The Economic Burden of Eosinophilic Gastritis and Eosinophilic Enteritis in the United States

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ABSTRACT

Introduction: Eosinophilic gastritis and eosinophilic enteritis (EoG/EoN) are associated with a substantial clinical burden. However, limited information is available regarding the economic burden of EoG/EoN. This study was conducted to compare healthcare resource use (HRU) and costs among patients with EoG/EoN versus without EoG/EoN in the USA.

Methods: Administrative claims data from the IBM MarketScan® Commercial Claims and Encounters (CxCAE) and Medicare Supplemental and Coordination of Benefits Databases (2009–2019) was used to identify two cohorts of patients. Patients without EoG/EoN were matched 3:1 to patients with EoG/EoN on sex, year of birth, and healthcare plan type. Study measures included demographic characteristics, select comorbidities, all-cause HRU, and costs. Comparisons were made over a 1-year period following EoG/EoN diagnosis for patients with EoG/EoN and an eligible date for patients without EoG/EoN.

Results: A total of 2219 patients with EoG/EoN and 6657 patients without EoG/EoN were analyzed. Significantly higher proportions of patients with EoG/EoN versus without EoG/EoN had comorbid conditions. Rates of all-cause HRU were significantly higher among patients with EoG/EoN versus patients without EoG/EoN (adjusted rate ratio [95% confidence interval]: inpatient visits, 6.26 [5.26, 7.46]; outpatient visits, 1.17 [1.16, 1.19]; emergency department visits, 2.11 [1.98, 2.25]; all p < 0.001). Patients with EoG/EoN incurred significantly higher costs versus patients without EoG/EoN (adjusted mean cost difference $31,180; p < 0.001). Cost differences were largely due to outpatient (adjusted mean cost difference $14,018; p < 0.001) and inpatient (adjusted mean cost difference $11,224; p < 0.001) costs.

Conclusion: The economic burden associated with EoG/EoN is substantial, with patients with EoG/EoN having a higher rate of HRU and incurring $31,180 more than patients without EoG/EoN on average. Most of the cost difference was attributable to outpatient and inpatient costs. Cost-saving strategies to lower the burden of illness in this patient population are needed.

Keywords: Economic burden; Eosinophilic gastritis; Eosinophilic enteritis; Healthcare resource utilization
**Key Summary Points**

**Why carry out this study?**
While the clinical and quality of life burdens associated with eosinophilic gastritis and eosinophilic enteritis (EoG/EoN) have been documented, limited information is available regarding the associated healthcare costs and healthcare resource use (HRU) in this patient population.

This retrospective study used administrative claims data to quantify and compare healthcare costs and HRU among patients with EoG/EoN relative to patients without EoG/EoN in the USA.

**What was learned from the study?**
In the USA, patients with EoG/EoN incurred significantly greater costs than patients without EoG/EoN, with the main contributors to the increased costs observed being inpatient and outpatient services.

It may be helpful to focus cost-saving strategies on care received in the inpatient and outpatient settings.

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**INTRODUCTION**

Eosinophilic gastritis (EoG) and eosinophilic enteritis (EoN) are two types of eosinophilic gastrointestinal disorders (EGIDs) characterized by the pathologic accumulation of eosinophils in the stomach and small intestine, respectively [1]. The standardized estimated prevalence rates of EoG and EoN in the USA are 6.3 and 8.4 cases per 100,000, respectively [2]. However, a considerable portion of cases may be undetected as there is no dedicated consensus on how to diagnose the condition [3]. Therefore, the true prevalence of EoG/EoN is unknown and likely underestimated. Unlike some EGIDs such as eosinophilic esophagitis, EoG/EoN do not show a clear sex predilection [4]. EoG/EoN can present with varying symptoms which are often debilitating and may include abdominal pain, nausea, and diarrhea [5]. The chronic nature of EoG/EoN [6–9] can significantly impair patients’ health-related quality of life. Results from a qualitative health-related quality of life assessment showed that patients reported that symptoms associated with EoG/EoN negatively impacted their social functioning, ability to engage in activities involving food, and impaired perceptions of their body image and ability to sleep [9].

Currently, no treatments have been approved by the US Food and Drug Administration for EoG/EoN. The clinical management of EoG/EoN focuses on supportive care to manage symptoms [10]. Standard approaches include a combination of dietary modifications (e.g., eliminating consumption of foods that exacerbate symptoms), corticosteroids (e.g., prednisone), proton pump inhibitors, and immunosuppressants (e.g., azathioprine) [1, 11]. For patients with severe manifestations, such as intestinal obstruction, surgery may be warranted [8, 10, 12]. Despite the range of therapeutic approaches, symptomatic relief is typically short-lived [3] and prolonged use of therapies such as corticosteroids increases the risk of serious adverse events [7]. Additionally, dietary restrictions and food elimination may negatively impact quality of life [9, 13]. Furthermore, many patients require ongoing treatment and continue to experience chronic gastrointestinal (GI) symptoms despite treatment [14].

As most of the available literature on EoG/EoN focuses on characterizing its clinical burden and impact on patients’ health-related quality of life, less is known regarding the associated healthcare resource use (HRU) and costs [15]. While clinical burden is important to understand, it is also important to understand the economic impact of this condition. To our knowledge, this is one of the first large, claims-based studies to examine HRU and cost among this population. To fully capture the burden of illness associated with EoG/EoN and provide healthcare stakeholders with a benchmark to
guide efforts aimed at reducing the burden of illness, we used a large administrative claims database to compare HRU and costs incurred among patients with EoG/EoN versus patients without EoG/EoN in the USA. The aim of this study was to understand the healthcare costs and HRU associated with EoG/EoN in the USA.

METHODS

Data Source

This study used data from the IBM MarketScan® Commercial Claims and Encounters (CCAE) and Medicare Supplemental and Coordination of Benefits Databases (2009–2019). MarketScan® claims data include comprehensive information on enrollment history, dates of service, claims for medical and pharmacy services, as well as some patient demographic variables. The database includes information collected from about 100 different insurance companies and represents about 25 million beneficiaries annually from all US census regions. The Medicare Supplemental and Coordination of Benefits database includes information on patients 65 years old and older with Medicare coverage as well as employer-paid commercial plans. As the data were de-identified, ethics approval was not required for this study.

Compliance with Ethics Guidelines

Institutional review board approval and informed consent were not required for the conduct of this study. All of the information from the databases is de-identified and compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act.

Study Design and Sample Selection

In this retrospective matched cohort study, two cohorts of patients were analyzed: patients with EoG/EoN and patients without EoG/EoN. The initial data sample included patients with EoG/EoN who had at least two diagnoses on separate dates (International Classification of Diseases Ninth Revision, Clinical Modification [ICD-9-CM] codes 535.70, 558.41; International Classification of Diseases Tenth Revision, Clinical Modification [ICD-10-CM] code K52.81), and patients without EoG/EoN matched 10:1 to patients with EoG/EoN on sex, year of birth, and capitated/non-capitated plan type. Patients without EoG/EoN were required to not have a diagnosis for EoG/EoN. As a result of the potential for EoG/EoN to be misdiagnosed as other gastrointestinal conditions [16, 17], patients with eosinophilic esophagitis (EoE), functional dyspepsia, or irritable bowel syndrome (IBS) were excluded.

For patients with EoG/EoN the index date was defined as a randomly selected date with a diagnosis code of EoG/EoN that allowed for 6 months of continuous enrollment prior to (baseline period) and 12 months of continuous enrollment after the index date (study period). For patients without EoG/EoN, the index date selected was an eligible date, allowing for 6 months of continuous enrollment prior to and 12 months of continuous enrollment after the index date, that was closest to the matched patient with EoG/EoN’s index date.

After all inclusion/exclusion criteria were applied, the final sample included patients without EoG/EoN matched 3:1 to patients with EoG/EoN on sex, year of birth, and capitated/non-capitated plan type as this was the ratio that allowed one to maximize the retention of patients. When there were more than three matches for patients with EoG/EoN, three matched patients without EoG/EoN were randomly selected.

Study Measures and Outcomes

Study measures and outcomes that were described and compared between patients with and without EoG/EoN during the baseline period included demographics (e.g., age, sex, region of residence), select comorbidities, and medications used to treat EoG/EoN. All-cause HRU and all-cause medical (i.e., inpatient, outpatient, and emergency department) and pharmacy costs were also described and compared.
Statistical Analyses

Patient characteristics, HRU, and costs were described using means and standard deviations for continuous variables and counts and percentages for categorical variables. Statistical comparisons between patients with and without EoG/EoN were conducted using generalized estimating equations (GEE) to account for matching.

For HRU, unadjusted and adjusted rate ratios were estimated. For healthcare costs, unadjusted and adjusted mean costs and mean cost differences were estimated with GEEs used to conduct statistical comparisons. For the adjusted analyses, the model adjusted for age at index date, sex, region, index year, and plan type. As a sensitivity analysis, the Charlson Comorbidity Index (CCI), in addition to the same covariates as the main model, was included.

The study analyses were conducted in duplicate.

RESULTS

Patient Characteristics

A total of 2219 patients with EoG/EoN and 6657 matched patients without EoG/EoN met the patient selection criteria and were included in the study (Fig. 1). The mean age of patients with EoG/EoN and without EoG/EoN was 31.3 and 31.5 years, respectively with 61.2% of patients with EoG/EoN and 61.5% of patients without EoG/EoN age 18 years or older at index (Table 1). Nearly half of all patients were male (47.0%) and overall most patients had plans without capitation (88.8%). Of the comorbid conditions assessed, patients with EoG/EoN were more significantly likely to have atopic conditions (47.0% vs. 13.5%, \( p < 0.001 \)) and gastrointestinal symptoms (70.8% vs. 7.4%, \( p < 0.001 \)) during the baseline period than patients without EoG/EoN. The most common gastrointestinal symptoms among patients with EoG/EoN were abdominal pain (48.7%), nausea/vomiting (27.4%), and diarrhea (20.5%). Among patients without EoG/EoN, the prevalence of gastrointestinal symptoms at baseline was low overall (7.4%). The most common medications used by patients with EoG/EoN were corticosteroids (46.0%) and proton pump inhibitors (45.2%) (Table 1).

Healthcare Resource Use

The unadjusted and adjusted incidence rate ratios and risk ratios of HRU measured during the 12-month study period are summarized in Table 2. A significantly higher proportion of patients with EoG/EoN had at least one inpatient stay (17.6% vs. 2.8%), outpatient visit (99.7% vs. 84.9%), and emergency department visit (45.0% vs. 21.3%) in the 12-month study period compared to patients without EoG/EoN (all \( p < 0.001 \)). No appreciable difference was observed in the mean length of inpatient stay between cohorts (5.49 vs. 5.58 days; \( p = 0.88 \)). Patients with EoG/EoN had significantly higher rates of adjusted all-cause HRU during the study period compared to patients without EoG/EoN (adjusted rate ratio [RR]: inpatient visits, 6.26 (95% confidence interval [CI] 5.26, 7.46); outpatient visits, 1.17 (95% CI 1.16, 1.19); emergency department visits, 2.11 (95% CI 1.98, 2.25; all \( p < 0.001 \)). In the sensitivity analysis after an additional adjustment for CCI, results remained statistically significant with the RRs slightly smaller than the main model (e.g., main model RR for inpatient visits was 6.26, sensitivity was 5.36).

Healthcare Costs

The mean, unadjusted, total healthcare costs for patients with EoG/EoN were $32,722 during the 12-month study period, compared to $4179 for patients without EoG/EoN (Fig. 2). Patients with EoG/EoN incurred significantly higher adjusted all-cause total costs during the study period compared to patients without EoG/EoN (adjusted mean cost difference $31,180, \( p < 0.001 \))
The difference in total costs was largely driven by differences in outpatient costs (adjusted mean cost difference $14,018, \( p < 0.001 \)) as the difference in outpatient costs accounted for 45\% of the adjusted total cost difference during the 12-month study period. The unadjusted mean cost difference between cohorts was significant, although slightly lower than the adjusted cost difference (unadjusted mean cost difference $28,593; adjusted mean cost difference $31,180; both \( p < 0.001 \)). Unadjusted mean cost difference in inpatient costs was $9787, while adjusted mean cost difference in inpatient costs was $11,224 (both \( p < 0.001 \)). Similarly, unadjusted mean cost difference in outpatient costs was $12,714, while adjusted mean cost difference in outpatient costs was $14,018 (both \( p < 0.001 \)). Cost differences from the sensitivity analysis where CCI was additionally adjusted for were statistically significant with the cost difference between cohorts lower than the main model (main model mean adjusted total cost difference $31,180; sensitivity analysis mean adjusted total cost difference $25,263).
Table 1  Demographics and clinical characteristics measured during the baseline period

| Characteristic                          | Patients with EoG/EoN (N = 2219) | Patients without EoG/EoN (N = 6657) | p valuea |
|----------------------------------------|----------------------------------|-------------------------------------|----------|
| Age on index date (years), mean ± SD  | 31.3 ± 21.2                      | 31.5 ± 21.0                         | < 0.001  |
| Age ≥ 18 years on index date, n (%)   | 1358 (61.2%)                     | 4097 (61.5%)                        | 0.0976   |
| Sex, n (%)                             |                                  |                                     |          |
| Male                                   | 1044 (47.0%)                      | 3132 (47.0%)                        | –        |
| Female                                 | 1175 (53.0%)                      | 3525 (53.0%)                        | –        |
| Region of residence, n (%)             |                                  |                                     |          |
| Northeast                              | 429 (19.3%)                       | 1247 (18.7%)                        | 0.5742   |
| North Central                          | 547 (24.7%)                       | 1431 (21.5%)                        | < 0.01   |
| South                                  | 785 (35.4%)                       | 2664 (40.0%)                        | < 0.001  |
| West                                   | 447 (20.1%)                       | 1213 (18.2%)                        | 0.0679   |
| Unknown                                | 11 (0.5%)                         | 102 (1.5%)                          | < 0.001  |
| Index year, n (%)                      |                                  |                                     |          |
| 2010                                   | 198 (8.9%)                        | 301 (4.5%)                          | < 0.001  |
| 2011                                   | 272 (12.3%)                       | 687 (10.3%)                         | < 0.01   |
| 2012                                   | 225 (10.1%)                       | 746 (11.2%)                         | < 0.05   |
| 2013                                   | 259 (11.7%)                       | 1098 (16.5%)                        | < 0.001  |
| 2014                                   | 223 (10.0%)                       | 748 (11.2%)                         | < 0.001  |
| 2015                                   | 257 (11.6%)                       | 872 (13.1%)                         | < 0.001  |
| 2016                                   | 274 (12.3%)                       | 831 (12.5%)                         | 0.7084   |
| 2017                                   | 262 (11.8%)                       | 773 (11.6%)                         | 0.5466   |
| 2018                                   | 249 (11.2%)                       | 601 (9.0%)                          | < 0.001  |
| Health plan type, n (%)                |                                  |                                     |          |
| Plans with capitation                  | 248 (11.2%)                       | 747 (11.2%)                         | 0.8956   |
| Plans without capitation               | 1971 (88.8%)                      | 5910 (88.8%)                        | 0.8956   |
| Charlson Comorbidity Index (CCI), mean ± SD | 0.5 ± 1.1                      | 0.1 ± 0.5                            | < 0.001  |
| Comorbid conditions, n (%)             |                                  |                                     |          |
| Atopic conditions                      | 1042 (47.0%)                      | 900 (13.5%)                         | < 0.001  |
| Allergic conjunctivitis                | 48 (2.2%)                         | 34 (0.5%)                           | < 0.001  |
| Allergic rhinitis                      | 485 (21.9%)                       | 290 (4.4%)                          | < 0.001  |
| Asthma                                 | 399 (18.0%)                       | 198 (3.0%)                          | < 0.001  |
| Atopic dermatitis/eczema               | 186 (8.4%)                        | 184 (2.8%)                          | < 0.001  |
| Food allergy                           | 329 (14.8%)                       | 26 (0.4%)                           | < 0.001  |
| Characteristic                              | Patients with EoG/EoN (N = 2219) | Patients without EoG/EoN (N = 6657) | p value<sup>a</sup> |
|--------------------------------------------|----------------------------------|-------------------------------------|--------------------|
| Sinusitis                                  | 269 (12.1%)                      | 368 (5.5%)                          | < 0.001            |
| Urticaria                                  | 70 (3.2%)                         | 35 (0.5%)                           | < 0.001            |
| Celiac disease                             | 39 (1.8%)                         | 3 (0.0%)                            | < 0.001            |
| Chronic gastritis/enteritis/duodenitis     | 804 (36.2%)                       | 61 (0.9%)                           | < 0.001            |
| Eosinophilic esophagitis                   | 515 (23.2%)                       | 0 (0.0%)                            | –                  |
| Functional dyspepsia                       | 131 (5.9%)                        | 0 (0.0%)                            | –                  |
| Gastroesophageal reflux disease            | 653 (29.4%)                       | 11 (0.2%)                           | < 0.001            |
| Gastrointestinal symptoms                  | 1571 (70.8%)                      | 494 (7.4%)                          | < 0.001            |
| Abdominal pain                             | 1080 (48.7%)                      | 208 (3.1%)                          | < 0.001            |
| Chest pain/throat pain                     | 251 (11.3%)                       | 148 (2.2%)                          | < 0.001            |
| Constipation                               | 282 (12.7%)                       | 54 (0.8%)                           | < 0.001            |
| Diarrhea                                   | 455 (20.5%)                       | 40 (0.6%)                           | < 0.001            |
| Dysphagia                                  | 237 (10.7%)                       | 14 (0.2%)                           | < 0.001            |
| Esophageal perforation                     | 2 (0.1%)                          | 0 (0.0%)                            | –                  |
| Other esophageal conditions<sup>b</sup>    | 56 (2.5%)                         | 3 (0.0%)                            | < 0.001            |
| Weight loss/failure to thrive              | 252 (11.4%)                       | 28 (0.4%)                           | < 0.001            |
| Gas/bloating                               | 121 (5.5%)                        | 8 (0.1%)                            | < 0.001            |
| Gastrointestinal bleeding                  | 130 (5.9%)                        | 22 (0.3%)                           | < 0.001            |
| Heartburn                                  | 33 (1.5%)                         | 4 (0.1%)                            | < 0.001            |
| Nausea/vomiting                            | 609 (27.4%)                       | 90 (1.4%)                           | < 0.001            |
| Inflammatory bowel disease                 | 114 (5.1%)                        | 15 (0.2%)                           | < 0.001            |
| Ulcerative colitis                         | 50 (2.3%)                         | 6 (0.1%)                            | < 0.001            |
| Crohn’s disease                            | 76 (3.4%)                         | 11 (0.2%)                           | < 0.001            |
| Irritable bowel syndrome                   | 104 (4.7%)                        | 0 (0.0%)                            | –                  |
| Medication classes, n (%)                  |                                  |                                    |                    |
| Antihistamines                             | 293 (13.2%)                       | 96 (1.4%)                           | < 0.001            |
| H2 receptor blockers                       | 263 (11.9%)                       | 34 (0.5%)                           | < 0.001            |
| Leukotriene antagonists                    | 331 (14.9%)                       | 119 (1.8%)                          | < 0.001            |
| Proton pump inhibitors                     | 1002 (45.2%)                      | 103 (1.5%)                          | < 0.001            |
| Corticosteroids                            | 1020 (46.0%)                      | 709 (10.7%)                         | < 0.001            |
| Fluticasone                                | 322 (14.5%)                       | 217 (3.3%)                          | < 0.001            |

<sup>a</sup> p values indicate statistical significance.
DISCUSSION

This retrospective claims-based study quantified and compared HRU and costs incurred by patients with EoG/EoN versus patients without EoG/EoN in the USA. The findings from this analysis demonstrated that patients with EoG/EoN experienced a significantly greater economic burden compared to patients without EoG/EoN over the 1-year study period. The major drivers of the high economic burden observed were costs incurred in the inpatient and outpatient settings. More specifically, the difference in outpatient costs accounted for 45% of the adjusted total cost differences during the 1-year study period and inpatient costs accounted for 36% of the cost differences.

In this study, significantly higher proportions of patients with EoG/EoN versus without EoG/EoN had the selected comorbidities during the baseline period. The higher prevalence of comorbid conditions in addition to gastrointestinal symptoms, relapse, and recurrence that is common in EoG/EoN is likely to have contributed to the large number of outpatient visits and inpatient visits and increased inpatient and outpatient costs experienced by patients with EoG/EoN [6–8]. It is also possible that the downstream health effects of EoG/EoN such as growth retardation and delayed puberty in childhood and adolescence, and social functioning involving food and eating and psychological distress, which are currently understudied, have an impact on the high economic burden observed in this study [8, 9].

To the best of our knowledge, this is the first large, claims-based study to assess the HRU and cost burden of EoG/EoN in the USA. Most of the available studies to date have focused primarily on the clinical burden associated with EoG/EoN or eosinophilic gastrointestinal disorders in general without descriptions of the direct cost burden. For example, a survey study published in 2019 that assessed the clinical impact of eosinophilic gastrointestinal disorders found that 64% of survey respondents reported stress due to high out-of-pocket disease-related costs, which posed a substantial barrier to healthcare [15]. In a qualitative assessment of health-related quality of life, patients with EoG/EoN reported a range of negative physiological impacts including poor emotional and mental well-being, inability to engage in activities involving food, and impaired perceptions of their body image [9]. The current study provides the direct cost burden of EoG/EoN to complement the previously well-documented impact of EoG/EoN on health-related quality of life. Despite the debilitating impact of EoG/EoN, the disorder has been underdiagnosed and under-recognized. The present study demonstrated the substantial direct burden of EoG/EoN via high

| Characteristic                      | Patients with EoG/EoN (N = 2219) | Patients without EoG/EoN (N = 6657) | p value\(^a\) |
|------------------------------------|----------------------------------|------------------------------------|---------------|
| Budesonide                         | 284 (12.8%)                      | 19 (0.3%)                         | < 0.001       |
| Prednisone                         | 424 (19.1%)                      | 200 (3.0%)                        | < 0.001       |
| Other systemic corticosteroids\(^c\) | 400 (18.0%)                      | 370 (5.6%)                        | < 0.001       |
| Elemental diet                     | 121 (5.5%)                       | 0 (0.0%)                          | –             |

The baseline period was defined as the 6-month period prior to the index date (randomly selected date with an EoG/EoN diagnosis for patients with EoG/EoN or date closest to index date of matched case for patients without EoG/EoN).

**EoG** eosinophilic gastritis, **EoN** eosinophilic enteritis, **N** number, **SD** standard deviation

\(^a\)\(p\) values were estimated using generalized estimating equations (GEE). \(p\) values are not shown for variables the data is exactly matched on or when there are no observations in one cohort.

\(^b\) Other esophageal conditions include esophageal foreign body, stricture, web, and congenital stenosis

\(^c\) Other systemic corticosteroids include betamethasone, dexamethasone, methylprednisolone, prednisolone, and cortisone
Table 2 Unadjusted and adjusted incidence rate ratios and risk ratios of healthcare resource utilization measured during the 12-month study period

| All-cause healthcare resource utilization | Unadjusted | Risk/rate ratio of patients with EoG/EoN vs. without EoG/EoN (95% CI) | p value | Adjusted<sup>a</sup> | Risk/rate ratio of patients with EoG/EoN vs. without EoG/EoN (95% CI) | p value |
|-----------------------------------------|------------|-----------------------------------------------------------------|--------|------------------------|-----------------------------------------------------------------|--------|
|                                         | Patients with EoG/EoN (N = 2219) | Patients without EoG/EoN (N = 6657) |        |                        |                                                                 |        |
| Inpatient                               |            |                                                                  |        |                        |                                                                 |        |
| Any admission, n (%)                    | 390 (17.58%) | 185 (2.78%)                                                       | 6.32 (5.31, 7.53) | < 0.001                | 6.26 (5.26, 7.46)                                                  | < 0.001|
| Number of admissions, mean ± SD         | 0.30 ± 0.92 | 0.03 ± 0.21                                                       | 9.33 (7.59, 11.48) | < 0.001                | 9.17 (7.46, 11.27)                                                  | < 0.001|
| Total inpatient days, mean ± SD<sup>c</sup> | 2.17 ± 8.34 | 0.19 ± 2.06                                                       | 11.53 (8.44, 15.75) | < 0.001                | 11.26 (8.23, 15.41)                                                  | < 0.001|
| Outpatient                              |            |                                                                  |        |                        |                                                                 |        |
| Any visit, n (%)                        | 2212 (99.68%) | 5650 (84.87%)                                                    | 1.17 (1.16, 1.19) | < 0.001                | 1.17 (1.16, 1.19)                                                  | < 0.001|
| Number of visits, mean ± SD             | 24.66 ± 29.17 | 6.53 ± 10.40                                                      | 3.78 (3.54, 4.03) | < 0.001                | 3.75 (3.52, 4.00)                                                  | < 0.001|
| Emergency department                    |            |                                                                  |        |                        |                                                                 |        |
| Any visit, n (%)                        | 999 (45.02%) | 1419 (21.32%)                                                     | 2.11 (1.98, 2.25) | < 0.001                | 2.11 (1.98, 2.25)                                                  | < 0.001|
| Number of visits, mean ± SD             | 1.23 ± 3.38 | 0.35 ± 1.26                                                       | 3.56 (3.08, 4.11) | < 0.001                | 3.56 (3.09, 4.10)                                                  | < 0.001|

<sup>a</sup>The adjusted risk ratios and incidence rate ratios controlled for the following: age at index date, sex, region, index year and plan type

<sup>b</sup>Risk ratios, incidence rate ratios, 95% confidence intervals, and p values were estimated using generalized estimating equations with a Poisson distribution

<sup>c</sup>Total inpatient days is calculated among all patients in the sample and includes all inpatient stays that overlap with the 12-month study period. If the inpatient stay started before the index date or ends after the end of the study period, only the days that fall within the study period were considered.

CI confidence interval, EoG eosinophilic gastritis, EoN eosinophilic enteritis, N number, SD standard deviation
healthcare costs. However, given the challenges clinicians face to accurately diagnose EoG/EoN, the conditions are underdiagnosed or misdiagnosed [14, 17]. As a result, the total healthcare cost burden this disease inflicts on the healthcare system is likely larger than we observed in this study despite the rarity of the conditions.

The absence of an approved therapy by the US Food and Drug Administration for patients with EoG/EoN is among the major contributors to the unmet need in patients with EoG/EoN. Existing treatment options include both non-pharmacological (diet) and pharmacological approaches, although the efficacy of dietary approaches has not been validated and patients’ adherence and tolerability remain important drawbacks [7]. Prolonged corticosteroid which remains the mainstay of treatment has been shown to be effective therapeutically but carries the risk of serious adverse effects [18]. The drawbacks associated with current therapies are noticed among patients. In a survey of patients with eosinophilic gastrointestinal disorders in general, the vast majority of patients indicated that the treatment options (e.g., dietary elimination, steroids, immunomodulators) were not easy to adhere to or convenient [15]. Collectively, the limitations associated with the current standard of care for EoG/EoN coupled with the substantial burden the disease imposes underscore the urgency of the unmet needs in this patient population.

Considering the paucity of available literature describing the direct cost burden associated with EoG/EoN, this study has important strengths. The commercial claims dataset used in this study contained a large sample of patients with EoG/EoN that provided robust, up-to-date estimate of the economic burden of EoG/EoN. Second, to increase the accuracy of our assessment of the magnitude of the disease burden, patients with EoG/EoN were matched to patients without EoG/EoN on sex, region, index year and plan type. In addition, the HRU and cost analyses were adjusted for multiple potential confounders including age at index date, sex, region, index year, and plan type. A sensitivity analysis was conducted which further adjusted for CCI did not result in significant changes to the findings.
| All-cause healthcare costs ($)\(^d\) | Unadjusted results\(^a\) | Adjusted results\(^b\) |  |
|--------------------------------------|-------------------------|------------------------|--|
|                                      | Patients with EoG/EoN\(^c\) (N = 2219) | Patients without EoG/EoN\(^c\) (N = 6657) | Mean cost difference | p value | Patients with EoG/EoN (N = 2219) | Patients without EoG/EoN (N = 6657) | Mean cost difference | p value |
| Total costs                          | 32,772 ± 84,677          | 4179 ± 21,624          | 28,593             | < 0.001 | 35,151             | 3971             | 31,180             | < 0.001 |
| Medical costs                        | 27,476 ± 81,044          | 3076 ± 17,949          | 24,400             | < 0.001 | 29,155             | 2934             | 26,221             | < 0.001 |
| Inpatient                            | 10,723 ± 58,486          | 937 ± 15,356           | 9787               | < 0.001 | 12,073             | 848              | 11,224             | < 0.001 |
| Outpatient                           | 14,550 ± 29,968          | 1836 ± 7121            | 12,714             | < 0.001 | 15,750             | 1732             | 14,018             | < 0.001 |
| Emergency department                 | 2204 ± 9652             | 304 ± 1748             | 1900               | < 0.001 | 2201               | 304              | 1898               | < 0.001 |
| Pharmacy costs                       | 5296 ± 13,565            | 1103 ± 11,303          | 4193               | < 0.001 | 6016               | 1039             | 4978               | < 0.001 |

The 12-month study period was defined as the period following and including the index date.

EoG eosinophilic gastritis, EoN eosinophilic enteritis, IQR interquartile range, N number, SD standard deviation

\(^a\) Unadjusted results include average costs ± standard deviation. Statistical comparisons were conducted using generalized estimating equations.

\(^b\) Adjusted results include predicted costs and p values, estimated using generalized estimating equations with a Tweedie distribution. The adjusted models controlled for the following: age at index date, sex (female), region, index year and plan type (capitation).

\(^c\) Costs presented as mean ± SD.

\(^d\) All costs were inflated to 2021 USD.
While this study does provide helpful insight for healthcare stakeholders that can serve as a useful benchmark for future studies, this analysis should be considered within the context of certain limitations, some of which are inherent to observational claims-based studies. First, as with all studies using retrospective databases, the data may have been subject to missing data or coding errors. Second, administrative claims data only contain diagnostic and procedure codes that are recorded for reimbursement purposes, rather than research purposes. Third, as patients with EoG/EoN are believed to be underdiagnosed in clinical practice [16, 19], it is possible that there may have been control patients included in this analysis that had undiagnosed EoG/EoN, or those considered EoG/EoN could have been examples of more severe EoG/EoN. However, the percentage of undiagnosed patients with EoG/EoN in the control cohort is expected to be low and have minimal impact on the sample. Additionally, patients with IBS and functional dyspepsia were excluded from the control cohort to help minimize the misclassification between cases and controls. However, this exclusion may impact the generalizability of our results since it is a comparison of patients with EoG/EoN to patients without EoG/EoN and other gastrointestinal conditions, eosinophilic esophagitis, functional dyspepsia or irritable bowel syndrome. Finally, as patients included in the data were required to have employer-based health insurance, the results of this study may not be representative of patients who are uninsured or insured by public health plans (e.g., Medicaid).

CONCLUSIONS

Results from this study highlight the substantial HRU and cost burden associated with EoG/EoN in the USA. The main drivers of the economic burden observed in this study were inpatient and outpatient settings. The limitations of the current standard of care for EoG/EoN coupled with the substantial burden of the disease underscore the urgency of the unmet needs in this patient population.

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Compliance with Ethics Guidelines. Institutional review board approval and informed consent were not required for the conduct of this study. All of the information from the databases is de-identified and compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act.

Data Availability. The dataset analyzed in this study is not publicly available due to licensing agreement with IBM.
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