Eosinophilic esophagitis in 2026: Which therapy, when?

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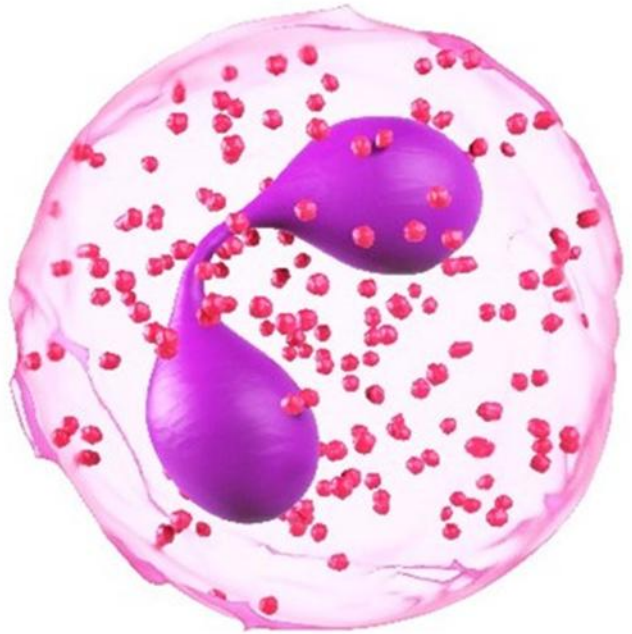
Eosinophilic Esophagitis - Definition

- Chronic allergen/immune mediated disease
- Characterized by symptoms of esophageal dysfunction
- Histologically with eosinophilic infiltration of the esophageal mucosa
  - >15 eos/hpf
- Absence of secondary causes of eosinophilia

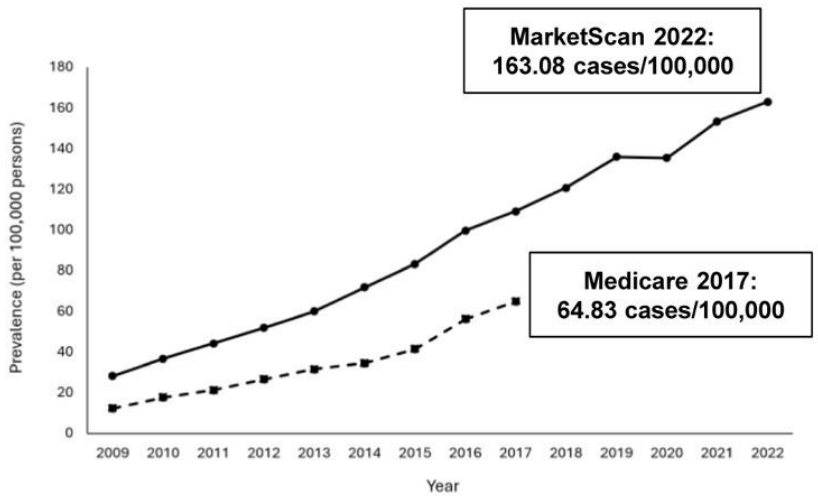


Dellon ES et al. *Gastroenterology*. 2018;155(4):1022-1033.e10.

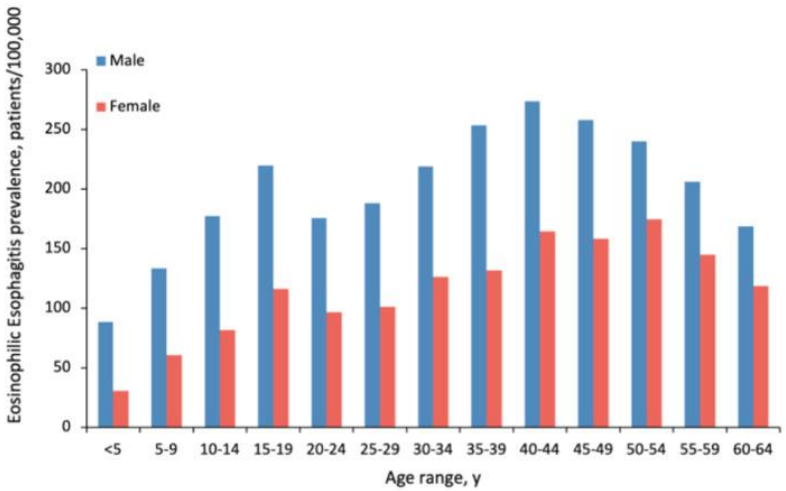
Prevalence and Cost of EoE in the US

Continually Rising Prevalence of EoE in the United States

Analysis of administrative claims data for the U.S. shows > 5-fold prevalence increase since 2009

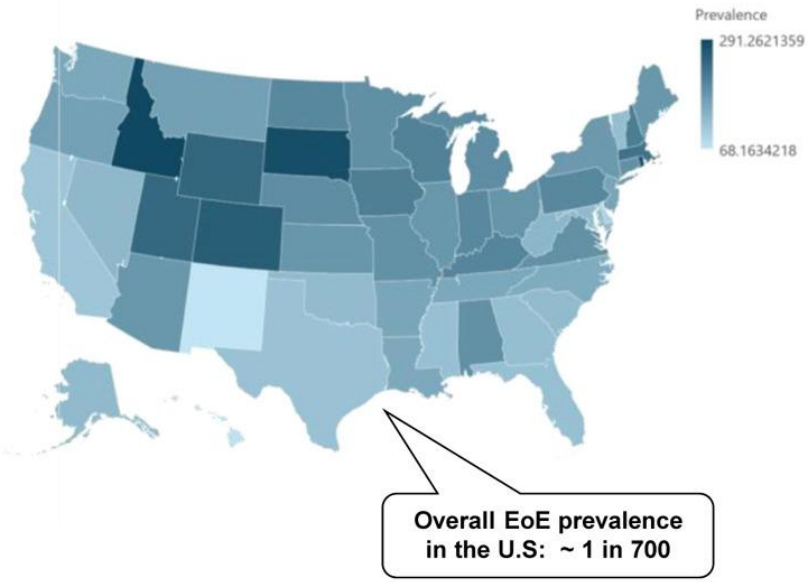


EoE prevalence by age and sex in 2022 (MarketScan)



Prevalence increased in all age strata an in both sexes

EoE prevalence per 100,000 by state



Clinical Gastroenterology and Hepatology

Thel, Hannah L. et al. *Clinical Gastroenterology and Hepatology.* 23(2):272-280.e8.

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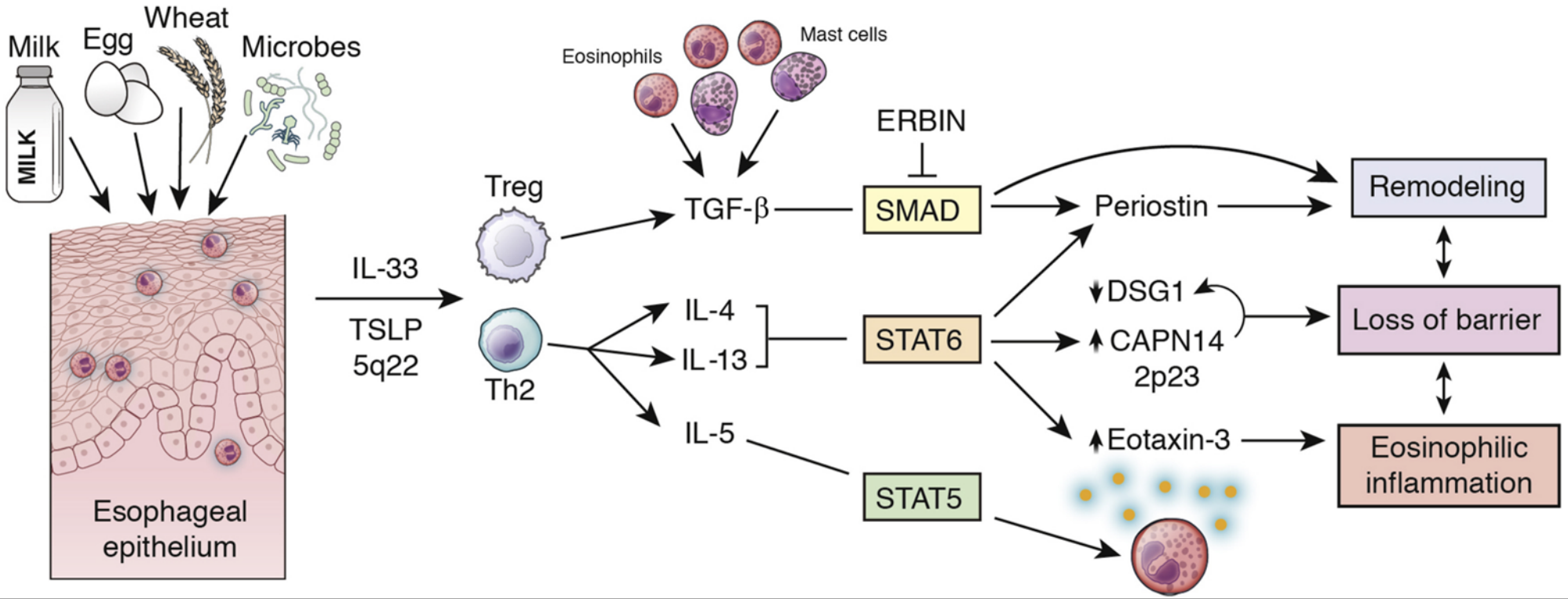
EoE pathophysiology

- Th2- mediated condition
  - Activated Th2 lymphocytes increase tissue levels of Th2 cytokines (eg, IL-4, IL-5 and IL-13)
  - Results in chronic esophageal inflammation and dysfunction



Common Symptoms of EoE

Adults and Adolescents

- Solid food dysphagia
  - 60-100% of patients
- Food impaction – 25%
- Heartburn – 30-60%
- Chest Pain 8-44%

Children

- Nausea and vomiting
- Regurgitation
- Heartburn
- Abdominal pain
- Chest pain
- Food refusal
- Failure to thrive

Dellon, CGH 2009. Dellon, Med Clin N am 2019. Hiremath, DDS 2015

Eating Adapatations in EoE

”IMPACT”

I - **I**mbibe fluids with meals

M - **M**odify food (cutting into small pieces, pureeing)

P - **P**rolong mealtimes

A - **A**void hard texture foods

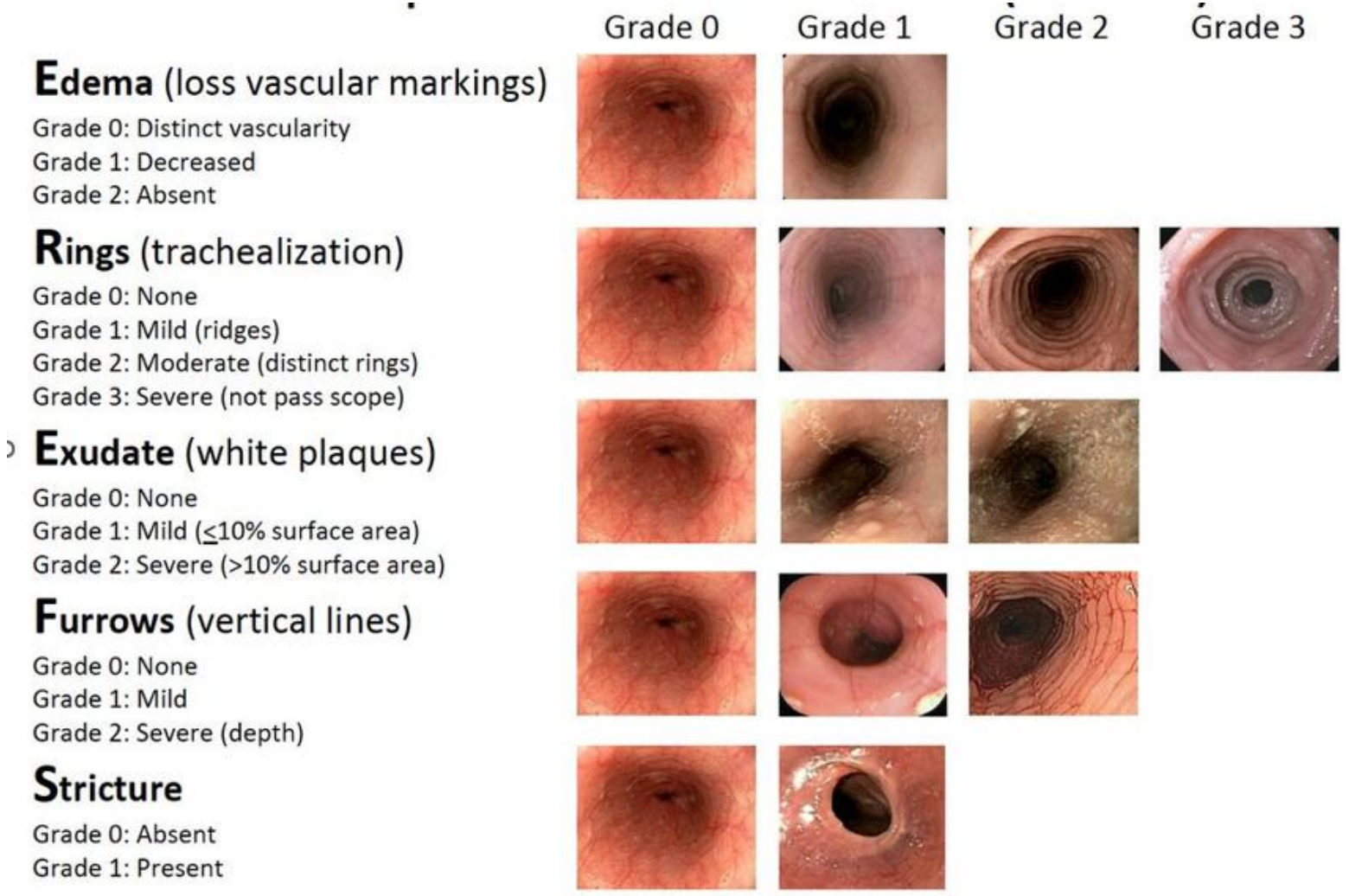
C - **C**hew excessively

T - **T**urn away tablets/pills

- Eating adaptations may hide and help control dysphagia, which may lead to delays in diagnosis

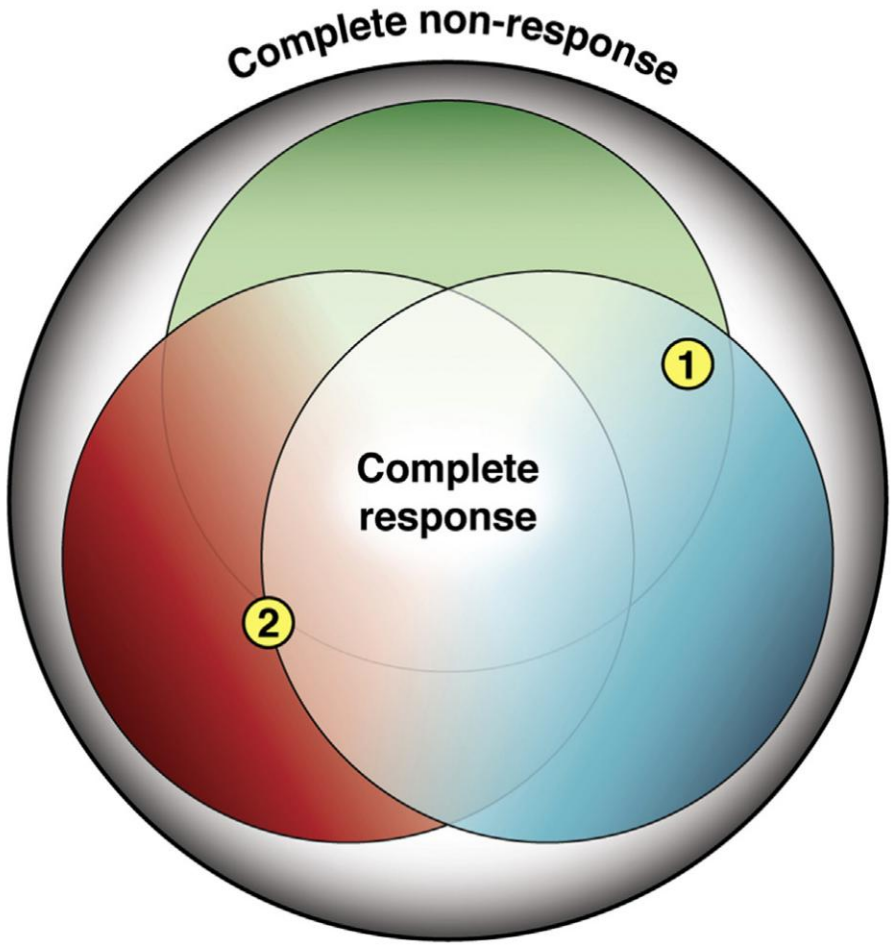
- People with EoE may also have emotional distress or anxiety related to eating, an may avoid social or work activities involving food or meals

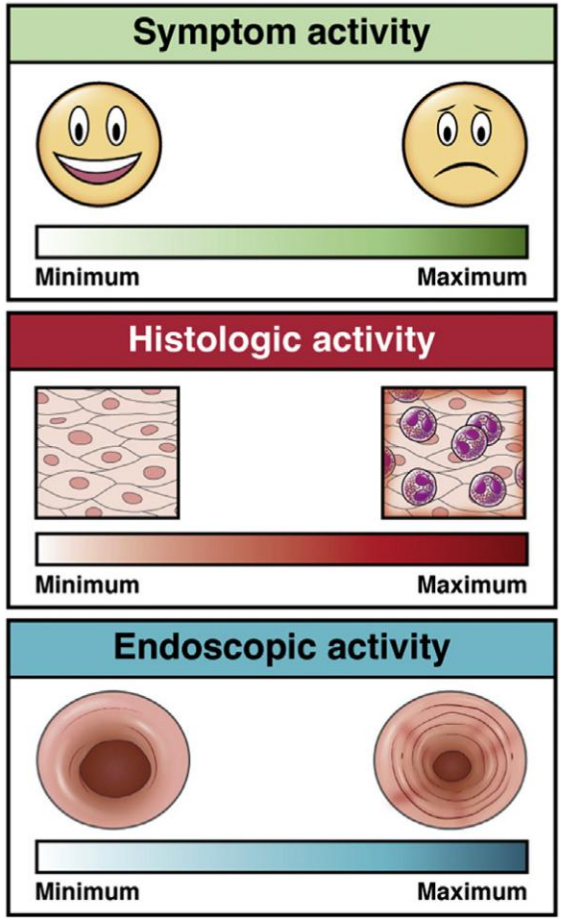
EoE Endoscopic Reference Score (EREFS)



Hirano et al. Gut. 2014; 62(4):489-95

Treatment Goals in EoE Management





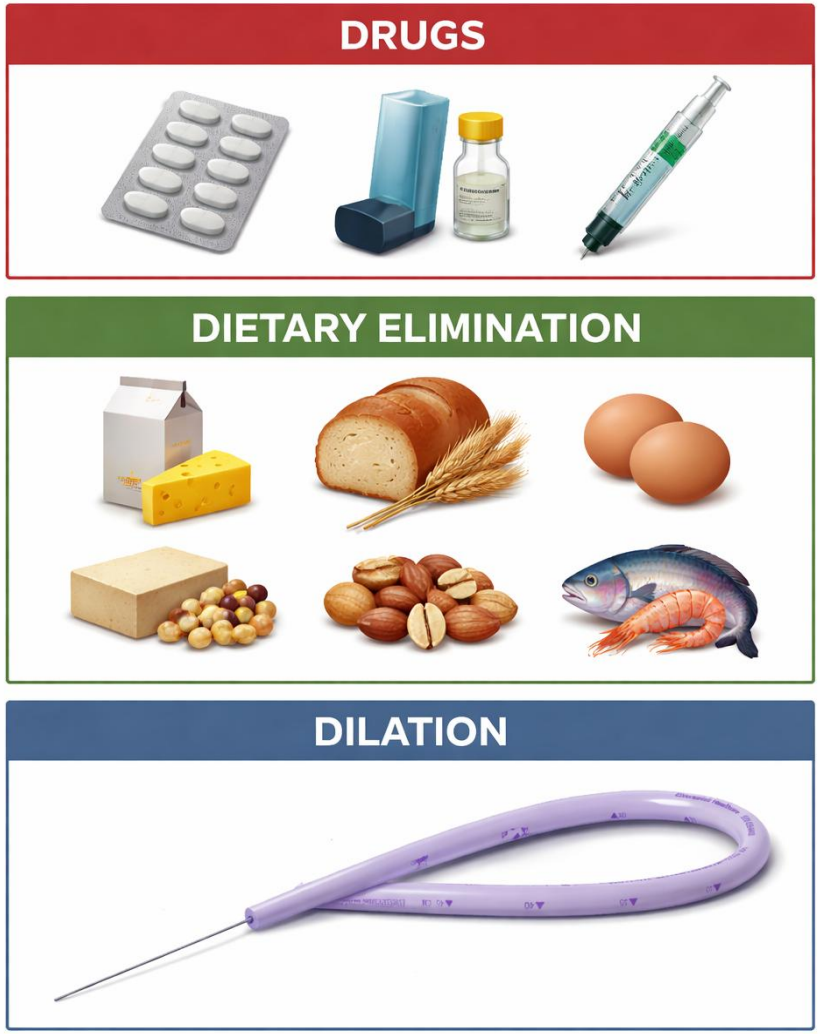
Symptoms
Resolution of dysphagia without the need to avoid food based on texture

Histopathology
Resolution of esophageal eosinophilic inflammation (< 5-15 eos/hpf)

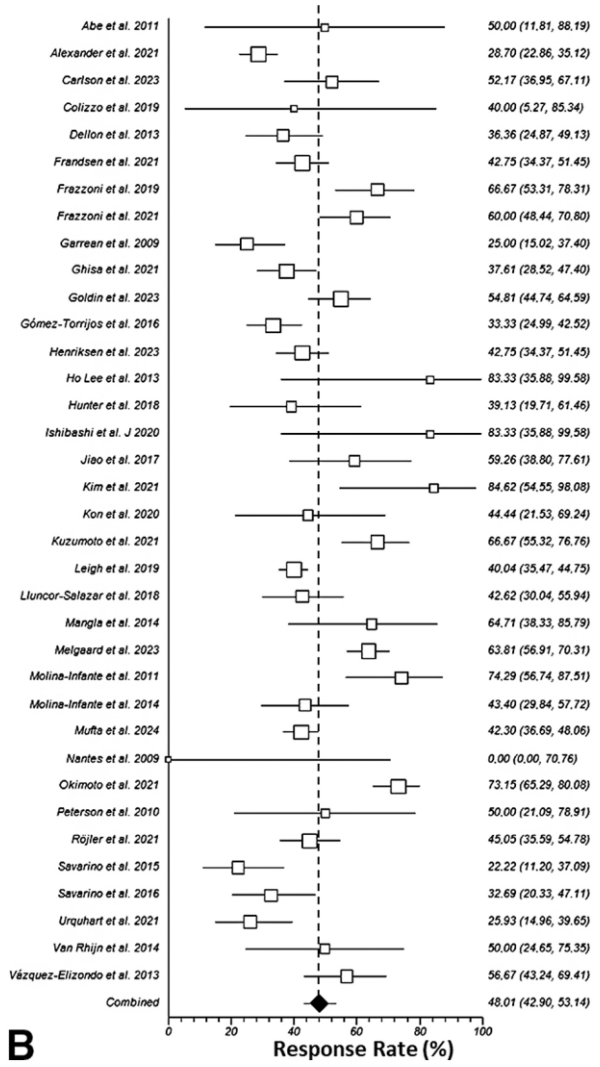
Endoscopy
Improvement in inflammatory features and strictures (Diameter >15 mm)

Treatment Modalities

- Drugs
  - Proton pump Inhibitors (PPI)
  - Topical Corticosteroids
  - Biologics
- Dietary Elimination
- Dilation



PPI efficacy



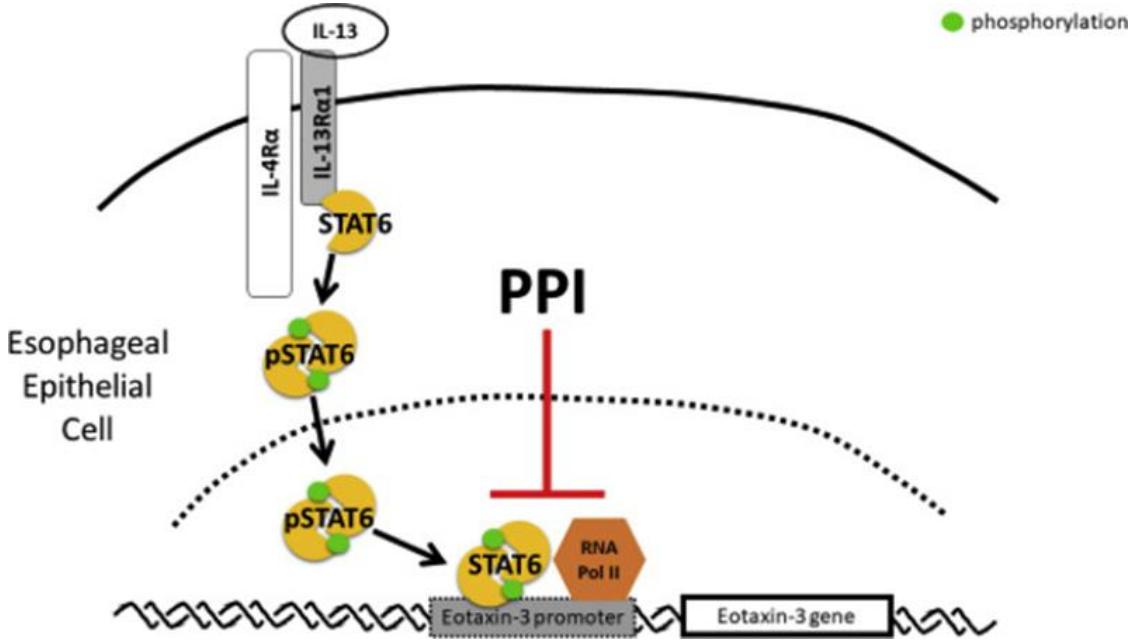
- Histologic remission rate (<15 eos/hpf)
  - **45.4%** pooled remission rate
  - No significant difference between adult and pediatric population
  - **34.1%** Deep remission (<5 eos/hpf)
- Clinical Response: **65%**

Lucendo AJ, et al. Clin Gastroenterol Hepatol. 2025 Nov;23(12):2115-2127.e21.

PPIs treat EoE Through Multiple Mechanisms

- **Esophageal Acid Dependent**
  - Restore esophageal mucosal barrier integrity
  - Reduced acid-mileu decreases eotaxin-3 release

- **Esophageal Acid Independent**
  - Inhibition of inflammatory cell H+-ATPases that pump acid into extracellular space/lysosomes
  - Inhibit oxidative burst, cell migration and phagocytosis
  - Inhibit adhesion molecule expression
  - Reduce STAT6 and RNA Pol II binding to eotaxin-3 promotor



Dellon ES. Gastro. 2018 Oct;155(4):1022-1033.e10.

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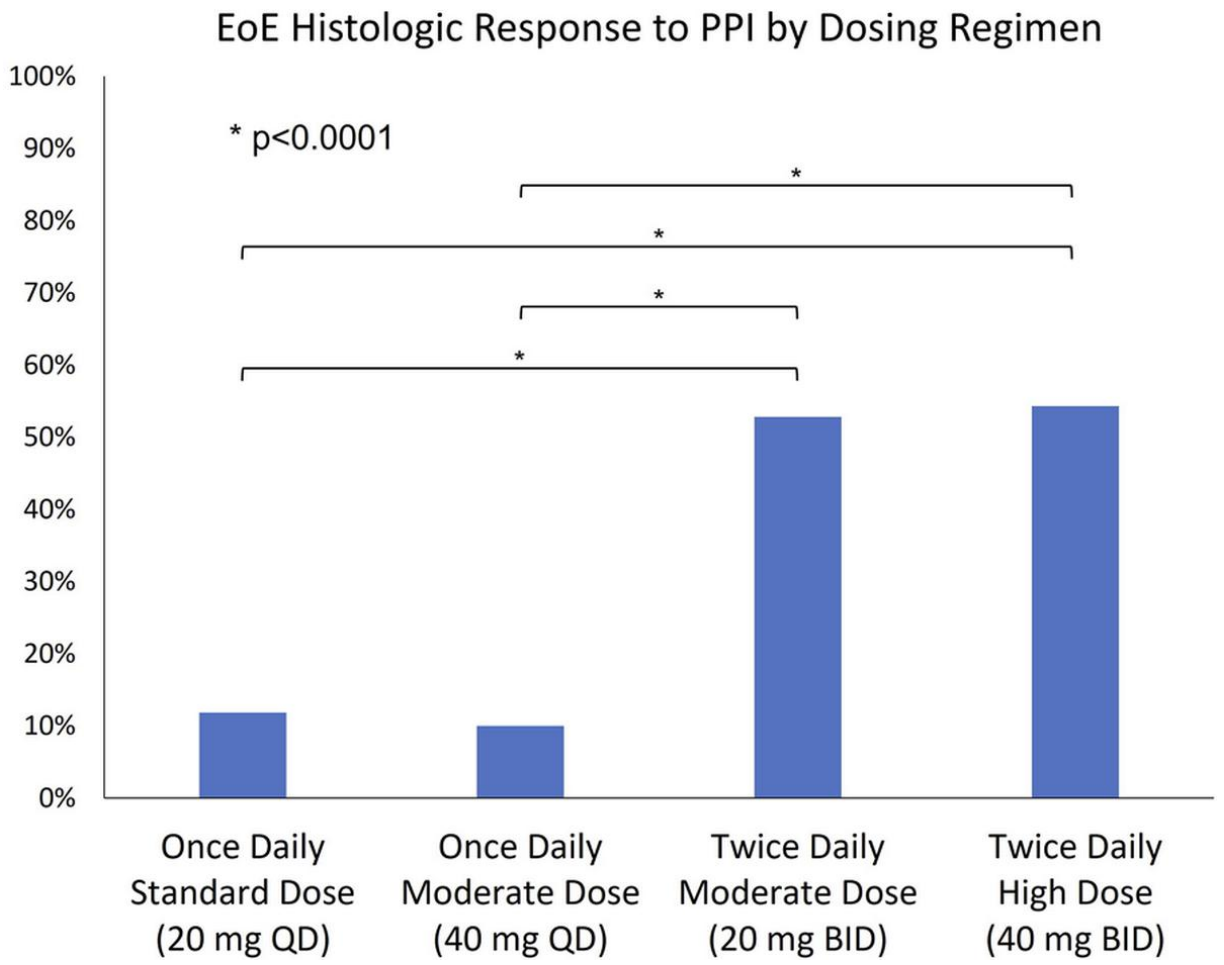
Optimal PPI Dosing

Medication	Dosing
PPIs	
Children	2 mg/kg per day (or 1 mg/kg twice daily)
Adults	Double the approved reflux dose per day (e.g., omeprazole 20 mg twice daily or 40 mg daily or other PPI equivalent)



Muftah M, et al. Am J Gastroenterol. 2024 May 1;119(5):991-995.
Dellon ES, Am J Gastroenterol. 2025 Jan 1;120(1):31-59.

Predicting PPI response

PPI responsive

- Higher MNBI in proximal esophagus compared to distal esophagus
- Isolated distal elevation in eosinophils at index endoscopy

PPI non-response

- Positive food allergy testing and increased environmental allergens
- Proximal predominant eosinophilic infiltration (middle/proximal > distal eosinophil density by $\gtrsim$ 10/hpf
- Inability to pass an endoscope
- Elevated peripheral eosinophil count
- Young age
- Lower BMI (< 25.2)

Alexander, R, et al. Digestive Diseases and Sciences (2021) 66:3096–3104
Hartnett DA, et al. Clin Gastroenterol Hepatol. 2025 Jul 16:S1542-3565(25)00608-1.

PPI Maintenance Therapy Considerations

- No consensus on standard maintenance regimen

- Lucerno AJ, et al. 2025 Metanalysis of 7 studies with PPI reduced to half induction dose
  - 68.2% maintained histologic remission on half dose

- Molina-Infante, et al. 2015 followed 75 adults with PPI tapered to lowest effective dose in prospective cohort
  - 73% maintained histologic remission on low dose PPI
  - 9/12 patients regained response with PPI intensification

- Laserna-Mendieta EJ, et al. (EoE CONNECT database)
  - ~70% of patients maintain histologic remission after stepping down to standard dosing
  - Maintenance success higher if in deep remission

Takeaway:

Generally reasonable to try to reduce to lowest effective dose

Lucendo AJ, et al. Clin Gastroenterol Hepatol. 2025 Nov;23(12):2115-2127.e21.
Molina-Infante J, et al. Am J Gastroenterol. 2015 Nov;110(11):1567-75.
Laserna-Mendieta EJ, et al. Aliment Pharmacol Ther. 2020 Sep;52(5):798-807.

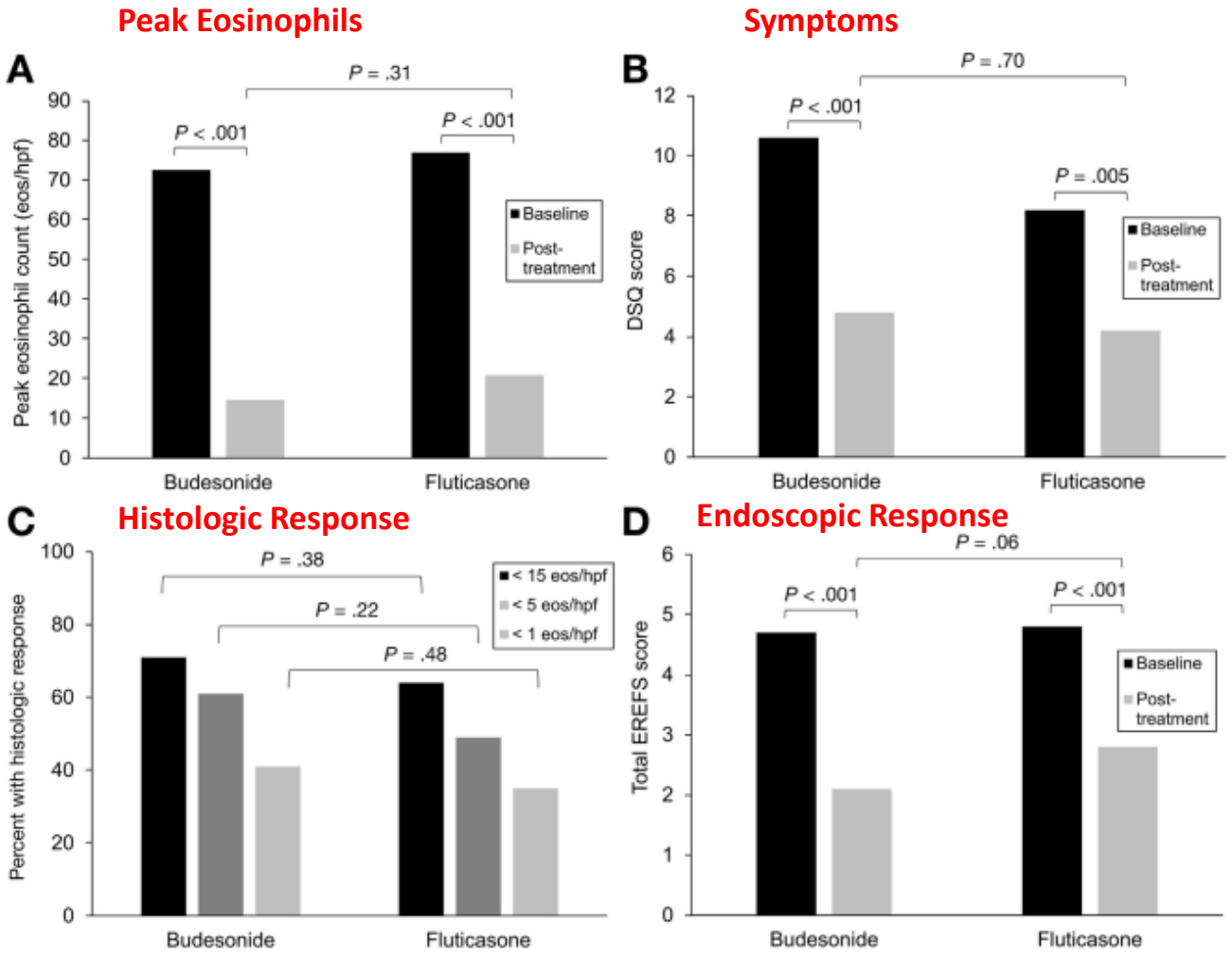
Topical Steroids

- Effective for inducing remission
- Can reduce esophageal remodeling
- One US FDA approved formulation
  - Adults and children 11 years and older
  - Budesonide oral suspension: 2mg BID x12 weeks
- Adapted Formulations
  - Fluticasone HFA
  - Budesonide Respules
  - Compounded budesonide

Topical Steroids: Practical tips

- Dosing of “adapted” formulations:
  - 2 mg/d of budesonide
  - 1760 mcg/d of fluticasone from inhaler
- Take after breakfast and/or before bed – no eating/drinking for 30-60 mins
- Can rinse mouth and spit
- Take adequate time to explain dosing to patients

What is the efficacy of topical steroids?



- 8 Week RCT of Budesonide (1mg BID) vs. Fluticasone (880 µg BID)
- Histologic response (< 15 eos/hpf)
  - Budesonide 71%
  - Fluticasone 64%

Budesonide 〓 Fluticasone

Dellon ES et al. Gastroenterology. 2019 Jul;157(1):65-73.e5

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Twice Daily vs. Daily Steroid Dosing

	Daily (n=122)	Twice daily (n = 400)	P value
Type of steroid used, n (%) Fluticasone Budesonide	 22 (18) 100 (82)	 143 (36) 257 (64)	< .001
Mean steroid dose, µg ± SD	1519 ± 686	1706 ± 733	.01
Symptom response, n (%)	38 (78)	104 (76)	.82
Histologic response, n (%) < 15 eos/hpf ≤6 eos/hpf 0 eos/hpf	 68 (56) 58 (48) 33 (27)	 232 (58) 205 (51) 124 (31)	 .66 .47 .41

- Outcomes did not differ by daily or twice daily dosing
- Daily dosing associated with less candida esophagitis (3% vs. 8%)

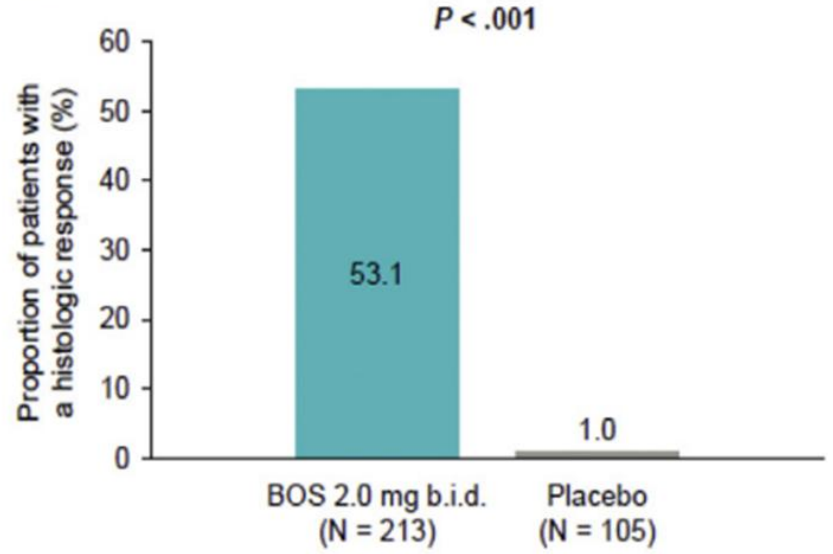
Reed CC, et al. Clin Gastroenterol Hepatol. 2025 May;23(6):946-953.e1

Budesonide Oral Suspension

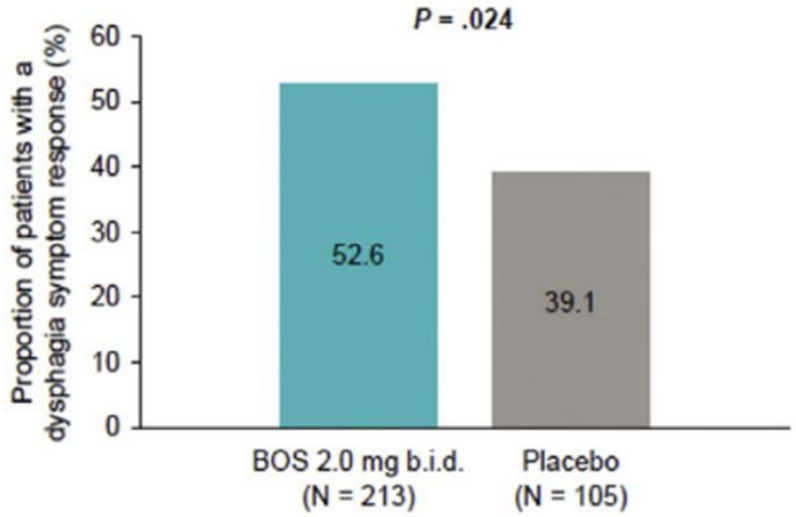
- Improved both histology and symptoms
- Only FDA approved oral therapy
- Approved for 12 weeks of therapy

< 15 eos/hpf: 62%

Stringent histologic response (≤6 eos/hpf)[a]



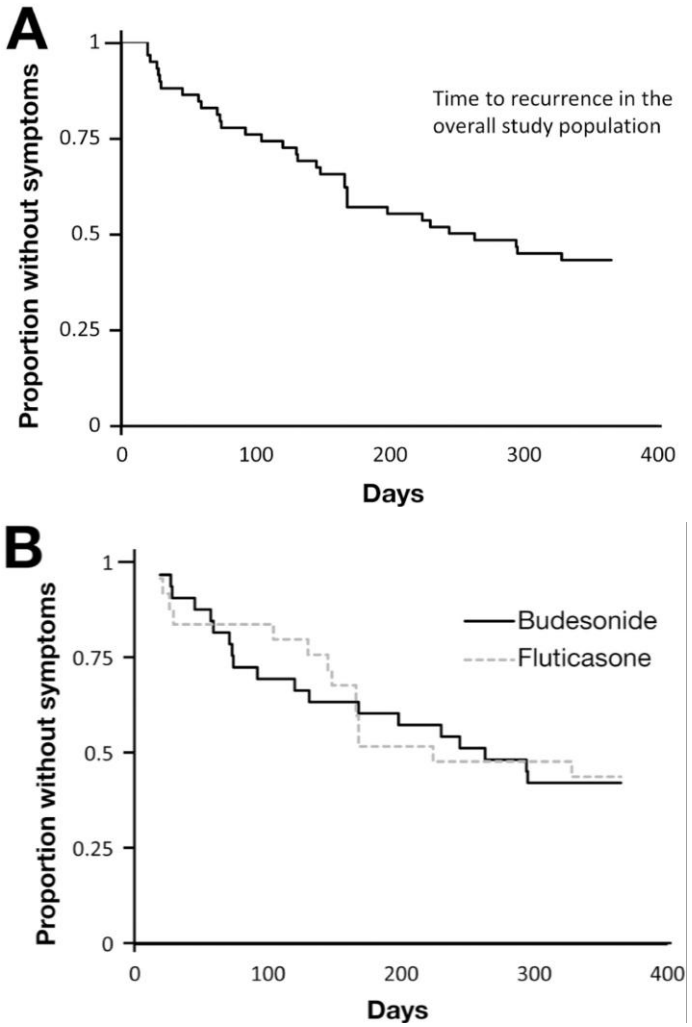
Dysphagia symptom response (≥30% reduction in DSQ score)[b]



Hirano I, et al. Clin Gastroenterol Hepatol. 2022 Mar;20(3):525-534.e10

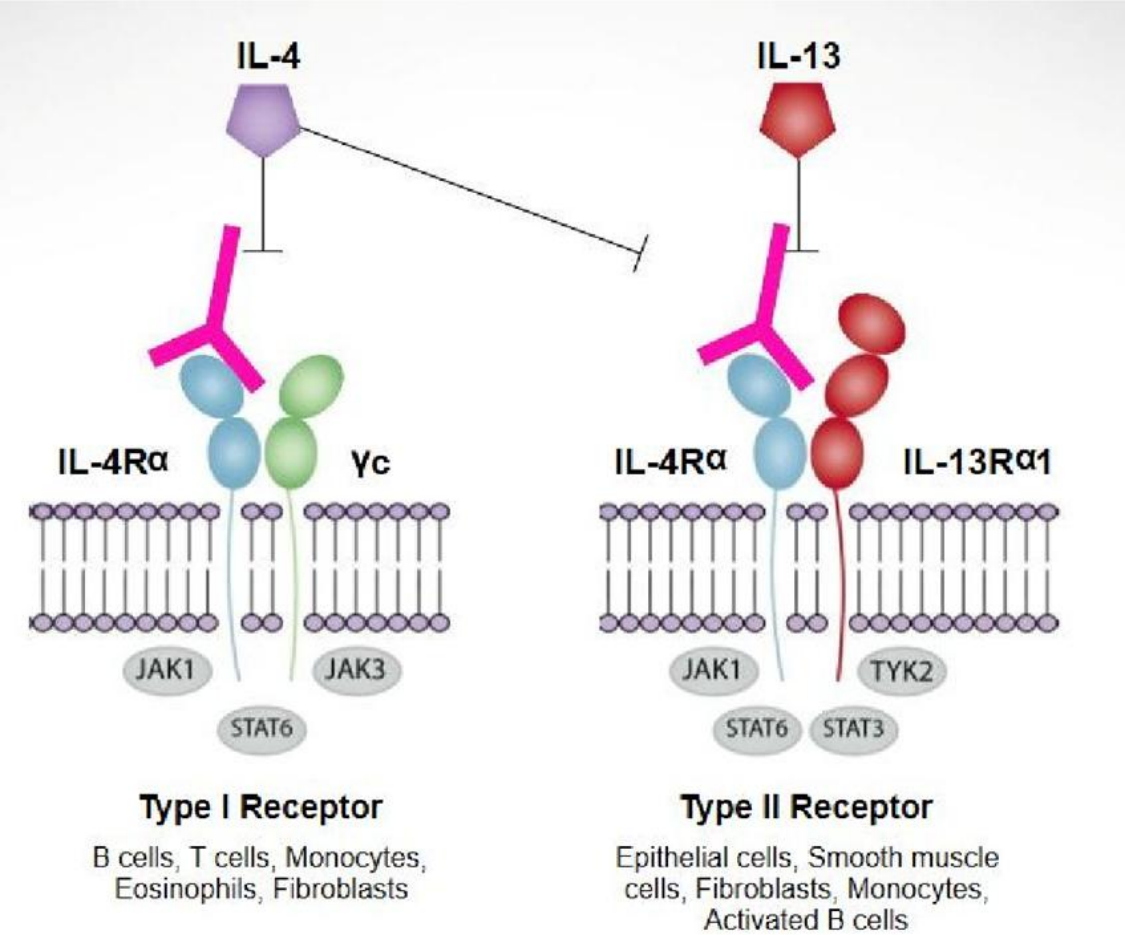
Rapid Recurrence of EoE After Treatment

- **Study Design:**
  - Randomized, double-blind, double-dummy trial observing EoE recurrence after treatment discontinuation
- **Key Findings:**
  - 57% (33/58) had symptom recurrence within 1 year (median 244 days)
  - No difference between oral budesonide vs fluticasone inhalation therapy (HR 1.04, 95% CI 0.52–2.08)
  - 78% had histologic relapse (≥15 eos/hpf) despite clinical appearance



Dellon ES et al. *Clin Gastroenterol Hepatol*. 2020;18(7):1483-1492

Dupilumab: Anti-IL-4Rα Monoclonal Ab

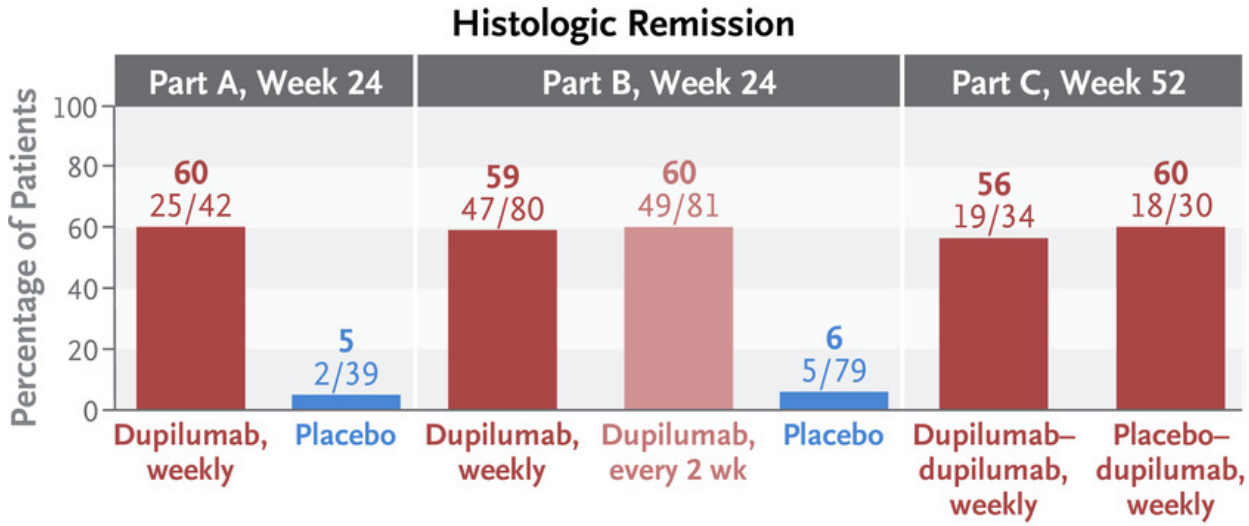


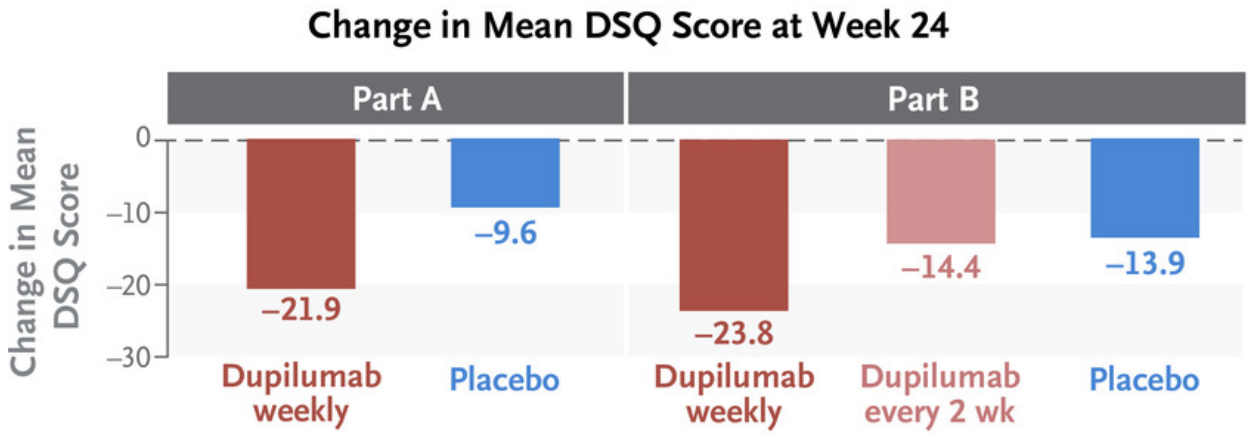
- Inhibits signaling of both IL-4 and IL-13
- Prior FDA approval for
  - Moderate-to-Severe Atopic Dermatitis
  - Moderate-to-Severe Asthma with eosinophilic phenotype or OCS-dependent
  - Chronic Rhinosinusitis with Nasal Polyposis

Dellon ES et al. N Engl J Med 2022;387:2317-2330

Dupilumab Phase III Trial Results

- Histologic Remission:
  - Significantly more common with Dupilumab weekly and every 2 weeks VS placebo in part A and B
- Dysphagia Scores:
  - Larger reduction from baseline with weekly dosing per DSQ in part A and part B
  - NO statistically significant decrease with Dupilumab every 2 week dosing





Dellon ES et al. N Engl J Med 2022;387:2317-2330

Dupilumab Safety

- Serious adverse events are rare
  - 3-6% across study parts A-C
  - Only one assessed thought related to trial regimen
- Majority common of adverse events were related to injection-site reactions

Table 2. Incidence of Adverse Events during the Treatment Period (Safety Analysis Set).*

Event	Part A		Part B			Part A–C Group in Part C	
	Dupilumab, 300 mg weekly (N=42)	Placebo (N=39)	Dupilumab, 300 mg weekly (N=80)	Dupilumab, 300 mg every 2 wk (N=81)	Placebo (N=78)	Dupilumab–dupilumab (N=40)	Placebo–dupilumab (N=37)
	number of patients (percent)						
Deaths	0	0	0	0	0	0	0
Adverse event	36 (86)	32 (82)	67 (84)	63 (78)	55 (71)	24 (60)	27 (73)
Serious adverse event†	2 (5)	0	5 (6)	1 (1)	1 (1)	0	1 (3)
Adverse event leading to discontinuation†	1 (2)	0	2 (2)	2 (2)	2 (3)	0	2 (5)
Adverse event occurring in ≥10% of patients in any group‡							
Injection-site reaction	7 (17)	4 (10)	16 (20)	18 (22)	16 (21)	4 (10)	8 (22)
Injection-site erythema	3 (7)	5 (13)	8 (10)	18 (22)	9 (12)	4 (10)	5 (14)
Injection-site pain	4 (10)	3 (8)	7 (9)	10 (12)	4 (5)	2 (5)	3 (8)
Injection-site swelling	3 (7)	1 (3)	10 (12)	7 (9)	2 (3)	2 (5)	0
Nasopharyngitis	5 (12)	4 (10)	2 (2)	4 (5)	3 (4)	1 (2)	3 (8)
Headache	2 (5)	4 (10)	6 (8)	5 (6)	9 (12)	3 (8)	2 (5)
Acne	0	1 (3)	0	2 (2)	3 (4)	0	4 (11)
Rash	0	4 (10)	2 (2)	4 (5)	0	1 (2)	0

* The safety analysis set included all the patients who had undergone randomization and received at least one dose or part of a dose of dupilumab or placebo; data were analyzed according to whether the patients received dupilumab or placebo, regardless of trial group assignment. The Part A–C group comprised the eligible patients from Part A who continued the trial in Part C; placebo–dupilumab indicates those who received placebo in Part A and dupilumab at a weekly dose of 300 mg in Part C, and dupilumab–dupilumab indicates those who received dupilumab at a weekly dose of 300 mg in Parts A and C.

† None of the adverse events or serious adverse events that were assessed were considered by the trial investigators to be related to the trial regimen, with the exception of one serious adverse event of systemic inflammatory response syndrome; the patient with this event was continued to be followed in the trial, and the event did not recur (further details are provided in Table S9).

‡ Adverse events in this category were reported according to the preferred terms in the *Medical Dictionary for Regulatory Activities*, version 23.0.

When should dupilumab be considered first line?

- Patients with multiple comorbid atopic conditions
  - Moderate, persistent, or difficult to control asthma
  - Moderate, persistent, or difficult to control atopic dermatitis
  - Difficult to control chronic sinusitis with nasal polyps
- Patients with a strong preference to avoid dietary restriction or topical swallowed steroids

When to consider Dupilumab for step up therapy

- Eosinophilic esophagitis that is difficult to treat
- Failure to thrive, poor growth or significant weight loss due to EoE
- Frequent use of rescue therapies (oral steroids, dilations)
- Severe diet restriction or requiring amino acid formula
- Clinically significant esophageal strictures or narrow caliber esophagus
- Refractory to current therapy
  - Persistent symptoms, persistent esophageal inflammation, adverse effects of current therapy, intolerance of current therapy, inability to adhere to current therapy

Other emerging treatments

Medication	Mechanism	Status
Cendakimab (SQ)	IL-13 monoclonal antibody	Phase 3 Completed/Published
Fluticasone orally dissolving (APT-1011)	Broad steroid anti-inflammatory effects	Phase 3 (FLUTE-3)
tezepelumab	Anti-TSLP	Phase 3 (CROSSING)
solrikitug (NSI-8226) (SQ)	Anti-TSLP	Phase 2 (ALAMERE)
CALY-002 (IV)	Anti-IL-15	Prelim phase 1 completed EoE/celiac
vedolizumab (IV)	Anti-α4β7 integrin	Case reports in EoE/EGID
etrasimod (PO)	Sphingosine 1-phosphate (S1P) receptor modulator	Phase 2 EoE (completed)
zemaira (IV)	Alpha—1-trypsin inhibitor	Phase 2
Vonoprazan (PO)	Potassium Competitive Acid Blocker	Phase 2
AQ280 (PO)	Jak1 Inhibitor	Phase 2 trials planned

Clinical trial status and data retrieved from ClinicalTrials.gov.

Elimination Diet

- Eliminate common triggers followed by reintroduction

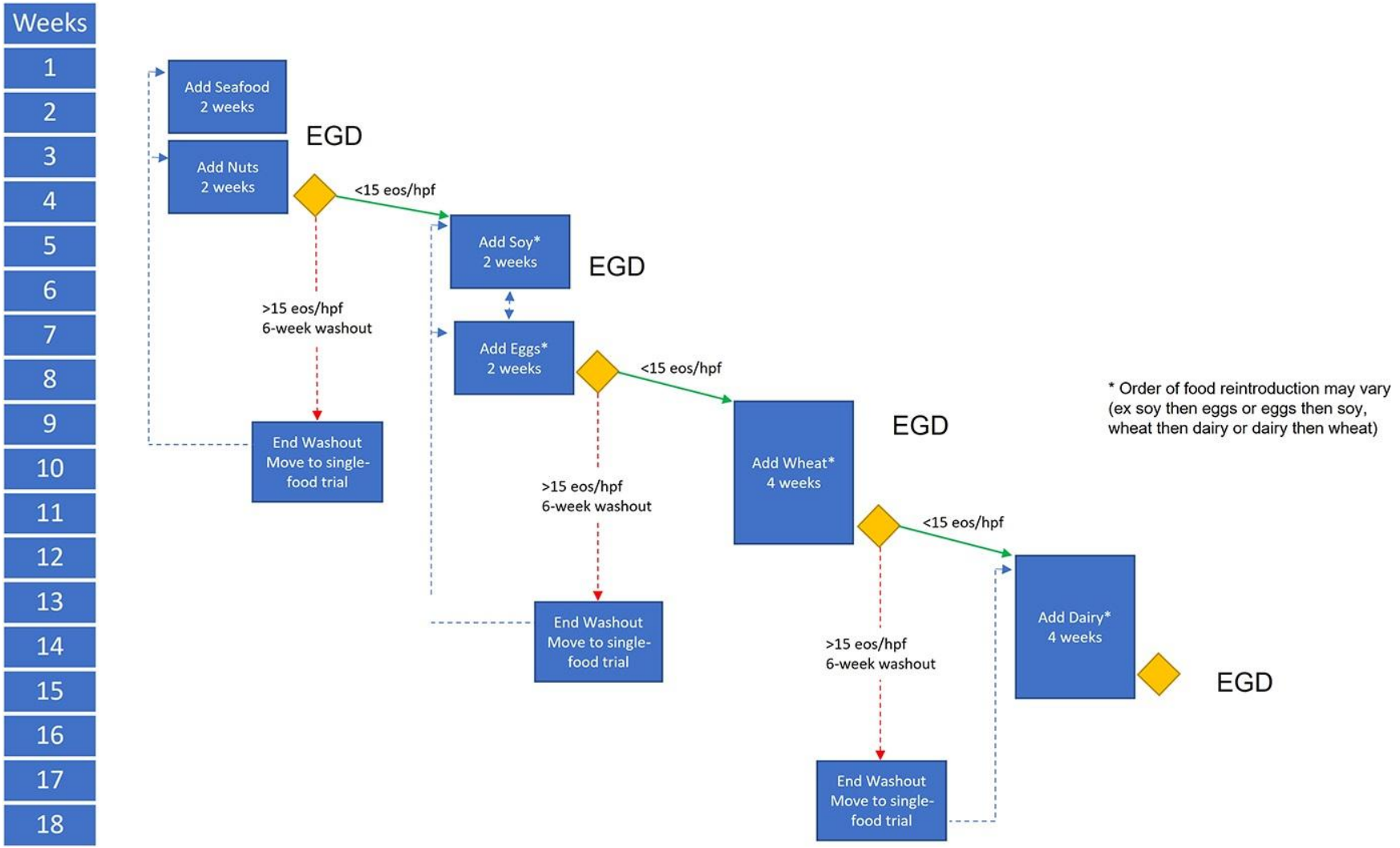
	6FED	4FED	2FED	1FED
Diary	☑	☑	☑	☑
Wheat	☑	☑	☑	
Egg	☑	☑		
Soy	☑	☑		
Tree nuts/peanuts	☑			
Fish/Shellfish	☑			

Dietary Therapy Efficacy in Eosinophilic Esophagitis

Histologic Response Rates (AGA/JTF Guideline 2020)

Hirano et al., Ann Allergy Asthma Immunol 2020

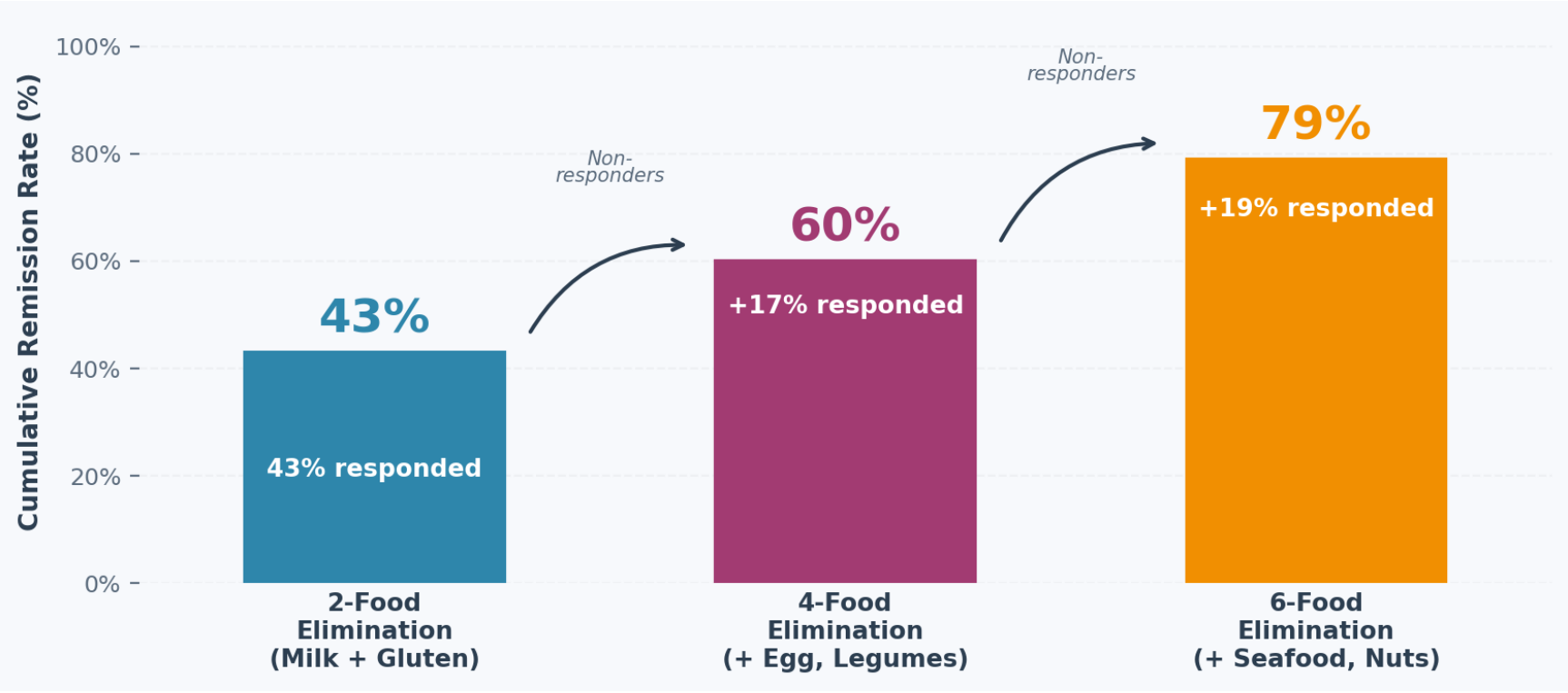
Reintroduction of Eliminated Foods



Zalewski A et al. Am J Gastroenterol. 2022 Dec 1;117(12):1963-1970.

Step-Up 2-4-6 Elimination Diet: Cumulative Remission

Prospective Multicenter Study | 130 EoE Patients (Adults & Children) | Molina-Infante et al. 2018



STUDY HIGHLIGHTS

The concept: Start with the least restrictive diet and escalate only in non-responders, rather than starting everyone on the most restrictive 6-food diet.

Adult vs. pediatric: Similar remission at each step. Adults: 44% → 60% → 80%. Children: 40% → 57% → 76%.

Efficiency gains: Compared to starting with 6-food elimination, the step-up approach saves ~20% of endoscopies and ~30% of diagnostic time.

Remission defined as <15 eos/hpf on esophageal biopsies after 6-week dietary elimination.

WHY THIS MATTERS

43% Respond to Just 2 Foods

Nearly half of patients achieve remission by removing only milk and gluten. Most never need a more restrictive diet, reducing patient burden and improving long-term adherence.

79% Cumulative Remission

The step-up approach reaches the same high remission rate as starting with SFED, but with far less dietary restriction for the majority of patients who respond early.

Fewer Scopes, Faster Answers

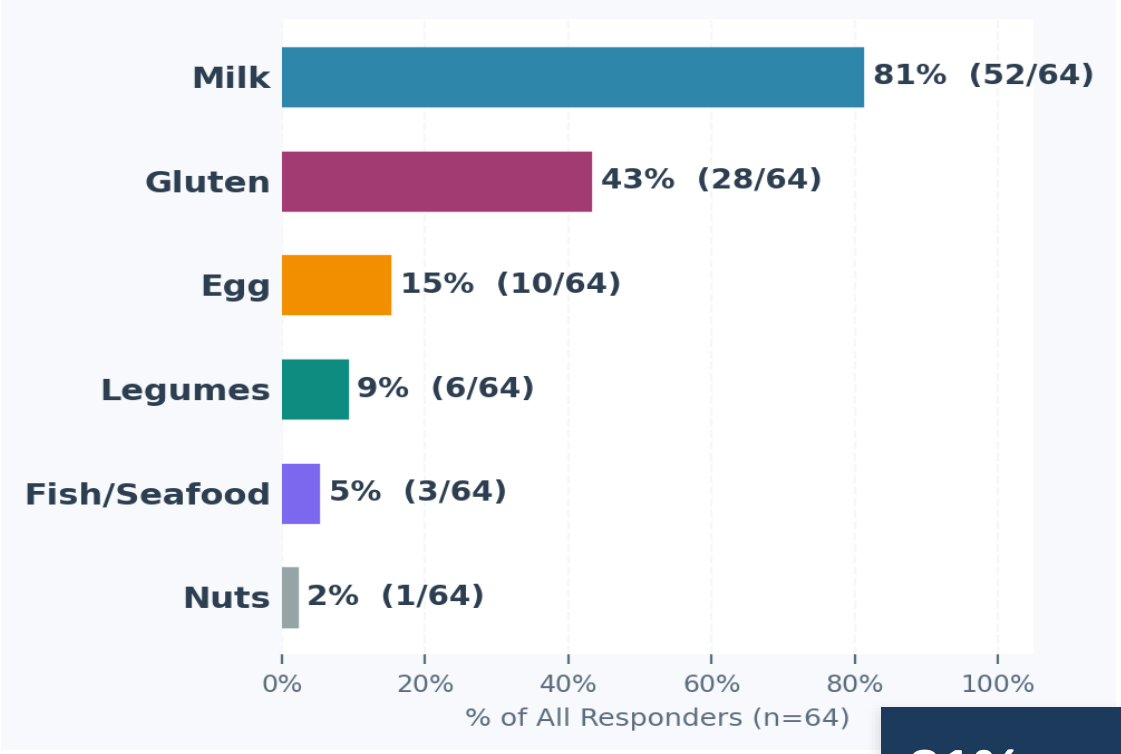
By identifying responders at each step, the 2-4-6 protocol avoids unnecessary endoscopies and cuts diagnostic workup time by nearly a third compared to traditional top-down approaches.

Molina-Infante J et al. J Allergy Clin Immunol. 2018 Apr;141(4):1365-1372

Food Trigger Identification in EoE: The 2-4-6 Results

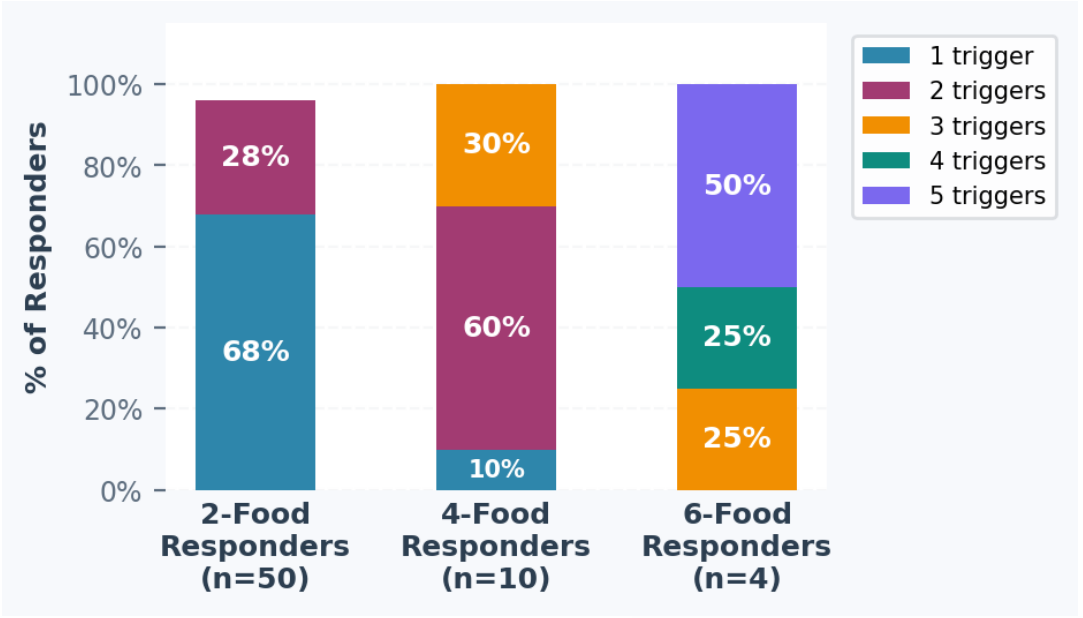
Food Reintroduction Data from 64 Responders | Molina-Infante et al. 2018

TRIGGER FREQUENCY ACROSS ALL RESPONDERS



81% of all responders had **milk** as a trigger

NUMBER OF TRIGGERS PER PATIENT



92% of 2-Food/4-Food responders had only 1-2 triggers

TRIGGER PATTERNS BY ELIMINATION STEP

2-Food Responders (n=50)
Milk alone: 52% (26/50)
Gluten alone: 16% (8/50)
Both milk + gluten: 28% (14/50)
96% had only 1-2 triggers

4-Food Responders (n=10)
Milk + egg: 30% (3/10)
Milk + legumes: 30% (3/10)
Milk + gluten + egg: 20% (2/10)
70% had 1-2 triggers

6-Food Responders (n=4)
All had 3-5 food triggers
50% had 5 triggers
These patients are rare but need the full restriction approach

Molina-Infante J et al. J Allergy Clin Immunol. 2018 Apr;141(4):1365-1372

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One Food Elimination Diet – SOFEED Trial

- Open label RCT 1FED (animal milk) vs. 6FED
  - 129 patients
    - n = 67 1FED
    - n = 62 6FED
  - Primary endpoint < 15 eos/hpf

- No difference in histologic response at 6 weeks
    - **34% in 1FED vs. 40% in 6FED** (p=0.58)

- No difference in mean changes from baseline in symptom scores (EoEHSS)

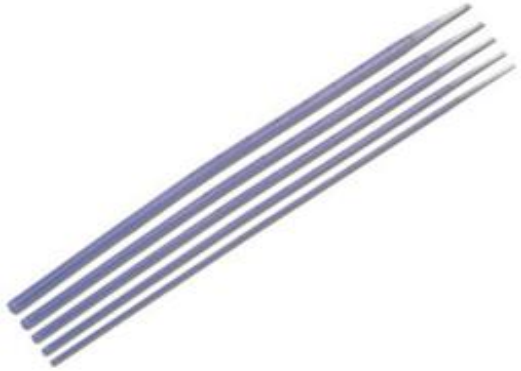
	1FED (n=67)	6FED (n=62)	Percentage point difference*	p value
<15 eos/hpf†	23 (34%; 23 to 46)	25 (40%; 28 to 53)	6% (−11 to 23)	0·58
≤10 eos/hpf	20 (30%; 19 to 41)	23 (37%; 25 to 49)	7% (−9 to 24)	0·46
≤6 eos/hpf	12 (18%; 9 to 27)	20 (32%; 21 to 44)	14% (−0 to 29)	0·069
≤1 eos/hpf	4 (6%; 0 to 12)	12 (19%; 10 to 29)	13% (2 to 25)	0·031

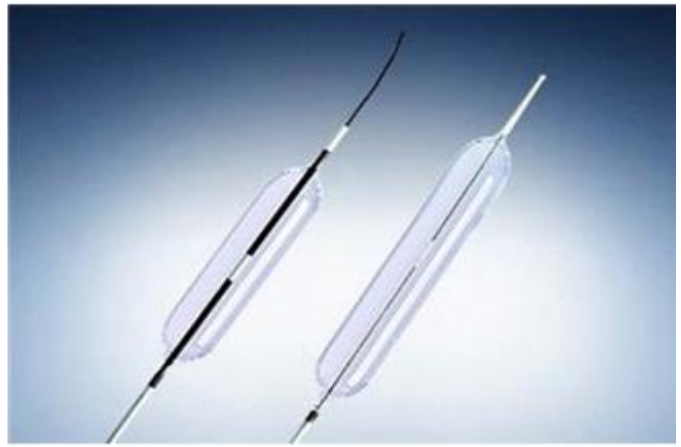
Data are n (%; 95% CI) or % (95% CI). p values were calculated with Fisher's exact test. 1FED=one-food elimination diet. 6FED=six-food elimination diet. eos/hpf=eosinophils per high-power field. *6FED versus 1FED. †Primary endpoint.

Table 2: **Proportion of patients in histological remission (intention-to-treat population)**

Dilation for EoE

- Who?
  - All patient with EoE + esophageal stricture with dysphagia
  - In combination with medical and/or dietary therapy
  - Consider if ongoing dysphagia despite histologic remission
- How much?
  - Goal: Relieve dysphagia and food impaction (typically at least 16-18mm)
  - Over 1 or more sessions
- Bougie or Balloon?
  - Depends on stricture location, length, endoscopist preference

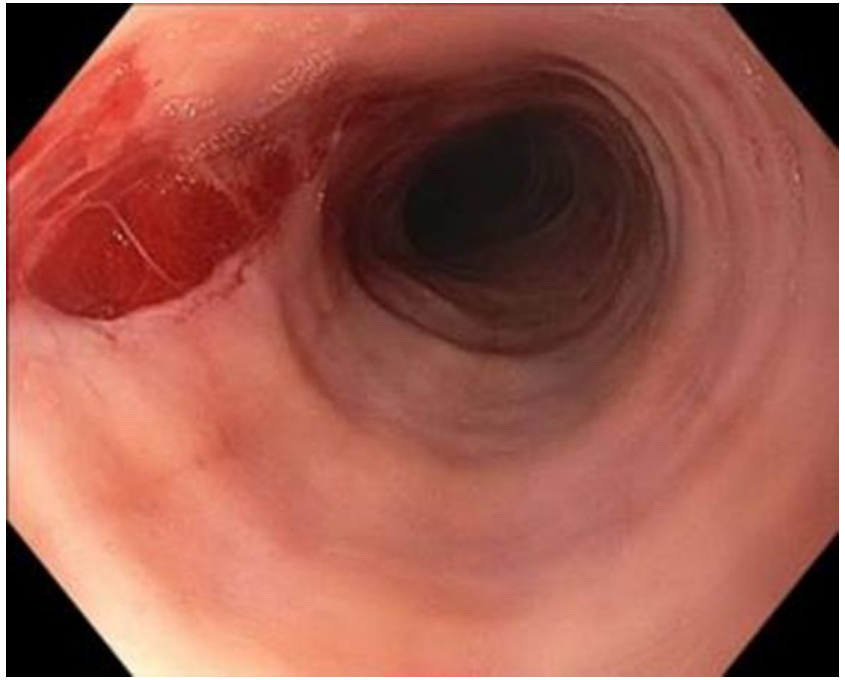




Aceves SS, et al. *Gastrointest Endosc*. 2022;96(4):576-592.e1.

Dilation for EoE

- Careful dilation is safe
- 58% require 2nd dilation; 75% within a year
- Start low and go slow
  - Small increases over multiple sessions
  - Helpful to reinspect with endoscopy after each bougie dilator
  - Stop session when mucosal tear, disruption, or laceration is noted
- Short-term chest pain is common; inform patients



Dellon ES, et al. *Am J Gastroenterol*. 2013;108(5):679-693.

EoE Management: Cost-Effectiveness by Perspective & Time Horizon

Markov Model | PPI-First vs SFED-First vs Steroid-First | Ranked by Total Cost & QALYs

KEY TAKEAWAYS

Payer perspective favors SFED-First at 5 years — diet-based approach has lowest cost to insurers.

Societal perspective favors PPI-First at both horizons — elimination diets carry hidden costs (productivity loss, dietary burden).

Steroid-First ranks last in nearly every scenario — highest costs with no QALY advantage.

All strategies assume dupilumab rescue at $7,311/quarter for refractory patients.

DUPILUMAB PRICE THRESHOLD

At current pricing ($7,311/quarter), no strategy incorporating dupilumab is cost-effective at $100K/QALY.

Price must drop to **$2,039/quarter** for dupilumab-inclusive strategies to become cost-effective.

Hiramoto B, et al. Am J Gastroenterol. 2025 Jan 1;120(1):161-172.

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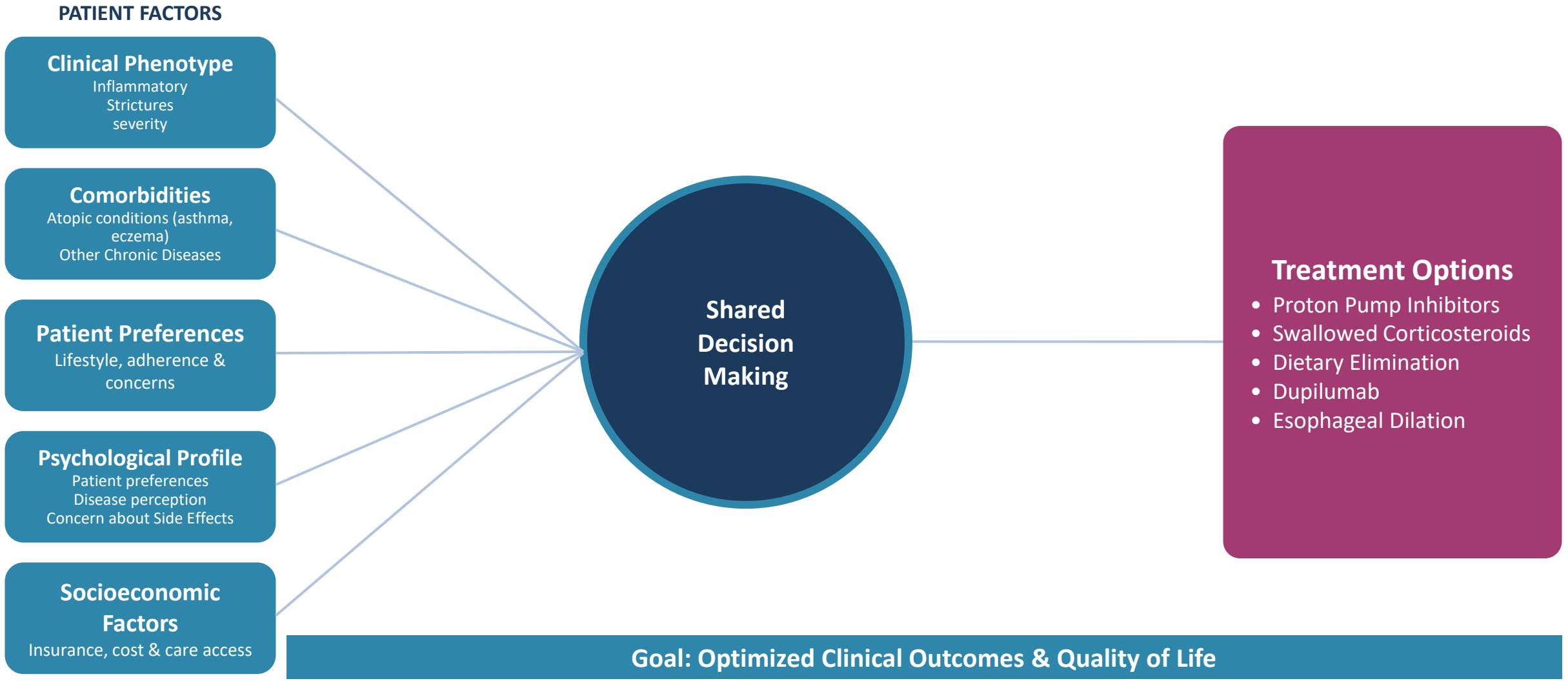
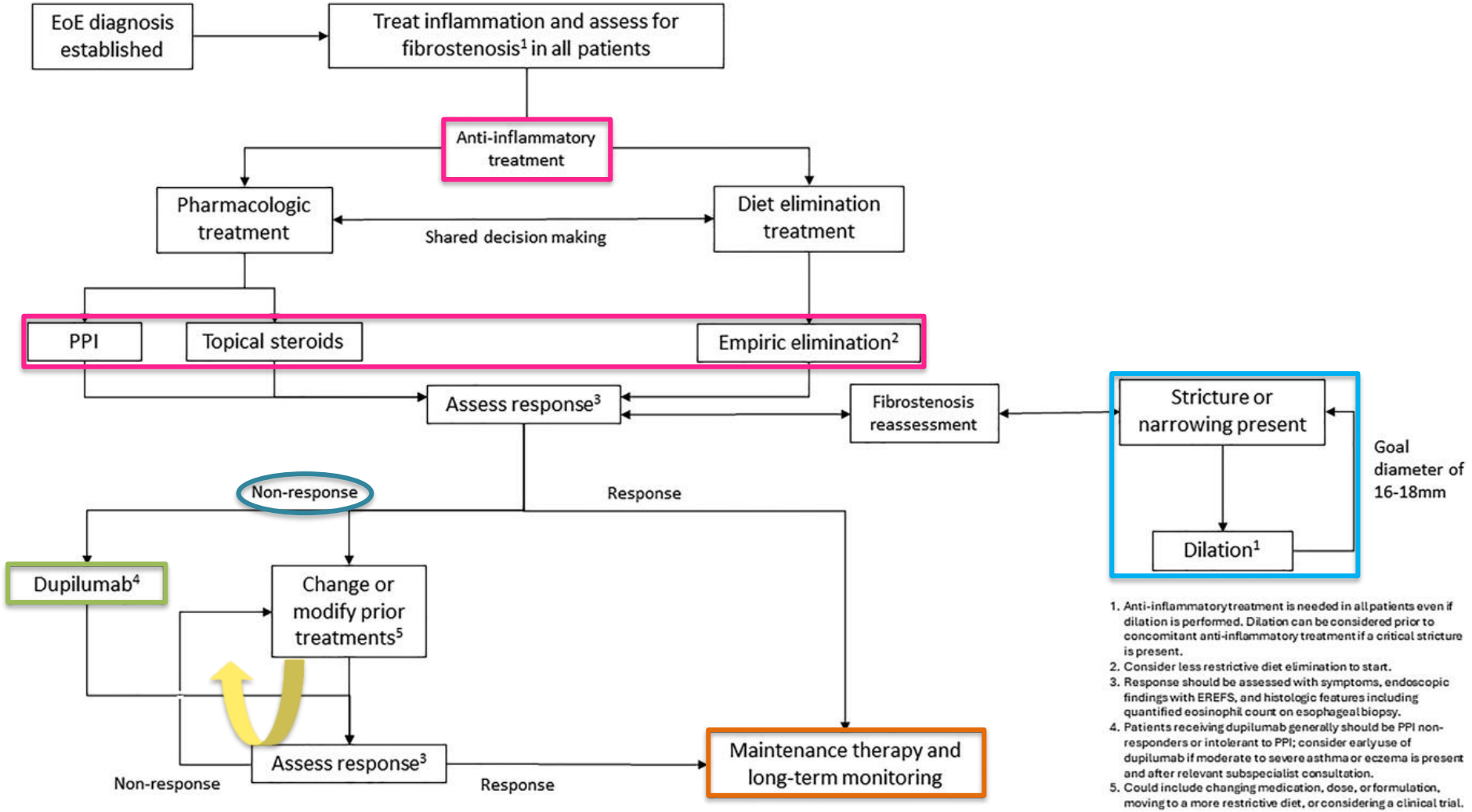
Personalizing EoE Therapy: A Shared Decision-Making Approach

Patient-Centered Framework for Initial Therapy Selection



Ottoni M, et al. Expert Rev Clin Immunol. 2025 Oct;21(10):1373-1382.

ACG Clinical Guidelines: Management Algorithm



1. Anti-inflammatory treatment is needed in all patients even if dilation is performed. Dilation can be considered prior to concomitant anti-inflammatory treatment if a critical stricture is present.
2. Consider less restrictive diet elimination to start.
3. Response should be assessed with symptoms, endoscopic findings with EREFS, and histologic features including quantified eosinophil count on esophageal biopsy.
4. Patients receiving dupilumab generally should be PPI non-responders or intolerant to PPI; consider early use of dupilumab if moderate to severe asthma or eczema is present and after relevant subspecialist consultation.
5. Could include changing medication, dose, or formulation, moving to a more restrictive diet, or considering a clinical trial.

Dellon ES, et al. Am J Gastroenterol 2025

Thank You

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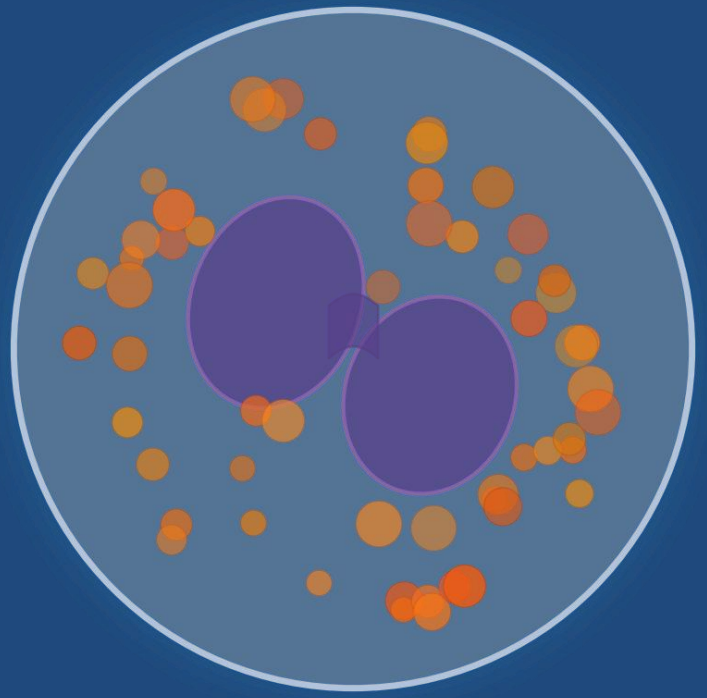

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