

# High Discovery Rate of Eosinophilic Gastritis and/or Duodenitis Among Patients with Chronic Unexplained Gastrointestinal Symptoms

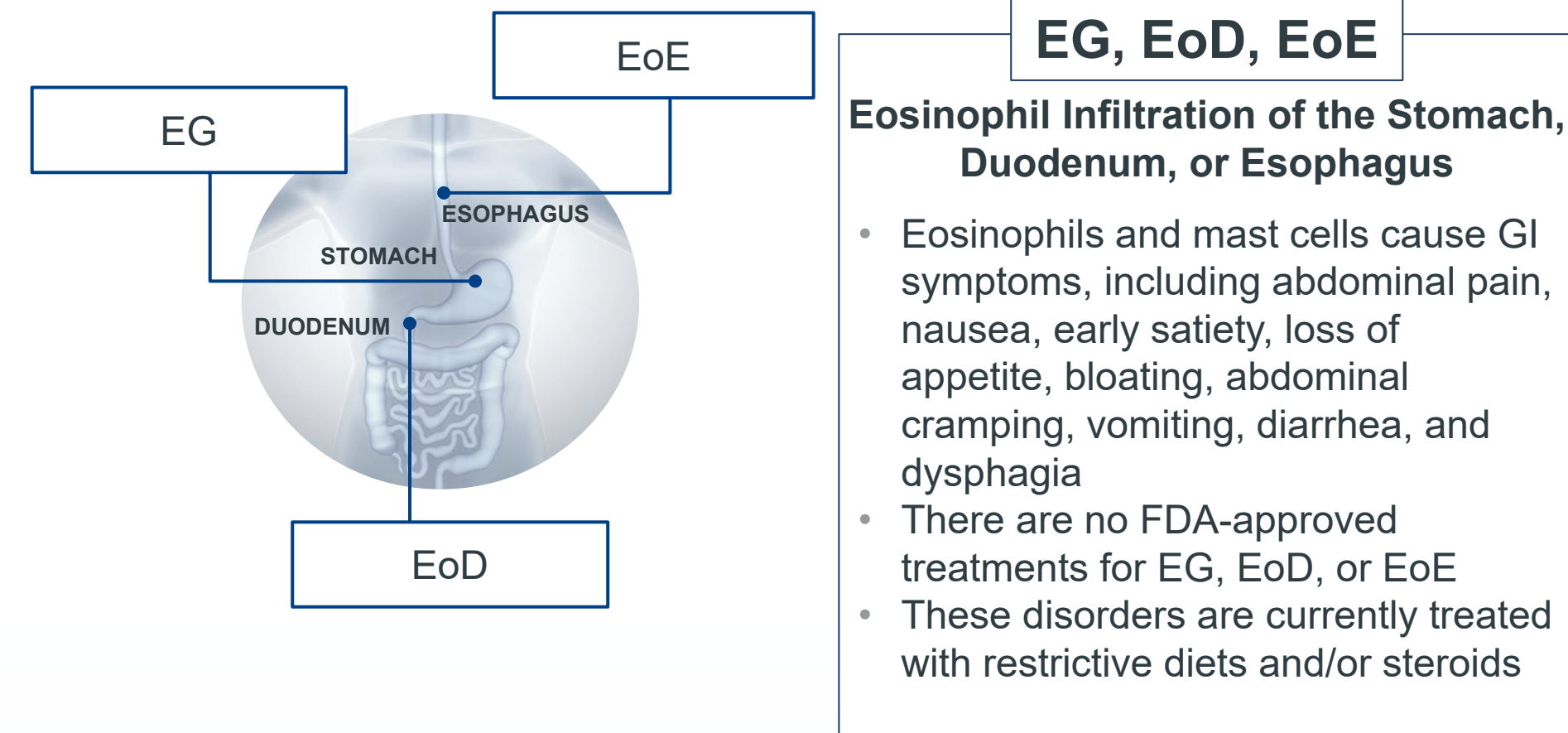
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## BACKGROUND

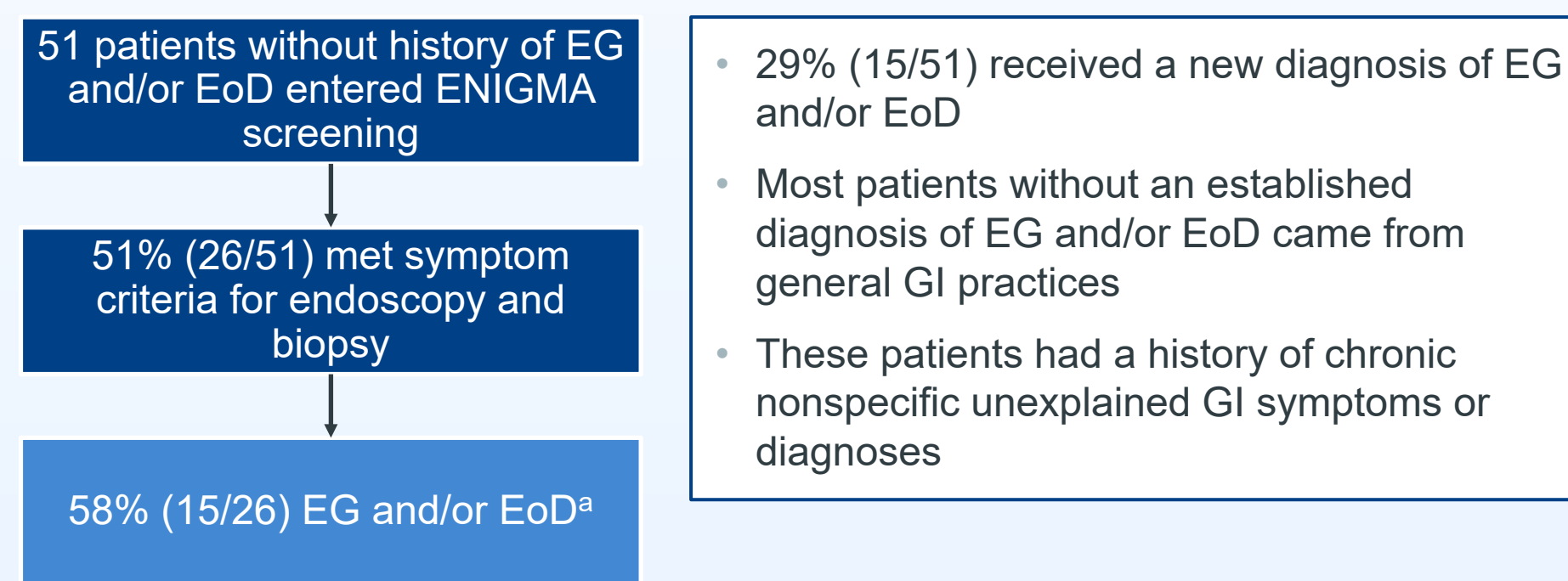
- Pathologic accumulation and over-activation of eosinophils and mast cells are implicated in chronic inflammatory diseases of the gastrointestinal (GI) tract, including eosinophilic esophagitis (EoE), gastritis (EG), duodenitis (EoD), and colitis—collectively termed eosinophilic gastrointestinal diseases (EGIDs)<sup>1,2</sup>
- Patients with EGIDs have decreased quality of life due to chronic and often debilitating symptoms such as dysphagia, abdominal pain, bloating, nausea, early satiety, vomiting, and diarrhea<sup>3</sup>

Figure 1. Eosinophilic GI Disorders



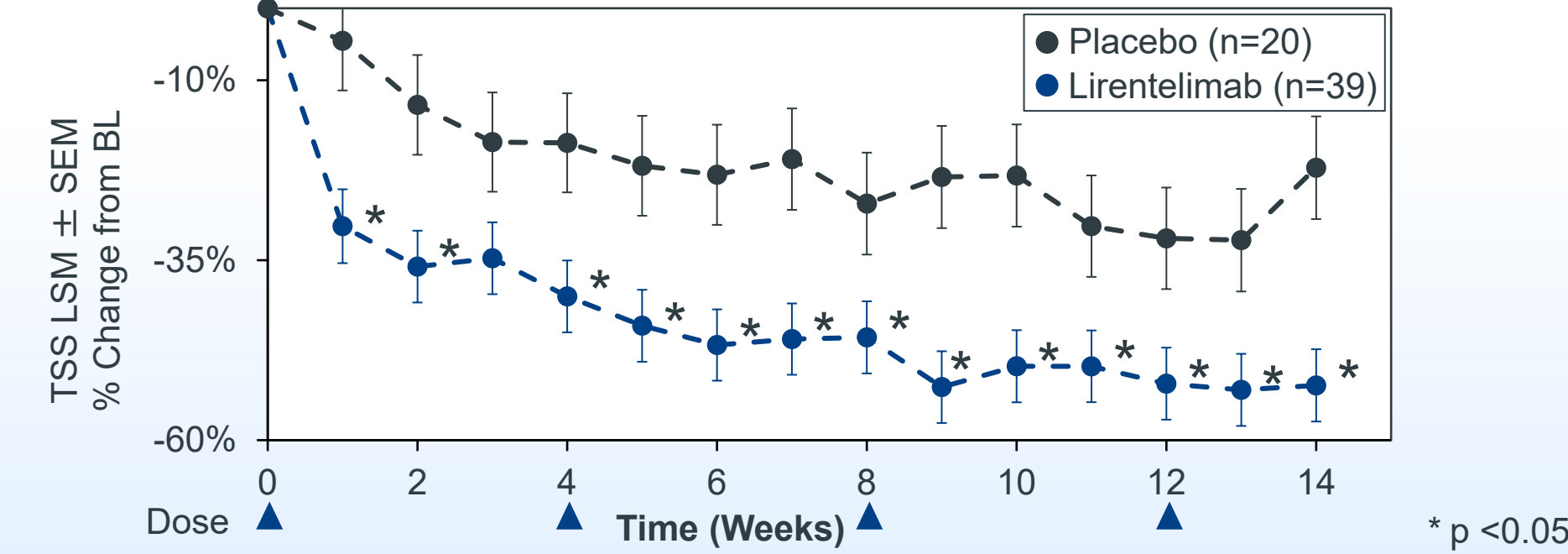
- EG and/or EoD are thought to affect 45,000–50,000 persons in the US; this could be an underestimate. There is evidence that these diseases are as common as inflammatory bowel diseases<sup>4,5</sup>
- EG and/or EoD have been described as rare conditions found in individuals with atopy and increased peripheral eosinophils and/or total IgE. However, this conclusion was based on retrospective studies that included patients already diagnosed with EG and/or EoD<sup>6,7</sup>
- Current treatment options, such as diet restriction and corticosteroids, have limited efficacy and/or are inappropriate for chronic use
- New therapies are needed

Figure 2. High Rate of Detection of New Cases of EG and/or EoD in the ENIGMA Study Indicates Underdiagnosis of These Diseases<sup>8</sup>



- Lirentelimab, an investigation medicine, is a humanized monoclonal antibody against Siglec-8, produced histologic and symptom improvements in patients with EG and/or EoD in a Phase 2, randomized, placebo-controlled study (ENIGMA)<sup>8</sup>.
- A recent analysis of ENIGMA screening data revealed that multiple biopsies are required to optimize diagnostic yield, due to the patchiness of gastroduodenal eosinophils<sup>9</sup>

Figure 3. Lirentelimab Significantly Reduced Patient Symptoms in the ENIGMA Study<sup>5</sup>



## OBJECTIVE

- We conducted a prospective study to evaluate the prevalence of EG and/or EoD among patients with moderate–severe chronic unexplained GI symptoms and clinical features, to inform diagnostic protocols

## METHODS

- Patients with ≥6-month history of GI symptoms without an identified cause and no response to pharmacologic or dietary interventions, or patients with previous diagnoses of irritable bowel syndrome and/or functional dyspepsia were screened

### EG/EoD GI Symptom Questionnaire<sup>®</sup>

- Developed in accordance with FDA guidance, a patient-reported outcome tool measures each of the following symptoms, daily, on a scale of 0–10:

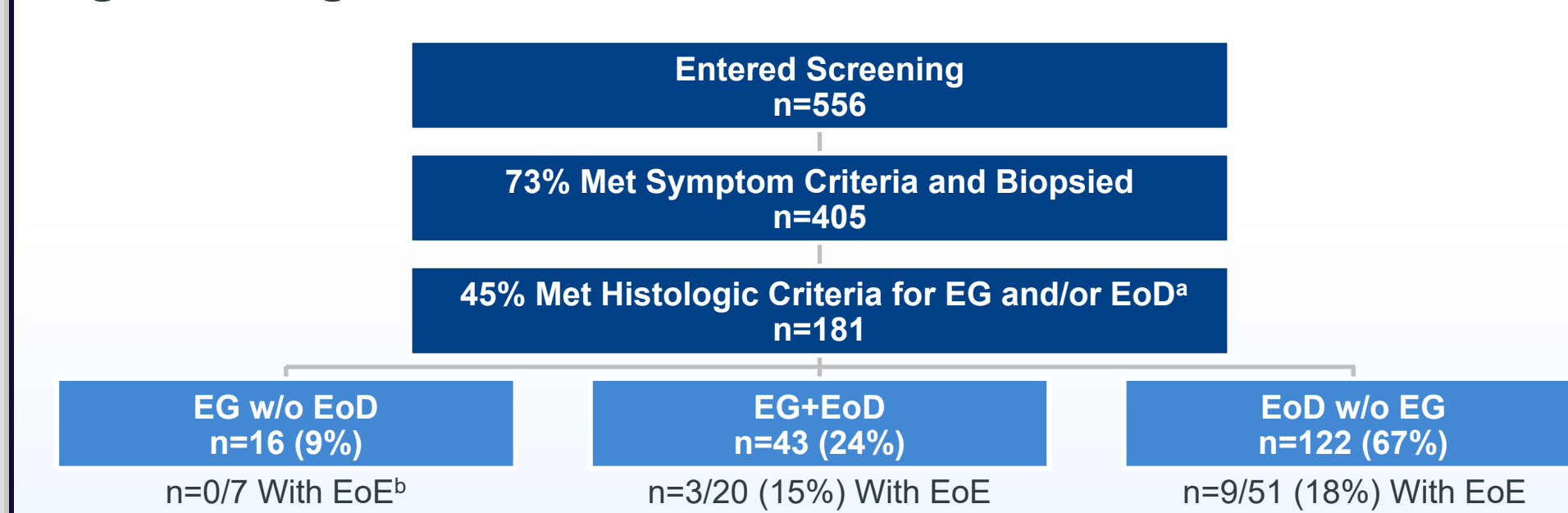
- Abdominal pain
- Nausea
- Vomiting
- Early satiety
- Loss of appetite
- Abdominal cramping
- Bloating
- Diarrhea

- Patients had daily scores of ≥3 (range 0–10) for any individual symptom and Total Symptom Scores (TSS) ≥10
- Controls had an average daily score ≤1 for all symptoms and no daily score ≥3, on any day, for any symptom

- Patients who reported active moderate–severe symptoms per the EG/EoD Questionnaire qualified for systematic biopsy collection
- Biopsy samples were collected during esophagogastroduodenoscopy (EGD)
  - Minimum of 12 gastric and duodenal biopsies (4 gastric antrum, 4 gastric corpus, and 4 from duodenum, plus additional biopsies from areas of interest)
  - Up to 4 esophageal biopsies (2 distal and 2 mid/proximal) from patients with histories of EoE, esophageal abnormalities during EGD, or for other reasons
- Primary endpoints were the proportion of patients who underwent biopsy and met the histologic criteria for EG and/or EoD (≥30 eos/hpf in 5 gastric or 3 duodenal hpfs)
- A separate study of asymptomatic controls was conducted for comparison

## RESULTS

Figure 4. High Prevalence of EG and/or EoD



- 33% (181/556) of patients with chronic unexplained GI symptoms and 45% (181/405) of patients with moderate–severe symptoms who underwent biopsy met histologic criteria for EG and/or EoD

<sup>a</sup> Patients who met symptom criteria and ≥30 eos/hpf in 5 gastric hpfs and/or ≥30 eos/hpf in 3 duodenal hpfs  
<sup>b</sup> 12 of 78 (15%) patients with esophageal biopsies met histologic criteria for EoE (≥15 eos in 1 hpf) and EG and/or EoD

Table 1. Features of Patients with EG and/or EoD and Controls

Patient Characteristics	Met Histologic <sup>a</sup> Criteria for EG and/or EoD n=181	Asymptomatic Controls n=33	
Mean age, years (range)	45 (19–78)	34 (18–51)	
Female sex, %	73%	39%	
White, %	85%	100%	
Weight, median, kg	83	80	
Blood eosinophils	Cells/μL, median (IQR)	170 (100–250)	70 (50–150)
	Blood eos ≥250 cells/μL, %	27%	9%
	Blood eos ≥500 cells/μL, %	4%	0
	Blood eos ≥1500 cells/μL, %	0	0
Immunoglobulin E	kU/L, median (IQR)	34 (14–103)	18 (9–60)
	IgE ≥ 70 kU/L, %	36%	21%
TSS [0–80], mean ±SD	31.3±11.2	0.1±0.2	
Previous Diagnosis	GI symptoms <sup>b</sup> , mean years	11	-
	GERD, IBS, FD, and/or EoE, %	93%	0
	GERD, %	65%	0
	IBS, %	55%	0
	FD, %	15%	0
	EoE, %	2%	0
	Atopy <sup>c</sup> , %	48%	15%

<sup>a</sup> Patients who met symptom criteria and ≥30 eos/hpf in 5 gastric hpfs and/or ≥30 eos/hpf in 3 duodenal hpfs  
<sup>b</sup> Diagnoses of other functional GI disorders, such as chronic abdominal pain or functional diarrhea  
<sup>c</sup> Asthma, allergic rhinitis, atopic dermatitis and/or food allergy

Figure 5. Symptoms in Patients With EG, EoD, and EG+EoD

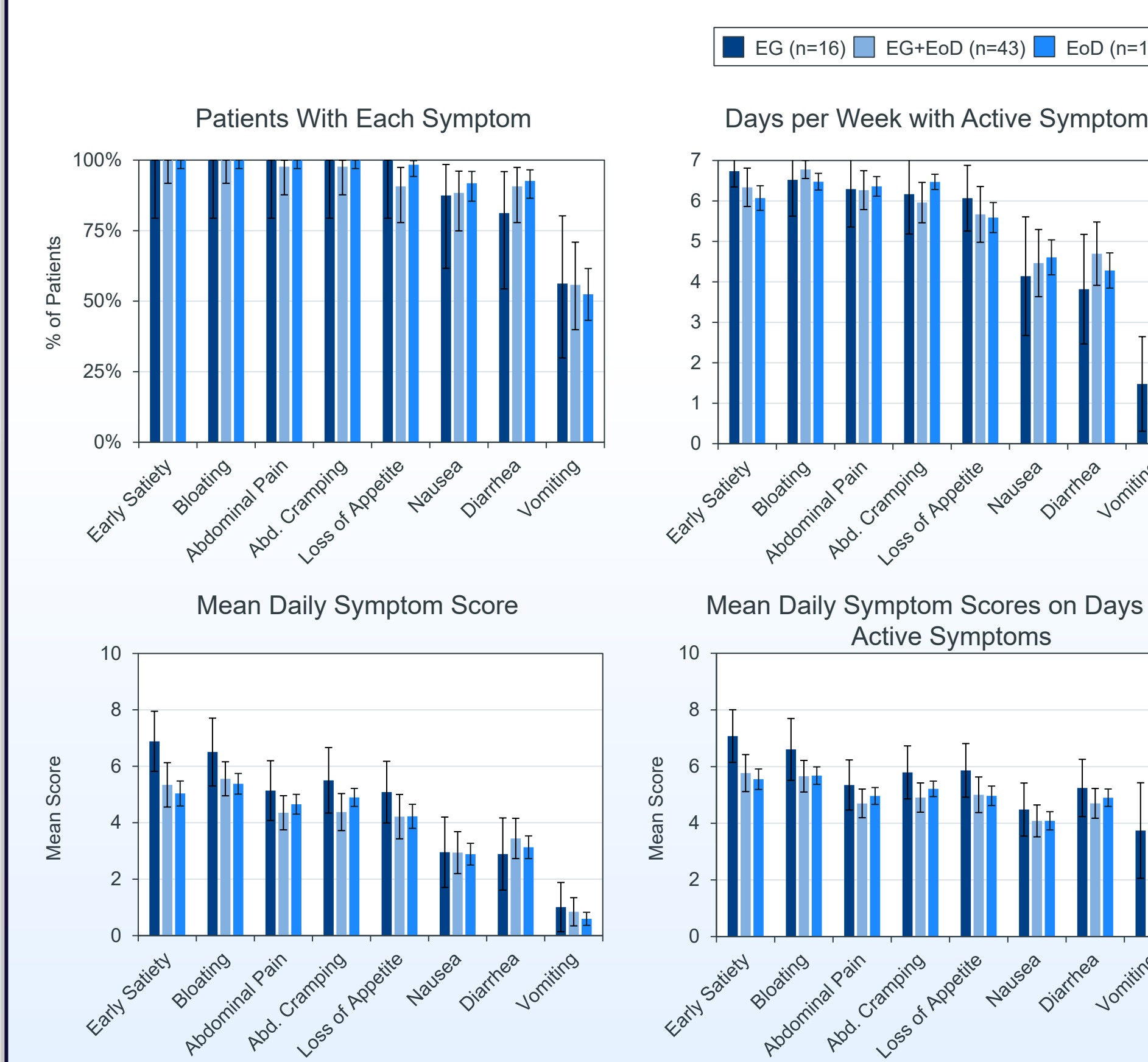
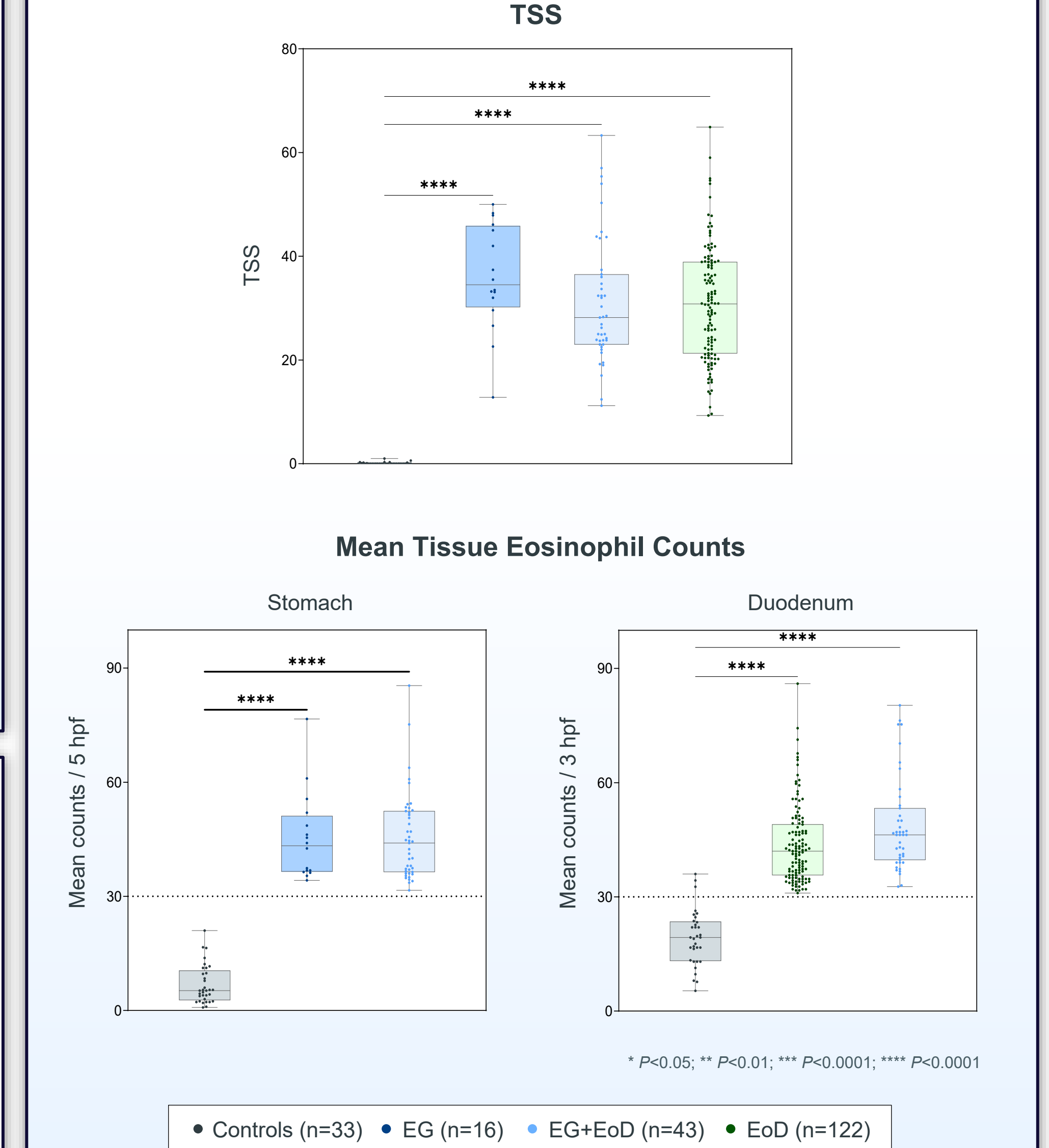


Figure 6. Total Symptom Score (TSS) and Mean Eosinophil Counts in Patients vs Controls



45% (181/405) of patients and 6% (2/33) of asymptomatic controls<sup>a</sup> met histologic criteria for EG and/or EoD (odds ratio, 12.52; 95% CI, 3.0–53.0; P<0.001)

<sup>a</sup> Patients and controls used the same patient-reported-outcome questionnaire and underwent identical biopsy protocols. Histologic evaluation for both groups were performed by the same central pathologists

## CONCLUSIONS/DISCUSSION

- Endoscopy and systematic biopsy of patients with moderate–severe GI symptoms found that 45% met histologic criteria EG and/or EoD
- Symptom burden, measured by intensity and frequency, was similar among patients with EG, EoD, and EG and EoD
- EG and/or EoD should be considered in symptomatic patients regardless of baseline peripheral eosinophil levels
- Patients with chronic moderate–severe unexplained GI symptoms should undergo EGD with collection of gastric and duodenal biopsies and counting of eosinophils to identify those with EG and/or EoD
- Endoscopy with systematic biopsy and assessment of tissue eosinophils may lead to a precise diagnosis, including EG and/or EoD