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Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA

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Recording by Melissa Roberts

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DISCLOSURES

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Introduction and objectives

- Despite the availability of ICS-LABA combination therapies:
  - 30–50% of patients with asthma on ICS-LABA remain uncontrolled.[1-4]
  - About one third of US patients with asthma experienced ≥1 exacerbation in the past 12 months.[5]
- The burden of severe exacerbations in patients using ICS-LABA is well described, unlike the burden of moderate exacerbations.[2]
- There is disagreement on how to apply the ATS/ERS[6] definitions of moderate exacerbations to retrospective claims-based analyses, and there is also a wide variation in the estimates of the burden of these events.
- Here we describe claims-based definitional algorithms for moderate and severe exacerbations that were developed and applied to a large administrative claims database to define the frequency of exacerbations in patients with asthma treated with ICS-LABA.

ATS/ERS definitions of moderate and severe exacerbations

- **Moderate:** ≥1 of deterioration in symptoms, deterioration in lung function, increased rescue bronchodilator use; features should last for ≥2 days, not severe enough to warrant SCS use and/or hospitalization. ED visits for asthma that do not require SCS may also be classified as moderate.
- **Severe:** events that require urgent action on the part of the patient and physician to prevent a serious outcome and include ≥1 of use of SCS or increase from a stable maintenance dose for ≥3 days, a visit to an ED for asthma requiring SCS, or a hospital admission for asthma requiring SCS.

ATS, American Thoracic Society; ED, emergency department; ERS, European Respiratory Society; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; SCS, systemic corticosteroids

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Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

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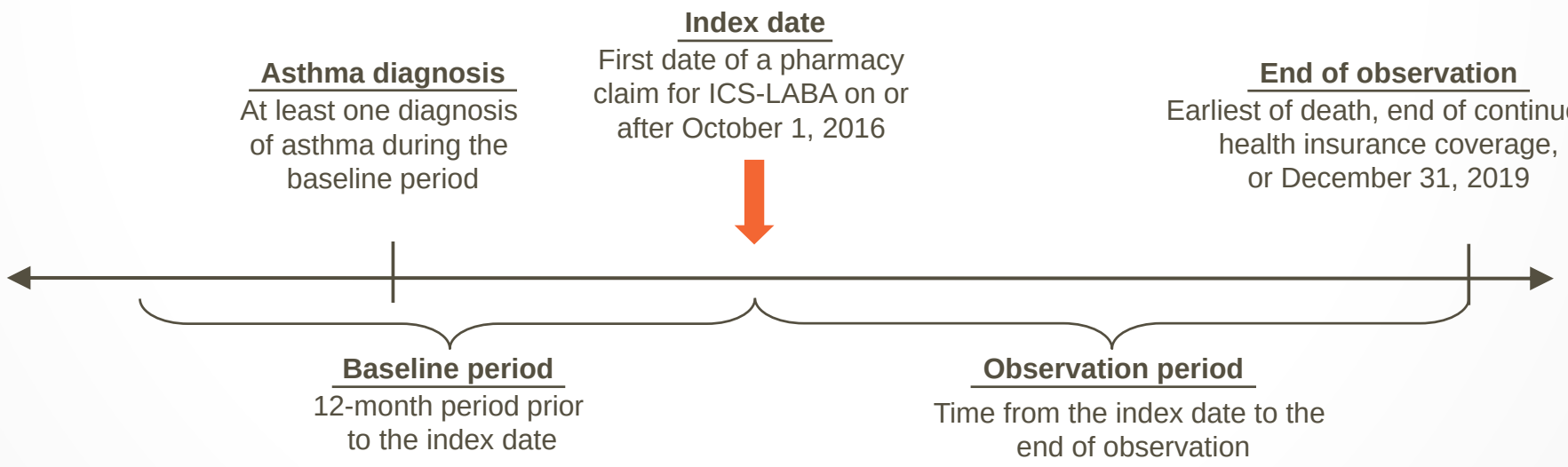
Methods

- This retrospective cohort study utilized the Optum's de-identified Clinformatics® Data Mart Database (2007–2020), a US claims database with national geographical coverage.
- Algorithms to operationalize the ATS/ERS moderate and severe asthma exacerbation definitions were developed by a multidisciplinary clinical and epidemiology team based on medical and pharmacy claims data.
- Using the algorithms, the post-index rate of exacerbations per patient and the proportion of patients experiencing exacerbations during the 12-months post-index period were calculated.

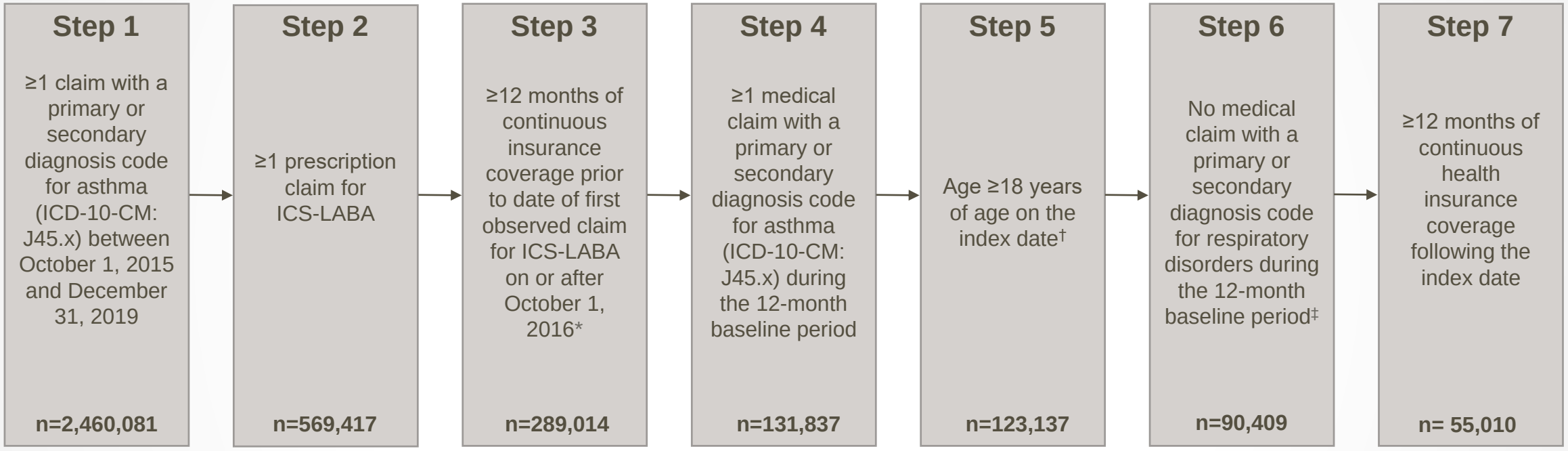
Study design



ATS, American Thoracic Society; ERS, European Respiratory Society; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist

Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

Eligibility criteria and sample selection



- Median follow-up in the cohort was 2.1 years

*The 12 months prior to the index date was defined as the baseline period; †the index date was defined as the first date of a pharmacy claim for ICS-LABA on or after October 1, 2016; ‡in total, 32,728 (26.58%) patients were excluded: 71 (0.06%) with active tuberculosis, 32,236 (26.18%) with COPD, 100 (0.08%) with cystic fibrosis, and 1,211 (0.98%) with lung cancer. Patients could have more than one of the exclusionary respiratory disorders.

COPD, chronic obstructive pulmonary disease; ICD-10-CM, International Classification of Diseases, 10th revision, Clinical Modification; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist

Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

American Thoracic Society
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May 14–19, 2021

Baseline demographics and clinical characteristics

Demographics	Overall population (N=55,010)
Age at index, years	
Mean (SD)	57.6 (16.7)
Median (IQR)	59.0 (46.0, 71.0)
Male, n (%)	17,497 (31.8)
Geographic region of USA, n (%)	
South	23,454 (42.6)
West	12,852 (23.4)
Midwest	12,303 (22.4)
Northeast	6,345 (11.5)
Unknown	56 (0.1)
Insurance type, n (%)	
Commercial	30,455 (55.4)
Medicare	24,555 (44.6)

Clinical characteristics	Overall population (N=55,010)
Asthma-related comorbidities, n (%)	
Hypertension	29,653 (53.9)
Allergic rhinitis	21,430 (39.0)
GERD	17,112 (31.1)
History of severe asthma exacerbation*, n (%)	14,989 (27.2)
Elixhauser Comorbidity Index, mean (SD)	2.5 (6.3)
Concomitant medication use†, n (%)	
SABA	25,011 (45.5)
SCS	18,465 (33.6)
LTRA	15,630 (28.4)
SABA-SAMA FDC	2,950 (5.4)
ICS	2,044 (3.7)
LAMA	1,797 (3.3)
SAMA	786 (1.4)
Biologics	647 (1.2)
PDE-4	324 (0.6)

*Severe exacerbations were defined as events requiring treatment with systemic corticosteroids (3–28 days' supply dispensed within 14 days after an ED or outpatient visit for asthma or asthma symptoms) OR inpatient hospital stay of ≥2 days for asthma or asthma symptoms; †concomitant medication use was defined as any prescription for respiratory medication other than ICS-LABA in the 30 days before and after the index date. Medications used by ≥0.5% of patient population are listed in the table.

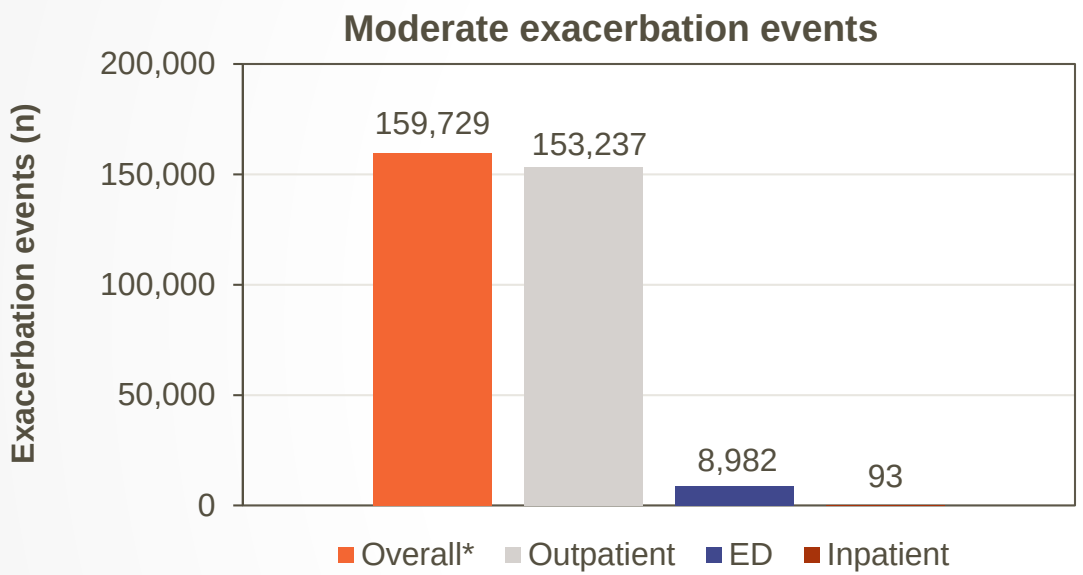
FDC, fixed-dose combination; GERD, gastro-esophageal reflux disease; ICS, inhaled corticosteroids; IQR, interquartile range; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; PDE-4, phosphodiesterase type 4 inhibitors; SABA, short-acting β_2-agonist; SAMA, short-acting muscarinic antagonist; SCS, systemic corticosteroids; SD, standard deviation

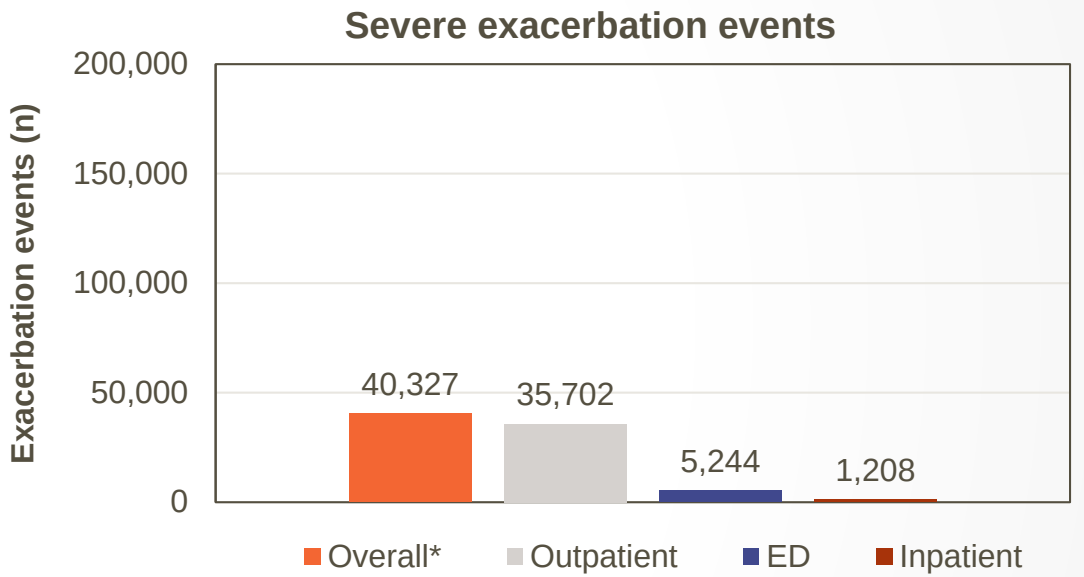
Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

American Thoracic Society
Annual Meeting 2021
May 14–19, 2021

Events meeting the algorithmic definition for moderate exacerbations were more common than severe events

- Observation period in total cohort (N=55,010): mean (SD) 2.2 (0.7) years; median 2.1 years.





Moderate exacerbation events defined as follows

- Diagnoses of acute asthma exacerbations (excluding status asthmaticus) in outpatient, ED or inpatient (<2 days) settings that did not meet criteria for a severe exacerbation.

OR

- Outpatient, ED, or inpatient visit (<2 days) for asthma or asthma symptoms (ie, dyspnea, coughing, wheezing, chest pain, fatigue, bronchospasm, acute bronchitis, reactive airways dysfunction syndrome) followed by a pharmacy claim for a respiratory medication (excluding systemic corticosteroids) within 14 days, and where the criteria for a severe exacerbation event was not met.

Severe exacerbation events defined as follows

- Requiring treatment with systemic corticosteroids (3–28 days' supply dispensed within 14 days after an ED or outpatient visit for asthma or asthma symptoms).

OR

- Inpatient hospital stay of ≥2 days for asthma or asthma symptoms.

*Overall represents the number of events that were presented in outpatient, ED, or inpatient settings.
ED, emergency department; SD, standard deviation

Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

The annualized rate and number of events meeting the algorithmic definition for moderate exacerbations were substantially higher than for severe events

- Observation period in total cohort (N=55,010): mean (SD) 2.2 (0.7) years; median 2.1 years.

	Exacerbation rate per patient year, post-index (95% CI)*	Proportion of patients with exacerbations in the 12-month post-index period		
		None	1 event	≥2 events
Moderate exacerbations	1.116 (1.110, 1.122)	38.4%	31.1%	30.5%
Severe exacerbations	0.278 (0.275, 0.281)	78.0%	16.2%	5.9%

Moderate exacerbation events defined as follows
- Diagnoses of acute asthma exacerbations (excluding status asthmaticus) in outpatient, ED or inpatient (<2 days) settings that did not meet criteria for a severe exacerbation.

OR
- Outpatient, ED, or inpatient visit (<2 days) for asthma or asthma symptoms (ie, dyspnea, coughing, wheezing, chest pain, fatigue, bronchospasm, acute bronchitis, reactive airways dysfunction syndrome) followed by a pharmacy claim for a respiratory medication (excluding systemic corticosteroids) within 14 days, and where the criteria for a severe exacerbation event was not met.

Severe exacerbation events defined as follows
- Requiring treatment with systemic corticosteroids (3–28 days' supply dispensed within 14 days after an ED or outpatient visit for asthma or asthma symptoms).

OR
- Inpatient hospital stay of ≥2 days for asthma or asthma symptoms.

*Rate of asthma exacerbations per person year was calculated as the sum of exacerbation events divided by the sum of person-years in the observation period, and the corresponding 95% CI was calculated as rate ± 1.96 × √(sum of exacerbation events / [sum of person-years in the observation period]). The rate was calculated using data from the total observation period (≥12 months per patient).
CI, confidence interval; ED, emergency department; ICS, inhaled corticosteroids; LABA, long-acting β_2-agonist; SD, standard deviation

Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

Asthma-related HCRU and healthcare costs at baseline were generally higher as the number of exacerbations in the post-index period increased

	Overall	Frequency of moderate asthma exacerbations in the 12-month post-index period			Frequency of severe asthma exacerbations in the 12-month post-index period		
	N=55,010	None N=21,119	1 event N=17,103	≥2 events N=16,788	None N=42,889	1 event N=8,886	≥2 events N=3,235
Asthma-related healthcare resource utilization* ≥1 visit, n (%)							
Inpatient visits	6,387 (11.6)	2,365 (11.2)	1,839 (10.8)	2,183 (13.0)	4,806 (11.2)	1,051 (11.8)	530 (16.4)
Emergency department visits	9,952 (18.1)	3,226 (15.3)	3,108 (18.2)	3,618 (21.6)	6,907 (16.1)	2,014 (22.7)	1,031 (31.9)
Outpatient visits	52,063 (94.6)	19,574 (92.7)	16,219 (94.8)	16,270 (96.9)	40,458 (94.3)	8,500 (95.7)	3,105 (96.0)
Other visits†	3,404 (6.2)	917 (4.3)	903 (5.3)	1,584 (9.4)	2,346 (5.5)	676 (7.6)	382 (11.8)
Asthma-related healthcare costs‡ in USD, median (IQR)							
Total healthcare costs	2,146 (619–6,074)	1,578 (461–4,775)	2,026 (599–5,341)	3,226 (1,007–9,155)	1,966 (569–5,493)	2,536 (765–7,068)	4,125 (1,284–13,981)
Pharmacy costs	416 (70–1,962)	286 (57–1,576)	383 (67–1,827)	713 (129–2,594)	387 (63–1,893)	469 (102–2,010)	765 (161–2,724)

*Patient HCRU was assessed during the baseline period, defined as the 12-month period prior to the index date. A medical service claim was considered asthma-related if it was associated with a primary or secondary diagnosis of asthma; †other visits include physical medicine and rehabilitations, durable medical equipment, home care services, and hospice; ‡patient healthcare costs were assessed during the baseline period, defined as the 12-month period prior to the index date. All costs were inflated to 2019 US dollars using the medical care component of the Consumer Price Index.
HCRU, healthcare resource utilizaition; IQR, interquartile range

Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

American Thoracic Society
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Conclusions

- In our cohort of ICS-LABA-treated adult patients with asthma, we observed a nearly 4-fold higher rate of events meeting the algorithmic definition for moderate versus severe exacerbations.
  - Over 60% of patients experienced ≥1 moderate exacerbation in the 12-months post-index period.
- In general, asthma-related healthcare resource utilization and healthcare costs at baseline were lowest for patients with no moderate exacerbations during 12-month post-index period and were highest for patients experiencing ≥2 moderate exacerbations during the same period.
  - Similar trends were observed for severe exacerbation events.
- Collectively, these observations highlight the considerable burden associated with moderate exacerbations.
- The definitional algorithms for asthma exacerbations may be used as a case-finding tool in health claims data.
- Results are based on working version of the algorithm.
  - Further work is planned to validate the exacerbation algorithm using chart review.

ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist

Roberts M, et al. Development of Claims-based Definitional Algorithms for Moderate and Severe Asthma Exacerbations and Quantification of Exacerbation Rates in Adult Asthmatic Patients Treated With ICS-LABA.

CO-AUTHORS' DISCLOSURES

- A Czira, A Fowler, D Slade, S Zhang, and W Meeraus are employees of GSK and hold stocks or shares in GSK. M Tabberer was an employee of GSK at the time of the study and holds stocks or shares in GSK. D Mapel received research funding for this study from Analysis Group, Inc., and in the past 5 years, has also received respiratory-related research support from AstraZeneca, Boehringer Ingelheim, Pfizer, and Sunovion Pharmaceuticals. MS Duh, M Wu, R Chang, S Park, and WY Cheng are employees of Analysis Group, Inc., which received research funding from GSK to conduct this study.