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Prevalence of Eosinophilic Granulomatosis With Polyangiitis and Associated Health Care Utilization Among Patients With Concomitant Asthma in US Commercial Claims Database

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Objective: To estimate the prevalence and associated disease burden of eosinophilic granulomatosis with polyangiitis (EGPA) in patients with asthma from a US claims database.

Methods: Two cohorts were defined using enrollees (aged ≥18 years) from the Optum deidentified Clinformatics Datamart claims database 2010–2014, based on validated EGPA case definitions with varying specificity: EGPA 1 (main cohort; more specific; patients with 2 codes [in any combination] within 12 months of each other for eosinophilia, vasculitis, or mononeuritis multiplex) and EGPA 2 (sensitivity analysis cohort; less specific; patients with 2 codes of above conditions and/or neurologic symptoms within 12 months of each other). Patients had 3 or more asthma medications in the 12-month baseline before index date (date of the second code). Eosinophilic granulomatosis with polyangiitis prevalence, asthma severity during the baseline period, oral corticosteroid (OCS) use, and health care utilization during the 12-month follow-up period were determined.

Results: Overall, 88 and 604 patients were included in main cohort EGPA 1 and sensitivity analysis cohort EGPA 2, respectively; corresponding annual EGPA prevalence rates were 3.2 to 5.9 and 23.4 to 30.7 cases/million patients. Approximately 75% of patients were prescribed OCS and ~30% experienced 1 or more hospitalization; 75% in EGPA 1 and 52% in EGPA 2 with 1 or more non-OCS prescription in the 90 days before index date had severe asthma.

Conclusions: Eosinophilic granulomatosis with polyangiitis prevalence estimates varied based on specificity of the case definition but were generally consistent with previous country-specific estimates. Despite differences in prevalence, both cohorts displayed a generally similar, high burden of OCS use and health care utilization, highlighting the substantial disease burden among patients with EGPA and the need for specific treatments.

Key Words: asthma, Churg-Strauss syndrome, Eosinophilic granulomatosis with polyangiitis, prevalence, vasculitis

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Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss syndrome, is a rare, systemic, necrotizing vasculitis of small- to medium-sized vessels characterized by asthma and eosinophilia.[1–3] Country-specific estimates for the prevalence of EGPA have been reported to range from 2 to 38 cases per million people,[4,5] with an incidence ranging from 0.6 to 3.4 cases per million.[3,4] Patient survival has increased over time based on improved awareness and treatment patterns, including the use of oral corticosteroids (OCSs) to achieve remission, as recommended by the EGPA Consensus Task Force.[1] Patients with relapsing or refractory EGPA, however, frequently require intense immunosuppression to induce and maintain remission.[1] The long-term use of immunosuppressive agents and maintenance OCS is associated with a high burden of adverse events.[6,7]

Various classification criteria are used to identify EGPA, but the American College of Rheumatology criteria, with a sensitivity of 85% and specificity of 99.7%, are the most common.[8] Diagnosis of EGPA is frequently delayed as it often takes several years for a patient to fulfill the criteria or find a specialist to determine the diagnosis. Partly because of difficulties in diagnosing EGPA, coupled with the rarity of the disease, data on the prevalence of EGPA in the United States and associated health care utilization are limited. Ascertaining accurate prevalence data has been further complicated by the lack of specific *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes for EGPA. In the absence of a specific *ICD-9* code, a claims-based method, using algorithms comprising combinations of *ICD-9* diagnostic and procedural codes to identify individuals with EGPA among patients with asthma in the United States, was developed in 2004.[9] A number of algorithms, termed *case definitions*, were developed and validated to identify EGPA cases with varying levels of specificity (based on positive predictive value [PPV]).[9] Importantly, the development of these algorithms relied on input from varying populations, health care systems, and coding conventions that may impact their generalizability.[9] While these case definitions do not replace a specific *ICD* code for EGPA and their accuracy in identifying EGPA cases is a function of specificity of the algorithms, they do provide an estimate of the boundaries of EGPA prevalence, which can be used as a basis for further research.

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The aim of this study was to estimate the boundaries of annual EGPA prevalence and disease burden and to assess health care utilization in these EGPA cohorts, using data from a US commercial claims database.

MATERIALS AND METHODS

Data Source

This was a descriptive cohort study (GSK ID: HO-13-9845) of patients enrolled in the Optum deidentified Clinformatics Datamart (CDM) database between 2010 and 2014. The CDM database contains verified, deidentified commercial health plan data on millions of enrollees, along with historic claims for Managed Medicaid and Medicare + Choice (known as Medicare Advantage since 2003) members, comprising medical claims, pharmacy claims, inpatient confinement, standard pricing, and member eligibility data for billing purposes. Laboratory results and clinical information are available only for a small subset of patients.

Because there is no specific EGPA *ICD-9* code to identify EGPA patients, 2 claims-based EGPA case definitions were used in this study to examine the range of estimates of disease burden and health care utilization associated with EGPA. Two EGPA cohorts were defined using validated case definitions based on *ICD-9* and current procedural terminology codes.[9] The first cohort, EGPA 1, was the main cohort and comprised patients with 2 codes (in any combination) within 12 months of each other for either eosinophilia (code 288.3) and vasculitis (codes 447.6, 446.4, 447.8, 446.20, 362.18, 695.2) or vasculitis and mononeuritis multiplex (code 354.5); its PPV was 80% implying high specificity or greater. As sensitivity analysis, we created a second cohort, EGPA 2, based on a case definition with a lower PPV of 40% or greater and included patients with 2 codes (in any combination) within 12 months of each other for either eosinophilia and vasculitis, vasculitis and mononeuritis multiplex, or vasculitis and the additional codes for neurologic symptoms (codes 356.9, 356.4, 354.0–4, 354.8–9, 20 200, 20 206, 20 205, 64 795, 04.11, 04.12, 04.19, 83.21). EGPA 1 was, by definition, more restrictive than EGPA 2, indicating higher likelihood of avoiding false-positives in EGPA 1. However, this came at a cost of excluding patients with neurologic symptoms, which may also present clinically in EGPA. Therefore, as sensitivity analysis, this study explored an additional broader cohort (EGPA 2) to capture additional patients with neurologic symptoms, even if it involved a risk of including false-positives. The outcomes presented for these 2 cohorts therefore provide a range of estimates of prevalence and health care utilization ranging from a very specific, narrow EGPA 1 cohort to a broader EGPA 2 cohort.

The date of the second code was defined as the date of EGPA diagnosis (index date). The 12-month period before the index date was defined as the baseline period and 12 months after as the follow-up period.

Patient Selection Criteria

Eligible patients were 18 years or older on the index date and had been continuously enrolled in the database during the baseline and follow-up periods. The majority of patients with EGPA also have asthma,[10] and the case definitions used in this study were validated in a population of adult patients with asthma. Therefore, patients in this study were required to have 3 or more asthma medication claims in the baseline period, which could include short-acting β_2-agonists, inhaled corticosteroids, inhaled corticosteroids and long-acting β_2-agonist combinations, leukotriene receptor antagonists, OCS, cromolyn or nedocromolyn, theophylline/xanthine, omalizumab, or anticholinergics. Patients with a diagnosis of chronic obstructive pulmonary disease at any time during the study period, or with a history of chronic obstructive pulmonary disease prior to the study, were excluded.

Study Variables

The prevalence of EGPA for each year between 2010 and 2014 was assessed, calculated as the number of adult patients with EGPA in a calendar year divided by the total number of enrollees 18 years or older enrolled continuously throughout the same year.

Outcomes evaluated during the follow-up period were health care utilization (any hospitalizations, any emergency room [ER] visits, asthma-related hospitalizations, any asthma-related ER visits, and any home health service) and the use of EGPA maintenance medications (including OCS, rituximab, immunosuppressive therapy with azathioprine and methotrexate, and cyclophosphamide). OCS use was further characterized in terms of the average daily dose (calculated as the doses from all OCS prescriptions divided by the total days-supplied across all prescriptions) and adherence (calculated as the proportion of days covered [PDC] during the follow-up period) during the 12-month follow-up period. Proportion of days covered (1-year adherence) of OCS use during follow-up was calculated as the total number of days-supply of OCS from all prescriptions divided by 365 days. OCS users were further classified based on their average daily OCS dose expressed as prednisone equivalent (<4, 4 to <7.5, and ≥ 7.5 mg/d).

Asthma severity was assessed in the 90 days before the index date, based on the asthma medications prescribed during this period, and patients were categorized based on the stepwise approach to asthma management (steps 1–5) recommended by Global Initiative for Asthma (GINA).[11] Claims data cannot be used to distinguish the indication of a particular OCS prescription (asthma or EGPA). Therefore, to avoid misclassification of patients with EGPA as patients with asthma on OCS (i.e., GINA step 0 or unclassified per the current GINA step algorithm), the GINA step analyses were conducted in restricted cohorts of patients with EGPA who had at least 1 prescription of a non-OCS asthma medication in the 90 days before the index date.

Outcomes assessed during the 12-month baseline period prior to the index date included the frequency of asthma-related exacerbations (defined using hospitalization, ER visit, or OCS use) and the presence of baseline comorbidities, based on any diagnosis codes available in the claim record. The comorbidities evaluated were markers of disease progression and organ involvement that are associated with the severity and burden of EGPA.

Data Analysis

This was a descriptive study. With the exception of the prevalence estimates (reported as cases per million patients per year), only the total number, per-patient averages, proportions, and associated confidence intervals were reported for variables. Analyses were conducted separately for the main cohort EGPA 1 and sensitivity analysis cohort EGPA 2.

This research represents analysis of the deidentified data from the CDM database, and as such, this analysis did not require approval from an ethics committee or institutional review board. The deidentified data are only accessible to organizations with appropriate data governance processes in place.

RESULTS

EGPA Cohorts

A total of 88 patients with EGPA were included in the main cohort (EGPA 1), and 604 patients were included in the sensitivity

TABLE 1. Characteristics of Patients With EGPA During the Baseline Period (Optum CDM Database, 2010–2014)

	EGPA 1[a] (n = 88)	EGPA 2[b] (n = 604)
Age at EGPA diagnosis, mean (SD), y	52.7 (14.8)	58.4 (14.4)
<50 y, n (%)	30 (34.0)	156 (25.8)
≥50 y, n (%)	58 (65.9)	448 (74.1)
Female, n (%)	54 (61.4)	439 (72.7)
Comorbidities, n (%)		
Cutaneous		
Gangrene	0 (0)	4 (0.6)
Purpura	21 (23.8)	101 (16.7)
Ear, nose, and throat		
Allergic rhinitis	38 (43.2)	142 (23.5)
Sinusitis	40 (45.4)	193 (31.9)
Chest		
Pulmonary infiltrates	3 (3.4)	25 (4.1)
Cardiovascular		
Alveolar or pulmonary hemorrhage	0 (0)	2 (0.3)
Cardiomyopathy	0 (0)	4 (0.6)
Congestive heart failure	6 (6.8)	39 (6.4)
Abdominal		
Polyposis	9 (10.2)	13 (2.1)
Renal		
Chronic kidney disease	0 (0)	25 (4.1)
Glomerular nephritis	3 (3.4)	34 (5.6)
Nervous system		
Neuropathy	17 (19.3)	186 (30.7)
Mononeuritis multiplex	13 (14.8)	13 (2.1)
Polyneuropathy	17 (19.3)	163 (26.9)
Stroke	5 (5.6)	39 (6.4)

[a]EGPA 1, is the main cohort based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, or vasculitis and mononeuritis multiplex; PPV ≥80%.

[b]EGPA 2 is the sensitivity analysis cohort based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, vasculitis and mononeuritis multiplex, or vasculitis and neurologic symptoms; PPV ≥40%.

analysis cohort EGPA 2, between 2010 and 2014 (Supplementary Figure 1, http://links.lww.com/RHU/A163). At diagnosis, the median age of patients in the EGPA 1 and EGPA 2 cohort was 53 and 58 years, respectively; the majority of patients were 50 years or older and female (Table 1).

Prevalence

The annual prevalence of EGPA from 2010 to 2014 varied depending on the case definition used (Fig. 1); the range of annual prevalence (lowest to highest) using EGPA 1 (more specific) definition was 3.2 to 5.9 cases per million compared with 23.4 to 30.7 cases per million using EGPA 2 (sensitivity analysis cohort, less specific) definition.

Health Care Utilization

Approximately 30% of the patients in each cohort experienced at least 1 hospitalization (Fig. 2). There were more asthma-related hospitalizations but fewer home health service visits in EGPA 1 cohort compared with EGPA 2 cohort (15% vs 5% and 16% vs 25%, respectively). In both the main (EGPA 1) and sensitivity analysis (EGPA 2) cohorts, health care utilization generally increased with increasing daily OCS dose, but this was based on very small sample sizes (Supplementary Table 1, http://links.lww.com/RHU/A163).

Medication Use During Follow-up

Approximately 75% of the patients in both cohorts were prescribed OCS during the 1-year follow-up period (Table 2). In total, 82.6% of the EGPA 1 cohort and 74.2% of the EGPA 2 cohort had an average daily OCS dose of at least 7.5 mg/d; the median doses in cohorts 1 and 2 were 18.25 and 15.75 mg/d, respectively (Table 2). In cohorts 1 and 2, 43.5% and 28.4% of patients, respectively, had received 5 or more OCS prescriptions, and 65.1% and 49.8%, respectively, were prescribed OCS for at least 6 of the 12 months after EGPA diagnosis, based on a 1-year PDC 0.5 or greater (Table 2). Other forms of maintenance medication used in the 1-year follow-up period included rituximab, cyclophosphamide, and the immunosuppressants, azathioprine, and methotrexate. Rituximab use was similar in the EGPA 1 and 2 cohorts (5.7% vs 4.6%), as was cyclophosphamide use (2.2% vs 2.3%). The proportion of patients using methotrexate was slightly higher in the EGPA 1 cohort than in the EGPA 2 cohort (18.2% vs 15.7%), and the use

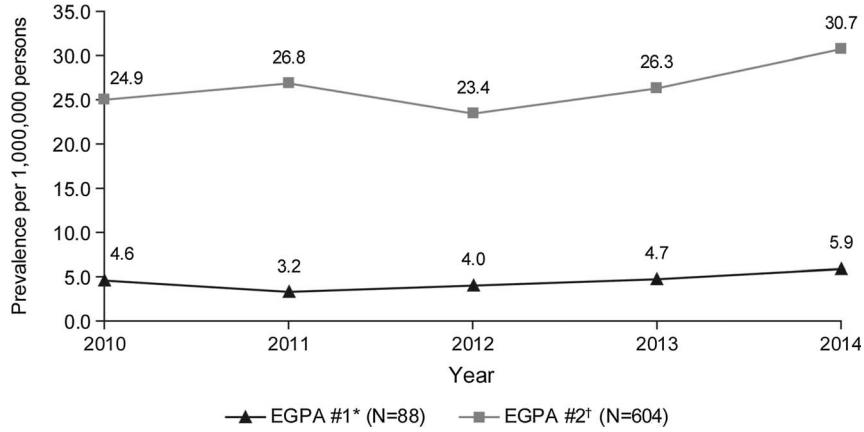

FIGURE 1. Eosinophilic granulomatosis with polyangiitis prevalence (Optum CDM database, 2010–2014). *EGPA 1 (main cohort) based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, or vasculitis and mononeuritis multiplex; PPV ≥80%; †EGPA 2 (sensitivity analysis cohort) based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, vasculitis and mononeuritis multiplex, or vasculitis and neurologic symptoms; PPV ≥40%.

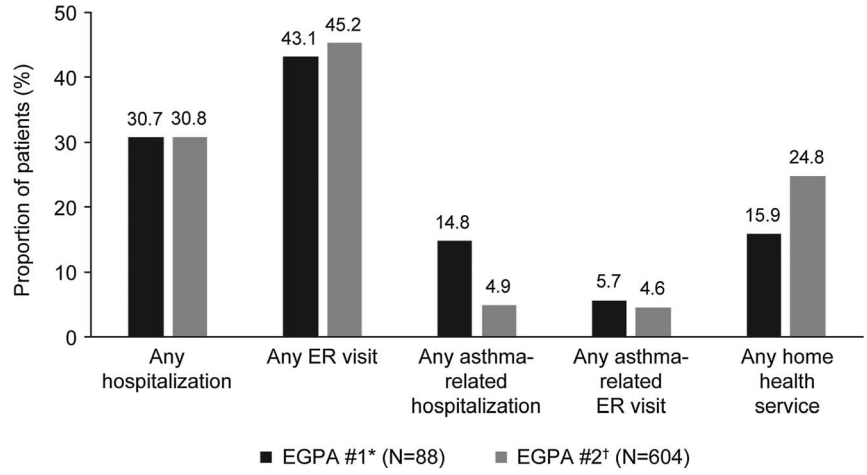

FIGURE 2. Health care utilization among patients with EGPA during the 1-year follow-up period (Optum CDM database, 2010–2014). *EGPA 1 (main cohort) based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, or vasculitis and mononeuritis multiplex; PPV ≥80%; †EGPA 2 (sensitivity analysis cohort) based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, vasculitis and mononeuritis multiplex, or vasculitis and neurologic symptoms; PPV ≥40%.

of azathioprine was also markedly higher in the EGPA 1 cohort (23.8% vs 11.2%).

Severity of Asthma (GINA Step) and Asthma Exacerbations

In total, 75% of the patients in the EGPA 1 cohort who had at least 1 prescription of a non-OCS asthma medication in the 90 days before the index date and 52% of the corresponding patients in the EGPA 2 cohort were classified as having severe asthma (GINA step 4 or 5). Most patients in both cohorts did not experience asthma exacerbations in the baseline period (Table 3). In the EGPA 1 cohort, 15.9% of patients had an asthma exacerbation requiring OCS, whereas only 8.3% had an exacerbation requiring OCS in the EGPA 2 cohort.

Baseline Comorbidities

The most common baseline comorbidities, based on the presence of diagnosis codes in patient records, consisted of respiratory conditions, but other comorbidities indicating involvement of other organs were also prevalent. The most common comorbidities in the main cohort (EGPA 1) were sinusitis (45.4%), allergic rhinitis (43.2%), and purpura (23.8%); in the sensitivity analysis cohort (EGPA 2), they were sinusitis (31.9%), neuropathy (30.7%), and polyneuropathy (26.9%) (Table 1).

DISCUSSION

This study provided a range of estimates for the annual EGPA prevalence and associated health care utilization among patients with asthma enrolled in a US commercial claims database. Given the absence of a specific EGPA *ICD-9* code, this study used previously validated claims-based definitions to define cohorts with varying specificity in identifying EGPA patients. This is the first large-scale study to evaluate EGPA prevalence across the United States using real-world administrative claims data. Given the scarcity of data on EGPA disease burden in the literature, this study provides valuable information on this debilitating condition.

Historically, EGPA was categorized as part of a group of antineutrophil-associated vasculitides, the symptoms and disease trajectories of which are varied. Based on the variation across these vasculitides, a specific EGPA diagnosis code was created in the *ICD-10* disease classification system. However, this code was not adopted in the United States until October 2015; therefore, capturing EGPA diagnoses accurately was difficult in claims databases created prior to 2015. In the absence of a specific *ICD-9* code for EGPA, in the current study, 2 previously published case definitions with different degrees of specificity for identifying EGPA cases were used to define 2 EGPA cohorts—more specific cohort EGPA 1 and a second cohort EGPA 2 (sensitivity analysis), which was more inclusive potentially at the cost of including more false-positives. As expected, the prevalence of EGPA varied

TABLE 2. EGPA Maintenance Medication Use and Burden of OCS Use During the Follow-up Period (Optum CDM Database, 2010–2014)

	EGPA 1[a] (n = 88)	EGPA 2[b] (n = 604)
At least 1 prescription of OCS, n (%)	69 (78.4)	450 (74.5)
OCS average daily dose		
Mean (SD)	21.27 (14.71)	20.14 (19.81)
Median	18.25	15.75
OCS categories based on average daily dose among OCS users, n (%)		
<4 mg	1 (1.5)	24 (5.3)
4 to <7.5 mg	11 (15.9)	92 (20.4)
≥7.5 mg	57 (82.6)	334 (74.2)
No. OCS prescriptions among OCS users, n (%)		
1	6 (8.7)	77 (17.1)
2–4	13 (18.8)	156 (34.6)
5–9	30 (43.5)	128 (28.4)
≥10	20 (28.9)	89 (19.7)
PDC ≥0.5 among OCS users (OCS use for ≥6 out of 12 mo), %	65.2	49.8

[a]EGPA 1, the main cohort based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, or vasculitis and mononeuritis multiplex; PPV ≥80%.

[b]EGPA 2, the sensitivity analysis cohort based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, vasculitis and mononeuritis multiplex, or vasculitis and neurologic symptoms; PPV ≥40%.

TABLE 3. Asthma Severity[a] and Frequency of Exacerbations During the Baseline Period (Optum CDM Database, 2010–2014)

	EGPA 1[b] (n = 40)	EGPA 2[c] (n = 140)
GINA step,[d] n (%)		
Step 1	6 (15.0)	24 (17.1)
Step 2	2 (5.0)	29 (20.7)
Step 3	2 (5.0)	14 (10.0)
Step 4	15 (37.5)	47 (33.6)
Step 5	15 (37.5)	26 (18.6)
Asthma exacerbations during the 12-mo baseline period,[e] n (%)		
	n = 88	**n = 604**
Requiring ER visit		
0	84 (95.5)	588 (97.4)
1	3 (3.4)	14 (2.3)
≥2	1 (1.1)	2 (0.3)
Requiring hospitalization		
0	84 (95.5)	590 (97.6)
1	2 (2.2)	11 (1.8)
≥2	2 (2.2)	3 (0.5)
Requiring OCS		
0	74 (84.1)	554 (91.7)
1	3 (3.4)	30 (4.9)
2	7 (7.9)	13 (2.1)
≥3	4 (4.5)	7 (1.1)

[a]GINA step analyses were conducted in restricted cohorts of patients with EGPA who had at least 1 prescription of a non-OCS asthma medication in the 90 days before the index date to avoid misclassification of patients with EGPA as patients with asthma on OCS treatment.

[b]EGPA 1, the main cohort based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, or vasculitis and mononeuritis multiplex; PPV ≥80%.

[c]EGPA 2, sensitivity analysis cohort based on at least 2 diagnosis codes (in any combination) for either eosinophilia and vasculitis, vasculitis and mononeuritis multiplex, or vasculitis and neurologic symptoms; PPV ≥40%.

[d]Disease severity increases from GINA step 1 (least severe) to step 5 (most severe).

[e]Exacerbations were defined as those requiring an asthma hospitalization (hospitalization with an asthma diagnosis code [*ICD-9*: 493.xx] in either the primary or secondary position of the claim), an asthma ER visit (ER visit with an asthma diagnosis code [*ICD-9*: 493.xx] in either the primary or secondary position), or a claim for a physician office visit or an outpatient visit and service (with an asthma diagnosis code [*ICD-9*: 493.xx] in either the primary or the secondary position), which was accompanied by an OCS dispensation within 7 days (either before or after the visit). An OCS-defined exacerbation was defined as treatment with OCS with an average daily dose of ≥20 mg prednisone (or equivalent) that lasted for ≥3 days but ≤28 days (or 4 weeks) with an asthma medical code recorded within ±2 weeks. All other OCS use was considered maintenance therapy or non–asthma related).

depending on the case definition, with an approximately 6-fold difference between the 2 definitions during 2010 to 2014. Annual prevalence in the EGPA 1 cohort ranged from 3.2 to 5.9 cases per million, whereas the prevalence in the EGPA 2 cohort ranged from 23.4 to 30.7 cases per million, remaining more or less constant throughout the study period within each case definition. These results based on the main cohort EGPA 1 (a narrow specific cohort) and a sensitivity analysis cohort EGPA 2 (a broader inclusive cohort) can be considered boundaries for the true prevalence of EGPA, and the true prevalence is expected to lie somewhere in between these estimates. The range of estimates provided in the current study is generally consistent with previous country-specific EGPA prevalence estimates of 2 to 38 cases per million patients.[4,5] Indeed, a recently published study found the prevalence of EGPA in Olmstead County in Minnesota to be 42.1 cases per 100,000, based on patient medical records.[12]

Based on current literature, the burden of disease in patients with EGPA is high.[13,14] Results from this study are generally congruent with the limited existing literature on the EGPA burden of disease and add information on specific health care utilization frequencies, demonstrating very high levels of OCS use, substantial health care resource utilization, and a broad range of organ involvement. Although the prevalence of EGPA varied between the 2 cohorts, as expected a priori, both cohorts had an overall high burden of disease and health care use. More frequent exacerbations requiring OCS, more patients with GINA step 4/5 asthma, and more patients requiring asthma-specific hospitalizations and OCS use in cohort 1 versus 2 indicate that the burden of EGPA may have been slightly higher in cohort 1, although no formal statistical comparisons were made between the cohorts. Most patients in both the cohorts were OCS users, with immunosuppressant therapy being the second most common maintenance treatment during the follow-up period, consistent with findings from other studies.[15] Moreover, around three-quarters of patients had an average daily OCS dose of 7.5 mg/d or greater; 7.5 mg/d is considered by the European League Against Rheumatism to be the threshold at which EGPA remission is defined in terms of OCS use, although it should be noted that a Birmingham Vasculitis Activity Score of 0 is also required to meet the European League Against Rheumatism remission criteria.[16] Approximately half of the patients were receiving OCS for at least 6 of the 12 months following EGPA diagnosis, and health care utilization broadly increased with OCS use, highlighting the severity of disease in patients with higher OCS use. However, the small sample size for these groups, particularly in the lower-dose categories, means these findings should be interpreted with caution. In general, health care utilization was high in both cohorts, with approximately a third of patients being hospitalized. These findings are consistent with previous reports of hospitalization, which show high levels of hospitalization for a broad range of comorbidities in patients with EGPA.[17,18]

The severity of asthma in the population was considerable, with half to three-quarters of patients with at least 1 non-OCS asthma prescription in the 90 days before the index date, classified as having severe asthma based on the GINA step classification. Despite this, only 16% to 20% of patients experienced asthma exacerbations requiring OCS use, hospitalization, or ER visit, equating to a rate of ~0.2 exacerbations per person-year. This rate is much lower than the previously reported exacerbation rates in patients with severe asthma, including a rate of 0.5 exacerbation per patient-year during the 12 months following asthma diagnosis reported by Suruki et al.[19] in patients with GINA step 5 asthma. The apparent underestimation of the exacerbation rate in our study may be influenced by the difference in patient populations between studies, as well as the different index dates as anchors for measurements. Furthermore, the proportion of OCS-defined exacerbations may have been underestimated as many patients with EGPA require OCS over long periods; therefore, short bursts of OCS use in these patients may not have been accurately identified as exacerbations. Notwithstanding this apparent underestimation of exacerbations in the population, high rates of comorbidities were identified across the 2 EGPA cohorts. In general, patients experienced similar proportions of respiratory, cutaneous, and neurological comorbidities when compared with other studies of patients with EGPA with a high prevalence of asthma,[20–22] although a higher rate of sinusitis (41.8%–92.1%) was reported elsewhere,[20,22]

as were higher rates of neuropathy (35%–47%),[21] mononeuritis multiplex (46.0%), and lung infiltrates (38.6%).[22]

Interestingly, while there was an approximately 6-fold difference in the estimated prevalence of EGPA using the EGPA 1 and EGPA 2 case definitions, health care utilization was generally similar in both cohorts, with the exception of asthma inpatient hospitalizations, OCS use, and asthma severity, which were higher in EGPA 1. The difference between the 2 case definitions was the inclusion of patients with additional codes of neurological symptoms in EGPA 2, creating a wider EGPA population. As this directly affects the numerator in prevalence estimation, a difference in prevalence estimates between the 2 cohorts was expected. The similar proportion of patients with general health care use in the 2 cohorts can potentially be explained by the additional patients in EGPA 2 with neurologic symptoms not having a markedly different distribution of health care use than the patients with other conditions that were included in both the definitions. The observed differences in comorbidities could also be driven by the additional neurologic codes, but the examination of health care use stratified by the conditions used to define EGPA was outside the scope of this study and a subject of further research.

This study has some notable limitations. Importantly, there is no specific *ICD-9* code for EGPA, which means the accuracy of identifying EGPA cases from the database depends on the validity of the case definitions, which themselves were based on very small sample sizes. EGPA 2, the sensitivity analysis cohort in our study, was, by definition, more inclusive and included more false-positives than the main cohort EGPA 1. However, EGPA 1 was very restrictive and excluded EGPA patients with less common symptoms. This study therefore used both cohorts with varying specificities to provide a range of estimates for the outcomes of interest. *ICD-10* has been available since October 2015, and this is likely to improve opportunities for research in this area. However, although physicians in the United States must use *ICD-10* codes in order to be reimbursed by payers for services provided, it should be noted that not all specialists agree with using the *ICD-10* code "M30.1 polyarteritis with lung involvement [Churg-Strauss]" for EGPA because it is categorized under "M30 polyarteritis nodosa and related conditions," which is broader than EGPA and therefore may include patients with other diagnoses. Furthermore, the sensitivity of the algorithms used was not assessed in the original study because of the type of data sources available for validation.[9] In addition, both patients with EGPA and patients with asthma are prescribed OCS, but the US claims database used here cannot distinguish between conditions associated with a particular pharmacy claim. To mitigate this for the GINA analyses, only patients with at least 1 non-OCS prescription in the 90 days preindex were included. Without an EGPA discharge diagnosis code, EGPA-specific hospitalizations or ER visits could not be captured. It is likely that, in the absence of a specific EGPA *ICD-9* code, alternative diagnoses were used to describe EGPA symptoms. Nonetheless, by limiting the follow-up period to 12 months after EGPA diagnosis, it can be assumed that the majority of the resource use identified here can be attributed to EGPA management, including comorbidities. It should also be noted that the results of this study may not be representative of patients in the United States who receive health care through other government organizations (e.g., Medicaid) or who lack health insurance. In addition, the results may not be directly generalizable to other countries that may have different clinical management settings.

CONCLUSIONS

This study used real-world data to show high levels of OCS use and frequent health care utilization in the 2 cohorts of patients with EGPA in the United States, highlighting disease burden and the persistence of symptoms. These findings indicate a potential unmet need for specific EGPA treatments to improve symptom control and outcomes.

KEY POINTS

1. This study estimated the annual prevalence and associated disease burden of EGPA in patients with asthma using data from a US commercial claims database, using 2 different validated case definitions for identifying EGPA patients.
2. Eosinophilic granulomatosis with polyangiitis annual prevalence estimates varied 3.2 to 30.7 per million patients depending on the case definition used and are generally consistent with the global estimates.
3. Despite the differences in prevalence, both the cohorts displayed generally similar health care utilization, with some differences in the burden of severe asthma, OCS use, and asthma inpatient stays.
4. High-dose OCS use, along with the frequency of health care resource utilization, highlights the severity and persistence of symptoms among EGPA patients with asthma, pointing toward a potential need for EGPA-specific medications in these patients.

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