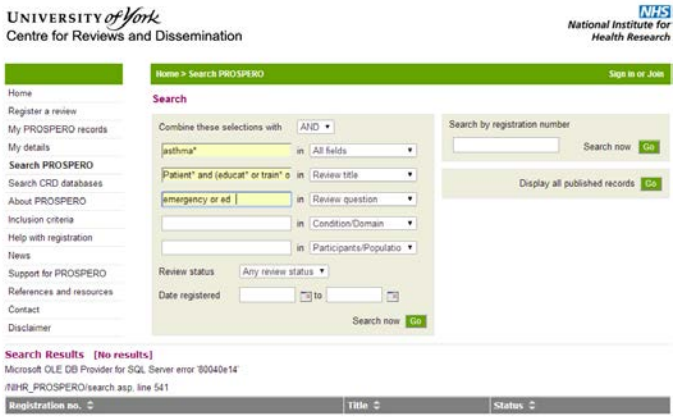
9. Prospero



Appendix 3-2 List of excluded articles.

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4 ENGAGING PATIENTS AND PRIMARY CARE PROVIDERS IN THE DESIGN OF NOVEL OPINION LEADER BASED INTERVENTIONS FOR ACUTE ASTHMA IN THE EMERGENCY DEPARTMENT: A MIXED METHODS STUDY

4.1 Introduction

Asthma is a chronic lung disease characterized by airway inflammation punctuated by episodes of instability, often in response to a variety of triggers. Despite improved understanding of the pathophysiology of asthma[183] and therapeutic advances, asthma control remains elusive for many patients.[121] This loss of control results in frequent exacerbations which may result in emergency department (ED) visits.[184]

While the pharmacologic ED management of acute asthma has been recognized as "evidence-based",[147] there is a need to facilitate the transitions in care between acute care settings such as the ED and community-based follow-up with primary care providers (PCPs). Important knowledge and care gaps have been identified in adults presenting to EDs with asthma exacerbations;[119] some of these gaps are more common in subjects at high risk of admissions and relapses.[139, 185] In addition, follow-up visits with a PCP after ED discharge have shown to be delayed or non-existent.[120] Recently published and widely disseminated asthma guidelines have highlighted the essential role of patient education and the establishment of post-ED care partnerships after an asthma exacerbation.[1] These strategies are designed to maintain asthma control,

prevent poor health outcomes and maximize patient quality of life; however, the evidence supporting such guidance is mixed.[117, 118] and this makes any plan for sustained implementation a complex and challenging endeavor.[186]

Opinion leaders (OL) are recognized as local educational specialists capable of influencing their colleagues with their knowledge.[187] Effective, safe and responsive OL-based interventions have shown to improve professional practice and health outcomes;[188] active OL-based multifaceted interventions targeting different barriers to change have been proposed as novel strategies for knowledge transfer.[189] The involvement of OLs in the implementation of quality improvement and educational interventions in health care is not necessarily effective under all circumstances, their benefits seem to be intervention and disease specific.[190]

Emergency department-directed OL-based interventions targeting chronic conditions, such as osteoporosis, have facilitated PCPs linkages, improved PCP follow-up and resulted in large improvements in appropriate testing and treatment compared with usual care.[191, 192] While community-based influential physicians have been shown to influence the behaviour of peers, reduce their need to participate in traditional educational programs and improve care in patients with chronic obstructive disease (COPD),[193] ED-based studies comparing OL-endorsed treatment recommendations for ambulatory asthma and COPD with usual care found

no increase in PCP follow-up visits at 30 days or reduction of relapses at 90 days.[162]

To date, the effectiveness of OL-based multifaceted interventions facilitating the transitions in care between the ED and the primary care setting improve health outcomes after asthma exacerbations has not been established. In addition, the specific value of letting patients and PCPs' perceptions and expectations influence the content of these interventions has been infrequently studied.[194, 195] Therefore, the aim of the current study was to seek input from patients and PCPs on the design of novel OL-based multifaceted interventions for acute asthma.

4.2 Methods

4.2.1 Study design:

A sequential explanatory mixed methods design was employed, which involved quantitative (survey) and qualitative (focus groups) data collection. The structure of the mixed-methods approach is QUAN → qual, in which quantitative methods precede qualitative and the quantitative methods are dominant.[196] This sequential approach serves the function of convergence and complementarity to seek elaboration and clarification of survey results. The study was approved by the University of Alberta Health Research Ethics Board (Pro00023191; Appendix 1). Written informed consent was waived; patients and PCPs' voluntary responses/participation reflected their consent to take part in the study.

4.2.2 Quantitative methods (surveys):

Over a four month period, a consecutive sample of at least 50 patients with physician-diagnosed asthma who had ever presented to the ED for acute asthma were invited by trained research assistants to complete a self-administered non-validated survey, regardless of their reason for ED presentation to the University of Alberta Hospital. Information on demographics, primary care support and perceptions of an ideal local OL in ambulatory asthma care was collected; preferences regarding the content, style and delivery methods of OL-based interventions in acute asthma directed from EDs were also gathered. The survey took approximately 10 minutes to complete.

During the same period of time, a random sample of 50 PCPs (family physicians from the Edmonton area) was chosen from the College of Physicians and Surgeons of Alberta website (www.cpsa.ab.ca) and each was invited to participate in an electronic survey. Due to a *null* response to the electronic survey, surveys were subsequently faxed to a second random sample of 150 PCPs chosen from the same website. Due to a *low* response to this second attempt, surveys were distributed during an academic event involving family physicians from the Edmonton area. Apart from the same information collected in the patient survey, training designation and years of clinical experience were documented.

At the end of both surveys, patients and PCPs were invited to participate in separate focus groups to discuss their responses, to further

explore their preferences and expectations regarding the delivery of ED-directed interventions for asthma care involving OLs, and to debate their potential impact on clinical practice.

4.2.3 Qualitative methods (Focus groups):

Focus group questions were developed following a semi-structured format with open-ended questions.[197] Introductory questions were developed to build rapport and encourage an open discussion among participants. After introductions, survey results were presented and focus group moderators asked a series of probing questions about participants' preferences on the delivery of ED-directed educational interventions for asthma care involving OLs; the ideal content, style and delivery methods to improve patient-PCP linkages were also sought. Potential barriers for intervention implementation and knowledge uptake were also explored.

Two focus group discussions (2 hours each) were conducted with the same instructions and questions. One researcher with experience in qualitative research moderated them with the aid of two clinician-researchers. Focus groups were audio recorded; however, two process facilitators also completed field notes that documented the main themes of the session and any observations pertinent to the study aims. Focus group discussions and notes were transcribed verbatim.

4.2.4 Data analysis:

The results of the surveys were analyzed and summarized using descriptive statistics: proportions for categorical variables and medians with percentiles and interquartile range (IQR: P_{25}, P_{75}) for continuous variables (due to a non-normal distribution). Data were analyzed using Stata Statistical Software® Release 13.0 (College Station, TX, Stata Corporation).

A conventional approach to content analysis was used to create coding categories and identify themes and patterns derived directly from the lived experience at the focus groups.[198, 199] Patient and PCPs' responses (including the identification of barriers and facilitators for potential implementation) were interpreted from the content of text data and not from a pre-existing theoretical framework. Data transcripts were condensed into text segments that were coded based upon emergent themes that were continually refined and compared to each other. Finally, categories were aggregated into broader themes related to participants' preferences, expectations and views on barriers and facilitators for the delivery of ED-based education interventions for asthma. Excerpts from participants' narratives were used to illustrate the main themes derived from focus group discussions.

4.3 Results

Figure 4-1 summarizes the study recruitment strategies and the response/participation for the surveys and the focus groups, respectively.

4.3.1 Patient survey results:

A total of 54 patients with asthma completed the survey; their median age was 44 (IQR: 27, 58) years and 55% were female. Overall, 65% of patients reported a family physician frequently managed their asthma; 39% preferred to receive guidance regarding their asthma exacerbation from a Respirologist, 44% during their ED visit and 56% through one-on-one discussions. In addition, 55% expressed interest in having PCP follow-up within a week of being discharged from the ED; however, the difficulty obtaining a follow-up visit was reported as moderate on a 1-7 Likert scale ranging from very difficult (1) to very easy (7); the median was 4 (IQR: 3, 6).

4.3.2 Primary care provider survey results:

The response rates to the PCP faxed-surveys and to the surveys handed-out in an academic event were 11% (n = 17/150) and 63% (n=22/35), respectively. A total of 39 PCPs completed the survey; 39% of them were in the 46-55 years age category and 72% were female. A Respirologist was identified as an ideal OL in ambulatory asthma by 59% of the respondents. All PCPs expressed interest in receiving notification of their patients' ED acute asthma presentation; 62% considered personalized, guideline-based, recommendations to be the ideal content of an educational intervention directed from the ED and 39% were inclined to receive this guidance through an educational pamphlet faxed to their offices. Finally, 54% preferred this notification within a week of ED

discharge including details on: ED treatment (95%), final diagnosis (92%), and post-ED treatment (87%).

4.3.3 Focus group results:

Findings include a description of participants' characteristics, preferences, expectations and views on barriers and facilitators for the delivery of OL-based educational interventions for asthma directed from the ED. Table 4-1 summarizes patients and PCPs' illustrative statements for the main themes that emerged from these activities.

4.3.3.1 Patients:

From 24 patients with asthma who completed the survey and agreed to participate in the focus group, six attended. Their median age was 54.5 years (IQR: 52, 58) and six were females. All but one patient had a PCP (family doctor) and reported current regular use of medication to control asthma. Analysis revealed four main themes that emerged from the focus group discussions:

4.3.3.1.1 Theme 1: Preference for specialized knowledge:

Patients recognized the benefits of asthma education uptake while in the ED and expressed preference for specialized education (from a Respirologist) regarding the asthma episode that brought them to the ED. While great value was given to the specialized knowledge of Respirologists (e.g., about the role of different medication options) patients recognized these physicians may not be available for the provision of post

discharge self-management education. Other health care providers working in the ED (e.g., nurses, respiratory therapists or pharmacists) were identified as alternative clinicians who could address these topics (**Table 1**).

4.3.3.1.2 Theme 2: Anxiety as a barrier for information uptake during the ED visit:

One of the most profound themes was the role of anxiety as a barrier for asthma education in the ED. Patients reported that asthma exacerbation episodes typically trigger high levels of anxiety. The predominant message was that anxiety acted as a potential deterrent to knowledge uptake as it adversely interfered with complex cognitive processing of information (Table 1).

4.3.3.1.3 Theme 3: Role, content and provider of "teachable moments" in the ED:

Participants agreed that the ED offers a short window of time to receive education about asthma; however, they considered the opportunity and content of "teachable moments" may vary according to symptom severity and anxiety levels during the ED stay. Although receptive, participants expressed concerns about information overload that could prevent them from accurately remembering concepts after discharge. They mentioned that information provided in the ED sometimes is not clear and leaves them confused and with several doubts about future steps. Patients recognized the uptake of fragmented information from their

interaction with several health providers during their ED stay (e.g., nurse, respiratory therapist, pharmacist, ED physician). For example, some participants acknowledged the importance of receiving information from a pharmacist regarding the appropriate use of inhalers prior to discharge; however, discussions about comprehensive chronic self-management were preferred to occur outside the ED (Table 1).

4.3.3.1.4 Theme 4: Importance of transitions of care from emergency to the primary care settings:

Participants acknowledged the importance of ongoing education after ED discharge to support their self-management skills. There was almost unanimous feeling that disconnection between the ED, PCP and Respirologists' recommendations are an important barrier for a successful continuum of care.

They emphasized the importance of timely one-on-one, follow-up after discharge. There were discussions about whether follow-up should occur with their PCP (family doctor) or with a specialist. Patients indicated that a long-term relationship with a family physician facilitates follow-up with this care provider; however, patients also felt the lack of specialized training in respiratory medicine would limit their ability to order and conduct specialized tests for monitoring their condition (Table 1).

4.3.3.2 Primary Care Providers:

A total of 11 PCPs who completed the survey and initially indicated their interest in participating in the focus group were contacted by

telephone and electronic mail. None of them accepted the invitation for the focus groups and therefore, a snowball sampling strategy was used to recruit additional research participants. Six PCPs (3 males and 3 females; all family physicians with median year of graduation: 1994 (IQR: 1989, 2004) took part in the focus group discussion. Four main themes emerged from the focus group discussions with the PCPs:

4.3.3.2.1 Theme 1: Notification and timing of follow-up after ED discharge:

Participants stressed the importance of having a prompt notification and follow-up with their patients after they are discharged from the ED (e.g., within one day to one week after ED discharge) and while they are still on the medication prescribed during the ED visit (Table 1).

4.3.3.2.2 Theme 2: Content of ED discharge letters and education:

Most participants expressed preference for receiving personalized educational information instead of general asthma information or educational pamphlets faxed to their offices. There was consensus about the importance of receiving discharge letters explicitly indicating the final ED diagnosis and discharge medications. They expressed the content of the letter would be useful to determine how soon the follow-up appointment should take place (Table 1).

4.3.3.2.3 Theme 3: Opinion leaders for ambulatory asthma care and education:

In contrast to PCP survey respondents, participants in the focus group expressed that family physicians would be the best OLs for ambulatory asthma care and education. Participants acknowledged the value of Respirologists as OLs though, particularly in those patients not having family physicians or for practitioners in the “late majority” category of innovation uptake. They also perceived Respirologists might be able to offer advice about patients not responding to traditional management strategies. Participants felt that family physicians had a more relatable perspective and that because many of the challenges of ambulatory asthma care are not related to treatment choices but to socio-economic issues, a family physician would be more equipped to act as an OL for education on ambulatory asthma care (Table 1).

4.3.3.2.4 Theme 4: Time constraints for proper post –ED follow-up and education:

There was general consensus that time constraints are an important barrier for asthma education in ambulatory care settings. Participants expressed that other health providers such as asthma educators and chronic care managers could help overcoming the challenges and gaps in the delivery of asthma education in the ambulatory care setting (Table 1).

4.4 Discussion

Input from patients and PCPs regarding the content, style and delivery methods of OL-based interventions in acute asthma directed from the ED provided valuable information for the design and implementation of novel multifaceted interventions (NCT01079000). The identification of Respirologists as local OLs; of the first week after ED discharge as a practical window for education; and of one-on-one vs. personalized written materials faxed to offices as desirable delivery methods for patients and PCPs, respectively, are concrete examples of how contributions from patients and PCPs helped tailor the future study interventions. The focus groups allowed the reconciliation of the discrepancies with the survey responses through the identification of the main driver behind the OL-selection: the preference for specialized knowledge. They also facilitated the identification of potential determinants for implementation.

The fact that Respirologists were nominated by most of the survey respondents as the ideal clinicians to guide education after an asthma attack reflect their earned professional leadership role, trust and respect among individuals with different technical competences and status in the health system.[190] Respirologists' knowledge, ability to order/conduct specialized tests and ability to manage patients with complex respiratory conditions were their most valued assets. While participants in the PCPs focus group expressed the belief that family physicians would be the best OLs for ambulatory asthma care and education, the value of

Respirologists as OLs was still acknowledged. Both patients and PCPs, however, recognized the limited availability of Respirologists for the provision of post discharge self-management education and discussed the potential benefit derived from empowering other health care providers working in or outside the ED to assume that role. The assistance that trained asthma educators, nurses, respiratory therapists and pharmacists can provide in transitions in asthma care between the ED and the primary care setting has been previously described.[75, 76] Finally, time constraints were identified as an important barrier for an effective post-ED interaction with PCPs.

The first week of ED discharge was identified as a practical time frame for the provision of asthma education by patients and PCPs. While there is no clear evidence regarding the most effective time for the provision of asthma education, their preference would be aligned with the current guideline recommendations for PCP contact/follow-up.[200] Additional initiatives referred to by PCP-survey respondents such as faxing them a copy of the patients' ED chart and a personalized-letter including details on their patients' final diagnosis, ED and ED post-treatment were also considered of value.[194] These efforts have the potential to influence physicians' behaviors (e.g., initiating contact with their patients, adjusting medication, making referrals, etc.); however, they are not part of "regular practice" in Canada and should only be

recommended for implementation elsewhere after their cost-effectiveness is assessed using rigorous research methods.[201]

Given the weak evidence of benefit derived from asthma education provided in the ED,[202, 203] its not surprising that controversy exists regarding the superiority of this compared to other settings.[46, 147] In a chaotic environment like the ED, time for the delivery of anything but brief educational interventions directly related to the discharge and follow-up of a condition, may be difficult. Moreover, patients identified anxiety as a potential barrier for the delivery of educational interventions in the ED. The increasing comorbidity of anxiety disorders in patients with asthma,[204] which are usually triggered by episodes of loss of asthma control, could be a key and rarely-explored element influencing knowledge uptake in acute settings. Finally, asthma is a complex chronic disease with considerable knowledge and care gaps among those afflicted by it, and the delivery of such interventions may be better left to those with specific training in the area and time to provide appropriate guidance.

4.4.1 Limitations

The sequential explanatory mixed methods used in this study constitutes the main strength of this initiative to consider the perceptions of patients and PCPs in the design of ED-directed OL-based educational interventions in acute asthma. Nonetheless, our findings may not represent the perception of all asthmatics in Canada (or elsewhere) nor be generalizable to those presenting to all EDs. Efforts were made by the

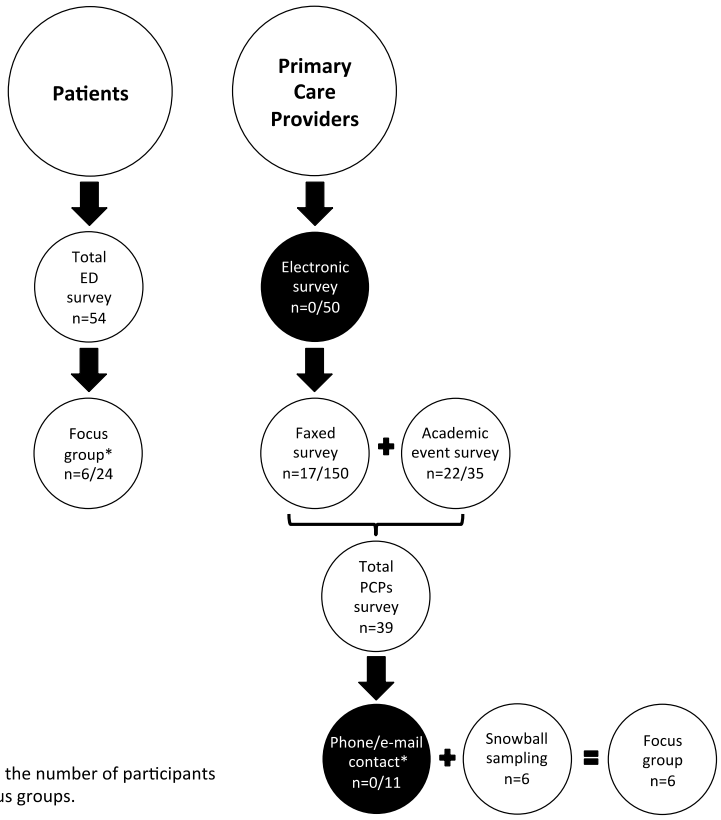
research staff to reach non-selective samples; however, difficulty accessing and receiving responses from PCPs, either for the survey or the in-person focus group, led to a potentially biased sample of highly engaged clinicians. The response issues presented here are consistent with previous efforts[205] and represent important information from which other researchers or health administrators can learn. In addition, the patient sample may have been biased as well, as the respondents were older and more often female than the samples engaged in ED-based asthma trials. While alternative practitioners (e.g., nurse practitioners) are generally not available to patients in this community and the potential role of non-traditional practitioners (e.g., acupuncturists, physiotherapists, holistic practitioners) was not explored for the same reasons, their inclusion in other settings may be quite reasonable. Finally, the sample sizes were small and data saturation was not formally assessed;[206] however, consistency in the qualitative responses was observed.

4.5 Conclusions

Messages and recommendations arising from patients and PCPs helped tailor ED-directed OL-based multifaceted interventions in acute asthma to meet the local needs and expectations. Further in depth discussions of the survey responses helped to identify the main drivers of their preferences (e.g., professional trust for OL selection), as well as potential barriers and facilitators for knowledge uptake and for the implementation of our and similar interventions. Particularly, non-

conventional effect-modifiers (e.g., patient anxiety levels and timing of the intervention) might not have been discovered had a mixed methods approach not been employed. While the effectiveness of the tailored interventions are currently being investigated using clinical trial methods (NCT01079000), the value that both patients and PCPs provide to health professional liaisons as education providers is a key finding that may facilitate the translation of research results into clinical practice.

Figure 4-1 Study recruitment strategies.



Note: *The denominator is based on the number of participants who agreed to participate in the focus groups.

Table 4-1 Patients and primary care providers' statements for the main themes that emerged from the focus groups.

Participants	Main themes	Statements
Patients with asthma	Preference for specialized knowledge in the delivery of ED asthma education	*"They know what to prescribe to you. They are a lot more specialized or they will have more idea what to give you for what your symptoms are".*
	Anxiety as a barrier for the uptake of information during the ED visit	*"You are scared, you're terrified; you are focused on your breathing. Honestly I thought I was dying".*
	Role, content and provider of "teachable moments" in the ED:	*"I would sit with a nurse or whoever and talk while I am in the actual emergency area. But I don't think I am taking information in. You could talk to me until I'm blue in the face but if I'm not well and having an asthmatic attack, I'm telling you I'm not taking the information in because I am not thinking".*
	Transitions of care from emergency to the primary care settings	*"Sometimes you go to see your family doctor and although they are trying to give you the best care that they can, they are so overwhelmed a lot of times with their practice that they don't always have full time for you, whereas if you go to see your lung specialist, that's basically all they are there for your problem. Your family doctor can't do the tests that the asthma doctors do".*
Primary care providers	Notification and timing of follow-up after ED discharge	*"Why can't get this a day after?; everybody wants notification that his/her patient has been in Emerg. Realistically within a day is not going to happen, but it has to be as soon as practical. If they don't recover from the episode, I want to know that day. If they weren't given prednisone or ICS, it would be good to know. Three weeks later, they're going to be in real trouble".*
	Content of ED	*"Diagnosis is the key part here. The*

	discharge letters and education	*diagnosis of asthma would make me act, it's not about doubting the diagnosis, it's used like a red flag/alert (it's nice to be able to read the diagnosis/be given a diagnosis, then you know what to do."*
	Role of OLs for ambulatory asthma care and education	*"Family physician perspective is better, more relatable, getting taught by people that know your experience, less of a top down approach".*
	Time constraints for proper post – ED follow-up and education	*"Physicians often can't spend hour with patients; asthma educators can review environmental changes, be more didactic; they can show pictures and graphs."*

Note: ED/Emerg = Emergency department; ICS = Inhaled corticosteroids; OL = Opinion leader.

Appendix 4-1 Notification of ethics approval.

Notification of Approval (Renewal)

Date:	May 24, 2013
Amendment ID:	Pro00023191_REN2
Principal Investigator:	Brian Rowe
Study ID:	MS3_Pro00023191
Study Title:	**Tailoring Educational Interventions in Acute Asthma: Does the Engagement of Knowledge Users Improve the Design of Emergency Medicine Trials involving Opinion-Leaders?**
Sponsor/Funding Agency:	CIHR - Canadian Institutes for Health Research CIHR

RSO-Managed Funding:

	Project ID	Project Title	Speed Code	Other Information
View	RES0011584	Tailoring Educational Interventions in Acute Asthma: Does the Engagement of Knowledge Users Improve the Design of Emergency Medicine Trials involving Opinion-Leaders?	Not available yet	

Approval Expiry Date:	July 7, 2014

Thank you for submitting this renewal application. Your application has been reviewed and approved.

This re-approval is valid for another year. If your study continues past the expiration date as noted above, you will be required to complete another renewal request. Beginning at 30 days prior to the expiration date, you will receive notices that the study is about to expire. If you do not renew on or before the renewal expiry date, you will have to re-submit an ethics application.

All study related documents should be retained so as to be available to the Health REB upon request. They should be kept for the duration of the project and for at least 5 years following study completion.

Sincerely,

Dr. Glen J. Pearson, BSc, BScPhm, PharmD, FCSHP
Associate Chair, Health Research Ethics Board - Health Panel

5 OUTPATIENT CARE GAPS IN PATIENTS PRESENTING TO EMERGENCY DEPARTMENTS WITH ACUTE ASTHMA

5.1 Introduction

A visit to the emergency department (ED) for acute asthma commonly corresponds to a patient who has been experiencing worsening respiratory symptoms and whose attempts to alleviate them have been unsuccessful and/or not evidence-based; in other words, ED presentations for acute asthma are usually the reflection of loss of asthma control. While most patients presenting to the ED with acute asthma respond to therapy and are subsequently discharged,[207] a significant proportion of relapses occur after these visits.[139] Asthma relapses following ED discharge represent important negative outcomes for the patient, their families and the health care system.[208, 209]

Several patients with asthma have poor understanding of their respiratory condition, its triggers and manifestations; therefore, they don't have the appropriate knowledge and skills to effectively self-manage their exacerbations.[210, 211] Moreover, others don't receive appropriate outpatient care. Finally, it is common to find patients with a combination of the above presenting to the ED.[212, 213] Limited or no access to health care providers, medications and preventive resources are additional barriers that patients with asthma face on a regular basis. Consequently, the ED may provide an important group of patients with a unique opportunity to identify their outpatient gaps in asthma care, receive asthma education and establish

important partnerships for the continuum of their care (e.g., link them with a primary care provider [PCP] or a specialist).[214-216]

Care gaps include a variety of scenarios in which effective interventions involved in the process of care are not part of routine clinical practice.[189] While treatment guidelines[1, 217] and consensus documents have been stressing for many years the importance of offering focused patient-education at every asthma encounter, including ED visits for acute asthma,[155, 218] the cost-effectiveness of identifying outpatient asthma care gaps and targeting them through educational strategies directed from the ED remains unclear.[117, 118]

In a study published 16 years ago, a network of ED/respiratory researchers across North America (The Multicenter Airway Research Collaboration [MARC]) was invited to prioritize teaching topics for the routine asthma education in the ED.[219] Survey respondents believed preventive actions (e.g., reviewing proper inhaler techniques, rationale for medication, recognition of asthma triggers and use of spacer devices) were key targets for ED-based asthma education; other preventive actions such as the use of written asthma action plans (AAPs), medication compliance and peak flow techniques/diaries were considered less important. Potentially important outpatient interventions (e.g., influenza vaccination, smoking cessation and referral to asthma education) were not specifically examined.

The objective of this study was to explore outpatient care gaps

associated with preventive actions among patients presenting to the ED for an asthma exacerbation who are subsequently discharged.

5.2 Methods

5.2.1 Study design and population:

This was a cross-sectional analysis of data obtained in a prospective, randomized, blinded endpoints ascertainment study (*NCT01079000*) conducted in two cities (Edmonton and Calgary) in AB, Canada. Prospective data used for this analysis were obtained from standardized baseline questionnaires and a medical chart review of patients between 17-55 years of age presenting to EDs for acute asthma before being discharged back to the community; screening and data collection were performed on a daily basis by trained research staff. Patients with >55 years of age, those with chronic obstructive pulmonary disease (COPD) or another end-stage lung disease, and those with an inability to consent were excluded.

5.2.2 Study variables:

Demographic factors (e.g., age, sex, racial/cultural background [visual assessment], marital status, level of education, and occupation) were considered for this analysis. Chronic asthma factors, resource utilization and medication at ED presentation were also explored. Finally, aspects related to clinical presentation and ED management were described.

5.2.3 Preventive actions-related measurements:

Two clinician-investigators (CVR, BHR) independently reviewed the enrolment data and adjudicated patients' needs based on the frequency of the following preventive actions at ED presentation: spacer devices, written AAPs and asthma medication; influenza immunization, cigarette smoking, and referral to asthma education. A random 30% sample of the study cases was used to assess the agreement between the adjudicators.

5.2.4 Statistical analysis:

The results of descriptive analysis were summarized with numbers and proportions or medians with interquartile range (IQR: P_{75}, P_{25}) due to a non-normal distribution of the continuous data. The agreement between the preventive action-adjudicators was calculated based on the kappa (k) statistics.

5.2.5 Ethical considerations:

The Health Ethics Research Board at the University of Alberta granted ethics approval for the *NCT01079000* study (Pro00029699; Appendix 1); all patients provided informed written consent and additional consent was not required for this particular analysis.

5.3 Results

5.3.1 Patient characteristics:

A total of 367 patients provided consent to participate in the primary study. Emergency department interview and chart review data were available for all the study patients and therefore included in this analysis. The median age of the study population was 28 years, more than half of them were female and single, and the majority visually identified themselves as of White/Commonwealth/European racial or cultural background (Table 5-1).

Almost half of the study population had never smoked and there was an overall long asthma history. No patients were hospitalized for asthma in the previous year and the median time since their last ED visit was 1.5 years. Overall, 26% of patients reported not having a regular family physician, and only 61% stated that their family physician most frequently treated their asthma.

Almost a quarter of the study population, took action before presenting to the ED; most of them visited their family physician or a physician at a walk-in-clinic. Most, however, did not take evidence-based actions to prevent or mitigate the ED visit. Finally, 72% of patients reported that health insurance helped them with medication costs; patients covered a median of 20% of medication costs (Table 5-1). At ED presentation, more patients reported being prescribed inhaled corticosteroids/long-acting β-agonists (ICS/LABA) than ICS alone; 38% of

the study population were corticosteroid naïve at ED presentation (Figure 5-1).

5.3.2 Acute asthma presentation:

In the ED, most patients were classified as “urgent” according to the Canadian Triage and Acuity Scale (CTAS) (Table 5-2). Overall, ED management followed current guideline recommendations; however, most SABA and inhaled anticholinergics seem not be administered within the first hour of admission. The use of pre-post spirometry was not common and almost half of the patients were ordered chest radiography. The majority of the population were discharged from the ED in less than six hours.

5.3.3 Patients’ needs at ED presentation:

The results of the external adjudication of the preventive actions among the 367 patients included in this study revealed that more than half of them required spacer devices (patients reported not to have one despite being indicated). Among those who reported having a spacer device 42% reported not using it; “difficulties to carry it around” was identified as the most common reason for not using the spacer device. Very few patients with asthma reported having a written AAP (3%). Thirty-seven percent reported receiving influenza vaccination in the past year and only 7% reported being referred to an asthma education program in the last 10 years. At ED presentation, following the recommendations of the current

asthma guidelines, 38% of the patients with asthma required the initiation of ICS, 11% required the addition of ICS/LABA combination agents (step-up approach due to lack of asthma control with adequate ICS doses) and 39% required reinforcement of compliance with preventer medications (either ICS or ICS/LABA). Finally, a third of the study population (current smokers) required counselling on smoking cessation (Table 5-3). The agreement between the independent adjudicators in the 30% random sample was 98% (k=0.96).

5.4 Discussion

This study characterized adults treated and discharged from the ED for an asthma exacerbation and explored their needs with regards to preventive actions at ED presentation. Most of them were young, single and perhaps Caucasian workers with long asthma history who consulted the ED for worsening respiratory symptoms that limited they daily activities. Indicators of prior asthma severity such as previous ED visits, hospitalizations and intubations were not frequent among the study population; however, the study sample may represent a select group of patients with previous high levels of asthma control. Factors associated with an increased risk of relapse such as female sex and current use of ICS/LABA agents were highly prevalent.[139]

A considerable proportion of patients were not linked to a family physician who took care of their asthma. This important finding was addressed in the design of the comparative effectiveness trial that this

cross-sectional analysis was based on due to the potential differential effects (misclassification) derived from this exposure (see Chapter 6). Management strategies prior to the ED presentation were not explored in detail; however, the fact that only 15% (56/367) of the patients were assessed by PCPs prior to the ED visit (either by their family physician or by a physician at a walk-in-clinic) jeopardizes the proposed role for these health care professionals in the ambulatory management and control of asthma. [46] [47] Importantly, it reveals that the evidence-based management approach recommended by the current guidelines was not followed by the study population.[1] Active and shared participation of patients and PCPs in the management of asthma exacerbations has been strongly promoted[1, 220] in an attempt to focus the efforts and resources available in acute care facilities (e.g., EDs or equivalent settings) to the provision of care of severe asthma exacerbations and those episodes of acute asthma not controlled with initial treatment strategies.

Several outpatient gaps in asthma care were identified in this study; the evidence supporting the associated preventive actions is summarized below. The benefits derived from the use of spacer devices (improved delivery and reduced side-effects) for patients prescribed pressurized metered dose inhalers (pMDIs) have been documented for many years;[221] adequate inhaler techniques are well recognized as key determinants for their effectiveness.[222] [223] Despite this evidence, 60% of the study participants reported not owning a spacer device. Moreover, a

considerable proportion of patients owning a spacer device required reinforcement on compliance.

Randomized controlled trials (RCTs) and systematic reviews (SRs) have demonstrated clear benefits associated with the use of individualized written AAPs in conjunction with education and regular medical review on the reduction of health care utilization, absenteeism and symptoms, and the improvement of quality of life.[83] Strategies to improve the understanding, uptake and early self-activation of written AAPs like their adaptation to patients' level of asthma control and health literacy have been associated with a significant reduction of undesired outcomes related to asthma exacerbations.[49] The uptake of written AAPs in this study was considerably lower than proportions reported by other studies involving patients with acute episodes of asthma; however, important variations among studies could explain this difference.[224-228] This study was restricted to ED presenters, didn't include children and details on the AAPs content were considered during the adjudication of the preventive actions; only written and appropriate ones (in terms of content) were considered valid.

Current asthma guidelines recommend encouraging smoking cessation by patients with asthma and their family. Most of these recommendations are supported by observational studies revealing an increased risk of more severe asthma symptoms, frequent exacerbations, health care resource utilization, and worse lung function and quality of life

in patients with asthma who smoke when compared to those who don't smoke.[229-231] Few studies have specifically studied the role of smoking cessation on asthma outcomes.[232, 233] In this study, based on their current smoking status, 30% of the participants required counseling on this matter.

Patients with asthma are encouraged to have an influenza vaccination every year;[234] this recommendation is extrapolated from the higher risk of complications and increased health care costs associated with influenza in healthy adults between 18-64 years.[235] The evidence supporting universal influenza vaccination for patients with asthma is still subject to debate.[236] Based, on the current guideline recommendations,[1] a considerable proportion of the study population required direction on annual influenza vaccination.

All asthma guidelines strongly advocate for patient education. While a variety of educational and self-assessment programs have been developed for adults frequently presenting to the EDs for acute asthma,[83, 157] the effectiveness of educational interventions directed from the ED has not been evaluated with the same rigor as asthma medications.[147] In this study, referral to asthma education was required by 93% of the study population.

Treatment with regular daily doses of ICS[57-59] or ICS/LABA[60, 62, 237-240] is recommended for patients with asthma based on their positive impact on the reduction of asthma symptoms, improving lung function, and mitigating the risk of severe exacerbations, hospitalizations and death.

The fact that almost 40% of the study population experiencing an asthma exacerbation was corticosteroid naïve at ED presentation, that 11% required step-up in management, and that a considerable proportion of patients prescribed with ICS agents required reinforcement of compliance may reflect a general under-recognition of the importance of anti-inflammatory agents in controlling symptoms and reducing exacerbations by the PCPs, patients, or both.[39]

Several barriers to the application of evidence in clinical practice may be influencing the presence of the gaps in asthma care identified in the study population.[189, 241] For example, some of the current recommendations for preventive care are supported by interventions of uncertain clinical significance (e.g., smoking cessation and influenza vaccination strategies); the evidence for other (e.g., referral to asthma education programs) relies on interventions with limited scope and external validity. For those preventive actions supported by robust evidence (e.g., corticosteroid treatment, and use of spacer devices and of written AAPs), patients' and clinicians' preferences, expectations and knowledge could influence their adherence and effectiveness in real-world settings; this may explain some of the variations in asthma management observed within and across individual practices. Finally, contextual factors such as differential access, resources, affordability and incentives to change may have an important effect on patients' and physicians' attitudes and practices, respectively. Strategies targeting the sustained

implementation of various recommendations infrequently support current guideline recommendations. [1, 44, 116]

5.4.1 Limitations

There are several limitations to this analysis that require discussion. First, given that the exploration of outpatient asthma care gaps at ED presentation was not the main objective of the *NCT01079000* study, details on other preventive actions recommended by the guidelines (e.g., physical activity, nutrition and avoidance of occupational exposures/medications/environmental pollutants that make asthma worse) were not collected. Analyses were mainly descriptive and limited to the preventive factors obtained in the study through ED interview and chart review data-collection methods (susceptible to recall and reporting bias); a more detailed exploration and analysis of some of these outpatient care gaps (e.g., training received regarding the appropriateness of inhaler techniques, type education patients' have been referred to and compliance to it, and content/structure/adaptation of written AAPs, type of counseling on smoking cessation patients' have received) would have been very informative. The comprehensiveness and accuracy of the data presented rely on information collected in a standardized manner by trained research staff and on a systematic and reliable adjudication process. Second, the study was conducted in six urban EDs (mostly academic) in two Canadian cities, so the generalizability of results to other centers and jurisdictions, might be of concern. Finally, this study did not examine admitted patients,

patients with mixed entities (e.g., asthma-COPD overlap syndrome), and those with complicated presentations, perhaps also limiting the external validity of these findings.

The identification and discussion of gaps in asthma ED care such as the potential underuse of spirometry and overuse of other procedures (e.g., chest radiography, laboratory tests) were not the focus of this analysis. These gaps may also be influenced by the lack of evidence on their benefits, risks and costs.

5.5 Conclusion

While there is no consensus on the preventive actions that all patients with asthma should be considering as part of their integral management, this analysis provided a good description of some of the most common preventive actions identified as priorities for action by experts in the field. Despite a long history of asthma and relative stability reported by this sample of patients with acute asthma, a large number of associated care gaps were identified. These gaps were identified in patients facing an exacerbation that resulted in an ED presentation with no hospital admission; evidence, patients', clinicians', and contextual factors that could be influencing these observations have been highlighted. Insufficient evidence may exist to support some of the recommendations provided in the current asthma guidelines, which could partially explain these findings. Future research should focus on novel strategies aiming to close of the existing gaps in asthma care.

Table 5-1 Characteristics of the study population.

	Study population n= 367
Demographics, n (%)	
Age (years)	28 (22, 37)
Female sex	232 (63.2%)
Marital status (most common: single)	213 (58.0%)
Post-secondary education	209 (56.9%)
White racial or cultural background	271 (73.8%)
Chronic asthma factors	
Smoking status, n (%)	
Never	177 (48.2%)
Previous	80 (21.8%)
Current	110 (30.0%)
Asthma history (years), median (IQR)	20 (13, 25)
Had last ED visit (years), median (IQR)	1.5 (0.5,5)
Hospitalizations for asthma in past two years, median (IQR)	0 (0, 0)
Ever intubated for asthma, n(%)	29 (7.9%)
Health care utilization	
Have a Family doc, n (%)	273 (74.4%)
Family physician most frequently treats his/her asthma, n (%)	225 (61.3%)
ED is the usual site for acute asthma care, n (%)	191 (52.0%)
Contacted a heath care provider prior to the ED visit, n (%)	87 (23.7%)
Contacted his/her family physician/physician at a Walk-in Clinic	30/87

Insurance status	
Health insurance helps with cost of asthma medication, n (%)	264 (71.9%)
Percentage of asthma medication costs paid by patients with health insurance, median (IQR)	20 (0, 20)

Note: ED = emergency department; interquartile range (IQR) is presented as 25th and 75th percentiles.

Table 5-2 Acute asthma presentation and ED management.

	Study population n= 367
Clinical presentation	
CTAS Score, n (%)	
1,2	64 (17.4%)
3	245 (66.8%)
4,5	58 (15.8%)
Arived by EMS, n (%)	19 (5.2%)
Days with respiratory symptoms getting worse, median (IQR)	2 (0.5, 5)
Days with activity limitation due to asthma, median (IQR)	1 (0, 3.5)
Number of inhaled β-agonist puffs within 24 hours of ED, median (IQR)	8 (2, 16)
Vital signs, median (IQR)	
Pulse	98 (88, 110)
Respiratory rate	20 (18, 24)
SaO_2 (On room air)	97 (95, 98)
Temperature (C^o)	36.5 (36.2, 36.8)
ED management	
Received inhaled β-agonists in the ED, n (%)	349 (95.1%)
Number of puffs in the first hour, median (IQR)	0 (0, 4)
Number of puffs over ED stay, median (IQR)	12 (4, 18)
Given any systemic corticosteroid treatment, n (%)	279 (76.0%)
Time in min to systemic corticosteroid treatment, median (IQR)	28 (15, 53)
Received inhaled anticholinergics, n (%)	318 (86.7%)

Number of puffs in the first hour, median (IQR)	0 (0, 4)
Number of puffs over ED stay, median (IQR)	10 (4, 15)
$MgSO_4$ medication in the ED, n (%)	18 (4.9%)
Lung Function, median (IQR)	
Earliest PEF (n=294)	294 (220, 350)
Final PEF (n=344)	350 (299, 425)
Change in PEF (n=217)	71 (35, 131)
Earliest %Predicted PEF (n=292)	60 (47, 76)
Final %Predicted PEF (n=344)	76 (61, 90)
Change in %Predicted PEF (n=217)	16 (7, 28)
FEV_1 % Predicted at discharge (n=344)	78 (62, 93)
FEV_1/FVC % (n=344)	76 (66, 84)
Other tests	
Blood work, n (%)	75 (20.4%)
Chest radiography, n (%)	179 (48.8%)
Electrocardiogram, n (%)	48 (13.1%)
Sputum collection, n (%)	2 (0.5%)
ED length of stay, median (IQR)	
ED length-of-stay (hours)	4.2 (3.2, 5.5)
ED length-of-stay ≥ 6 hours	75 (20.4%)

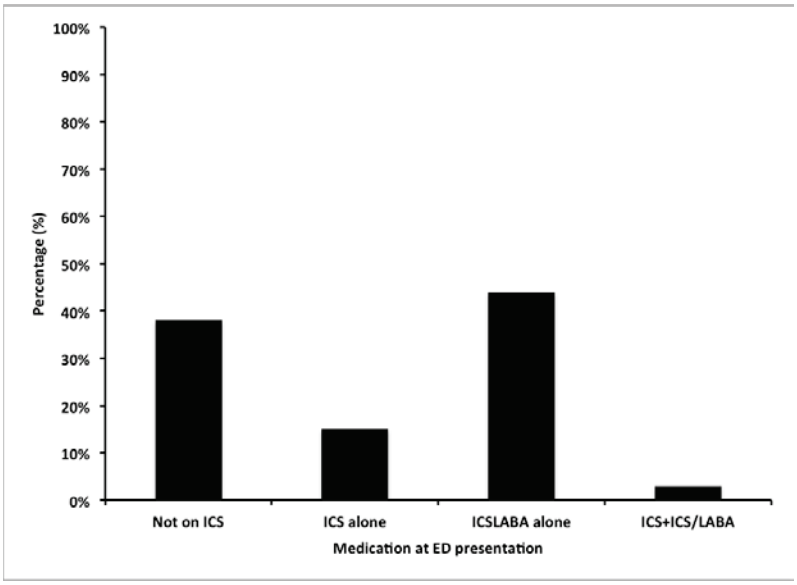
Note: CTAS = Canadian Triage and Acuity Scale; EMS = emergency medical services; ED = emergency department; SaO_2 = oxygen saturation; $MgSO_4$ = magnesium sulfate; PEF = peak expiratory flow; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; interquartile range (IQR) is presented as 25^{th} and 75^{th} percentiles.

Table 5-3 Patient needs at emergency department presentation.

Factors	Study population n= 367
Spacer device, n (%)	
Required	215 (58.6%)
Need reinforcement of compliance	57 (15.5%)
Influenza vaccination, n (%)	233 (63%)
Asthma Action Plan (AAP), n (%)	
Required	357 (97%)
Need reinforcement of compliance	4 (1.1%)
Counselling on smoking cessation (current smokers only), n (%)	113 (30.8%)
Referral to asthma education, n (%)	341 (92.9%)
Medication, n (%)	
Need reinforcement of compliance with preventer medication	144 (39.2%)
Add preventer medication/ICS	138 (37.6%)
Add ICS/LABA combination agents	39 (10.6%)

Note: ICS = Inhaled corticosteroids; ICS/LABA = Inhaled corticosteroids/long-acting β-agonists.

Figure 5-1 Medication at emergency department presentation.



Note: ICS = Inhaled corticosteroids; ICS/LABA = Inhaled corticosteroids and long-acting β_2-agonist.

Appendix 5-1 Notification of ethics approval.

Approval

Date:	May 25, 2012
Study ID:	Pro00029699
Principal Investigator:	Brian Rowe
Study Title:	ED-directed interventions to improve outcomes after asthma exacerbations
Protocol Number:	Version 1
Protocol Date (first submitted):	5/1/2012
Approval Expiry Date:	May 24, 2013
Sponsor/Funding Agency:	CIHR - Canadian Institutes for Health Research CIHR

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel . Your application, including revisions received today, has been reviewed and approved on behalf of the committee.

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. Subject consent for access to identifiable health information is required for the research described in the ethics application, and appropriate procedures for such consent have been approved by the Health Research Ethics Board - Health Panel. In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (May 24, 2013), you will have to re-submit an ethics application.

The membership of the Health Research Ethics Board - Biomedical Panel complies with the membership requirements for research ethics boards as defined in Division 5 of the Food and Drug Regulations and the Tri-Council Policy Statement. The HREB - Biomedical Panel carries out its functions in a manner consistent with Good Clinical Practices.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health approval should be directed to (780) 407-6041. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,

Doug Gross, Ph.D.
Associate Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

6 EMERGENCY-DEPARTMENT DIRECTED INTERVENTIONS TO IMPROVE OUTCOMES AFTER ASTHMA EXACERBATIONS: A RANDOMIZED TRIAL

6.1 Introduction

Despite increased understanding of its diagnosis and effective management, asthma remains a major public health problem.[7, 242, 243] Negative outcomes resulting from exacerbations include frequent emergency department (ED) visits and hospitalizations, school and work absenteeism, impaired health related quality of life (HRQoL), significant costs to the health care system, and, occasionally, death.

The most recent asthma guidelines have added dedicated content to the assessment of asthma control, the minimization of the risk of adverse outcomes and highlighted the essential role that individualized care, patient education and effective partnerships between patients and their primary care providers (PCPs) play in the achievement of these goals.[1] Regardless of these recommendations, many Canadians visit EDs for asthma exacerbations. Furthermore, a significant proportion of those who are treated and discharged relapse within four weeks of their visit, even when provided with evidence-based ED care.[139] Importantly, some ED patients with asthma have limited or no access to PCPs and when they have it, some patients don't consider a post-discharge follow-up necessary.[120] Finally, when a post-ED follow-up visit with a PCP occurs, many encounters don't address important gaps in care nor are they

evidence-based. As a result, a proportion of patients leave their PCP office without instructions on how to recognize early warning signs of loss of asthma control and on the steps to follow in response to those signs.[121]

A gap between evidence-based best practices and the actual care delivered to patients with asthma exists; this gap may explain the suboptimal quality of care and poor health outcomes after asthma exacerbations. While a number of pharmacologic interventions have been associated with a reduction in relapses after ED visits for asthma,[90,102] only a few non-pharmacologic interventions focused on individualized PCP and patient -centered approaches have been examined using rigorous research methods.[117, 118, 244] In addition, the following elements of high-quality care have not been well described or deployed: education components; strategies targeting the sustained implementation of various recommendations;[147] and methods to facilitate the transitions in care between the ED and community-based follow-up with PCPs.[245]

The primary objective of this study was to determine if ED-directed interventions focused on increasing PCPs-patient follow-up using an incremental approach of local opinion leader (OL) letter to PCPs or the addition of a care manager (CM) educating patients on self-management, reduced relapses within 90 days compared to usual care (UC) in patients with moderate to severe acute asthma discharged from the ED.

The secondary objectives of this study aimed to determine if the proposed interventions: a) decreased relapses (number) and increased

the time to relapse within 90 days of the ED visit; b) increased the proportion of follow-up visits with a PCP within 30 days of the ED visit; c) improved patients' HRQoL within 90 days of the ED visit.

6.2 Method

6.2.1 Study design:

Prospective, randomized, open label, blinded endpoints ascertainment (PROBE) study with a 1:1:1 allocation ratio to three intervention arms.

***Changes to the study design:** Due to an error in the allocation ratio in one of the main study sites (2:1:1), the allocation ratio was changed to 0.1:1:1 during the last four months of study enrolment. This protocol deviation was detected on 29th August 2015 and reported to the University of Alberta (UofA) health ethics research board (HERB) (see Appendix 1 for more details).

6.2.2 Participants:

This study involved adult patients presenting to one of six EDs in Edmonton and Calgary (Alberta, Canada) who received treatment for acute asthma that resulted in discharge between June 2012 and December 2015. The study protocol was registered (Clinical Trials.gov: https://clinicaltrials.gov; NCT01079000) and approved by the UofA HREB (Pro00029699).

6.2.2.1 ***Selection criteria:***

6.2.2.1.1 Inclusion criteria:

1. Age 17-55 years old;
2. Patients treated and discharged from one of the study sites with a physician diagnosis of acute asthma during the study period;
3. Patients must have had a previous physician-diagnosis of asthma and an exacerbation diagnosed by the ED physician (e.g., past asthma history, increased asthma symptoms, recorded response to short acting β_2-agonists (SABA) in the ED, and). In the event of a new diagnosis, the patient was still eligible for the study if the treating physician felt that the history was compatible with a diagnosis of asthma.

6.2.2.1.2 Exclusion criteria:

1. Patients with asthma who were primarily cared for by a Respirologist;
2. Patients not seen by an emergency physician in the ED (e.g., direct referrals);
3. Physician diagnosis of acute exacerbation of chronic obstructive pulmonary disease (COPD);
4. Radiologically *confirmed* pneumonia during the 10 days preceding study entry;
5. Patients with an active history of bronchiectasis, cystic fibrosis, or lung cancer;

6. Clinically confirmed congestive heart failure at ED presentation;
7. Patients not able/unwilling to perform spirometry or peak expiratory flow (PEF) assessment;
8. Inability to provide informed consent or comply with the study protocol due to cognitive impairment, language barrier, or no contact details;
9. Previous participation in the study;
10. Ongoing enrolment in another clinical study.

6.2.3 Study setting:

Study sites included urban teaching centres: four Edmonton EDs (University of Alberta Hospital [UAH], North East Community Health Centre [NECHC], Grey Nuns Hospital [GNH] and Sturgeon Community Hospital [SCH]) and two Calgary EDs (Foothills Medical Centre and Peter Lougheed Centre).

6.2.4 Interventions:

After ED discharge study participants were randomized to one of the following intervention arms:

6.2.4.1 Usual care:

Provision of verbal instructions by the treating emergency physician; and of standardized written discharge instructions/plan (2-page pamphlets detailing medications and expected health outcomes until follow-up with their PCP), asthma action plan (AAP; stepped approach to

mitigate asthma exacerbation severity) and information on asthma medications (the last two available from the Canadian Thoracic Society [CTS]) by a research nurse. Finally, a copy of the ED chart was faxed to the patient's PCP office within the 24 hours of enrolment [48 hours during weekends]) (Appendix 2);

6.2.4.2 Usual care described above + personalized fax to the patients' PCPs (OL-letter):

Input from patients with asthma and PCPs helped tailoring the content, style and delivery methods of the personalized fax to the patients' PCPs-study intervention (Chapter 4). The OL-letter included a brief report of the patient ED diagnosis, treatment and post-ED prescription, and a summary of the current asthma guideline-recommendations for ambulatory care follow-up timing and content based on the gaps in care identified at ED presentation (standardized focus on spacer device use, influenza immunization, written AAP use, smoking cessation, asthma education and long-term medication recommendations - Appendix 3) signed by a local Respirologist (one in Edmonton [MB] and one in Calgary [RL]). The OLs were volunteers who were recruited through solicitation (personal approach) by the principal investigator of this study; they are both Respirologists who are locally and nationally recognized for their academic and clinical leadership roles in asthma care.[246] They self-identify as OLs and local physicians similarly agree. Since no universal evidence-based recommendation existed regarding the timing of the PCP follow-up,

a review of the patient within 1-2 weeks of the ED visit was recommended. The OL-letter was faxed to the patient's PCP office within the 24 hours of enrolment [48 hours during weekends]).

6.2.4.3 Usual care described above + personalized fax to the patients' PCPs described above + involvement of a care manager educating patients on self-management:

Via telephone, a certified asthma educator (with background on nursing or respiratory therapy) reviewed patients' symptoms, self-management strategies (potential asthma triggers and early warning signs, AAP) and encouraged follow-up with their PCP within the first week of ED discharge using standardized scripts (Appendix 4). These scripts were designed following the *five major steps to intervention (Five A's model: Ask, Advise, Assess, Assist and Arrange);*[247] duration of the phone call as well as any additional activities performed as per patients' request were documented (e.g., second call).

- For those patients who reported not to be linked to a PCP at ED presentation, a PCP from the Edmonton/Calgary area (accepting patients) was assigned before or immediately following ED discharge by the clinical research staff.

6.2.5 Pre-specified outcomes:

6.2.5.1 Primary outcome (proportion of first asthma relapse):

Relapse occurrence (yes/no) in this study was defined as *an unscheduled medical visit to a walk-in clinic, family doctor's office or an ED resulting from the patient's perceived need for further asthma treatment* within 90 days of ED discharge. This outcome has been used successfully, and is widely accepted as a clinically relevant outcome.[248-251] Relapses were assessed at 30 and 90 days (+/- 5 days) by patient self-report (Appendices 5 and 6).

6.2.5.2 Secondary outcomes (SOs):

SO1 and 2: Total number of asthma relapses and time to relapse: The number of relapses up to 90 days and time to first asthma relapse were recorded.

SO3: Follow-up with a PCP (proportion of first follow-up with a PCP): The occurrence of a self-reported follow-up with a PCP (yes/no) in this study was defined as a patient having a face-to-face meeting with their PCP (or equivalent) within 30 days after discharge. Telephone interactions with the PCP's office were classified as "no PCP follow-up".

SO4: Health related quality of life: Health related quality of life was assessed at baseline, 30 and 90 days (+/- 5 days) using a disease specific, validated instrument for asthma patients (asthma quality of life questionnaire [AQLQ]; Appendix 7).[252 253 254 255]

Other outcomes of interest were measured such as hospitalizations and deaths during the study period, as well as the proportion of patients on inhaled corticosteroids (ICS) and combination controller agents (inhaled corticosteroids/long-acting β_2-agonists [(ICS/LABA]) at 90 days.

6.2.5.3 Outcome verification process:

The primary and secondary outcomes (SO1, 2 and 3) were measured by patient self-report at 30 and 90 days after discharge and validated by obtaining charts and ED records when possible. Outcome verification was systematically performed by the research team at 90 days through *Net*Care (the provincial electronic medical record for Alberta), the Emergency Department Information System (EDIS) in Edmonton and the Sunrise Clinical Manager (SCM [with historical data from Regional Emergency Department Information System-REDIS]) in Calgary, and by calling the PCPs' offices. A standardized form was used (Appendix 8).

6.2.5.4 Adjudication of the primary outcome:

For each suspected relapse, study personnel prepared a full report describing the circumstances of the suspected relapse (including patient report and verified information). Two study investigators (BHR and CVR), blinded to the study interventions, independently reviewed the data and reported as to whether the relapse satisfied the study operational definition. Disagreements were resolved by consensus prior to un-blinding.

- Asthma relapses included verified/patient self-report of an event that matched the definition of the primary outcome (first event resulting or not in change in treatment and/or in hospital admission).
- Follow-up with a PCP included verified/ patient self-report of an event that matched the definition of this secondary outcome (first event resulting or not in change in treatment).

6.2.6 Sample size:

The study protocol sample size included a total of 366 patients (122 per group), this number took into consideration potential ~10% attrition. Sample size calculations were based on the primary outcome (proportion with first relapse at 90 days)[164, 256, 257] and a chi-square test of association and post-hoc tests (UC vs. PF, PF vs. CM). Approximately 40% of the UC group were expected to have a relapse based on estimates from previous studies.[120] Based on minimal clinically important differences (MCID) reported in other acute asthma trials,[258] a clinically relevant effect was considered to be a 50% relative reduction to 20% in the PF group and 5% in the CM group on 90-day relapses. A sample size of 110 per group was estimated to permit the detection of a moderate effect size of at least 0.171 (80% power, $\alpha = 0.05$), a more dramatic effect than the 50% MCID for the three groups, and a difference between UC and PF of 50% (i.e., 40% vs. 20%) and between PF and CM of 75% (i.e., 20% vs. 5%) using two-sided z-tests, 80% power, $\alpha=0.025$.

6.2.7 Patient sequence generation, allocation to the study interventions and blinding:

Trained research staff screened consecutive patients presenting to the study sites for shortness of breath, wheezing, cough/congestion and chest pain on a daily basis in Edmonton (UAH: 08:00-23:00 M-F; 10:00-18:00 S&S; NECHC/SCH: 10:00-18:00 M-F; GNH: respiratory therapist dependent) and Calgary (on-call research assistants: daily) during the study period (Appendix 9). Following treatment by the physician (pre-post treatment pulmonary function tests, nebulized SABA, etc.) and once the discharge decision was made, those fulfilling the enrolment criteria and providing written informed consent (Appendix 10) were interviewed for the collection of baseline information (Appendix 11); relevant ED information was collected using chart review methods (Appendix 12). All eligible patients were reported to one of two study investigators (BHR or CVR) as soon as possible after enrolment. These investigators allocated each patient to one of the three study arms using computer generated random number services provided by an independent organization (EPICORE Centre; www.epicore.ualberta.ca). Patients were allocated using centralized permuted block randomization with variable block sizes at each site to maintain balance over seasons and study sites. Finally, two research staff (one in Edmonton and one in Calgary) not involved in patient enrolment or in outcome assessment, delivered the corresponding study intervention UC: fax of ED record to PCP; PF: fax of ED

record and OL-letter to PCP; CM: fax of ED record and OL-letter to PCP, and notification of CM).

The two study investigators in charge of the randomization were not blinded to the assigned interventions; however, neither kept track of the sequence of randomization. The treating ED physicians, and the research staff in charge of patient enrolment and outcome assessment were blinded to the allocation status. Patients and staff involved in the CM arm were not blinded to their intervention.

6.2.8 Statistical analyses:

Analyses were performed using Stata Statistical Software® (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Baseline characteristics were summarized (e.g., frequencies and medians and interquartile ranges [P_{25}, P_{75}] as continuous variables were non-normally distributed) and compared among the allocation groups (intention to treat [ITT] approach) using Kruskal-Wallis tests and chi-square tests for discrete variables (or Fisher's Exact tests). The proportion with first asthma relapse (primary outcome) was reported by study intervention arm and associated 95% confidence intervals (CIs) were calculated. A chi-square test of association compared proportions among groups and *if statistically significant ($p<0.05$)* separate proportion tests compared pairs of groups (e.g., UC vs. PF) adjusted for multiple testing (Bonferroni correction). The intra-cluster correlation coefficient (ICC) was calculated to assess for potential contamination among those PCPs who were assigned more than one patient

in the study. A multivariate analysis using generalized estimation equations was performed to adjust estimates of effect for important factors with potential clinical imbalance in the baseline comparisons as well as to adjust for the potential of site-specific differences in effectiveness.[259] Odds ratios (OR) and associated 95% CIs were reported.

Secondary outcomes were summarized by study intervention arm and estimates and 95% CIs were reported. Kruskal-Wallis tests assessed differences in the total number of relapses (SO1) by group and differences in HRQoL at different time points (SO4) by group. Kaplan-Meier curves displayed time to relapse within 90 days (SO2) by group (if relapse did not occur, data were censored at 90 days) and log-rank tests compared groups. A chi-square test of association compared the proportion with PCP follow-up within 30 days (SO3) by group.

No interim analysis was planned or conducted for this study. Finally, some post-hoc sensitivity and subgroup analyses were conducted to explore the primary outcome results. For the sensitivity analyses, different operational definitions of the primary outcome, as well as considering a different analytic approach (per protocol [PCP vs. no PCP visits after ED discharge]), were explored. For the subgroup analyses, study, patient, health provider (emergency physicians and PCPs) and system relevant factors were explored. Basic information (e.g., sex, year of graduation, specialty, interests) regarding the PCPs was obtained from the College of Physicians and Surgeons of Alberta public website (http://www.cpsa.ca).

6.2.9 Data management and quality assurance:

During the study period a screening/enrolment log was maintained; Refusals, Misses and Other exclusions (RMO) were documented to determine the generalizability of the sample.

Study data were collected and managed (including the outcome adjudication) using Research Electronic Data Capture (REDCap; Vanderbilt University; Nashville, TN, USA) tools hosted at the University of Alberta.[260] REDCap is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The REDCap databases mirrored the data collection forms and had required/restricted values, which allowed centralized checking and monitoring. Periodic site monitoring and feedback activities were performed.

6.2.10 Funding source:

This study was co-funded by the Canadian Institutes of Health Research (CIHR operating grant # RES0011584), knowledge translation (KT) Canada, and the Emergency Medicine Research Group (EMeRG); these funding sources had no role in the design, conduct or knowledge dissemination products of this study.

6.3 Results

A total of 943 patients presenting to the Edmonton and Calgary study sites with respiratory symptoms compatible with asthma were screened for inclusion between June 2012 and December 2015. Figure 6-1 summarizes the number of patients randomized (n=367) after considering exclusions and those patients who were consented but were not enrolled. Twenty-three patients met exclusion criteria after providing consent to participate in the study (late exclusions) and 23 were admitted after consent and enrolment (screen failures); four protocol violations were detected and reported to the UofA HERB (see Appendix 1 for more details). While some patients were lost to follow-up, data on the main study outcome and SO1, 2 and 3 were available for the total study sample through the outcome verification process.

The study population was younger than the population screened but not enrolled (median age: 28 [IQR: 22, 37] vs. 35 [IQR: 25, 48]; $p<0.001$); however, their sex distribution was similar (female sex: 64% vs. 59%; $p=0.362$). No significant baseline differences were observed among the study groups (Tables 6-1 and 6-2).

6.3.1 Intervention fidelity

Fidelity to theory: The education provided in this study followed the recommendations of the current clinical practice guidelines.[1] The OL-based intervention was tailored based on the input from patients and PCPs engaged in the cross-sectional study (Chapter 3). While no specific

theoretical framework supported the study interventions, several strategies aiming behavior change in both patients and PCPs were targeted: education, communication and guideline recommendations.[261]

Provider training and intervention implementation: No changes in the pre-defined strategies described in the methods section occurred during the study conduct.

Intervention receipt: Approximately 90% of the OL-letters (one-page personalized summary and list of recommendations) were successfully sent via fax within the 48-hour time frame and confirmation of successful delivery at the PCP office was received in all the study cases assigned to the PF arm. The CM telephone contact occurred within 7 days in more than 80% of cases, and 62% of the 94 effective contacts (17 patients could not be reached after 5 attempts) resulted in a request for a second contact.

Intervention enactment: Factors that could have reflected that either patients or PCPs put new behaviours into practice were measured and monitored during the study period; these factors were considered during the post-hoc exploratory sub-group analyses that were completed in this study.

6.3.2 Study outcomes

The primary and secondary outcomes reported by the study participants and those adjudicated are summarized in Tables 6-3 and 6-4.

The study interventions (PF and CM) significantly increased the proportion of first PCP follow-up visits within 30 days when compared to UC (PF: 45.5%; CM: 47.7%; UC: 29.5%; p=0.004). Based on an absolute increased risk of 0.16 (95% CI: 0.03, 0.28), the number needed to treat (NNT) for benefit with the PF was 6 (95% CI: 3.5, 30.5). These differences were diluted at 90 days when approximately half of the patients allocated to the three study arms had visited a PCP (Figure 6-2). The median time to first PCP follow-up visit within 90 days was significantly lower in the study intervention arms when compared to UC (PF: 13 days; CM: 16 days; UC: 24 days; p=0.036).

Most of the first asthma relapses occurred within the first 30 days of ED discharge and the proportion of first asthma relapses within 90 days of ED discharge was significantly higher in the intervention arms when compared to UC (PF: 28.2%; CM: 18.9%; UC: 12.3%; p=0.006) (Figure 6-3). Based on an absolute increased risk of 0.16 (95% CI: 0.05, 0.25), the NNT for harm was 6 (95% CI: 3.9, 19.0) for the PF. A statistically significant decrease in the time to asthma relapse was observed in the intervention arms at 90 days (Log-rank test= 0.007; Figure 6-4). A median number of one asthma relapse occurred within 90 days in the three study arms. The PF intervention was associated with a statistically significant increase in relapses when compared to UC: unadjusted OR=3.1; 95% CI: 1.6 to 6.1. This association was attenuated (adjusted OR=2.8; 95% CI: 1.7 to 4.6) after controlling for factors with potential clinical imbalance in the

baseline comparisons (sex, post-secondary education, time since last ED visits, usual site for acute asthma care [ED], ICS/LABA medication at presentation, stepped-up treatment approach at ED discharge, and length of stay [LOS]>6 hours); however, ICS/LABA at presentation was independently and significantly associated with relapse (adjusted OR=1.8; 95% CI: 1.1 to 3.1) (Table 6-5).

A consistent improvement in HRQoL (based on the AQLQ overall scoring) was observed at 30 days when compared to baseline among all three study groups and this improvement persisted at the 90-day follow-up; however, no differences were found among the groups (Figure 6-5).

No statistically significant increase in the proportion of hospitalizations within 90 days was observed among the treatment arms and no deaths were documented during the study period. Finally, the proportion of patients on ICS medication at 90 days was very similar to the one at ED presentation (Figure 6-6).

6.3.3 Sensitivity analyses

In the three study arms, the proportion of relapses at 30 and 90 days consistently and progressively increased when exploring outcome data obtained from 1) self-report, 2) adjudication, 3) adjudication considering those PCP follow-up visits that included the *addition of prednisone*, and 4) those PCP follow-up visits that included the *addition of prednisone or antibiotics* as asthma relapses. A considerable proportion of PCP visits including the *addition of prednisone* and the *addition of*

prednisone or antibiotics occurred in the PF and CM arms (Figure 6-7); the addition of prednisone was not related to the lack of prescription at ED discharge.

Twenty-one percent (43 of 210) of those patients who had a PCP within 90 days of ED discharge had an asthma relapse. Among those patients who relapsed, 39% (n=27) were never seen by their PCP during the study period, 26% (n=18) had a PCP visit before relapse occurrence, 29% (n=20) had a PCP visit after relapse occurrence, one patient relapsed the same day they visited their doctor and in four patients the date of PCP visit was unknown (patients didn't report dates and we were unable to confirm them during the verification process). The distribution between those who had a PCP visit before and after the asthma relapse was similar in the UC arm (before: 4/18 vs. after: 4/18) and in the PF arm (before: 9/31 vs. after: 8/31) but not in the CM arm (before: 5/21 vs. after: 8/21).

Sub-group analyses

Study factors: No statistically significant differences were found among the three study arms when comparing the proportion of new PCPs assigned in the study (UC: 34%; PF: 30%; CM: 22%) and the proportion of patients sharing a PCP (UC: 40%; PF: 37%; CM: 39%). A hundred and forty-one (38%) patients shared a PCP and the maximum number of patients seen by the same PCP was 5 (ICC=0.201).

Patient-related factors: Apart from those summarized in Tables 6-1 and 6-2, no statistically significant differences were found among the three

study arms when comparing the proportion of patients taking prednisone (UC: 89%; PF: 87%; CM: 97%) or using steroid inhalers (UC: 71%; PF: 63%; CM: 75%) as prescribed at 30 days (both considered proxy measures for intervention enactment).

Health provider-related factors (emergency physicians): No statistically significant differences were found among the three study arms when comparing the proportion of ICS medication prescribed at discharge (Figure 5); however, their treatment decisions at ED discharge (stepped-up vs. non stepped-up approach were different among the study groups: (UC: 58% vs. PF: 48% and CM: 41%). The proportion of patients in whom no change in treatment occurred during an asthma relapse was higher in the PF intervention arm within 30 days (UC: 1.4% vs. PF: 5.5% and CM: 1.8%) and 90 days (UC: 3.4% vs. PF: 9.1% and CM: 3.6%).

Health provider-related factors (PCPs): Primary care provider characteristics were very similar among the three study arms; most physicians were male (62%), family doctors (59%); the median year of graduation was 1992 [IQR= 1984,2001]) and 3.8% reported special interest in asthma. Overall, in the PCP follow-up visits documented within 90 days (patient self-report), more of the preventive actions identified by the adjudicators were discussed in the intervention arms when compared to the UC arm (Table 6-6). The proportion of patients in whom no change in treatment occurred during a PCP visit was higher in the PF intervention arm within 30 days (UC: 14% vs. PF: 24% and CM: 20%) and 90 days

(UC: 24% vs. PF: 31% and CM: 29%). These two measures were also considered proxy measures for intervention enactment.

System factors: No statistically significant differences were found among the three study arms when comparing insurance coverage and medication use in the last year (Table 6-1).

6.4 Discussion

Discharge after assessment and treatment is the most common outcome in patients presenting to the ED with acute asthma in Canada and the Unites States (US).[207] Despite adequate evidence-based care, many patients do not receive effective follow-up or interventions to target gaps in care.[139] This study was designed to increase the frequency, timeliness and effectiveness of these follow-up visits in the hope of reducing relapses, improving HRQoL and impacting asthma care. Using randomized controlled trial methods, patients were allocated to receive UC, personalized OL-letters faxed with recommendations to their PCPs or CM guidance on self-management to patients, in an incremental approach to achieving these goals.

Primary care provider guidance on follow-up care by a local OL and CM guidance on patients' self-management similarly increased the proportion of PCP follow-up visits within 30 days; however, this difference was mitigated by 90 days. Moreover, this outcome would still be considered sub-optimal (only half of the patients on each study group was seen by their PCP after 90 days of being discharged). Times to PCP

follow-up visits within 30 days suggested most patient symptom review and medication adjustment occurred at approximately the second week of ED discharge with these extra-efforts (faxing a copy of the ED chart and the OL-letter, and contacting the patient within the first week of ED discharge).

Counterintuitive results were observed on the primary study outcome; the proportion of asthma relapses within 90 days was significantly higher in the study intervention arms, particularly in the group which received the PF. Patients allocated to the intervention arms also relapsed sooner than those allocated to UC. Most of the relapses occurred within the first 30 days and times to asthma relapse suggested these undesired events occurred most commonly within the first week of ED discharge.

Health related quality of life improved in all study patients at 30 days regardless of the study intervention and this improvement persisted at 90 days. The asthma relapses that occurred during the follow-up period didn't seem to negatively influence patient scoring of the factors included in each of the AQLQ domains. Finally, while the proportion of hospitalizations within 90 days was higher in the study intervention arms than in the UC arm, it was lower than the current admission patterns in North America.

Asthma is a complex respiratory condition and poor health outcomes after asthma exacerbations may be influenced by suboptimal

quality of care resulting from a combination of issues (e.g., delayed/no medical follow-up, non-evidence based management, barriers to medication or primary care access, poor patient adherence/compliance). This study assessed the effectiveness of multifaceted and tailored ED directed interventions based on promising strategies to influence clinical practice (local OL-guidance to PCPs)[188] and increased patients' capacity to self-manage their asthma (CM-guidance on self-management to patients).[262] The results don't support the original hypothesis that increased follow-up by the PCP after an asthma exacerbation would necessarily decrease the resource utilization. One may reasonably ask: "How are these results explained?" Several study design, patient, health provider and system factors could have influenced these results; these factors were explored when possible.

6.4.1 Study factors:

The statistical balance among the three study arms in the patient factors examined in the study suggests the protocol deviation that resulted in an alteration of the allocation ratio for the study randomization sequence was compensated by the complete recruitment of the originally planned sample size and the assessment/verification of all of the study primary outcomes. It's unlikely that this error had differential effects in the study results.[263]

The UC arm in fact represents *enhanced* UC. A copy of the ED chart was faxed to all PCPs in an effort to disentangle potential *reminder*

and *Hawthorne* effects derived from written materials sent to the PCPs. Discharge plan packages (including written AAPs) are not always provided to patients in the ED; they were provided to all study patients in an effort to control for potential differential effect of these interventions. While we underestimated the beneficial effects of the UC arm components, these effects don't explain the counterintuitive results observed for the primary outcome.

One component of the fidelity of the UC and PF interventions was not completely assessed (intervention receipt).[159] The research staff who sent the fax (either the ED chart or the ED chart + OL-letter) to the PCP office obtained confirmation of receipt in all study participants; however, the study didn't measure if the PCPs red these materials or the action they took after reading it (e.g., giving directions to their nurses/receptionist to divert patients if there was limited capacity to assess them). Finally, the CM intervention was delivered as intended to 85% of the population assigned to that study arm. Different levels of exposure related to these factors should be balanced among the study arms due to the randomization and analytic (ITT) methods employed. Other components of intervention fidelity were either standardized (provider characteristics, training and intervention implementation) or explored in the post-hoc subgroup exploratory analyses with no significant findings (proxy measures for intervention enactment).

A new linkage to a PCP compared to an established relationship

with a PCP, had the potential to influence the study results; however, the proportion of new PCPs assigned to the study patients was similar among the study groups. It's unlikely that this exposure factor had differential effects in the study results.

6.4.2 Patient factors:

Patient factors examined in this study (e.g., asthma history, severity, ED management, medication at presentation and discharge) were statistically balanced among the study groups. Patient factors with potential clinical imbalance were included in the adjusted analyses and the direction of the association between the intervention arms and the risk of relapse occurrence remained the same. Medication at presentation (ICS/LABA) was associated with an increased risk of relapsing within 90 days which supports previous research findings indicating a strong association between this factor and relapse in patients who are seen and discharged from the ED for acute asthma.[139] Patients' skills to learn, understand and implement effective-self management were not measured at baseline or during the follow-up. Less health literacy has been associated with poor longitudinal asthma outcomes; however, this issue was not measured in the current study.[264]

6.4.3 Health provider-related factors (emergency physicians):

ED physicians were blinded to the study objectives and to the allocation of the interventions. Differences in the level/intensity of their

verbal instructions to patients should have been balanced among the study arms due to the randomization process. In addition, ED management and prescriptions were balanced among the study groups; while not ideal, differential evidence-based treatment decisions at ED discharge (stepped-up vs. non stepped-up) are unlikely to explain the study results.

6.4.4 Health provider-related factors (PCPs):

The fact that more than one study patient could have been followed-up by the same PCP introduced the chance for contamination; which have been controlled in similar studies using cluster randomized designs.[265] The proportion of patients with a shared physician was similar among the study arms; most physicians were male, family doctors with long practice history and low documentation of special interest in asthma. The ICC was low and the ITT statistical approach should have addressed for any potential bias derived from statistical clustering effect.

6.4.5 System factors:

Patient's had similar insurance coverage and medication use during the year prior to ED presentation suggesting that differential access to medication would be unlikely to explain the study results. A series of proxies of their socio-demographic profile (income/Aboriginal status/employment) were explored and none of these factors could appear to provide explanations for the study results.

Analyzing the study data from a different perspective (per protocol vs. ITT) helped clarifying that almost 40% of the patients who relapsed didn't have a follow-up with their PCP during the study period. As a result, they were never exposed to the effects of the OL-letter recommendations given to their PCPs. While most relapses did occur before the PCP encounters, differences in the timing of this encounter could not explain the results observed in this study.

The outcome adjudication process allowed the identification of another un-intended and consequence of this study (overtreatment). The addition of prednisone or/and antibiotics at the PCP encounters could have been related to worsening symptoms; however, these could also be the result of early and excessive management approaches triggered by the OL-letter recommendations. Finally, the proportion of patients on ICS medication at 90 days was very similar to the original ED presentation. This result provides two important insights: 1) the low adherence with controller medication in this group at three months contributed to the undesired asthma related outcomes (including new exacerbations);[266] and 2) three months may be an appropriate timing for the assessment of ambulatory medication patterns in patients who visit the ED for an asthma exacerbation as some are clearly are receiving sub-optimal treatment.[267]

6.4.6 Strengths and limitations

Despite the un-blinded nature of the study interventions, the internal

validity of the results relies on the strong research methods employed (e.g., randomization, concealment of allocation and blinded ascertainment of endpoints), on the systematic adjudication of care gaps addressed in the OL-letter intervention, and on the fidelity of the delivery of the interventions. The OL-selection followed a self-selection approach, which was cost-effective; while the two OLs who participated in this study were highly motivated individuals with special interest in asthma, it is possible that some members of the PCP community didn't recognize these specific professionals as OLs and therefore ignore their recommendations.[246] The outcome adjudication process helped minimize the influence of social desirability bias likely impacting the health outcomes originally obtained by patient self-report.[268] While the direction of the estimates derived from analyses based on the adjudication process and from patient self-report was the same, their magnitude reflected a more precise measure of the outcomes of interest.

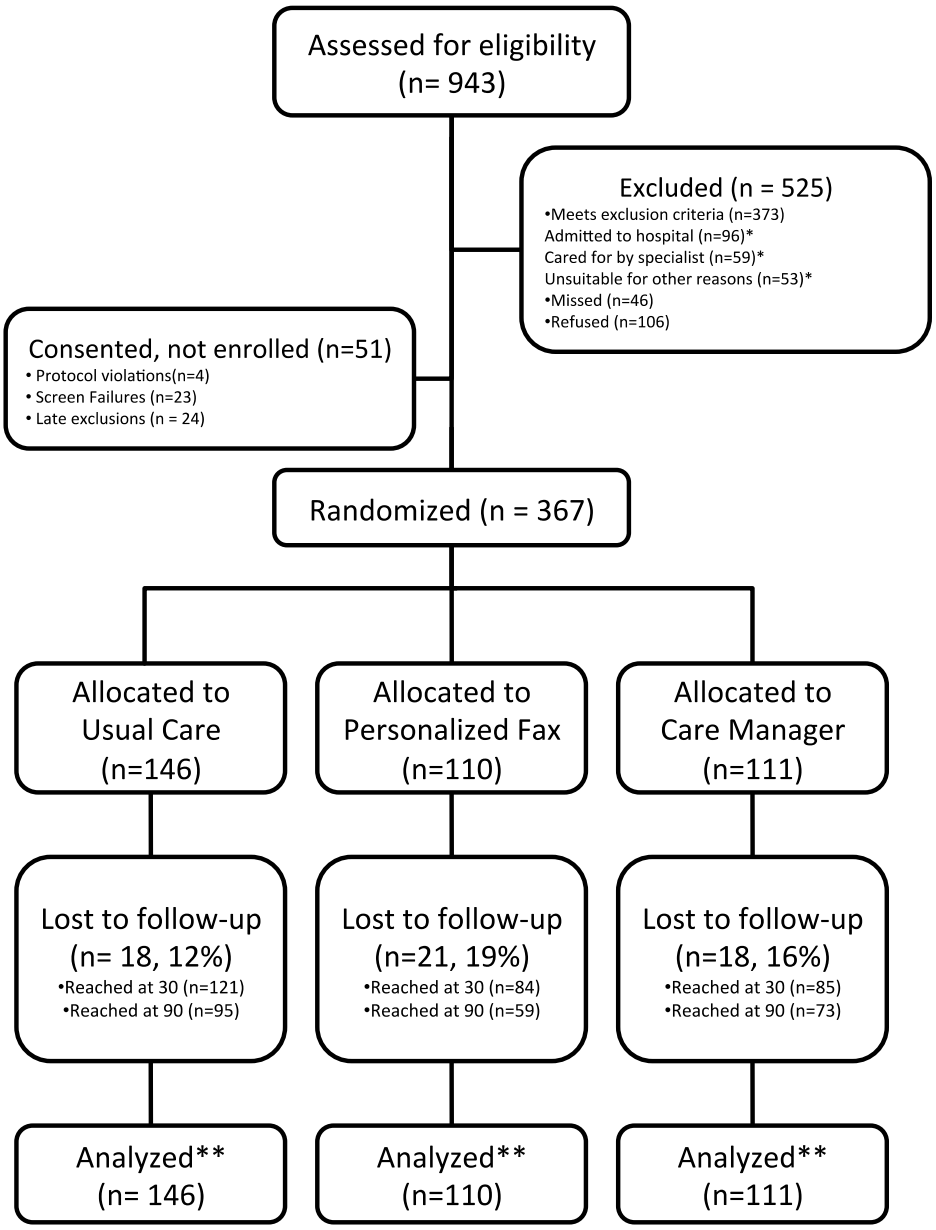
Importantly, patients were the unit of randomization and analysis in this study; however, patient management and their health outcomes may have been differentially influenced by specific PCP characteristics (e.g., knowledge, skills, treatment approaches, availability for a short-term follow-up, etc.) that were not measured/explored in this study.

6.5 Conclusion

Intended and un-intended consequences arose from the multifaceted and tailored ED-directed interventions implemented in this

study. Both, PCP guidance on follow-up care by a local OL and CM guidance on patients' self-management increased the proportion of PCP follow-up after an ED visit for acute asthma in the short-term; the study interventions were moderately effective in improving the post-ED linkage between patients and PCPs. Most importantly, the interventions were associated with increased resource utilization after the ED for acute asthma. The results suggest that the faxed OL-letter influenced PCP behavior and patient management. Exploration of patient (e.g., history, severity, past and ED management, adherence), PCP (e.g., established vs. new PCP; age, sex, years of practice), and system (e.g., medication coverage, proxies for socio-economic status) factors failed to identify potential causes of these results. The most likely explanation to the study results is that lack of sub-acute follow-up capacity in PCP offices may have contributed to referral to acute care settings and to early and excessive treatment after the arrival of the fax. Costs of the implementation were not directly considered in this thesis project; however, the costs required to implement such interventions would not be warranted given the effects on health outcomes and the unintended consequences of the study interventions.

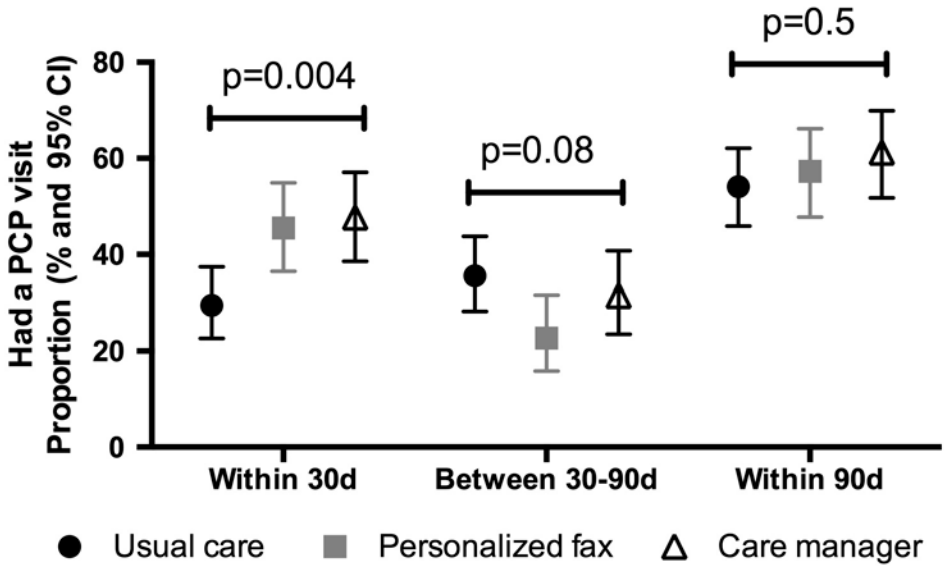
Figure 6-1 Flow diagram of emergency department directed interventions to improve outcomes after asthma exacerbations



*Top three reasons for exclusion

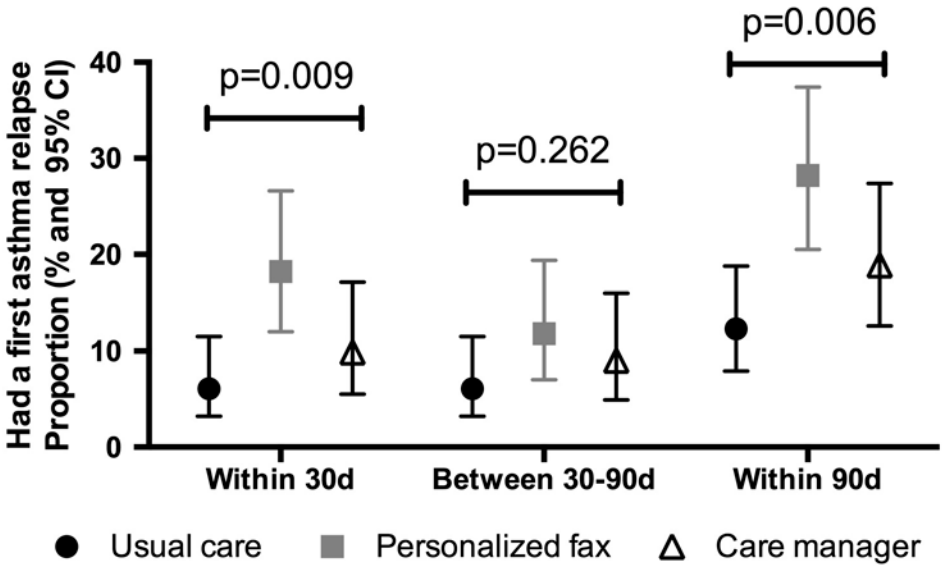
** Primary outcome data were available on all study patients.

Figure 6-2 Proportion of first primary care provider follow-up visits within 90 days by study intervention arm



Note: PCP = Primary care provider; CI = confidence interval.

Figure 6-3 Proportion of first asthma relapse within 90 days by study intervention arm



Note: CI = confidence interval.

Figure 6-4 Time to asthma relapse by study intervention arms within 90 days

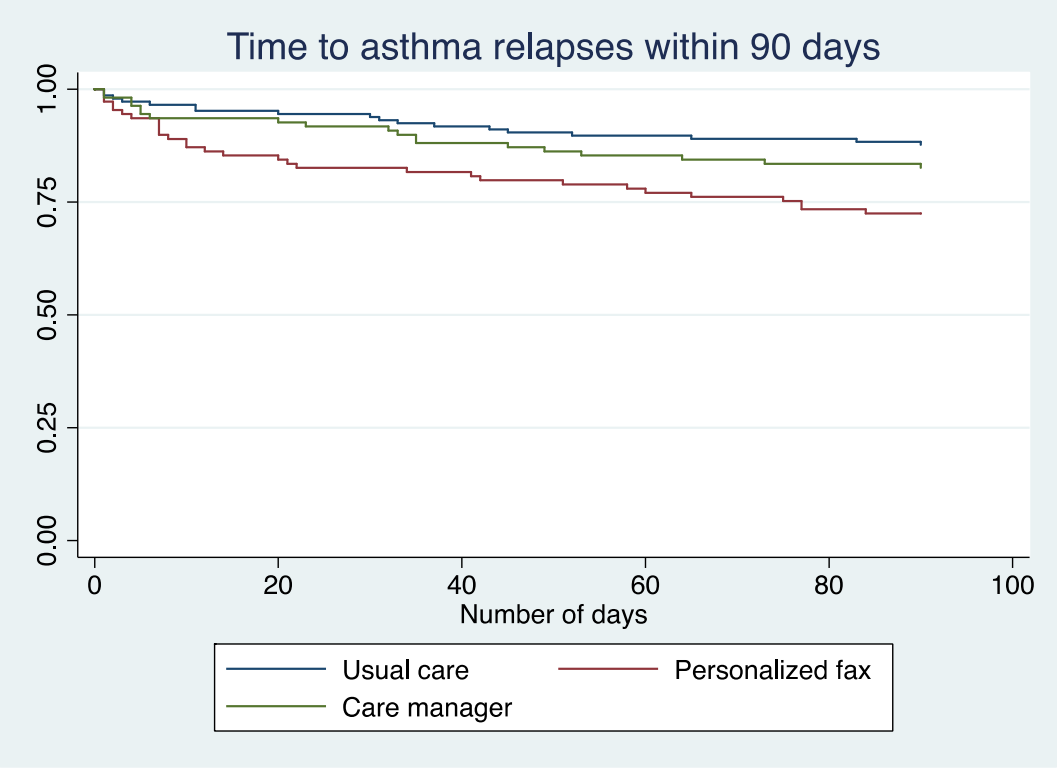


Figure 6-5 Changes in the overall score of the asthma quality of life questionnaire (AQLQ) by study arm

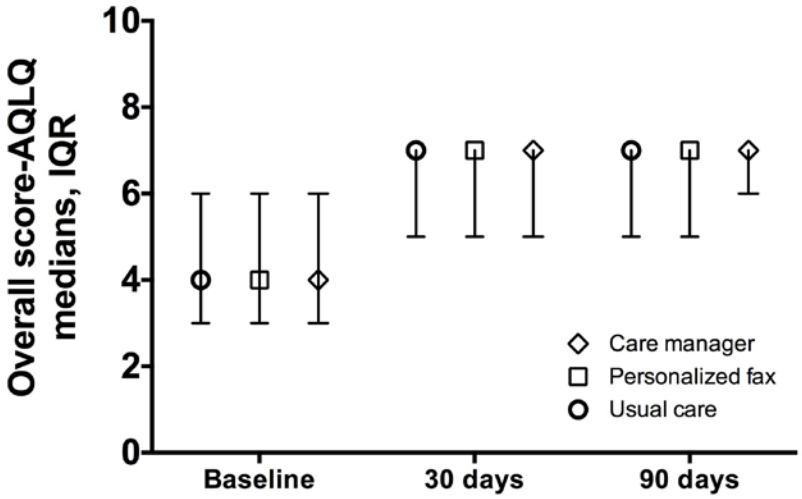
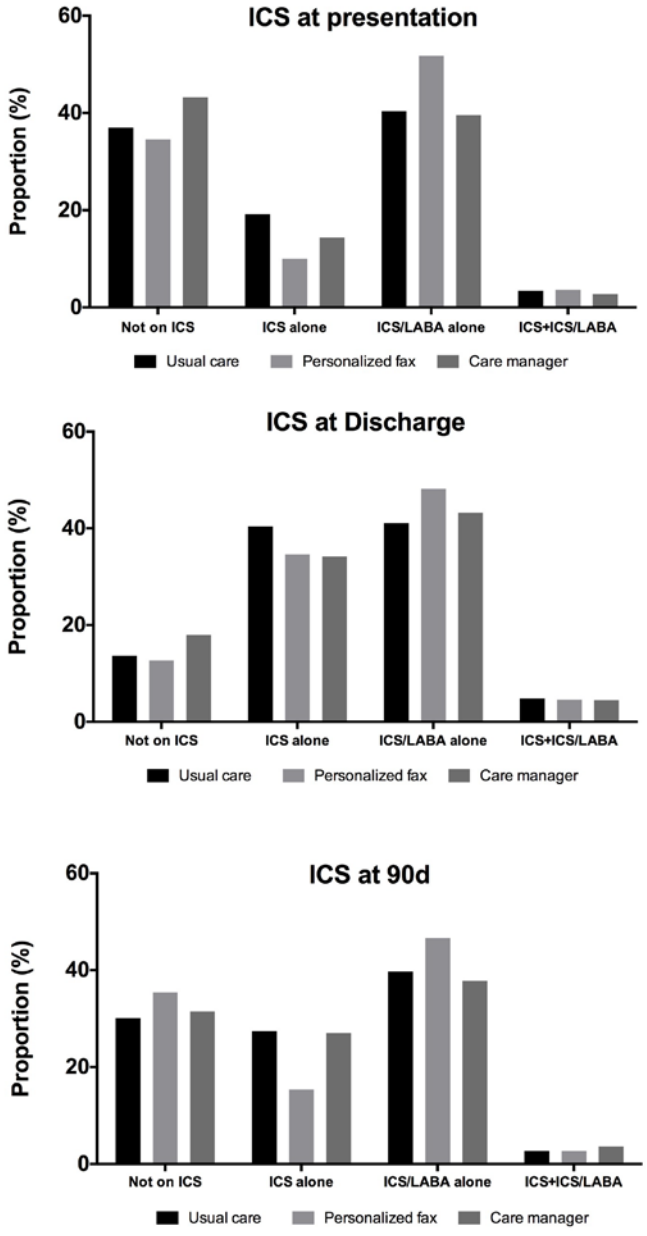
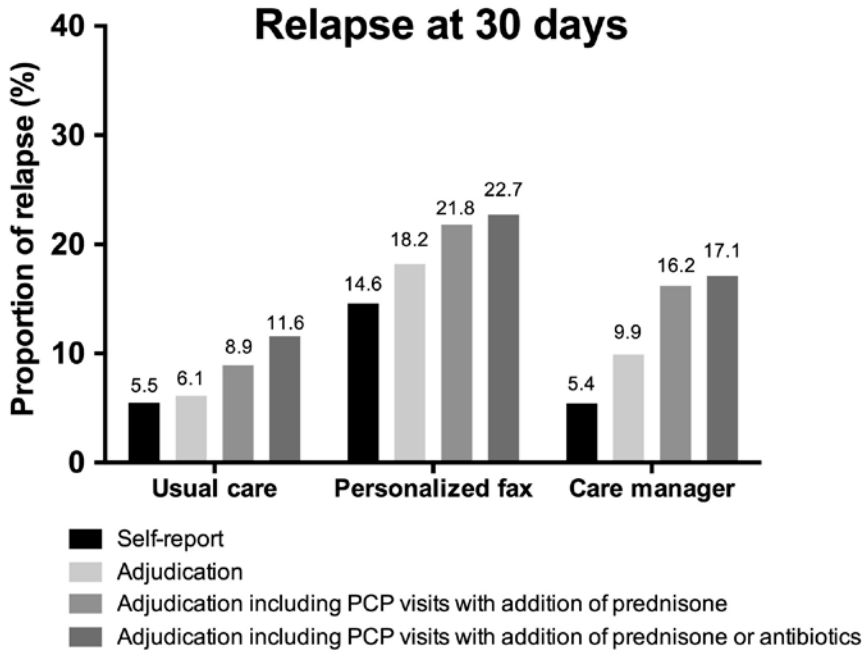


Figure 6-6 Changes in the proportion of patients prescribed with anti-inflammatory medication at emergency department presentation 30 and 90 days by study arm



Note: ICS = Inhaled corticosteroids; ICS/LABA = Inhaled corticosteroids and long-acting β_2-agonist

Figure 6-7 Sensitivity analyses considering different operative definitions of the primary outcome



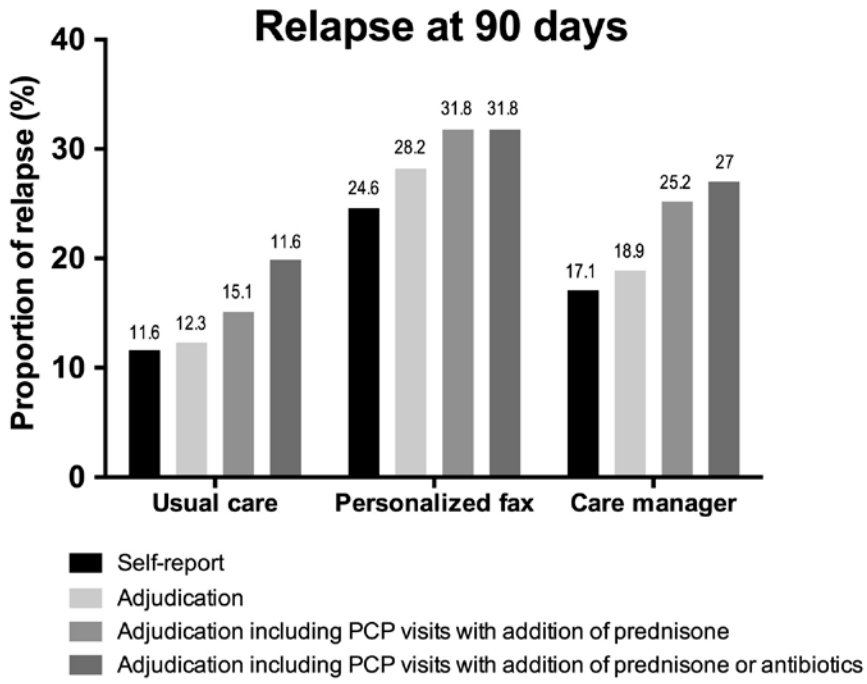


Table 6-1 Baseline characteristics of the study population at emergency department presentation

	Usual Care (n=146)	Personalized Fax (n=110)	Care Manager (n=111)
Socio-demographic factors			
Age (years), median (IQR)	28 (22, 35)	29 (23, 42)	29 (23, 37)
Female sex, n (%)	91 (62.3%)	74 (67.3%)	67 (60.4%)
Ethnicity, n (%)			
Caucasian	112 (76.7%)	75 (68.2%)	84 (75.7%)
Other	34 (23.3%)	35 (31.8%)	27 (24.3%)
Highest level of education, n (%)			
Post-secondary education	90 (61.6%)	58 (52.7%)	61 (54.9%)
Marital status (single), n (%)	90 (61.6%)	60 (54.6%)	63 (56.8%)
Working for pay or profit during the last year, n (%)	101 (69.2%)	76 (69.1%)	87 (78.4%)
Income in the last year, median (IQR)*	70537 (57606, 96594)	78326 (58400, 100173)	78614 (59952, 98631)
Preventive factors			
Have an "asthma action plan", n (%)	73 (50%)	61 (55.5%)	63 (56.8%)
Written asthma action plan	3/73	0/61	2/63
Use inhalers, n (%)	134 (91.8%)	98 (89.1%)	101 (91.0%)
Own a spacer device	69/134	36/98	47/101
Have had immunization during the last influenza season, n (%)	59 (40.4%)	51 (46.4%)	45 (40.5%)
Have been referred to asthma education, n (%)	24 (16.4%)	15 (13.6%)	17 (15.3%)
Smoking status, n (%)			
Never	67 (45.9%)	52 (47.3%)	58 (52.3%)
Current	48 (32.8%)	34 (30.9%)	28 (25.2%)
Previous	31 (21.8%)	24 (21.8%)	25 (22.5%)

Resource utilization			
Have a family physician, n (%)	103 (70.6%)	81 (73.6%)	90 (81.1%)
Family physician most frequently treats his/her asthma, n (%)	87 (59.6%)	68 (61.8%)	70 (63.1%)
ED is the usual site for acute asthma care, n (%)	82 (56.2%)	52 (47.3%)	57 (51.3%)
Time since last ED visit (years), median (IQR)	1 (0.3, 3)	2 (0.5, 8)	1.5 (0.5, 5)
Hospitalizations for asthma in past two years, median (IQR)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Insurance status			
Medication coverage, n (%)	111 (76.0%)	75 (68.2%)	78 (70.3%)
Percentage of asthma medication paid by the patient, median (IQR)	20 (0, 20)	20 (0, 20)	10 (0, 20)
Reported less medication use due to cost, n (%)	38 (26.0%)	21 (19.1%)	26 (23.4%)
Chronic asthma factors			
Asthma history (years), median (IQR)	20 (13, 20)	20 (10, 25)	19 (13, 26)
Have a seasonal component to asthma symptoms, n (%)	119 (81.5%)	83 (75.5%)	88 (79.3%)
Ever intubated for asthma, n (%)	7 (4.8%)	12 (10.9%)	10 (9.0%)
Medication at presentation to the ED, n (%)			
Inhaled short-acting β_2-agonists (SABA)	126 (86.3%)	89 (80.9%)	94 (84.7%)
Inhaled corticosteroids (ICS)	33 (22.6%)	15 (13.6%)	19 (17.1%)
Inhaled long-acting β_2-agonists (LABA)	1 (0.7%)	0	0
Inhaled corticosteroids/long-acting β_2-agonists (ICS/LABA)	64 (43.8%)	61 (55.5%)	47 (42.3%)

Oral corticosteroids (Prednisone)	7 (4.8%)	6 (5.5%)	5 (4.5%)
Leukotriene modifier/antagonist	8 (5.6%)	6 (5.5%)	7 (6.3%)
Anticholinergics	12 (8.2%)	6 (5.5%)	7 (6.3%)
Combined SABA + anticholinergics	0	0	1 (0.9%)
Theophylline	0	0	0
Antibiotics	3 (2.1%)	2 (1.8%)	2 (1.8%)

Note: IQR = Interquartile range (P_{75}, P_{25}); ED = Emergency department.

- Canadian dollars.

Table 6-2 Clinical characteristics and length of stay

	Usual Care (n=146)	Personalized Fax (n=110)	Care Manager (n=111)
Clinical factors at ED presentation			
Canadian Triage Acuity Scale (CTAS) score, n (%)			
1,2	29 (19.9%)	21 (19.1%)	14 (12.6%)
3	90 (61.6%)	70 (63.6%)	85 (76.6%)
4,5	27 (18.5%)	19 (17.3%)	12 (10.8%)
Duration of symptoms, median (IQR)			
Days with respiratory symptoms getting worse	2 (0.5, 4)	3 (0.6, 6)	2 (0.7, 5)
Days with activity limitation due to asthma	2 (1, 4)	1 (0, 3)	1 (0, 3)
No. of inhaled β_2-agonist puffs within 24 hours of ED	8 (2, 16)	8 (1, 20)	8 (3, 15)
Vital signs, median (IQR)			
Pulse	100 (89, 108)	99 (86, 113)	95 (86, 112)
Respiatory rate	20 (18, 24)	20 (18, 26)	20 (18, 23)
SaO_2 (On room air)	97 (95, 98)	97 (95, 98)	97 (95, 98)
Temperature	36.6 (36.2, 36.8)	36.4 (36.1, 36.7)	36.5 (36.2, 36.8)
ED course			
Received inhaled β_2-agonists in the ED, n (%)	140 (95.9%)	105 (95.5%)	104 (93.7%)
No. of treatments in the first hour (puffs), median (IQR)	0 (0, 0)	0 (0, 5)	0 (0, 5)
No. of treatments over ED stay, median (IQR)	10 (4, 8)	12 (4, 18)	11 (4, 19)
Given any corticosteroid treatment, n (%)	113 (77.4%)	85 (77.3%)	81 (72.9%)
Received inhaled anticholinergics, n (%)	129 (88.4%)	97 (88.2%)	92 (82.9%)
No. of treatments in the first hour, median (IQR)	0 (0, 3)	0 (0, 5)	0 (0, 5)
No. of treatments over ED stay, median (IQR)	8 (4, 15)	12 (4, 16)	9 (4, 15)
$MgSO_4$ medication in the ED, n (%)	7 (4.8%)	7 (6.4%)	4 (3.6%)
Lung Function			
Earliest PEF (n=294), median (IQR)	278 (222, 350)	300 (205, 373)	300 (225, 350)

Final PEF (n=344), median (IQR)	350 (300, 419)	340 (296, 411)	353 (300, 449)
Change in PEF (n=217), median (IQR)	79 (42, 136)	71 (30, 124)	71 (39, 149)
Earliest %Predicted PEF (n=292), median (IQR)	58 (47, 73)	61 (45, 84)	60 (49, 71)
Final %Predicted PEF (n=344), mean (SD)	76 (19.7)	74 (22.1)	77 (20.3)
Change in %Predicted PEF (n=217), median (IQR)	18 (7, 29)	17 (5, 26)	13 (8, 30)
FEV_1 % Predicted at discharge (n=344), median (IQR)	84 (63, 94)	76 (59, 93)	78 (60, 90)
FEV_1/FVC % (n=344), median (IQR)	75 (55, 85)	77 (66, 83)	76 (65, 85)
Medication at ED discharge, n (%)			
Inhaled short-acting β_2-agonists (SABA)	141 (96.6%)	108 (98.2%)	108 (97.3%)
Inhaled corticosteroids (ICS)	66 (45.2%)	43 (39.1%)	43 (38.7%)
Inhaled long-acting β_2-agonists (LABA)	1 (0.7%)	0	0
Inhaled corticosteroids/long-acting β_2-agonists (ICS/LABA)	67 (45.9%)	58 (52.7%)	53 (47.8%)
Oral corticosteroids (Prednisone)	108 (74.0%)	87 (79.1%)	86 (77.5%)
Leukotriene modifier/antagonist	10 (6.8%)	3 (2.7%)	4 (3.6%)
Anticholinergics	30 (20.6%)	20 (18.2%)	28 (25.2%)
Combined SABA + anticholinergics	27 (18.5%)	20 (18.2%)	27 (24.3%)
Theophylline	0	0	0
Antibiotics	18 (12.3%)	5 (4.6%)	9 (8.1%)
ED outcomes			
ED length-of-stay (hours), median (IQR)	4.4 (3.2, 5.8)	4.3 (3.2, 5.6)	4 (3.0, 5.1)
ED length-of-stay > 6 hours, n (%)	35 (24.0%)	26 (24.0%)	14 (12.6%)

Note: IQR = Interquartile range (P_{75}, P_{25}); ED = Emergency department; PEF = Peak expiratory flow; FEV_1 = Forced expiratory flow in 1 second; FEV_1/FVC = Forced expiratory flow in 1 second and forced vital capacity ratio.

Table 6-3 Proportion of primary care provider visits and asthma relapses within 30 and 90 days by study intervention (patient self-report)

Study outcomes	Usual Care (n=146)	Personalized Fax (n=110)	Care Manager (n=111)	p value
Had a first PCP visit within 30 days, % and (95% CI)	32.9% (25.7, 40.9)	49.1% (39.8, 58.4)	51.4% (42.0, 60.6)	**0.004$^{\varphi}$**
Time to first PCP visit in days, median (IQR)	8 (4, 18)	10 (5, 19)	10 (6, 19)	0.591
Had a first PCP visit between 30-90 days, % and (95% CI)	36.6% (29.1, 44.9)	31.1% (22.8, 40.7)	34.6% (26.0, 44.3)	0.664
Time to first PCP visit in days, median (IQR)	64 (46, 80)	58 (50, 78)	57 (45, 67)	0.399
Had a first PCP visit within 90 days, % and (95% CI)	56.8% (48.6, 64.7)	61.8% (52.4, 70.5)	65.8% (56.4, 74.0)	0.342
Time to first PCP visit in days, median (IQR)	23 (8, 51)	14 (6, 24)	15 (8, 30)	**0.029$^{\theta}$**
Had a first asthma relapse within 30 days, % and (95% CI)	5.5% (2.8, 10.6)	14.6% (9.1, 22.5)	5.4% (2.4, 11.6)	**0.021$^{\phi}$**
Time to first asthma relapse in days, median (IQR)	5 (2, 11)	8 (4, 11)	5 (1, 19)	0.694
Had a first asthma relapse between 30-90 days, % and (95% CI)	6.2% (3.2, 11.5)	11.8% (7.0, 19.4)	10.8% (6.2, 18.1)	0.227
Time to first asthma relapse in days, median	45 (33, 65)	61 (42, 75)	49 (35, 64)	0.190

(IQR)				
Had a first asthma relapse within 90 days, % and (95% CI)	11.6% (7.4, 18.0)	24.6% (17.4, 33.5)	17.1% (11.2, 25.4)	**0.025** [δ]
Time to first asthma relapse in days, median (IQR)	31 (5, 44)	14 (7, 61)	35 (19, 53)	0.752
Number of asthma relapses within 90 days, median (IQR)	1 (1, 1)	1 (1,2)	1 (1, 1)	0.356
Hospitalizations within 90 days, % and (95% CI)	1.4% (0.3, 5.4)	4.5% (1.9, 10.5)	2.7% (0.9, 8.1)	0.262
Time to hospitalization in days, median (IQR)	17 (2, 31)	58 (2, 69)	1 (0, 90)	0.645

Note: IQR = Interquartile range (P_{75}, P_{25}); PCP = primary care provider; ED = Emergency department.

[φ] Bonferroni correction: UC vs Fax: 0.027; UC vs CM: 0.009; Fax vs CM: 2.211.

[θ] Bonferroni correction: UC vs Fax: 0.036; UC vs CM: 0.174; Fax vs CM: 1.443.

[Φ] Bonferroni correction: UC vs Fax: 0.039; UC vs CM: 1.809; Fax vs CM: 0.057.

[δ] Bonferroni correction: UC vs Fax: 0.021; UC vs CM: 0.63; Fax vs CM: 0.522.

Table 6-4 Proportion of primary care provider visits and asthma relapses within 30 and 90 days by study intervention (results from the outcome adjudication)

Study outcomes	Usual Care (n=146)	Personalized Fax (n=110)	Care Manager (n=111)	p value
Had a first PCP visit within 30 days, % and (95% CI)	29.5% (22.6, 37.4)	45.5% (36.3, 54.9)	47.7% (38.6, 57.1)	**0.004φ**
Time to first PCP visit in days, median (IQR)	7 (4, 16)	10 (5, 17)	12 (7, 19)	0.162
Had a first PCP visit between 30-90 days, % and (95% CI)	35.6% (28.2, 43.8)	22.7% (15.8, 31.6)	31.5% (23.5, 40.8)	0.082
Time to first PCP visit in days, median (IQR)	61 (42, 76)	51 (35, 71)	55 (45, 70)	0.553
Had a first PCP visit within 90 days, % and (95% CI)	54.1% (45.9, 62.1)	57.3% (47.8, 66.2)	61.2% (51.8, 69.9)	0.517
Time to first PCP visit in days, median (IQR)	24 (6, 57)	13 (6, 24)	16 (8, 30)	**0.036θ**
Had a first asthma relapse within 30 days, % and (95% CI)	6.1% (3.2, 11.5)	18.2% (12.0,26.6)	9.9% (5.5, 17.1)	**0.009ϕ**
Time to first asthma relapse in days, median (IQR)	6 (2, 11)	7 (2, 11)	4 (1, 6)	0.494
Had a first asthma relapse between 30-90 days, % and (95% CI)	6.1% (3.2, 11.5)	11.8% (7.0, 19.4)	9.0% (4.9, 16.0)	0.262

Time to first asthma relapse in days, median (IQR)	44 (35, 59)	58 (42, 75)	45 (35, 53)	0.185
Had a first asthma relapse within 90 days, % and (95% CI)	12.3% (7.9, 18.8)	28.2% (20.5, 37.4)	18.9% (12.6, 27.4)	**0.006δ**
Time to first asthma relapse in days, median (IQR)	30 (6, 43)	12 (4, 51)	22 (4, 40)	0.840
Number of asthma relapses within 90 days, median (IQR)	1 (1, 1)	1 (1,2)	1 (1, 2)	0.208
Hospitalizations within 90 days, % and (95% CI)	1.4% (0.3, 5.4)	5.5% (2.5, 11.7)	3.6% (1.3, 9.3)	0.168
Time to hospitalization in days, median (IQR)	17 (2, 31)	8 (2, 18)	1 (1, 45)	0.623

Note: IQR = Interquartile range (P_{75}, P_{25}); PCP = primary care provider; ED = Emergency department.

φ Bonferroni correction: UC vs Fax: 0.024; UC vs CM: 0.009; Fax vs CM: 2.199.

θ Bonferroni correction: UC vs Fax: 0.033; UC vs CM: 0.528; Fax vs CM: 0.621.

ϕ Bonferroni correction: UC vs Fax: 0.009; UC vs CM: 0.801; Fax vs CM: 0.231.

δ Bonferroni correction: UC vs Fax: 0.003); UC vs CM: 0.435); Fax vs CM: 1.305.

Table 6-5 Unadjusted and adjusted analyses for the main study outcome

Risk of having an asthma relapse within 90 days		
Study intervention	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Personalized fax*	3.1 (1.6 to 6.1)	**2.8 (1.7 to 4.6)**
Care manager*	1.8 (0.8, 4.2)	1.8 (0.7, 4.8)
Female sex Ref: Male sex		0.8 (0.5, 1.5)
Post-secondary education Ref: High-school education or less		1.4 (0.9, 2.2)
ED-usual site for acute asthma care Ref: ED- not an usual site for acute asthma care		1.8 (0.9, 3.6)
Number of years since last ED visit (continuous)		1.0 (0.9, 1.1)
ICS/LABA medication at ED presentation Ref: No ICS/LABA medication at ED presentation		**1.9 (1.1, 3.2)**
Stepped-up treatment approach at ED discharge Ref: No stepped-up treatment approach at ED discharge		0.8 (0.4, 1.5)
ED-length of stay>6 hours Ref: ED-length of stay ≤6 hours		1.4 (0.7, 3.1)

Note: Ref= reference category; OR= odds ratio; CI= confidence interval; ED= emergency department; ICS-LABA= Inhaled corticosteroids/long-acting β_2-agonists

* Logistic regression using GEE and considering UC as the reference category.

Table 6-6 Preventive actions discussed at the primary care provider follow-up visits documented within 90 days (patient self-report)

	Intervention 1 (n=128)*	Intervention 2 (n=89)*	Intervention 3 (n=93)*
Preventive action	**Number, (%)**		
Education referral	14 (10.9%)	12 (13.5%)	20 (21.5%)
Written asthma action plan provided in the emergency department	13 (10.1%)	20 (22.5%)	19 (20.4%)
Smoking cessation**	17 of 55 (30.9%)	10 of 45 (22.2%)	10 of 46 (21.7%)
Immunization	8 (6.3%)	11 (12.4%)	18 (19.4%)
Compliance/adherence with inhalers	47 (36.7%)	30 (33.7%)	38 (40.9%)

* Number of patients who were reached either at 30 or 90 days after emergency department discharge.

** Percentages are based on the number of patients who reported to smoke at the primary care provider follow-up visit.

Appendix 6-1 List of study protocol deviations and violations reported to the Health Ethics Research Board at the University of Alberta.

Protocol Deviation

Description:

Change in the allocation ratio for the study randomization sequence.

- The study protocol stipulated a 1:1:1 allocation ratio to one of the three arms (usual care/personalized fax to the primary care provider/patient asthma education by care manager [CM]).
- The independent organization that was contracted and paid to provide the randomization services made an error and assigned a 2:1:1 ratio to main study sites.
- This error was detected and corrected by this organization close on August 20th 2015; however, based on the recruitment of the originally planned sample size (n=367) and the assessment/verification of all of the study primary outcomes we should have enough power to detect statistically significant differences among the study arms.

Protocol Violation #1

Patient ID: (RMV) 05 01 052

Description:

Patient randomized to the CM education arm of the study and received usual care.

- Enrolled October 24th 2014 and randomized to receive CM education.
- After files sent to Edmonton site, there was an absence of follow up and CM forms.
- Follow up with Calgary CM confirmed that there was no referral for this patient.

Protocol Violation #2

Patient ID: (RMV) 05 01 052

Description:

Missing original patient files.

- After receiving all of the original documentation in Edmonton, Calgary was notified on June 29th 2015 that original documentation was missing.
- On March 11th 2016 it was concluded that the original documentation was missing including: original consent, baseline visit forms, 30 day follow up forms, and CM forms.
- The original patient file contains personal health identifiable information (such as PHN, full name, DOB, full address, phone number, secondary contact information, and medical history).
- The study coordinator from Calgary confirmed on March 17th 2016 that the original patient files were lost representing a breech of privacy.

Protocol Violation #3

Patient ID: (ELT) 05 02 043
Description:
No record of randomization.

- Enrolled August 12th 2014 in Calgary.
- Checklist received indicated “usual care” assigned by the study coordinator from Calgary.
- Searches revealed no information regarding patient enrollment was sent to Edmonton site.
- Searches revealed no record of randomization through randomization service.

Protocol Violation #4

Patient ID: (MCZ) 05 03 010
Description:

- Patient randomized to receive a personalized opinion letter (OL) fax to his/her primary care provider and received CM education.
- Patient was enrolled Sunday, September 22, 2013 in Calgary.
- Information emailed to Edmonton site Monday September 23rd for randomization. Following review, some clarification was requested before randomization could be completed.
- The final information for randomization was sent from Calgary to Edmonton on 9:17am on September 24rd.
- Dr. Rowe randomized the patient on September 25th 2013 to receive a personalized fax from the Calgary OL to the Family Physician.
- Dr. Rowe sent an email to the Calgary site on September 25th confirming the randomization allocation with the OL-letter attached.
- During data cleaning process it was discovered that this patient study enrollment checklist was assigned to the CM arm, the

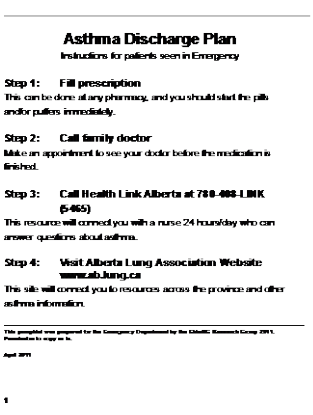
patient file includes 2 CM phone call records.

Protocol Violation #5

Patient ID: (GCA) 01 04
Description:
File received outside of timeframe eligible for randomization.

- Patient provided consent to participate in the study and baseline study forms were completed on June 25th 2013 by the research staff. The file was not provided on time for randomization by the study coordinator from Edmonton.

Appendix 6-2 Discharge package (asthma discharge plan, asthma handbook [section 4: medications] and written asthma action plan).



Asthma Discharge Plan

Instructions for patients seen in Emergency

Step 1: Fill prescription

This can be done at any pharmacy, and you should start the pills and/or puffers immediately.

Step 2: Call family doctor

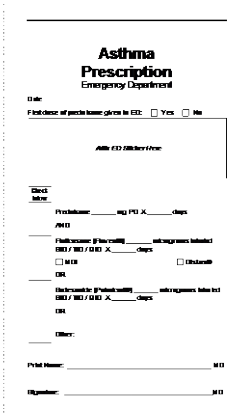
Make an appointment to see your doctor before the medication is finished.

Step 3: Call Health Link Alberta at 780-408-LINK (5465)

This resource will connect you with a nurse 24 hours/day who can answer questions about asthma.

Step 4: Visit Alberta Lung Association Website: www.ab.lung.ca

This site will connect you to resources across the province and other asthma information.



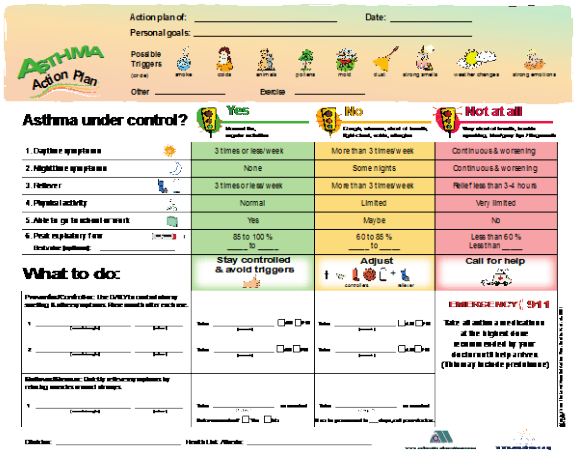
Asthma Prescription

Emergency Department

THE LUNG ASSOCIATION

ASTHMA HANDBOOK

www.lung.ca



Asthma Action Plan

Action plan of: _____ Date: _____

Personal goals: _____

Possible Triggers

Other _____ Exercise _____

Asthma under control?

	Yes	No	Not at all
1. Daytime symptoms	3 times or less/week	More than 3 times/week	Continuous & worsening
2. Nighttime symptoms	None	Some nights	Continuous & worsening
3. Reliever	3 times or less/week	More than 3 times/week	Relief less than 3-4 hours
4. Physical activity	Normal	Limited	Very limited
5. Able to go to school or work	Yes	Maybe	No
6. Peak expiratory flow	85 to 100 % ____ to ____	60 to 85 % ____ to ____	Less than 60 % Less than ____
What to do:	Stay controlled & avoid triggers	Adjust	Call for help

Appendix 6-3 Opinion leader-letter.

UNIVERSITY OF ALBERTA

ED-directed Interventions in Acute Asthma

Date:

Dear Dr. _____,

This letter is being sent on behalf of **your patient**: _____

Your patient was seen in the Emergency Department (ED) at the University of Alberta Hospital on _____ with an exacerbation of asthma.

The patient was managed by the Emergency Physician and was deemed to be safe for discharge with the following prescriptions:

- ☐ Prednisone 50mg/day x ____ days
- ☐ Fluticasone (Flovent) 500µg twice a day x 4 weeks; or
- ☐ Fluticasone/Salmeterol (Advair) 500µg/50µg twice a day x 4 weeks.
- ☐ Salbutamol (100 µg) 2 puffs QID prn

In keeping with best practice principles from established guidelines, a **follow up** visit with your patient within **1-2 weeks** is recommended, to ensure resolution and review of chronic management issues. This notice is to **inform** you of the presentation to the ED, so you can arrange the appropriate follow up with yourself.

Patients who experience an exacerbation of asthma are at **increased** risk of further **morbidity** and occasional **mortality** within the year after an exacerbation. Highlighted below are management issues to be considered with your patient in order to optimize their management. This review with your patient will be valuable in **altering** the disease course and **improving** long term outcomes.

Management Issues for your consideration:

Immunization:	☐ Influenza vaccination
Prevention	☐ Asthma Self Management/Action Plan
Counseling:	☐ Smoking Cessation Counseling
Referral	☐ Asthma Education
Medication change:	☐ Addition of regular inhaled corticosteroid (ICS) agent
	☐ Addition of ICS/long-acting beta-agonist (LABA) combination
	☐ Addition of leukotriene receptor antagonist agents
Reminder:	☐ Importance of long-term compliance

We hope you have found this information useful. For more information please visit www.lung.ca/cts.

Sincerely,

[OL name], MD, FRCPC
Department/Division of [division name] Medicine
University of [university name]

Faculty of Medicine & Dentistry
1G1.43 Walter C. Mackenzie Centre · 8440 – 112 Street · University of Alberta · Edmonton · Alberta · Canada · T6G 2B7
Telephone: (780) 407-6707 · Fax: (780) 407-3982
www.emergencymed.medualberta.ca

Appendix 6-4 Care manager form.

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
(Centre - Collector - Consecutive)

This follow-up interview should be completed within the first week post-discharge (maximum Day 10)

Email contact ☐ Yes ☐ No

Date: _____/_____/_____ Time: ___ ___ : ___ _
dd mm yyyy (00:00-23:59)

Telephone Contact Information

1. Date: _____/_____/_____ Time: ___ ___ : ___ _ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
2. Date: _____/_____/_____ Time: ___ ___ : ___ _ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
3. Date: _____/_____/_____ Time: ___ ___ : ___ _ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
4. Date: _____/_____/_____ Time: ___ ___ : ___ _ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
5. Date: _____/_____/_____ Time: ___ ___ : ___ _ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____

Were you able to complete this follow-up? ☐ Yes ☐ No

If yes, follow-up date: _____/_____/_____
dd mm yyyy

If no, interview status:

- ☐ Refused follow-up interview
- ☐ Unreachable x 5 over at least 5-days
- ☐ Other, specify _____

☐ Complete as much information as possible (from the study participant)

Source: _____ Date: _____/_____/_____
dd mm yyyy

Details: _____

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Opening Dialogue

Hello, may I speak with _____. My name is _____ and I work at the _____ Emergency Department in _____. I am calling to find out how you are doing with your asthma management and self care for the Asthma Study you are taking part in. Is this a good time to talk for about 10-15 minutes?
If NO – 'When would be a better time to contact you'? _____
If YES – 'Great, please remember that all of your answers will be kept confidential and will be used for research purposes only'.

Medication Assessment

When you were discharged from the hospital, were you were given a prescription for a steroid (_____)?

☐ Yes ☐ No ☐ Unsure

Were you able to take the steroid as prescribed or instructed to use? ☐ Yes ☐ No

How many days have you taken the steroid? _____days

In case you have not taken this medication as prescribed or instructed, please think about why you haven't done so. As I read you the following list, please let me know the **most important** reason why you have not taken this medication as prescribed (Check all that apply)

- ☐ I couldn't afford the medication
- ☐ I felt better and did not feel it was necessary
- ☐ I experienced side effects
- ☐ I was scared about possible side effects
- ☐ The treatment plan was too complicated
- ☐ I lost the medication
- ☐ I forgot to take it
- ☐ I was told to stop after it was finished
- ☐ Other, specify _____

Was any intervention provided by the care manager?

☐ Yes ☐ No

- ☐ Compliance/adherence encouragement
- ☐ Education regarding prednisone mechanism/rationale
- ☐ Management care

Specify _____

When you were discharged from the hospital, were you were given a prescription for a steroid inhaler or instructions to continue to use your existing steroid inhaler (_____)?

☐ Yes ☐ No ☐ Unsure

Are you taking this steroid inhaler? ☐ Yes ☐ No

If no, for how many days did you actually take the inhaler (any amount of inhalations)? _____ days

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

In case you have not taken this medication as prescribed or instructed, please think about why you haven't done so. As I read you the following list, please let me know the **most important** reason why you have not taken this medication as prescribed (Check all that apply)

- ☐ I couldn't afford the medication
- ☐ I felt better and did not feel it was necessary
- ☐ I experienced side effects
- ☐ I was scared about possible side effects
- ☐ The treatment plan was too complicated
- ☐ I lost the medication
- ☐ I forgot to take it
- ☐ Other, specify _____

Was any intervention provided by the care manager?

☐ Yes ☐ No

☐ Compliance/adherence encouragement
☐ Education regarding ICS or ICS/LABA mechanisms/rationale
☐ Management care

Specify _____

When you were discharged from the hospital, were you were given a prescription for Ventolin or Bricanyl inhaler?

☐ Yes ☐ No ☐ Unsure

Over the past 24 hours, have you used your Ventolin or Bricanyl inhaler? ☐ Yes ☐ No

If yes, how many puffs did you take? _____ puffs (if greater than 10 puffs, the patient will be referred to the ED)

In case you have not taken this medication as prescribed or instructed, please think about why you haven't done so. As I read you the following list, please let me know the **most important** reason why you have not taken this medication as prescribed (Check all that apply)

- ☐ I couldn't afford the medication
- ☐ I felt better and did not feel it was necessary
- ☐ I experienced side effects
- ☐ I was scared about possible side effects
- ☐ The treatment plan was too complicated
- ☐ I lost the medication
- ☐ I forgot to take it
- ☐ Other, specify _____

Was any intervention provided by the care manager?

☐ Yes ☐ No

☐ Compliance/adherence encouragement
☐ Education regarding SABA mechanisms/rationale
☐ Management care

Specify _____

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

When you were discharged from the hospital, were you were given ***any other*** prescription including spacer device (e.g., aerochamber)?

☐ Yes ☐ No

Specify _____

Are you taking this/these medication(s)? ☐ Yes ☐ No

If no, for how many days did you actually take this/these medication(s)? _____ days

In case you have not taken this/these medication(s) as prescribed or instructed, please think about why you haven't done so. As I read you the following list, please let me know the **most important** reason why you have not taken this/these medication(s) as prescribed (Check all that apply)

- ☐ I couldn't afford the medication
- ☐ I felt better and did not feel it was necessary
- ☐ I experienced side effects
- ☐ I was scared about possible side effects
- ☐ The treatment plan was too complicated
- ☐ I lost the medication
- ☐ I forgot to take it
- ☐ I was told to stop after it was finished
- ☐ Other, specify _____

Was any intervention provided by the care manager?

☐ Yes ☐ No

☐ Compliance/adherence encouragement
☐ Education regarding mechanisms/rationale
☐ Management care

Specify _____

Patient medication concerns

Do you have any further questions regarding your asthma medications?

☐ Yes ☐ No

If yes, specify_____

Was any intervention provided by the care manager?

☐ Yes ☐ No

☐ Compliance/adherence encouragement
☐ Education regarding mechanisms/rationale
☐ Management care

Specify _____

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Follow-up visit with primary care provider

Since you were seen in the emergency department on _____, have you seen a primary care health provider to review your asthma management?

☐ Yes ☐ No

If yes, Date of visit: ___/___/_____
dd mm yyyy

Please specify,
- ☐ You initiated the visit with your Family Doctor.
- ☐ Your Family Doctor contacted you to come in for a review of your ASTHMA plan.

Where did this visit take place?
- ☐ Family physician, nurse practitioner or internist
- ☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
- ☐ Walk-in/urgent care clinic
- ☐ Other, specify:_____

Name of Health Care Provider or Clinic:_____

Location:_____

Did the health provider change your asthma medicines or treatment plan? ☐ Yes ☐ No

Did you discuss any of the following with your health provider since the ED visit?

Asthma education referral	☐ Yes	☐ No	
Written Asthma Action Plan	☐ Yes	☐ No	
Smoking cessation	☐ Yes	☐ No	☐ N/A
Immunization	☐ Yes	☐ No	☐ N/A
Compliance/adherence with inhalers	☐ Yes	☐ No	☐ N/A
Referral for spirometry/lung testing	☐ Yes	☐ No	
Referral to a specialist	☐ Yes	☐ No	
Other, specify _____	☐ Yes	☐ No	
Other, specify _____	☐ Yes	☐ No	

Do you have an appointment booked to see your primary care health provider to review your asthma management?

☐ Yes ☐ No

If yes, Date of visit: ___/___/_____
dd mm yyyy

If no, why not?_____

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Were any of the following options offered?

☐ Do you want more information on the causes of asthma or what asthma is?
Specify _____

☐ Do you want more information on smoking cessation? or ☐ N/A
Specify _____

☐ Do you want more information on immunization? or ☐ N/A
Specify _____

☐ Do you want more information on the written Asthma Action Plan? or ☐ N/A
Specify _____

☐ Do you want more information regarding an asthma education referral? or ☐ N/A
Specify _____

☐ Do you want me to book an appointment for you with your Family doctor? or ☐ N/A
Specify _____

Signs and Symptoms assessment

Since the ED visit, have you returned to doing the normal activities that you were performing before the exacerbation?

☐ Yes ☐ No

Do you still have any of the following symptoms?

Cough	☐ Yes	☐ No
Wheezing	☐ Yes	☐ No
Insomnia/waking at night	☐ Yes	☐ No
Hoarseness/voice change	☐ Yes	☐ No
Swelling (anywhere)	☐ Yes	☐ No
Sore throat	☐ Yes	☐ No
SOB	☐ Yes	☐ No
Nausea	☐ Yes	☐ No
Other, specify _____	☐ Yes	☐ No

Was any intervention provided by the care manager?

☐ Yes ☐ No

☐ Preventer compliance/adherence encouragement
☐ Education regarding symptoms
☐ Management care

Specify _____

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Second call

Patient agreed to a second call offered by the care manager after their primary care health provider visit:

☐ Yes ☐ No

If yes, Date: _____/_____/_____ Time: ___ ___ : ___ _
dd mm yyyy (00:00-23:59)

Closing Dialogue

That's it! Do you have any questions or comments? If yes, record below.

_____

_____

On behalf of Dr. _____and the _____hospital, I want to thank you again for your help with this important Asthma Study.

Appendix 6-5 Thirty-day follow-up form.

30-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
(Centre - Collector - Consecutive)

This follow-up interview should be completed between Day 30 (minimum Day 25, maximum Day 35)

Telephone Contact Information

1. Date: _____/_____/_____ (dd/mm/yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
2. Date: _____/_____/_____ (dd/mm/yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
3. Date: _____/_____/_____ (dd/mm/yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
4. Date: _____/_____/_____ (dd/mm/yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____
5. Date: _____/_____/_____ (dd/mm/yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials [ ][ ][ ]
   Comments: _____

Were you able to complete this follow-up? ☐ Yes ☐ No

If yes, follow-up date: _____/_____/_____ (dd/mm/yyyy)

If no, interview status:

- ☐ Refused follow-up interview
- ☐ Unreachable x 5 over at least 5-days
- ☐ Other, specify _____

☐ Complete as much information as possible (from the study participant or family member)

Source: _____ Date: _____/_____/_____ (dd/mm/yyyy)

Details: _____

30-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Opening Dialogue

Hello, may I speak with _____. My name is _____ and I work at the _____ Emergency Medicine Research Group at the University of Alberta. I am calling to find out how you are doing with your asthma and complete the follow-up for the Asthma Study you are taking part off. Is this a good time to talk for about 10-15 minutes?
If NO – 'When would be a better time to contact you'? _____
If YES – 'Great, please remember that all of your answers will be kept confidential and will be used for research purposes only'.

Medication Assessment

When you were discharged from the hospital, were you were given a prescription for a steroid?
☐ Yes ☐ No ☐ Unsure

If yes, please specify the agent: _____ Daily dose: _____ug

Were you able to take the steroid as prescribed or instructed to use? ☐ Yes ☐ No

How many days did you take the steroid? _____days

In case you did not take this medication as prescribed or instructed, please think about why you did not do so. As I read you the following list, please let me know the **most important** reason why you did not take this medication as prescribed (Check all that apply)

☐ I felt better and did not feel it was necessary
☐ I experienced side effects
☐ I was scared about possible side effects
☐ The treatment plan was too complicated
☐ I lost the medication
☐ I forgot to take it
☐ I was told to stop after it was finished
☐ Other, specify _____

When you were discharged from the hospital, were you were given a prescription for a steroid inhaler **or** instructions to continue to use your existing **steroid inhaler**?
☐ Yes ☐ No ☐ Unsure

If yes, please specify the agent: _____ Daily dose: _____ug

Are you still taking this steroid inhaler? ☐ Yes ☐ No

If no, for how many days did you actually take the inhaler (any amount of inhalations)? _____ days

In case you did not take this medication as prescribed or instructed, please think about why you did not do so. As I read you the following list, please let me know the **most important** reason why you did not take this medication as prescribed (Check all that apply)

☐ I felt better and did not feel it was necessary
☐ I experienced side effects
☐ I was scared about possible side effects
☐ The treatment plan was too complicated
☐ I lost the medication
☐ I forgot to take it
☐ I was told to stop after it was finished
☐ Other, specify _____

30-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - ___ - ___ (Centre - Collector - Consecutive)

At this point, you might encourage compliance with the inhaled medications. The exact approach will vary, of course, from patient to patient. Although participants are under no obligation to comply, a sympathetic and respectful conversation, along with some encouragement, may get them back on medication. Regardless, be sure to thank them for their help before proceeding with interview.

Follow-up visit with primary care provider:
Since you were seen in the emergency department on _____, have you seen a health provider to review your asthma management?
☐ Yes ☐ No

If yes, Date of visit: ___/___/_____ (dd mm yyyy)

Where did this visit take place?
- ☐ Family physician, nurse practitioner or internist
- ☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
- ☐ Walk-in/urgent care clinic
- ☐ Emergency department
- ☐ Other, specify:_____

Name of Health Care Provider or Clinic:_____

Location:_____

Did the health provider change your asthma medicines or treatment plan? ☐ Yes ☐ No

If yes, check all that apply:
- ☐ Added inhaled beta-agonist or anticholinergic
- ☐ Increased inhaled corticosteroids dose
- ☐ Addition of inhaled corticosteroids (only if was not prescribed ICS when discharged)
  Agent:_____ Daily dose: _____ug
- ☐ Addition of oral corticosteroids
  Agent:_____ Daily dose: _____mg # days_____
- ☐ Added antibiotics
- ☐ Change in treatment plan but then discharged home
- ☐ Change in treatment plan and then transferred to an ED

  Name of hospital _____

  Date of Admission: ___/___/_____ (dd mm yyyy) Date of Discharge: ___/___/_____ (dd mm yyyy)
- ☐ Other, specify_____

Did you discuss any of the following with your health provider since the ED visit?

Asthma education referral	☐ Yes	☐ No	
Asthma Action Plan	☐ Yes	☐ No	
Smoking Cessation	☐ Yes	☐ No	☐ N/A

30-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - ___ - ___ (Centre - Collector - Consecutive)

Referral for spirometry/lung testing	☐ Yes	☐ No
Referral to a specialist	☐ Yes	☐ No
Current asthma control	☐ Yes	☐ No
Other, specify _____	☐ Yes	☐ No
Other, specify _____	☐ Yes	☐ No

Do you still have any of the following symptoms?

Cough	☐ Yes	☐ No
Insomnia	☐ Yes	☐ No
Hoarseness	☐ Yes	☐ No
Swelling	☐ Yes	☐ No
Sore throat	☐ Yes	☐ No
Nausea	☐ Yes	☐ No
Other, specify _____	☐ Yes	☐ No

Relapse Assessment

Since you were seen in the emergency department on _____, have you had a **worsening** of your asthma that led you to seek **urgent** medical treatment?

☐ Yes ☐ No

If yes, **when** did you **first** seek **urgent** medical treatment for worsening of your asthma?

Date: ___/___/_____ (dd mm yyyy)

Where did you go for this **urgent** asthma visit?

- ☐ Primary care provider (e.g. family physician, nurse practitioner or internist)
- ☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
- ☐ Walk-in/urgent care clinic
- ☐ Emergency department
- ☐ Other, specify: _____

Name of Health Care Provider or Clinic: _____

Location: _____

Was a change made to your asthma medications or treatment plan? ☐ Yes ☐ No

If yes, check all that apply:

- ☐ Added inhaled beta-agonist or anticholinergic
- ☐ Increased inhaled corticosteroids dose
- ☐ Addition of inhaled corticosteroids (only if was not prescribed ICS when discharged)
  Agent:_____ Daily dose: _____ug
- ☐ Addition of oral corticosteroids
  Agent:_____ Daily dose: _____mg # days_____
- ☐ Added antibiotics
- ☐ Change in treatment plan but then discharged home

30-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] (Centre / Collector) - [ ][ ][ ] (Consecutive)

☐ Change in treatment plan including overnight admission to hospital

Name of hospital _____

Date of Admission: ___/___/____ (dd mm yyyy) Date of Discharge: ___/___/____ (dd mm yyyy)

☐ Other, specify_____

Have you had any **OTHER** episodes of **worsening** of your asthma that led you to seek **urgent** medical treatment? ☐ Yes ☐ No

If yes, how many? _____ episodes

If no, continue (this is a final attempt to elicit an acute asthma relapse)

What **medications** are you currently taking for your asthma and have you missed taking any of these medications over the **past two weeks**?

Medication (Check Agent)	Prescribed	Uses	Daily Dose	Missed
Inhaled corticosteroids (ICS) ☐ Flovent® ☐ Qvar® ☐ Pulmicort®	☐ Yes ☐ No	☐ Yes ☐ No	_____ µg/day	☐ Yes ☐ No
Short-acting beta-agonists (SABA) ☐ Ventolin® ☐ Bricanyl®	☐ Yes ☐ No	☐ Yes ☐ No	☐ daily ☐ prn	☐ Yes ☐ No
Long-acting beta-agonists (LABA) ☐ Oxeze® ☐ Serevent®	☐ Yes ☐ No	☐ Yes ☐ No	☐ daily ☐ prn	☐ Yes ☐ No
Inhaled anticholinergics ☐ Atrovent® ☐ Spiriva®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Combined SABA & anticholinergic ☐ Combivent®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Combined ICS + LABA ☐ Advair® ☐ Symbicort®	☐ Yes ☐ No	☐ Yes ☐ No	ICS dose _____ µg/day	☐ Yes ☐ No
Theophylline ☐ Theodur® ☐ Uniphyl®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Antileukotrienes ☐ Accolate® ☐ Singulair®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Oral corticosteroids ☐ Prednisone ☐ Dexamethasone	☐ Yes ☐ No	☐ Yes ☐ No	_____ mg/day x ___ days	☐ Yes ☐ No
Other, specify: _____	☐ Yes ☐ No	☐ Yes ☐ No	_____ mg/day x ___ days	☐ Yes ☐ No

Over the past 24 hours, have you used your β-agonist (Ventolin or Bricanyl) inhaler? ☐ Yes ☐ No

If yes, how many puffs did you take? _____ puffs

Over the past 24 hours, have you used a β-agonist (Ventolin) nebulizer? ☐ Yes ☐ No

If yes, how many nebulizers did you take? _____ treatments

30-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # | 0 | 1 | - | | | - | | | |
Centre Collector Consecutive

Note: If patient refers dyspnea, encourage patient to contact their primary care provider for assistance or return to the Emergency Department. Please describe situation below:
_____

Closing Dialogue:
That's it! Do you have any questions or comments? If yes, record below.
_____
_____
On behalf of Dr. _____and the _____hospital, I want to thank you again for your help with this important Asthma Study.

Appendix 6-6 Ninety-day follow-up form.

90-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - ___ - ___

Centre Collector Consecutive

This follow-up interview should be completed between Day 90 (minimum Day 85, maximum Day 95)

Telephone Contact Information

1. Date: ____/____/____ (dd mm yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials ☐☐☐

   Comments: _____

2. Date: ____/____/____ (dd mm yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials ☐☐☐

   Comments: _____

3. Date: ____/____/____ (dd mm yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials ☐☐☐

   Comments: _____

4. Date: ____/____/____ (dd mm yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials ☐☐☐

   Comments: _____

5. Date: ____/____/____ (dd mm yyyy) Time: ___ ___ : ___ ___ (00:00-23:59) Caller Initials ☐☐☐

   Comments: _____

Were you able to complete this follow-up? ☐ Yes ☐ No

If yes, follow-up date: ____/____/____ (dd mm yyyy)

If no, interview status:

- ☐ Refused follow-up interview
- ☐ Unreachable x 5 over at least 5-days
- ☐ Other, specify _____

Complete as much information as possible (from the study participant or family member)

Source: _____ Date: ____/____/____ (dd mm yyyy)

Details: _____

90-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Opening Dialogue

Hello, may I speak with _____. My name is _____ and I work at the _____ Emergency Medicine Research Group at the University of Alberta. I am calling to find out how you are doing with your asthma and complete the follow-up for the Asthma Study you are taking part off. Is this a good time to talk for about 10-15 minutes?
If NO – 'When would be a better time to contact you'? _____
If YES – 'Great, please remember that all of your answers will be kept confidential and will be used for research purposes only'.

Follow-up with primary care provider:
Since our last phone call on ___/___/_____, did you follow up with your primary care provider?
dd mm yyyy

☐ Yes ☐ No

If yes, Date of visit: ___/___/_____
dd mm yyyy

Please specify,
☐ You initiated the visit with your Family Doctor.
☐ Your Family Doctor contacted you to come in for a review of your ASTHMA plan.

Where did this visit take place?
☐ Primary care provider (e.g. family physician, internist, nurse practitioner)
☐ ASTHMA specialist (e.g. pulmonologist, ASTHMA clinic)
☐ Walk-in/urgent care clinic
☐ One of the above and then transferred to an ED
☐ Other, specify:_____

Name of Health Care Provider or Clinic:_____

Location:_____

At this visit, did you seek additional treatment for **worsened** lung condition/ASTHMA since your recent asthma attack?

☐ Yes ☐ No

Did the doctor change your lung condition/ASTHMA medicines or treatment plan? ☐ Yes ☐ No

If yes, check all that apply:

☐ Inhaled beta-agonist or anticholinergic from health provider
☐ Increased/addition of inhaled corticosteroids (ICS) dose (if applicable)
Agent:_____ Daily dose: _____ug
☐ Increased/addition of ICS/LABA combination inhaler (if applicable)
Agent:_____ Daily dose: _____ug
☐ Addition of oral corticosteroids
Agent:_____ Daily dose: _____mg #days_____
☐ Antibiotics from health provider
Agent:_____ Daily dose: _____mg #days_____
☐ Change in treatment plan but then discharged home
☐ Change in treatment plan and then transferred to an ED

90-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Were you admitted to hospital? ☐ Yes ☐ No

If yes, what hospital?_____

Date of Admission: ___/___/_____ Date of Discharge: ___/___/_____
dd mm yyyy dd mm yyyy

☐ Other, specify _____

Since we last talked, have you been referred to an asthma education program?
☐ Yes ☐ No

Are you still smoking?
☐ Yes ☐ No ☐ N/A

If so, did your primary care provider counsel you on smoking cessation?
☐ Yes ☐ No

Since we last talked, did your primary care provider discuss your vaccination status with you?
☐ Yes ☐ No ☐ N/A

Since we last talked, did your primary care provider discuss an Asthma Action Plan (AAP) to prevent the next flair-up?
☐ Yes ☐ No ☐ N/A

Since we last talked, did your primary care provider discuss medication adherence or compliance with you?
☐ Yes ☐ No ☐ N/A

Since we last talked, have you returned to doing the normal activities that you were performing before the exacerbation?
☐ Yes ☐ No

Relapse Assessment
Since you were seen in the emergency department on _____, have you had a **worsening** of your asthma that led you to seek **urgent** medical treatment?
☐ Yes ☐ No

If yes, **when** did you **first** seek **urgent** medical treatment for worsening of your asthma?

Date: ___/___/_____
dd mm yyyy

Where did you go for this **urgent** asthma visit?
- ☐ Primary care provider (e.g. family physician, nurse practitioner or internist)
- ☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
- ☐ Walk-in/urgent care clinic
- ☐ Emergency department
- ☐ Other, specify: _____

90-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Name of Health Care Provider
or Clinic: _____

Location: _____

Was a change made to your asthma medications or treatment plan? ☐ Yes ☐ No

If yes, check all that apply:

- ☐ Added inhaled beta-agonist or anticholinergic
- ☐ Increased inhaled corticosteroids dose
- ☐ Addition of inhaled corticosteroids (only if was not prescribed ICS when discharged)
  Agent:_____ Daily dose: _____ug
- ☐ Addition of oral corticosteroids
  Agent:_____ Daily dose: _____mg # days_____
- ☐ Added antibiotics
- ☐ Change in treatment plan but then discharged home

☐ Change in treatment plan including overnight admission to hospital

Name of hospital _____

Date of Admission: ___/___/____ Date of Discharge: ___/___/_____
dd mm yyyy dd mm yyyy

☐ Other, specify _____

Have you had any **OTHER** episodes of **worsening** of your asthma that led you to seek **urgent** medical treatment? ☐ Yes ☐ No

If yes, how many? _____ episodes

If no, continue (this is a final attempt to elicit an acute asthma relapse)

90-day Follow-up form

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

What **medications** are you currently taking for your asthma and have you missed taking any of these medications over the **past two weeks**?

Medication (Check Agent)	Prescribed	Uses	Daily Dose	Missed
Inhaled corticosteroids (ICS) ☐ Flovent® ☐ Qvar® ☐ Pulmicort®	☐ Yes ☐ No	☐ Yes ☐ No	_____ µg/day	☐ Yes ☐ No
Short-acting beta-agonists (SABA) ☐ Ventolin® ☐ Bricanyl®	☐ Yes ☐ No	☐ Yes ☐ No	☐ daily ☐ prn	☐ Yes ☐ No
Long-acting beta-agonists (LABA) ☐ Oxeze® ☐ Serevent®	☐ Yes ☐ No	☐ Yes ☐ No	☐ daily ☐ prn	☐ Yes ☐ No
Inhaled anticholinergics ☐ Atrovent® ☐ Spiriva®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Combined SABA & anticholinergic ☐ Combivent®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Combined ICS + LABA ☐ Advair® ☐ Symbicort®	☐ Yes ☐ No	☐ Yes ☐ No	ICS dose _____ µg/day	☐ Yes ☐ No
Theophylline ☐ Theodur® ☐ Uniphyl®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Antileukotrienes ☐ Accolate® ☐ Singulair®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Oral corticosteroids ☐ Prednisone ☐ Dexamethasone	☐ Yes ☐ No	☐ Yes ☐ No	_____ mg/day x ___ days	☐ Yes ☐ No
Other, specify: _____	☐ Yes ☐ No	☐ Yes ☐ No	_____ mg/day x ___ days	☐ Yes ☐ No

Over the past 24 hours, have you used your β-agonist (Ventolin or Bricanyl) inhaler? ☐ Yes ☐ No

If yes, how many puffs did you take? _____ puffs

Over the past 24 hours, have you used a β-agonist (Ventolin) nebulizer? ☐ Yes ☐ No

If yes, how many nebulizers did you take? _____ treatments

Note: If patient refers dyspnea, encourage patient to contact their primary care provider for assistance or return to the Emergency Department. Please describe situation below:

_____

Closing Dialogue:
That's it! Do you have any questions or comments? If yes, record below.

_____

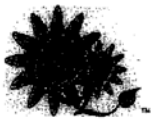
_____

On behalf of Dr. _____and the _____hospital, I want to thank you again for your help with this important Asthma Study.

Appendix 6-7 Asthma Quality of Life Questionnaire (AQLQ).

ASTHMA QUALITY OF LIFE QUESTIONNAIRE WITH STANDARDISED ACTIVITIES (AQLQ(S))

SELF-ADMINISTERED



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Developement and validation supported by GLAXO WELLCOME, INC.

OCTOBER 2000

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID_____

SELF-ADMINISTERED DATE_____

Please complete **all** questions by circling the number that best describes how you have been during the **last 2 weeks as a result of your asthma.**

HOW **LIMITED** HAVE YOU BEEN **DURING THE LAST 2 WEEKS** IN THESE ACTIVITIES **AS A RESULT OF YOUR ASTHMA?**

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
1. STRENUOUS ACTIVITIES (such as hurrying, exercising, running up stairs, sports)	1	2	3	4	5	6	7
2. MODERATE ACTIVITIES (such as walking, housework, gardening, shopping, climbing stairs)	1	2	3	4	5	6	7
3. SOCIAL ACTIVITIES (such as talking, playing with pets/children, visiting friends/relatives)	1	2	3	4	5	6	7
4. WORK-RELATED ACTIVITIES (tasks you have to do at work*) **If you are not employed or self-employed, these should be tasks you have to do most days.*	1	2	3	4	5	6	7
5. SLEEPING	1	2	3	4	5	6	7

HOW MUCH **DISCOMFORT OR DISTRESS** HAVE YOU FELT **DURING THE LAST 2 WEEKS?**

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None
6. How much discomfort or distress have you felt over the last 2 weeks as a result of CHEST TIGHTNESS?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID_____

SELF-ADMINISTERED DATE_____

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
7. Feel CONCERNED ABOUT HAVING ASTHMA?	1	2	3	4	5	6	7
8. Feel SHORT OF BREATH as a result of your asthma?	1	2	3	4	5	6	7
9. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO CIGARETTE SMOKE?	1	2	3	4	5	6	7
10. Experience a WHEEZE in your chest?	1	2	3	4	5	6	7
11. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF CIGARETTE SMOKE?	1	2	3	4	5	6	7

HOW MUCH **DISCOMFORT OR DISTRESS** HAVE YOU FELT **DURING THE LAST 2 WEEKS?**

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None
12. How much discomfort or distress have you felt over the last 2 weeks as a result of COUGHING?	1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
13. Feel FRUSTRATED as a result of your asthma?	1	2	3	4	5	6	7
14. Experience a feeling of CHEST HEAVINESS?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID_____

SELF-ADMINISTERED DATE_____

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
15. Feel CONCERNED ABOUT THE NEED TO USE MEDICATION for your asthma?	1	2	3	4	5	6	7
16. Feel the need to CLEAR YOUR THROAT?	1	2	3	4	5	6	7
17. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO DUST?	1	2	3	4	5	6	7
18. Experience DIFFICULTY BREATHING OUT as a result of your asthma?	1	2	3	4	5	6	7
19. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF DUST?	1	2	3	4	5	6	7
20. WAKE UP IN THE MORNING WITH ASTHMA SYMPTOMS?	1	2	3	4	5	6	7
21. Feel AFRAID OF NOT HAVING YOUR ASTHMA MEDICATION AVAILABLE?	1	2	3	4	5	6	7
22. Feel bothered by HEAVY BREATHING?	1	2	3	4	5	6	7
23. Experience asthma symptoms as a RESULT OF THE WEATHER OR AIR POLLUTION OUTSIDE?	1	2	3	4	5	6	7
24. Were you WOKEN AT NIGHT by your asthma?	1	2	3	4	5	6	7
25. AVOID OR LIMIT GOING OUTSIDE BECAUSE OF THE WEATHER OR AIR POLLUTION?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID_____

SELF-ADMINISTERED DATE_____

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
26. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO STRONG SMELLS OR PERFUME?	1	2	3	4	5	6	7
27. Feel AFRAID OF GETTING OUT OF BREATH?	1	2	3	4	5	6	7
28. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF STRONG SMELLS OR PERFUME?	1	2	3	4	5	6	7
29. Has your asthma INTERFERED WITH GETTING A GOOD NIGHT'S SLEEP?	1	2	3	4	5	6	7
30. Have a feeling of FIGHTING FOR AIR?	1	2	3	4	5	6	7

HOW LIMITED HAVE YOU BEEN **DURING THE LAST 2 WEEKS?**

	Most Not Done		Several Not Done		Very Few Not Done		No Limitation
31. Think of the OVERALL RANGE OF ACTIVITIES that you would have liked to have done during the last 2 weeks? How much has your range of activities been limited by your asthma?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID_____

SELF-ADMINISTERED DATE_____

HOW LIMITED HAVE YOU BEEN **DURING THE LAST 2 WEEKS?**

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at All Limited
32. Overall, among ALL THE ACTIVITIES that you have done during the last 2 weeks, how limited have you been by your asthma?	1	2	3	4	5	6	7

DOMAIN CODE:

Symptoms: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 29, 30
Activity Limitation: 1, 2, 3, 4, 5, 11, 19, 25, 28, 31, 32
Emotional Function: 7, 13, 15, 21, 27
Environmental Stimuli: 9, 17, 23, 26

Appendix 6-8 Ninety-day outcome verification form.

OUTCOMES VERIFICATION USING EDIS/Net*CARE/PCP CONTACT*
EDucate Asthma Study

Study ID # ☐☐ - ☐☐ - ☐☐☐
Centre Collector Consecutive

Date: _____/_____/_____
dd mm yyyy

Follow-up visit with primary care provider (PCP):
Source:

☐ PCP office contact

Since the date the patient was discharged from the Emergency Department, is there evidence that he/she visited a PCP to review their asthma management?
☐ Yes ☐ No

If yes, date of visit: ___/___/_____
dd mm yyyy

Where did this visit take place?
- ☐ Family physician, nurse practitioner or internist
- ☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
- ☐ Walk-in/urgent care clinic
- ☐ Other, specify:_____

Name of Health Care Provider or Clinic:_____

Is there evidence that the health provider changed the patient asthma medicines or treatment plan?
☐ Yes ☐ No

If yes, check all that apply:
- ☐ Added inhaled beta-agonist or anticholinergic
- ☐ Increased inhaled corticosteroids dose
- ☐ Addition of inhaled corticosteroids (only if was not prescribed ICS when discharged)
  Agent:_____ Daily dose: _____ug
- ☐ Addition of oral corticosteroids
  Agent:_____ Daily dose: _____mg # days_____
- ☐ Added antibiotics
- ☐ Change in treatment plan but then discharged home
- ☐ Change in treatment plan and then transferred to an ED
  Name of hospital _____
  Date of ED presentation: ___/___/____
  dd mm yyyy
- ☐ Change in treatment plan and admitted
  Date of Admission: ___/___/____ Date of Discharge: ___/___/_____
  dd mm yyyy dd mm yyyy
- ☐ Other, specify_____

Is there evidence that the health provider discussed any of the following with the patient since the ED visit?
☐ Yes ☐ No

OUTCOMES VERIFICATION USING EDIS/Net*CARE/PCP CONTACT*
EDucate Asthma Study

Study ID # ☐☐ - ☐☐ - ☐☐☐
Centre Collector Consecutive

If yes, check all that apply:

Asthma education referral	☐ Yes	☐ No	☐ N/A
Written Asthma Action Plan	☐ Yes	☐ No	☐ N/A
Smoking cessation	☐ Yes	☐ No	☐ N/A
Immunization	☐ Yes	☐ No	☐ N/A
Compliance/adherence with inhalers	☐ Yes	☐ No	☐ N/A
Referral for spirometry/lung testing	☐ Yes	☐ No	
Referral to a specialist	☐ Yes	☐ No	
Other, specify _____	☐ Yes	☐ No	
Other, specify _____	☐ Yes	☐ No	

If the patient didn't show up to this visit, is there evidence that an appointment was booked with the primary care provider to review the patient's asthma management?
☐ Yes ☐ No

If yes, who booked this appointment?
- ☐ The patient
- ☐ The primary care provider
- ☐ Other, specify:_____
- ☐ ND

Date of visit: ___/___/_____
dd mm yyyy

Relapse Assessment:
Source:
- ☐ EDIS/NetCARE
- ☐ PCP office contact

Since the date the patient was discharged from the Emergency Department, is there evidence that he/she has had a **worsening** of his/her asthma that led them to seek **urgent** medical treatment?
☐ Yes ☐ No

If yes, **when** did he/she **first** seek **urgent** medical treatment for worsening of his/her asthma?

Date: ___/___/_____
dd mm yyyy

Where did he/she go for this **urgent** asthma visit?
- ☐ Primary care provider (e.g. family physician, nurse practitioner or internist)
- ☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
- ☐ Walk-in/urgent care clinic
- ☐ Emergency department
- ☐ Other, specify: _____

Name of Primary Care Provider or Clinic: _____

OUTCOMES VERIFICATION USING EDIS/Net*CARE/PCP CONTACT*
EDucate Asthma Study

Study ID # ☐☐ - ☐☐ - ☐☐☐
Centre Collector Consecutive

If yes, is there evidence that a change was made to his/her asthma medications or treatment plan?
☐ Yes ☐ No

If yes, check all that apply:

☐ Added inhaled beta-agonist or anticholinergic
☐ Increased inhaled corticosteroids dose
☐ Addition of inhaled corticosteroids (only if was not prescribed ICS when discharged)
Agent:_____ Daily dose: _____ug
☐ Addition of oral corticosteroids
Agent:_____ Daily dose: _____mg # days_____
☐ Addition of ICS/LABA agent
Agent:_____ Daily dose: _____mg # days_____
☐ Added antibiotics
☐ Change in treatment plan but then discharged home
☐ Change in treatment plan and then transferred to an ED
Name of hospital _____
Date of ED presentation: ___/___/____ (dd mm yyyy)

☐ Change in treatment plan and admitted to hospital
Date of Admission: ___/___/____ (dd mm yyyy) Date of Discharge: ___/___/____ (dd mm yyyy)

☐ Other, specify_____

☐ Change in treatment plan including overnight admission to hospital
Name of hospital _____

Date of Admission: ___/___/____ (Dd mm yyyy) Date of Discharge: ___/___/____ (dd mm yyyy)

☐ Other, specify_____

Is there evidence that the patient has had any **OTHER** episodes of **worsening** of his/her asthma that led them to seek **urgent** medical treatment?
☐ Yes ☐ No

If yes, how many? _____ episodes

Appendix 6-9 Screening checklist.

Screening Checklist

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study screening ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Screening date: [ ][ ] / [ ][ ] / [ ][ ][ ][ ]
dd mm yyyy

Inclusion criteria (Exclude the patient if **ANY** of the answers to the following questions is "No")

Between 17 and 55 years of age; ☐ Yes ☐ No

Treated and discharged from the emergency department for acute asthma; ☐ Yes ☐ No

Satisfies the clinical diagnosis of acute asthma as evidenced by all of the following: ☐ Yes ☐ No
- Experiencing increasing asthma symptoms (cough, wheeze, and/or shortness of breath) requiring assessment **and** has a history of similar episodes previously;
- Responding (clinically or symptomatically) to inhaled bronchodilator therapy (beta-agonists and/or anticholinergics);
- Clinical history compatible with "asthma" (previous MD or new ED diagnosis).

Evidence of airflow obstruction on presentation at the ED (FEV_1 or PEF <80% of predicted); ☐ Yes ☐ No

Have a family physician, nurse practitioner or internist with whom to follow-up or one was found. ☐ Yes ☐ No

Exclusion criteria (Exclude the patient if **ANY** of the answers to the following questions is "Yes")

Primarily cared for by a Respirologist/Pulmonologist; ☐ Yes ☐ No

Direct referrals (i.e. not seen by an emergency physician); ☐ Yes ☐ No

History of more than 20 pack-years of smoking; ☐ Yes ☐ No

Physician diagnosis of acute COPD (e.g., failure of FEV_1 or PEF to respond to ED treatment and a FEV_1/FVC ratio ≤ 70%); ☐ Yes ☐ No

Radiographically ***confirmed*** pneumonia during the 10 days preceding trial entry; ☐ Yes ☐ No

History of bronchiectasis, cystic fibrosis, or lung cancer; ☐ Yes ☐ No

Diagnosed with congestive heart failure in the ED; ☐ Yes ☐ No

Not able to perform spirometry assessment; ☐ Yes ☐ No

Inability to provide informed consent or comply with the study protocol due to cognitive impairment, language barrier, or no contact details; ☐ Yes ☐ No

Has previously participated in the study; ☐ Yes ☐ No

In the opinion of the investigator are unsuitable for enrolment. ☐ Yes ☐ No
Please specify reason _____

Eligibility

Is this patient eligible for enrollment in the study? ☐ Yes ☐ No

If yes:

Study enrollment ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Appendix 6-10 Informed consent form.

Alberta Health Services

UNIVERSITY OF ALBERTA

PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study:	ED-Directed Interventions to Improve Outcomes after Asthma Exacerbations.
Principal Investigator:	Dr. Brian Rowe, MD, MSc, CCFP(EM) Department of Emergency Medicine, University of Alberta
Co-Investigators:	Dr. Mohit Bhutani, MD, FRCPC Division of Pulmonary Medicine, University of Alberta
	Dr. Cristina Villa-Roel, MD, PhD (Candidate) Department of Emergency Medicine, University of Alberta

Background and purpose of this study: You have been seen and treated in the Emergency Department for worsening of your asthma. This worsening is called an ***exacerbation*** of your asthma. Your emergency doctor has determined that you are safe to be discharged home.

The Emergency Medicine Research Group (EMeRG) at the University of Alberta is conducting a study to help improve the communication between you and your primary care provider (your family doctor, nurse practitioner or internist).

In this study, we are testing whether simple educational interventions given in the Emergency Department help improve the quality of outpatient care for adult patients (>17 years of age) who are treated for worsening of their asthma and then sent home. You have an equal chance (33%) of being in one of the three treatment arms of the study. You will not be able to tell which arm you are in and the three arms represent different methods to improve communications between the emergency site and your doctors.

Participating in this study will involve: If you agree to participate, our research staff will interview you before you leave the ED and contact you by telephone within the next week in order to check the status of your asthma. The purpose of the interview today is to collect information about your general health, asthma history, severity of the current exacerbation, quality of life and general socio-demographic data (e.g., sex, level of education, marital status, access to health care services and to a primary care provider). You will be provided with reading materials from the Canadian Thoracic Society to help you better understand asthma. Your primary care provider will be notified of your visit to the Emergency Department.

Information on your asthma exacerbation will be sent to your family physician, all patients will receive educational materials/pamphlets, and some patients will receive enhanced care through a telephone contact. Thirty and 90 days after your discharge from the Emergency Department, our research staff will contact you by phone and see how you are recovering. A series of questions about your general health will be asked; the total time for the personal and phone interviews will be less than 15 minutes.

Possible Benefits: The possible benefits to you for participating in this study are: 1) We are

planning to follow you during for three months after your ED presentation; the telephone contact will provide you with an opportunity to discuss your asthma status with a health care professional; and 2) In case you don't have a primary care provider, one will be assigned to you.

Possible Risks: Your treatment will not be affected by this study. We won't interfere with the decisions made or medications given or prescribed by your emergency doctor. As far as we know, due to the nature of this intervention (education) we do not think there are any risks to you from taking part in this study.

Procedures: Today, we will collect information on your past and current asthma and your emergency treatment. The study staff may need to look at your personal electronic (NetCare) or paper health records held at the study doctor's office, and/or kept by other health care providers that you may have seen in the past (i.e., your family doctor). We will explore your use of other heath services (like emergency department visits and diagnostic tests) after leaving the emergency today. Any personal health information that we obtain from these records will be only what is needed for the study. During research studies it is im portant that the data we obtain is accurate. For this reason your health data, including your name, may be looked at by people from the University of Alberta Health Research Ethics Board. By signing this consent form you are agreeing to allow the study staff to collect, use and disclose information about you from your personal health records as described above.

Confidentiality: During the study we will be collecting health data about you. We will do everything we can to make sure that this data is kept private. No data relating to this study that includes your name will be released outside of the study office or published by the researchers. Sometimes, by law we may have to release your information with your name and so we cannot guarantee absolute privacy. However, we will make every legal effort to make sure that your health information is kept private.

After the study is completed we will still need to securely store your health data that was collected as part of the study. At the University of Alberta we keep data stored for 5 years. If you leave the study, we will not collect new health information about you, but we will need to keep the data that we already have.

Voluntary Participation: You are free to withdraw from this study at any time, and your continuing medical care will not be affected in any way. If the study is not undertaken or if it is discontinued at any time, the quality of your medical care will not be affected. People who do not enroll in the study will be treated with usual care by the emergency doctor. If any knowledge gained from this or any other study becomes available which could influence your decision to continue in the study, you will be promptly informed.

Further Information: If you have concerns about any aspect of this study, you may contact the Health Research Ethics Board Office at (780) 492-2615. This office has no affiliations with the study investigators. They have no affiliation with the study investigators. Please contact any of the individuals identified below if you have any questions or concerns: Dr. Rowe (investigator) at (780) 407-6707 or Jennifer Victor (study coordinator) at (780) 407-3742.

Alberta Health Services

UNIVERSITY OF ALBERTA

Patient Consent

Title of Study:	ED-Directed Interventions to Improve Outcomes after Asthma Exacerbations.
Principal Investigator: **Co-Investigators:**	Dr. Brian Rowe, Emergency Medicine [780-407-6707] Dr. Mohit Bhutani, Pulmonary Medicine [780-407-1832] Dr. Cristina Villa-Roel, Emergency Medicine [780-492-9671] All at the University of Alberta

Please answer the following questions:

Do you understand that you have been asked to be in a research study?	☐ Yes	☐ No
Have you read and received a copy of the attached information sheet?	☐ Yes	☐ No
Do you understand the benefits and risks involved in taking part in this research study?	☐ Yes	☐ No
Have you had an opportunity to ask questions and discuss this study?	☐ Yes	☐ No
Do you understand that you are free to refuse to participate or withdraw from the study at any time? You do not have to give a reason and it will not affect your future medical care.	☐ Yes	☐ No
Has the issue of confidentiality been explained to you? Do you understand who will have access to your electronic and paper medical records (including personal identifiable information)?	☐ Yes	☐ No
Do you want the study investigators to notify your primary care provider (your family doctor or nurse practitioner) that you are participating in this research study? If yes, please give his/her name: _____	☐ Yes	☐ No

This study was explained to me by: _____

I agree to take part in this study.

_____ Signature of participant

_____ Printed name

Consent date: ☐☐ / ☐☐ / ☐☐☐☐ (dd / mm / yyyy)

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of research staff

Date: ☐☐ / ☐☐ / ☐☐☐☐ (dd / mm / yyyy)

A COPY OF THIS INFORMATION AND CONSENT FORM MUST BE GIVEN TO EACH STUDY PARTICIPANT

Appendix 6-11 Chart review form.

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Emergency Department Evaluation

Vital Signs (earliest documented in ED):

Respiratory Rate _____ _____ / min

Pulse Rate _____ _____ _____ / min

Temperature _____ _____ . _____ °C ☐ Oral ☐ Tympanic ☐ Not documented

Oxygen saturation by pulse oximetry _____ _____ _____ % ☐ Not documented

On room air? ☐ Yes ☐ No

If no, oxygen route: ☐ Mask ☐ Nasal prong Flow _____ L/min

Earliest airway measure ☐ _____ _____ _____ ml ☐ _____ . _____ _____ L/min ☐ Not done

Date and time of airway measure _____/_____/_____ ___ ___ : ___ ___
dd mm yyyy (00:00-23:59)

When were spirometry results recorded?

☐ Before first nebulize/inhaler (MDI) treatment
☐ After first nebulizer/inhaler (MDI) treatment
☐ Unknown

Was a chest x-ray performed? ☐ Yes ☐ No

Was an ECG performed? ☐ Yes ☐ No

Was a sputum specimen obtained? ☐ Yes ☐ No

Was a blood culture obtained? ☐ Yes ☐ No

Was a blood work drawn? ☐ Yes ☐ No →: ☐ CBC. ☐ Electrolytes ☐ Cardiac enzymes

Were ABGs drawn? ☐ Yes ☐ No

If yes, date and time of earliest ABG: _____/_____/_____ ___ ___ : ___ ___
dd mm yyyy (00:00-23:59)

pH _____ / $PaCO_2$ _____ / PaO_2 _____

EMS Arrival ☐ Yes ☐ No (if no, go to **Emergency Department Management)**

Vital Signs (earliest documented)

Respiratory Rate _____ _____ / min

Pulse Rate _____ _____ _____ / min

Temperature _____ _____ . _____ °C ☐ Oral ☐ Tympanic ☐ Not documented

Oxygen saturation by pulse oximetry _____ _____ _____ % ☐ Not documented

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Inhaled β-agonist ☐ Yes ☐ No

Number of treatments in EMS _____ nebs _____ puffs (100 µg/puff)

Total dose in first 60 minutes: _____ _____ . _____ mg

Number of treatments over entire EMS care _____ nebs _____ puffs

Total dose during stay in ED _____ _____ . _____ mg

Inhaled anticholinergic ☐ Yes ☐ No

Number of treatments in EMS _____ nebs _____ puffs (20 µg/puff)

Total dose in first 60 minutes: _____ _____ . _____ mg

Number of treatments over entire EMS care _____ nebs _____ puffs

Total dose during stay in ED _____ _____ . _____ mg

Other Asthma Treatments: ☐ Yes ☐ No If yes, check all that apply

☐ Subcutaneous beta-agonist: ☐ Epinephrine ☐ Beta-agonist, e.g. terbutaline
☐ IV aminophylline
☐ IV magnesium
☐ Oxygen
☐ Other, specify _____

Emergency Department Management

Inhaled β-agonist ☐ Yes ☐ No

Number of treatments in first 60 minutes (from ED triage time) ___ nebs ___ puffs (100µg/puff)

Total dose in first 60 minutes: _____ _____ . _____ mg

Number of treatments over entire ED stay _____ nebs _____ puffs

Total dose during stay in ED _____ _____ . _____ mg

Inhaled anticholinergic ☐ Yes ☐ No

Number of treatments in first 60 minutes (from ED triage time) _____ nebs _____ puffs (20 µg/puff)

Total dose in first 60 minutes: _____ . _____ _____ mg

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - ___ - ___

Number of treatments over entire ED stay _____ nebs _____ puffs

Total dose during stay in ED _____ . _____ _____ mg

Corticosteroid (if more than one dose, check first administered) ☐ Yes ☐ No

- ☐ Prednisone
- ☐ IV Methylprednisolone (Solu-Medrol)
- ☐ IV Hydrocortisone (Solu-Cortef)
- ☐ Other, specify _____

Dose ____ ____ ____mg

Actual date and time of first steroid given ____/____/_____ (dd mm yyyy) ____ ____ : ____ ____ (00:00-23:59)

Assisted Ventilation: ☐ Yes ☐ No If yes, check all that apply

- ☐ Non-invasive ventilation (BiPAP, CPAP, PAV, etc)
- ☐ Intubation
- ☐ Other, specify: _____

Other Asthma Treatments: ☐ Yes ☐ No If yes, check all that apply

- ☐ Subcutaneous beta-agonist: ☐ Epinephrine ☐ Beta-agonist, e.g. terbutaline
- ☐ IV aminophylline
- ☐ IV magnesium
- ☐ Oxygen
- ☐ Other, specify _____

Are previous PFTs available from the chart? ☐ Yes ☐ No If yes: ____/____/_____ (dd mm yyyy)

Record the results of the last PFT (post-bronchodilator) done before today's visit.

FEV_1 _____ L

% predicted _____

PEFR _____L/min

% predicted _____

FVC _____

FEV_1/FVC _____ %

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - ___ - ___ (Centre - Collector - Consecutive)

Spirometry – if performed or if possible (i.e., not intubated, on NIV, or too ill)

Earliest		**Latest (prior to discharge)**	
☐ Pre ☐ Post ☐ Not Done		☐ Pre ☐ Post	
FEV_1	_____ L	FEV_1	_____ L
% predicted	_____	% predicted	_____
PEFR	_____L/min	PEFR	_____L/min
% predicted	_____	% predicted	_____
FVC	_____	FVC	_____
FEV_1/FVC	_____ %	FEV_1/FVC	_____ %
Date: ___/___/_____ (dd mm yyyy) Time: ___ ___: ___ ___ (00:00-23:59)		Date: ___/___/_____ (dd mm yyyy) Time: ___ ___: ___ ___ (00:00-23:59)	

Respiratory Medications Prescribed at discharge

Medication (Check Agent)	**Prescription / Admission Orders**	**Daily Dose**
Inhaled corticosteroids (ICS) ☐ Flovent® ☐ Qvar® ☐ Pulmicort®	☐ Existing ☐ New ☐ N/A	_____µgs ☐ QD ☐ BID ☐ TID ☐ QID X ____days
Short –acting beta-agonists (SABA) ☐ Ventolin® ☐ Bricanyl®	☐ Existing ☐ New ☐ N/A	☐ daily ☐ prn
Long-acting beta-agonists (LABA) ☐ Oxeze® ☐ Serevent®	☐ Existing ☐ New ☐ N/A	☐ daily ☐ prn
Inhaled anticholinergics ☐ Atrovent® ☐ Spiriva®	☐ Existing ☐ New ☐ N/A	
Combined SABA & anticholinergic ☐ Combivent®	☐ Existing ☐ New ☐ N/A	
Combined ICS + LABA ☐ Advair® ☐Symbicort®	☐ Existing ☐ New ☐ N/A	ICS dose _____µgs ☐ QD ☐ BID ☐ TID ☐ QID X ____days
Corticosteroids ☐ Prednisone ☐ Dexamethasone ☐ Other, specify:_____	☐ Existing ☐ New ☐ N/A	_____mgs ☐ PO ☐ IV X_____days
Antibiotics ☐ Specify:_____	☐ Existing ☐ New ☐ N/A	_____mgs ☐ QD ☐ BID ☐ TID ☐ QID ☐ PO ☐ IV
Other, specify:_____	☐ Existing ☐ New ☐ N/A	

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

ED Consultations: ☐ Yes ☐ No

☐ Medicine
☐ Pulmonary/Respirology
☐ Other: _____

Date and time of discharge from consult: _____/_____/_____ ___ ___ : ___ ___
dd mm yyyy (00:00-23:59)

Disposition

☐ Home of Usual Residence
☐ Transferred out to extended care facility (if minimal/assisted living only)
☐ Other, specify _____

Date and time of discharge from ED: _____/_____/_____ ___ ___ : ___ ___
dd mm yyyy (00:00-23:59)

Post-ED Referral: ☐ Yes ☐ No

☐ General Medicine
☐ Pulmonary/Respirology
☐ Asthma Educator
☐ Other: _____

Appendix 6-12 Emergency department visit form.

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - ___ - ___ (Centre - Collector - Consecutive)

Triage information

Sex: ☐ Male ☐ Female PHN #: ☐☐☐☐☐☐☐☐☐☐ Age (years): ☐☐ Height (inches): ☐☐ Weight (pounds): ☐☐☐

CTAS Score: ☐☐ Not documented: ☐ Triage PEF: ☐ No ☐ Yes → Value: ☐☐☐

Triage date: ☐☐ / ☐☐ / ☐☐☐☐ (dd / mm / yyyy) Triage time: ☐☐ : ☐☐ (00:00-23:59)

General Health

Have you ever had a diagnosis of:

☐ Yes	☐ No	COPD
☐ Yes	☐ No	Chronic bronchitis
☐ Yes	☐ No	Asthma
☐ Yes	☐ No	Emphysema
☐ Yes	☐ No	Lung problems
☐ Yes	☐ No	ED MD provided 1st time asthma diagnosis

How long have you had asthma?

_____ ☐ Months ☐ Years

☐ New diagnosis

How long ago did you last visit an emergency department (*greater than 8 hours in the ED*) for treatment of your asthma?

_____ ☐ Days ☐ Weeks ☐ Months ☐ Years

☐ Unknown ☐ Never

In the past two years, how many times have you required hospitalization for your asthma?

_____ times ☐ Unknown

Have you ever been intubated (a tube put into your lungs to help you breath)?

☐ Yes ☐ No ☐ Unknown

Have you ever been admitted to an intensive care unit for your asthma?

☐ Yes ☐ No ☐ Unknown

Which primary care provider do you see most frequently for the routine treatment of your asthma?

☐ Family physician
☐ Nurse practitioner

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

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Centre Collector Consecutive

- ☐ Internal Medicine specialist
- ☐ Respirologist
- ☐ Other, specify: _____
- ☐ No regular physician

For how long have you been seeing this primary care provider?

_____ ☐ Days ☐ Weeks ☐ Months ☐ Years

☐ Unknown ☐ N/A

How long ago did you last visit your primary care provider because your asthma was worse?

_____ ☐ Days ☐ Weeks ☐ Months ☐ Years

☐ Unknown ☐ N/A

Do you have a family physician?

☐ Yes ☐ No

If yes, name: Dr. _____ _____
First Name Last name

Do you see your family physician regularly?

☐ Yes ☐ No ☐ N/A

How long ago did you last visit your family physician?

_____ (*circle one*: days / weeks / months / years) ago ☐ Unknown ☐ N/A

Do you use an inhaler? ☐ Yes ☐ No

If yes, some patients use a 'spacer device' or an aerochamber when taking their inhalers. Do you own one of these devices for your inhalers?

☐ Yes ☐ No

If yes, do you regularly use one of these devices with your inhalers?

☐ Yes ☐ No

If you do **not** use a spacer device or an aerochamber, why not?

- ☐ Never been prescribed by a doctor
- ☐ Prescribed, but not instructed how to use it
- ☐ Too difficult to carry around
- ☐ Forget to use it
- ☐ Don't think it works
- ☐ Other, specify: _____

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

In general, do you have an "action plan" to use in the case of deterioration/worsening of your asthma?

☐ Yes ☐ No

If yes, is it: ☐ Written ☐ Verbal ☐ Both

Describe your action plan: _____

_____

_____

Did you use this action plan prior to coming to the ED on this visit?

☐ Yes ☐ No

When your asthma is getting worse, where do you usually go? (check all that apply)

☐ Primary care provider (e.g. family physician, nurse practitioner. internist)
☐ Asthma specialist (e.g. pulmonologist, allergist, asthma clinic)
☐ Walk in/urgent care clinic
☐ Emergency department
☐ Other, specify: _____
☐ N/A (newly diagnosed by ED physician)

Do you have a seasonal component to your asthma symptoms? ☐ Yes ☐ No

If yes, which season(s) is the worst for you? (check all that apply)

☐ Spring
☐ Summer
☐ Fall
☐ Winter

Do you have any asthma triggers?

Inhalant	Cats	☐ Yes	☐ No	☐ Unknown
	Other animals	☐ Yes	☐ No	☐ Unknown
	House dust mites	☐ Yes	☐ No	☐ Unknown
	Indoor mold	☐ Yes	☐ No	☐ Unknown
	Environmental	☐ Yes	☐ No	☐ Unknown
Occupational irritants, specify _____		☐ Yes	☐ No	☐ Unknown
	Tobacco smoke	☐ Yes	☐ No	☐ Unknown
	Household chemicals	☐ Yes	☐ No	☐ Unknown
	Perfumes	☐ Yes	☐ No	☐ Unknown
	Pollution	☐ Yes	☐ No	☐ Unknown
	Woodburning stove/fireplace	☐ Yes	☐ No	☐ Unknown
	Work environment	☐ Yes	☐ No	☐ Unknown

Do other factors affect your asthma?

	ASA/NSAIDS	☐ Yes	☐ No	☐ Unknown
	Exercise	☐ Yes	☐ No	☐ Unknown
	Food/Food Additives	☐ Yes	☐ No	☐ Unknown

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

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Centre Collector Consecutive

Acid Reflux	☐ Yes	☐ No	☐ Unknown
Respiratory Infection	☐ Yes	☐ No	☐ Unknown
Weather	☐ Yes	☐ No	☐ Unknown
Other, specify_____	☐ Yes	☐ No	☐ Unknown

Smoking history

Do you smoke? ☐ Yes ☐ No

If yes, please classify yourself:
☐ Current Smoker ☐ Former Smoker

If **former** smoker, how long ago did you quit smoking?

_____ ☐ Days ☐ Weeks ☐ Months ☐ Years

If **current or former** smoker:

Average number of packs/day (1 pack = 25 cigarettes): _____

Number of years spent smoking: _____ years

Number of 'pack years' smoked: _____ years
(Calculation: # of packs per day X # years smoked = # pack years)

Immunizations

Have you had a Pneumococcal vaccine? ☐ Yes ☐ No ☐ Unknown

If yes, how long ago? _____ (*circle one*: days / weeks / months / years) ago ☐ Unknown

Have you had an Influenza vaccine recently? ☐ Yes ☐ No ☐ Unknown

If yes, how recently?

☐ Within the current flu season ☐ More than a year ago
☐ Last year ☐ Unknown

Did you receive an H1N1 ("Swine Flu") vaccine last year? ☐ Yes ☐ No ☐ unknown

If yes, how recently?

☐ within the current flu season ☐ more than a year ago

☐ last year ☐ unknown

Asthma education

Have you ever been referred to an **Asthma education** program?

☐ Yes ☐ No ☐ unknown

If yes, how long ago? _____ (*circle one*: days / weeks / months / years) ago ☐ unknown

If yes, where? ☐ Private office ☐ Asthma clinic ☐ Other: _____ ☐ can't recall

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

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Centre Collector Consecutive

Concurrent Medications

Are you **currently prescribed** any of the following asthma medications at home and have you **missed** taking any of these medications over the **past two weeks**?

Medication (Check Agent)	Prescribed	Uses	Daily Dose	Missed
Inhaled corticosteroids (ICS) ☐ Flovent® ☐ Qvar® ☐ Pulmicort®	☐ Yes ☐ No	☐ Yes ☐ No	_____ ug/day	☐ Yes ☐ No
Short-acting beta-agonists (SABA) ☐ Ventolin® ☐ Bricanyl®	☐ Yes ☐ No	☐ Yes ☐ No	☐ daily ☐ prn	☐ Yes ☐ No
Long-acting beta-agonists (LABA) ☐ Oxeze® ☐ Serevent®	☐ Yes ☐ No	☐ Yes ☐ No	☐ daily ☐ prn	☐ Yes ☐ No
Inhaled anticholinergics ☐ Atrovent® ☐ Spiriva®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Combined SABA & anticholinergic ☐ Combivent®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Combined ICS + LABA ☐ Advair® ☐ Symbicort®	☐ Yes ☐ No	☐ Yes ☐ No	ICS dose _____ ug/day	☐ Yes ☐ No
Theophylline ☐ Theodur® ☐ Uniphyl®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Antileukotrienes ☐ Accolate® ☐ Singulair®	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No
Oral corticosteroids ☐ Prednisone ☐ Dexamethasone	☐ Yes ☐ No	☐ Yes ☐ No	_____ mg/day x ___ days	☐ Yes ☐ No
Other, specify: _____	☐ Yes ☐ No	☐ Yes ☐ No		☐ Yes ☐ No

For the asthma attack that caused you to come in to the Emergency Department today, please answer the following questions:

When did your asthma start getting worse?

_____ ☐ Hours ☐ Days ☐ Weeks

☐ Unknown

During the past two weeks, how many days have you been unable to complete your regular daily activities, because you were not feeling well due to your asthma?

_____ Days

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

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Centre Collector Consecutive

How many activations of your beta-agonist (ventolin, salbutamol, berotec, bricanyl, etc.,) have you used in the past 24 hours?

_____ puff(s) _____ Nebulizer(s)

Recent symptoms *(please check all that the patient has experienced in the last 7 days)*

- ☐ Increased shortness of breath
- ☐ Increased sputum purulence *(check all that apply)*
  - ☐ Increased sputum thickness
  - ☐ Change in sputum color
- ☐ Increased sputum volume
- ☐ Fever
- ☐ Chills/rigors
- ☐ Increased cough
- ☐ Increased wheezing
- ☐ Chest pain
- ☐ Runny nose
- ☐ Other, specify _____

To what do you attribute the cause of this asthma attack? (*check all that apply*)

- ☐ Cold or flu
- ☐ Contact with something you were allergic to, specify _____
- ☐ The weather
- ☐ Exercise
- ☐ Other, specify _____
- ☐ Unknown

If your asthma gets worse in the next month, describe your possible actions. (DO NOT READ *to patient, just check answers as patient replies).*

- ☐ Call doctor immediately
- ☐ See doctor immediately (check where: ☐ office ☐ walk in clinic ☐ ED
- ☐ Increase use of ß-agonist
- ☐ Increase use of ICS
- ☐ Increase use of oral corticosteroids
- ☐ Increase use of other medications, specify _____
- ☐ Other strategies, specify _____

Although the answers to the following questions are not necessary for treatment, they will help us evaluate the effect asthma has on your life.

Demographics

What is your marital status?

- ☐ Married
- ☐ Common-law
- ☐ Living with a partner
- ☐ Single (never married)
- ☐ Widowed
- ☐ Separated

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

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Centre Collector Consecutive

- ☐ Divorced
- ☐ Refused to answer

What have you been doing for most of the past 12 months?

- ☐ Caring for family
- ☐ Working for pay or profit
- ☐ Caring for family and working for pay or profit
- ☐ Going to school
- ☐ Recovering from illness/on disability
- ☐ Looking for work
- ☐ Retired
- ☐ Other, specify _____
- ☐ Refused to answer

Which of the following represents the highest level of schooling you have completed?

- ☐ Some high school or less
- ☐ Finished high school (secondary diploma)
- ☐ Some college/university courses
- ☐ Post secondary certificate or diploma
- ☐ Undergraduate university degree completed
- ☐ One or more graduate degrees
- ☐ Don't know
- ☐ Refused to answer

* Research staff's **visual assessment** of ethnic origin:

- ☐ Caucasian
- ☐ Aboriginal
- ☐ Oriental
- ☐ East Indian
- ☐ Black
- ☐ Other, specify _____

DISCHARGE Pulmonary Functions

FEV_1 (L)		% predicted	
PEFR (L/min)		% predicted	
FVC		FEV_1/FVC (%)	

ED-Directed Interventions To Improve Outcomes After Asthma Exacerbations

Study ID # 0 1 - [ ][ ] - [ ][ ][ ]
Centre Collector Consecutive

Respiratory Medications Prescribed at discharge

Medication (Check Agent)	Prescription / Admission Orders	Daily Dose
Inhaled corticosteroids (ICS) ☐ Flovent® ☐ Pulmicort® ☐ Qvar®	☐ Existing ☐ New ☐ N/A	_____ugs ☐ QD ☐ BID ☐ TID ☐ QID X ____days
Short –acting beta-agonists (SABA) ☐ Ventolin® ☐ Bricanyl®	☐ Existing ☐ New ☐ N/A	☐ daily ☐ prn
Long-acting beta-agonists (LABA) ☐ Oxeze® ☐ Serevent®	☐ Existing ☐ New ☐ N/A	☐ daily ☐ prn
Inhaled anticholinergics ☐ Atrovent® ☐ Spiriva®	☐ Existing ☐ New ☐ N/A	
Combined SABA & anticholinergic ☐ Combivent®	☐ Existing ☐ New ☐ N/A	
Combined ICS + LABA ☐ Advair® ☐ Symbicort®	☐ Existing ☐ New ☐ N/A	ICS dose _____ugs ☐ QD ☐ BID ☐ TID ☐ QID X ____days
Corticosteroids ☐ Prednisone ☐ Dexamethasone ☐ Other, specify:_____	☐ Existing ☐ New ☐ N/A	_____mgs ☐ PO ☐ IV X_____days
Leukotriene modifiers ☐ Accolate® ☐ Singulair®	☐ Existing ☐ New ☐ N/A	
Antiobiotics ☐ Specify:_____	☐ Existing ☐ New ☐ N/A	_____mgs ☐ QD ☐ BID ☐ TID ☐ QID ☐ PO ☐ IV
Other, specify:_____	☐ Existing ☐ New ☐ N/A	

7 DISCUSSION AND CONCLUSIONS

7.1 Summary of results

The chapters of this thesis introduce (Chapters 1 and 2), present (Chapters 3 to 6) and discuss (Chapter 7) the results of three studies that were conducted in an effort to synthesize the evidence, identify patient and physician preferences, and improve outcomes using multifaceted interventions after emergency department (ED) visits for acute asthma. The knowledge to action (KTA) model developed by Graham and Straus[133, 134] was adapted (Figure 7-1) to provide a conceptual framework that could help answering the following research question: Using randomized controlled trial (RCT) methods (**D**esign), in adult patients with acute asthma discharged from the ED (**P**opulation), will opinion leader (OL) or care manager (CM)-based interventions directed from the ED (**I**ntervention) reduce relapses and improve outcomes (**O**utcomes) compared to usual care (**C**ontrol)?

This section summarizes the main results of these three studies and their contributions to the overall knowledge in the field:

7.1.1 Systematic review and meta-analysis on the effectiveness of educational interventions to increase primary care follow-up for adults seen in the emergency department for acute asthma:

This systematic review (SR) provided conclusive evidence to

support the consideration of ED-directed educational interventions targeting either adult patients or providers as effective strategies to increase office follow-up visits with a primary care provider (PCP) after asthma exacerbations (Table 7-1). Meta-analysis of data from five RCTs conducted in North America,[162-166] revealed that such interventions led to a greater likelihood of having follow-up with a clinician after ED discharge for an asthma exacerbation. Approximately six patients would need to receive ED-directed educational interventions after being discharged in order to generate one additional office follow-up visit with a PCP. This review didn't provide conclusive evidence to support the consideration of ED-directed educational interventions targeting either adult patients or providers as effective strategies to improve important patient-oriented outcomes, such as relapses and hospital admissions, after asthma exacerbations.

A variable description of intervention fidelity was identified in the included studies (Table 7-1).[170] The majority of the interventions focused on educating patients with asthma about warning signs, acute medical management, ED-discharge efforts to improve PCP follow-up, and indications to return to the ED for re-evaluation. Importantly, the educational interventions included co-interventions such as the provision of a short course of oral corticosteroids, transportation vouchers and letters faxed to the patient's PCP office.

This SR followed structured and rigorous methods in order to minimize the risk of publication and selection bias;[148] it also assessed

study validity and intervention fidelity[159] in order to facilitate the interpretation and applicability of the evidence-based inferences. Due to the small number of studies for each comparison, the potential for publication bias was not formally assessed. Study inclusion was restricted to RCTs based on the interest in summarizing the highest quality evidence to provide support to inform guideline recommendations.

This review contributed to the overall thesis project by summarizing high-quality evidence on ED-directed educational interventions focused on improving PCP follow-up after asthma exacerbations. It revealed that most of these educational interventions were multifaceted. No specific studies were found on the effectiveness of personalized OL-letters delivered to their PCPs or CM guidance, in an incremental approach. It also confirmed that knowledge users have not been engaged in the design of such interventions. All these aspects helped reinforce that the research question supporting this PhD project was feasible, of interest, novel and ethically relevant.[269]

7.1.2 Engaging patients and primary care providers in the design of novel OL-based interventions for acute asthma in the emergency department: a mixed-methods study:

Using sequential explanatory mixed methods, input from patients and PCPs helped tailor OL-based interventions in acute asthma directed from the ED; they also allowed the identification of potential barriers and facilitators for knowledge uptake and for the implementation of these and

similar interventions.

Nomination of a Respirologist as the preferred OLs for guidance on ambulatory asthma care reflects their earned professional leadership role, trust and respect among individuals with different technical competences and status in the health system.[190] Both patients and PCPs, however, recognized the limited availability of Respirologists for the provision of post discharge self-management education and discussed the potential benefit derived from empowering other health care providers working in or outside the ED to assume that role.

The first week of ED discharge was identified as a practical time frame for the provision of asthma education. Additional components of a proposed initiative were requested by PCP respondents such as faxing them a copy of the patients' ED chart and a personalized letter including details on their patients' final diagnosis, ED and ED post-treatment.

Patients identified anxiety during an asthma attack as a potential barrier for the delivery of interventions in the ED. Finally, time constraints were identified as an important barrier for an effective post-ED interaction with PCPs.

This study contributed to the overall thesis project by providing valuable information to refine the ED-directed OL-based multifaceted interventions to be evaluated in the comparative effectiveness trial. In depth discussions of the survey responses helped identify the main drivers of patients and PCPs' preferences for OL-selection, as well as potential

barriers and facilitators for knowledge uptake and for the potential implementation of these and similar interventions. The value that both patients and PCPs provided to health professional liaisons as education providers was a key finding that helped with the interpretation of the applicability of the overall project results. Potential effect-modifiers of these interventions (e.g., patient anxiety levels and timing of the intervention) might not have been discovered had a mixed methods approach not been employed.

7.1.3 Emergency-Department Directed Interventions to improve outcomes after asthma exacerbations:

This comparative effectiveness trial included adults treated and discharged from the ED for an asthma exacerbation. Several gaps in asthma care were identified in the study population at ED presentation; the prevention actions associated with these care gaps underwent a structured adjudication process and were addressed in one of the study arms.

Multifaceted and tailored ED-directed interventions including personalized OL-letters faxed to the PCPs or OL ***plus*** CM guidance on self-management to patients were moderately effective in improving the linkage between patients and PCPs after an ED visit for acute asthma; however, this effect was attenuated by 90 days. Unfortunately, approximately 50% of patients in all groups still had not received a guideline recommended PCP visit by the 90-day end of study deadline.

The study interventions were not effective in reducing resource utlization or improving quality of life (QoL). Importantly, counterintuitive results were observed on the primary study outcome and overtreatment was documented during the PCP follow-up visits. Finally, the proportion of patients on inhaled corticosteroid medication at 90 days was very similar to the pattern seen at ED presentation, suggesting that long-term adherence to preventer medications remains an issue in the post-ED period.

The internal and external validity of the study results rely on the strong research methods employed, the structured adjudication of care gaps addressed in the OL-letter intervention, the fidelity of the delivery of the interventions and the verification of health outcomes originally obtained by patient self-report (Table 7-1).

7.2 Interpretation of the thesis results

Asthma is a complex respiratory condition in which the dynamic interaction of a number of factors including patient, environmental, pharmacologic and non-pharmacologic (including system features) influence its level of control (Figure 7-2). [20, 21] Deficiencies or issues in one or more of these factors may affect their interaction and increase the risk of exacerbations due the loss of asthma control.[38, 39]

Loss of asthma control often results in ED visits for acute asthma. In the ED, synergism among a number of actions also influence immediate and short-medium term outcomes like medical disposition (admission vs.

discharge) and relapses, respectively. The provision of evidence-based management while in the ED and at discharge, and of clear discharge instructions/written plans have been shown to have a significant impact on patient oriented outcomes. [90, 112, 113, 117]

In those patients who are discharged (~90% in Canada), a follow-up visit with a PCP after ED presentation constitutes the ideal scenario for the review of symptoms, pharmacologic treatment (e.g., reinforcement of the importance of adherence to/continuation of the ED prescription), self-management strategies and the discussion of relevant preventive actions (e.g., proper inhaler techniques, smoking cessation, referral for asthma education).[1, 44, 116] The quality of the care offered to patients at this encounter influences the complete resolution of the exacerbation (regain of asthma control) or the occurrence of undesired events (relapses).

The results of the systematic review and of the comparative effectiveness trial included in this thesis suggest that a variety of multifaceted interventions directed from the ED, are effective strategies to increase PCP follow-up visits after asthma exacerbations. Nonetheless, the PCP interaction often fails to achieve the desired result of a granular evaluation of pharmacological or non-pharmacological factors designed to regain asthma control. The conclusive and counterintuitive results of the comparative effectiveness trial do not support the adoption of *OL-letters faxed to the PCPs* or *OL **plus** CM guidance to improve patients' self-*

management as valid approaches to reduce resource utilization or improve QoL (Table 7-1).

The comparative effectiveness trial addressed an important limitation identified in the SR; the fidelity of the delivery of the study interventions was described in detail. Briefly, the majority of the OL-letters were successfully delivered via fax within the 48-hour time frame, received by the PCP office, and contained the requested information in no more than a one-page summary. Similarly, the CM telephone contact occurred within 7 days in more than 80% of the cases, and frequently (62%) resulted in a request for a second contact.

In addition, the verification and external adjudication of the study outcomes provided a more precise measure of the outcomes of interest than the one obtained from patient self-report. The counterintuitive results and un-intended consequences suggest that the faxed OL-letter influenced PCP behaviour and patient management. The exploration of study, patient, health provider, and system factors failed to identify additional causes of these results apart from those that could have been derived by the effect of the faxed OL-letter. The lack of sub-acute follow-up capacity in PCP offices may have contributed to early and excessive ambulatory treatment, and referral to acute care settings after the arrival of the fax. The cost-effectiveness of implementing these interventions is yet to be determined; however, investing in such interventions seems

unwarranted given the weak benefits on health outcomes and the unintended consequences of the study interventions.

7.3 Study significance and implications for patients, health care professionals, policy makers and researchers

Knowledge-to-practice gaps in complex clinical conditions like asthma will only be closed by the successful implementation of valid evidence at low risk of bias; this is only possible when factors affecting practice, behaviour or policy change are anticipated and evaluated using rigorous research methods.

This is the first study in the asthma literature that examines if ED-directed interventions focused on increasing PCPs-patient follow-up using an incremental approach of OL-letter to PCPs alone or in addition to CM guidance on self-management, improve outcomes in patients with moderate to severe acute asthma being discharged from the ED.

The results of this thesis project are methodologically, clinically and contextually relevant since they 1) synthesize the evidence on high-quality interventions targeting the transitions in care between the ED and PCPs for asthma and identify factors that may influence their effectiveness; 2) highlight the value of considering KTA frameworks, of engaging potential knowledge users, and of using mixed-methods in comparative effectiveness studies of multifaceted interventions; and 3) reveal important information about the occurrence of desired and undesired outcomes after acute asthma visits to Canadian EDs.

The KTA model developed by Graham and Straus[133, 134] has been the framework for the development, implementation and evaluation of several quality-improvement initiatives promoting evidence-based practices in Canada.[270] The novelty of this project relies on the generation of new evidence based on a dynamic, theory-based and stepped-approach (using integrated knowledge translation principles and high-quality research methods) in an attempt to bridge the gap between knowledge generation and its adoption into practice. [271]

An important message for patients with asthma derived from this program of research is that a follow-up visit with their family doctor is still considered a key step in regaining asthma control following an ED visit. Interventions like the ones evaluated in this thesis project, however, are not effective strategies to reduce their visits to acute care settings for perceived need of further treatment if there is limited capacity to follow-them up effectively after an ED visit for acute asthma.

The main message to emergency physicians is that while the overall quality of the ED management observed in this thesis could be perceived as “evidence-based”, there is still a window for improvement on specific components like their treatment decisions at discharge (a stepped-up approach is always recommended). A careful assessment of patients’ history, severity of presentation, response to treatment and predictors for relapse should guide all disposition decisions and discharge instructions. The identification of high levels of anxiety in their patients

during the acute episode should be followed by the selection of alternative strategies (e.g., assistance from allied health professionals) for the delivery of asthma education and guidance.[114, 144]

The main message to PCPs treating patients with asthma is that arranging an effective post-ED follow-up in their patients may have an significant impact on their outcomes. An effective follow-up includes reviewing their symptoms, reinforcing the importance of adherence to asthma controller medication, and assessing preventive actions. Limited capacity for short-term follow-up in offices should initiate the search for alternative cost-effective strategies for timely patient assessment such as post-ED follow-up by allied health professionals (e.g., respiratory therapists, pharmacists, asthma educators) from the primary care network. In addition, when possible, health care interventions should be adapted to patients' levels of health literacy. Finally, Respirologists will benefit from knowing value that both patients with asthma and PCPs give to their guidance in ambulatory asthma care.

There are important implications from the results of this thesis for policy makers. Unless large and definitive, the results of a single study should not immediately change practice or policy. The implementation of interventions targeting complex conditions like asthma should rely on the evaluation of their effectiveness using high-quality, socially accountable and context-sensitive research methods such as the ones used in this program of research. The description of the fidelity of the study

interventions should help reflecting on the potential risks and benefits derived from similar interventions that can or cannot be easily implemented in clinical practice. Moreover, this research reinforces the caution of implementing even well intended interventions/strategies avoided unless they are accompanied by rigorous assessment of their effectiveness and the costs to the health care system.[272, 273]

Finally, a key message for researchers is that un-intended consequences of study interventions need to be carefully explored and interpreted. The solid rationale, theory and research methods supporting this thesis proposal allowed the discussion of factors that could have influenced its counterintuitive and un-intended results.

7.4 Future directions

The results from this research allowed the identification of opportunities for future research initiatives including, but not limited to, the following areas:

1. The assessment of the impact that different ED treatment decisions (non stepped-up vs. stepped-up approaches) have on the health outcomes of patients who are discharged home after being treated for an asthma exacerbation.
2. The assessment of the quality of asthma care provided at the primary care level after an ED visit for acute asthma, and of the impact that the provision of different levels of evidence-based interventions has on patients' health-related outcomes.

3. The exploration of the impact that different delivery methods of the "active ingredients" of ED directed OL-leader and CM interventions (e.g., face to face encounters, summaries of guidelines or evidence) has on patients' health outcomes.
4. The evaluation of alternative care providers (e.g., nurse practitioners, asthma educators, pharmacists, physicians with an interest in asthma) in the provision of urgent post-ED reassessment, medication reconciliation and adjustment, and relapse prevention.
5. The evaluation of alternative PCP intervention delivery models (e.g., same-day booking, primary care networks, etc.) on urgent post-ED reassessment, medication reconciliation and adjustment, and relapse prevention.
6. The evaluation of the use of electronic applications for physicians (e.g., computerized decision support systems) and/or patients (e.g., texts, social media) to generate reminders and evidence-based guidance after a patient ED visit for acute asthma.
7. The use of the KTA conceptual framework and mixed-research methods employed in this program of research to answer similar research questions in other clinical conditions.

7.5 Conclusions

Asthma is a complex chronic respiratory disease and exacerbations place patients at increased risk of sub-optimal outcomes, impaired QoL and poor asthma control in the future. One important, often missing component of care after an ED visit for acute asthma is a timely re-assessment by a PCP using evidence-based approaches. Multifaceted and tailored ED-directed interventions including personalized OL-letters faxed to the PCPs or CM guidance on self-management to patients, in an incremental approach appear to be moderately effective in improving the linkage between patients and PCPs after an ED visit for acute asthma; however, the effect is attenuated over time. The study interventions, however, were not effective in reducing resource utilization or improving QoL. Moreover, un-intended consequences including overtreatment at the patient-PCP follow-up encounters were associated with the study interventions.

This research adds to the asthma literature by providing robust comparative evidence of novel ED-directed strategies designed to improve health-related outcomes for asthma. The use of a KTA conceptual framework favoured a reflective and synergistic research process with the involvement of potential end users. Regardless of the outcome of the comparative effectiveness study, the interpretability of these results and their potential applicability was enhanced by the previous contact with the

practice environment and the anticipation of potential barriers and facilitators for knowledge implementation.

Figure 7-1 Knowledge to action (KTA) model supporting this thesis project.

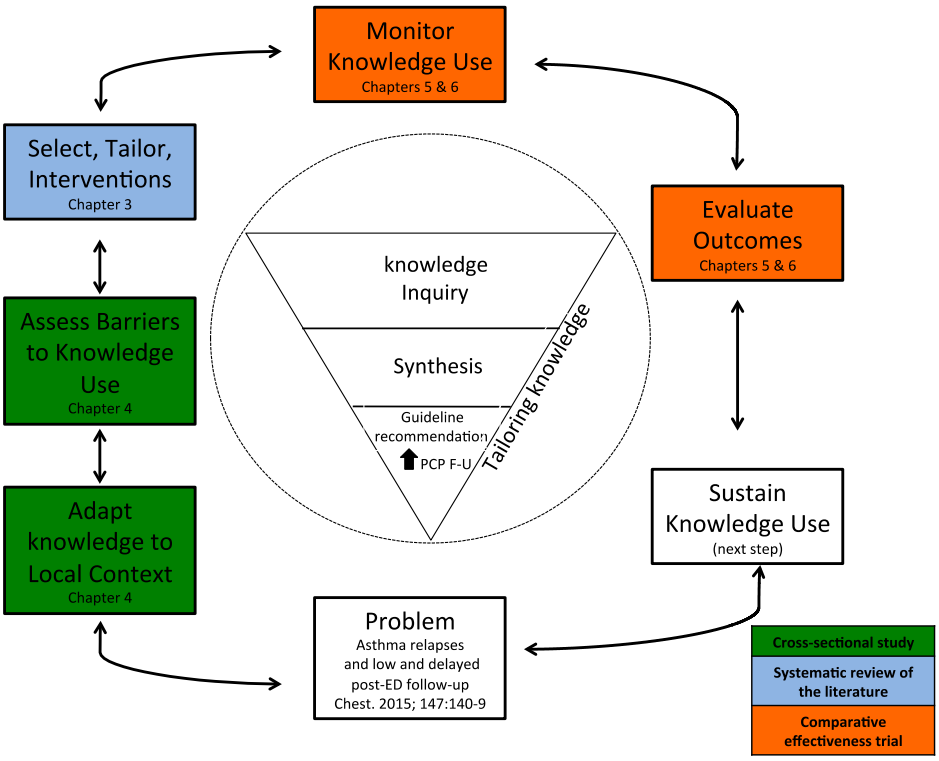
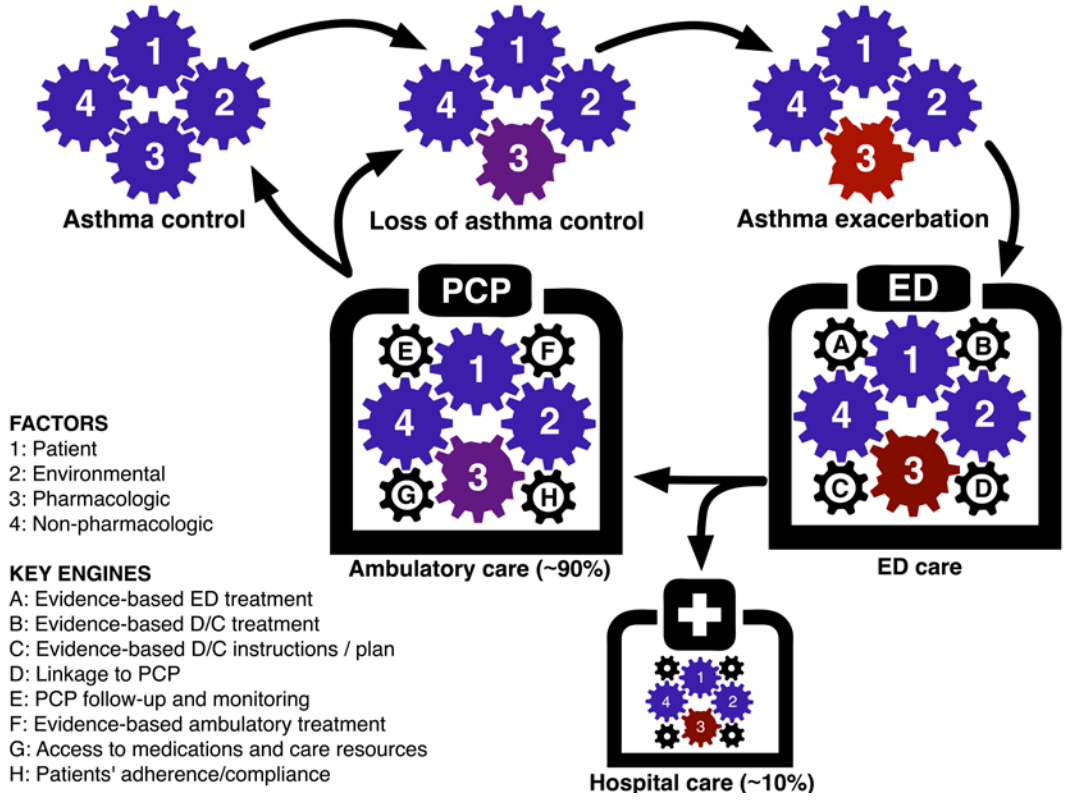


Figure 7-2 Factors influencing the loss of asthma control and the potential outcomes resulting from the care provided in emergency departments and in the ambulatory care setting.



Note: ED= emergency department; PCP = primary care provider; D/C = discharge

Table 7-1 Comparison between the characteristics and results of the systematic review and the comparative effectiveness trial included in this thesis project.

	Systematic Review	Comparative effectiveness trial
Population	Patients discharged from the ED after being treated for acute asthma	Patients discharged from the ED after being treated for acute asthma
Interventions	Multifaceted	Multifaceted
Number/type of studies	5 RCTs	1 RCT
Sample size	n=825	n=367
Intervention fidelity	Poorly described	Well described
Outcomes source/type	Patient report/pooled	Verified/adjusted
PCP follow-up visits within 30 days	1.6 (95%CI: 1.3 to 1.9)	PF vs. UC: 2.2 (95%CI: 1.3 to 3.7) CM vs. UC: 2.1 (95%CI: 1.2 to 3.89)
Relapses within 90 days	1.3 (95%CI: 0.8 to 2.0)	PF vs. UC: 2.8 (95%CI: 1.7 to 4.6) CM vs. UC: 1.8 (95%CI: 0.7 to 4.8)

Note: ED= emergency department; RCT = randomized controlled trial; PCP = primary care provider; PF = personalized fax (study intervention); CM = care manager (study intervention); CI= confidence interval.

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