

Supplementary Materials

Supplementary Methods

Incident EGPA case definition

Persons with at least one inpatient diagnosis or two outpatient diagnoses (≥ 90 days apart) of eosinophilic granulomatosis with polyangiitis (EGPA) (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM] code M30.1) during the study selection window (January 1, 2017, through June 30, 2021) in the Merative™ MarketScan® Commercial Claims and Encounters database or Medicare Supplemental databases. Patients were excluded who had the EGPA diagnosis prior to January 1, 2017 or a first observed diagnosis of microscopic polyarteritis nodosa (ICD-10-CM code M31.7), giant cell arteritis (ICD-10-CM codes M31.5 and M31.6), Takayasu arteritis (ICD-10-CM code M31.4), or hypereosinophilic syndrome (ICD-10-CM D72.11) after the last observed EGPA diagnosis.

Matched severe uncontrolled asthma cohort definition

Inclusion Criteria

Patients were available for selection if they met all of the following criteria on or after January 1, 2017:

- At least one criterion from Part A, plus at least one criterion from Part B, plus at least one criterion from Part C (note: the criteria for Parts B and C must have occurred on or after January 1, 2017; the criteria from Part C must have occurred after the patient fulfilled the criteria from Part B. The criteria from Part A may have occurred at any point in time, including before January 1, 2017). The index date (ID) was determined based on Part C criteria, as described following.

Part A:

- At least one claim for an emergency department visit with a diagnosis of asthma (ICD-10-CM code J45.), or
- At least one claim for hospitalization with asthma as the primary diagnosis on the claim, or

- At least four outpatient claims on different dates (at least 7 days apart) with an asthma diagnosis in any position on the claim plus at least two pharmacy claims for asthma controller medications (inhaled corticosteroid [ICS], ICS in combination with a long-acting β_2 agonist [LABA], leukotriene receptor antagonist [LTRA] or theophylline) in 1 year (note: the four outpatient claims and two pharmacy claims must have all occurred within 365 days of each other; claims may have occurred in any order; outpatient claims must have been at least 7 days apart from one another; pharmacy claims must have been at least 60 days apart from each other, and no minimum number of days' supply was required for pharmacy claims), or
- At least one outpatient claim with an asthma diagnosis in any position, plus at least four pharmacy claims for any asthma medication in 1 year (note: the one outpatient claim and four pharmacy claims must all have occurred within 365 days of each other; claims may have occurred in any order; pharmacy claims must have been at least 60 days apart from one another, and no minimum number of days' supply was required for pharmacy claims).

Part B:

- Receipt of at least one claim with a medium- to high-dose of ICS, ICS/LABA, ICS/long-acting muscarinic antagonist (LAMA), or ICS/LTRA.
- At least 180 cumulative days' supply of oral glucocorticoids (OGCs); gaps present between fills that totaled ≥ 180 days were allowed.

Part C:

- At least one claim for hospitalization with asthma as the primary diagnosis on the claim (note: this could have been the same hospitalization as identified for Part A, so long as it occurred after the Part B criteria; the ID was defined as the date of admission), or
- At least two outpatient visits (ie, excluding inpatient stays) for asthma followed by treatment with systemic corticosteroids within a week (1 dose of intravenous steroids or at least 3 days of OGCs) (note: outpatient visits should have occurred between 30 and 365 days apart, provided that they occurred after the Part B criteria were fulfilled; each outpatient visit should have steroids dispensed within 1 week of the visit; the ID was defined as the date of the first outpatient visit with steroids dispensed), or

- At least four claims for a short-acting β 2 agonist (SABA) within any 12-month period (note: the four SABA claims within a 12-month period should have been identified after the Part B criteria were met; each pharmacy claim was at least 30 days apart, and the ID was defined as the date of the first SABA claim).

Index Date

The ID was defined as the date the first Part C criterion was fulfilled on or after January 1, 2017 (note: all patients must have fulfilled the Part B criteria before the Part C criteria could be assessed).

Patients were required to have at least 1 year of continuous health plan enrolment before ID.

Exclusion Criteria

Patients were excluded from the matched asthma cohort if they had a diagnosis of EGPA (ICD-10-CM code M30.1) at any time.

Supplementary Table 1 Comorbidity Diagnosis Codes

Condition	ICD-10-CM Code
Acute myeloid leukemia	C92.0, C92.4, C92.5, C92.6, C92.A
Anxiety	F06.4, F40, F41, F43.1
Arrhythmia	I47, I48, I49
Arterial thrombosis	I63.0, I63.3, I74
Asthma	J45
Atopic dermatitis, eczema	L20, L30.9
Back pain (dorsalgia)	M54.0, M54.1, M54.4, M54.5, M54.6, M54.8, M54.9
B-cell lymphoma	C82, C83, C85, C88.0, C88.2, C88.3, C88.4
Cervical cancer	C53
Chronic eosinophilic pneumonia	J82.81
Chronic myeloid leukemia	C92.1, C92.2
Chronic obstructive pulmonary disease	J41, J42, J43, J44, J98.2
Colorectal cancer	C18, C19, C20
Deep vein thromboembolism	I80.1, I80.2, I80.3, I81, I82.2, I82.3, I82.4, I82.5, I82.62, I82.72, I82.9
Depression	F06.31, F06.32, F25.1, F31.3, F31.4, F31.5, F31.6, F31.7, F31.8, F31.9, F32, F33, F34.1, F41.8, F43.21, F43.23
Diffuse eosinophilic fasciitis	M35.4
Dyslipidemia	E78, E88.81
Eosinophilic asthma	J82.83
Eosinophilic cellulitis	L98.3
Eosinophilic colitis	K52.82
Eosinophilic endomyocardial disease	I42.3
Eosinophilic esophagitis	K20.0
Eosinophilic gastritis or gastroenteritis	K52.81
Gastro-oesophageal reflux disease	K21
Hodgkin's lymphoma	C81
Hypereosinophilic syndrome	D72.11
Hyperthyroidism	E05
Insomnia	F51.0, G47.0
Interstitial pulmonary disease	J84, D86.0, D86.2
Irritable bowel syndrome	K58
Ischemic heart disease	I20, I21, I22, I23, I24, I25

Lung cancer	C34
Malignancy (all cancers)	C
Nasal polyps	J33
Obesity	E66.0, E66.1, E66.2, E66.8, E66.9, Z68.3, Z68.4
Obstructive sleep apnea	G47.33
Polycythemia	D45
Primary myelofibrosis	D47.1
Primary (essential) thrombocythemia	D47.3
Pulmonary eosinophilia	J82
T-cell lymphoma	C84, C86, C91.5
Throat or chest pain	R07
Vitamin D deficiency	E55

Abbreviations: ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

Supplementary Table 2 BVAS Events

Organ System	Event (ICD-10-CM code)
Major BVAS events	Gastrointestinal ischemia or infarction (K55.0, K55.1, K55.8, K55.9) Retinal change (retinal vasculitis, thrombosis, exudate or hemorrhage) (H34, H35.0, H35.2, H35.6, H35.7) Sensorineural hearing loss (H90.3, H90.4, H90.5, H90.6, H90.7, H90.8, H90.A2, H90.A3) Hemoptysis or alveolar hemorrhage (R04.2, R04.89) Respiratory failure (J96) Ischemic cardiac pain (I20.9) Cardiomyopathy (I25.5, I42.0, I42.1, I42.2, I42.3, I42.4, I42.5, I42.7, I42.8, I42.9, I43, O90.3) Congestive heart failure (I11.0, I13.0, I13.2, I26.0, I27.22, I50) Hematuria (N02, R31) Creatinine: stage IV–V chronic kidney disease, end-stage renal disease, or dialysis (G0049, G0052, G0257, G2170, G2171) Cerebrovascular accident (I60, I61, I62, I63, I67.6, I68, I69) Spinal cord lesion (G95.1) Cranial nerve palsy (G51.0, G51.2, H49.0, H49.1, H49.2, H49.3) Mononeuritis multiplex (G58.7)
Non-major BVAS events	
General	Myalgia (M79.1) Arthralgia (M25.5) Fever (R50.81, R50.9)
Skin	Purpura (D69.0, D69.2) Skin ulcer (L97, L98.4, E08.621, E08.622, E09.621, E09.622, E10.621, E10.622, E11.621, E11.622, E13.621, E13.622) Urticaria (L50) Nodules (R22) Erythema nodosum (L52)
Mucous membrane	Mouth ulcers (K12.3) Genital ulcers (N48.5, N76.5, N76.6)
Eyes	Other specified disorders of eye and adnexa (H57.89) Proptosis (H05.2) Scleritis or episcleritis (H15.0, H15.1) Conjunctivitis, blepharitis or keratitis (H01.0, H10, H16) Moderate/severe visual impairment or blindness (H54.0, H54.1, H54.2, H54.3, H54.7, H54.8)

	Uveitis (H20)
Ear, nose, and throat	Bloody nasal discharge, crusts, nasal ulcers or nasal granulomata (J34.0, J34.8) Subglottic stenosis (J38.6) Conductive hearing loss (H90.0, H90.1, H90.2, H90.6, H90.7, H90.8, H90.A1, H90.A3) Acute or chronic sinusitis (J01, J32)
Chest	Wheeze (R06.2) Lung nodules or cavities (R91) Pleural effusion or pleurisy/pleuritis (J90, J91.8, R09.1) Endobronchial involvement (J98.09)
Cardiovascular	Valvular heart disease (I34, I35, I36, I37) Pericarditis or pericardiectomy (I30.0, I30.8, I30.9, I31.0, I31.1, I31.9)
Abdominal	Peritonitis (K65)
Renal	Hypertension (I10, I11, I12, I13, I14, I16, I67.4) Proteinuria (R80.0, R80.1, R80.9) Creatinine: stage II–III chronic kidney disease (I12.9, I13.0, I13.10, N18.2, N18.3, N18.9)
Nervous system	Headache (G44.0, G44.1, G44.5, G44.8, R51) Meningitis (G03) Organic confusion (R41.0) Seizure (G40, R56.9) Sensory peripheral neuropathy (R20.2)

Note: Events were based on version 3.0 of the BVAS.

Abbreviation: BVAS, Birmingham Vasculitis Activity Score.

Supplementary Table 3 Demographics, Clinical Characteristics, and Insurance Type for the Full Incident EGPA Cohort (Prior to Match), Matched EGPA Cohort A, and Matched General Insured Cohort

	Full Incident EGPA Cohort (N = 236)	Matched EGPA Cohort A (n = 213)	Matched General Insured Cohort (n = 779)
Age at index date, mean (SD)	50.4 (14.5)	49.6 (14.3)	50.6 (13.7)
[range], years	[1.0–85.0]	[1.0–85.0]	[2.0–85.0]
Age at index date, n (%)			
<18 years	4 (1.7)	4 (1.9)	12 (1.5)
18–34 years	34 (14.4)	31 (14.6)	78 (10.0)
35–49 years	66 (28.0)	66 (31.0)	242 (31.1)
50–64 years	104 (44.1)	90 (42.3)	372 (47.8)
65–79 years	23 (9.7)	18 (8.5)	62 (8.0)
80+ years	5 (2.1)	4 (1.9)	13 (1.7)
Female, n (%)	136 (57.6)	125 (58.7)	459 (58.9)
Follow-up duration from index date, mean (SD), months	21.7 (14.6)	20.8 (14.3)	20.7 (14.3)
Duration of follow-up from index date, n (%)			
<6 months	39 (16.5)	38 (17.8)	145 (18.6)
6–11 months	39 (16.5)	37 (17.4)	128 (16.4)
12–17 months	31 (13.1)	28 (13.1)	107 (13.7)
18–23 months	33 (14.0)	30 (14.1)	113 (14.5)
24–29 months	32 (13.6)	30 (14.1)	110 (14.1)
30+ months	62 (26.3)	50 (23.5)	176 (22.6)
Year of index date, n (%)			
2017	67 (28.4)	59 (27.7)	223 (28.6)
2018	50 (21.2)	44 (20.7)	158 (20.3)
2019	63 (26.7)	58 (27.2)	210 (27.0)
2020	37 (15.7)	34 (16.0)	120 (15.4)
2021	19 (8.1)	18 (8.5)	68 (8.7)
Commercial insurance, n (%)	208 (88.1)	191 (89.7)	703 (90.2)
Medicare Supplement/Medicare Advantage, n (%)	28 (11.9)	22 (10.3)	76 (9.8)
Geographic region, n (%)			
Northeast	50 (21.2)	43 (20.2)	156 (20.0)
North Central	42 (17.8)	41 (19.2)	155 (19.9)
South	97 (41.1)	86 (40.4)	317 (40.7)
West	47 (19.9)	43 (20.2)	151 (19.4)

Abbreviations: EGPA, eosinophilic granulomatosis with polyangiitis; SD, standard deviation.

Supplementary Table 4 History of Comorbidities in Matched EGPA Cohort A and the Matched General Insured Cohort

Comorbidity	Percentage Prevalence (95% CI)		Prevalence Ratio (95% CI)	P-value
	Matched EGPA Cohort A (n = 213)	Matched General Insured Cohort (n = 779)		
Asthma				
Persistent	70.4 (64.6, 76.8)	2.7 (1.8, 4.1)	26.1 (17.0, 40.2)	< .001
Severe	65.7 (59.7, 72.4)	1.2 (0.6, 2.2)	56.9 (29.5, 109.7)	< .001
Severe uncontrolled	45.1 (38.9, 52.3)	0.4 (0.1, 1.2)	117.0 (37.5, 365.6)	< .001
Throat or chest pain	46.0 (39.8, 53.2)	17.1 (14.6, 19.9)	2.7 (2.2, 3.3)	< .001
Dyslipidemia	40.4 (34.3, 47.5)	39.2 (35.9, 42.7)	1.0 (0.9, 1.2)	.745
Gastro-oesophageal reflux disease	37.1 (31.1, 44.2)	16.7 (14.3, 19.5)	2.2 (1.8, 2.8)	< .001
Back pain	32.9 (27.1, 39.8)	26.4 (23.5, 29.7)	1.2 (1.0, 1.6)	.058
Nasal polyps	30.0 (24.5, 36.9)	0.5 (0.2, 1.4)	58.5 (21.6, 158.9)	< .001
Vitamin D deficiency	25.4 (20.1, 31.9)	17.6 (15.1, 20.5)	1.4 (1.1, 1.9)	.009
Obesity	25.4 (20.1, 31.9)	23.6 (20.8, 26.8)	1.1 (0.8, 1.4)	.598
Anxiety	25.4 (20.1, 31.9)	20.9 (18.3, 24.0)	1.2 (0.9, 1.6)	.160
COPD	19.7 (15.0, 25.9)	3.0 (2.0, 4.4)	6.7 (4.1, 10.9)	< .001
Arrhythmia	19.7 (15.0, 25.9)	6.5 (5.0, 8.5)	3.0 (2.1, 4.4)	< .001
Obstructive sleep apnea	19.7 (15.0, 25.9)	14.8 (12.5, 17.5)	1.3 (1.0, 1.8)	.076

Atopic dermatitis/eczema	18.3 (13.8, 24.3)	6.5 (5.0, 8.5)	2.8 (1.9, 4.1)	< .001
Depression	17.8 (13.4, 23.8)	16.4 (14.0, 19.3)	1.1 (0.8, 1.5)	.624
Ischemic heart disease	17.8 (13.4, 23.8)	5.4 (4.0, 7.2)	3.3 (2.2, 5.0)	< .001
Pulmonary eosinophilia	16.9 (12.5, 22.8)	0.1 (0.0, 0.9)	131.7 (18.2, 954.7)	< .001
Interstitial pulmonary disease	12.2 (8.5, 17.5)	0.3 (0.1, 1.0)	47.5 (11.4, 198.7)	< .001
Any malignancy	10.3 (7.0, 15.3)	6.8 (5.2, 8.8)	1.5 (0.9, 2.4)	.084
Deep vein thromboembolism	5.2 (2.9, 9.2)	0.9 (0.4, 1.9)	5.7 (2.3, 14.6)	< .001
Primary (essential) thrombocythemia	3.8 (1.9, 7.4)	0.3 (0.1, 1.0)	14.6 (3.1, 68.4)	< .001
Eosinophilic esophagitis	3.8 (1.2, 6.3)	0	—	—
Irritable bowel syndrome	3.3 (1.6, 6.8)	3.3 (2.3, 4.9)	1.0 (0.4, 2.2)	.971
Hyperthyroidism	3.3 (1.6, 6.8)	0.4 (0.1, 1.2)	8.5 (2.2, 32.7)	.002
Hypereosinophilic syndrome	2.3 (0.3, 4.4)	0	—	—
Eosinophilic gastritis or gastroenteritis	1.4 (0.0, 3.0)	0	—	—
Eosinophilic endomyocardial disease	1.4 (0.0, 3.0)	0	—	—

Note: History of comorbidities in the baseline period (12 months prior to the index date) occurring in $\geq 1\%$ of patients in either Matched EGPA Cohort A or the Matched General Insured Cohort is shown.

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; EGPA, eosinophilic granulomatosis with polyangiitis.

Supplementary Table 5 Demographics, Clinical Characteristics, and Insurance Type for the Full Incident EGPA Cohort (Prior to Match), Matched EGPA Cohort B, and Matched SUA Cohort

	Full Incident EGPA Cohort (N = 236)	Matched EGPA Cohort B (n = 182)	Matched SUA Cohort (n = 640)
Age at index date, mean (SD) [range], years	50.4 (14.5) [1.0–85.0]	51.2 (14.0) [1.0–85.0]	51.7 (13.6) [2.0–86.0]
Age at index date, n (%)			
<18 years	4 (1.7)	4 (2.2)	11 (1.7)
18–34 years	34 (14.4)	22 (12.1)	66 (10.3)
35–49 years	66 (28.0)	50 (27.5)	168 (26.3)
50–64 years	104 (44.1)	86 (47.3)	325 (50.8)
65–79 years	23 (9.7)	15 (8.2)	55 (8.6)
80+ years	5 (2.1)	5 (2.7)	15 (2.3)
Female, n (%)	136 (57.6)	108 (59.3)	390 (60.9)
Follow-up duration from index date, mean (SD), months	21.7 (14.6)	19.9 (13.3)	18.8 (12.6)
Duration of follow-up from index date, n (%)			
<6 months	39 (16.5)	31 (17.0)	111 (17.3)
6–11 months	39 (16.5)	33 (18.1)	132 (20.6)
12–17 months	31 (13.1)	27 (14.8)	99 (15.5)
18–23 months	33 (14.0)	29 (15.9)	104 (16.3)
24–29 months	32 (13.6)	24 (13.2)	76 (11.9)
30+ months	62 (26.3)	38 (20.9)	118 (18.4)
Year of index date, n (%)			
2017	67 (28.4)	49 (26.9)	171 (26.7)
2018	50 (21.2)	42 (23.1)	154 (24.1)
2019	63 (26.7)	50 (27.5)	168 (26.3)
2020	37 (15.7)	29 (15.9)	106 (16.6)
2021	19 (8.1)	12 (6.6)	41 (6.4)
Commercial insurance, n (%)	208 (88.1)	162 (89.0)	569 (88.9)
Medicare Supplement/Medicare Advantage, n (%)	28 (11.9)	20 (11.0)	71 (11.1)
Geographic region, n (%)			
Northeast	50 (21.2)	40 (22.0)	150 (23.4)
North Central	42 (17.8)	33 (18.1)	123 (19.2)
South	97 (41.1)	74 (40.7)	249 (38.9)
West	47 (19.9)	35 (19.2)	118 (18.4)

Abbreviations: EGPA, eosinophilic granulomatosis with polyangiitis; SD, standard deviation; SUA, severe uncontrolled asthma.

Supplementary Table 6 History of Comorbidities in the Matched EGPA Cohort B and Matched SUA Cohort

Comorbidity	Percentage Prevalence (95% CI)		Prevalence Ratio (95% CI)	P-value
	Matched EGPA Cohort B (n = 182)	Matched SUA Cohort ^a (n = 640)		
Asthma				
Persistent	70.3 (63.7, 77.0)	–	–	–
Severe	64.3 (57.3, 71.2)	–	–	–
Severe uncontrolled	42.9 (35.7, 50.0)	–	–	–
Dyslipidemia	43.4 (36.8, 51.2)	48.9 (45.2, 52.9)	0.9 (0.7, 1.1)	.203
Throat or chest pain	42.9 (36.2, 50.7)	37.0 (33.5, 41.0)	1.2 (1.0, 1.4)	.144
Gastro-oesophageal reflux disease	39.0 (32.5, 46.8)	36.3 (32.7, 40.2)	1.1 (0.9, 1.3)	.491
Back pain	31.9 (25.8, 39.4)	41.1 (37.5, 45.1)	0.8 (0.6, 1.0)	.032
Nasal polyps	28.0 (22.2, 35.4)	4.7 (3.3, 6.6)	6.0 (3.9, 9.1)	< .001
Anxiety	27.5 (21.7, 34.8)	28.9 (25.6, 32.6)	1.0 (0.7, 1.2)	.707
Vitamin D deficiency	26.4 (20.7, 33.6)	23.3 (20.2, 26.8)	1.1 (0.9, 1.1)	.384
Obesity	24.7 (19.2, 31.9)	41.7 (38.1, 45.7)	0.6 (0.5, 0.8)	< .001
COPD	21.4 (16.2, 28.3)	22.7 (19.6, 26.1)	0.9 (0.7, 1.3)	.727
Depression	20.3 (15.2, 27.1)	23.3 (20.2, 26.8)	0.9 (0.6, 1.2)	.407
Arrhythmia	19.8 (14.8, 26.5)	10.5 (8.3, 13.1)	1.9 (1.3, 2.7)	< .001
Obstructive sleep apnea	19.2 (14.3, 25.9)	29.7 (26.4, 33.4)	0.6 (0.5, 0.9)	.008

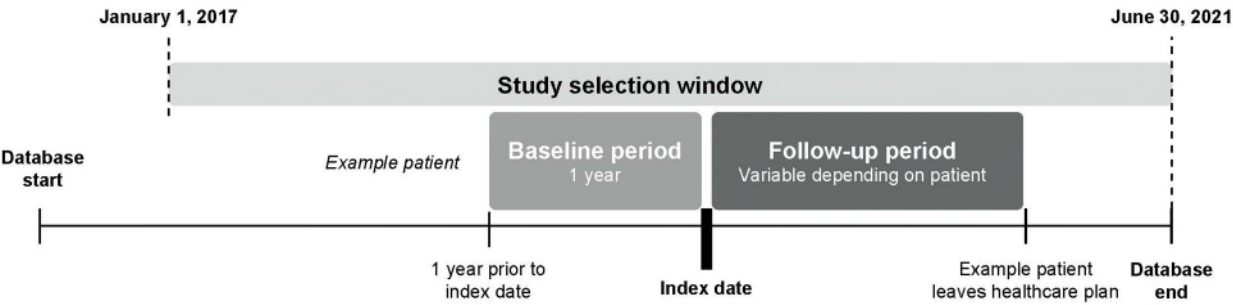
Ischemic heart disease	18.7 (13.8, 25.3)	12.0 (9.8, 14.8)	1.6 (1.1, 2.2)	.019
Atopic dermatitis/eczema	18.7 (13.8, 25.3)	11.9 (9.6, 14.7)	1.6 (1.1, 2.3)	.016
Pulmonary eosinophilia	16.5 (11.9, 22.9)	0.5 (0.2, 1.4)	35.2 (10.9, 113.9)	< .001
Interstitial pulmonary disease	12.6 (8.6, 18.5)	3.1 (2.0, 4.8)	4.0 (2.3, 7.2)	< .001
Any malignancy	11.0 (7.3, 16.6)	8.8 (6.8, 11.2)	1.3 (0.8, 2.0)	.355
Deep vein thromboembolism	4.9 (2.6, 9.3)	2.3 (1.4, 3.9)	2.1 (0.9, 4.7)	.071
Hyperthyroidism	4.9 (2.6, 9.3)	1.6 (0.8, 2.9)	3.2 (1.3, 7.7)	.011
Primary (essential) thrombocythemia	4.4 (2.2, 8.7)	0.2 (0.0, 1.1)	28.1 (3.5, 223.5)	.002
Eosinophilic esophagitis	3.8 (1.9, 8.0)	1.1 (0.5, 2.3)	3.5 (1.2, 9.9)	.017
Irritable bowel syndrome	3.3 (1.5, 7.2)	5.5 (4.0, 7.5)	0.6 (0.3, 1.4)	.243
Eosinophilic endomyocardial disease	2.2 (0.1, 4.3)	0	—	—
Arterial thrombosis	1.6 (0.5, 5.1)	0.5 (0.2, 1.4)	3.5 (0.7, 17.3)	.122
Eosinophilic gastritis or gastroenteritis	1.6 (0.5, 5.1)	0.2 (0.0, 1.1)	10.5 (1.1, 100.8)	.041
B-cell lymphoma	1.1 (0.3, 4.4)	0.8 (0.3, 1.9)	1.4 (0.3, 7.2)	.0682
Hypereosinophilic syndrome	1.1 (0.0, 2.6)	0	—	—

Notes: ^aAll patients in the SUA cohort had persistent, severe, and severe uncontrolled asthma.

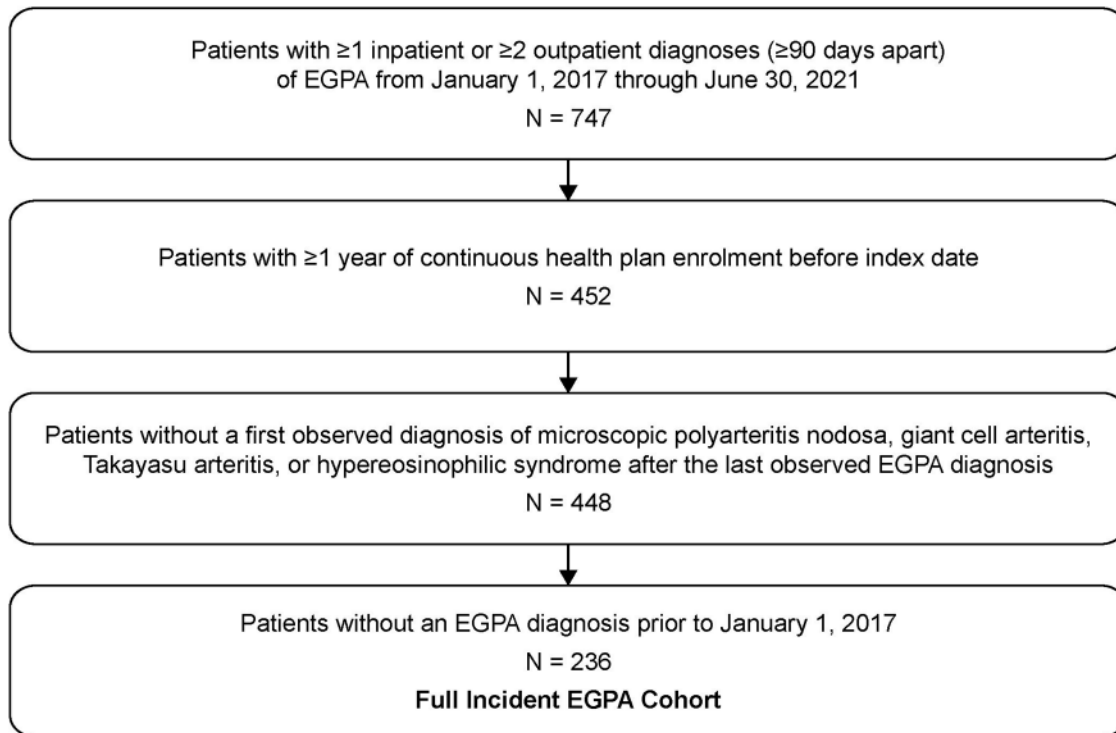
History of comorbidities in the baseline period (12 months prior to the index date) occurring in ≥ 1% of patients in either the EGPA Matched Cohort B or Matched SUA Cohort is shown.

Abbreviations: CI, confidence interval, COPD, chronic obstructive pulmonary disease; EGPA, eosinophilic granulomatosis with polyangiitis, SUA, severe uncontrolled asthma.

Supplementary Figure 1 Study Design.



Supplementary Figure 2 Patient selection and attrition for the Full Incident EGPA Cohort.



Abbreviation: EGPA, eosinophilic granulomatosis with polyangiitis.