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# One-year outcomes of inhaled controller therapies added to systemic corticosteroids after asthma-related hospital discharge

Mohsen Sadatsafavi <sup>a,b,\*</sup>, Larry D. Lynd <sup>c,d</sup>, Mary A. De Vera <sup>c</sup>, Zafar Zafari <sup>d</sup>, J. Mark FitzGerald <sup>a,b</sup>

<sup>a</sup> Institute for Heart and Lung Health, Department of Medicine, The University of British Columbia, Vancouver, Canada

<sup>b</sup> Centre for Clinical Epidemiology and Evaluation, The University of British Columbia, Vancouver, Canada

<sup>c</sup> Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, The University of British Columbia, Vancouver, Canada

<sup>d</sup> Centre for Health Evaluation and Outcome Sciences, The University of British Columbia, Vancouver, Canada

Received 11 August 2014; accepted 30 December 2014

Available online 7 January 2015

## KEYWORDS

Asthma;  
Resource use;  
Outcomes;  
Comparative effectiveness;  
Propensity score;  
Treatment

## Summary

**Background:** Much of the evidence on the early use of inhaled controllers after severe asthma exacerbations is about their short-term benefit, leaving a gap in evidence on their longer-term outcomes.

**Methods:** We used administrative health data from British Columbia, Canada (2001–2012) to evaluate readmission rate (primary outcome), adherence to controller medications, and use of reliever medications associated with different inhaled controller treatments as an add-on to systemic corticosteroids (SCS) over one-year following discharge from an asthma-related admission in individuals 12–55 years of age. Exposure was assessed in the 60 days after discharge, and categorized as monotherapy with SCS (*SCS-only*) versus SCS plus inhaled controller therapy (*SCS + inhaler*); the latter was further divided into SCS + inhaled corticosteroid (*SCS + ICS*) and SCS + ICS and long-acting beta agonists (*SCS + ICS/LABA*). Propensity score-adjusted regression models were used to estimate relative rates (RR) of outcomes across exposure groups.

**Abbreviation:** ANCOVA, analysis of covariance; B/F, budesonide + formoterol; CI, confidence interval; F/S, fluticasone + salmeterol; ICD, international classification of diseases; ICS, inhaled corticosteroids; LABA, long-acting beta-agonists; LTRA, leukotriene receptor antagonists; MPR, medication possession ratio; P, P-value; RR, rate ratio; SABA, short-acting beta agonists; SCS, systemic corticosteroids.

\* Corresponding author. Centre for Clinical Epidemiology and Evaluation, 7th Floor, 828 West 10th Avenue, Research Pavilion, Vancouver, BC V5Z 1M9, Canada. Tel.: +1 604 875 5178; fax: +1 604 875 5179.

E-mail address: [msafavi@mail.ubc.ca](mailto:msafavi@mail.ubc.ca) (M. Sadatsafavi).

<http://dx.doi.org/10.1016/j.rmed.2014.12.014>

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**Results:** The final cohort included 2,272 post-discharge periods (43.0% *SCS-only*, 26.9% *SCS + ICS*, and 30.1% *SCS + ICS/LABA*). Readmission rate was significantly lower in the *SCS + inhaler* versus *SCS-only* (RR = 0.74 [95%CI 0.59–0.93]), but similar between *SCS + ICS* and *SCS + ICS/LABA* (RR = 0.78 [95%CI 0.59–1.04]). Long-term adherence, defined as medication possession ratio, to controller medications was 83% higher in *SCS + inhaler* than *SCS-only*, and 64% higher in *SCS + ICS/LABA* than in *SCS + ICS*. The use of reliever medications was similar across exposure groups.

**Conclusion:** Early initiation of inhaled controllers after discharge from an asthma-related hospitalization was associated with significantly better long-term adherence to controller medications as well as reduced rate of readmissions. Combination therapy with ICS/LABA seems to be at least as effective as mono-therapy with ICS in reducing the risk of readmission, with the added benefit of better long-term adherence.

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## Introduction

Patients who have experienced a recent asthma exacerbation requiring inpatient care constitute a group of severe asthma patients at high risk of subsequent adverse events [1,2]. The role systemic corticosteroids (SCS) to achieve asthma control and reduce the rate of exacerbation in this group of patients is well established [3,4]; nevertheless, the benefit of early initiation of inhaled controllers alongside SCS is less studied. Randomized trials in this patient population have focused on short-term (often within 30 days) outcomes [5,6]. Nevertheless, early inhaled controller therapy might alter the risk of longer-term effects, either directly or through setting the course for the longer-term treatment the patient receives. A previous observational study demonstrated that not having controller medication at discharge after an emergency department or inpatient visit was associated with a 79% higher risk of experiencing another similar event in the next 6 months [7]. This important finding signifies the window of opportunity that exists to use established and available treatments to improve the outcomes in this high risk group of asthma patients. This study, however, did not evaluate the effect of inhaler treatment as an add-on to SCS, nor did it investigate the role of adherence in explaining the results. We hypothesize that the outpatient care in the immediate post-discharge period is a critical time to ensure long-term, evidence-based treatment is provided to the individual, and that patients who only receive short-term SCS in this period might miss the opportunity of receiving maintenance inhaler treatment once the exacerbation episode resolves.

Further, it is not obvious which classes of inhaled controllers provide the best effectiveness and safety profile. On one hand, evidence suggests that combination of ICS and long-acting beta-agonists (LABA) is the most effective inhaler therapy [3,8]. On the other hand, there are concerns regarding the safety of LABAs in terms of increased risk of adverse asthma-related outcomes even with concomitant ICS use [9]. These concerns are heightened in the post-discharge period given these individuals are already at high risk of adverse asthma-related outcomes. In summary, there seems to be a substantial gap in evidence

on the long-term consequences of inhaled controller therapies as an add-on to SCS after asthma-related hospitalizations.

Population-based administrative health data are a valuable resource to fill this evidence gap as they are based on representative population, capture outcomes under real-world settings, and have sample sizes that surpass those of clinical studies. Indeed, administrative health data have played important role in improving our understanding of the real-world safety and effectiveness of asthma treatments [10,11]. The objective of this study was to evaluate the comparative outcomes of the addition of inhaled controller to systemic corticosteroids in one year after discharge from an asthma-related admission.

## Methods

**Data sources:** We used the administrative health records from British Columbia (BC), a Canadian province with a population of approximately 4.2 million, from April 2001 (the first year that ICS + LABA as a combination inhaler became available in the province) to March 2012. BC has a public health care system in place, the administrative needs of which has resulted in centralized datasets that captures resource use for all legal residents, all care providers (public or private), and all prescribed medications regardless of any insurance coverage. We had access to consolidation files [12] and all records of inpatient [13] and outpatient [14] encounters, as well as filled prescriptions [15] during this period. Databases are linkable at the individual level with very low rate of missing, underreporting, or misclassification [16–18]. Since all legal residents of BC receive universal health-care, the data are representative of the whole population. Ethics approval for the use of the data was obtained from the University of British Columbia Institutional Review Board (Human Ethics H08-01287), and permission was granted by the Ministry of Health for the study.

**Study cohort:** We created a cohort of individuals who, between the ages 12 and 55, 1) had been discharged from at least one episode of asthma-related hospitalization, 2) had filled prescription for SCS in the 60-days post-discharge period, and 3) had been continuously registered with the

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