Long-term Outcomes After Stepping Down Asthma Controller Medications

A Claims-Based, Time-to-Event Analysis

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BACKGROUND: Long-term outcomes after stepping down asthma medications are not well described.

METHODS: This study was a retrospective time-to-event analysis of individuals diagnosed with asthma who stepped down their asthma controller medications using a US claims database spanning 2000 to 2012. Four-month intervals were established and a step-down event was defined by a $\geq 50\%$ decrease in days-supplied of controller medications from one interval to the next; this definition is inclusive of step-down that occurred without health-care provider guidance or as a consequence of a medication adherence lapse. Asthma stability in the period prior to step-down was defined by not having an asthma exacerbation (inpatient visit, ED visit, or dispensing of a systemic corticosteroid linked to an asthma visit) and having fewer than two rescue inhaler claims in a 4-month period. The primary outcome in the period following step-down was time-to-first asthma exacerbation.

RESULTS: Thirty-two percent of the 26,292 included individuals had an asthma exacerbation in the 24-month period following step-down of asthma controller medication, though only 7% had an ED visit or hospitalization for asthma. The length of asthma stability prior to stepping down asthma medication was strongly associated with the risk of an asthma exacerbation in the subsequent 24-month period: < 4 months' stability, 44%; 4 to 7 months, 34%; 8 to 11 months, 30%; and ≥ 12 months, 21% ($P < .001$).

CONCLUSIONS: In a large, claims-based, real-world study setting, 32% of individuals have an asthma exacerbation in the 2 years following a step-down event.

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ABBREVIATIONS: ICS = inhaled corticosteroid; IP = inpatient admission; OLDW = Optum Laboratories Data Warehouse; SCS = systemic corticosteroid

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The goal of asthma management is to use the least amount of medication necessary to optimally manage asthma symptoms while decreasing the burden associated with the treatments. Accomplishing this goal often involves stepping down medications to test whether taking less asthma medication will result in similar asthma outcomes. Decisions about stepping down depend heavily on understanding the associated risks of worsening asthma outcomes when making such an adjustment.

While asthma guidelines suggest that step-down be considered if asthma is stable for 3 months or longer, the evidence to support these recommendations is weak.^{1,2} Three meta-analyses examined the risks of specific asthma controller reductions all in patients determined to have stable asthma³⁻⁵; however, there remains a wide

gap in our understanding of the risks associated with stepping down asthma medications. One of the widest gaps is the assessment of long-term outcomes; there are very few studies that have followed individuals for > 1 year after a step-down event. Understanding longer-term outcomes is very important to individuals and their clinicians as they discuss possible adjustments in asthma medications. A second key gap is that there are very few studies that have documented asthma outcomes for periods longer than 3 months prior to the step-down event; the length of stability prior to stepping down may be an important factor to consider when estimating the likelihood of favorable long-term outcomes. To address these gaps, we analyzed a longitudinal claims database to describe the long-term outcomes of stepping down asthma controller medications in patients with different levels of stability.

Materials and Methods

Study Design

The study was a retrospective claims analysis using Optum Labs Data Warehouse (OLDW), a longitudinal health-care database that contains deidentified data from > 100 million individuals enrolled in commercial insurance or Medicare Advantage plans over a 20-year period.⁶ Administrative claims extracted for this study included medical and pharmacy claims as well as eligibility information from 2000 to 2012. Individuals in OLDW are geographically diverse across the United States, with the greatest representation in the south and midwest US census regions. The study was exempt from institutional review board approval due to the preexisting and deidentified nature of the data.

Study Cohort

Individuals who had an asthma diagnosis code from 2000 to 2012 were identified. In the OLDW, individuals > 85 years old are labeled as 85 years old in the data due to the risk of reidentification due to extreme age. Next, individuals not having an asthma controller medication claim in the database between 2002 and 2012 were excluded. The cohort was further refined to individuals with continuous medical and pharmacy coverage for ≥ 3 years at some point between 2000 and 2012. Next, individuals with an identified step-down of asthma medications were selected. The cohort was further refined by retaining individuals with continuous enrollment of at least 1 year before and 2 years after the step-down event period. Finally, individuals with inconsistent medication filling patterns were excluded from the study. This was defined as having three or more intervals where no medication claims were present. The rationale for excluding these individuals is related to the concern that these individuals may not have been accessing health care through the insurance coverage and, therefore, not reporting health-care events into this database.

Definitions

A step-down event was defined by a $\geq 50\%$ decrease in days-supplied of controller medications from one evaluation period to the next. Only the first occurrence of a step-down event per individual was used for analysis. It is important to note that we captured step-down decisions based on pharmacy dispensing, and, therefore, included those who were recommended by their provider to step down, those who were making this choice independent of a provider's recommendation, and those who were identified as stepping down as a consequence of a medication

adherence lapse. Four-month intervals were selected for this study rather than 3-month intervals (the current guideline-recommended period of stability prior to step-down) to allow for 3-month pharmacy dispensing to be counted more evenly across intervals. Each individual was thus followed for 10 consecutive 4-month intervals: three prior to stepping down, one interval where the step-down occurred, and six intervals after the step-down. The cohort was then divided into groups based on the number of consecutive 4-month intervals of asthma stability they experienced prior to attempting a step-down (0-3 months of stability, 4-7 months of stability, 8-11 months of stability, and ≥ 12 months of stability). Asthma stability in the period prior to step-down was defined by not having an asthma exacerbation (inpatient visit, ED visit, or dispensing of a systemic corticosteroid linked to an asthma visit) and having fewer than two rescue inhaler claims in a 4-month period. The definition of asthma exacerbation used in this study is based on recommendations made in an asthma outcomes workshop⁷ and is similar to the definition recently used in a clinical trial of stepping down asthma medication.⁸ The number of rescue inhaler dispensing using administrative claims is associated with a measure of asthma control.⁹

Outcome Measurements

The primary outcome in the period following step-down was time-to-first asthma exacerbation; secondary outcomes were time to having at least two rescue inhalers dispensed in 4 months and time to returning to or exceeding the baseline days-supplied of asthma controller medication prior to the step-down event. Baseline days of asthma controller medication were defined based on the number of days supplied of the medication based on dispensing data over the 4-month interval.

Asthma medications were defined as controller and rescue medications as previously described.¹⁰ Briefly, short-acting bronchodilators were classified as rescue medications while inhaled corticosteroids (ICSs), ICS-long-acting β -agonist combination, leukotriene modifiers, theophylline, mast cell stabilizers, and omalizumab were classified as controller medications. To prevent any individuals from having an outcome attributed to an event on day 0, 1 day was added for all time calculations. Additional data for each individual were collected and used in the analysis, including (1) age at the time of the step-down event; (2) sex; (3) season, based on midpoint of the period just prior to stepping down; (4) asthma medication ratio, defined as the number of controller medications dispensed divided by the sum of the controller and rescue medications dispensed¹¹; (5) asthma controller medication days supplied, categorized as > 149, 90-149, and < 90 days; (6) Charlson comorbidity

index; and (7) number of outpatient visits for asthma during the two periods prior to the step-down event period.

Analysis

First, the frequency of achieving primary and secondary asthma outcomes (ie, asthma exacerbations, at least two rescue inhalers in 4 months, returning to or exceeding baseline asthma controller medication use) over the 24 months following the step-down event was calculated for the entire cohort, as well as according to length of stability prior to step-down. Then, a time-to-event analysis was conducted with time 0 defined as the end of the 4-month interval during which the step-down occurred and failure defined by first asthma exacerbation. To determine the most appropriate time-to-event model, we first estimated a Cox proportional hazards model including only the stability group and rejected the proportional hazards assumption based on Schoenfeld residuals.¹²

We then compared parametric time-to-event models with exponential, Gompertz, log-logistic, Weibull, log-normal, and γ distributions, again including only the stability group, and compared the models using Akaike information criterion, Bayesian information criterion, and log likelihood; based on all three statistics, the γ distribution was selected as the most appropriate for time-to-asthma exacerbation. We then estimated a separate time-to-event parametric model with a γ distribution for three outcome categories: asthma exacerbation (primary outcome), inpatient or ED visit for asthma, or meeting any possible of the primary or secondary outcomes. In addition to prior stability, each model included age category, race, sex, season of step-down, Charlson comorbidity index, and number of days of asthma controller medication dispensed in the pre-step-down period. All analyses were performed using Stata 12.1 (StataCorp LP) and SAS 9.3 (SAS Institute Inc).

Results

Participants

We identified 26,292 individuals who met our criteria for inclusion. Figure 1 is a flowchart of cohort selection. Table 1 summarizes the characteristics of the individuals who were assigned to the groups based on length of stability prior to the step-down event. Statistical differences between the assigned groups were noted for age, sex, race, season of step-down, baseline days of asthma controller medication dispensing, Charlson comorbidity index, outpatient visits for asthma, the number of months from incident asthma diagnosis to step-down event, and asthma medication ratio.

Main Outcomes

Thirty-two percent of the 26,292 included individuals had an asthma exacerbation in the 24-month period following step-down of asthma controller medication, though only 7% had an ED visit or hospitalization for asthma. The length of asthma stability prior to stepping down asthma medication was strongly associated with the risk of an asthma exacerbation in the subsequent 24-month period: < 4 months' stability, 44%; 4 to 7 months, 34%; 8 to 11 months, 30%; and ≥ 12 months, 21% ($P < .001$) (Fig 2). The number and percentage of individuals grouped by length of asthma stability before step-down who had specific asthma outcomes are summarized in Table 2. Notably, most individuals had one of the asthma outcomes (ED/inpatient admission [IP], systemic corticosteroid [SCS], at least two rescue inhalers in 4 months, or returning to baseline controller therapy) over the course of 2 years, suggesting that evidence of underlying asthma remained for most of the cohort.

Variables Associated With Asthma Outcomes

Variables associated with specific asthma outcomes, displayed at time-to-asthma outcome ratios, are sum-

marized in Table 3. Several variables are significantly associated with a shortened time-to-asthma exacerbation: age 0 to 19 years old ($P < .001$), female sex ($P < .001$), black race ($P < .001$), Charlson comorbidity

Figure 1 – Cohort selection.

TABLE 1] Characteristics of Patients Included in Study

Characteristics	Group				All	P Value
	0-3 mo Stability Before Step-down	4-7 mo Stability Before Step-down	8-11 mo Stability Before Step-down	≥12 mo Stability Before Step-down		
Age, y						< .001
18-64	5,438 (70.9)	2,914 (68.8)	2,022 (69.8)	8,961 (77.9)	19,335 (73.5)	
5-17	1,380 (18.0)	895 (21.1)	638 (22.0)	1,769 (15.4)	4,682 (17.8)	
65+	331 (4.3)	152 (3.6)	103 (3.6)	511 (4.4)	1,097 (4.2)	
0-4	519 (6.8)	272 (6.4)	132 (4.6)	255 (2.2)	1,178 (4.5)	
Sex						.169
Male	3,523 (45.9)	1,882 (44.5)	1,289 (44.5)	5,103 (44.4)	11,797 (44.9)	
Female	4,145 (54.1)	2,351 (55.5)	1,606 (55.5)	6,391 (55.6)	14,493 (55.1)	
Race						< .001
Black	669 (8.7)	334 (7.9)	223 (7.7)	790 (6.9)	2,016 (7.7)	
Other	729 (9.5)	428 (10.1)	281 (9.7)	865 (7.5)	2,303 (8.8)	
Unknown	1,103 (14.4)	576 (13.6)	418 (14.4)	1,532 (13.3)	3,629 (13.8)	
White	5,167 (67.4)	2,895 (68.4)	1,973 (68.2)	8,309 (72.3)	18,344 (69.8)	
Season of step-down						< .001
Fall	1,639 (21.4)	1,060 (25.0)	736 (25.4)	2,873 (25.0)	6,308 (24.0)	
Spring	2,159 (28.2)	1,031 (24.4)	698 (24.1)	2,837 (24.7)	6,725 (25.6)	
Summer	2,196 (28.6)	1,195 (28.2)	754 (26.0)	3,071 (26.7)	7,216 (27.4)	
Winter	1,674 (21.8)	947 (22.4)	707 (24.4)	2,715 (23.6)	6,043 (23.0)	
Days supplied controller medicines prior to step-down						< .001
91-149	1,737 (22.7)	790 (18.7)	590 (20.4)	2,608 (22.7)	5,725 (21.8)	
< 90	2,841 (37.1)	1,893 (44.7)	1,288 (44.5)	4,135 (36.0)	10,157 (38.6)	
> 149	3,090 (40.3)	1,550 (36.6)	1,017 (35.1)	4,753 (41.3)	10,410 (39.6)	
Charlson morbidity index						< .001
0	744 (9.7)	499 (11.8)	465 (16.1)	2,791 (24.3)	4,499 (17.1)	
1	5,783 (75.4)	3,181 (75.1)	2,034 (70.3)	7,263 (63.2)	18,261 (69.5)	

(Continued)

TABLE 1] (continued)

Characteristics	Group				All	P Value
	0-3 mo Stability Before Step-down	4-7 mo Stability Before Step-down	8-11 mo Stability Before Step-down	≥12 mo Stability Before Step-down		
2	632 (8.2)	314 (7.4)	215 (7.4)	810 (7.0)	1,971 (7.5)	
3	281 (3.7)	132 (3.1)	102 (3.5)	363 (3.2)	878 (3.3)	
4+	228 (3.0)	107 (2.5)	79 (2.7)	269 (2.3)	683 (2.6)	
Outpatient visits						<.001
1	2,216 (28.9)	1,700 (40.2)	1,303 (45.0)	5,774 (50.2)	10,993 (41.8)	
2	4,066 (53.0)	2,226 (52.6)	1,420 (49.1)	5,355 (46.6)	13,067 (49.7)	
3+	1,386 (18.1)	307 (7.3)	172 (5.9)	367 (3.2)	2,232 (8.5)	
No. of months after incident asthma diagnosis and before the step-down event						<.001
13-18	2,481 (32.4)	1,386 (32.7)	675 (23.3)	3,567 (31.0)	8,109 (30.8)	
19-24	1,218 (15.9)	674 (15.9)	529 (18.3)	1,802 (15.7)	4,223 (16.1)	
25-30	1,221 (15.9)	638 (15.1)	505 (17.4)	1,840 (16.0)	4,204 (16.0)	
31-36	701 (9.1)	396 (9.4)	288 (9.9)	1,079 (9.4)	2,464 (9.4)	
37-42	630 (8.2)	356 (8.4)	273 (9.4)	1,014 (8.8)	2,273 (8.6)	
43-48	359 (4.7)	212 (5.0)	175 (6.0)	540 (4.7)	1,286 (4.9)	
49+	1,058 (13.8)	571 (13.5)	450 (15.5)	1,654 (14.4)	3,733 (14.2)	
Asthma medication ratio						<.001
≤0.5	4,244 (55.3)	1,704 (40.3)	1,094 (37.8)	2,531 (22.0)	9,573 (36.4)	
>0.5	3,424 (44.7)	2,529 (59.7)	1,801 (62.2)	8,965 (78.0)	16,719 (63.6)

Figure 2 – Time-to-event analysis for meeting IP, ED, or SCS criteria. IP = inpatient admission; SCS = systemic corticosteroid.

index ≥ 1 ($P < .001$), shorter length of stability period before stepping down ($P < .001$), and at least two outpatient asthma visits ($P < .001$).

Discussion

We found that 32% of individuals had an asthma exacerbation in the 24 months following a decrease in asthma controller medications by $\geq 50\%$ in a claims-based, real-world setting that did not select for provider-directed step-down events. In this dataset, length of asthma stability prior to stepping down asthma medication is strongly associated with asthma outcomes in the period following asthma step-down.

Compared with previous studies, the rates of asthma exacerbations reported in this study after stepping down asthma exacerbations were similar or slightly lower. There are very few studies with longer than 6 months' follow-up after stepping down asthma medication and, therefore, few studies for comparing our outcomes data. Martinez et al⁸ randomized patients with asthma, stable on low doses of ICS, to stop or reduce the ICS and followed them for 44 weeks, finding 49% who stopped had an asthma exacerbation, 35% who reduced ICS had an exacerbation, and 28% who maintained their ICS dose had an asthma exacerbation. At 44 weeks, the estimates for asthma exacerbations in our study ranged from 12% for those who had stable asthma for > 12 months to 30% for those who were stable for < 4 months. The lower asthma exacerbation risk in our study may reflect a real-world effect of including individuals who may not actually have asthma or may reflect lower exacerbation detection rates than would be captured in a clinical trial. Drawing direct comparisons between the study performed by Martinez et al⁸ and the current study is further challenged by the considerable difference in

TABLE 2] Twenty-Four Month Outcomes After Stepping Down Asthma Medications in Individuals Grouped by Length of Pre-Step-down Stability

Length of Stability Prior to Stepping Down, mo	No. (% Total)	Type of Asthma Outcome (% of Cohort) ^a			
		No Asthma Outcome Event	ED or IP Visit for Asthma	SCS	≥ 2 Rescue Inhalers in 4 mo
0-3	7,668 (29)	538 (7)	341 (4)	1,478 (19)	2,812 (37)
4-7	4,233 (16)	522 (12)	117 (3)	726 (17)	2,215 (52)
8-11	2,895 (11)	383 (13)	79 (3)	425 (15)	1,632 (56)
≥ 12	11,496 (44)	2,105 (18)	272 (2)	1,191 (10)	7,012 (61)
					Returning to Baseline Controller Therapy
					2,499 (33)
					653 (15)
					376 (13)
					916 (8)

IP = inpatient admission; SCS = systemic corticosteroid.

^aOnly the first asthma outcome was identified for each individual in the 2-y period following a step-down, with ED or IP visit for asthma counting first, then systemic corticosteroid, then ≥ 2 rescue inhalers in 4 mo, then returning to baseline controller therapy.

TABLE 3 Variables Associated With Asthma Outcomes After Stepping Down Asthma Controller Medications

Variable	Meeting Any Asthma Outcome* Time Ratio (95% CI)	P Value	Wald P Value	IP/ED Time Ratio (95% CI)	P Value	Wald P Value	IP/ED/SCS (Asthma Exacerbation) Time Ratio (95% CI)	P Value	Wald P Value
Group, mo stability			<.001			<.001			<.001
≤ 4	Ref	...		Ref	...		Ref	...	
4-7	1.46 (1.37, 1.56)	<.001		1.80 (1.52, 2.12)	<.001		1.36 (1.25, 1.47)	<.001	
8-11	1.51 (1.40, 1.63)	<.001		1.76 (1.45, 2.14)	<.001		1.60 (1.45, 1.76)	<.001	
≥ 12	1.59 (1.51, 1.68)	<.001		2.39 (2.07, 2.76)	<.001		2.33 (2.17, 2.51)	<.001	
Age (category), y			<.001			.004			<.001
18-64	Ref	...		Ref	...		Ref	...	
5-19	1.14 (1.08, 1.20)	<.001		1.12 (0.96, 1.30)	.164		0.75 (0.70, 0.81)	<.001	
> 65	0.91 (0.82, 1.01)	.068		0.74 (0.58, 0.94)	.014		1.13 (0.98, 1.32)	.098	
< 5	1.08 (0.97, 1.19)	.16		0.79 (0.62, 1.00)	.048		0.51 (0.45, 0.58)	<.001	
Sex			.32			<.001			<.001
Male	Ref	...		Ref	...		Ref	...	
Female	1.02 (0.98, 1.07)	.32		0.78 (0.70, 0.88)	<.001		0.86 (0.81, 0.91)	<.001	
Race			.003			<.001			<.001
Black	Ref	...		Ref	...		Ref	...	
Other	1.08 (0.97, 1.19)	.14		1.35 (1.04, 1.74)	.024		1.19 (1.04, 1.35)	.011	
Unknown	0.92 (0.84, 1.01)	.066		0.69 (0.55, 0.85)	.001		1.17 (1.03, 1.32)	.012	
White	0.96 (0.89, 1.04)	.30		1.38 (1.14, 1.68)	.001		1.24 (1.12, 1.37)	<.001	
Season of step-down			<.001			.73			.048
Fall	Ref	...		Ref	...		Ref	...	
Spring	1.15 (1.09, 1.22)	<.001		1.06 (0.91, 1.24)	.46		1.06 (0.98, 1.15)	.13	
Summer	1.01 (0.95, 1.07)	.76		0.98 (0.84, 1.13)	.75		0.97 (0.90, 1.05)	.47	
Winter	1.06 (1.00, 1.13)	.039		1.02 (0.87, 1.20)	.80		1.06 (0.98, 1.16)	.13	
Baseline days of controller medications			<.001			.27			.46
91-149	Ref	...		Ref	...		Ref	...	
< 90	0.54 (0.51, 0.57)	<.001		1.04 (0.90, 1.20)	.61		0.97 (0.90, 1.05)	.48	
> 149	1.50 (1.41, 1.58)	<.001		1.12 (0.97, 1.29)	.13		0.95 (0.89, 1.03)	.21	

(Continued)

TABLE 3] (continued)

Variable	Meeting Any Asthma Outcome ^a Time Ratio (95% CI)	P Value	Wald P Value	IP/ED Time Ratio (95% CI)	P Value	Wald P Value	IP/ED/SCS (Asthma Exacerbation) Time Ratio (95% CI)	P Value	Wald P Value
Charlson comorbidity index			.002						
0	Ref	...		Ref	...		Ref	...	
1	0.99 (0.93, 1.05)	.66		0.69 (0.57, 0.84)	<.001		0.61 (0.56, 0.68)	<.001	
2	0.87 (0.79, 0.95)	.003		0.55 (0.43, 0.71)	<.001		0.58 (0.51, 0.67)	<.001	
3	0.90 (0.80, 1.02)	.11		0.37 (0.27, 0.50)	<.001		0.53 (0.45, 0.63)	<.001	
4+	0.84 (0.73, 0.97)	.014		0.34 (0.25, 0.47)	<.001		0.54 (0.45, 0.65)	<.001	
Outpatient asthma visits			.22						<.001
1	Ref	...		Ref	...		Ref	...	
2	1.01 (0.97, 1.06)	.58		0.81 (0.71, 0.92)	.001		0.63 (0.59, 0.67)	<.001	
3+	0.95 (0.87, 1.03)	.19		0.42 (0.35, 0.50)	<.001		0.31 (0.28, 0.34)	<.001	
Months after incident diagnosis			.29			.32			.61
13-18	Ref	...		Ref	...		Ref	...	
19-24	0.98 (0.92, 1.04)	.52		1.01 (0.86, 1.19)	.87		0.98 (0.90, 1.07)	.66	
25-30	1.00 (0.94, 1.06)	.96		1.05 (0.89, 1.24)	.58		0.97 (0.89, 1.06)	.54	
31-36	0.96 (0.89, 1.04)	.33		1.00 (0.82, 1.21)	.97		0.93 (0.83, 1.03)	.14	
37-42	1.07 (0.99, 1.16)	.094		1.17 (0.94, 1.45)	.15		1.05 (0.94, 1.17)	.36	
43-48	0.94 (0.86, 1.04)	.26		1.11 (0.85, 1.45)	.43		0.95 (0.83, 1.09)	.44	
49+	0.97 (0.91, 1.04)	.39		1.23 (1.03, 1.47)	.025		0.98 (0.90, 1.08)	.73	
Asthma medication ratio			<.001			.019			.13
≤ 0.5	Ref	...		Ref	...		Ref	...	
> 0.5	1.20 (1.15, 1.26)	<.001		1.15 (1.02, 1.29)	.019		1.05 (0.99, 1.11)	.13	

Ref = reference group. See Table 2 legend for expansion of other abbreviations.

^aIndividuals who had IP/ED visits for asthma, SCS for asthma, ≥ 2 rescue inhalers in 4 mo, or a return to baseline controller level.

sampling—children with mild persistent asthma in Martinez et al⁸ compared with all ages and all severity levels in the current study. Haahtela et al¹³ randomized individuals with asthma to step-down from low-dose ICS and followed them for 52 weeks, finding that 33% had asthma exacerbations. Visser et al¹⁴ randomized patients with asthma to step-down ICSs and followed them for 26 weeks, finding that 23% had asthma exacerbations. In summary, the current study suggests that the asthma exacerbation risk after stepping down asthma medications is similar to previous reports despite differences in patient selection, study setting, and length of follow-up.

The secondary outcomes reported in this study also offer some lessons about outcomes after stepping down asthma medications. First, 33% of individuals who had stable asthma for < 4 months returned to their baseline level of asthma controller therapy, considerably higher than the 15%, 13%, and 8% for individuals who had stable asthma for 4 to 7 months, 8 to 11 months, and > 12 months, respectively (Table 2). Likely, these individuals had a lapse in adherence which was corrected in the subsequent period. The other secondary outcome we collected, ≥ 2 rescue inhalers in a 4-month period, was intended to be a surrogate marker for asthma control.⁹ However, over one-half of our cohort met this criteria during the 24-month outcome period (Table 2). These findings could be interpreted to suggest that the majority of individuals who step down their asthma medication experience asthma that is not in control in the subsequent 24 months or that using rescue inhaler dispensing numbers ≥ 2 in 4 months from claims data may be oversensitive as a marker for asthma control. Additional studies with patient-reported outcomes will help clarify the outcome of asthma control after stepping down medications.

Depending on which individuals are selected for step-down, the future-risk asthma exacerbation may vary considerably—this is clearly reflected in the current study where we identified several variables associated with asthma exacerbations in the outcome period. The length of asthma stability before stepping down appeared to have the strongest association with asthma exacerbation outcomes, with time ratios lengthening in a “dose-dependent” manner (Table 3). The time that an individual has had “stable” asthma for this study is defined using claims data; however, the variables that are used depend primarily on knowing whether an exacerbation occurred last. Considering length of stability, even beyond the 3 months that is currently suggested, may improve risk

prediction and allow for more individualized recommendations. However, there remains a need for improving risk prediction for those deciding about stepping down.

There are a few limitations that suggest caution with interpreting the findings from this study. First, we did not include individuals who did not step down in our analysis; therefore, the 32% risk of an asthma exacerbation is an absolute risk not adjusted for baseline risk of those who had asthma exacerbations despite continuation of asthma controller medication. Second, our cohort included individuals who were continuously enrolled in a health insurance plan, and, therefore, may not be applicable to those who are uninsured or who have different types of insurance plans. Third, from our dataset, it is unclear whether decisions to step down were made in consultation with a health-care provider—the role of the health-care provider in guiding these decisions is likely very important. Finally, using observational data prevents collection of all desired variables, many of which may be important predictors of stability after asthma step-down such as spirometry, sputum for eosinophils, exhaled nitric oxide, or other biomarkers.¹⁵ As a corollary, the definition used for stability prior to step-down may not correspond directly to guideline-determined stability given the lack of some variables in our dataset. The strengths of the study are the sample size, the long-term pre-step-down and post-step-down measurement periods, and the identification of multiple factors associated with the outcome of interest.

Several additional steps will help clarify decisions about stepping down asthma medications. Effectiveness studies comparing those with similar characteristics who step down and those who do not will provide additional context for individuals and their providers to consider. Prospective study designs that allow for better delineation between individuals who have a lapse of adherence and those who intend to step down will also be important, as will studies that clarify the role of health-care provider guidance.

Conclusions

Individuals and their providers can cautiously apply the data from this study to decisions about stepping down asthma medications. The novel insights from this analysis that contribute to this decision-making process are consideration to the length of stability prior to step-down and the rate of asthma exacerbations in the 24 months following step-down.

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