Prevalence of Eosinophilic Gastritis, Gastroenteritis, and Colitis: Estimates From a National Administrative Database

*Elizabeth T. Jensen, †Christopher F. Martin, ‡Michael D. Kappelman, and *Evan S. Dellon

See ''Eosinophilic Gastrointestinal Disorders Affect More Than Just the Esophagus'' by Furuta et al on page 1.

ABSTRACT

Objectives: Eosinophilic esophagitis (EoE) is becoming increasingly more common, but the prevalence of other eosinophilic gastrointestinal disorders (EGIDs) is unknown. Our objective was to estimate the prevalence of eosinophilic gastritis, gastroenteritis, and colitis in the United States.

Methods: We used the IMS Health LifeLink PharMetrics Plus Claims Database, data representative of a US national commercially insured population containing medical and pharmaceutical claims for >75 million individuals. We restricted our sample to patients ages 0 to 64 with continuous enrollment between July 1, 2009, and June 30, 2011. We identified patients with eosinophilic gastritis, gastroenteritis, and colitis as defined by ≥1 instance of the *International Classification of Diseases, Ninth Revision* codes 535.70, 558.41, and 558.42, respectively. We calculated the prevalence of the codes in the database and then standardized the estimates to the US population by age and sex.

Results: The standardized estimated prevalences of eosinophilic gastritis, gastroenteritis, and colitis were 6.3/100,000, 8.4/100,000, and 3.3/100,000, respectively. The prevalence of eosinophilic gastroenteritis was the highest among children age <5 years, whereas eosinophilic gastritis was more prevalent among older age groups. We observed no age differences for eosinophilic colitis. Among affected patients, there was a high proportion of coexisting allergic conditions, 38.5% for eosinophilic gastritis, 45.6% for gastroenteritis, and 41.8% for colitis. Concomitant allergic disease was most commonly identified in pediatric patients.

Conclusions: The prevalence of non-EoE EGIDs remains rare in the United States, with <50,000 total patients affected. There appears to be a female predominance and a high co-occurrence of atopic comorbidities.

What Is Known

- The prevalence of noneosinophilic esophagitis eosinophilic gastrointestinal disorders is poorly described in the literature.
- The introduction of the *International Classification of Diseases, Ninth Revision* codes for these conditions provided the opportunity to estimate the prevalence of these conditions in the United States.

What Is New

- Eosinophilic gastritis, gastroenteritis, and colitis are rare, with a standardized prevalence of 6.3/100,000, 8.4/100,000, and 3.3/100,000, respectively.
- The prevalence of eosinophilic gastroenteritis was the highest among children age <5 years, whereas eosinophilic gastritis was more prevalent among older age groups. We observed no age differences for eosinophilic colitis.

Key Words: administrative data, eosinophil, prevalence, United States

(*JPGN* 2016;62: 36–42)

Eosinophilic gastrointestinal disorders (EGIDs) are characterized by abnormal eosinophilic infiltration of different segments of the gastrointestinal (GI) tract in the absence of an identifiable secondary cause. Eosinophilic esophagitis (EoE) is the most common of these conditions (1–3), with a recent prevalence estimate of 57 patients/100,000 individuals in the United States (4). Eosinophilic gastritis, eosinophilic gastroenteritis, and eosinophilic colitis are thought to be less common than EoE,

Received November 17, 2014; accepted May 12, 2015.

From the *Center for Esophageal Diseases and Swallowing, Division of Gastroenterology and Hepatology, Department of Medicine, †Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, and the ‡Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, University of North Carolina School of Medicine, Chapel Hill.

Address correspondence and reprint requests to Evan S. Dellon, MD, MPH, CB No. 7080, 4140 Bioinformatics Building, 130 Mason Farm Rd, University of North Carolina, Chapel Hill, NC 27599-7080 (e-mail: edellon@med.unc.edu).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (*www.jpgn.org*).

This study was funded, in part, by a University of North Carolina Junior Faculty Development Grant (E.S.D.) and National Institutes of Health Awards K23 DK090073 (E.S.D.) and K08 DK088957 (M.D.K.), and uses resources from the University of North Carolina's Center for Gastrointestinal Biology and Disease (P30 DK34987).

The authors report no conflicts of interest.

DOI: 10.1097/MPG.0000000000000865

although the prevalence of these other EGIDs has not been well described.

Many features of these diseases, including atopic comorbidities or clinical presentation, have been described only in the setting of case series studies or small, single-center studies (5–10). The population-level burden of these diseases, the age- and sex-based distributions, and associations with other conditions are unknown. The potential for estimating the prevalence of these other EGIDs, at the national level, was made possible in 2008 with the approval of an *International Classification of Diseases, Ninth Revision* (ICD-9) codes for eosinophilic gastritis (535.70), eosinophilic gastroenteritis (558.41), and eosinophilic colitis (558.42), but to date there have been no studies utilizing these codes.

The aim of the present study was to use a large health plan claims database to identify and characterize patients with eosinophilic gastritis, eosinophilic gastroenteritis, and eosinophilic colitis and estimate the prevalence of each of these EGIDs in the United States. We also sought to characterize the epidemiology of these diseases with respect to age, sex, clinical presentation, and concomitant allergic diseases.

METHODS

Study Design, Data Source, and Case Definition

We performed a retrospective analysis of the IMS Health LifeLink Claims Database (IMS Health, Plymouth Meeting, PA). This database contains longitudinal, integrated, fully adjudicated medical and pharmaceutical claims for >75 million individuals from >80 health plans, from all of the 50 states in the United States, and has been shown to be representative of a US national commercially insured population (11,12). These data are aggregated after a sufficient period of time has elapsed to ensure completeness of billing data. Data were not linkable to the patient medical record; however, enrollees' demographic data including age, sex, and census region (northeast, south, midwest, and west) were available. Regional designations correspond to the US census regions.

We restricted the data set to subjects continuously enrolled from July 1, 2009, through June 30, 2011, and estimated a 2-year, period prevalence, accounting for the delay in uptake for the new code that was noted after its introduction in 2008 and allowing an adequate amount of time for the code to be used (13). We excluded enrollees age ≥65 years because their claims data are likely to be incomplete because of coinsurance provided through Medicare.

Eosinophilic gastritis, gastroenteritis, and colitis were defined based on a patient having ≥1 instance of the ICD-9 codes 535.70, 558.41, and 558.42, respectively. We did not include the ICD-9 code of 558.3 because this is a more general code for allergic gastroenteritis and colitis and would lead to overestimation of the number of patients. Patients with EoE were identified as described formerly, for the purposes of comparison for concomitant allergic disease (4).

Descriptive Factors and Allergic Disease

In addition to the codes for eosinophilic gastritis, gastroenteritis, and colitis, data on other ICD-9 diagnostic codes were extracted. These included ICD-9 codes for the atopic disorders of rhinitis, sinusitis, dermatitis, urticaria, asthma, and food allergies (supplementary Table 1, *http://links.lww.com/MPG/A483*). Food allergy and other allergic conditions were characterized by ≥1 instance of the use of the corresponding allergic disease–related ICD-9 code during the study period. Because these allergic conditions could represent prevalent conditions, we did not require any accompanying procedure code. We also extracted data on census region of residence, sex, and age. Age was characterized in 5-year increments to allow standardizing of prevalence estimates to the age and sex distribution of residents in the United States per the 2010 Census data. In each of the non-EoE EGID conditions, we examined the frequency of concomitant functional dyspepsia (536.9) and IBS (564.1). Finally, we extracted data on ICD-9 codes (supplementary Table 1, *http://links.lww.com/MPG/A483*) for a number of upper and lower GI symptoms of interest.

Statistical Analysis

We used descriptive statistics to characterize demographics, symptoms, and concomitant allergic diseases, and to estimate the proportion of patients with >1 EGID condition (for example, superimposed eosinophilic gastritis and eosinophilic colitis). We also estimated the proportion of patients with superimposed EoE, using a formerly validated claims-based definition for EoE (≥1 instance of the ICD-9 code 530.13) (14). Pearson χ^2 tests were used to evaluate whether the distributions of sex, age, census region, the presence of allergic diseases, and the proportions of upper and lower GI symptoms differed between patients with EGID and the source population.

To calculate period prevalence, we divided the number of patients who met the case definition for each EGID during the 2-year period by the total number of enrolled patients during the same 2 years (the study population). The overall prevalence, prevalence by sex, prevalence by census region, and prevalence by 5-year age increments were estimated using the source population. We standardized the overall prevalence estimate to the US population by age and sex using 2010 census data for individuals <65 years of age, to allow us to estimate the absolute number of patients with eosinophilic gastritis, gastroenteritis, and colitis in the United States.

We performed sensitivity analyses using more restrictive case definitions for the EGIDs. Specifically, we estimated the prevalence of eosinophilic gastritis, gastroenteritis, and colitis after excluding patients with ICD-9 codes suggestive of possible competing causes of GI tract eosinophilia, including ulcerative colitis (556.x), Crohn disease (555.x), and diseases with an infectious etiology (ICD-9 codes 120.0–127.9). The University of North Carolina's institutional review board exempted this study from review.

RESULTS

Characteristics of Patients With EGIDs

Of the 11,569,217 individuals continuously enrolled during the study period, 774 (0.007%) met the criteria for eosinophilic gastritis, 954 (0.008%) met the criteria for eosinophilic gastroenteritis, and 404 (0.003%) met the criteria for eosinophilic colitis. The mean (±SD) number of claims, on different days, for eosinophilic gastritis, gastroenteritis, and colitis was 1.3 (±1.6), 1.7 (±2.4), and 1.8 (±3.9) claims, respectively. There were 104 patients with >1 non-EoE EGID, representing 4.9% of patients with an EGID (101 with 2 conditions and 3 with all of the 3 conditions). Of the 954 patients with eosinophilic gastroenteritis, 51 (5.3%) had diagnostic codes for both eosinophilic gastritis and eosinophilic gastroenteritis. The proportion of patients with superimposed EoE was similar across conditions, specifically 10.6% for eosinophilic gastritis, 12.0% for eosinophilic gastroenteritis, and 10.9% for eosinophilic colitis. Assessment of the frequency of concomitant functional dyspepsia and IBS in each of the non-EoE EGID conditions identified that for eosinophilic gastritis 0.7% and 5.6% had coexisting functional dyspepsia and IBS codes, respectively. For eosinophilic gastroenteritis, 0.4% and 8.6% had functional dyspepsia and IBS codes, respectively, and for eosinophilic colitis, 1.2% had concomitant functional dyspepsia and 13.4% had concomitant IBS.

TABLE 1. Demographic characteristics of patients with eosinophilic GI disease

	Source population	Eosinophilic gastritis		Eosinophilic gastroenteritis		Eosinophilic colitis	
	n = 11,569,217 (%)	Patients, n = 774 (%)	$P^{\dagger}$	Patients, n = 954 (%)	$P^{\dagger}$	Patients, n = 404 (%)	$P^{\dagger}$
Age <20 y*	3,587,571 (31.0)	159 (20.5)	<0.01	385 (40.4)	<0.01	153 (37.9)	<0.01
Male	5,544,574 (47.9)	299 (39.6)	<0.01	423 (44.3)	0.03	173 (42.8)	0.05
Region of country‡							
Northeast	2,226,470 (19.2)	111 (14.3)	<0.01	126 (13.2)	<0.01	78 (19.3)	<0.01
South	4,529,151 (39.1)	346 (44.7)		401 (42.0)		197 (48.8)	
Midwest	3,569,432 (30.9)	263 (34.0)		366 (38.4)		92 (22.8)	
West	1,244,164 (10.8)	54 (7.0)		61 (6.4)		37 (9.2)	

Data calculated for the time frame July 1, 2009, through June 30, 2011, for those enrolled continuously for 24 months. GI = gastrointestinal. Data adapted from IMS Health LifeLink, PharMetrics Plus Claims Database, January 2001 to November 2011, IMS Health Incorporated.

* Children were defined as age <20 years for purposes of standardization in 5-year increments of age.

† P value for χ^2 test for difference in distributions among patients versus source population.

‡ US census regions (*https://www.census.gov/geo/maps-data/maps/pdfs/reference/us_regdiv.pdf*).

The mean (SD) age of patients with eosinophilic gastritis, gastroenteritis, and colitis was 39.8 (±17.4), 30.2 (±19.9), and 33.5 (±20.5) years, respectively. The patient distribution by age (pediatric or adult), census region (northeast, south, midwest, and west), and sex (men or women) was statistically different from that of the source population (Table 1).

Upper and lower GI symptoms differed according to condition (Table 2). Patients with eosinophilic gastritis were more likely than patients with eosinophilic gastroenteritis or colitis to have had chest or throat pain. Patients with eosinophilic colitis more commonly had presented with diarrhea (41%) and GI bleeding (14%). Abdominal pain, however, was present in a high proportion of patients across all conditions and in nearly 60% of those with eosinophilic colitis. For all of the disease conditions, more than one fourth of patients had presented with nausea and/or vomiting. The proportion of upper and lower GI symptoms was significantly higher than observed in the source population (Table 2).

Coexisting allergic conditions were relatively common in patients with eosinophilic gastritis, gastroenteritis, and colitis, at 38.5%, 45.6%, and 41.8% respectively, and these comorbidities were significantly higher than in the source population (supplementary Table 2, *http://links.lww.com/MPG/A484*). The most commonly reported allergic condition was rhinitis (28%–30%). Asthma was reported in 16% of patients with eosinophilic gastritis, 19% of patients with eosinophilic gastroenteritis, and 15% of patients with eosinophilic colitis (supplementary Table 2, *http://links.lww.com/MPG/A484*). Similar to that which has been documented in EoE (15), the proportion of patients with concomitant allergic disease was higher among pediatric patients (age <19 years). For example, 58.9% of pediatric patients with eosinophilic gastritis also had documentation of an allergic condition, compared with 33.6% of adults with eosinophilic gastritis. For eosinophilic gastroenteritis, 51.6% of pediatric patients had allergic disease compared with 41.8% of adults. With eosinophilic colitis, 52.0% of pediatric patients had concomitant allergic disease compared with 35.9% of adults.

Prevalence and Distribution of EGIDs in the United States

In the source population the prevalence of eosinophilic gastritis, gastroenteritis, and colitis was 6.7, 8.2, and 3.5 patients/100,000, respectively (Table 3). The female predominance for disease was most evident for eosinophilic gastritis, in which the prevalence for women was 7.9 patients/100,000 as compared with

TABLE 2. Upper and lower GI symptoms of patients with eosinophilic GI disease

	Source population	Eosinophilic gastritis		Eosinophilic gastroenteritis		Eosinophilic colitis	
Symptom	n (%) n = 472,222	n (%) n = 774	P^{*}	n (%) n = 954	P^{*}	n (%) n = 404	P^{*}
Dysphagia	52 (0.01)	0 (0.0)	<0.01	0 (0.0)	<0.01	0 (0.0)	<0.01
Heartburn	2649 (0.6)	41 (5.3)	<0.01	21 (2.2)	<0.01	20 (5.0)	<0.01
Abdominal pain/dyspepsia	66,578 (14.1)	402 (51.9)	<0.01	474 (49.7)	<0.01	239 (59.2)	<0.01
Chest pain/throat pain	49,799 (10.6)	226 (29.2)	<0.01	200 (21.0)	<0.01	94 (23.3)	<0.01
Nausea/vomiting	29,289 (6.2)	195 (25.2)	<0.01	276 (28.9)	<0.01	113 (28.0)	<0.01
Failure to thrive	797 (0.2)	13 (1.7)	<0.01	25 (2.6)	<0.01	14 (3.5)	<0.01
Diarrhea	18,426 (3.9)	131 (16.9)	<0.01	293 (30.7)	<0.01	165 (40.8)	<0.01
Gas/bloating	3846 (0.8)	42 (5.4)	<0.01	52 (5.5)	<0.01	32 (7.9)	<0.01
GI bleeding	7074 (1.5)	69 (8.9)	<0.01	66 (6.9)	<0.01	58 (14.4)	<0.01

Data calculated for those enrolled continuously from July 1, 2009, through June 30, 2011, for claims arising within this period, claims data for the source population represent claims for a 5%, random sample of the total study population. GI = gastrointestinal. Data adapted from IMS Health LifeLink, PharMetrics Plus Claims Database, January 2001 to November 2011, IMS Health Incorporated.

* P value for test for difference in proportions between patients with eosinophilic gastritis, gastroenteritis, and colitis, as compared with a random sample of the source population meeting study eligibility criteria for enrollment period.

TABLE 3. Prevalence of eosinophilic GI diseases by age, sex, and region

	Source population (n)	Eosinophilic gastritis		Eosinophilic gastroenteritis		Eosinophilic colitis	
		Patients (n)	Prevalence (per 100,000)	Patients (n)	Prevalence (per 100,000)	Patients (n)	Prevalence (per 100,000)
Age, y*							
<20	3,587,571	159	4.4	385	10.7	153	4.3
20–64	7,981,646	615	7.7	569	7.1	251	3.1
Sex							
Male	5,544,574	299	5.4	423	7.6	173	3.1
Female	6,024,643	475	7.9	531	8.8	231	3.8
Region†							
Northeast	2,226,470	111	5.0	126	5.7	78	3.5
South	4,529,151	346	7.6	401	8.9	197	4.3
Midwest	3,569,432	263	7.4	366	10.3	92	2.6
West	1,244,164	54	4.3	61	4.9	37	3.0
Overall prevalence	**11,569,217**	**774**	**6.7**	**954**	**8.2**	**404**	**3.5**

Data calculated for those enrolled continuously from July 1, 2009, through June 30, 2011, for claims arising within this period. GI = gastrointestinal. Data adapted from IMS Health LifeLink, PharMetrics Plus Claims Database, January 2001 to November 2011, IMS Health Incorporated.

*Children were defined as age <20 years for purposes of standardization in 5-year increments of age.

†US census regions (*https://www.census.gov/geo/maps-data/maps/pdfs/reference/us_regdiv.pdf*).

5.4 patients/100,000 for men. Regional differences were observed for eosinophilic gastritis and gastroenteritis, as the prevalence in the south and midwest was nearly twice that of the prevalence in the northeast and west. In contrast, no regional difference in prevalence was observed for eosinophilic colitis (Table 3).

Examination of the prevalence, by age and sex, for each of the EGIDs suggested differences between the conditions. For eosinophilic gastritis, particularly among women, the prevalence increased with age, with peak prevalence in the oldest age group (14.4 patients/100,000 in women for ages 60–64 years) (Fig. 1A). Eosinophilic gastroenteritis prevalence gradually decreased with age, with highest prevalence for both boys and girls in patients under the age of 5 years, 17.6 patients/100,000 and 16.7 patients/100,000, respectively (Fig. 1B). There was little difference in the prevalence of eosinophilic colitis by age and sex (Fig. 1C).

When age and sex were standardized to the US population, the estimated prevalence of eosinophilic gastritis was 6.3/100,000, the prevalence of eosinophilic gastroenteritis was 8.4/100,000, and the prevalence of eosinophilic colitis was 3.3/100,000. Applying these prevalences to the 2010 US population, we estimate there are 16,952 patients with eosinophilic gastritis, 22,548 patients with eosinophilic gastroenteritis, and 8982 patients with eosinophilic colitis, for a total of 48,482 affected individuals between ages 0 and 64 years in the United States, during the study period.

In sensitivity analyses, in which a more restrictive case definition was used to exclude patients with possible competing conditions, we observed similar prevalence estimates to those obtained using the primary definitions for eosinophilic gastritis and gastroenteritis but not colitis. Eosinophilic gastritis prevalence was 6.0/100,000 after excluding 34 patients with inflammatory bowel disease (IBD) codes and 2 patients with infectious disease codes, and the prevalence of eosinophilic gastroenteritis was 7.7/100,000, after excluding 72 patients with IBD codes and 8 patients with infectious disease codes. Nearly 30% of patients with eosinophilic colitis, however, had codes for either IBD (n = 114) or infectious disease (n = 6), reducing the prevalence to 2.4 patients/100,000. Using these more restrictive prevalence estimates, an estimated 43,203 individuals are affected by one of these conditions in the United States.

DISCUSSION

In the present study, we estimated the prevalence of eosinophilic gastritis, eosinophilic gastroenteritis, and eosinophilic colitis in the United States. To our knowledge, estimates of the prevalence of each of these conditions in the United States have not been directly calculated from national level data. Our results indicate that these conditions are rare and much less common than EoE. For the first time, we are also able to present age- and sex-specific prevalence for these conditions, show a female predominance for eosinophilic gastritis, gastroenteritis, and colitis, and demonstrate an association with allergic diseases. Because of the large database that we used, we were able to identify many-fold more patients with EGID than have been described earlier.

One other study estimated the overall prevalence of the non-EoE EGIDs using a methodology in which allergists and gastroenterologists were surveyed about their practice data, and the results were extrapolated nationally (16). They found a prevalence of 28/100,000 for combined patients with eosinophilic gastroenteritis and eosinophilic colitis, higher than our estimate. They also found higher prevalence in the northeast region, whereas we found higher prevalence in the south and midwest.

The age distribution of patients in our study suggested that most patients were adults. The ability to identify a larger set of patients than earlier described, from which age distributions could be examined, was a strength of this study. Although often associated with young children, mean age of patients with eosinophilic colitis was 33.5, and only 11 of the 404 patients were among children <2 years of age at the time of diagnosis (3 patients were <1 year of age). Adult patients with eosinophilic colitis have been described in smaller, single-center studies, including a recent study of 11 patients with eosinophilic colitis in which the mean age was 22 (17,18).

There have been several published case series of patients with EGIDs (8,9,19–21). Case series from single centers suggest that these EGIDs are associated with significant morbidity and that the clinical presentation differs depending on the location of the eosinophilia in the GI tract, and the depth of inflammation through the bowel wall (9,19,20). Patients with eosinophilic colitis may present with abdominal pain, diarrhea, and rectal bleeding. Patients with eosinophilic gastritis and gastroenteritis may present with

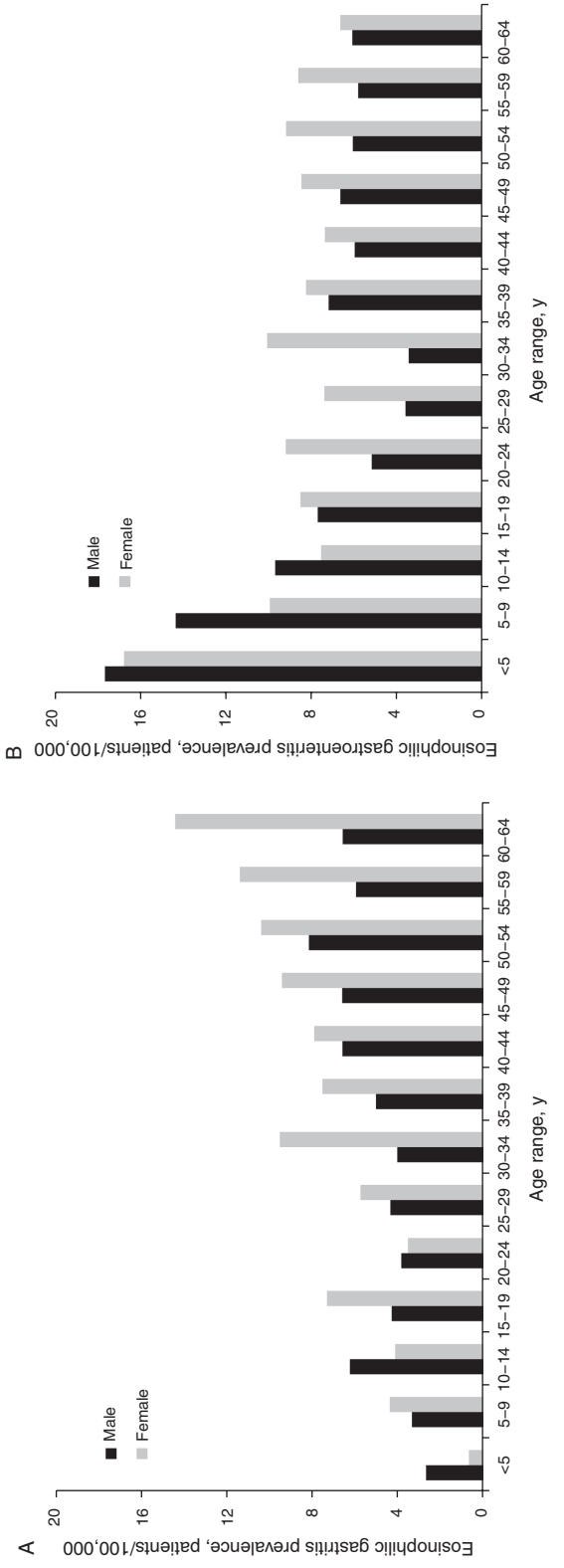

FIGURE 1. A, Prevalence of gastritis (patients/100,000) in the database between July 1, 2009, through June 30, 2011, for those enrolled continuously for 24 months, as stratified by sex and by 5-year increments of age. B, Prevalence of eosinophilic gastroenteritis (patients/100,000) in the database between July 1, 2009, through June 30, 2011, for those enrolled continuously for 24 months, as stratified by sex and by 5-year increments of age. C, Prevalence of eosinophilic colitis (patients/100,000) in the database between July 1, 2009, through June 30, 2011, for those enrolled continuously for 24 months, as stratified by sex and by 5 year increments of age. (Male patients are the black bars and females are the gray bars.) Data adapted from IMS Health LifeLink, PharMetrics Plus Health Plan Claims Database, January 2001 to November 2011, IMS Health Incorporated.

abdominal pain, nausea, and vomiting (7–9,20–22). The upper and lower GI symptoms described for patients in these smaller studies are consistent with the patient symptoms documented in the present study.

Our data show that patients with the non-EoE EGIDs have frequent associated atopic conditions, though the proportion is not as high as has been formerly reported for EoE (23–25). In our own data, the proportion of patients with non-EoE EGID and concomitant EoE was also less than the proportion of patients with EoE and atopy (Table 3). Several case series or single-center studies have identified allergic disease comorbidity in many patients with eosinophilic gastritis and gastroenteritis (5,6,8,26,27). In a case series of 42 patients, Zhang et al (10) found that 30% of the patients with eosinophilic gastroenteritis had concomitant allergic rhinitis or asthma. Similarly, Caldwell et al (5) found that 7 of 14 patients diagnosed with eosinophilic gastritis tested positive for food or aeroallergens with skin prick testing. This same study provided molecular profiling data to support the assertion that eosinophilic gastritis is a T_H2-assocated disease. Still, some patients with EGIDs have no evidence of concomitant allergic disease, and there is some suggestion there may be an autoimmune component to these diseases (28,29). Our finding of increased diagnosis of atopy among patients with eosinophilic colitis is a novel finding, perhaps a reflection of the larger sample from which these associations could be examined. It may also be that patients with a chronic health condition are more likely to seek care for other comorbidities and that the increased diagnosis of atopic illness is reflecting increased health care utilization among these patients.

There are some limitations to the estimates presented. Although this is the first, large-scale administrative claims data approach to estimating the prevalence of these conditions, there is the potential that we may have underestimated or overestimated the number of patients. Of note, the ICD-9 codes for the non-EoE EGIDs have not been validated against other data sources; therefore, misclassification of identified patients may be possible. Given the rarity of these diseases and the relative newness of these diagnostic codes, however, we would hypothesize that our estimates are most likely an underestimate of the true number of patients. In our study validating the ICD-9 code for EoE, we found that it was highly specific but much less sensitive (14). We would postulate that it would be similarly unlikely for a provider to use one of the EGID ICD-9 codes for a patient without an EGID, but cannot confirm this in the present study because our claims data are deidentified and not linked to patient records. To attempt to account for this potential misclassification, we performed sensitivity analyses using a more restrictive coding case definition, excluding patients with codes for possible competing conditions. With this, the estimates changed minimally. In addition, the validity of our definitions are supported by the observation that the associated symptom codes for patients with these disorders are consistent with what is known about the clinical presentation of these conditions. Nonetheless, it is important that, to date, there are no published guidelines on case definitions for these conditions, so clinical diagnosis of these relatively new entities is likely a heterogeneous process too. Although there are some investigations assessing eosinophil levels in the GI tract (29), there are no formal cut-points for the number of eosinophils in the stomach, small intestine, and colon in the EGIDs, and there are no published guidelines as of yet for the diagnosis of these non-EoE EGIDs.

In addition to potential misclassification, we are limited in our analyses of the data captured in the claims database. Therefore, we cannot comment on patient race/ethnicity, socioeconomic status, practice setting, endoscopic findings, histologic features, or depth of involvement in the wall of the GI tract. Time trends and incidence calculations are also not possible given the recent introduction of these ICD-9 codes. The patients in this database are representative of a commercially insured population. It is possible that some patients are underinsured, and thus less likely to obtain the services necessary to reach a diagnosis, and we do not capture patients who are uninsured, on Medicaid, or on Medicare. This could result in an underascertainment of the number of patients.

The patients examined also represented prevalent cases, and use of the diagnostic codes could reflect care received during follow-up treatment for the EGID, rather than at initial diagnosis. Therefore, we felt that requiring a procedure code for histopathologic examination could underestimate case prevalence. It is possible too that patients may have been misclassified as having 1 EGID, later to be diagnosed with a different condition. The proportion of patients with both eosinophilic colitis and an IBD diagnosis may be indicative of diagnostic confusion for eosinophilic colitis. We found little evidence to support increased functional disorders in patients with an EGID and minimal overlap in the proportion of patients with >1 EGID.

In examining the presence of upper and lower GI symptoms, we were only able to evaluate symptom codes. Furthermore, we did not restrict the occurrence of these symptom codes to before or on the date on which the claims were made. Therefore, some of these symptoms may be unrelated to the EGID diagnosis. Because these are prevalent cases, however, we anticipate that there may be instances in which the GI symptom may occur after the diagnosis is made. In future studies, with additional years of follow-up after the introduction of the code, incident cases may be examined, and a more complete description of presenting symptoms at diagnosis can be ascertained.

There are several strengths of this study, including that we have used a large, national database demonstrated to be representative of all of the patients in the United States with commercial insurance (11,12). This allowed us to present details on the largest population of EGID patients yet reported in the literature and make national prevalence estimates standardized to the population of the United States, ages 0 to 64 years.

In conclusion, we demonstrate that the non-EoE EGIDs are very rare diseases, with prevalences ranging from 3.3 to 8.4 patients/100,000, and with fewer than 50,000 people affected in the United States with one of these conditions. Moreover, we find that the conditions tend to be more common in women and are associated with high upper and lower GI morbidity. The high proportion of coexisting atopic illness suggests these conditions may arise, in some instances, from a similar pathogenesis as EoE. Differences in sex ratios (female predominance for these other EGIDs as compared with male predominance for EoE), however, indicates that there may be important pathogenic differences for these conditions. As the time since introduction of these diagnostic codes increases, it will allow for additional studies to be conducted, which examine incidence and prevalence changes over time, and long-term disease sequelae.

REFERENCES

1. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology* 2007;133:1342–63.
2. Dellon ES. Diagnosis and management of eosinophilic esophagitis. *Clin Gastroenterol Hepatol* 2012;10:1066–78.
3. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol* 2011;128:3.e6–20.e6.
4. Dellon ES, Jensen ET, Martin CF, et al. The prevalence of eosinophilic esophagitis in the United States. *Clin Gastroenterol Hepatol* 2014;12:589.e1–96.e1.

5. Caldwell JM, Collins MH, Stucke EM, et al. Histologic eosinophilic gastritis is a systemic disorder associated with blood and extragastric eosinophilia, TH2 immunity, and a unique gastric transcriptome. *J Allergy Clin Immunol* 2014;134:1114–24.
6. Ko HM, Morotti RA, Yershov O, et al. Eosinophilic gastritis in children: clinicopathological correlation, disease course, and response to therapy. *Am J Gastroenterol* 2014;109:1277–85.
7. Lee CM, Changchien CS, Chen PC, et al. Eosinophilic gastroenteritis: 10 years experience. *Am J Gastroenterol* 1993;88:70–4.
8. Reed C, Woosley JT, Dellon ES. Mo1854 clinical characteristics, treatment outcomes, and resource utilization in children and adults with eosinophilic gastroenteritis. *Dig Liver Dis* 2015;47:197–201.
9. Talley NJ, Shorter RG, Phillips SF, et al. Eosinophilic gastroenteritis: a clinicopathological study of patients with disease of the mucosa, muscle layer, and subserosal tissues. *Gut* 1990;31:54–8.
10. Zhang L, Duan L, Ding S, et al. Eosinophilic gastroenteritis: clinical manifestations and morphological characteristics, a retrospective study of 42 patients. *Scand J Gastroenterol* 2011;46:1074–80.
11. Stempel DA, Mauskopf J, McLaughlin T, et al. Comparison of asthma costs in patients starting fluticasone propionate compared to patients starting montelukast. *Respir Med* 2001;95:227–34.
12. Kappelman MD, Rifas-Shiman SL, Kleinman K, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol* 2007;5:1424–9.
13. Jensen ET, Cook S, Allen JK, et al. Mo1119 What Is the Burden of GI Illness in the United States? It Depends on How You Ask. *Gastroenterology* 2014;146:S-561–2.
14. Rybnicek DA, Hathorn KE, Pfaff ER, et al. Administrative coding is specific, but not sensitive, for identifying eosinophilic esophagitis. *Dis Esophagus* 2013;27:703–8.
15. Dellon ES, Jensen ET, Martin CF, et al. Prevalence of eosinophilic esophagitis in the United States. *Clin Gastroenterol Hepatol* 2014;12:589.e1–96.e1.
16. Spergel JM, Book WM, Mays E, et al. Variation in prevalence, diagnostic criteria, and initial management options for eosinophilic gastrointestinal diseases in the United States. *J Pediatr Gastroenterol Nutr* 2011;52:300–6.
17. Bates AW. Diagnosing eosinophilic colitis: histopathological pattern or nosological entity? *Scientifica (Cairo)* 2012;2012:682576.
18. Reed C, Woosley JT, Dellon ES. Clinical characteristics, treatment outcomes, and resource utilization in children and adults with eosinophilic gastroenteritis. *Dig Liver Dis* 2015;47:197–201.
19. Chang JY, Choung RS, Lee RM, et al. A shift in the clinical spectrum of eosinophilic gastroenteritis toward the mucosal disease type. *Clin Gastroenterol Hepatol* 2010;8:669–75.
20. Klein NC, Hargrove RL, Sleisenger MH, et al. Eosinophilic gastroenteritis. *Medicine (Baltimore)* 1970;49:299–319.
21. Ko HM, Morotti RA, Yershov O, et al. Eosinophilic gastritis in children: clinicopathological correlation, disease course, and response to therapy. *Am J Gastroenterol* 2014;109:1277–85.
22. Lucendo AJ, Arias A. Eosinophilic gastroenteritis: an update. *Expert Rev Gastroenterol Hepatol* 2012;6:591–601.
23. Markowitz JE, Spergel JM, Ruchelli E, et al. Elemental diet is an effective treatment for eosinophilic esophagitis in children and adolescents. *Am J Gastroenterol* 2003;98:777–82.
24. Spergel JM. Eosinophilic esophagitis in adults and children: evidence for a food allergy component in many patients. *Curr Opin Allergy Clin Immunol* 2007;7:274–8.
25. Simon D, Marti H, Heer P, et al. Eosinophilic esophagitis is frequently associated with IgE-mediated allergic airway diseases. *J Allergy Clin Immunol* 2005;115:1090–2.
26. Bischoff SC. Food allergy and eosinophilic gastroenteritis and colitis. *Curr Opin Allergy Clin Immunol* 2010;10:238–45.
27. Odze RD, Bines J, Leichtner AM, et al. Allergic proctocolitis in infants: a prospective clinicopathologic biopsy study. *Hum Pathol* 1993;24:668–74.
28. Talley NJ. Gut eosinophilia in food allergy and systemic and autoimmune diseases. *Gastroenterol Clin North Am* 2008;37:307–32.
29. Hurrell JM, Genta RM, Melton SD. Histopathologic diagnosis of eosinophilic conditions in the gastrointestinal tract. *Adv Anat Pathol* 2011;18:335–48.