

PREDICTORS

Moderate Symptom-Based Exacerbations as Predictors of Severe Claims-Based Exacerbations in Asthma

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Objectives. Asthma exacerbations have well-established clinical and economic impact, yet lack consensus on characterization of an episode's severity. Asthma treatment guidelines outline the concept of a moderate asthma exacerbation; however, a clear definition that can be operationalized has not been proposed. **Methods.** Adult asthma (ICD-9: 493.XX) patients, with at least 9 months of continuous enrolment in the Fallon Community Health Plan were included in the retrospective cohort study. Patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD) or other lower respiratory tract conditions were excluded. The first reported asthma-related event following a 2-week symptom-free period was designated as the index event. Asthma-related events were categorized as (1) moderate exacerbations (symptom-based) or (2) severe exacerbations (claims-based). Timing between and temporal sequence of asthma-related events along with average costs were calculated. **Results.** Of 3126 eligible patients, 55% reported an asthma-related event followed by a recurrent event(s). Moderate exacerbations followed by recurrent moderate exacerbations were most frequent (20%) with the shortest interval between exacerbations (mean: 83 days [SD 87]). Moderate exacerbations followed by severe exacerbations occurred in 16% of patients with an average of 176.74 (SD 176.94) days between events. **Conclusions.** Patient report of asthma bothersome enough to initiate contact with a clinician, but not requiring oral corticosteroid (OCS), is a definition for a moderate exacerbation that can be operationalized for research purposes. Further work is needed to demonstrate whether identification of moderate exacerbations will allow interventions that impact the frequency and timing of future exacerbations.

Keywords claims-based exacerbations, cost of asthma-related event, interval between exacerbations, moderate exacerbation, severity of exacerbation

INTRODUCTION

Asthma is a chronic airway disorder characterized by bronchoconstriction and respiratory symptoms, marked by periods of acute deterioration (exacerbation). Exacerbations can be life-threatening events, are often associated with a significant decrease in quality of life, and have widespread and substantial negative socioeconomic impact. Patients having frequent exacerbations (~20% of those with asthma) incur 80% of the total direct costs for asthma care (1), which have been estimated at \$50.1 billion in the United States (2). In addition, the treatment of exacerbations accounts for between 35% and 50% of all medical expenditures for asthma (1).

Several national and international guidelines recognize the prevention of asthma exacerbation as a major goal of asthma treatment and the number of exacerbations as an important factor to assess optimal asthma control (3).

However, there is no consensus about how to characterize an episode's severity or whether differentiating the severity of exacerbations has any utility.

Previous definitions of exacerbations have used a wide panel of unvalidated or partly validated criteria. Recently published American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines (4) define a severe asthma exacerbation as an event requiring oral corticosteroid (OCS) use, a visit to an emergency department (ED) or hospital admission. This definition of severe exacerbation that includes an intervention such as the use of systemic corticosteroids, an ED/urgent care (UC) visit, or a hospitalization has clinical relevance and is one of the central components distinguishing intermittent from persistent asthma in the Expert Panel Report 3 guidelines (5). The definition of severe exacerbations in the literature is variable and has not consistently used the ATS/ERS definition (6–10). The ATS/ERS statement also defines a moderate asthma exacerbation; an asthma event sufficiently bothersome to the patient to induce a temporary change in treatment to restore asthma control; however, we could not identify any studies using the ATS/ERS

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concept of a moderate asthma exacerbation. Further, a recent workshop was convened by the National Institutes of Health (NIH) to recommend a set of asthma outcomes for routine use in asthma clinical research (11). The recently published report from the exacerbations subcommittee, emphasized the lack of a validated way to define moderate exacerbations or to distinguish a moderate exacerbation from just a variation in the level of asthma control. Therefore, the committee did not distinguish moderate versus severe exacerbations in their recommendations for defining asthma exacerbations. The committee suggested further investigation is needed to operationalize a definition of moderate asthma exacerbations.

Studies defining moderate exacerbations are limited and conflicting. For instance, one study defined a moderate exacerbation as the use of OCSs (12), yet another as an increased use of controller therapy (OCSs/inhaled corticosteroids/long-acting β_2 -agonist/theophylline) (13). Recent work suggests that symptoms may be strong predictors of exacerbations. Ng et al. (14) reported symptoms to be more predictive of recurrent ED visits and hospitalization than forced expiratory flow (FEV_1). Malo et al. (15) found that a diary of symptoms had a comparable ability to detect asthma flare-ups, as did serial peak expiratory flow rate (PEFR) monitoring. Chan-Yeung et al. (6) found that an increase in symptoms preceded a reduction in PEFR in asthma exacerbations and that symptoms were more sensitive predictors than PEFR.

The purpose of our study was to evaluate a proposed definition for a moderate exacerbation; based on the ATS/ERS definition a moderate asthma exacerbation is an asthma event sufficiently bothersome to the patient to induce a temporary change in treatment to restore asthma control. We operationalized this definition to identify events where a patient initiated contact with a health care provider (HCP) regarding asthma symptoms; yet, the event did not meet criteria for a severe exacerbation as outlined by ATS/ERS. By reaching out to their HCP the patient is verifying the symptoms have reached a threshold that motivates them to feel an intervention is needed. Using this definition of moderate exacerbation, we then assessed the relationship of moderate (symptom-based) asthma exacerbations to severe (claims-based) asthma exacerbations in a sample of the US asthma patient population.

METHODS

This retrospective cohort study of adult asthma patients used data from the Fallon Clinic (now known as Reliant Medical Group), a large multi-specialty medical group practice serving 200,000 members throughout Central Massachusetts, in cooperation with the Fallon Community Health Plan. Institutional Review Board approval was obtained through the Western Institutional Review Board (#2010335). The electronic medical records (EMRs) and claims data from patients obtaining medical care from the Fallon Clinic from 2007–2009 were linked and deidentified to form the dataset used. Symptoms were recorded in a complaint log that allowed for recording of one symptom per encounter (office

visit or phone contact) by the office nurse or physician and integrated into the EMR. Multiple symptom complaints were defined as distinct symptom(s) reported within 3 days of the initial symptom complaint. Symptoms reported beyond 3 days of the initial symptom complaint were considered a separate exacerbation.

The first moderate or severe encounter with a primary or secondary asthma diagnosis (ICD-9 code of 493.xx) during the 3-year-study period was defined as the index event, with the provision that the patient must not have reported a symptom within the 2-weeks prior to the index event. Data for patients ≥ 18 years old on the index date, who had an encounter within the 3-month pre-index period (exclusive of the 2-week symptom-free period) and who were enrolled for at least 6 months post-index were analyzed. The requirement for an encounter in the health system in the 3 months prior to the pre-index period was to ensure the subject was being seen in the health care system prior to the index event. Patients were excluded if they had a medical claim with either a primary or secondary diagnosis of respiratory tract cancer (larynx, trachea, or pleura), COPD (ICD-9-CM codes 491.xx, 492.xx, 496.xx) or allied conditions such as bronchiectasis, tuberculosis, cystic and pulmonary fibrosis, pneumoconioses, pneumonitis, pneumonopathy, or other upper and lower non-asthma respiratory tract and lung conditions.

Asthma exacerbations were categorized by severity of the event as recommended by the ATS/ERS definition (4). Severe (claims-based) exacerbations (i.e., health care claims with a primary diagnosis of 493.x) included: UC visits, ED visits, inpatient (IP) hospitalizations, or OCS claims. Moderate (symptom-based) exacerbations were defined as patient report, to a HCP, of asthma symptoms including: nighttime awakening, shortness of breath, coughing, wheezing, chest tightness, fatigue, and use of rescue β -agonist.

ANALYSIS

Demographic and medical characteristics were tabulated. Counts and percentages were calculated for categorical variables, and means and medians were calculated for each event category including means of health care costs by type of event.

Event pair categories were not mutually exclusive, and each event to recurrent event was counted as one event pair. In addition, event pairs had to be contiguous events. For example, if a patient had three separate exacerbations during the observation period, we would identify two-event pairs; the first pair would involve the 1st and 2nd exacerbations and the second pair would involve the 2nd and 3rd exacerbations. The primary analysis estimated the mean days from an initial report of a moderate exacerbation to the report of a second exacerbation of any severity. The timing and pattern of moderate exacerbations escalating to severe asthma exacerbations was of interest. In addition, we assessed the relationship of the number of days between a moderate and severe exacerbation and the number of follow-up clinic visits. Moderate

exacerbations were stratified by the type and number of symptoms reported. Symptom groups included patients with single symptoms requiring a change in asthma medication, breathing difficulties, complaints of coughing, complaints of chest tightness, complaints of sleep disruptions, or complaints of wheezing, and patients with two or more symptoms.

We also compared the economic impacts for moderate versus severe exacerbations. Asthma-related costs within 3 days of the symptom complaint were used to estimate the mean symptom unit costs, stratified by single, multiple, or any reported symptoms. Unit costs reported were based on the charges to the health plan—the actual amount paid for the services by the health plan plus the patient's co-payment. Mean unit costs for severe exacerbations were stratified into categories of OCS, physician office, UC/ED, and IP. Costs used in calculations included OCS claims plus all costs incurred on the day of the fill (excluding any UC, ED, or IP costs), physician office, UC/ED, and hospitalization claims with a primary diagnosis of 493.x, including nebulizers, equipment, and so on. The final calculation of the mean asthma-related moderate and severe exacerbation costs was inflated to 2009 dollars based on the consumer price index. All analyses were conducted with SAS v 9.2 for Windows (SAS Institute, Cary, NC, USA).

RESULTS

A total of 3126 patients met the inclusion and enrolment criteria for the primary analysis (Table 1). The average age was 50 (SD 19.9) with 1909 (61.1%) patients aged 25–64 years old. Two-thirds were women, and comorbid conditions were common; 929 (29.7%) had a history of hypertension, 529 (16.9%) had a history of diabetes, 314 (10%) had a history of depression, and 307 (9.8%) had a history of obesity.

A total of 2573 (82.3%) patients reported at least one exacerbation during the study period with 180 (5.8%) reporting only one moderate (symptom-based) exacerbation and 660 (21.1%) reporting a single severe (claims-based) exacerbation during the 3-year observation period (Table 2). Of the 1733 patients with a recurrent asthma-related event, a total of 3988 event pairs were analyzed for the association and timing of recurrent events. Of the 3988 event pairs, 20% included a moderate exacerbation based on report of a single symptom followed by either a recurrent moderate exacerbation based on the same symptom or a different single symptom, with on average 82.9 (SD 87.01) days between events. Moderate exacerbations based on report of multiple symptoms were less common (2.4%) and occurred with a longer average time between events (Table 3). A total of 640 (16.1%) of the event pairs included a single symptom moderate exacerbation followed by a severe exacerbation with a mean of 176.74 (SD 176.94) days between events.

The average number of clinic visits between a moderate and severe exacerbation was positively correlated to the time between events. For example, the time from a single symptom moderate exacerbation to severe exacerbation based on OCS claim had on average 149 days between events with an

TABLE 1.—Asthma population.

	Total	
	n	%
Number of patients	3126	100%
Age (mean/SD)	50	(19.86)
18–24	397	(12.70)
25–39	637	(20.38)
40–54	856	(27.38)
55–64	416	(13.31)
65–74	375	(12.00)
75 plus	445	(14.24)
Sex		
Female	2087	(66.76)
Male	1039	(33.24)
Comorbid Conditions		
(Pts (%) with any Dx history)		
Alcohol abuse	41	(1.31)
Anemia	195	(6.24)
Arythmia	191	(6.11)
Asthma	3126	(100.00)
Congestive heart failure	76	(2.43)
Deficiency anemias	195	(6.24)
Depression	314	(10.04)
Diabetes (complicated)	121	(3.87)
Diabetes (uncomplicated)	408	(13.05)
Heart failure	76	(2.43)
Hypertension	929	(29.72)
Hypothyroidism	196	(6.27)
Obesity	307	(9.82)
Obstructive sleep apnea	136	(4.35)
Other neurological disease	67	(2.14)
Peripheral vascular	124	(3.97)
Psychoses	282	(9.02)
Renal failure	51	(1.63)
Rheumatoid arthritis	70	(2.24)
Valvular disease	58	(1.86)

TABLE 2.—Patients stratified by Event, no Event, and no Recurrent Event.

	n	%
	3126	100
No exacerbation (symptom or claims based)	553	17.69
Initial symptom based exacerbation without recurrent event	180	5.76
Initial claims based exacerbation without recurrent event	660	21.11
Patients with no event plus patients without recurring event	1393	44.56
Patients with recurrent event	1733	55.44

Note: Symptom-based events were defined as patient report to a health care provider of asthma symptoms including: nighttime awakening, shortness of breath, coughing, wheezing, chest tightness, fatigue, and use of a rescue beta-agonist. Claims-based exacerbations were defined as healthcare claims with a primary diagnosis of 493.x.

average 0.28 follow-up visits between events ($p < .0001$), and a single symptom moderate exacerbation to a severe exacerbation (based on UC/ED/Hosp claim) had on average 217 days between events with on average 0.26 follow-up visits between events ($p < .0001$) (Table 4).

When stratified by the individual type of symptom reported, no specific symptom or symptom complex was associated with a significantly shorter time to a recurrent moderate or severe exacerbation (data not shown).

TABLE 3.—Event types for patients with Recurrent Events and unadjusted mean days to Recurrent Event.

Event categories for N = 1733 patients	# of event pairs	% of total event pairs	mean ^d	(SD)	Range
Symptom (single) based to recurrent symptom (single) based	798	20.01	82.99	(87.01)	4–355
Symptom (single) based to oral steroid claim (OCS) ^a	306	7.67	149.24	(174.24)	1–683
Symptom (single) based to UC, ED, or Hosp ^b	436	10.93	217.66	(181.15)	1–692
Symptom (single) based to OCS, UC, ED, or Hosp ^c	640	16.05	176.74	(176.94)	1–689
Symptom (multiple) based to recurrent symptoms (multiple) based	95	2.38	177.46	(105.69)	4–361
Symptom (multiple) based to oral steroid claim ^a	40	1.00	148.63	(180.12)	1–706
Symptom (multiple) based to UC, ED, or Hosp ^b	60	1.50	205.57	(185.35)	1–609
Symptom (multiple) based to OCS, UC, ED, or Hosp ^c	82	2.06	171.00	(178.87)	1–706
Oral Steroid claim to recurrent oral steroid claim	761	19.08	187.01	(190.22)	4–964
Oral steroid claim to UC, ED, or Hosp	453	11.36	265.58	(220.28)	1–954
UC/Emergency Department to Hospitalization	239	5.99	309.78	(269.39)	1–995
Hospitalization to recurrent hospitalization	78	1.96	214.60	(211.92)	6–938
Total number of event pairs	3988				

Note: Event categories are not mutually exclusive, each symptom complaint or event followed by recurrent event is counted as one event pair, patients can have more than one event pair over the 3 year study period. ^a Only those events where OCS occurred before UC, ED, or IP. ^b Those seeking urgent/emergent care regardless of prior OCS claim. ^c Symptom followed by any type of severe event. ^d Means based on patients with recurrent event, a given subject may contribute multiple events in different categories. N = 1733 patients; Total number of event pairs = 3988.

TABLE 4.—Relationship of days between moderate and severe exacerbations and clinic visits.

Event categories for N = 1733 patients	Subsequent		Intervening follow-up clinic visits			
	n	%				
	3126	100%	Mean ^d	(SD)	Spearman correlation coefficient ^c	P value
Symptom (single) based to recurrent symptom (single) based	798	(25.53)	0.23	(0.52)	0.03	0.18
Symptom (single) based to oral steroid claim (OCS) ^a	306	(9.79)	0.94	(1.85)	0.28	<.0001
Symptom (single) based to UC, ED, or Hosp ^b	436	(13.95)	0.64	(1.57)	0.26	<.0001
Symptom (single) based to OCS, UC, ED, or Hosp ^c	640	(20.47)	0.67	(1.55)	0.24	<.0001
Symptom (multiple) based to recurrent Symptoms (multiple) based	95	(3.04)	0.21	(0.57)	−0.06	0.43
Symptom (multiple) based to oral steroid claim ^a	40	(1.28)	0.76	(1.24)	0.27	0.00
Symptom (multiple) based to UC, ED, or Hosp ^b	60	(1.92)	0.38	(0.90)	0.21	0.02
Symptom (multiple) based to OCS, UC, ED, or Hosp ^c	82	(2.62)	0.45	(0.92)	0.13	0.08
Oral Steroid claim to recurrent oral steroid claim	761	(24.34)	0.28	(0.71)	0.23	<.0001
Oral steroid claim to UC/ED/Hosp	453	(14.49)	0.70	(1.57)	0.34	<.0001

Note: Event categories are not mutually exclusive, each symptom complaint or event followed by recurrent event is counted as one event pair, patients can have more than one event pair over the 3 year study period. ^a Only those events where OCS occurred before UC, ED, or IP. ^b Those seeking urgent/emergent care regardless of prior OCS claim. ^c Symptom followed by any type of severe event. ^d Means based on patients with recurrent event, a given subject may contribute multiple events in different categories. ^e P value for Spearman correlation: Prob > |r| under H0: Rho = 0. N = 1733 patients; Total number of event pairs = 3988.

The most frequent pattern (19.1%) for recurrent severe exacerbations was an OCS claim followed by a second OCS claim (Table 3), with an average of 187 (SD190.2) days between claims. A smaller subset (11.4%) included an OCS claim followed by an event requiring a higher level of care (UC/ED/Hosp claim) with on average 265.58 (SD 220.28) days between claims. We found the occurrence of an UC/ED visit followed by a recurrent hospitalization to have the longest mean number of days between events (309.78 [SD 269.39]).

In determining the cost of an exacerbation by severity, we found the mean unit cost for a moderate exacerbation to be \$85.23 (SD 315.08). Mean unit costs for severe exacerbations were \$64.91 (SD 185.03) for OCS, \$445.69 (SD 684.68) for ED visit, and \$7,237.86 (SD 4935.15) for hospitalization (Table 5).

DISCUSSION

We report on a symptom-based definition for moderate asthma exacerbation and the relationship of moderate

TABLE 5.—Event unit cost^a.

N = 3126	Mean	SD	Count
<i>Symptoms^b</i>			
Symptom (single)	\$ 85.23	(315.08)	1042
Symptoms (multiple)	\$ 336.39	(1258.44)	573
Symptom(s) any	\$ 174.34	(799.83)	1615
<i>Exacerbations</i>			
Oral steroid claim	\$ 64.91	(185.03)	717
Emergency Department	\$ 445.69	(684.68)	65
Hospitalization	\$ 7,237.86	(4935.15)	18

Symptoms included: night time awakening, shortness of breath, coughing, wheezing, increased albuterol use, and activity limitation. ^aBased on subjects with claims. ^bSymptom unit costs based on actual asthma-related charges to the health plan within 3 days of symptom report.

(symptom-based) and severe (claims-based) asthma exacerbations from a sample of the adult US asthmatic population. Among our population, comorbid conditions were slightly lower than reported in a population of American asthmatics published in 2000 (29.7% compared

with 42% respectively); in which the most prevalent being allergy(s) (22%), hypertension (15%), depression (10%), and arthritis (9%) (16). Our study population had a similar prevalence of comorbid depression, yet higher prevalence of hypertension.

Over 80% (82.3%) of our sample presented with either a moderate or severe exacerbation during the study period. Over half (55%) of our study population had more than one exacerbation and in many (39.2%) of the exacerbations, a moderate exacerbation preceded a severe exacerbation. In addition, the average number of days between a single symptom moderate exacerbation and a recurrent single symptom moderate exacerbation was on average 47% less than for any other exacerbation pair. Of all event unit costs, the costs associated with an OCS claim were the lowest at \$64.91 (SD 185.03).

The uniqueness of this study was use of an EMR database to examine the relationship between moderate and severe asthma exacerbations to assess a proposed definition for moderate (symptom-based) exacerbations that can be operationalized. A majority of our sample experienced an exacerbation during the study period. Only 32.6% of these experienced a single exacerbation, of which a majority (78.6%) was a severe exacerbation. By our definition, a moderate exacerbation involved a change in asthma status bothersome enough for a patient contact their HCP.

In our study, 22% of the recurrent event pairs were a moderate (based on single or multiple symptoms) exacerbation followed by another moderate exacerbation, whereas only 18 % had a moderate exacerbation followed by a severe exacerbation. In addition, a positive correlation was found for the time between events (average number of days) and the number of follow-up clinic visits; as the average number of days between events increased so does the average number of ambulatory visits. These findings validate the importance of symptom monitoring as a component of asthma management. Regular follow-up of patients with asthma, reassessment of symptoms and level of control, and directed intervention could potentially prevent recurrent severe exacerbations. Asthma self-management—accompanied by regular review of medications and asthma control by a medical practitioner—has been shown to improve health outcomes significantly more than usual care (17). There are data on the association of level of control and risk of exacerbations (18), but data on prospective assessment of control and the impact of intervening with an asthma action plan are sparse. Our findings support other research showing recent exacerbations were predictive of future exacerbations (19).

The mean number of days between a single symptom and moderate exacerbation was considerably less than between any other type of event pair. In an asthma population, drawn from a managed care organization, with a range of asthma severity, the expected exacerbation rate is relatively infrequent; therefore, our findings of a fairly lengthy time (149 days) to the escalation to a severe exacerbation is not surprising. Although our definition for moderate exacerbation is symptom-based, it required contact with an HCP. Symptom complaints to the HCP

provide an opportunity to identify factors that precipitate worsening of asthma, such as exposure to an allergen, irritant, or respiratory virus, and allow for education on minimizing such exposures. Symptom complaints reported to a HCP also provide an opportunity to educate patients on the use of an asthma management plan including daily record keeping of symptoms and PEFs as directed in the GINA recommendations (3); to review adherence to medication treatment plans, and proper inhaler technique; and to prompt change in medications to prevent recurrent exacerbation(s). Severe exacerbations are, in general, more costly, so intervening for a moderate event—to the degree this prevents recurrent severe exacerbations—is a more cost-efficient use of resources.

Direct costs for asthma treatment in the United States are estimated to be \$500 per patient with asthma-related hospitalizations and ED visits the costliest component of asthma management (20). In this study, the average unit cost for a moderate exacerbation (based on reporting of a single symptom) was \$85.23, whereas patients complaining of more than one symptom within 3 days, symptom (multiple) had an average unit cost of \$336.39, which by definition were events that involved repeated contact with the HCP and potentially used more resources. Yet, costs for care following a moderate exacerbation were less than for a severe exacerbation. The costs associated with an OCS were similar to a moderate exacerbation, likely due to the OCS being frequently prescribed during a telephone encounter, of note, the telephone encounter itself is not billable and not captured as a “cost” in this analysis.

Symptoms outside a patient’s usual range of day-to-day asthma are a reasonable means to define a moderate exacerbation and should be explored further. In our analysis, we used the fact that the symptoms were troubling enough to be reported to their HCP to categorize them as outside a patient’s usual range of day-to-day asthma. This appears reasonable and supportive of the ATS Task Force definition: “events that are troublesome to the patient, and that prompt a need for a change in treatment, but are not severe” (4, p. 61). ATS/ERS guidelines suggest exacerbations should be recognized and treated before the exacerbation becomes severe. Patient reported symptoms are an important aspect in developing an asthma self-assessment plan and are a central component of asthma control instruments that can aid in identifying changes in asthma health status. Importantly, ensuring that patients understand and follow their self-management plan, including contacting their HCP when indicated, is essential to avoiding severe exacerbations.

Finally, our data suggest that our definition does have value; we observed that a recurrent moderate exacerbation occurs, on average, sooner than an escalation to a severe exacerbation. It allows the recognition that there is an issue with a patient’s underlying baseline control, whether due to their controller regimen, recognition or avoidance of triggers, and so on, and allows implementation of a change in management (either pharmacologic or non-pharmacologic) to potentially avoid escalation to a severe exacerbation.

Limitations of this study include the imperfect capability of claims data to discern key aspects of the patient's condition, including asthma severity, asthma control, or the relationship of patients' asthma to comorbid conditions. However, having a baseline level of asthma control or asthma severity does not negate the value of our analysis. Our definition of moderate exacerbations has value independent of baseline level of severity. Patients with intermittent, mild/mod/severe persistent disease can all have asthma exacerbations and a definition of moderate exacerbations is of value for all categories of asthma severity. In addition, asthma control, while related to asthma severity, is a distinct concept and by definition is heterogeneous in response to a wide array of influences. Having a baseline level of asthma control for the population does not give us an accurate indication of the level of asthma control over time (21). In addition, the frequency of moderate exacerbations would underestimate the level of asthma-related symptoms in a population.

It is unknown whether instructions to take a previously prescribed steroid were given when a symptom/complaint was reported to a clinician or if a new prescription was ordered. Moderate exacerbations relied upon clinician recording at least one symptom. Multiple symptoms per episode were determined by capturing all symptoms within a 3-day window, symptoms beyond 3 days were considered as a separate asthma episode. Analysis of combinations of specific symptoms was inconclusive due to the limited sample size. Patients with limited access to health services may utilize the ED for other than severe exacerbations including mild and moderate asthma symptoms, limiting the generalizability of our study to patients with access to health services.

CONCLUSIONS

Recognizing a moderate exacerbation and providing clinical intervention before a recurrent event or escalation to severe exacerbation is important for asthma control and cost management. A change in symptoms precipitating an interaction with a HCP, but not requiring OCS, is a definition for a moderate exacerbation that can be operationalized and quantified. Further work is needed to demonstrate whether identification of moderate exacerbations will impact the frequency and timing of future exacerbations.

DECLARATION OF INTEREST

Sandi J. Lane was an employee of Lovelace Respiratory Research Institute during the study design, analysis, and interpretation of the results, and is currently an employee of Appalachian State University. Anne L. Fuhlbrigge has served as a consultant for the design and analysis of epidemiologic studies for LRRI, Merck Inc. and GSK. She has served on a Respiratory specialist advisory panel for Merck Inc. and Sunovion and is a member of the Joint

Adjudication Committee for ICON Medical Imaging. She has received funding from AHRQ and NIH. Hans Petersen is an employee of Lovelace Respiratory Research Institute. James M. Seltzer is a member of the speaker's bureau for GlaxoSmithKline.

Christopher M. Blanchette has received research funding in areas related to this topic from GlaxoSmithKline, Merck, AstraZeneca, and Novartis. Prakash Navaratnam is a senior partner in DataMed Solutions LLC and was engaged as a paid consultant by the study sponsor to help design and conduct this study. Felicia Allen-Ramey is an employee and shareholder of Merck & Co., Inc. Financial support was provided by Merck & Co Inc. to conduct this research.

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