7-12-2021

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Recommended Citation

Nanishi M, Press VG, Miller JB, Eastin C, Aurora T, Crocker E, Fujiogi M, Camargo CA, Jr., and Hasegawa K. Hospital-Initiated Care Bundle, Posthospitalization Care, and Outcomes in Adults with Asthma Exacerbation. J Allergy Clin Immunol Pract 2021.

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Original Article

Hospital-Initiated Care Bundle, Posthospitalization Care, and Outcomes in Adults with Asthma Exacerbation

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What is already known about this topic? Hospitalization for asthma exacerbation is an opportune setting for initiating preventive care for high-risk patients. However, little is known about the effect of implementing an evidence-based preventive care bundle during hospitalization on subsequent risk of asthma exacerbation.

What does this article add to our knowledge? In this study of adults hospitalized for asthma exacerbation, implementation of a hospital-initiated care bundle not only improved the quality of post-hospitalization asthma care but also reduced the rate of severe asthma exacerbation up to 30%.

How does this study impact current management guidelines? The present study underscores the importance of implementing evidence-based preventive asthma care in patients hospitalized with asthma exacerbation.

BACKGROUND: Hospitalization for asthma exacerbation is an opportune setting for initiating preventive efforts. However, hospital-initiated preventive asthma care remains underdeveloped and its effectiveness is uncertain.

OBJECTIVE: To examine the effectiveness of a hospital-initiated asthma care bundle on posthospitalization asthma care and clinical outcomes.

METHODS: Prospective multicenter study of adults (18-54 years) hospitalized for asthma exacerbation in 2017 to 2019. During the hospitalization, we implemented an asthma-care bundle (inpatient laboratory testing, asthma education, and discharge care), and prospectively measured chronic asthma care (eg, immunoglobulin E testing, specialist care) and asthma exacerbation (ie, systemic corticosteroid use, emergency department [ED] visit, hospitalizations) outcomes. By applying a self-controlled case series method, we examined within-person changes in these outcomes before (2-year period) and after (1-year period) the bundle implementation.

RESULTS: Of 103 adults hospitalized for asthma exacerbation, the median age was 40 years and 72% were female. Compared with the preimplementation period, the postimplementation period had improved posthospitalized asthma care, including serum specific immunoglobulin E testing (rate ratio [RR] 2.18; 95% confidence interval [95% CI] 0.99-4.84; $P = .051$) and evaluation by asthma specialist (RR 2.66; 95% CI 1.77-4.04; $P < .001$). Likewise, after care bundle implementation, patients had significantly lower annual rates of systemic corticosteroid use (4.2 vs 2.9 per person-year; RR 0.70; 95% CI 0.61-0.80; $P < .001$), ED visits (3.2 vs 2.7 per person-year; RR 0.83; 95% CI 0.72-0.95; $P = .008$), and hospitalizations (2.1 vs 1.8 per person-year; RR 0.82; 95% CI 0.69-0.97; $P = .02$). Stratified analyses by sex, race/ethnicity, and health insurance yielded consistent results.

CONCLUSIONS: After hospital-initiated care bundle implementation, patients had improved posthospitalization care and reduced rates of asthma exacerbation. **© 2021 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2021;■:■-■)**

Key words: *Asthma exacerbation; Hospitalization; Quality of care; Asthma management; Outcomes*

INTRODUCTION

Asthma is a significant health problem in the United States. In 2018, 25 million individuals had asthma,[1] with an estimated

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This study was funded by a grant from Novartis Pharmaceuticals Corporation to Massachusetts General Hospital (K. Hasegawa). The sponsor had no role in the conduct of the study, collection, management, analysis, or interpretation of the data or preparation or approval of the manuscript.

Conflicts of interest: C. A. Camargo, Jr, has participated in scientific advisory boards for AstraZeneca and GSK. K. Hasegawa has received a research grant from Novartis. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication April 13, 2021; revised June 20, 2021; accepted for publication June 24, 2021.

Available online ■■

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2213-2198

https://doi.org/10.1016/j.jaip.2021.06.044

Abbreviations used
COPD- Chronic obstructive pulmonary disease
ED- Emergency department
ICS- Inhaled corticosteroids
IgE- Immunoglobulin E
IL- Interleukin
MARC-41- The 41st Multicenter Airway Research Collaboration
RCT- Randomized controlled trial

direct health cost of $50 billion.[2] Asthma exacerbations contribute to a substantial portion of this problem—approximately 1.7 million emergency department (ED) visits and 180,000 hospitalizations in 2016 alone.[3] In this context, the U.S. government has identified improving asthma care as an objective in *Healthy People 2030,* with a goal to reduce asthma exacerbations, ED visits, and hospitalizations.[4]

Despite its clinical and public health importance, recent studies have demonstrated a suboptimal quality of ED,[5-9] inpatient,[10-12] and transitional[12,13] care in patients with asthma exacerbation. For example, a retrospective study of hospitalized patients with asthma reported that guideline-recommended transition of care to specialists was suboptimal (only 27% of hospitalized adults received a referral to an asthma specialist at hospital discharge).[10] Within the sparse literature, clinical trials of adults with asthma exacerbation have examined the effect of single or limited elements of asthma care—such as asthma education,[14-16] individual action plan,[17-19] or facilitated referral[20]—on subsequent asthma outcomes. Although hospitalization for asthma exacerbation is an opportune setting for initiating high-quality asthma care for these costly and high-risk patients, little is known about the effect of implementing an evidence-based preventive care bundle[21] during hospitalization on subsequent risk of asthma exacerbation.

To address the knowledge gap, we conducted a prospective multicenter study of adults hospitalized for asthma exacerbation to examine the effectiveness of a hospital-initiated asthma care bundle on posthospitalization asthma care and clinical outcomes.

METHODS

Study design, setting, and participant

This is a multicenter, prospective, before-after study—the 41st Multicenter Airway Research Collaboration (MARC-41)—that investigates the effectiveness of the hospital-initiated preventive care bundle in adults hospitalized for asthma exacerbation. By applying a self-controlled case series design, we compared each participant's rate of outcomes over a 3-year period (ie, 2 years before vs 1 year after the implementation of the care bundle). This design enables each participant to function as his or her own control.[22] Accordingly, it has a major advantage that effects of any time-invariant covariates (eg, the genetics, sex, race/ethnicity, site) are implicitly controlled, thereby mitigating unmeasured confounding.[22-25]

In 2017 to 2019, we enrolled adults (aged 18-54 years) with a physician diagnosis of asthma, current use of inhaled corticosteroids (ICS), and a history of frequent severe exacerbations (defined by ≥2 bursts of systemic corticosteroids [≥3 days each] in a 1year period[26]) who were hospitalized for asthma exacerbation at 1 of the 5 geographically diverse U.S. hospitals—Henry Ford Hospital (Detroit, MI), Massachusetts General Hospital (Boston, MA), University of Arkansas for Medical Science (Little Rock, AR), University of Chicago Medical Center (Chicago, IL), and Virginia Commonwealth University Medical Center (Richmond, VA). We limited the study to patients aged 18 to 54 years in order to minimize misspecification with chronic obstructive pulmonary disease, according to previous studies.[6,10] We excluded patients with nonadherence to ICS (ie, use of ICS once a week or less—based on the screening interview and medical record review at enrollment) and those without a permanent address or phone number. The institutional review board at each of the participating hospitals approved the study (as a quality improvement study). Informed consent was obtained from all study participants.

Exposure—hospital-initiated asthma care bundle

Immediately after hospital admission, the participating site implemented the inpatient asthma care bundle consisting of 3 major areas with a total of 10 core elements (Table E1; available in this article's Online Repository at www.jaci-inpractice.org): (1) laboratory testing (serum total immunoglobulin E [IgE] as well as complete blood count with differential [including eosinophil quantification]); (2) education (development of written action plan, education of inhaler use technique, issuing peak flowmeter, and smoking cessation assistance [for smokers]); (3) hospital discharge (or transitional) care (prescription of systemic corticosteroids, modification of ICS, and instruction/scheduling of follow-up by asthma specialist). In addition to these core (mandatory) elements, the sites also implemented optional elements (eg, pharmacy, asthma care manager consult) based on the availability of resources at each site. These optional elements did not contribute to the overall bundle examined. The item selection of the care bundle was based on the national and international asthma guidelines,[27,28] systematic literature review of high-quality evidence (including the Cochrane Database of Systematic Reviews and meta-analysis of clinical trials), and input from the multidisciplinary project team (eg, allergists, emergency physicians, internists, pulmonologists). The overall goal of the bundle was to reduce the risk of severe asthma exacerbations after the index hospitalization.

Outcome measures

The primary clinical outcome was severe asthma exacerbation—the use of systemic corticosteroids for 3 or more days, ED visit, or hospitalization for asthma exacerbation—during the pre- and postimplementation periods, according to previous studies.[26,29,30] The secondary (process measure) outcomes were asthma care, including laboratory testing (total and specific IgE measurement, environmental allergen skin testing), adjustment to long-term controller medications (eg, initiation of biologic agents), and evaluation by an asthma specialist (eg, allergist, pulmonologist). We measured these outcomes—in both the preimplementation period (retrospectively) and the postimplementation period (prospectively)—through structured interviews and medical record review by nonblinded investigators using a standardized protocol, which has been used in previous studies.[6,10,31] Structured interviews and medical record review were conducted at enrollment and during hospitalization as well as at 1 month, 6 months, and 12 months after enrollment to abstract the data on asthma care (including the electronic documentation of medication use), clinical outcomes, medical history, and laboratory testing during the pre- and postimplementation periods. All data were reviewed at the EMNet Coordinating Center at Massachusetts General Hospital, and site investigators were queried about missing data and discrepancies identified by data checks.

TABLE I. Characteristics of adults hospitalized for asthma exacerbation*

Characteristics	n = 103
Patient characteristics	
Demographics	
Age, y, median (IQR)	40 (32-49)
Female sex, n (%)	74 (72)
Race/ethnicity, n (%)	
Non-Hispanic White	19 (18)
Non-Hispanic Black	69 (67)
Hispanic ethnicity	12 (12)
Others	3 (3)
Health insurance, n (%)	
Private	38 (37)
Public	62 (60)
No insurance	3 (3)
Household income, $, median (IQR)†	37,942 (27,540-54,164)
Having primary care physician, n (%)	95 (92)
Current smoking, n (%)‡	22 (21)
BMI, kg/m^2, median (IQR)§	35 (28-43)
Medical history	
History of eczema, n (%)	32 (31)
History of allergic rhinitis, n (%)	66 (64)
Coexistent illnesses, n (%)‖	
COPD	13 (13)
Gastroesophageal reflux	12 (12)
Psychiatric disorder	10 (10)
Congestive heart failure	7 (7)
Pneumonia	6 (6)
Asthma-related history	
ED visit for asthma in the preimplementation period, n (%)	96 (93)
Hospitalized for asthma in the preimplementation period, n (%)	79 (77)
Frequency of hospitalizations, median (IQR)	2 (1-5)
History of intubation for asthma, n (%)	30 (29)
Current use of oral corticosteroids, n (%)	45 (44)
Current use of ICS, n (%)	103 (100)
Current use of long-acting beta-agonist, n (%)	70 (68)
Current use of leukotriene receptor antagonists or modifiers, n (%)	54 (52)
Asthma Control Test in the past 4 wk, median (IQR)	9 (7-12)
Having PEF meter	76 (74)
Having PEF measured in the past 4 wk¶	42 (55)
Having asthma action plan	47 (46)
Laboratory values during hospitalization	
WBC, cells/μL, mean (SD)	10,480 (4,130)
Eosinophils, cells/μL, mean (SD)	297 (430)
Serum total IgE level, IU/μL, mean (SD)#	412 (880)
Presentation and inpatient course	
Initial hospitalization location, n (%)	
ED observation unit	55 (53)
Hospital ward or stepdown unit	36 (35)
ICU	12 (11)
Mechanical ventilation**	12 (12)
Disposition, n (%)	
Discharged to home	101 (98)
Left against medical advice	2 (2)

BMI, Body mass index; *ICU,* intensive care unit; *IQR,* interquartile range; *PEF,* peak expiratory flow; *WBC,* white blood cell count.
*Percentages are not equal to 100 because of rounding.
†Estimated from patient's residence ZIP code.
‡Among 97 patients who gave the information of smoking status.
§Among 90 patients who gave the information of body height and weight.
‖Including COPD, pneumothorax, pneumonia, nasal polyps, rhinitis, sinusitis, vocal code dysfunction, significant arrhythmia, congestive heart failure, psychiatric disorder (eg, schizophrenia), and gastroesophageal reflux.
¶Among 76 patients who had a PEF meter before the index hospitalization.
#Among 77 patients who underwent serum total IgE measurement during the index hospitalization.
**Including noninvasive and invasive positive-pressure ventilation.

Statistical analysis

In the current study, we applied a self-controlled case series method to multicenter data. This design relies on within-individual comparisons in a study sample with both the exposure and the outcomes of interest.[22] Specifically, to examine the effectiveness of the care bundle on the posthospitalization asthma care and clinical outcomes, we examined the within-individual changes for each outcome between the pre- and the postimplementation periods. We fit conditional Poisson regression models to estimate rate ratios (RRs) with 95% confidence intervals (95% CIs)—with the pre-implementation period (2-year period) as the reference period—for the postimplementation 1-year period. To account for the difference in period intervals, the model incorporated an offset term (ie, natural logarithm of the interval). Because each patient is matched to her or his own reference period, the RRs from the conditional Poisson regression model are equivalent to having fixed effects in the model.

We conducted a series of sensitivity analyses. First, in the stratified analyses that examine the potential heterogeneity in the effect of care bundle,[32-35] we repeated the analysis with stratification by sex, race/ethnicity, insurance, baseline smoking status, obesity (body mass index $\geq$ 30 kg/m^2), history of intubation, recent oral corticosteroid use, and initial disposition (ie, ED observation unit, hospital ward or stepdown, and intensive care unit). Second, to minimize the potential misclassification with chronic obstructive pulmonary disease (COPD), we have conducted a subgroup analysis excluding patients with a history of COPD. Third, to address the potential effect of increased availability of biologic agents in recent years, we repeated the analysis by excluding patients who initiated anti-interleukin-4 (IL-4)/IL-5 therapy after hospital discharge. Fourth, we repeated the analysis by dividing the postimplementation period into 2 6-month intervals (1-6 months and 7-12 months after the index hospitalization). Lastly, to address the point that exacerbations events are recurrent and nonindependent, we modeled the outcome events as binary variables. The original target sample size was 90 patients hospitalized for asthma exacerbation. We estimated that the study would have had a power of greater than 80% to detect a 30% decrease in the incidence of severe asthma exacerbation, from 2.40 per year in the preimplementation period to 1.68 per year in the postimplementation period at a 2-sided significance level of .05. We analyzed the data using R version 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria). All *P* values were 2-tailed, with *P* less than .05 considered statistically significant.

Outcome	Rate (%)		RR (95% CI)‡	*P* value
	Pre implementation*	Post implementation†		
Serum specific IgE measurement	6	13§	2.18 (0.99-4.84)	.051
Allergen skin testing	<1	4	4.02 (0.78-29.0)	.11
Use of omalizumab	1	<1	0.67 (0.03-5.23)	.77
Use of anti-IL-4/IL-5 therapy‖	<1	5	10.1 (1.62-192.4)	.04
Asthma specialist visit	19	52	2.66 (1.77-4.04)	<.001

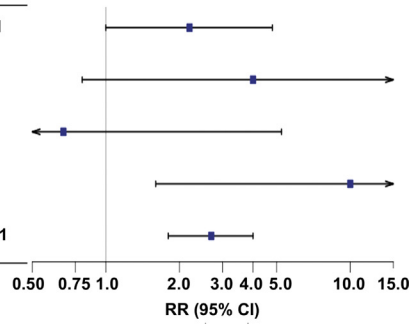

FIGURE 1. Within-individual comparisons of chronic asthma care between the pre- and the postimplementation periods. Arrows indicate that the 95% CI of the RR exceeds the lower or higher limit of the x-axis. *Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle. †In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle (including the index hospitalization). ‡RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals. §Serum specific IgE measurement after the index hospitalization. ‖Including dupilumab, benralizumab, mepolizumab, and reslizumab.

RESULTS

Patient characteristics

The MARC-41 study enrolled 103 adults hospitalized for asthma exacerbation at 1 of the 5 participating hospitals during 2017 to 2019. Data of the 12-month postimplementation period were available in 102 patients (99%), with the other patient contributing to 6-month postimplementation period data owing to loss to follow-up (ie, a total of 1,230 person-month follow-up). In this cohort, the median age was 40 years (interquartile range, 32-49 years); 72% were women, 67% non-Hispanic Black, and 12% Hispanic (Table I). In addition, 60% had public health insurance and 3% had no insurance. As expected, the study patients had a large asthma burden in the pre-implementation period, reflected by 93% having at least 1 ED visit and 77% having hospitalization for asthma exacerbation; the index hospitalization was consistent with their chronic asthma trajectory. Despite their substantial morbidity, patients reported suboptimal quality of asthma care components in the pre-implementation period, such as only 46% of patients having an asthma action plan prior to their index hospitalization. At the index hospitalization, 53% were admitted to the observation unit, 35% to the ward or stepdown unit, and 11% to the intensive care unit.

Comparisons of asthma care between the pre- and the postimplementation of care bundle

After implementation of a hospital-initiated asthma care bundle during the index hospitalization, the patients had improved quality of chronic asthma care (Figure 1). For example, after the implementation of the care bundle, there was a nonsignificant increase in the rate of specific IgE measurement (RR 2.18; 95% CI 0.99-4.84; $P = .051$) and a significant increase in the rate both for anti-IL-4/IL-5 therapies (RR 10.1; 95% CI 1.62-192.4; $P = .04$) and for asthma specialist visit (RR 2.66; 95% CI 1.77-4.04; $P < .001$) with adjusting for the difference in the period interval. In the sensitivity analyses, despite their limited statistical power, the association of care bundle implementation with an increased rate of asthma specialist visits was similar across sex (Table E2; available in this article's Online Repository at www.jaci-inpractice.org), race/ethnicity (Table E3; available in this article's Online Repository at www.jaci-inpractice.org), and health insurance (Table E4; available in this article's Online Repository at www.jaci-inpractice.org) strata.

Comparisons of clinical outcomes between the pre- and the postimplementation of care bundle

After the implementation of the in-hospital care bundle, the study patients had a significantly lower rate of severe asthma exacerbation (Figure 2). Specifically, the annualized rate of systemic corticosteroid use decreased from 4.2 per person-year in the preimplementation period to 2.9 per person-year in the postimplementation period, with a corresponding RR 0.70 (95% CI 0.61-0.80; $P < .001$). Likewise, there was a significant reduction in the rate for both ED visits (3.2 vs 2.7 per person-year; RR 0.83; 95% CI 0.72-0.95; $P = .008$) and hospitalizations (2.1 vs 1.8 per person-year; RR 0.82; 95% CI 0.69-0.97; $P = .02$) after implementation of the asthma care bundle.

In the sensitivity analyses, despite the relatively limited sample size, the relationship between care bundle implementation and decreased rate of severe asthma exacerbation was generally consistent across the sex (Table E5; available in this article's Online Repository at www.jaci-inpractice.org), race/ethnicity (Table E6; available in this article's Online Repository at www.jaci-inpractice.org), and health insurance (Table E7; available in this article's Online Repository at www.jaci-inpractice.org) strata. For example, the rate of ED visits and hospitalizations significantly decreased in both non-Hispanic White and Hispanic individuals, whereas the estimated effect was not significant in non-Hispanic Black individuals ($P_{interaction} < .01$ and $P_{interaction} = .02$, respectively; Table E6). With stratification by insurance, the estimated downward effects were also consistent with the main analysis in both public and private insurance strata. Likewise, similar relationships were observed in the stratified analysis by smoking status (Table E8; available in this

Outcome	Mean annualized incidence (per person-year)		RR (95% CI)‡	*P* value
	Pre implementation*	Post implementation†		
Systemic corticosteroid use	4.2	2.9	0.70 (0.61-0.80)	<.001
ED visits	3.2	2.7	0.83 (0.72-0.95)	.008
Hospitalization	2.1	1.8	0.82 (0.69-0.97)	.02

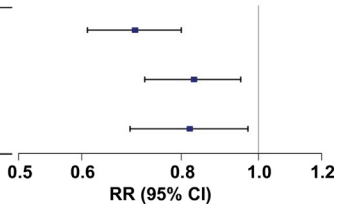

FIGURE 2. Within-individual comparisons of annualized incidence of severe asthma exacerbations between the pre- and the postimplementation periods. *Averaged over the 2-y period (a total of 206 person-years) before the implementation of hospital-initiated care bundle. †In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle. ‡RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

article's Online Repository at www.jaci-inpractice.org), obesity (Table E9; available in this article's Online Repository at www.jaci-inpractice.org), intubation history (Table E10; available in this article's Online Repository at www.jaci-inpractice.org), oral systemic corticosteroid use (Table E11; available in this article's Online Repository at www.jaci-inpractice.org), and disposition (Table E12; available in this article's Online Repository at www.jaci-inpractice.org). In the subgroup analysis of patients without COPD, the findings did not materially change (Table E13; available in this article's Online Repository at www.jaci-inpractice.org). In the sensitivity analysis excluding patients who initiated anti-IL-4/IL-5 therapy during the post-implementation period, the primary inference did not change materially—the annualized rate of systemic corticosteroid use decreased, with corresponding RR 0.71 (95% CI 0.62-0.81; $P <$ .001; Table E14; available in this article's Online Repository at www.jaci-inpractice.org). In the analysis dividing the post-implementation into 2 6-month periods, the rate reduction remained significant during the 7 to 12 months after the index hospitalization. (Tables E15 and E16; available in this article's Online Repository at www.jaci-inpractice.org). Lastly, in the analysis modeling the outcome events as binary variables, the findings were also consistent—reduced rate of ED visits with a corresponding RR of 0.21 (95% CI 0.07-0.70; $P = .01$; Table E17; available in this article's Online Repository at www.jaci-inpractice.org).

DISCUSSION

In this self-controlled case series analysis of a multicenter prospective study of 103 adults hospitalized for asthma exacerbation, the implementation of a hospital-initiated care bundle was associated with a significant improvement in post-hospitalization asthma care. Specifically, our data demonstrated an increase in the rate of biologic agent use and asthma specialist visit. Furthermore, there was a significant improvement in the clinical outcomes—an approximately 20% to 30% decrease in the rate of subsequent severe asthma exacerbations, defined by the use of systemic corticosteroids, ED visits, or hospitalizations. The current study demonstrated the effectiveness of an evidence-based, hospital-initiated care bundle on both chronic asthma care and clinical outcomes in adults with severe asthma exacerbation.

In agreement with our findings, previous studies—mostly focusing on individual elements of asthma care—have reported reductions in asthma disease burden.[14,36-38] For example, in a single-center randomized controlled trial (RCT) of children and adults with asthma exacerbation in the ED, Zeiger et al[37] found that, compared with continued management from nonspecialists, facilitated asthma specialist care not only increased the use of ICS but also decreased the frequency of asthma exacerbations and ED revisits. Furthermore, in another single-center RCT of adults hospitalized for asthma exacerbation in 1996 to 1999, Castro et al[38] reported that, compared with conventional care, multifaceted asthma care intervention (based on the 1997 Expert panel Report 2 [EPR-2] guidelines) reduced readmissions for asthma as well as health care (both direct and indirect) costs. In contrast, earlier reports have also shown no significant change in clinical outcomes.[17,39-41] For example, a Cochrane systematic review of 12 RCTs of educational intervention on adults with asthma exacerbation in the ED did not show a significant reduction in ED revisits.[39] These apparent discrepancies may be attributable to the differences in study design, setting, target populations, interventions of interest, or any combination of these factors. Regardless, the validity of our inference is strengthened by the self-controlled case series design. Its major advantage is that each individual serves as his or her own control and, hence, mitigates any time-invariant confounding, which cannot be addressed in conventional observational studies.[22] In addition, the study design removes between-individual variations, thereby yielding more precise estimates despite the relatively small sample size. The current study meets the assumptions of self-controlled case series in which we modeled transient exposures (ie, implementation of care bundle) and acute outcome events (ie, asthma exacerbations).[22] The current multicenter study builds on these prior reports and extends them by demonstrating the effectiveness of an evidence-based care bundle on both chronic asthma care and clinical outcomes in patients hospitalized with asthma exacerbation.

There are several potential explanations for the observed reductions in the frequency of severe asthma exacerbation after implementation of the hospital-initiated care bundle. First, the care bundle was, by definition, multifaceted (not as an isolated item) and was implemented in the inpatient setting—a time of heightened awareness and interest in health matters—reducing the outcome rates, at least partially, through an improvement in

both inpatient and posthospitalization care. Indeed, our data showed that the implementation of the bundle significantly improved posthospitalization asthma care (eg, the modest increase in biologic agent use and improved follow-up rate by an asthma specialist). Second, it is also possible that, after the implementation of asthma education, the patients changed their health behaviors (eg, better medication adherence), which the current study did not directly measure after the hospital discharge. Third, nonbundle elements of the study (eg, follow-up interviews) might have had an incremental benefit while its contribution is unlikely to have been substantial. However, despite the observed benefit of the care bundle, the morbidity burden of these patients remained large. This is partly because the implementation and effectiveness of the care bundle were imperfect in this real-world setting. Indeed, the implementation rate of some bundle elements was relatively low—67% for instruction for a follow-up visit with an asthma specialist and 31% for an appointment of a follow-up visit with an asthma specialist. Only 52% had a specialist visit during the postimplementation period whereas the rate significantly increased after the care bundle implementation. A prompt referral to a specialist at hospital discharge continued to be a challenge for administrative, financial, system-wide, and transportation reasons.[42] In addition, the current study did not directly intervene on postdischarge asthma care during the follow-up period (eg, guideline-concordant use of chronic asthma medications by the primary care physician). Furthermore, the observed heterogeneity of the effect between the race/ethnicity groups also suggests the potential need for context-specific implementations[43]; it also could have been due to the small subgroup sample sizes. Notwithstanding the complexity, the identification of an effective hospital-initiated preventive care bundle is an important finding. Our data, along with the previous studies, present cautious optimism that implementation of the evidence-based hospital-initiated asthma care bundle can not only improve the quality of asthma care but also reduce asthma morbidity burden.

Limitations

The study has several potential limitations. First, the data measurement relied, in part, on medical record review for the assessment of bundle implementation, asthma care, and outcomes; consequences of under documentation are possible. However, a prior study demonstrated that our data ascertainment methods had a high interrater agreement, including k coefficient of 0.95 (almost perfect) for clinical outcomes.[6] Second, we retrospectively measured the outcomes during the preimplementation period whereas we prospectively measured the outcome during the postimplementation period. This might have up- or downwardly biased the risk in the preimplementation period. Nevertheless, the measurement for both periods was performed using a standardized protocol. Third, the implementation of the bundle was imperfect and varied across the participating sites. Identifications of the barriers to its implementation merit further investigations. Fourth, as with any observational study, the causal inference might have been confounded by time-varying factors (eg, an increase in comorbidities over time). An RCT—with perfect adherence to the assigned intervention, no selection bias due to a differential loss to follow-up, and no postrandomization confounding—would yield a consistent estimate for the causal effect of interest. Fifth, the secular trend in asthma management may have affected the observed improvement in the patient outcomes. However, the observed 30% reduction in the primary outcome is unlikely to be fully explained by the secular change in asthma management alone. Sixth, in this current study, the sample size was not large. Regardless, we successfully identified significant effects of the bundle on the rate of severe asthma exacerbation. Lastly, our study sample comprised patients with frequent severe exacerbations in inner-city settings and excluded those with suboptimal medication adherence. Therefore, our inference might not be generalized to patients with mild-to-moderate asthma exacerbations or those with suboptimal adherence in nonurban or nonacademic hospitals. Nonetheless, our target population has a substantial asthma morbidity burden,[44] and hence, is the one for which targeted interventions are most urgently needed.

CONCLUSIONS

In sum, by applying a self-controlled case series method to prospective multicenter data of adults hospitalized for asthma exacerbation, we found that the implementation of an evidence-based asthma care bundle during hospitalization—an important opportunity for preventive care—was associated with significantly improved quality of asthma care and reduced rate of severe asthma exacerbation over the 1-year postimplementation period. These findings support a cautious optimism that the quality of asthma care can be further improved and asthma morbidity mitigated. For researchers, our study should advance research into building more robust evidence on hospital-initiated asthma care and identifying barriers for its implementation. For clinicians and hospitals, our data underscore the importance of continued efforts on the development and implementation of high-quality asthma care, which will, in turn, improve the outcomes of this population with large morbidity burden.

Acknowledgments

We thank the MARC-41 study hospitals and research personnel for their ongoing dedication to asthma research; and Ashley F. Sullivan, MS, MPH, and Ying Qi, MPH, (Massachusetts General Hospital) for their contributions to the MARC-41 study.

M. Nanishi and M. Fujiogi carried out the main statistical analysis, drafted the initial manuscript, and approved the final manuscript as submitted. J. B. Miller, V. G. Press, C. Eastin, and T. Aurora collected the data, reviewed and revised the manuscript, and approved the final manuscript as submitted. E. Crocker supervised the conduct of the study, reviewed and revised the manuscript, and approved the final manuscript as submitted. C. A. Camargo, Jr, conceptualized and designed the study, supervised the conduct of the study and the analysis, critically reviewed and revised the initial manuscript, and approved the final manuscript as submitted. K. Hasegawa conceptualized the study, obtained funding, supervised the statistical analysis, reviewed and revised the initial manuscript, and approved the final manuscript as submitted.

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ONLINE REPOSITORY

TABLE E1. Implementation of a hospital-initiated care bundle by item in patients hospitalized for asthma exacerbation

Bundle item	% (95% CI)
Core elements	
Inpatient laboratory testing*	97 (92-99)
Serum total IgE measurement	75 (65-83)
CBC with differential measurement	93 (87-97)
Inpatient asthma education†	82 (73-89)
Development of written action plan	54 (44-64)
Education of inhaler use technique	44 (34-54)
Provision of peak flowmeter‡	54 (33-73)
Smoking cessation assistance§	59 (36-79)
Hospital discharge care‖	96 (90-99)
Prescription of systemic corticosteroids	92 (85-97)
Modification of ICS	23 (16-33)
Instruction for follow-up visit to asthma specialist	67 (57-76)
Appointment of follow-up visit to asthma specialist	31 (22-41)
Optional elements	38 (29-48)
Pharmacy consult	15 (8-23)
Asthma case manager consult	31 (22-41)

CBC, Complete blood count.
*Any of the following 2 items.
†Any of the following 4 items. Asthma education was performed by the multidisciplinary project team (eg, emergency physicians, internists, allergists/immunologists, pulmonologists, respiratory therapists, advanced practice providers, study staff) during the index hospitalization.
‡Among 26 patients who did not have a peak flowmeter at hospitalization.
§Among 22 patients who were current smokers.
‖Any of the following 4 items.

TABLE E2. Within-individual comparisons of chronic asthma care between pre- and post-implementation periods, by sex

Outcome by sex	Rate (%)		RR (95% CI)‡	*P* value
	Preimplementation*	Postimplementation†		
Female (n = 74)				
Serum specific IgE measurement	7	11	1.45 (0.56-3.59)	.42
Allergen skin testing	1	1	1.00 (0.05-10.5)	.99
Use of omalizumab	<1	0	NA	NA
Use of anti-IL-4/IL-5 therapy§	<1	5.4	8.00 (0.89-71.6)	.06
Asthma specialist visit‖	20	54	2.76 (1.72-4.49)	<.001
Male (n = 29)				
Serum specific IgE measurement	2	17	10.2 (1.64-194.7)	.03
Allergen skin testing	0	0	NA	NA
Use of omalizumab	3	3	1.02 (0.05-10.6)	.99
Use of anti-IL-4/IL-5 therapy§	0	3	NA	NA
Asthma specialist visit‖	19	45	2.41 (1.08-5.48)	.03

NA, Not estimated given the absence of an outcome in a period.
*Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
†In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle (including the index hospitalization).
‡RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.
§Including dupilumab, benralizumab, mepolizumab, and reslizumab.
‖Including allergists, pulmonologists, and asthma clinic providers.

TABLE E3. Within-individual comparisons of chronic asthma care between pre- and post-implementation periods, by race/ethnicity

Outcome by race/ethnicity*	Rate (%)		RR (95% CI)§	*P* value
	Preimplementation†	Postimplementation‡		
Non-Hispanic White (n = 19)				
Serum specific IgE measurement	5	16	3.07 (0.51-23.3)	.22
Allergen skin testing	3	0	NA	NA
Use of omalizumab	3.0	0	NA	NA
Use of anti-IL-4/IL-5 therapy‖	0	16	NA	NA
Asthma specialist visit¶	32	58	1.88 (0.82-4.30)	.13
Non-Hispanic Black (n = 69)				
Serum specific IgE measurement	7	12	1.78 (0.67-4.65)	.24
Allergen skin testing	<1	0	NA	NA
Use of omalizumab	<1	0	NA	NA
Use of anti-IL-4/IL-5 therapy‖	<1	3	4.00 (0.38-86.0)	.26
Asthma specialist visit¶	18	54	2.96 (1.79-4.97)	<.001
Hispanic (n = 12)				
Serum specific IgE measurement	4	8	2.00 (0.08-50.5)	.62
Allergen skin testing	0	8	NA	NA
Use of omalizumab	4	0	NA	NA
Use of anti-IL-4/IL-5 therapy‖	0	0	NA	NA
Asthma specialist visit¶	8	25	3.00 (0.50-22.8)	.23

NA, Not estimated given the absence of an outcome in a period.
*There were only 3 patients in the other race/ethnicity category; therefore, no statistical inference was made.
†Averaged over the 2-y period (a total of 206 person-years) before the implementation of hospital-initiated care bundle.
‡In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle (including the index hospitalization).
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.
‖Including dupilumab, benralizumab, mepolizumab, and reslizumab.
¶Including allergists, pulmonologists, and asthma clinic providers.

TABLE E4. Within-individual comparisons of chronic asthma care between pre- and post-implementation periods, by primary health insurance

	Rate (%)			
Outcome by insurance*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Public insurance (n = 62)				
Serum specific IgE measurement	7	11	1.76 (0.62-4.91)	.27
Allergen skin testing	<1	2	2.02 (0.08-50.9)	.62
Use of omalizumab	2	2	1.01 (0.05-10.5)	.99
Use of anti-IL-4/IL-5 therapy‖	<1	3	4.03 (0.39-86.7)	.26
Asthma specialist visit¶	19	47	2.44 (1.42-4.22)	.001
Private insurance (n = 38)				
Serum specific IgE measurement	5	16	3.00 (0.86-11.7)	.09
Allergen skin testing	1	0	NA	NA
Use of omalizumab	1	0	NA	NA
Use of anti-IL-4/IL-5 therapy‖	0	8	NA	NA
Asthma specialist visit¶	21	58	2.75 (1.45-5.32)	.002

NA, Not estimated given the absence of an outcome in a period.
*There were only 3 patients with no insurance; therefore, no statistical inference was made.
†Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle (including the index hospitalization).
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.
‖Including dupilumab, benralizumab, mepolizumab, and reslizumab.
¶Including allergists, pulmonologists, and asthma clinic providers.

TABLE E5. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by sex

	Mean annualized incidence (per person-year)			
Outcome by sex*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Female (n = 74)				
Systemic corticosteroid use	4.0	2.8	0.71 (0.60-0.83)	<.001
ED visit	3.4	2.5	0.73 (0.62-0.86)	<.001
Hospitalization	2.2	1.6	0.76 (0.61-0.93)	.01
Male (n = 29)				
Systemic corticosteroid use	4.7	3.2	0.69 (0.54-0.87)	.002
ED visit	2.8	3.2	1.12 (0.87-1.45)	.37
Hospitalization	2.1	2.0	0.97 (0.71-1.33)	.87

*Test for the interactions between the care bundle and sex: $P_{interaction} = .86$ for systemic corticosteroid use, $P_{interaction} = .01$ for ED visit, and $P_{interaction} = .20$ for hospitalization.
†Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E6. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by race/ethnicity

	Mean annualized incidence (per person-year)			
Outcome by race/ethnicity*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Non-Hispanic White (n = 19)				
Systemic corticosteroid use	3.8	3.1	0.85 (0.63-1.15)	.31
ED visit	4.0	2.1	0.51 (0.35-0.72)	<.001
Hospitalization	2.8	1.5	0.54 (0.35-0.81)	.004
Non-Hispanic Black (n = 69)				
Systemic corticosteroid use	4.2	3.1	0.74 (0.63-0.86)	<.001
ED visit	3.1	3.1	0.99 (0.84-1.16)	.87
Hospitalization	2.2	2.1	0.96 (0.79-1.17)	.69
Hispanic (n = 12)				
Systemic corticosteroid use	5.3	1.8	0.35 (0.22-0.54)	<.001
ED visit	3.0	1.2	0.38 (0.21-0.66)	.001
Hospitalization	1.3	0.4	0.32 (0.11-0.76)	.02

*There were only 3 patients in the other race/ethnicity category; therefore, no statistical inference was made. Test for the interactions between the bundle and the race/ethnicity: in non-Hispanic Black patients, $P_{interaction} = .39$ for systemic corticosteroid use, $P_{interaction} < .001$ for ED visit, and $P_{interaction} = .02$ for hospitalization; in Hispanic patients, $P_{interaction} = .001$ for systemic corticosteroid use, for $P_{interaction} = .41$ for ED visit, and $P_{interaction} = .32$ for hospitalization.
†Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E7. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by primary health insurance

	Mean annualized incidence (per person-year)			
Outcome by insurance*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Public insurance (n = 62)				
Systemic corticosteroid use	4.7	3.0	0.64 (0.54-0.75)	<.001
ED visit	3.8	3.1	0.81 (0.68-0.95)	.01
Hospitalization	2.8	2.4	0.85 (0.70-1.03)	.10
Private insurance (n = 38)				
Systemic corticosteroid use	3.4	2.8	0.81 (0.64-1.01)	.06
ED visit	2.3	2.0	0.88 (0.67-1.15)	.35
Hospitalization	1.1	0.8	0.73 (0.48-1.09)	.13

*There were only 3 patients with no insurance; therefore, no statistical inference was made. Test for the interactions between the care bundle and primary health insurance: $P_{interaction} = .04$ for systemic corticosteroid use, $P_{interaction} = .58$ for ED visit, and $P_{interaction} = .40$ for hospitalization.
†Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 102.5 person-years) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E8. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by smoking status

	Mean annualized incidence (per person-year)			
Outcome by smoking status*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Nonsmoking (n = 75)				
Systemic corticosteroid use	4.4	3.3	0.75 (0.65-0.86)	<.001
ED visit	3.4	3.0	0.89 (0.76-1.03)	.13
Hospitalization	2.2	2.0	0.93 (0.76-1.12)	.45
Smoking (n = 22)				
Systemic corticosteroid use	3.3	1.7	0.52 (0.36-0.74)	<.001
ED visit	2.4	1.9	0.78 (0.54-1.11)	.18
Hospitalization	1.9	1.2	0.62 (0.39-0.95)	.03

*Among 97 patients who had the information of smoking status. Test for the interactions between the care bundle and the smoking status: $P_{interaction}$ = .08 for systemic corticosteroid use, $P_{interaction}$ = .53 for ED visit, and $P_{interaction}$ = .10 for hospitalization.
†Averaged over the 2-y period (a total of 150 person-years in the nonsmoking group and a total of 44 person-years in the smoking group) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 75 person-years in the nonsmoking group and a total of 21.5 person-years in the smoking group) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E9. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by obesity status

	Mean annualized incidence (per person-year)			
Outcome by obesity status*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Nonobesity (n = 28)				
Systemic corticosteroid use	4.8	3.6	0.75 (0.59-0.94)	.02
ED visit	2.5	3.5	1.38 (1.06-1.78)	.02
Hospitalization	1.9	2.0	1.04 (0.75-1.43)	.83
Obesity (n = 62)				
Systemic corticosteroid use	4.2	2.8	0.68 (0.57-0.80)	<.001
ED visit	3.8	2.7	0.72 (0.60-0.85)	<.001
Hospitalization	2.5	2.0	0.77 (0.62-0.94)	.01

BMI, Body mass index.
*Among 90 patients who had the information of body height and weight. Obesity was defined by BMI of $\geq$ 30 kg/m^2. Test for the interactions between the care bundle and the obesity status: $P_{interaction}$ = .49 for systemic corticosteroid use, $P_{interaction}$ < .001 for ED visit, and $P_{interaction}$ = .12 for hospitalization.
†Averaged over the 2-y period (a total of 56 person-years in the nonobesity group and a total of 124 person-years in the obesity group) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 28 person-years in the nonobesity group and a total of 61.5 person-years in the obesity group) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E10. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by history of intubation for asthma

Outcome by history of intubation for asthma*	Mean annualized incidence (per person-year)		RR (95% CI)§	*P* value
	Preimplementation†	Postimplementation‡		
No history of intubation (n = 72)				
Systemic corticosteroid use	4.0	2.7	0.68 (0.57-0.79)	<.001
ED visit	2.6	2.2	0.88 (0.73-1.05)	.16
Hospitalization	1.5	1.3	0.83 (0.65-1.06)	.14
History of intubation (n = 30)				
Systemic corticosteroid use	4.7	3.5	0.76 (0.60-0.94)	.01
ED visit	4.9	3.8	0.77 (0.62-0.96)	.02
Hospitalization	3.6	3.0	0.81 (0.63-1.04)	.10

*Among 102 patients who have the information of history of intubation for asthma. Test for the interactions between the care bundle and the history of intubation for asthma: $P_{interaction}$ = .42 for systemic corticosteroid use, $P_{interaction}$ = .39 for ED visit, and $P_{interaction}$ = .90 for hospitalization.
†Averaged over the 2-y period (a total of 144 person-years in the no-history of intubation group and a total of person-years in the history of intubation group) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 71.5 person-years in the no history of intubation group and a total of 30 person-years in the history of intubation group) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E11. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by use of oral corticosteroids before index hospitalization

Outcome by use of oral corticosteroids*	Mean annualized incidence (per person-year)		RR (95% CI)§	*P* value
	Preimplementation†	Postimplementation‡		
No use of oral corticosteroids (n =57)				
Systemic corticosteroid use	4.7	3.1	0.67 (0.56-0.79)	<.001
ED visit	3.6	2.9	0.79 (0.65-0.94)	.009
Hospitalization	2.4	2.0	0.85 (0.68-1.06)	.15
Use of oral corticosteroids (n = 45)				
Systemic corticosteroid use	3.6	2.7	0.76 (0.62-0.93)	.01
ED visit	2.8	2.5	0.90 (0.72-1.12)	.34
Hospitalization	1.9	1.4	0.76 (0.57-1.01)	.07

*Among 102 patients who have the information of use of oral corticosteroids before the index hospitalization. Test for the interactions between the care bundle and the use of oral corticosteroids: $P_{interaction}$ = .35 for systemic corticosteroid use, $P_{interaction}$ = .37 for ED visit, and $P_{interaction}$ = .56 for hospitalization.
†Averaged over the 2-y period (a total of 114 person-years in the nonuse of oral corticosteroids group and a total of 90 person-years in the use of oral corticosteroids group) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 56.5 person-years in the nonuse of oral corticosteroids group and a total of 45 person-years in the use of oral corticosteroids group) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E12. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods, by initial hospitalization location

	Mean annualized incidence (per person-year)			
Outcome by initial hospitalization location*	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
ED observation unit (n = 55)				
Systemic corticosteroid use	4.4	3.0	0.69 (0.57-0.82)	<.001
ED visit	2.6	2.4	0.92 (0.75-1.13)	.43
Hospitalization	1.4	1.3	0.90 (0.68-1.18)	.45
Hospital ward or stepdown unit (n = 36)				
Systemic corticosteroid use	4.1	3.0	0.73 (0.58-0.91)	.01
ED visit	3.6	3.3	0.93 (0.75-1.16)	.52
Hospitalization	3.0	2.4	0.80 (0.62-1.02)	.08
Intensive care unit (n = 12)				
Systemic corticosteroid use	3.4	2.3	0.69 (0.44-1.05)	.09
ED visit	4.9	1.8	0.37 (0.23-0.58)	<.001
Hospitalization	2.7	1.8	0.68 (0.41-1.08)	.11

*Test for the interactions between the bundle and the initial hospitalization location: in hospital ward or stepdown, $P_{interaction} = .66$ for systemic corticosteroid use, $P_{interaction} = .94$ for ED visit, and $P_{interaction} = .55$ for hospitalization; in intensive care unit, $P_{interaction} = .97$ for systemic corticosteroid use, for $P_{interaction} < .001$ for ED visit, and $P_{interaction} = .32$ for hospitalization.
†Averaged over the 2-y period (a total of 110 person-years in the ED observation unit group, a total of 72 person-years in the hospital ward or stepdown unit group, and a total of 24 person-years in the intensive care unit group) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 55 person-years in the ED observation unit group, a total of 35.5 person-years in the hospital ward or stepdown unit group, and a total of 12 person-years in the intensive care unit group) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E13. Within-individual comparisons of the annualized incidence of severe asthma exacerbations between pre- and postimplementation periods in patients without COPD

	Mean annualized incidence (per person-year)			
Outcomes	**Preimplementation***	**Postimplementation†**	**RR (95% CI)‡**	***P* value**
Systemic corticosteroid use	3.9	2.6	0.68 (0.58-0.78)	<.001
ED visit	3.3	2.4	0.74 (0.63-0.86)	<.001
Hospitalization	2.0	1.5	0.75 (0.62-0.92)	.01

*Averaged over the 2-y period (a total of 180 person-years) before the implementation of the hospital-initiated care bundle.
†In the 1-y period (a total of 90.5 person-years) after the implementation of the hospital-initiated care bundle.
‡RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E14. Within-individual comparisons of annualized incidence of severe asthma exacerbations between pre- and postimplementation periods in patients who did not initiate new biologic agents in the postimplementation period*

	Mean annualized incidence (per person-year)			
Outcome	**Preimplementation†**	**Postimplementation‡**	**RR (95% CI)§**	***P* value**
Systemic corticosteroid use	4.2	2.9	0.71 (0.62-0.81)	<.001
ED visit	3.1	2.7	0.76 (0.72-1.02)	.10
Hospitalization	2.0	1.8	0.88 (0.73-1.05)	.15

*Defined as anti-IL-4/IL-5 therapy including dupilumab, benralizumab, mepolizumab, and reslizumab.
†Averaged over the 2-y period (a total of 196 person-years) before the implementation of the hospital-initiated care bundle.
‡In the 1-y period (a total of 97.5 person-years) after the implementation of the hospital-initiated care bundle.
§RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E15. Within-individual comparisons of the annualized incidence of severe asthma exacerbations between pre- and postimplementation (0-6 mo after index hospitalization) periods

	Mean annualized incidence (per person-year)			
Outcome	Preimplementation*	Postimplementation†	RR (95% CI)‡	*P* value
Systemic corticosteroid use	4.2	3.1	0.74 (0.63-0.88)	<.001
ED visit	3.2	2.8	0.88 (0.73-1.05)	.15
Hospitalization	2.1	2.0	0.93 (0.75-1.15)	.52

*Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
†In the first 6-mo period after the implementation of the hospital-initiated care bundle (a total of 51.5 person-years).
‡RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E16. Within-individual comparisons of the annualized incidence of severe asthma exacerbations between pre- and postimplementation (7-12 mo after index hospitalization) periods

	Mean annualized incidence (per person-year)			
Outcome	Preimplementation*	Postimplementation†	RR (95% CI)‡	*P* value
Systemic corticosteroid use	4.2	2.7	0.66 (0.55-0.79)	<.001
ED visit	3.2	2.5	0.77 (0.64-0.93)	.007
Hospitalization	2.1	1.5	0.70 (0.55-0.89)	.004

*Averaged over the 2-y period (a total of 206 person-years) before the implementation of the hospital-initiated care bundle.
†In the second 6-mo period after the implementation of the hospital-initiated care bundle (a total of 51 person-years).
‡RRs are for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional Poisson regression models accounting for the difference in period intervals.

TABLE E17. Within-individual comparisons of the proportion of severe asthma exacerbations occurrence between pre- and postimplementation periods, modeling outcomes as binary variables

	Proportion (%)			
Outcome	Preimplementation	Postimplementation	OR (95% CI)*	*P* value
Systemic corticosteroid use	100	73	NA†	NA†
ED visit	93	69	0.21 (0.07-0.70)	.01
Hospitalization	77	58	0.59 (0.27-1.30)	.19

NA, Not applicable; *OR,* odds ratio.
*ORs for the occurrence of outcome event (yes vs no) for post- vs pre- (reference) implementation periods within individuals, as estimated by conditional logistic regression models accounting for the difference in period intervals.
†Not estimated because all patients had a systemic corticosteroid use in the preimplementation period as an inclusion criterion.