The Tortuous Path to Diagnosis of Eosinophilic Gastritis and Eosinophilic Gastroenteritis (EG/EGE) in the United States: A Real-World, Population-Based Study

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BACKGROUND

- Eosinophilic gastritis and eosinophilic gastroenteritis (EG/EGE) are rare diseases characterized by elevated eosinophils in gastrointestinal (GI) tract biopsies based on standard H&E histopathology, though no standardized diagnostic guidelines exist[1]
- Patients with EG/EGE suffer from a decreased quality of life due to debilitating GI symptoms, compounded by a lengthy path to diagnosis[2,3]
- Here we present a robust analysis of the medical history of patients with EG/EGE prior to diagnosis, utilizing a large, highly representative claims database of >295 million US individuals

METHODS

Data source
- Symphony Health's PatientSource® proprietary, longitudinal medical and pharmacy claims database (Aug 2008 – Oct 2018)

Study design
- Retrospective observational study
- Age groups defined as 0 to 10 years (y) of age (children), 11 to 17 y (adolescents), and ≥18 y (adults), based on age at initial symptom presentation
- Statistical significance tested using student's t-test (continuous variables) or Fisher's exact test (categorical variables)

Patient selection criteria
- ≥1 claim with ICD-CM diagnostic code for EG and/or EGE (K52.81)
- Claims capture ≥24 months prior to and ≥12 months after 1st EG/EGE claim
- Overall robust claims capture (75th percentile)
- ≥1 claim with code for relevant GI symptom and ≥1 claim with code for endoscopy procedure prior to EG/EGE diagnosis date
- A total of 3,250 patients (19% children, 10% adolescents, 71% adults) met all study inclusion criteria; baseline characteristics are presented in Table 1

Table 1. Patient baseline characteristics

	All Patients (n=3,250)	Patients 0-10 y (n=606)	Patients 11-17 y (n=318)	Patients ≥18 y (n=2,326)
Demographics				
Age, years, mean ± SD	38 ± 24	4 ± 4	14 ± 2	51 ± 15
Female, n (%)	2,062 (63%)	254 (42%)	169 (53%)	1,639 (70%)
Year of presentation, n (%)				
2008 to 2011	2,139 (66%)	397 (66%)	183 (58%)	1,559 (67%)
2012 to 2015	974 (30%)	192 (32%)	127 (40%)	655 (28%)
2016 to 2018	137 (4%)	17 (3%)	8 (3%)	112 (5%)
Comorbidities, n (%)				
Eosinophilic esophagitis	1,078 (33%)	345 (57%)	156 (49%)	577 (25%)
Eosinophilic colitis	111 (3%)	26 (4%)	9 (3%)	76 (3%)
Insurance coverage, n (%)				
Private/commercial	2,322 (71%)	449 (74%)	256 (81%)	1,617 (70%)
Medicare	352 (11%)	3 (0%)	1 (0%)	348 (15%)
Medicaid	393 (12%)	102 (17%)	48 (15%)	243 (10%)
Other government	31 (1%)	8 (1%)	2 (1%)	21 (1%)
Self-pay/uninsured	11 (0%)	1 (0%)	0 (0%)	10 (0%)
Unknown	141 (4%)	43 (7%)	11 (3%)	87 (4%)

RESULTS

Patients present with a variety of gastrointestinal symptoms

Figure 1. Frequency of GI symptoms prior to EG/EGE diagnosis (n=3,250)

*p<0.001 compared with adults (≥18 y)
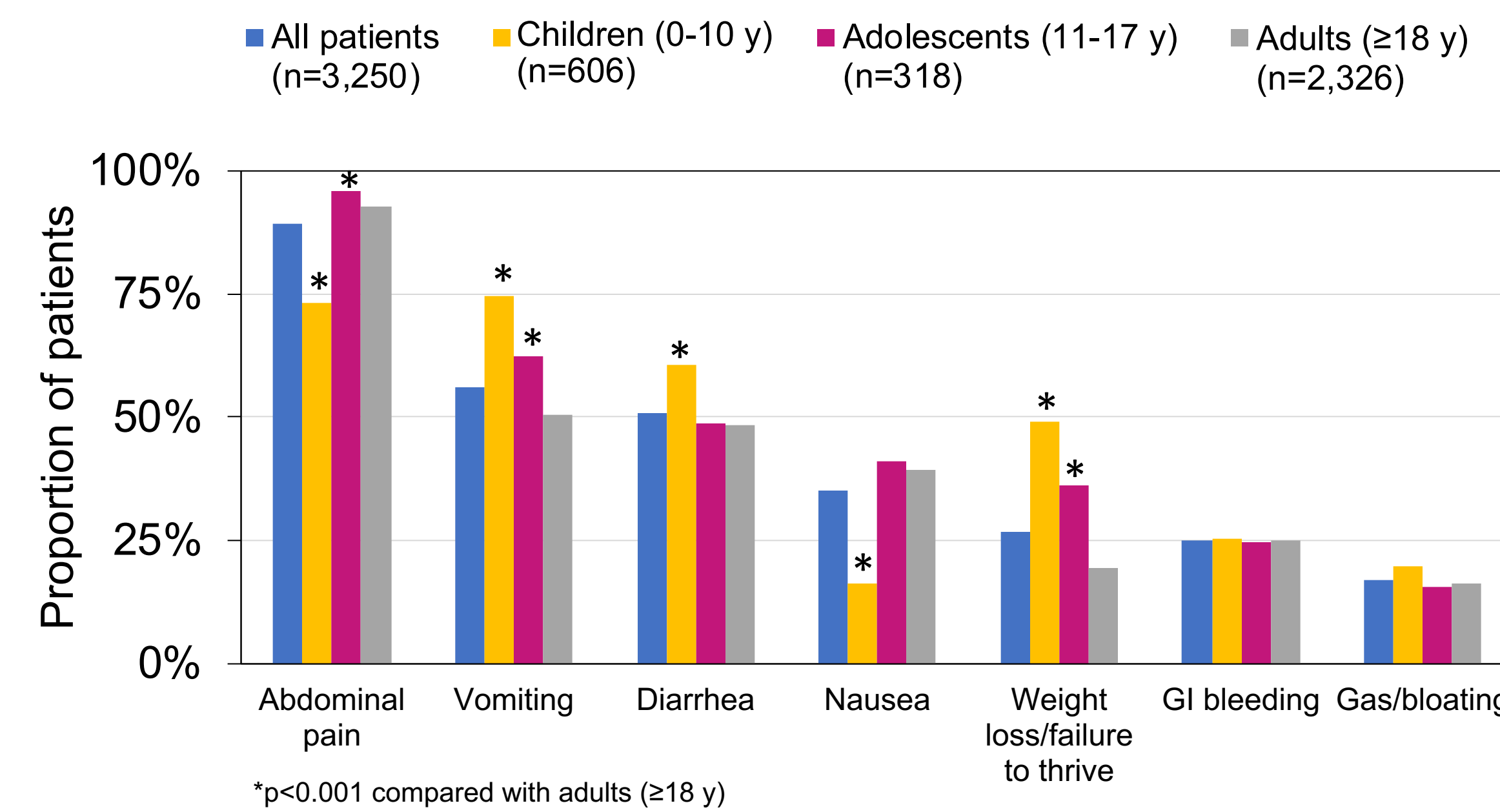
- Abdominal pain, vomiting and diarrhea were the most frequent GI symptoms experienced prior to EG/EGE diagnosis (Figure 1)
- Children and adolescents were significantly more likely to present with vomiting and weight loss/failure to thrive, and less likely to present with abdominal pain (Figure 1)
- Overall, 15% of patients initially presented to emergency medicine physicians; there were no difference between age groups
  - Patients were more likely to present to emergency medicine vs primary care if they experienced vomiting (p<0.001)

### Patients often initially receive non-specific GI diagnoses

Figure 2. Frequency of other GI diagnoses prior to EG/EGE diagnosis

*p<0.001 compared with adults (≥18 y)
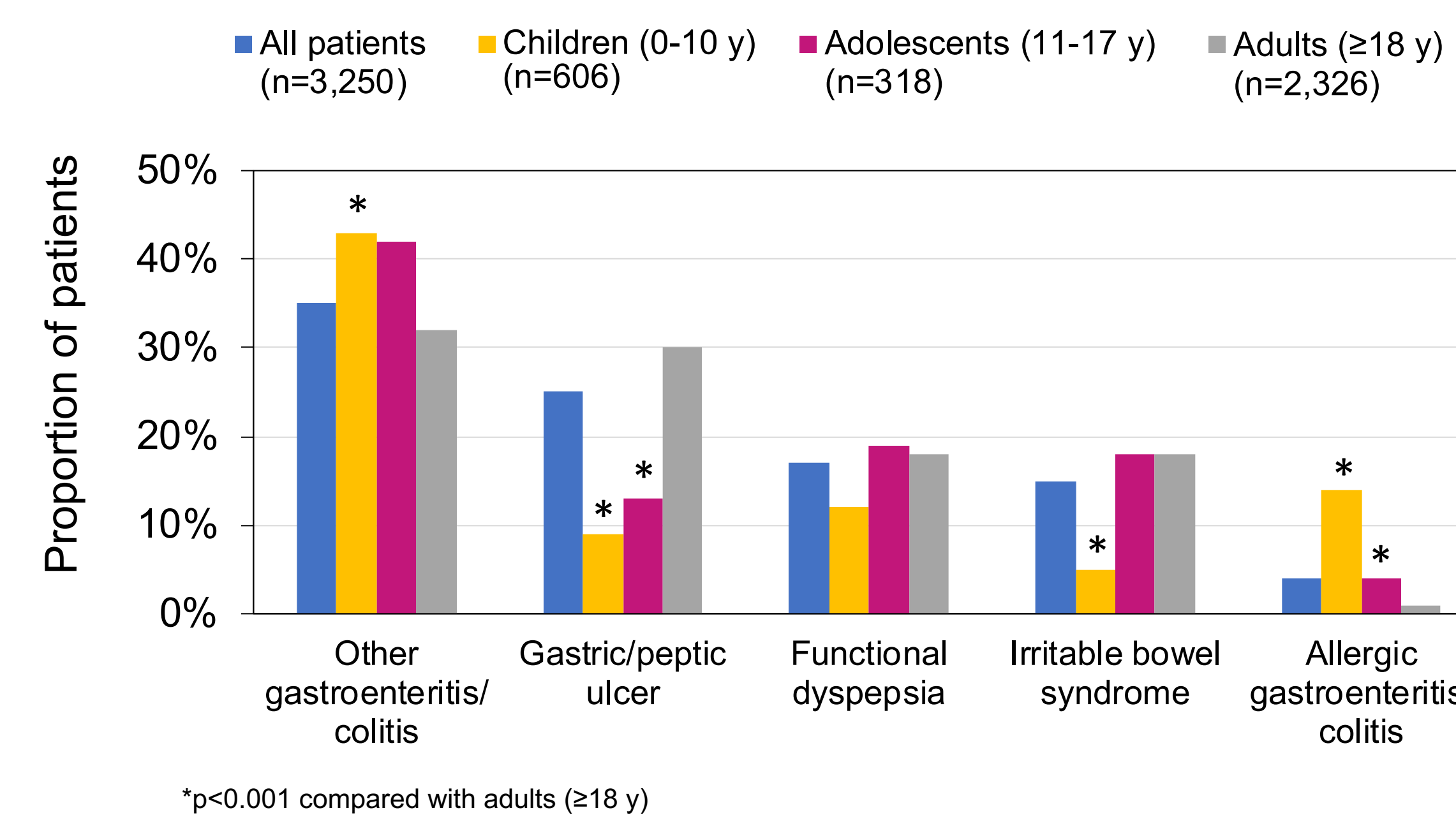
- Overall, 66% of patients received an alternate diagnosis of one or more non-eosinophilic GI conditions prior to their EG/EGE diagnosis (Figure 2)

EG/EGE diagnosis takes an average of 3.4 years

Figure 3. Mean time from presentation to diagnosis

*p<0.001 compared with adults (≥18 y)
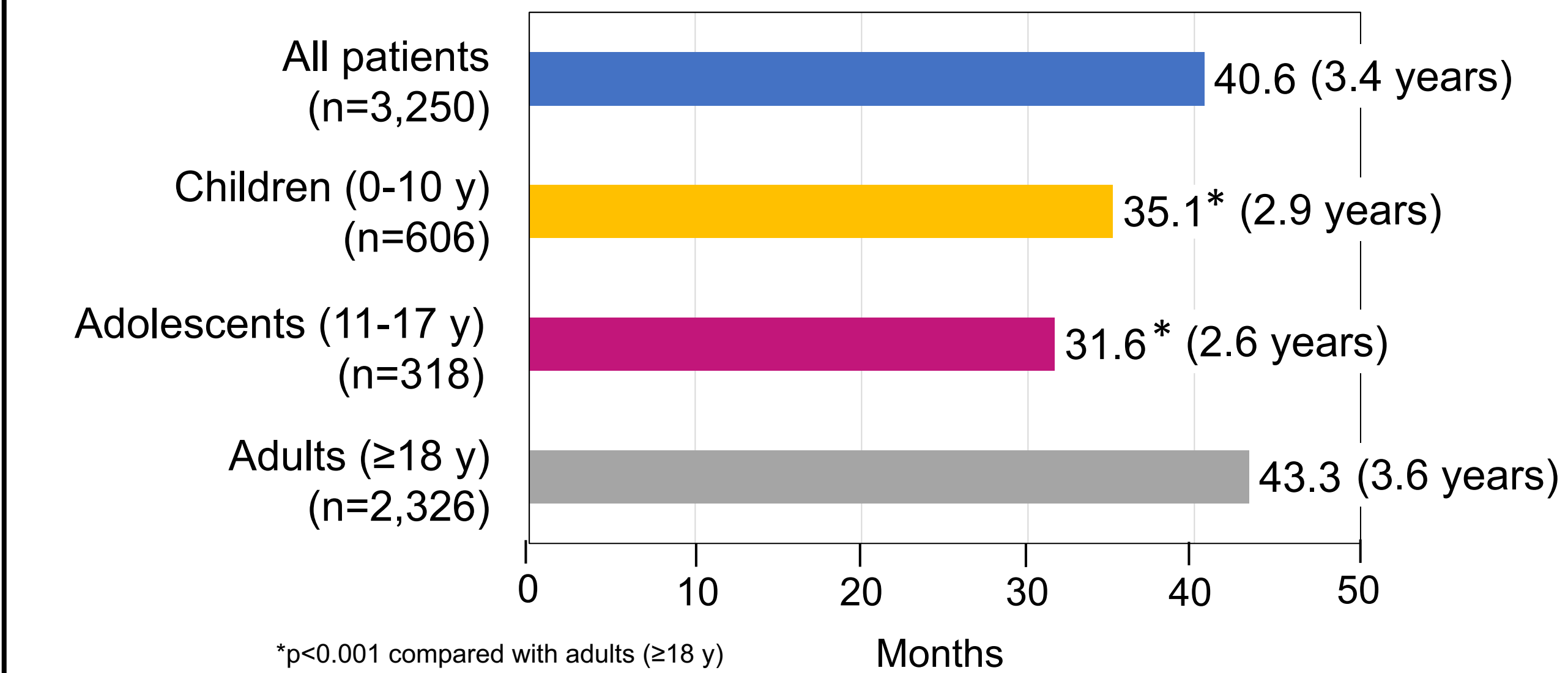
- Mean time from presentation to diagnosis was 40.6 months, and was significantly shorter for children and adolescents vs adults (Figure 3)

### Time to GI referral and/or endoscopy contributes to delayed diagnosis

Figure 4. Mean time from presentation to event, months

*p<0.001 compared with adults (≥18 y)
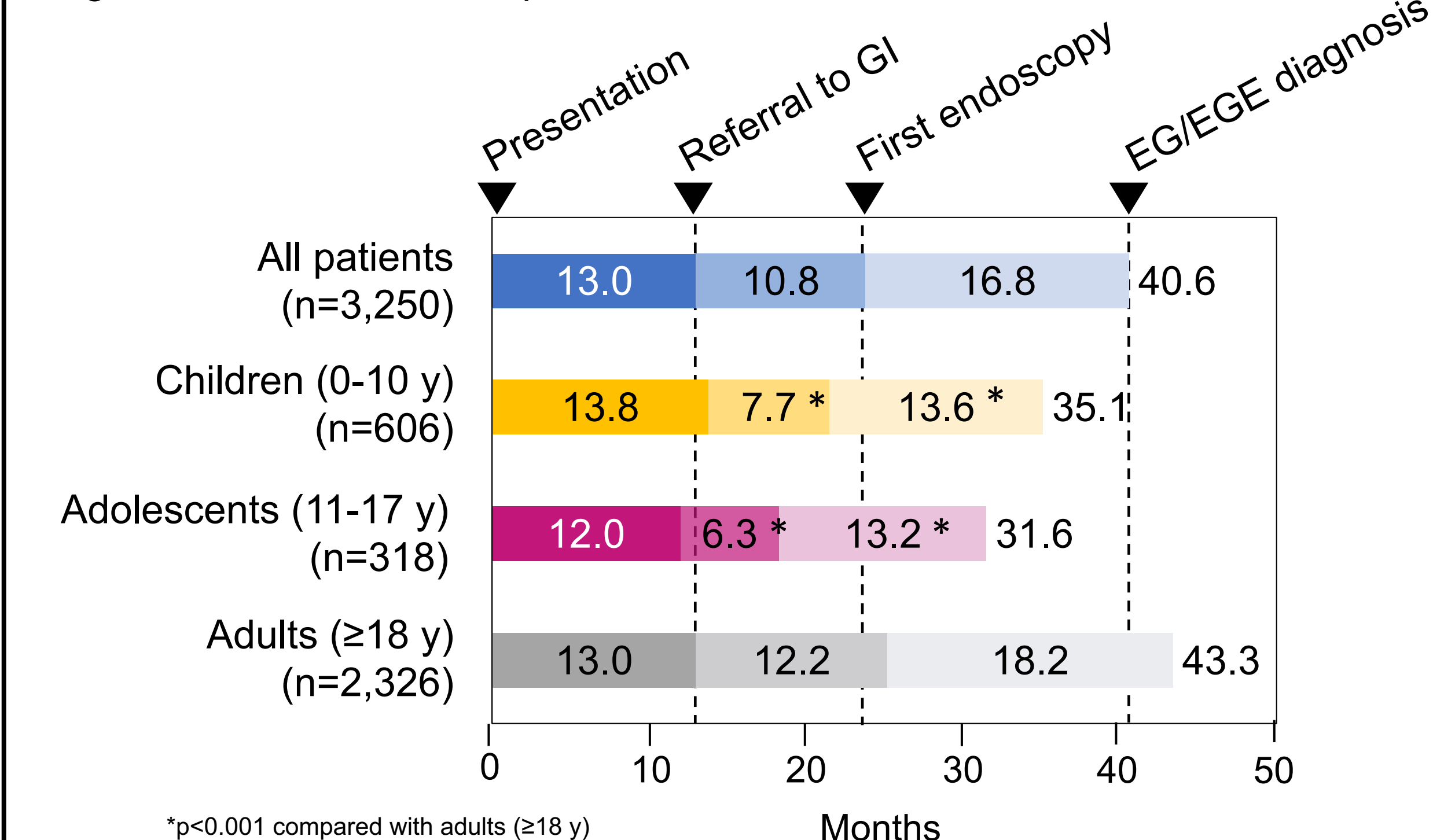
- Mean time from presentation to referral to a gastroenterologist (GI) was 13.0 months, with no differences between age groups (Figure 4)
- Mean time from GI referral to first endoscopy was 10.8 months, and was significantly shorter for children and adolescents vs adults (Figure 4)
- Mean time from first endoscopy to EG/EGE diagnosis was 16.8 months, and significantly shorter for children and adolescents vs adults (Figure 4)
- Overall, 56% of patients are diagnosed after first endoscopy; on average, patients received 2 endoscopies prior to diagnosis; there were no differences between age groups
- Mean time from first to repeat endoscopy was significantly shorter in children and adolescents vs adults (12.2 and 11.1 vs 23.0 months, p<0.001)

Biopsy/histopathology not performed routinely for all endoscopies

Figure 5. Frequency of biopsy and histopathology associated with endoscopy

*p<0.001 compared with adults (≥18 y)
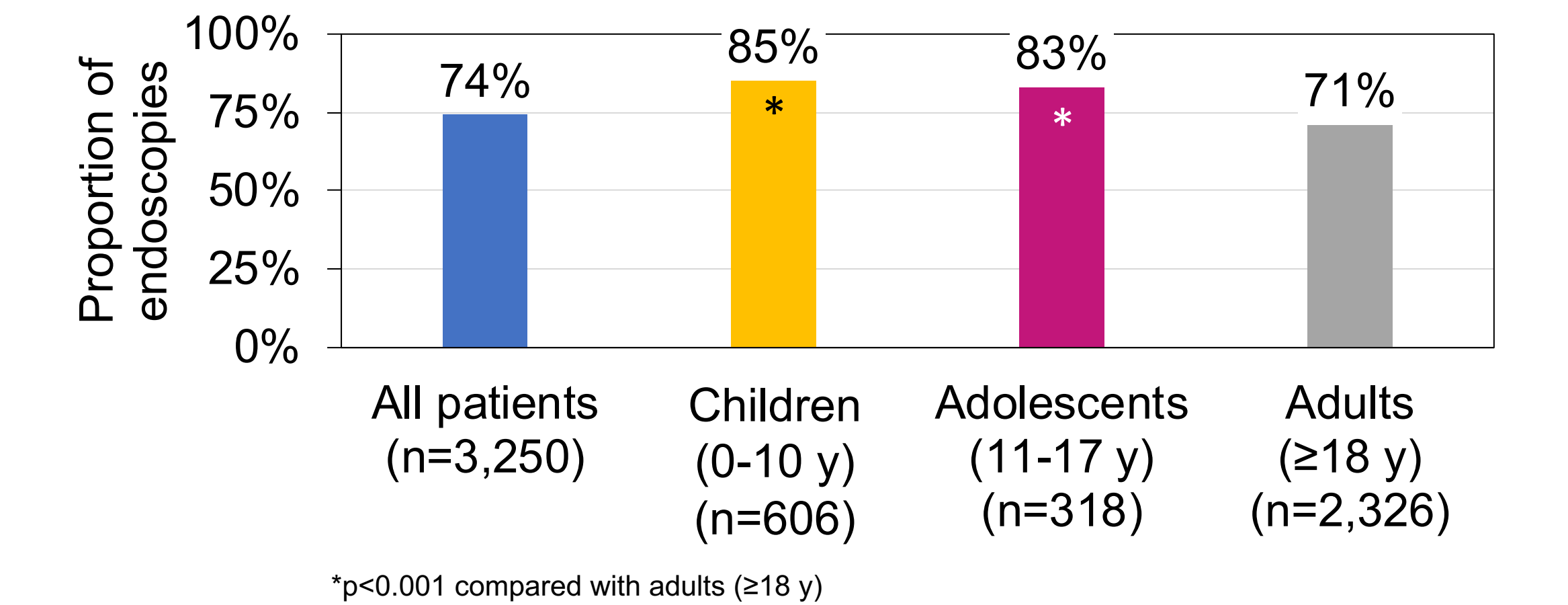
- Biopsy and histopathology were performed in 74% of all endoscopy procedures and were performed significantly more frequently in children and adolescents vs adults (Figure 5)

Patients with EG/EGE have a high prevalence of atopic comorbidities

Table 2. Frequency of atopic comorbidities

	All Patients (n=3,250)	Children (0-10 y) (n=606)	Adolescents (11-17 y) (n=318)	Adults (≥18 y) (n=2,326)
Allergic rhinitis	62%	76%*	75%*	57%
Asthma	46%	63%*	63%*	39%
Atopic dermatitis	30%	55%*	34%*	23%
Urticaria	12%	24%*	19%*	9%
Allergic conjunctivitis	10%	18%*	16%*	8%
Food allergy†	6%	20%*	10%*	2%

*p<0.001 compared with adults (≥18 y)
†Only food allergies reported by allergists were considered

- Atopic comorbidities were present in 80% of patients and were significantly more common in children and adolescents vs adults (Table 2)

CONCLUSIONS

- This study characterizes the lengthy journey to diagnosis for patients with EG/EGE, and highlights the unmet need for improved diagnostic practices and disease education
- Time to GI referral, failure to diagnose on first endoscopy, and lack of routine biopsy/histopathology likely contribute to delayed diagnosis
- Additional factors, such as failure to quantify eosinophils during histopathological exam of GI biopsies, likely cause further delay
- Shorter time to endoscopy and increased likelihood of biopsy/histopathology may contribute to the shorter mean time to diagnosis observed in children and adolescents
- Heightened disease awareness, tools to increase suspicion of EG/EGE (e.g., presence of atopic conditions, peripheral eosinophilia) and standardized criteria for endoscopy, biopsy, and histopathology may improve the time to diagnosis

References:
1) Gonsalves N, Furuta GT, Atkins D. (2016). Eosinophilic gastrointestinal disorders affect more than just the esophagus. J Pediatr Gastroenterol Nutr. 62(1):1-2.
2) Bedell A, Taft T, Craven MR, Guadagnoli L, Hirano I, Gonsalves N. (2017). Impact on Health-Related Quality of Life in Adults with Eosinophilic Gastritis and Gastroenteritis: A Qualitative Assessment. Dig Dis Sci. 63(5):1148-1157.
3) de Chambrun P, Gonzalez F, Canva JY, Gonzalez S, Houssin L, Desreumaux P, Cortot A, Colombel JF. (2011). Natural history of eosinophilic gastroenteritis. Clin Gastroenterol Hepatol. 9(11):950-956.