

# Prevalence of Eosinophilic Esophagitis in the United States

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**BACKGROUND & AIMS:** Eosinophilic esophagitis (EoE) has become a major cause of upper gastrointestinal morbidity in children and adults. However, there are few data on the nationwide prevalence of EoE. We aimed to estimate the prevalence of EoE in the United States.

**METHODS:** We collected health insurance claims from a large database that represented the U.S. commercially insured population. We analyzed data from 2008 to 2011, identifying cases of EoE by using a previously validated definition, and calculated a period prevalence by using data from 2009 to 2011. EoE was defined as any instance of the International Classification of Diseases, 9th revision code 530.13. We calculated the prevalence of the code in the database and standardized the estimate to the U.S. population.

**RESULTS:** Of 35,575,388 individuals in this database, 16,405 had at least 1 code for EoE. The mean age was 33.5 years, 65% were male, 55.8% had dysphagia, and 52.8% had a diagnostic code for at least 1 allergic condition. Among 11,569,217 individuals with continuous insurance coverage between mid-2009 and mid-2011, 6513 had at least 1 code for EoE. When standardized to the U.S. population, the estimated period prevalence of EoE was 56.7/100,000 persons, translating to approximately 152,152 cases in the U.S. Prevalence peaked in men 35–39 years old, with a rate of 114.6/100,000 persons.

**CONCLUSIONS:** Despite its relatively recent description, EoE is frequently diagnosed in the United States, with an estimated prevalence of 56.7/100,000 persons. This estimate depends on the accuracy of the International Classification of Diseases, 9th revision code, but it could be an underestimate, because knowledge of the code and recognition of EoE are increasing.

**Keywords:** Eosinophilic Esophagitis; Prevalence; Claims Data; Diagnosis.

**Podcast interview:** [www.gastro.org/cghpodcast](http://www.gastro.org/cghpodcast). Also available on iTunes; see editorial on page 597.

Eosinophilic esophagitis (EoE) is a recently recognized clinicopathologic entity that has become an increasingly common cause of upper gastrointestinal symptoms and morbidity in both children and adults.<sup>1,2</sup> It is currently defined as an allergic/immune-mediated disease characterized clinically by symptoms of esophageal dysfunction and histologically by a marked eosinophilic infiltrate in the esophageal mucosa in the absence of other competing causes of esophageal eosinophilia.<sup>3</sup> During the last decade there has been an exponential increase in the number of publications related to EoE, but many fundamental questions about EoE remain unanswered.

Although some aspects of the epidemiology of EoE are understood,<sup>4</sup> quantifying the prevalence of EoE in the United States has been hampered by the lack of a central medical record system in the United States, inconsistent application of EoE diagnostic definitions, and the difficulty of conducting population-based research at tertiary care referral centers with wide catchment areas. Nevertheless, a number of investigators have used a variety of strategies to report prevalence estimates ranging from less than 10 to more than 80 cases per 100,000.<sup>5–15</sup> The

**Abbreviations used in this paper:** EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; H2RB, histamine-2 receptor blocker; ICD-9, International Classification of Diseases, 9th revision; PPI, proton pump inhibitor.

potential for estimating EoE prevalence at the national level was made possible in 2008 with the approval of an International Classification of Diseases, 9th Revision (ICD-9) code for EoE (530.13). We have recently validated this code for use in administrative database research and found that the specificity of the code was extremely high.<sup>16</sup> To date, however, these codes have not been used on a national level in the United States to study the epidemiology of EoE.

The aims of the present study were to use a large health plan claims database to identify and characterize cases of EoE, to assess differences between children and adults with EoE, and to estimate the prevalence of EoE in the United States. These are important baseline data that can subsequently be used for appreciating the burden of this emerging disease.

## Methods

### *Study Design, Data Source, and Case Definition*

We performed a retrospective analysis of the IMS LifeLink PharMetrics Health Plan Claims Database (IMS Health Inc, Watertown, MA). This database contains longitudinal, integrated, fully adjudicated medical and pharmaceutical claims for more than 75 million individuals from more than 80 health plans and has been shown to be representative of a U.S. national commercially insured population.<sup>17,18</sup> Enrollees' demographic data including age, sex, and census region (East, South, Midwest, and West) were available.

EoE was defined as a single instance of the ICD-9 code 530.13, which was initially approved in 2008. We previously validated a single instance of this code for diagnosis of EoE by using health plan claims records among commercially insured patients and reported that this case definition has high specificity (>99%) balanced by a low sensitivity (37%).<sup>16</sup> Codes for gastroesophageal reflux disease (GERD) (530.81) and erosive esophagitis (530.11) were not used as exclusion criteria because the most recent consensus diagnostic criteria allow for the possibility for GERD and EoE to overlap,<sup>3</sup> erosive esophagitis does not distinguish EoE from GERD,<sup>19,20</sup> and the ICD-9 code for esophageal reflux may be nonspecific.

To characterize cases of EoE, data from 2008–2011 were analyzed in individuals ages 0–64 years who had at least 6 months of continuous health plan enrollment. To estimate a 2-year period prevalence, account for the delay in uptake for the new code that was noted after its introduction in 2008, and allow an adequate amount of time for the code to be used, data from July 1, 2009–June 30, 2011 were analyzed among individuals who had at least 24 months of continuous enrollment.

### *Associated Codes and Conditions of Interest*

In addition to the code for EoE, data on multiple other codes were extracted. These included ICD-9 codes for

upper gastrointestinal symptoms, esophageal disorders, and atopic disorders ([Supplementary Table 1](#)), as well as National Drug Codes for pharmaceutical agents such as histamine-2 receptor blockers (H2RBs), proton pump inhibitors (PPIs), corticosteroid agents that have been used topically or systemically to treat EoE such as fluticasone, budesonide, and prednisone,<sup>21–23</sup> and allergy medications.

### *Statistical Analysis*

Descriptive statistics characterized demographics, symptoms, associated diseases, and medications for subjects who met the study definition of EoE. Any patients meeting the case definition between 2008 and 2011 were included. For medication use, analyses were restricted to those patients with a pharmacy drug benefit ( $n = 12,390$ ). Bivariate analysis was performed to assess for differences in features of children (<18 years) and adults ( $\geq 18$  years) with EoE by using the Pearson  $\chi^2$  test.

To calculate the period prevalence, we identified all patients with continuous enrollment between July 1, 2009 and June 30, 2011. From these, we identified the number of patients who met the case definition for EoE during this period. We then divided this by the total number of patients in the database enrolled within this time frame. In restricting our estimate to patients continuously enrolled in this period, we assured that all patients included had equal opportunity for becoming a case if they had the disease. The overall prevalence, prevalence by sex, prevalence by census region, and prevalence by 5-year age increments were estimated within the database. Then, the overall prevalence estimate was standardized to the U.S. population by age and sex by using 2010 census data (for all individuals <65 years of age), and the absolute number of patients with EoE in the United States was extrapolated from the prevalence rate.

We also performed *a priori* sensitivity analyses with more restrictive coding definitions of EoE. These included (1) requiring one 530.13 code but excluding other conditions that could contribute to esophageal eosinophilia ([Supplementary Table 1](#)),<sup>3</sup> (2) requiring at least 2 occurrences of the 530.13 codes, and (3) requiring at least 2 occurrences of the 530.13 codes as well as excluding other conditions that could contribute to esophageal eosinophilia. Because it was the most conservative approach, data for this third definition are presented for the sensitivity analysis. This study was deemed exempt from review by the UNC Institutional Review Board.

## Results

### *Characteristics of Eosinophilic Esophagitis Cases*

A total of 35,575,388 individuals in the database from 2008–2011 with continuous enrollment of at least 6 months represented the initial source population. Of

these, 16,405 had at least 1 code for 530.13 and comprised the EoE case group. These patients were an average of 33.5 years old, and 64.9% were male (Table 1). The mean number of 530.13 ICD-9 claims per case was 7.4 (median, 4), and the number of identified cases substantially increased between 2008 and 2009, likely indicating increasing usage of the newly introduced code in 2008.

Cases of EoE frequently had associated ICD-9 codes for esophageal symptoms and conditions including dysphagia (55.8%), esophageal foreign bodies (12.5%), and esophageal strictures (28.7%) (Table 2). More than half of the EoE cases had an associated atopic disease, with rhinitis (41.8%) and asthma (23.4%) being most common. Approximately 10% of EoE patients had a prescription for an antihistamine, and the same proportion had a prescription for a leukotriene antagonist. PPIs were also commonly prescribed, with nearly half of patients receiving a prescription for a PPI (Table 2).

Children younger than the age of 18 comprised 24.0% of the cases of EoE. When children were compared with adults (Table 3), they were less likely to have dysphagia (32.1% vs 63.2%), esophageal foreign bodies (6.9% vs 12.5%), and esophageal strictures (5.5% vs 36.0%) and more likely to have abdominal pain (56.9% vs 43.7%), nausea or vomiting (42.7% vs 25.9%), failure to thrive (11.8% vs 0.4%), any allergic disease (65.6% vs 48.4%), asthma (37.7% vs 18.9%), and food allergies (9.8% vs 3.1%) ( $P < .001$  for all).

The distribution of demographic, symptom, and disease characteristics did not change on sensitivity analysis when the primary case definition was modified to exclude other conditions that could contribute to esophageal eosinophilia and/or to require at least two 530.13 diagnostic codes (data not shown).

**Table 1.** Demographic Characteristics of EoE Cases

|                                                                       | EoE cases <sup>a</sup><br>(N = 16,405) |
|-----------------------------------------------------------------------|----------------------------------------|
| Age (mean ± standard deviation, range) (y)                            | 33.5 ± 17.1<br>(0–64)                  |
| <18 years old, n (%)                                                  | 3933 (24.0)                            |
| Male, n (%)                                                           | 10,650 (64.9)                          |
| Number of 530.13 claims per person (mean ± standard deviation, range) | 7.4 ± 11.0<br>(1–335)                  |
| Region of country                                                     |                                        |
| East                                                                  | 3125 (19.1)                            |
| Midwest                                                               | 5512 (33.6)                            |
| South                                                                 | 5270 (32.1)                            |
| West                                                                  | 2498 (15.2)                            |
| Number of unique cases per year                                       |                                        |
| 2008                                                                  | 1227 (7.5)                             |
| 2009                                                                  | 5460 (33.3)                            |
| 2010                                                                  | 5270 (32.1)                            |
| 2011                                                                  | 4448 (27.1)                            |

NOTE. Data source: IMS LifeLink PharMetrics Health Plan Claims Database, January 2001–November 2011, IMS Health Incorporated. All Rights Reserved.  
<sup>a</sup>Patients with at least 1 or more instances of ICD-9 claim for 530.13 between 2008 and 2011.

**Table 2.** Clinical Features of EoE Cases

|                                                               | EoE cases <sup>a</sup><br>(N = 16,405) |
|---------------------------------------------------------------|----------------------------------------|
| Symptoms and diagnoses, n (%)                                 |                                        |
| Dysphagia                                                     | 9147 (55.8)                            |
| Esophageal foreign body                                       | 2043 (12.5)                            |
| Esophageal stricture                                          | 4709 (28.7)                            |
| Esophageal web/congenital stenosis                            | 846 (5.2)                              |
| Esophageal perforation                                        | 67 (0.4)                               |
| Abdominal pain/dyspepsia                                      | 7686 (46.9)                            |
| Heartburn                                                     | 1448 (8.8)                             |
| Pain in chest or throat                                       | 4669 (28.4)                            |
| Nausea or vomiting                                            | 4253 (25.9)                            |
| Failure to thrive                                             | 516 (3.1)                              |
| Allergic diseases, n (%)                                      |                                        |
| Any allergic disease                                          | 8663 (52.8)                            |
| Rhinitis                                                      | 6850 (41.8)                            |
| Sinusitis                                                     | 2493 (15.2)                            |
| Dermatitis                                                    | 1418 (8.6)                             |
| Urticaria                                                     | 297 (1.8)                              |
| Asthma                                                        | 3841 (23.4)                            |
| Food allergies                                                | 771 (4.7)                              |
| Medications, n (%) <sup>b</sup>                               |                                        |
| H2RBs                                                         | 459 (3.7)                              |
| PPIs                                                          | 6467 (52.2)                            |
| Systemic corticosteroids                                      | 3498 (28.2)                            |
| Steroid preparation that could be used topically <sup>c</sup> | 1431 (11.5)                            |
| Antihistamines <sup>d</sup>                                   | 1300 (10.5)                            |
| Leukotriene antagonists <sup>e</sup>                          | 1488 (12.0)                            |

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<sup>a</sup>Patients with at least 1 or more instances of ICD-9 claim for 530.13 between 2008 and 2011.

<sup>b</sup>Medication data derived from 12,390 EoE subjects with a pharmacy drug benefit.

<sup>c</sup>Asthma or nasal preparations of fluticasone, budesonide, beclomethasone, mometasone, ciclesonide, or flunisolide.

<sup>d</sup>Loratadine, desloratadine, fexofenadine, cetirizine, or levocetirizine.

<sup>e</sup>Montelukast, zafirlukast, or zileuton.

### Prevalence of Eosinophilic Esophagitis

A total of 11,569,217 individual subjects in the database from 2009–2011 with continuous enrollment of at least 24 months were used for the period prevalence calculations. In this population, there were a total of 6513 patients with at least 1 code for EoE, for an overall prevalence rate of 56.3/100,000 (Table 4). The prevalence was more than twice as high in male patients as in female patients (76.8 vs 37.4/100,000). For both genders, the peak prevalence was in the 35- to 39-year age range, and there was a decreasing prevalence after age 45 (Figure 1).

When the overall prevalence was standardized to the United States on the basis of age and sex, the rate was 56.7/100,000, which extrapolates to 152,152 cases in the United States. The prevalence in children (<20 years) was 50.5/100,000, and in adults (20–64 years) it was 58.9/100,000. After applying the more restrictive EoE case definition, we found 4515 cases of EoE in the

**Table 3.** Features of Adults vs Children With EoE

|                                                               | Children <sup>a,b</sup><br>(n = 3933) | Adults <sup>b</sup><br>(n = 12,472) |
|---------------------------------------------------------------|---------------------------------------|-------------------------------------|
| Age (mean ± standard deviation, range) (y)                    | 10.1 ± 5.0<br>(0–17)                  | 40.9 ± 12.1<br>(18–64)              |
| Male, n (%)                                                   | 2755 (70.1)                           | 7895 (63.3)                         |
| Region of country                                             |                                       |                                     |
| East                                                          | 888 (22.6)                            | 2237 (17.9)                         |
| Midwest                                                       | 1219 (31.0)                           | 4293 (34.4)                         |
| South                                                         | 1392 (35.4)                           | 3878 (31.1)                         |
| West                                                          | 434 (11.0)                            | 2064 (16.6)                         |
| Symptoms and diagnoses, n (%)                                 |                                       |                                     |
| Dysphagia                                                     | 1261 (32.1)                           | 7886 (63.2)                         |
| Esophageal foreign body                                       | 270 (6.9)                             | 2043 (12.5)                         |
| Esophageal stricture                                          | 218 (5.5)                             | 4491 (36.0)                         |
| Esophageal web/congenital stenosis                            | 25 (0.6)                              | 821 (6.6)                           |
| Esophageal perforation                                        | 4 (0.1)                               | 63 (0.5)                            |
| Abdominal pain/dyspepsia                                      | 2236 (56.9)                           | 5450 (43.7)                         |
| Heartburn                                                     | 144 (3.7)                             | 1304 (10.5)                         |
| Pain in chest or throat                                       | 682 (17.3)                            | 3987 (32.0)                         |
| Nausea or vomiting                                            | 1679 (42.7)                           | 4253 (25.9)                         |
| Failure to thrive                                             | 465 (11.8)                            | 51 (0.4)                            |
| Allergic diseases, n (%)                                      |                                       |                                     |
| Any allergic disease                                          | 2578 (65.6)                           | 6085 (48.8)                         |
| Rhinitis                                                      | 2135 (54.3)                           | 4715 (37.8)                         |
| Sinusitis                                                     | 567 (14.4)                            | 1926 (15.4)                         |
| Dermatitis                                                    | 669 (17.0)                            | 749 (6.0)                           |
| Urticaria                                                     | 126 (3.2)                             | 171 (1.4)                           |
| Asthma                                                        | 1481 (37.7)                           | 2360 (18.9)                         |
| Food allergies                                                | 387 (9.8)                             | 384 (3.1)                           |
| Medications, n (%) <sup>c</sup>                               |                                       |                                     |
| H2RBs                                                         | 206 (7.1)                             | 253 (2.7)                           |
| PPIs                                                          | 1589 (54.8)                           | 4878 (51.4)                         |
| Systemic corticosteroids                                      | 539 (18.6)                            | 2959 (31.2)                         |
| Steroid preparation that could be used topically <sup>d</sup> | 630 (21.7)                            | 801 (8.4)                           |
| Antihistamines <sup>e</sup>                                   | 473 (16.3)                            | 827 (8.7)                           |
| Leukotriene antagonists <sup>f</sup>                          | 665 (22.9)                            | 823 (8.7)                           |

NOTE. Analyses are for patients with at least 1 or more instances of ICD-9 claim for 530.13 between 2008 and 2011.

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<sup>a</sup>Children defined as <18 years of age.

<sup>b</sup>For comparisons between adults and children,  $P < .001$  for all rows except for sinusitis ( $P = .12$ ).

<sup>c</sup>Medication data derived from 12,390 EoE subjects (2900 children and 9490 adults) with a pharmacy drug benefit.

<sup>d</sup>Asthma or nasal preparations of fluticasone, budesonide, beclomethasone, mometasone, ciclesonide, or flunisolide.

<sup>e</sup>Loratadine, desloratadine, fexofenadine, cetirizine, or levocetirizine.

<sup>f</sup>Montelukast, zafirlukast, or zileuton.

database (Table 4), for a prevalence of 39.5/100,000. When standardized to the United States, the rate remained 39.5/100,000, which extrapolates to 105,977 cases.

## Discussion

During the past decade, EoE has emerged as a major cause of upper gastrointestinal morbidity in both children and adults.<sup>3,5–7,10,11,14,19,24,25</sup> However, estimates of the prevalence of EoE in the United States have been

limited by fragmented medical record systems and a lack of validated or consistently applied disease definitions. The aim of this study was to characterize cases of EoE and estimate the prevalence of EoE in the United States in a large database with methodology not previously possible in this field. By using a validated coding definition of EoE for detecting cases of EoE, we estimate that the prevalence of EoE in the United States is 56.7/100,000. We also note that the prevalence of EoE decreases after age 45, which is unexpected because for a chronic and nonfatal disease, prevalence should typically continue to increase with age. It is interesting to speculate whether this implicates an as yet unidentified early life exposure during the past 4 decades as an etiologic factor.

Our prevalence estimate, obtained from a large health plan claims database and with the largest number of cases yet analyzed in the EoE literature, is on the same order of magnitude of previously reported values from smaller studies (Table 5), lending empiric validity. For example, studies in children at single centers with well-defined catchment areas have estimated the prevalence of EoE to be 43–91/100,000.<sup>5,7,9,10</sup> In adults, several studies have previously reported the prevalence to be 23–55/100,000.<sup>6,11,14</sup> A recent administrative study in a military insurance population found a lower number of cases than expected, perhaps indicating lack of uptake of the ICD-9 code for EoE or a healthier population not representative of the United States.<sup>15</sup> There was also a survey of adult and pediatric gastroenterologists and allergists/immunologists that estimated the number of cases for each provider and calculated an EoE prevalence of 52/100,000.<sup>13</sup> Because of the large numbers of both individuals and EoE cases in the database in the present study, we believe that although our estimate is of the same order of magnitude as these other studies, it may be more precise. However, it is difficult to directly compare some of the prevalence values because ours is a 2-year period prevalence, and the previously reported values range from 1-year point prevalences to cumulative prevalences representing more than a decade of accrued cases.

To place our reported prevalence rates into context, it can be helpful to make a comparison with inflammatory bowel disease, another inflammatory condition of the gastrointestinal tract. The prevalences of Crohn's disease and ulcerative colitis in a pediatric population are 43 and 28/100,000, respectively, and in adults they are 201 and 238/100,000, respectively.<sup>18</sup> Therefore, within the relatively short time frame in which EoE has been recognized as a unique disease entity, the prevalence of EoE in all subjects has approached that of pediatric inflammatory bowel disease.

A key question in interpreting the results from an administrative database study such as this is whether the case definition is accurate and, if not, what degree of misclassification may be present. One answer can be provided by examining the clinical characteristics of the

**Table 4.** Prevalence of EoE in the Study Database<sup>a</sup>

| Source population  | Primary EoE case definition (at least one 530.13 code) |                          | Restrictive EoE case definition (>1 code + exclusions) |                          |
|--------------------|--------------------------------------------------------|--------------------------|--------------------------------------------------------|--------------------------|
|                    | EoE cases, n (%)                                       | Prevalence (per 100,000) | EoE cases, n (%)                                       | Prevalence (per 100,000) |
| Age group          |                                                        |                          |                                                        |                          |
| <20 y <sup>b</sup> | 3,587,571                                              | 1813 (27.8)              | 1348 (29.9)                                            | 37.6                     |
| 20–64 y            | 7,981,646                                              | 4700 (72.2)              | 3167 (70.1)                                            | 39.7                     |
| Sex                |                                                        |                          |                                                        |                          |
| Male               | 5,544,574                                              | 4257 (65.4)              | 2978 (66.0)                                            | 65.9                     |
| Female             | 6,024,643                                              | 2256 (34.6)              | 1537 (34.0)                                            | 34.0                     |
| Region             |                                                        |                          |                                                        |                          |
| East               | 2,226,470                                              | 1054 (16.2)              | 715 (15.8)                                             | 32.1                     |
| South              | 4,529,151                                              | 2507 (38.5)              | 1739 (38.5)                                            | 38.4                     |
| Midwest            | 3,569,432                                              | 2567 (39.4)              | 1809 (40.1)                                            | 50.7                     |
| West               | 1,244,164                                              | 385 (5.9)                | 252 (5.6)                                              | 20.3                     |
| Overall prevalence | 11,569,217                                             | 6513 (100)               | 4515 (100)                                             | 39.0                     |

NOTE. Data source: IMS LifeLink PharMetrics Health Plan Claims Database, January 2001–November 2011, IMS Health Incorporated. All Rights Reserved.

<sup>a</sup>Data calculated for time frame July 1, 2009–June 30, 2011 for those enrolled continuously for 24 months.

<sup>b</sup>Children were defined as age <20 years for purposes of standardization in 5-year increments of age.

identified EoE cases. We found the EoE cases to be relatively young, with a male predominance, numerous esophageal symptoms, and high rates of concomitant atopic disease. All of these features, including previously reported differences between adults and children, are expected for a population of EoE patients<sup>1,3,19,26–31</sup> and support that we are capturing true EoE cases. Related to this, an interesting point is that frequency of esophageal perforation in this patient sample, 0.4%, is essentially identical to what has been reported in a meta-analysis of perforation as a complication of esophageal dilation for treatment of esophageal strictures in EoE patients.<sup>32</sup> However, topical steroid medications were not

commonly prescribed (22% of children, 8% of adults). Although one explanation for this is that these are not true EoE patients, a more likely interpretation takes into account that this study detected prevalent, not incident, cases of EoE. Whereas one would expect incident EoE cases to frequently receive a topical steroid for initial treatment,<sup>33</sup> a prevalent case may be asymptomatic or on dietary restriction therapy and thus is not taking a medication, or may have had a medication previously prescribed outside of the enrollment window for this study.

Although it is reassuring that the clinical features of the patients identified in this study generally reflect what

**Figure 1.** Prevalence of EoE (cases per 100,000) as stratified by sex and by 5-year increments of age. Data source: IMS LifeLink PharMetrics Health Plan Claims Database, January 2001–November 2011, IMS Health Incorporated. All Rights Reserved.

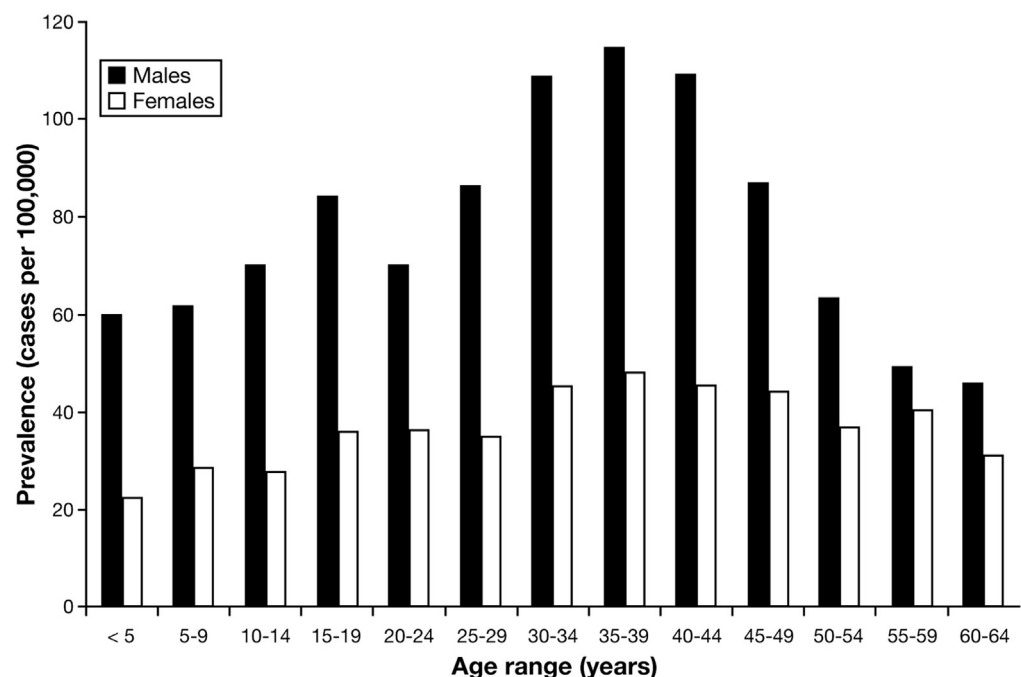


**Table 5.** Estimates of the Prevalence of EoE in the Medical Literature

| Author, year                  | Location                  | Study type, population                    | Population age      | N (population) | N (EoE) | Time of estimate | Prevalence estimate (per 100,000) |
|-------------------------------|---------------------------|-------------------------------------------|---------------------|----------------|---------|------------------|-----------------------------------|
| Noel, 2004 <sup>5</sup>       | Hamilton County, OH       | Single center, retrospective, pediatric   | Pediatric           | —              | 103     | 2000–2003        | 43.0                              |
| Cherian, 2006 <sup>7</sup>    | Perth, Australia          | Single center, retrospective, pediatric   | Pediatric           | —              | 285     | 1995, 1999, 2004 | 89.0                              |
| Gill, 2007 <sup>9</sup>       | Huntington region, WV     | Single center, retrospective, pediatric   | Pediatric           | ~600,000       | 44      | 1995–2004        | 73.0                              |
| Buckmeier, 2008 <sup>10</sup> | Hamilton County, OH       | Single center, retrospective, pediatric   | Pediatric           | —              | —       | 2000–2006        | 90.7                              |
| Dalby, 2010 <sup>12</sup>     | Southern Denmark          | Multicenter, prospective, pediatric       | Pediatric           | 256,164        | 6       | 2005–2007        | 2.3                               |
| Straumann, 2005 <sup>6</sup>  | Olten County, Switzerland | Single center, retrospective, adult       | Adult               | ~100,000       | 23      | 1989–2004        | 23.0                              |
| Ronkainen, 2007 <sup>8</sup>  | Northern Sweden           | Population-based, prospective, adult      | Adult               | 1,000          | 4       | 1998–2001        | 400                               |
| Hruz, 2011 <sup>14</sup>      | Olten County, Switzerland | Single center, retrospective, adult       | Adult               | ~90,000        | 39      | 1989–2009        | 42.8                              |
| Spergel, 2011 <sup>13</sup>   | United States             | Physician survey                          | —                   | 1,863 MDs      | —       | 2010             | 52.2                              |
| Prasad, 2009 <sup>11</sup>    | Omstead County, MN        | Population-based, retrospective, all ages | Pediatric and adult | ~140,000       | 78      | 1976–2005        | 55.0                              |
| Ally, 2012 <sup>15</sup>      | United States (military)  | Administrative data, all ages             | Pediatric and adult | 10,180,515     | 987     | 2009             | 9.7                               |
| Present study <sup>a</sup>    | United States             | Administrative data, all ages             | Pediatric and adult | 11,569,217     | 6513    | 2009–2011        | 56.7                              |

<sup>a</sup>Standardized to U.S. age distribution.

would be expected for EoE cases, an arguably more important strategy for minimizing misclassification is with validation of the case definition. Importantly, we previously validated our primary definition of EoE as at least one instance of the 530.13 ICD-9 code by using administrative claims data linked to individual patient records.<sup>16</sup> This definition was more than 99% specific by using a reference standard population that met consensus diagnostic guidelines for EoE,<sup>1,3</sup> and this level of specificity held without including an endoscopy code in the case definition. However, because this validation used administrative data from a tertiary care center,<sup>16</sup> it is possible that specificity might have been overestimated or that sensitivity and specificity could be lower in general practice and if consensus diagnostic guidelines are not fully followed.<sup>34</sup> It is also possible that some patients had esophageal eosinophilia caused by GERD and might have been misdiagnosed with EoE, and because PPIs are available over-the-counter, all PPI use cannot be captured in this database. Therefore, it is possible that some patients with PPI-responsive esophageal eosinophilia are misclassified as having EoE in the administrative data. To further address these possibilities of misclassification, we performed an analysis with an even more restrictive case definition of EoE.

Applying this definition, the clinical characteristics were unchanged when compared with the primary case definition. In addition, because almost 80% of the identified EoE cases had more than one ICD-9 claim for 530.13, with a mean number of these codes greater than 7 and a median greater than 4, we anticipate that it would be very unlikely that this frequency of diagnostic coding would represent misclassification or a coding error.

Because of the low sensitivity, it is likely that some cases of EoE have not been identified, and hence the prevalences reported here may, in fact, underestimate the true prevalence in the U.S. population. First, not all individuals with EoE come to medical attention, and others may be misdiagnosed or may not have undergone diagnostic evaluation for EoE. Second, not all individuals diagnosed with EoE are captured by the ICD-9 code, considering its recent introduction in 2008, so there are limitations of using a new ICD-9 code for a disease with an evolving definition and increasing recognition. To minimize this, we began our period-prevalence estimate a full year after code introduction. Nevertheless, the sensitivity of this code may be as low as 37%.<sup>16</sup> This implies that the true prevalence of EoE could be as high as 153.2/100,000, which extrapolates to 411,222 cases of EoE in the United States.

Besides misclassification, there are other potential limitations to this study that should be acknowledged. First, we are unable to present information that is not captured in administrative claims databases such as race/ethnicity, socioeconomic status, practice setting, endoscopic abnormalities, histology findings, over-the-counter medications, or indication for medication prescription (for example, was a topical steroid prescribed for asthma or EoE). We also do not have geographic data more specific than the 4 large census regions. Second, because the 530.13 code was newly introduced in 2008, we could not assess time trends and could not accurately estimate the incidence of the condition. Incidence calculations will be possible in planned future studies where there will be sufficient lead time without an EoE code to be confident that a diagnosis is incident, not prevalent.

These potential limitations are countered by the strengths of this study. This is a large database that has been demonstrated to be representative of all patients in the United States with commercial insurance.<sup>17,18</sup> As such, it yielded the largest sample of EoE cases yet to be reported in the literature. From this, we were able to calculate prevalence rates of EoE in the database and also standardize them to the U.S. population (ages 0–64), allowing extrapolation to the total number of EoE cases in this country.

In conclusion, this analysis of a large, nationally representative administrative database of commercially insured patients estimates that the prevalence of EoE in the United States is 56.7 cases/100,000. Although the limits on this estimate range from 39.5–153.2/100,000, these values may still underestimate the true prevalence because both knowledge of the new ICD-9 code and recognition of EoE are increasing. This estimated prevalence is approaching that of pediatric inflammatory bowel disease and represents a remarkable burden of disease for a condition that has only been recognized for the past 2 decades.

## Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at [www.cghjournal.org](http://www.cghjournal.org), and at <http://dx.doi.org/10.1016/j.cgh.2013.09.008>.

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**Supplementary Table 1.** ICD-9 Diagnostic Codes Used in This Study

|                                          | Code                                                 |
|------------------------------------------|------------------------------------------------------|
| Symptom or diagnosis related to EoE      |                                                      |
| Dysphagia                                | 787.2                                                |
| Esophageal foreign body                  | 935.1                                                |
| Esophageal stricture                     | 530.3                                                |
| Esophageal web/congenital stenosis       | 750.3                                                |
| Esophageal perforation                   | 530.4                                                |
| Abdominal pain/dyspepsia                 | 789.0x/536.8                                         |
| Heartburn                                | 787.1                                                |
| Pain in chest or throat                  | 784.1/786.5x                                         |
| Nausea or vomiting                       | 787.0x                                               |
| Failure to thrive                        | 779.3x/783.3                                         |
| Rhinitis                                 | 477.x/472.0                                          |
| Sinusitis                                | 473.x                                                |
| Dermatitis                               | 691.8, 692.1–692.6                                   |
| Urticaria                                | 708.0, 708.3                                         |
| Asthma                                   | 493.0x, 493.1, 493.81, 493.82, 493.9x                |
| Food allergies                           | 995.6x/995.7                                         |
| Symptom or diagnosis used for exclusions |                                                      |
| Esophageal malignancy                    | 150.x                                                |
| Achalasia                                | 530.0                                                |
| Eosinophilic gastroenteritis             | 535.7x/558.41                                        |
| Tracheoesophageal fistula                | 530.84                                               |
| Barrett's esophagus                      | 530.85                                               |
| Candidal esophagitis                     | 112.0/112.84                                         |
| Human immunodeficiency virus infection   | 0.42                                                 |
| Leukemias and related malignancies       | 200.x/201.x/202.x/203.x/204.x/205.x/206.x/207.x/208x |