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Hospitalization trends and determinants of inpatient costs for eosinophilic esophagitis patients in the United States: results from the Nationwide Inpatient Sample analysis

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Abstract

Background Inpatient care for patients with eosinophilic esophagitis (EoE) is thought to be uncommon, there are few data on inpatient care costs for individuals with EoE. The purpose of this study was to assess trends in inpatient admissions for EoE and examine factors that drive hospitalization costs.

Methods We examined EoE hospitalizations using ICD-9/10 codes, from 2010-2016 in the National Inpatient Sample. We also identified the diagnosis-related group codes, current procedural terminology codes, and common symptom codes documented during admission. We conducted 2 main analyses, primary (all EoE-related hospitalizations) and secondary (hospitalization with a primary diagnosis for EoE), and a sensitivity analysis using only hospitalizations with the secondary diagnosis for EoE, to determine the trend and cost of EoE-related hospitalizations. We used univariate and multivariate models to evaluate the effect of factors that drive hospitalization on total costs.

Results Our primary analysis showed that an estimated total of 33,467 EoE-related hospitalizations occurred in the US between 2010 and 2016, representing approximately 13 per 100,000 hospitalizations in the US. The admission rate increased by approximately 70% from 2010-2016 (9.26 to 15.75 per 100,000 hospitalizations), while the total annual and mean inflation-adjusted per-patient costs for EoE-related admissions were $24 million per year and $5135 (standard deviation $153), respectively. Patients and hospital characteristics were independently associated with cost of hospitalization.

Conclusion The rate of hospital admission for EoE has markedly increased in the US, as has the mean cost for EoE-related hospitalization, at a rate tenfold that of inflation from 2010-2016.

Keywords Eosinophilic esophagitis, hospitalization, inpatient, trend, cost

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Introduction

Evidence supporting an increase in the cases of eosinophilic esophagitis (EoE) diagnosed in the United States (US) and around the world has been widely reported [1,2]. In the US, the prevalence of EoE among children and adults is estimated at approximately 57 per 100,000 and EoE-related disease accounts for roughly $1 billion annually in healthcare expenditure. This is a substantial healthcare burden and cost for a relatively rare condition [3]. The management paradigm for EoE has evolved significantly over the past 2 decades. Commonly, the treatments comprise dietary therapy (elimination and elemental diets), acid suppressants (e.g., proton pump inhibitors), and topical glucocorticoids (e.g., fluticasone, budesonide) [4]. When strictures are present, esophageal dilatations are performed to relieve symptoms of dysphagia.

Typically, treatment and procedures for EoE are provided in the outpatient setting. The use of inpatient care for patients with EoE is thought to be uncommon, and perhaps primarily related to complications such as food impaction or esophageal perforation. However, there is little information about this treatment setting in caring for children and adults with EoE. In a study of health care utilization of EoE, Jensen *et al* found a median of zero inpatient claims was reported during the

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Conflict of Interest: None

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study period [5], but the data source for that study was not inpatient-specific, and the question of how common inpatient encounters are in EoE remains open. Therefore, the purpose of the study was to assess the pattern of inpatient care and cost for admissions with a diagnosis of EoE, using the Nationwide Inpatient Sample (NIS) data source.

Materials and methods

Study design

This study was a multi-year cross-sectional analysis of US hospitalizations in the NIS that occurred from January 1, 2010, to December 31, 2016, with a primary diagnosis of EoE. EoE cases were identified using ICD-9-CM 530.13 and ICD-10-CM K200, International Classification of Diseases ninth edition (ICD-9-CM), and tenth edition (ICD-10-CM) respectively; at least one code was required for case identification [6]. The transition from ICD-9-CM to ICD-10-CM coding occurred on October 1, 2015. We excluded hospitalizations with no corresponding ICD codes, EoE hospitalizations with patients who died during hospitalization (as we could not ascertain whether EoE was the primary cause of death; n=102), and hospitalizations with missing relevant cost or coding data. To estimate the number of EoE hospitalizations in the US, we incorporated the weight variable in the NIS that accounts for sampling design. The data from NIS are de-identified and considered non-human research; therefore, the study was exempt from review by the Institutional Review Board of the University of Alabama, Tuscaloosa-Alabama.

Data source

The NIS is a stratified probability sample maintained by the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality [7]. This database includes data from nearly 20% of hospitalizations in the United States. To minimize sampling bias, the NIS is stratified by geographic region, urban versus rural location, teaching status, and number of hospital beds. With probability sampling, hospitals within each of the different strata in the overall sample have an equal probability representation in the selected 20% sample. The data are weighted to provide a representative sample of the US population. Details regarding sample design, data collection, and weighting are described elsewhere [7]. The survey includes de-identified patient demographic information, diagnostic codes and procedure codes, length of stay, and total hospital charges.

Main outcome

The primary outcome of this study was total inpatient charges and costs for EoE. Total charges represent the amount billed for each hospitalization. Charges were controlled for inflation by adjusting the total hospital charge for hospitalization using the health services Consumer Price Index from the Bureau of Labor [8]. Costs represent the amount of money actually paid to the hospital, generally significantly less than the charges. To estimate costs, charges were converted using hospital-specific cost-to-charge ratio files in a dataset accompanying the NIS. These cost-to-charge ratio files are constructed using all-payer inpatient cost and charge information from the Centers for Medicare and Medicaid Services.

Predictor variables

Our predictor variables of interest in this study included: 1) patient demographics, such as age, sex, patient's place of residence, median household income by zip code of residence, payer source/insurance; 2) hospital factors, such as location, teaching status, number of beds and country region (a hospital was regarded as a teaching facility if it was affiliated with an American Medical Association-approved residency program, or was a member of the Council of teaching hospitals or had a full-time equivalent resident-to-patient ratio of ≥0.25); and 3) severity of illness subclass (minor with no complication, moderate, and major/extreme), calculated using software developed by 3M Health Information Systems by assigning all patients to a diagnosis-related group (DRG). The DRG appropriate for the date of discharge is assigned by the Medicare DRG Grouper algorithm during HCUP processing. In addition, using available diagnostics codes (ICD-9-CM and ICD-10-CM) and procedure codes (ICD-9-CM Procedure and ICD-10-CM Procedure), we identified common symptom and complication codes, and procedures documented in related admissions. Finally, we examined the effects of predictor variables on the cost of hospitalization. Details of diagnostic and procedure codes are provided in Supplementary Table 1.

Statistical analysis

Primary analysis

Our primary analysis was based on hospitalizations with either primary or secondary ICD 9 or 10 codes for EoE. We applied the discharge and strata weight variables provided in the NIS database to produce the national estimates of EoE hospitalizations and all inpatient stays at community hospitals across the US. We performed a descriptive statistical analysis of the distribution of the study data using the SURVEYFREQ procedure for categorical variables and the SURVEYMEANS procedure for continuous variables. We determined univariate associations of the covariates with outcomes using a χ^2 test for categorical variables and the Mann-Whitney nonparametric test for continuous variables. To account for the skewness in the data, we log10-transformed the total charge variable before using it in our modeling. Multivariable analyses to examine the determinants of cost for EoE hospitalizations were performed

Table 1 Weighted summary of characteristics of patients and hospitals among hospitalizations for eosinophilic esophagitis in the Nationwide Inpatient Sample, 2010-2016

Variable	Children (n=12,982) Weighted %	Adults (n=20,485) Weighted %	P-value
Patient characteristics			
Sex (female)	31.9	47.4	<0.001
Age, year (Mean, (SD))	9.2 (0.1)	47.2 (0.3)	
Length of hospital stay, days, mean (SD)	5 (1)	4 (1)	
Total hospitalization charge, US$, mean (SD)	4814.22 (244)	5448.31 (189)	
Race			<0.001
White	73.1	82.5	
Black	13.0	8.6	
Hispanic	8.1	5.3	
Other*	5.8	3.6	
Residence			0.1309
Large metropolitan	30.9	30.5	
Small metropolitan	29.1	27.3	
Non-metropolitan	40.0	42.2	
Percentile median household income by Zip			0.1287
0-25th	19.3	20.7	
26-50th	22.9	24.4	
51-75th	28.6	26.6	
76-100th	29.2	28.4	
Insurance			<0.001
Medicare/Medicaid	36.8	36.9	
Private including HMO	57.7	52.6	
Self-pay/no charge/other	5.6	10.6	
Hospital characteristics			
Urban location	98.5	95.4	<0.001
Teaching hospitals	91.2	63.6	<0.001
Admission source (Emergency Dept.)	51.2	69.4	<0.001
Hospital size			0.0673
Small	12.6	13.4	
Medium	23.3	25.4	
Large	64.0	61.2	
Hospital region			0.1406
Northeast	16.6	18.4	
Midwest	26.4	28.6	
South	32.5	31.0	
West	24.5	22.1	
Severity of illness subclass			<0.001
Minor (no comorbidity or complications)	21.7	29.5	
Moderate	47.3	39.8	
Major/Extreme	31.0	30.6	

*Other races include Asian/Pacific Islander, Native American and others

SD, standard deviation; HMO, health maintenance organization

using a SURVEYREG generalized least-squares estimation model. For multivariate analyses, costs were log-transformed to achieve a normal distribution. All multivariate models included the appropriate covariates, as listed in Table 1. We created final parsimonious models using the GLMSELECT, Least Absolute Shrinkage and Selection Operator (LASSO) and the Schwarz Bayesian Information Criterion. The GLMSELECT procedure supports a hierarchy among effects and any degree of interaction and nested effects [9]. We retransformed the results from log10 to the original scale using the smearing factor technique described by Duan [10]. All statistical analyses were conducted using Statistical Analysis Software (SAS) version 9.4 (SAS Institute, Inc., Cary, NC), with 2-sided tests and a significance level of 0.05.

Secondary analysis

In the secondary analysis, we focused on hospitalizations with only primary ICD-9 or -10 codes for EoE. This was an attempt to investigate the EoE-specific cause of hospitalization in this population. To do this, we repeated the analyses to ascertain the consistency of findings in our primary analysis regarding hospitalization rate and cost estimates that might be mainly attributable to EoE in the first, rather than the second position. Further, we assessed the indications for hospitalizations in urban vs. rural hospitals and teaching vs. non-teaching hospitals. We also performed a sensitivity analysis for hospitalizations with secondary diagnostic codes for EoE as opposed to the primary diagnosis, and then repeated the same analysis as above.

Results

Population, admission characteristics, and costs

After weighting the estimates, a total of 256,485,850 admissions occurred in US hospitals between 2010 and 2016. Of this number, 33,467 hospitalizations had a primary or a secondary diagnosis of EoE, representing approximately 13 per 100,000 (0.013%) of hospitalizations in the US. The mean age at admission was 32 years (standard deviation [SD], 1 year), and the mean length of stay was 5 days (SD 1 day). Discharges included in this analysis had more patients who were adults (age >18 years, 61%), male (58.7%), Whites (78.9%), and had private insurance (54.8%), located in the metropolitan area (58.7%). The admissions were more likely to be in hospitals in urban areas (96.6%), teaching hospitals (74.5%), with 500 beds or more (62.4%), in the southern region (31.5%). The most common source of admissions was the emergency department (62.3%). The descriptive data for EoE admission by age group is shown in Table 1.

The estimated total costs for EoE-related hospitalizations in the US over the 7-year study period were $168,572,413, resulting in an annual cost of over $24 million per year. The mean total charges per patient were $5135 (SD $153), with a maximum charge of $421,915. The median and interquartile ranges (IQR) were $2700 ($1229.85-5420.79). The mean cost for hospitalization increased at a rate tenfold that of inflation from 2010 to 2016 ($906 to $9576).

Table 2 lists the top 10 DRG codes and costs associated with EoE hospitalizations. About a quarter (n=8266) of identified admissions had analogous clinical conditions consistent with DRG 392, and 4% (n=1249) were grouped as DRG 391; both of these are related to esophagitis, gastroenteritis, and miscellaneous digestive disorders. The average length of stay for cases in DRG 391 was 6 days, with an estimated average hospitalization cost of $5085.

The trend analysis showed an increasing number of EoE-related admission in both adults and pediatric admissions (Fig. 1). Overall, the number of admissions increased by 56% from 2010 (N=3589) to 2016 (N=5655). The increase in the number of admissions was higher among the adult population, with EoE (70%) (n, 2113 in 2010 to 3605 in 2016) compared to the pediatric population (35%) (n, 1477 in 2010 to 2265 in 2016). The most common symptom and complication codes recorded were: EoE-related symptoms, including food impaction (6.2%), epigastric pain (5.8%) and/or failure to thrive (10.5%); EoE-related complications, including stricture of the esophagus (7.0%), laceration of the esophagus (1.5%), and/or spontaneous rupture of the esophagus (1.3%); gastroesophageal reflux symptoms (61.4%); and allergic comorbidities (Table 3).

Table 2 Top 10 Diagnosis Related Group (DRG) codes according to cost associated with hospitalization for eosinophilic esophagitis

DRG#	Description	Average cost per hospitalization ($)	Average length of stay (days)
391	Esophagitis, gastroenteritis and miscellaneous digestive disorders with MCC	5085	6
378	Gastrointestinal hemorrhage with CC	3649	3
641	Miscellaneous disorders of nutrition, metabolism, fluids and electrolytes	3266	5
394	Other digestive system diagnoses with complication or CC	3214	3
392	Esophagitis, gastroenteritis and miscellaneous digestive disorders without MCC	3099	4
379	Gastrointestinal hemorrhage without CC/ MCC	2950	3
202	Bronchitis and asthma with complication or CC/ MCC	2659	3
395	Other digestive system diagnoses without CC/ MCC	2104	1
203	Bronchitis & asthma without CC/MCC	1819	2

CC, comorbidity; MCC, major complications or comorbidity

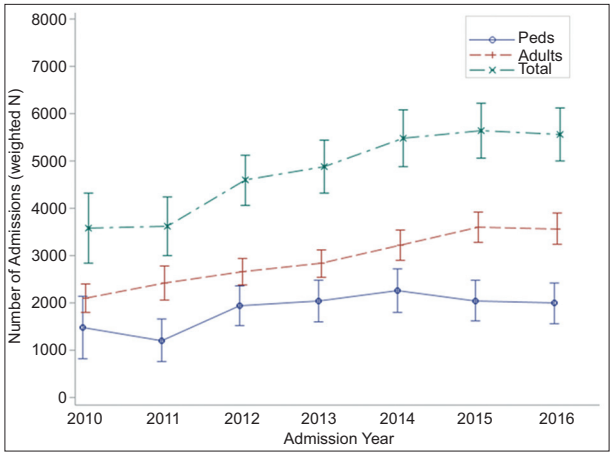

Figure 1 Trend in the number of admissions with diagnosis of eosinophilic esophagitis from 2010-2016 in United States hospitals, Nationwide Inpatient Sample data 2010-2016

Table 3 Common symptom and complication codes documented in hospitalizations related to eosinophilic esophagitis (EoE)

Description	Frequency (weighted %)
EoE-related symptoms	
Dysphagia	1060 (3.0)
Food impaction	2024 (6.0)
Persistent vomiting	2090 (6.2)
Failure to thrive	3523 (10.5)
Epigastric pain	1936 (5.8)
EoE-related complications	
Stricture of esophagus	2358 (7.0)
Spontaneous rupture of esophagus	450 (1.3)
Perforation of esophagus	173 (0.5)
Laceration of esophagus	518 (1.5)
Esophageal hemorrhage	149 (0.4)
Gastroesophageal reflux symptoms	
Esophageal reflux	1341 (19.8)
Reflux esophagitis	456 (1.4)
Esophagitis	151 (0.5)
Other esophagitis	279 (39.7)
Allergic comorbidities	
Asthma	5928 (17.7)
IgE food allergy	445 (1.3)
Atopic diseases	1185 (3.5)

Factors associated with the cost of inpatient care for EoE

In unadjusted analyses (Table 4), patients' characteristics, including sex, age, race, residence, income quartile and source of payment, had a significant effect on the EoE hospitalization charge. For example, females had about 18.9% higher costs than males. Compared to patients who lived in the non-metropolitan area, patients who lived in large or small metropolitan areas had 25.3% and 10.6% higher hospitalization charges, respectively. Further, patients with private insurance or other insurance (self-pay, uninsured) were significantly more likely to have lower hospitalization charges, by 23.5% and 22.3%, respectively, compared with public insurance (Medicare or Medicaid). Concerning hospital characteristics, admissions that occurred in urban locations compared to rural (P<0.001), or teaching hospitals compared to non-teaching (P<0.001), were more likely to have higher hospital charges. As expected, hospitalization charges increased according to the severity of the illness, with cases of major/extreme severity being charged 130% more than minor cases with no complication. The most common procedure performed in inpatients with a diagnosis of EoE was esophagogastroduodenoscopy (EGD) with biopsy (32%, n=10,761), adding to a total hospitalization cost of $47.7 million over 7 years and $6.8 million annually. The mean cost for each inpatient EGD procedure was $4483 (SD $167). About 4% of the hospitalizations had dilation of the esophagus, and the estimated average cost for each procedure was $4037 (SD $278).

For the multivariate analysis, the selection method (LASSO algorithm) retained 7 significant variables used for our final predictive modeling (Table 4). The female adult age group, metropolitan residence, hospital characteristics (urban, teaching, and west region), and severity of illness remained significant factors independently associated with an increase in total hospitalization charge. Comparing illness severity with or without complications, the adjusted hospitalization charge for severe EoE cases with complications was about 128% higher than for minor cases with no complication, whereas, predictors such as Black or other races compared to Whites, and hospitals located in the Midwest and South regions compared to Northeast, were significantly associated with lower hospital charges.

Secondary analysis

Our secondary analysis demonstrated that a weighted total of 5138 hospitalizations (15.5%) had a primary diagnostic code for EoE. The number of these hospitalizations decreased from 735 in 2010 to 630 in 2016. The mean age at admission was 28 years, and there was no increasing pattern in age at admission. The total cost for hospitalizations in this subgroup was $16,779,538. The average length of hospital stays and hospital charges in this population were 4 days and $3336, respectively. The proportion of admissions who underwent upper endoscopy with biopsy was 56%, while 6.5% underwent an esophageal dilatation procedure. We observed that the mean age of admission in children was 9 years while for adults was 47 years. The average length of hospital stay and hospital charges among children were 4 days and $3170, respectively. In the adult population, the mean admission age was 45 years, the average length of hospital stay was 3 days, and the mean hospital charge was $3,474.

The multivariate analysis demonstrated that the only significant predictor of hospital charge in this subgroup was disease severity scores. We observed that hospital charges increased with the severity of the disease. We also performed

Table 4 Univariate and multivariate results for hospitalization charges related to eosinophilic esophagitis, as predicted by patients, and hospital characteristics

Variable	Univariate association			Final multivariate model*		
	β	95%CI	P-value	β	95%CI	P-value
Patient characteristics						
Female (Ref: Male)	0.189	0.164-0.212	<0.001	0.124	0.072-0.178	<0.001
Age ≥19 y (Ref: 0-18 y)	0.271	0.230-0.313	<0.001	0.380	0.298-0.461	<0.001
Race (Ref: White)						
Black	0.058	0.021-0.096	0.002	-0.034	-0.122-0.054	0.451
Hispanic	0.316	0.277-0.355	<0.001	0.190	0.080-0.300	0.007
Other†	-0.136	-0.217-(-0.054)	0.001	-0.131	-0.234-(-0.028)	0.013
Patient residence (Ref: Non-Metropolitan)						
Large Metropolitan	0.253	0.206-0.301	<0.001	0.115	0.030-0.199	0.008
Small Metropolitan	0.106	0.067-0.145	<0.001	0.070	-0.010-0.151	0.088
Percentile median household income by Zip (Ref: 0-25th) N.S.						
26-50th	-0.165	-0.202-(-0.128)	<0.001			
51-75th	-0.117	-0.151-(- 0.083)	<0.001			
76-100th	-0.057	-0.097-(-0.016)	0.006			
Insurance (Ref: Medicare/Medicaid) N.S.						
Private including HMO	-0.235	-0.265-(-0.204)	<0.001			
Self-pay/no charge/other	-0.223	-0.261-(-0.185)	<0.001			
Hospital characteristics						
Hospital location (Ref: rural)	0.615	0.565-0.665	<0.001	0.434	0.291-0.577	<0.001
Hospital teaching status (Ref: Nonteaching)	0.212	0.182-0.243	<0.001	0.188	0.113-0.262	<0.001
Hospital size (Ref: Small) N.S.						
Medium	-0.114	-0.153-(-0.076)	<0.001			
Large	-0.085	-0.124-(-0.045)	<0.001			
Hospital Region (Ref: Northeast)						
Midwest	-0.110	-0.198-(-0.022)	0.014	-0.091	-0.198-(-0.016)	0.095
South	-0.121	-0.198-(-0.043)	0.002	-0.124	-0.232-(-0.015)	0.025
West	0.151	0.074-0.229	<0.001	0.181	0.057-0.305	0.004
Severity of illness subclass (Ref: minor with no complication)						
Moderate	0.648	0.599-0.696	<0.001	0.681	0.589-0.773	<0.001
Major/Extreme	1.288	1.240-1.336	<0.001	1.288	1.189-1.387	<0.001

*Represents final parsimonious hierarchical regression model

CI, confidence interval; N.S., not significant (not included in the final regression model); Ref, reference; HMO, health maintenance organizations

new sub-analyses to assess the indications of admission by urban vs. rural and academic vs. non-academic hospitals. The results showed that patients located in the metropolitan areas (P=0.006, Western hospital region (P<0.001), and those with private insurance (P=0.034) were significantly more likely to be hospitalized. Indications for teaching hospital compared to non-teaching hospitalization were children compared to adults (P=0.023), Blacks compared to Whites (P=0.004), large metropolitan residents compared to rural residents (P<0.001), private insurance compared to public insurance (P=0.035), and higher diseases severity score (P-values <0.001). The significant differences when comparing the secondary analysis and the primary analysis showed that the fraction of cost attributable to hospitalizations with a primary diagnostic code for EoE was strikingly lower ($16,779,538) compared to the cost estimate in the primary analysis ($171,239,618). In addition, the proportion of upper endoscopy and esophageal dilation observed was higher in the secondary analysis than the results of our primary analysis.

The sensitivity analysis results showed that a weighted total of 28,426 hospitalizations had secondary diagnostic codes for EoE, and that this group comprised about 85% of all the diagnoses of EoE-related hospitalizations. The majority of the patients were non-metropolitan (41%), males (58%), were in an urban hospital location (96%), and a hospital with a large number of beds (62%). Approximately 7% of the hospitalizations were associated with an esophageal stricture code, while 3.2% had codes for laceration of the esophagus. The proportion of hospitalizations related to esophageal dilations was 4%, while 28% had EGD with biopsy. The average cost of hospitalization per admission was $5536, and the median cost per hospitalization was $2825. The determinants of the cost of hospitalization were similar to the factors identified in our primary analysis.

Discussion

While the costs and healthcare burden of EoE have been growing, EoE is primarily managed in the outpatient setting and little is known about inpatient costs. Understanding hospitalization patterns and associated factors in this population is critical, providing a broader picture of the burden of this condition to patients, caregivers, and the hospital system, and can have policy implications. This study, which utilized a national data source, observed a growing and a substantial number of EoE-related admissions in US hospitals, with the hospitalization rate increasing by about 70% from 2010 to 2016. This pattern was seen across all age groups but was more prominent in the adult age range and accounted for more than $24 million annually. It is not clear whether this increasing trend in EoE admissions was due to more EoE diagnoses, greater EoE severity, or both. We also observed a significant association between patient characteristics, hospital features and severity of illness, and total EoE hospitalization charges. The association with increasing severity of illness was stronger for complications, hospital features (e.g., urban location, teaching status), and adult cases. We found no association between total hospitalization charge and patient income, source of payment, or hospital size (number of beds).

Several reports have documented an increasing number of EoE cases, and frequently patients with an established diagnosis of EoE attend the outpatient department for evaluation and monitoring, where they undergo procedures and receive care [5,11-14]. However, there are relatively few published data on inpatient EoE costs to contextualize our findings. In a study conducted by Jensen and colleagues in a large claims database with more than 8000 EoE cases [5], the annual total cost for care of EoE cases was close to US$1 billion, with a median cost of about $3300. Of this amount, about $2500 were attributable to the median cost for outpatient visits and $160 for pharmacy claims, with very little attributed to inpatient costs. In our study, which focused on inpatient data only rather than general claims, we found that an annual average of over $24 million was spent on approximately 4700 EoE-related hospitalizations with an average hospital stay of 5 days. In addition, our study showed that a unit increase in the hospitalization severity significantly increased the costs by an average of $6784 for extremely severe conditions and $1673 for moderate conditions. Compared with a previous publication that showed a median total outpatient cost per EoE case of $2508 [5], we observed an estimated median total charge per inpatient stay that ranged from $593 in 2010 to $5179 in 2016 [3,15-17]. The average cost of inpatient care for EoE-related admissions was significantly higher for adult admissions than for pediatric admissions. The mean cost of hospitalization increased at a rate tenfold that of inflation from 2010 to 2016 ($906 to $9576). This could be due to the increasing complexity and complications associated with the progression of the disease [18-23]. Still, additional prospective studies with more granular data would be needed to investigate these cases.

A large proportion of the EoE admissions had other associated comorbidities documented during admission, including allergic conditions (e.g., asthma, IgE-mediated food allergy and atopic comorbidities) and gastroesophageal reflux disease (GERD) (e.g., esophageal reflux, esophagitis) [24-30]. About 25% of hospitalized EoE cases had GERD-related symptoms, and 19% had asthma. Although our findings of the presence of these coexisting conditions among EoE hospitalization is consistent with other reports, we were unable to categorize whether the symptoms of the coexisting conditions or the symptoms/complications of EoE were the primary reason for admission. Since our sampling was based on hospitalizations with a primary diagnosis of EoE, we assume that either the presence of EoE symptoms, the severity of EoE symptoms and/or complications of EoE were the leading indication for hospitalization.

A significant strength of this study is that it used data nationally representative of EoE hospitalizations in the US. Another strength is that our research provides results for the actual healthcare dollars spent (costs), rather than charges. Nevertheless, our results should be interpreted with caution because of some limitations. First, the unit of analysis is a hospitalization, so we could not examine the effect of repeated events for the same individual. Second, hospital charges and cost estimates might not be precise. Although we adjusted yearly hospital charges for inflation using the Health services Consumer Price Index from the Bureau of Labor [8], the cost conversion method might not be exact. Third, since we used the ICD-9-CM and ICD-10 codes recorded in the NIS database, the inherent differences in the coding algorithm and transitioning could lead to misclassification bias and subsequently over- or underestimation of cases and estimated costs for EoE hospitalizations. Despite these limitations highlighted above, our findings should stimulate further research in this area using more rigorous data containing detailed information about inpatient utilization.

In conclusion, this study provides data on EoE hospitalization trends and the cost of inpatient care over the past 7 years in the US. We found that the average cost of care for EoE-related hospitalizations in US hospitals has increased remarkably over time. The high cost of inpatient care for EoE can be related to the patient's age, the severity of illness, and hospital features. Further research on the cost of care for EoE patients should be explored to improve cost-effective care for EoE patients.

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Summary Box

What is already known:

- There has been an increase in the diagnoses of eosinophilic esophagitis (EoE) in the United States (US) and around the world
- Typically, treatment and procedures for EoE are provided in the outpatient setting

What the new findings are:

- There is a substantial and growing number of EoE-related admissions in US hospitals
- A high cost of inpatient care for EoE can be related to the patient's age, the severity of illness, and hospital features

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Supplementary material

Supplementary Table 1 Description of diagnostic and procedure codes used in the study analyses

	Diagnostic codes	Procedure codes
Conditions	ICD-9-CM codes	ICD-10-CM codes
Eosinophilic esophagitis	530.13	K20.0
Eosinophilic gastroenteritis	558.41	k52.8
Gastroesophageal reflux disease	530.81, 530.10, 530.11, 530.19, and 530.3	K20.8, K20.9, K21.0, K21.9,
Dysphagia	78.72	R13.10 - R13.14
Epigastric pain	78.90	R10
Vomiting	536.2, 787.01	R11.10, R11.2
Esophageal obstruction or stricture	530.3	K22.2
Food impaction	935.1, 938	T18.100A, T18.108A, T18.110A, T18.118A, T18.120A, T18.128A, T18.190A, T18.198A
Maladaptive eating behaviors	307.59	Z72.4, Z59.4
Spontaneous ruptured esophagus	530.4	K22.3
Perforation of esophagus	862.22, 862.32	S27.813A, S27.819A
Laceration of esophagus	530.7, 998.2	k22.6, K91.71, K91.72
Esophageal hemorrhage	530.82	k22.8
Allergic and ectopic diseases		
Asthma	493.00 – 493.99	J45.0 – J45.998
IgE-mediated food allergy	995.3	Z91.01
Allergic rhinitis	447.9	J30
Atopic dermatitis & eczema	691.8, 692.9	L20-L30
Failure to thrive	783.2X, 783.4X	R62, R63

	Diagnostic codes	Procedure codes
	ICD-9-CM	ICD-10-PCS code
Dilation of the esophagus	42.92	0D754ZZ, 0D717DZ, 0D718DZ, 0D727DZ, 0D728DZ, 0D737DZ, 0D738DZ, 0D747DZ, 0D748DZ, 0D757DZ, 0D758DZ
Esophagogastroduodenoscopy with closed biopsy	45.16, 42.24	0D958ZX, 0DB58ZX, 0DD58ZX, 0D953ZX, 0D954ZX, 0D957ZX, 0DB53ZX, 0DB54ZX, 0DB57ZX, 0DB58ZX, 0DD53ZX, 0DD54ZX, 0DD58ZX
Repair of esophageal stricture	42.85	0D740DZ, 0D743DZ, 0D744DZ, 0D750DZ, 0D753DZ, 0D754ZZ
Suture of laceration of esophagus	42.82	0DQ50ZZ, 0DQ53ZZ, 0DQ54ZZ, 0DQ57ZZ, 0DQ58ZZ
Other esophagoscopy	42.23	0DJ08ZZ