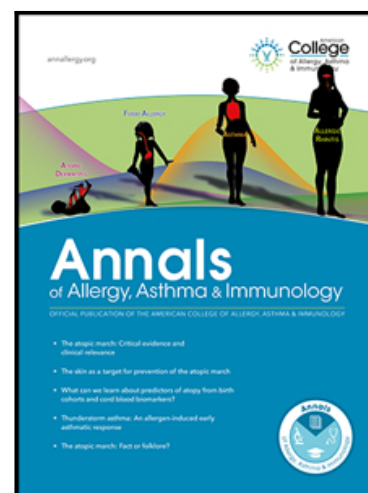


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An In-Depth Characterization of a Large Cohort of Adults Patients with Eosinophilic Esophagitis

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Title: An In-Depth Characterization of a Large Cohort of Adults Patients with Eosinophilic Esophagitis

Short Title: Characterization of a Large Adult EoE Cohort

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Abbreviations/Acronyms:

ADD – attention deficit disorder; ADHD – attention deficit hyperactivity disorder; AEC – Absolute eosinophil count; AR – allergic rhinitis; ASD – autism spectrum disorder; CI – confidence interval; DM – diabetes mellitus; EGD – esophagogastroduodenoscopy; EMR – Electronic Medical Record; EoE – Eosinophilic Esophagitis; Eos – Eosinophils; FFED – four food elimination diet; GERD – gastroesophageal reflux disease; HPF –high-powered field; H2R – Histamine 2 Receptor; IBD – inflammatory bowel disease; ICD –International Statistic Classification of Diseases and Related Health Problems; IRB – Institutional Review Board; OCD – obsessive compulsive disorder; PAR – perennial allergic rhinitis; PFAS – Pollen food allergy syndrome; PPI – proton pump inhibitor; PPI-REE – PPI responsive EoE; RR – relative risk; SAR – seasonal allergic rhinitis; SFED – six food elimination diet; SLE – systemic lupus erythematosus; UC – ulcerative colitis; UPenn – University of Pennsylvania; UPHS – University of Pennsylvania Health Systems

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47 Introduction

48 Eosinophilic esophagitis (EoE) is a chronic, allergic, immune-mediated disease
49 characterized by esophageal dysfunction thought to be mediated by food and environmental
50 allergen exposure.¹ Endoscopically, it is characterized by esophageal epithelial inflammation
51 with greater than 15 eosinophils per high-powered field (Eos/HPF) on esophageal biopsy.^{2,3} The
52 overall incidence and prevalence have been increasing over the last several decades, and in
53 addition to functional symptoms, it greatly detracts from patients' quality of life.⁴⁻⁷

54 There has been great interest in evaluating the association between EoE and a variety of
55 medical conditions. It has been widely shown that patients with EoE report personal or family
56 history of atopic conditions such as asthma, environmental allergies, atopic dermatitis, and food
57 allergies. Prior studies have estimated that 28-86% of adults and 42-93% of children with EoE
58 have at least one comorbid atopic condition.^{1,8-11} There have also been studies evaluating
59 associations between EoE and other conditions including celiac disease in pediatrics,⁹ chronic
60 rhinosinusitis, pollen food allergy syndrome, inflammatory bowel disease, connective tissue
61 disorders, and autism spectrum disorders.¹²⁻²⁰ However, the strength of these associations is not
62 well-delineated.

63 In this study, we perform an in-depth characterization of a large cohort of adult patients
64 with biopsy-proven EoE. In addition to evaluating the cohort's demographics, endoscopic
65 findings, therapy, associated atopic conditions, we evaluate additional parameters such as
66 smoking history, prevalence of pollen food allergy syndrome, drug allergy, anaphylaxis,
67 autoimmune and neuropsychiatric comorbidities, which have not been extensively evaluated in
68 previous studies, nor in such a large, manually verified adult cohort.

69

70 **Methods**

71 Cohort Generation and Data Extraction

72 The University of Pennsylvania Health Systems (UPHS) is one of the largest providers of
73 allergy care services in the tri-state area (Pennsylvania, New Jersey, and Delaware). We
74 extracted all available data since the advent of the UPHS electronic medical record (EMR; Epic
75 Penn Chart Systems) through 4/7/2017, which consisted of a total of 3,617,345 adult patients
76 aged 18 and older. The University of Pennsylvania (UPenn) institutional review board (IRB)
77 #827167 approved the study.

78 Associated medical conditions were identified by ICD-9 and ICD-10 codes (**eTable 1**).
79 For prevalence calculations, individual patients with each diagnosis were counted.

80

81 Validation of ICD Codes and Other Diagnoses via Chart Review

82 We performed manual chart review to determine the extent to which ICD codes and
83 extracted data correctly reflected the presence of each diagnosis of interest. We performed
84 manual chart review of all 1,218 EoE patients identified by ICD-9 and 10 codes. We also
85 performed a manual review of 100 charts of patients with diagnoses of asthma, allergic rhinitis,
86 eczema, food allergy, and celiac disease to ensure a more accurate estimation and comparison of
87 these diseases with those within the EoE population.

88 Requirement for inclusion in the EoE cohort was diagnosis of biopsy-proven EoE in
89 accordance with consensus guidelines, namely after a trial of proton pump inhibitor (PPI)
90 therapy.¹⁶ For about 10% of the 88 patients who were diagnosed in their childhood, data was not
91 available as to whether they had undergone an adequate trial of PPI prior to the biopsy results.
92 Diagnoses of asthma, allergic rhinitis, eczema, IgE-mediated food allergy, and celiac disease

were also made in accordance with established practice parameters.²¹⁻²⁵ Manual review of information listed under a patient's allergy tab were also used in conjunction with ICD codes to assist in identification of food allergies.

Parameters Evaluated

Via manual chart review, we evaluated standard demographic characteristics. We also evaluated family history of EoE, presenting symptom, number of Eos/HPF on the initial and most recent esophagogastroduodenoscopy (EGD), history of impaction and whether it required endoscopic intervention, history of end organ damage (stricture, rings, fibrosis) and whether this required endoscopic dilatation, serum absolute eosinophil count (AEC) and total serum IgE. For patients with multiple AEC or total serum IgE values available in their chart, we used the highest available values. We evaluated for other gastrointestinal characteristics such as comorbid symptoms of gastroesophageal reflux disease (GERD), diagnosis of proton pump inhibitor responsive EoE (PPI-REE), and history of *H. pylori* infection. (Given virtually all of the documentation in the charts reviewed were from before the newest consensus guidelines suggesting EoE and PPI-REE may be variations of the same disease entity,²⁶ we chose to report EoE and PPI-REE as separate entities). Therapy was divided into 4 categories: medical therapy, diet therapy, both, or neither. Patients who had concurrent IgE-mediated food allergies (and therefore avoided those respective food allergens) were not included in the diet therapy group. Finally, we also evaluated comorbid atopic, autoimmune, and neuropsychiatric conditions.

Results

Cohort Demographics and Social/Familial Characteristics

From the 3,617,345 adult UPHS database, we extracted 1,218 patients with a diagnosis code of EoE; 135,590 with asthma; 127,915 with seasonal and perennial allergic rhinitis; 107,499 with eczema; 19,311 with a diagnosis of food allergy, and 4,240 with a diagnosis of celiac disease (**Figure 1**).

After manual chart review of the 1,218 patients with EoE extracted via ICD-9 and ICD-10 codes (**eTable 1**), we confirmed the diagnosis of biopsy-proven EoE after a trial of proton pump inhibitor in 950 patients (78%). The accuracy of ICD codes after manual chart review ranged from 92-98% for the diagnoses of asthma, allergic rhinitis, eczema, food allergy, and celiac disease (**Figure 1**).

Demographic characteristics of these patients are supplied in **Table 1**. This population is primarily male and Caucasian, consistent with other studies.²⁷ The current median age of this cohort is 39 years (range 18-93 years). The median age of diagnosis was 33 years (range 5-89 years). The majority, 81%, were never smokers. A positive family history of EoE was seen in 32 patients (3.4%), of which the majority (84%) was in a first-degree relative (**Table 1**).

Laboratory and Endoscopic Findings

Presenting symptoms and EGD findings are listed in **Table 2**. The most common presenting symptom was dysphagia (64%). Five hundred twenty-four patients (55%) reported a history of at least one impaction including 200 (38%) that required at least one endoscopic removal. Five hundred twenty-seven patients (56%) had evidence of end organ damage on EGD, including strictures, rings, and fibrosis, with over half requiring at least one EGD dilatation (**Figure 2**).

We assessed serum laboratory studies (**Table 2**). Six hundred seventy-nine patients (72%) had at least one available complete blood count (CBC). The average AEC of this group was 446 K/uL (range 0-5,080 K/uL). The patient with an AEC of 5,080 had concomitant eosinophilic granulomatosis with polyangiitis (EGPA). Interestingly, the median and average total IgE values were within the normal range.

Treatments

Characteristics of therapy are outlined in **Figure 3a**. All data points reflect therapy at the time of chart review. The majority of patients were on medical therapy. A total of 175 patients were on diet therapy (this includes the “diet only” as well as the “diet and medical therapy” groups) (**Figures 3b-c**). Of these patients on diet therapy, 36% used the six-food elimination diet (SFED). Twenty percent used the four-food elimination diet (FFED), eliminating dairy, egg, wheat, and legumes. Thirty percent were on diets that removed two or more foods that historically caused EoE. The most common single food elimination diet was milk (13%). One percent each was on single food elimination of peanut/legumes, tree nuts, egg, and soy. Two

percent were on an elemental diet. Nineteen percent of all patients on diet therapy were documented reporting periodic noncompliance with their elimination diets.

Twenty-three patients (2% of the cohort) had tried diet therapy at some point and failed. These patients were not included in the overall diet therapy group. Of these, 16 patients had tried SFED but failed (i.e., unable to continue due to noncompliance or felt their symptoms had not improved with therapy). Seven patients had reported noncompliance with elemental diet in the past and are no longer on any diet therapy.

Eight hundred eighty-one patients (93%) were on ~~traditional EoE~~ medical therapy, such as a proton pump inhibitor (PPI) (61%) or swallowed steroids (14%) (**Figure 3b**). Of those on PPI monotherapy, 40% were in histologic remission on their most recent EGD. Fifteen percent had tried a swallowed steroid previously but stopped due to various reasons, including frequent noncompliance leading to termination, intolerance, lack of efficacy, and issues with insurance coverage. For those on swallowed steroids only, 63% took fluticasone; 35% took budesonide, and 1 patient took beclomethasone. Two hundred and twelve patients (24%) were on both a PPI and swallowed steroids. The majority of these patients (about 7 times more) were on PPI+swallowed fluticasone compared with PPI+swallowed budesonide. There was documentation that 5 patients reported non-compliance with swallowed steroids but continued with treatment. Three patients had stopped swallowed fluticasone due to thrush and 1 patient self-titrated off fluticasone; these patients were not included in the 129 on a swallowed steroid. Sixty-nine patients were on nontraditional medical therapy such as histamine 2 blockers (such as ranitidine), cromolyn, or sucralfate. Six patients (9%) reported good symptom control on ranitidine (of which 4 had documented symptoms of GERD). These patients' initial Eos/HPF ranged from 20 to 77 and all had documentation of end organ damage (strictures, rings, or

fibrosis) and/or history of impaction. Out of these 6, 5 had histologic improvement (down to 0 Eos/HPF) on their most recent EGD while on ranitidine only. One patient was on cromolyn (with no comorbid mast cell disorder), with report of good symptom control but no repeat EGD to evaluate histologic response. Two patients were documented as saying they were very reluctant to be on any medication for their EoE; they were not on any diet therapy either.

Other GI Characteristics: GERD, PPI-REE, and *H. pylori*

Five hundred and eight patients (54%) were documented by a gastroenterologist as having symptoms consistent with GERD, with eleven of these patients having documented barium esophagrams consistent with reflux. Three hundred and sixty-four patients (38%) were considered by a gastroenterologist to have possible PPI-REE upon initial evaluation, the majority ultimately confirmed after a trial of PPI and subsequent EGD. Eighteen patients (2%) had a documented history of infection with *H. pylori* and had undergone appropriate treatment.

Prevalence of Comorbid Atopic Conditions

Prior studies have shown a strong association between EoE and atopic conditions in both the adult and pediatric EoE populations.^{1,8-11} In our study, we made a similar observation for each atopic condition being 10-20 fold more common in the EoE cohort compared with the general UPHS population (**Table 3**). We could not investigate the seasonality component of increased EoE symptoms because this was generally not documented in patients' charts.

These features of increased atopic conditions extend to food allergy with a 50-fold increase (**Table 3**), 60-fold increase for medication allergy, with similar increase for latex allergy and anaphylaxis (**Table 3 and eTable 2**). The highest rate was for pollen-food allergy syndrome

(PFAS) with a 600-fold increase compared with the control population. Interestingly, the average IgE for the PFAS cohort was 311 IU/mL, slightly higher than the overall EoE cohort (243 IU/mL). The most common food allergens in the EoE cohort were tree nuts (24%), shellfish, (22%), and peanut (13%). The majority of patients had documented allergy to one food group only (64%).

Autoimmune Comorbidities

Due to publication on the association between EoE and autoimmune comorbidities,^{12,14,18} we examined all autoimmune diseases. In our population, 81 EoE patients (9%) had at least one comorbid autoimmune disease (**Table 3**), and many autoimmune diseases were more common in EoE with the exception of Type 1 diabetes mellitus and Graves' disease (**Table 4**). Nineteen EoE patients had comorbid celiac disease (2%) compared with the UPHS celiac disease prevalence of 0.11%.

Neuropsychiatric Comorbidities and Developmental Disorders

There have been reports in both the adult and pediatric populations about adverse psychosocial effects from the management of chronic EoE.²⁸ As a result, we evaluated neuropsychiatric comorbidities (**Table 5**) based on EMR documentation (medical problem listed, medications, neuropsychiatric evaluation). The overall prevalence of neuropsychiatric disorders in the entire cohort was 31% and was more prevalent in the EoE cohort compared with the general UPHS population. More recently, a pediatric study has shown an increased incidence of neuropsychiatric developmental disorders such as autism spectrum disorder (ASD) in patients with EoE.²⁹ In our study, 9 patients (1%) had documentation of an autism spectrum disorder

(ASD) compared with 0.03% in the UPHS population (**eTable 3**). The average age of diagnosis of EoE in these 9 ASD patients was 25 years of age, with an age range of 10-32 years.

Discussion

EoE remains a disease of increasing incidence associated with significant morbidity and decreased quality of life in both the adult and pediatric populations. Here we provide one of the largest in-depth characterizations of adult EoE patients in a large tertiary care and referral center.

The prevalence of EoE in our UPHS patient population, about 26 out of 100,000 patients, is about on par with data in the literature, estimated as 12.8 to 55 per 100,000.^{4,7,20} Demographics of our EoE population were overall consistent with what has been previously reported in the literature, predominantly non-Hispanic, Caucasian men in their thirties who presented with dysphagia.^{2-3,7,9,11,20}

Smoking and EoE

Our cohort consisted of predominantly never-smokers. It is unclear whether this may be a result of selection bias as EoE is most prevalent in middle-aged white males. While data on risk factors of EoE are limited, there are data that suggest an inverse correlation between smoking and EoE.³⁰ This finding is opposite to what has been previously hypothesized given the pro-inflammatory attributes of cigarette smoke. There have been studies that have consistently found that cigarette smoke has the ability to reduce eosinophilic inflammation in both mouse models and in patients with asthma.³¹

Endoscopic Findings and Intervention

In prior studies, impaction has been seen in up to 54% of EoE patients and esophageal strictures in up to 31% percent of patients. In our population the prevalence of food impaction was about the same as in the literature, but our incidence of strictures was higher, 56%. There was also a higher prevalence of endoscopic intervention than previously reported, possibly due to UPHS being an academic referral center and being solely adult practice.^{32,33}

Treatment

In terms of medical therapy, a large majority of patients were on PPI monotherapy, which may reflect difficulty with swallowed steroid compliance. And interestingly, for patients on swallowed steroids, fluticasone was two times more commonly prescribed as budesonide.

Curiously, five patients had clinical and histologic improvement on ranitidine only, which is not standard therapy for EoE. Recent studies have looked at the role of the histamine 2 receptor (H2R) in EoE pathogenesis. One study found increased histamine receptors in active EoE biopsies (compared with inactive EoE biopsies and controls) and that H2R was the most abundantly expressed of all the histamine receptors.³⁴ Further investigation into histamine receptor signaling in EoE is needed to see if H2R blockers may become a viable treatment in the future. Another possible explanation could be related to the role of aeroallergens in EoE pathogenesis. All five of these patients had documentation of SAR. Three out of five also had documentation of PFAS. It is quite possible that the time of evaluation was an “off season,” thereby contributing to (and confounding) clinical improvement, however data to support this hypothesis was not available from these patients’ charts. Alternatively, these patients could have been misdiagnosed and actually have had GERD.

Almost a fifth of patients on diet therapy reported periodic noncompliance, which serves to show how difficult and intrusive dietary changes can be for the adult patient, even for those on single food elimination diets. This is in contrast to the increased dietary compliance reported in younger children compared with adults and even older children.³⁵

Atopic Comorbidities

While atopic comorbidities such as asthma, allergic rhinitis, eczema, and food allergy in our population are similar to what has been reported in the adult and pediatric EoE populations,^{3,7-11,19} there was an increased prevalence of PFAS that has not been previously reported in such a large adult cohort, RR 486 (CI 441-535). While EoE and PFAS are both Th2-mediated immune mechanisms, the former, unlike the latter, is not traditionally characterized as IgE-mediated. Additional studies are needed to evaluate similarities in the pathogenesis of EoE and PFAS.

There was also an increased prevalence of anaphylaxis in our cohort, about 16%. In the industrialized nations, the lifetime prevalence of anaphylaxis from all causes is estimated to be about 0.05-2%.³⁶ This is on par with the general UPHS anaphylaxis prevalence of 0.24%. Our EoE cohort had about 67-fold increased association with anaphylaxis compared with that of the general UPHS population, RR 66.7 (CI 57.5-77.2). This increased incidence could be due to a higher prevalence of IgE-mediated food and medication allergy in the EoE cohort compared with the general UPHS population. This is a good reason for EoE patients to be followed by an allergist in addition to a gastroenterologist.

288 Autoimmune Comorbidities

289 Prevalence of comorbid autoimmune disease in EoE is an area that has been increasingly
290 studied over the last several years. The two most common autoimmune diseases in our
291 population were celiac disease and inflammatory bowel diseases. The RR of celiac disease in our
292 cohort was 17.4 (CI 11.1 – 27.2) and for IBD, the RR was 3.4 (CI 2.2-5.4).

293 Prior studies have shown an increased incidence of comorbid celiac disease of 50-70 fold
294 in the pediatric EoE population.¹² The prevalence of EoE in adult and pediatric patients with
295 celiac disease ranges from 3.2% to 10.7% based on American, Italian, and Australian studies.³⁷⁻³⁹
296 However, the converse scenario, the prevalence of celiac disease in patients with EoE, is less
297 well delineated. In our large adult EoE cohort, the prevalence of celiac disease was 2%. The
298 UPHS celiac disease prevalence is 0.11%, which is slightly lower than the estimated prevalence
299 in the US, 0.54%.³⁸

300 The prevalence of IBD (Crohn's disease and UC) was 2% in our EoE cohort. The
301 prevalence of adult UC in the U.S. is about 238 per 100,000 and the prevalence of Crohn's
302 disease is 201 per 100,000 population.⁴⁰ In the general UPHS population, the incidence of
303 Crohn's was similar, 0.27%, and UC was 0.31%. In our EoE cohort, Crohn's disease is about
304 five times more prevalent than in the U.S. as well as the UPHS populations.

305 The association between comorbid EoE and autoimmunity remains unknown. Celiac is
306 thought to be mediated by Th1-mediated immune responses and inflammatory bowel disease by
307 both Th1 and Th17-mediated immune responses.^{41,42} Conversely, EoE has traditionally been
308 thought to be a predominantly Th2-mediated immune disease.

309

310 Neuropsychiatric Comorbidities

311 Studies have shown that pediatric and adult patients with EoE have psychosocial
312 adjustment and coping problems due to challenges related to symptoms and management of their
313 disease that significantly affect their quality of life.⁴³ Unsurprisingly, about a fifth of our EoE
314 cohort had documentation of a comorbid neuropsychiatric condition. The overall prevalence of
315 each individual neuropsychiatric disorder was not significantly greater than that of the lifetime
316 prevalence of each individual disorder. However, all of the 6 most common neuropsychiatric
317 comorbidities were more prevalent in our EoE cohort compared with that of the general UPHS
318 population. Also, while the incidence of ASD in our EoE cohort was not greater than the overall
319 rising incidence in the general population,⁴⁴ there was a 33-fold increase compared with the
320 UPHS population, RR 5.23 (CI 3.6-7.6). This association has been seen predominantly in the
321 pediatric population,²⁹ so it is interesting to note that the average age of diagnosis of EoE in this
322 ASD cohort was in their mid-20s. Surprisingly, the prevalence of eating disorders was not as
323 high as we would have hypothesized given the stressful relationship with food in EoE.

325 Limitations

326 Our cohort of patients predominantly lives in urban and suburban settings, which should
327 be carefully considered when extrapolating our findings to rural areas or other regions of the
328 country. In addition, ours is an analysis of EMR patient health records at a single institution
329 within two main subspecialties (allergy and gastroenterology), which could lend itself to
330 selection bias. Also, choice of ICD code could be affected by administrative and/or billing
331 constraints. While some of the atopic conditions of interest showed high ICD code accuracy,
332 there was about 20% overestimation in the ICD coding for EoE, with some cases of GERD,

Barrett's esophagus, and other diagnoses erroneously coded as EoE. On the other hand, for certain diagnoses of interest, there could be a portion of the population that may have been missed when searched only by ICD codes. Finally, review of the available information in the EMR was one of the most vital aspects of our study, which is limited by the data available in each patient's chart. Documentation by medical providers is also subject to various limitations such as time, having providers outside the UPHS network (leading to fragmented documentation, missing records), and subspecialty knowledge and expertise. Certain diagnoses, such as drug or food allergy, could have been erroneously attributed, leading to over or underestimation. We did our best to correct for this with manual chart review.

Our study showed there were consistent findings in regards to demographics, therapy, and associated atopic conditions compared with previous studies in both the adult and pediatric literature.

Nevertheless, there were several findings that have heretofore not been evaluated in a large adult cohort of manually verified, biopsy-proven EoE. Our study shows that EoE patients are usually never smokers with an increased risk of pollen food allergy syndrome, anaphylaxis, and comorbid autoimmune and neuropsychiatric conditions compared with the general UPHS population. There was also an increased prevalence of impaction and stricture or fibrosis requiring endoscopic intervention compared with the pediatric population.

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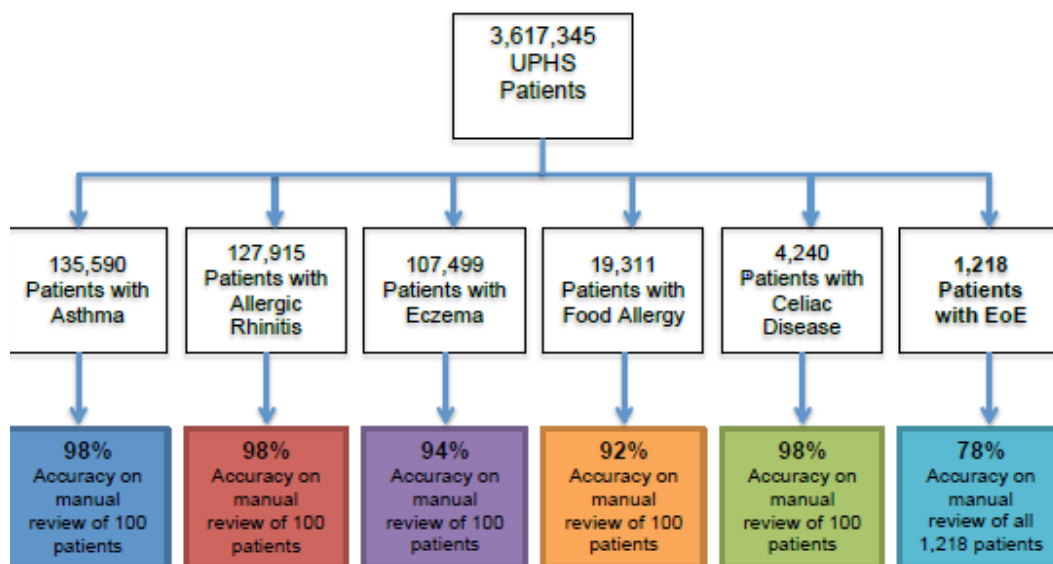
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470 **Figure Legend**

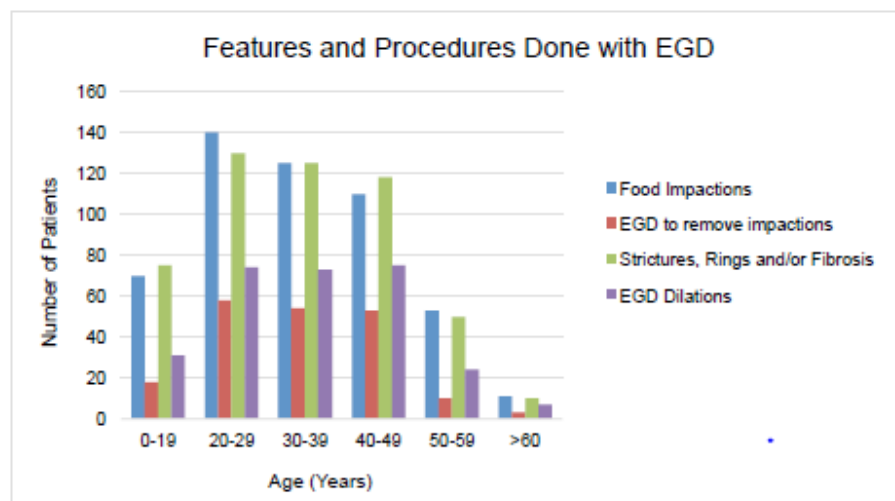
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Figure 1.

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473 **Figure 1.** Total number of UPHS EMR patients and patients with conditions extracted by ICD
 474 codes. Percent confirmed (true positive rate based on ICD codes) reflected in the colored boxes.

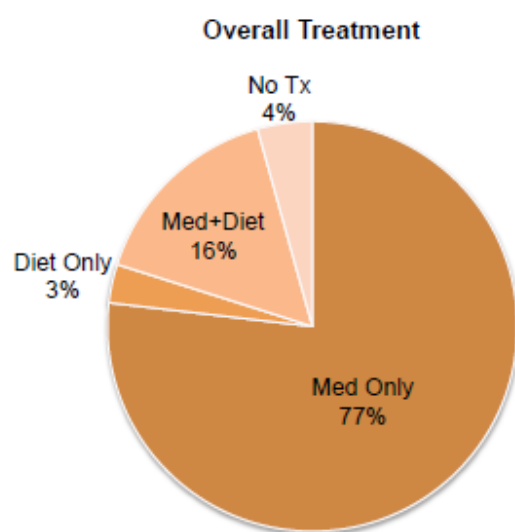
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Figure 2.

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477 **Figure 2.** Number of patients who developed: impactions and required endoscopic removal of
478 food, strictures or fibrosis requiring dilatation compared with their age of diagnosis. EGD-
479 esophagogastroduodenoscopy

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Figure 3 (A-C). Treatment



A.

Figure 3a-c. Treatment. Overall (a), Medical Therapy (b), Diet Therapy (c).

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Table 1. Demographic Characteristics of Cohort, N =950

Characteristic	Number (%)
Gender	
Male	611 (64%)
Female	339 (36%)
Race	
African American	69 (7%)
Asian	20 (2%)
Caucasian	842 (89%)
Other/Unknown	19 (2%)
Ethnicity	
Hispanic	24 (3%)
Non-Hispanic	926 (97%)
Smoking History	
Never Smoker	772 (81%)
<10 Pack Year Smoking History	122 (13%)
>10 Pack Year Smoking History	23 (2%)
Active Smoker	33 (4%)
Family History of EoE	
Positive History	32 (4%)
First Degree Relatives	27 (84%)
Second & Third Degree	5 (16%)
Two or More Relatives With EoE	5 (16%)
Age	Years
Median at Diagnosis of EoE	33
Average at Diagnosis of EoE	34
Range	5 – 89
Median Current Age	39
Average Current Age	40
Range	18-93

Abbreviations: EoE, eosinophilic esophagitis.

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Table 2. Laboratory and Endoscopic Findings

Presenting Symptom	Number (%)
Dysphagia	612 (64%)
Impaction	117 (12%)
Reflux	64 (7%)
Dyspepsia	14 (2%)
Other	139 (15%)
Unknown/Not documented	4 (<1%)
EGD Eos/HPF at Initial Diagnosis (N=763)	Eos/HPF
Median	40
Average	49
Range	15-500
EGD Eos/HPF at Most Recent EGD (N=651)	Eos/HPF
Median	14
Average	29
Range	0-240
History of Impaction	Number (%)
Positive History	524 (55%)
Requiring EGD Intervention	200 (38%)
Strictures, Fibrosis, Rings on EGD	Number (%)
Positive History	527 (56%)
Requiring Dilatation	297 (56%)
Absolute Eosinophil Count (AEC) (N=679)	Serum Value (K/uL)
Median	350
Average	446
Range	0 – 5,080
Total Serum IgE (N=152)	Serum Value (IU/mL)
Median	117
Average	243
Range	0 – 3,796

Abbreviations: EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis.

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Table 3. Comorbid Conditions

	EoE Cohort (%) (N=950)	UPHS Prevalence (%) (N=3,617,345)
Asthma	36%	3.7%
Allergic Rhinitis	70%	3.5%
Atopic Dermatitis	14%	2.8%
Food Allergy	24%	0.49%
Pollen Food Allergy Syndrome	34%	0.07%
Drug Allergy	30%	0.42%
Latex Allergy	3%	0.1%
Anaphylaxis	16%	0.24%
Autoimmune Disease	9%*	4%*
Psychiatric Disease	21%*	8%*

Abbreviations: EoE, eosinophilic esophagitis; UPHS, University of Pennsylvania Health Systems. * = (total of each type, subtypes listed in Tables 4 and 5)

Table 4. Autoimmune Comorbidities

		<u>Number (%)</u>
Patients with Comorbid Autoimmune Disease		81 (9%)
Patients with ≥ 2 Autoimmune Conditions		9 (11%)
Total Number of Individual Disorders		N=87
		<u>EoE Cohort – Number (%)</u>
		N=950
Celiac disease	19 (2%)	<u>UPHS Prevalence – Number (%)</u>
		(N=3,617,345)
IBD	19 (2%)	4,156 (0.11%)
Crohn's	14 (1.47%)	21,096 (0.58%)
UC	5 (0.53%)	9,642 (0.27%)
Psoriasis	12 (1.26%)	11,454 (0.31%)
AI Thyroiditis	10 (1.05%)	20,708 (0.57%)
SLE	10 (1.05%)	8,880 (0.25%)
Vitiligo	5 (0.53%)	14,530 (0.40%)
Type 1 DM	3 (0.32%)	9,954 (0.28%)
Graves' Disease	2 (0.21%)	18,573 (0.51%)
Dermatomyositis	2 (0.21%)	16,542 (0.46%)
Scleroderma	2 (0.21%)	1,245 (0.03%)
		1,366 (0.04%)

Abbreviations: AI, autoimmune; DM, diabetes mellitus; IBD, inflammatory bowel disease; SLE, systemic lupus erythematosus.

Table 5. Comorbid Psychiatric Comorbidities

		<u>Number (%)</u>
Patients with Comorbid Psychiatric Disease		200 (21%)
Patients with ≥ 2 Psychiatric Conditions		43 (22%)
Total Number of Individual Disorders		N=253
	<u>EoE Cohort – Number (%)</u> (N=950)	<u>UPHS Prevalence – Number (%)</u> (N=3,617,345)
Depression	117 (12%)	171,038 (4.7%)
Anxiety	88 (9.3%)	82,053 (2.3%)
ADD/ADHD	27 (2.8%)	19,662 (0.54%)
Bipolar disorder	10 (1.05%)	22,997 (0.64%)
OCD	6 (0.63%)	5,078 (0.14%)
Eating disorder	3 (0.32%)	3,928 (0.11%)
Other	2 (0.21%)	--

Abbreviations: ADD, attention deficit disorder; ADHD, attention deficit hyperactivity disorder; OCD, obsessive compulsive disorder.