

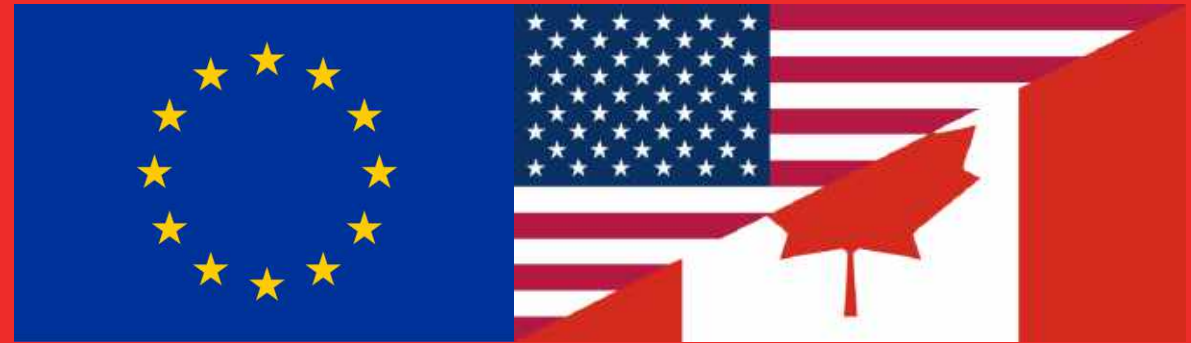
EoE Guidelines Under the Microscope



Harmonizing Care in EoE: A Dialogue Between European and North American Guidelines

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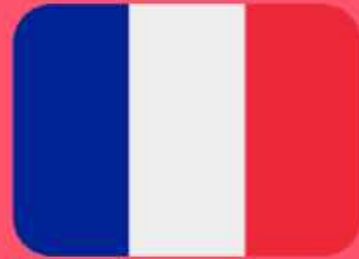
Disclosures

- Consulting fees: AbbVie, Alimentiv, Amgen, Anaptys Bio, AVIR Pharma Inc, Bristol Myers Squibb, Celltrion, Domain Therapeutics, Eupraxia, Eli Lilly, Ferring, Forte Biosciences, Fresenius Kabi, Gilead, Janssen, McKesson, Mirador Therapeutics, Pendopharm, Pfizer, Prometheus Biosciences Inc., Roche, Sanofi, Takeda, Tillotts Pharma
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- Royalties: Springer Publishing
- Research Support: AbbVie, Eli Lilly, Ferring, Pfizer

**REMEMBER WHEN WE WON THAT RYDER CUP
MATCH?**

YEAH, ME NEITHER.

Average time spent eating per day



France:

2 hours, 13 minutes



Italy:

2 hours, 7 minutes



Spain:

2 hours, 6 minutes



United States:

1 hour, 2 minutes

Data source: OCDE



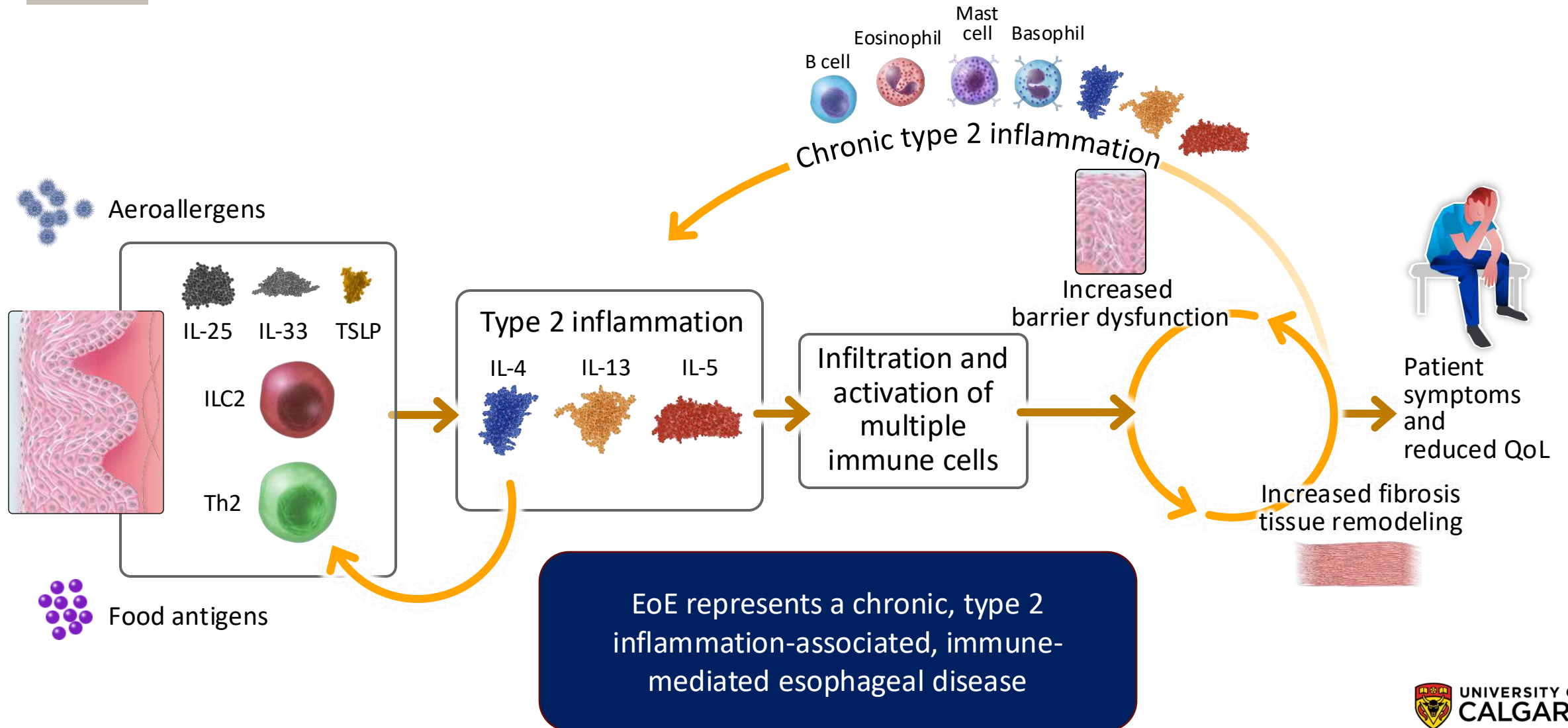
VS



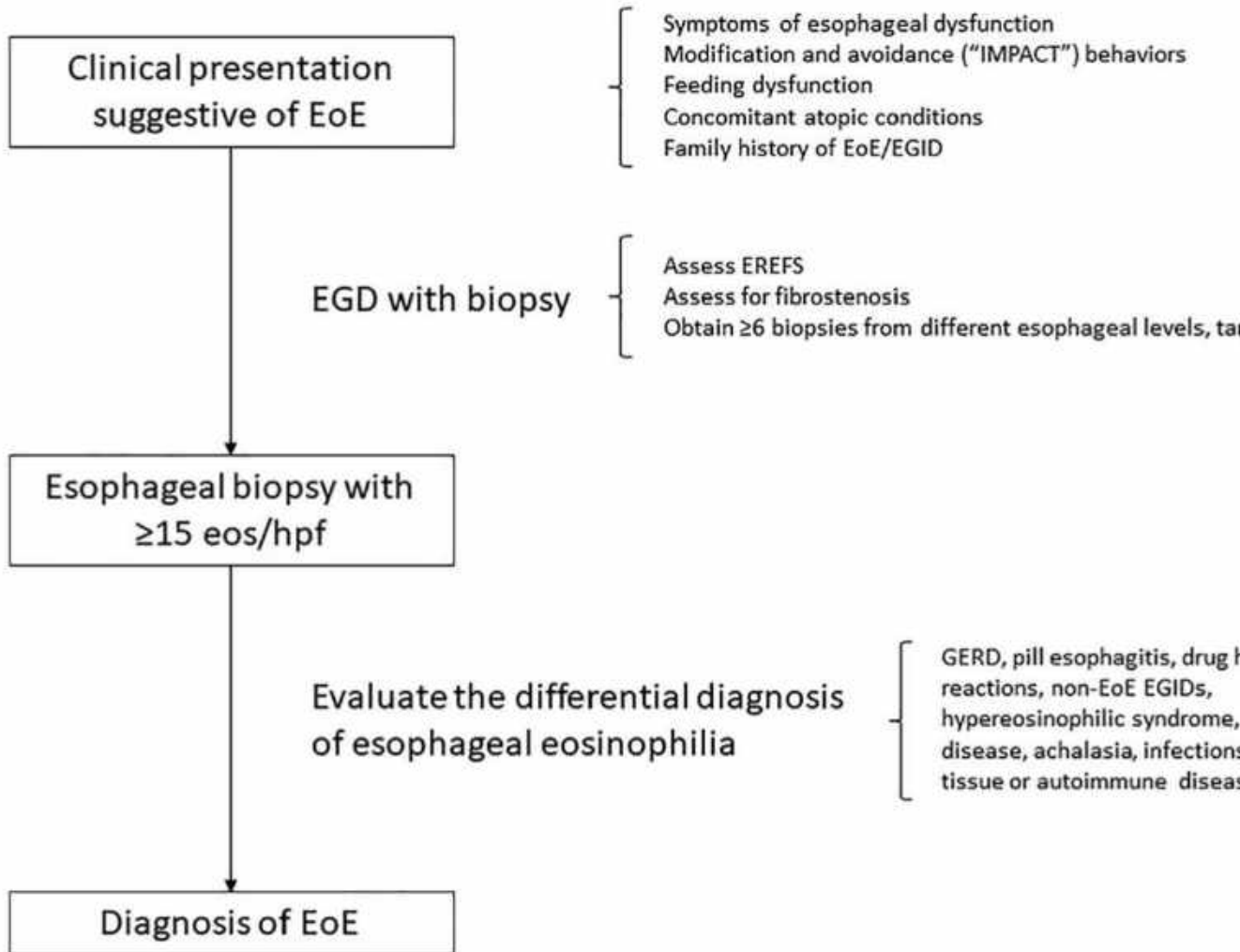
They both can't be right!

Key Recommendations for Diagnosis and Disease Evaluation

Conceptual definition of EoE as a clinicopathological diagnosis



Diagnostic criteria are established



Recommend EoE diagnosed on basis of symptoms of esophageal dysfunction and at least 15 eos/hpf, after evaluating for non-EoE disorders that can cause/contribute to EE

EoE and GERD are **different** entities, but may coexist, either unrelated or interacting and response to PPI is only partially driven by acid-suppressing effects

What should we do with **asymptomatic** EE? Similar in endoscopic and immunohistologic markers on tissue (? preclinical EoE)

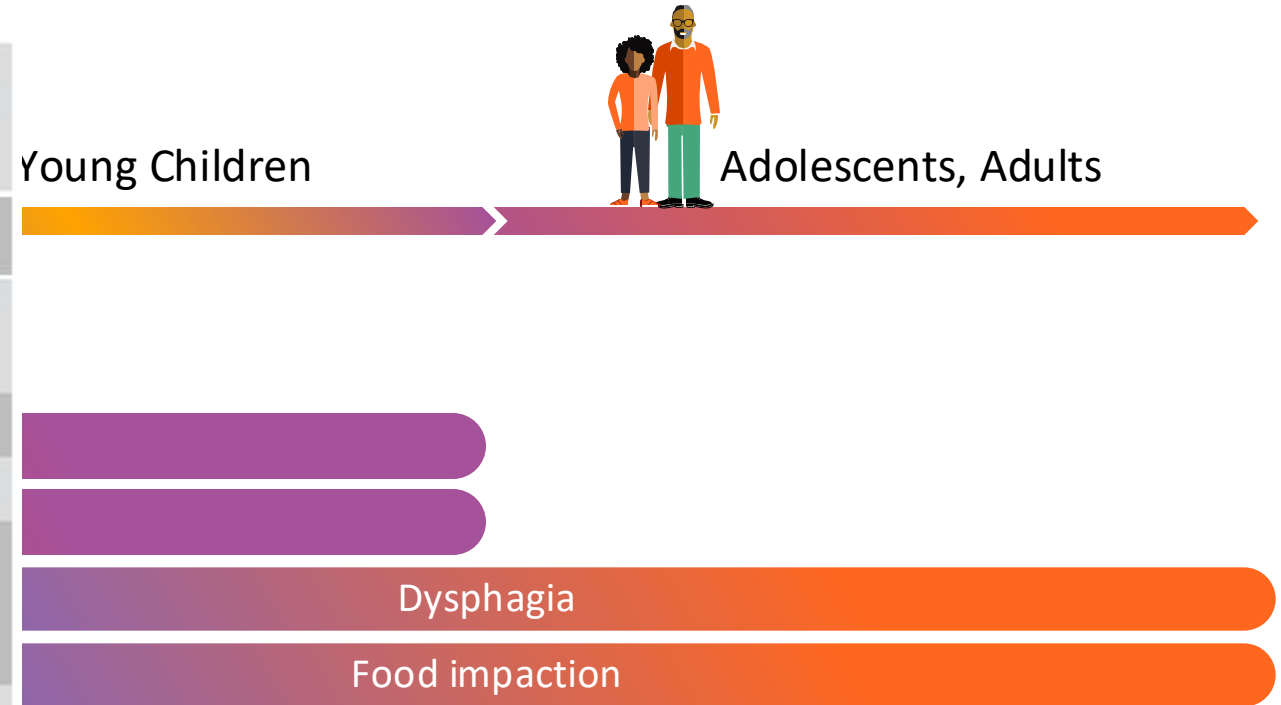
Care must be taken in disease evaluation: symptoms

Table 4. “IMPACT” behaviors to assess while taking a dysphagia history

Behavior	Description
Imbibe fluids	Drinking a lot of liquids to help get each bite down smoothly
Modify foods	Cutting foods into small pieces or pureeing foods
Prolong meal times	Eating slowly and being the “last one at the table”
Avoid hard texture foods	Meats, crusty breads, and foods with sticky consistencies are often removed from the diet to minimize symptoms
Chew excessively	Thorough chewing to achieve a mush-like consistency to allow easier swallowing
Turn away tablets/pills	Pill dysphagia is a subtle symptom of EoE and may be the only indication of swallowing dysfunction

EoE, eosinophilic esophagitis.

Adapted from Hirano and Furuta. *Gastroenterology*. 2020;158(4):840–51 (81).

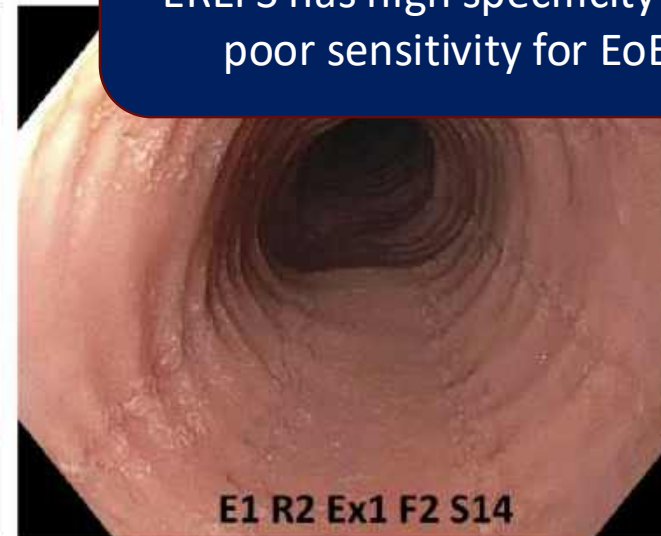
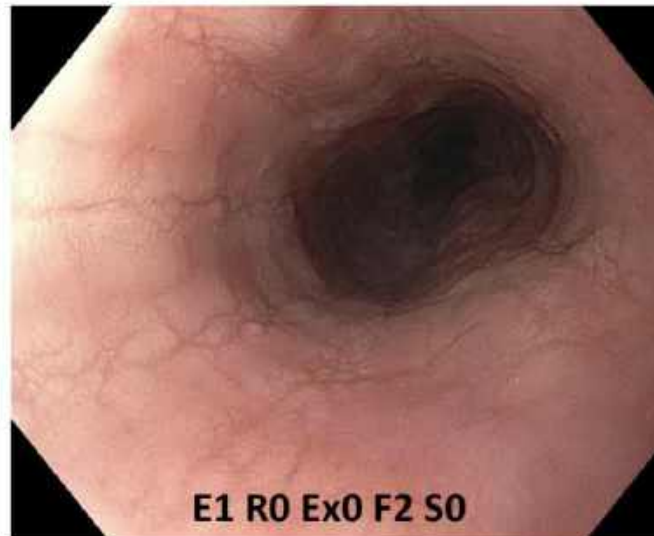
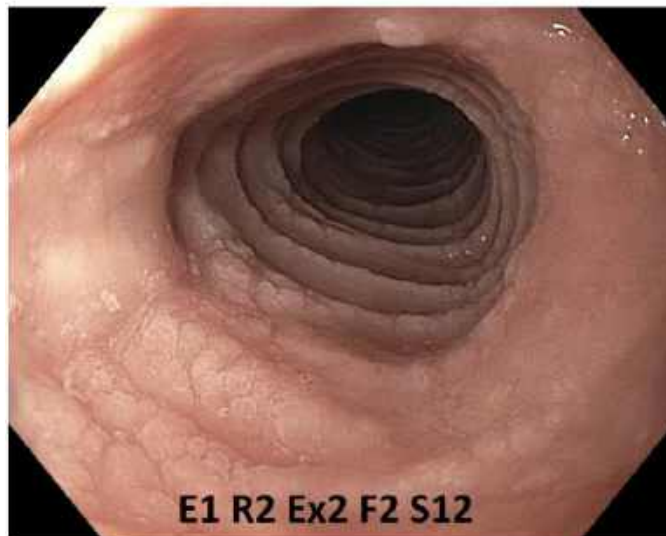


Care must be taken in disease evaluation: endoscopy

Finding	EREFS Scoring
Edema	1: Present (decreased vascularity)
Rings	1: Mild (ridges) 2: Moderate (does not impede scope passage) 3: Severe (standard scope does not pass)
Exudates	1: $\leq 10\%$ of surface area 2: $>10\%$ of surface area
Furrows	1: Mild 2: Severe (with appreciable depth)
Stricture	1: Present; also estimate diameter in mm

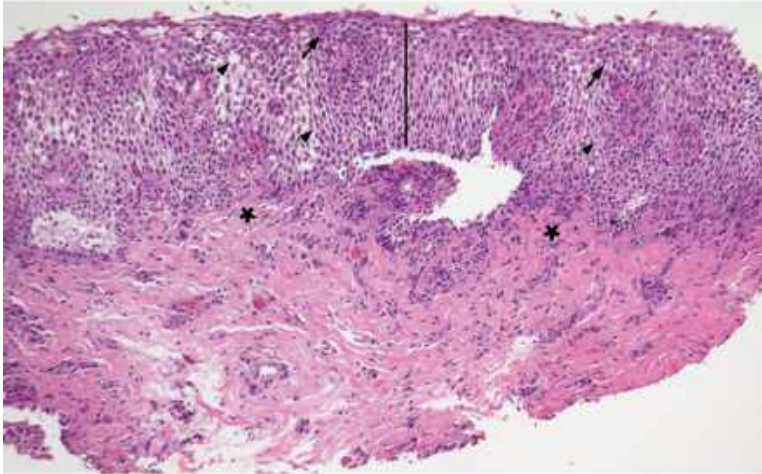


Only ~1/5 to 1/10 patients with EoE have a completely normal endoscopy; the EREFS has high specificity but relatively poor sensitivity for EoE diagnosis

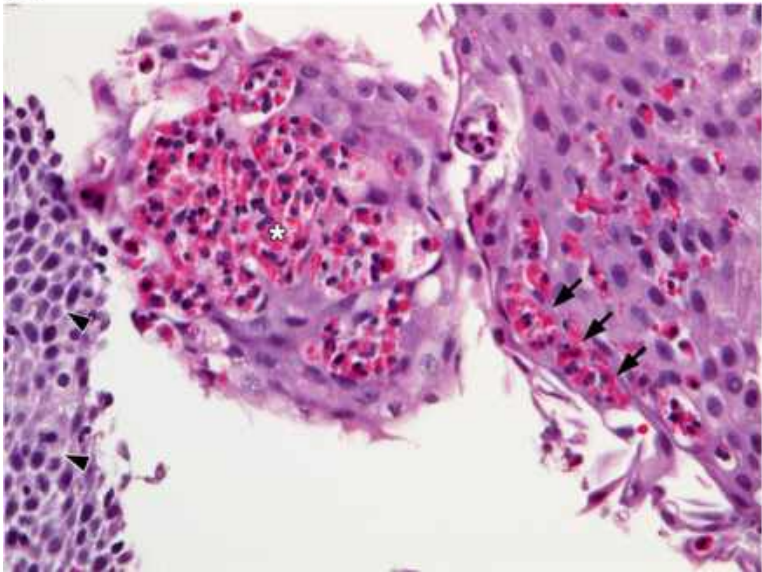


Care must be taken in disease evaluation: histopathology

(A)



(B)



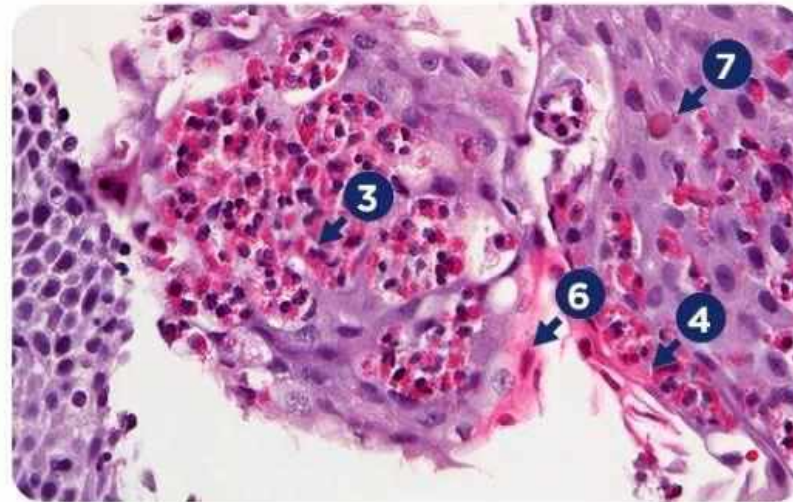
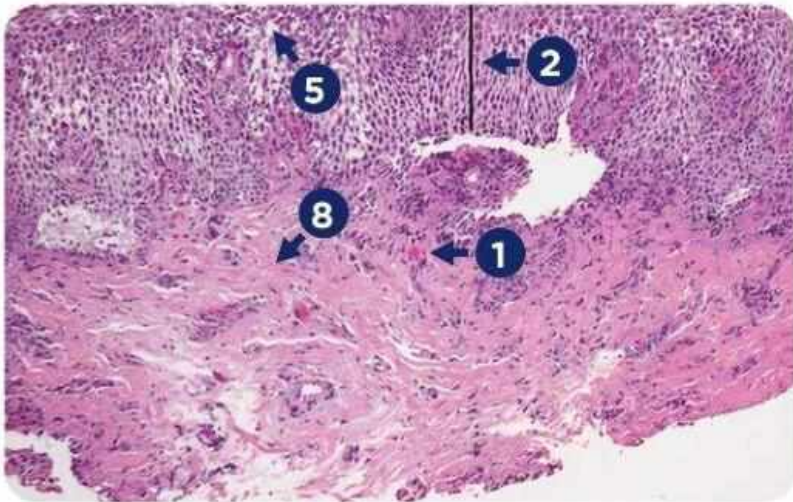
Recommend obtaining at least 6 esophageal biopsies from at least 2 esophageal levels (proximal/mid/distal), targeted to endoscopic findings



Recommend that eosinophil count be quantified on esophageal biopsies from every endoscopy performed for EoE

Care must be taken in disease evaluation: histopathology

1. Eosinophil information (EI)
2. Basal zone hyperplasia (BZH)
3. Eosinophil abscess (EA)
4. Eosinophil surface layering (SL)
5. Dilated intercellular spaces (DIS)
6. Surface epithelial alteration (SEA)
7. Dyskeratotic epithelial cells (DEC)
8. Lamina propria fibrosis (LPF)
Not commonly available in most biopsy samples.



Care must be taken in disease evaluation: histopathology

EoE + EG + EOD

0.6%

EoE + HP

2.6%

EoE + EG

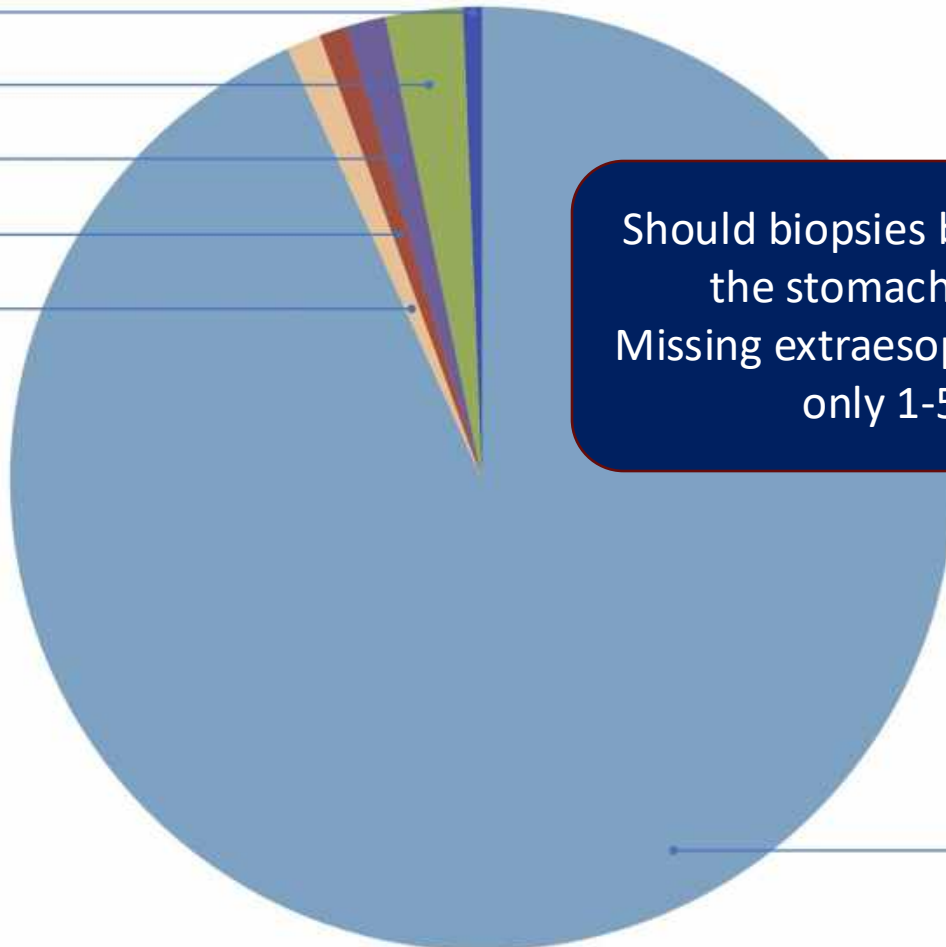
1.4%

EoE + EoD

0.9%

EoE + Celiac

1.2%



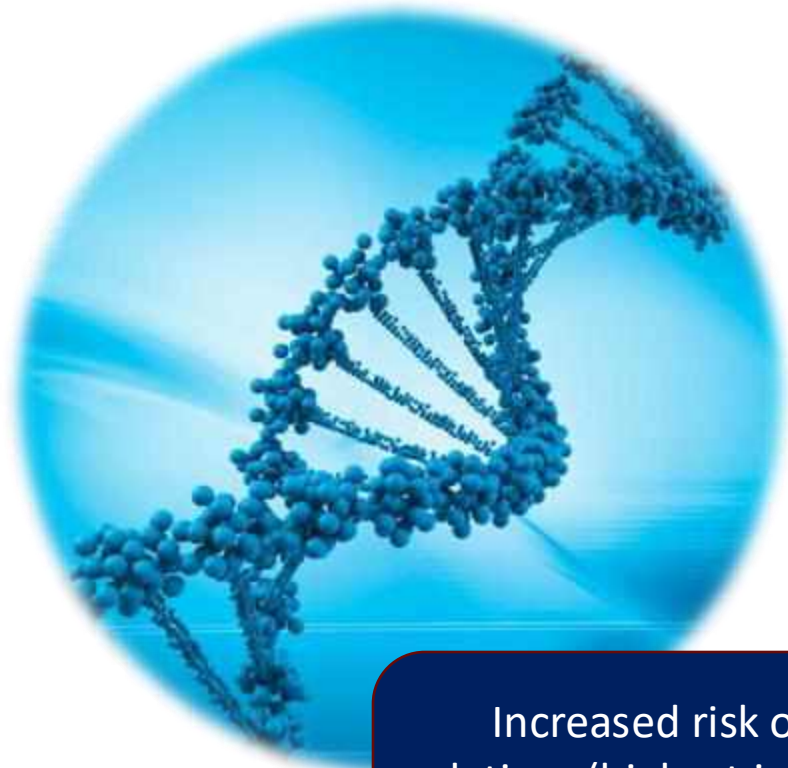
Should biopsies be routinely taken in the stomach or duodenum?
Missing extraesophageal pathology in only 1-5% of cases



Targeted collection in patients with endoscopic abnormalities or symptoms referring to stomach/duodenum

EoE
93.2%

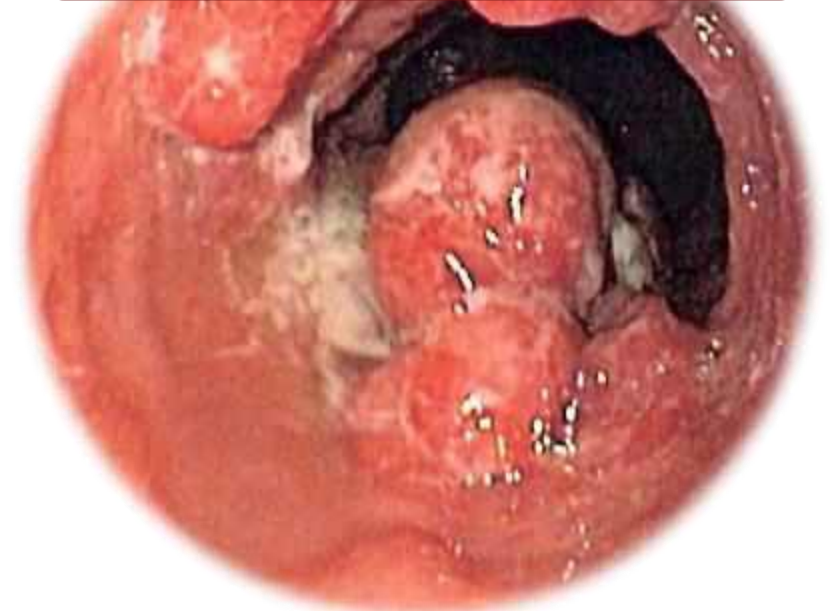
How do we counsel patients who have a new diagnosis of EoE?



Increased risk of EoE amongst relatives (highest in men and FDR) but impact of environment is high compared to genetic heritability

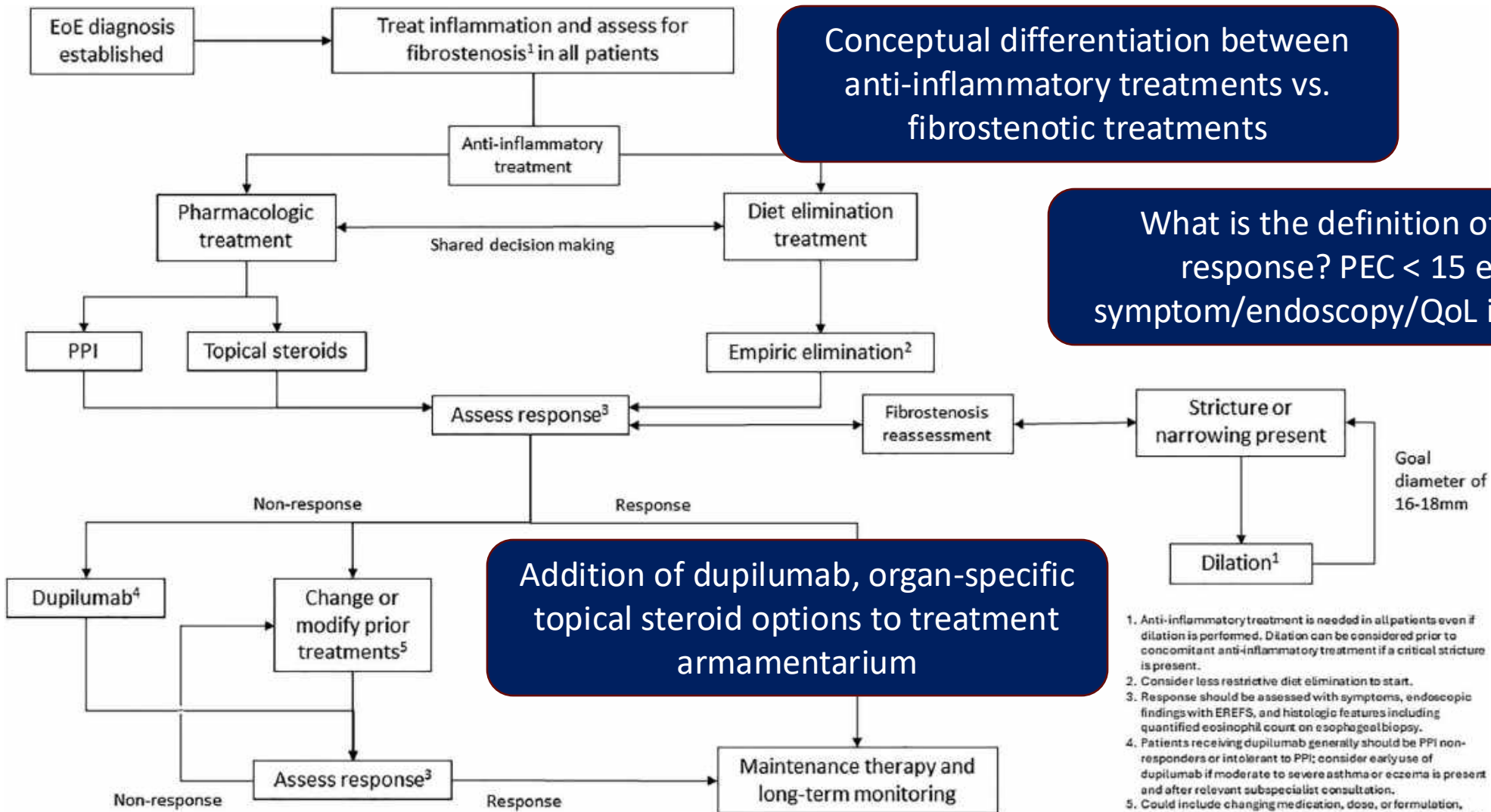


Risk of malignancy has not been demonstrated (recognizing limitations of long-term follow-up)



Key Recommendations for Treatment

Our treatment options have expanded significantly in managing patients with EoE

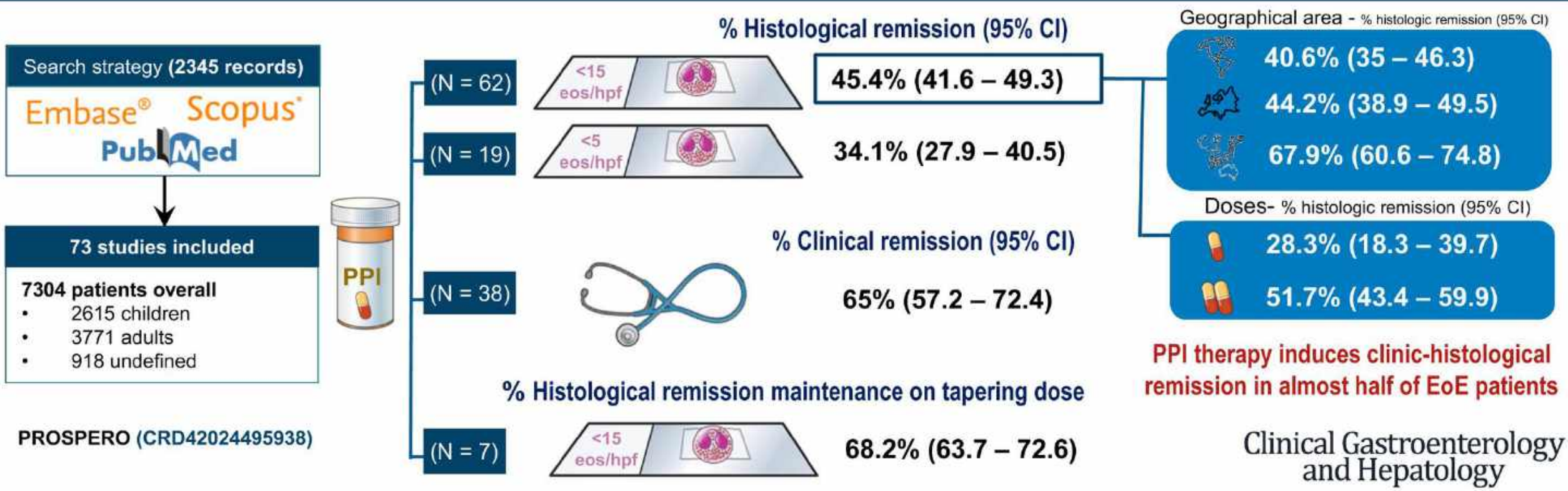


1. Anti-inflammatory treatment is needed in all patients even if dilation is performed. Dilation can be considered prior to concomitant anti-inflammatory treatment if a critical stricture is present.
2. Consider less restrictive diet elimination to start.
3. Response should be assessed with symptoms, 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.

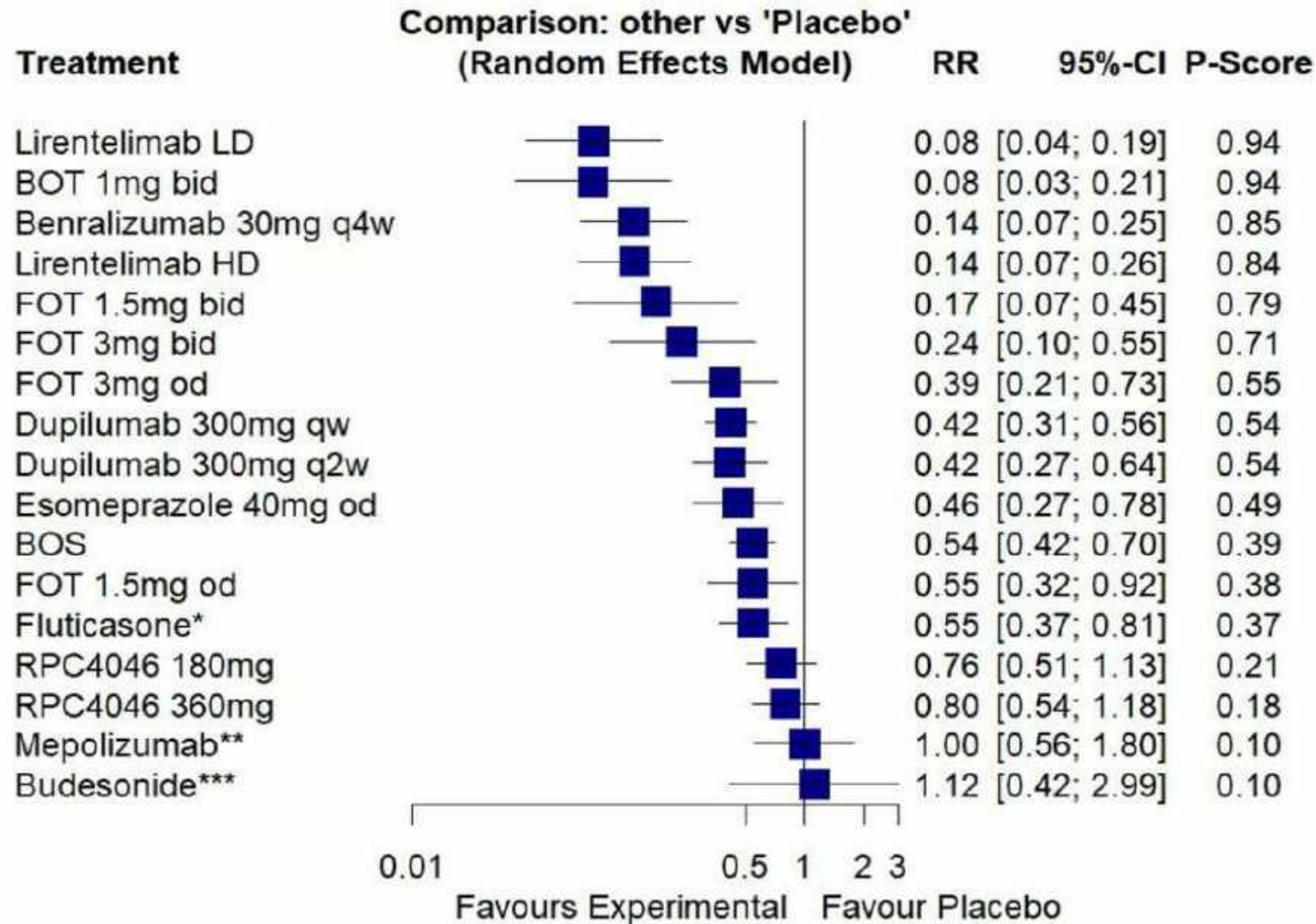
Using PPI therapy for EoE

PPIs are suggested for the treatment of EoE:
 Which dose should be used?
 What is the mechanism of EoE?
 Should we use PCABs?

Proton Pump Inhibitors for Inducing and Maintaining Remission in Eosinophilic Esophagitis: An Updated Systematic Review and Meta-Analysis



Swallowed topical corticosteroids remain a benchmark therapy for EoE

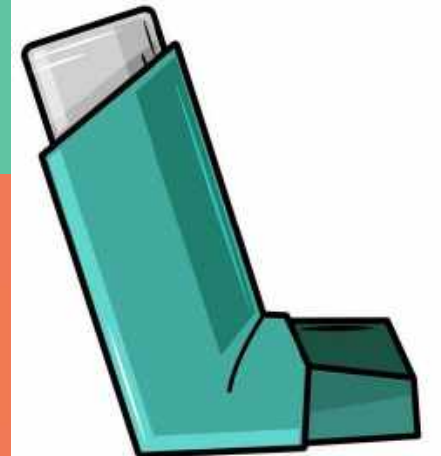
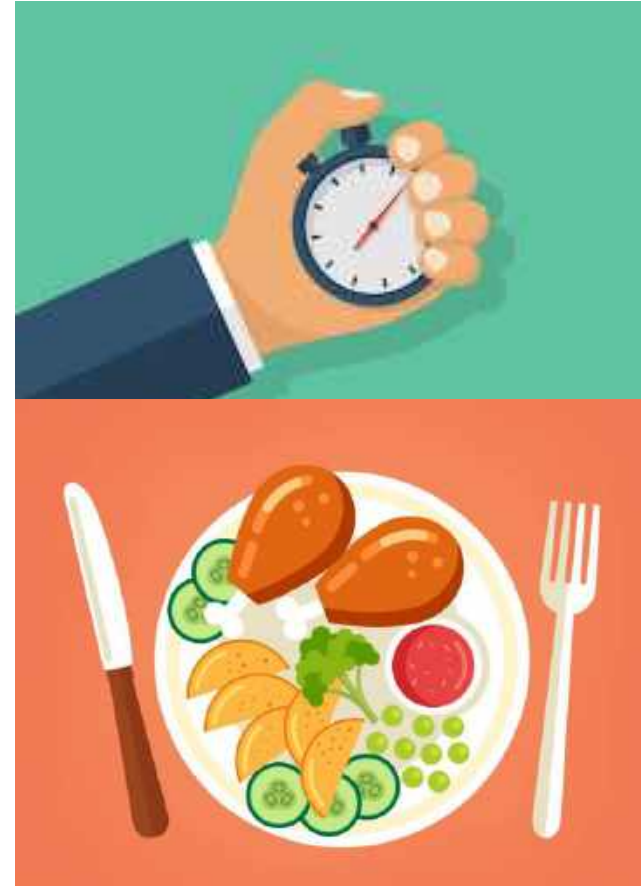


STCs are RECOMMENDED
as treatment for EoE

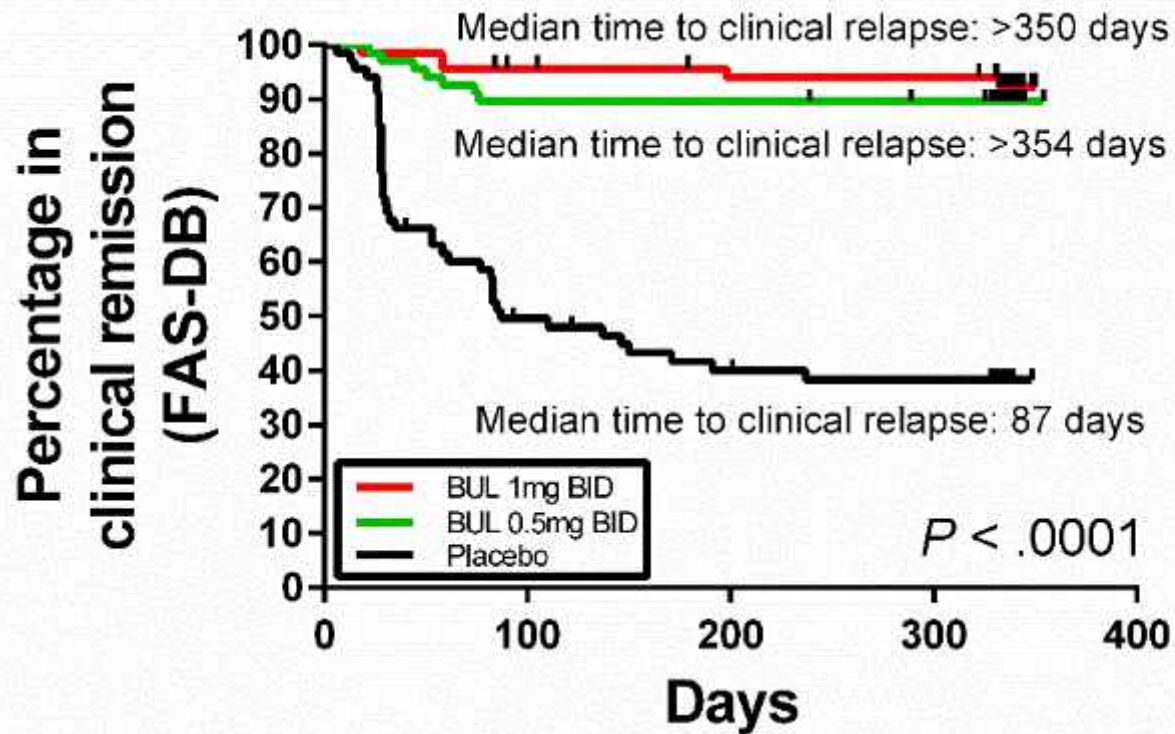
(Suggest fluticasone propionate or budesonide in patients with EoE being treated with topical corticosteroid)

Swallowed topical corticosteroids remain a benchmark therapy for EoE

STCs are the *most widely investigated therapy for EoE* with demonstrated superiority over placebo: at the same time, STCs as a group have been the most the most heterogeneous therapeutic alternative with variations in agent, dose, treatment duration, delivery system, and definitions of histologic remission



Swallowed topical corticosteroids remain a benchmark therapy for EoE



Budesonide orodispersible tablet is the most effective treatment for inducing histologic remission, is effective for maintaining EoE in remission, and is safe to use without severe side effects*

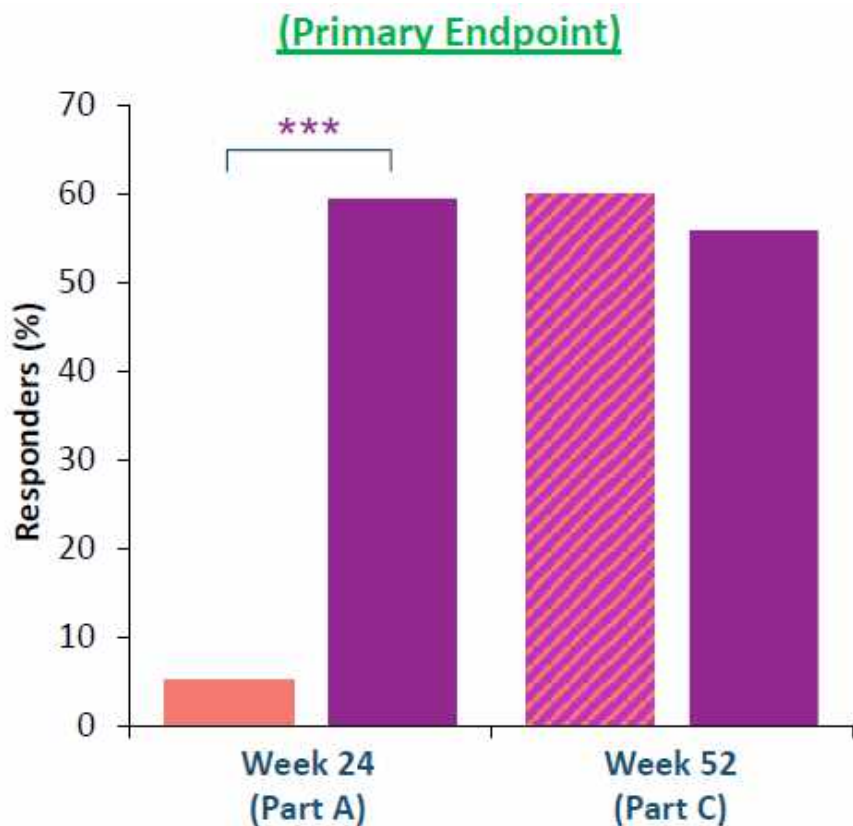
Kaplan–Meier plot displaying time to clinical relapse during the study

Hazard ratio (HR):

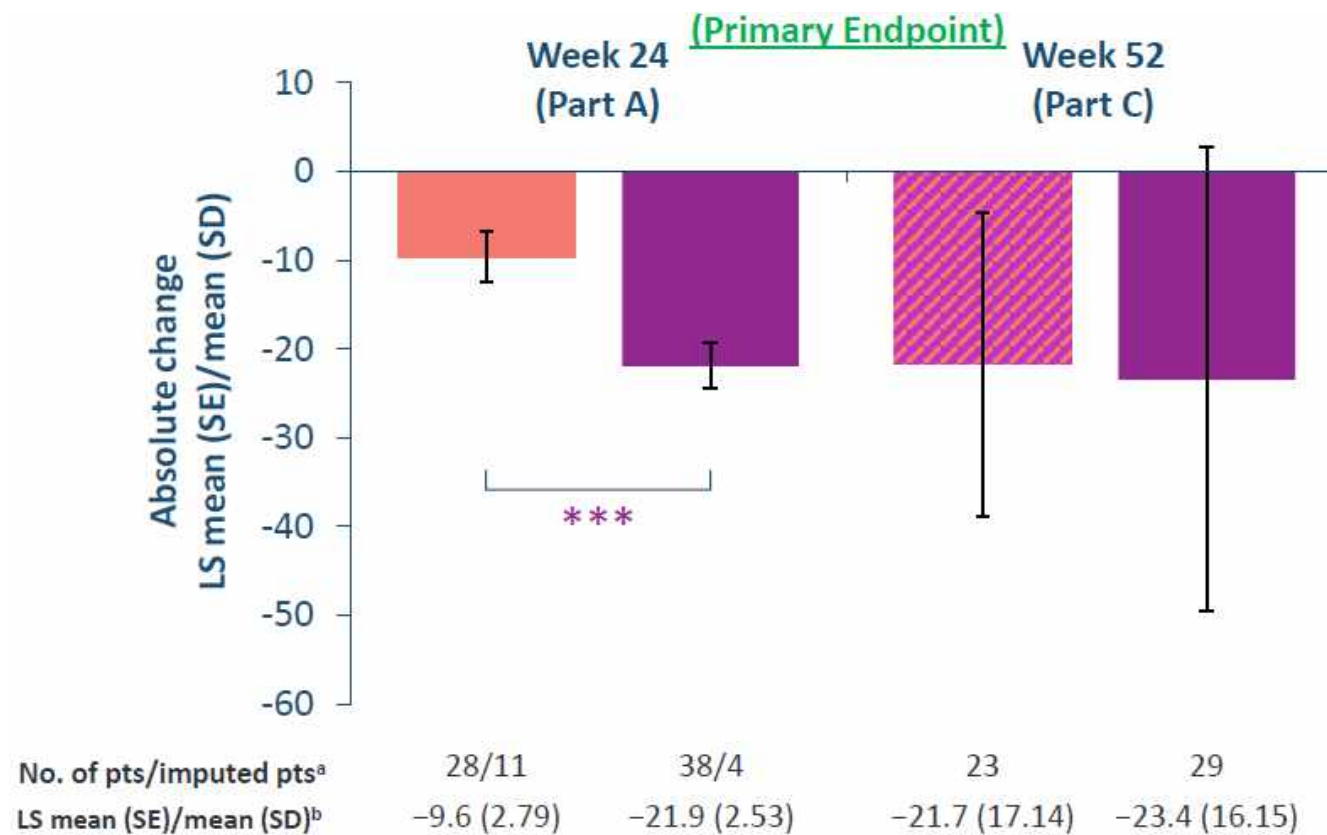
BUL1mg BID vs placebo: HR 0.086 ($P < .0001$)

BUL 0.5mg BID vs placebo: HR 0.120 ($P < .0001$).

Dupilumab - changing the game?



No. of pts	39	42	30	34
No. of responders (%)	(5.1)	(59.5)	(60.0)	(55.9)



No. of pts/imputed pts ^a	28/11	38/4	23	29
LS mean (SE)/mean (SD) ^b	-9.6 (2.79)	-21.9 (2.53)	-21.7 (17.14)	-23.4 (16.15)

■ Placebo
 ■ Dupilumab
 Placebo/dupilumab

Dupilumab - changing the game?

Dupilumab is suggested as a treatment for EoE in pediatric, adolescent, and adult populations (conditional) non-responsive to PPI

VS

Dupilumab is effective to induce and maintain clinical and histologic remission up to 52 weeks in EoE patients ≥ 12 years old (strongly in favor)



What is the correct *strategy* for using dupilumab?

Considerations for using a biologic in EoE

First Line Use	Second Line Use	Use in Fibrostenotic Disease
Comorbid asthma, atopic dermatitis, CRNP that requires dupilumab	Refractory or intolerant to therapy	Significant stricture/narrowing that requires repeated dilations or FBI
Strong preference to avoid dietary restriction or topical steroids	Difficult to treat populations who required systemic steroids or elemental diet	Narrow caliber esophagus poorly responsive to dilation
	Failure to thrive, poor growth, weight loss	
	Inability to adhere to current therapy	

6FED is not the only (nor the preferred!) way

Table 5. Dietary elimination therapy options

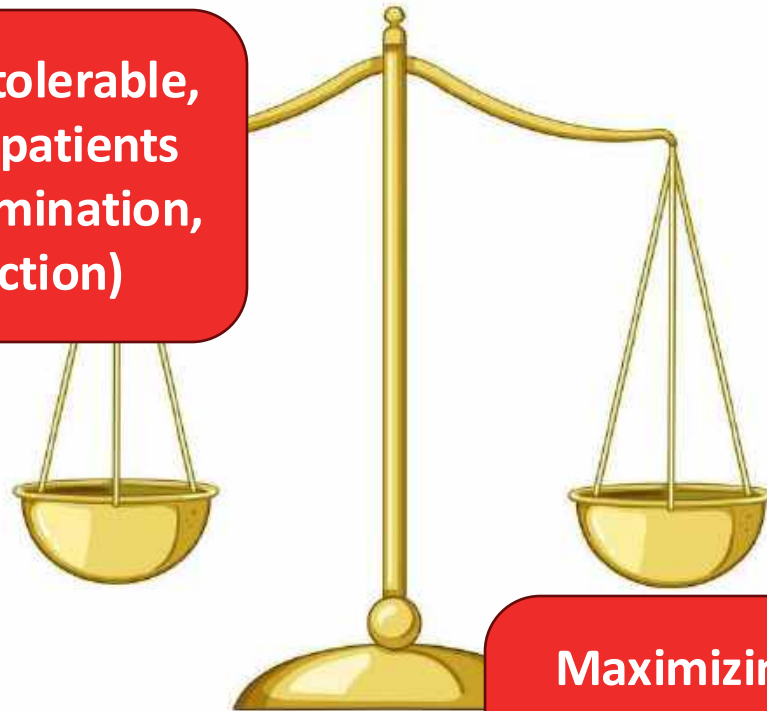
Diet	Details ^a	Efficacy range
1FED	Dairy elimination alone; also referred to as animal milk elimination ^b	35%–45%
2FED	Dairy and wheat elimination	40%–45%
4FED	Dairy, wheat, egg, and soy elimination	40%–50%
6FED	Dairy, wheat, egg, soy, nuts, and seafood elimination	40%–70%
Elemental formula	Amino acid–based hypoallergenic formula	>90% (if adherent)
Allergy test-directed	Not recommended ^c	—

Suggest empiric food elimination diet without allergy testing to direct avoidance

**Weakly against 6FED
Strongly in favor of simpler elimination diets (1FED cow's milk protein, 2FED, 4FED)**

6FED is not the only (nor the preferred!) way

What is practical, tolerable, and preferred by patients (less restrictive elimination, food reintroduction)



Maximizing efficacy from dietary elimination (in many patients to avoid drug therapy)



Dilation – the trusted partner to anti-inflammatory therapy for managing fibrostenotic complications



Dilation for ALL EoE patients with stricture + dysphagia

Target $\geq 16\text{mm}$ (can be done over multiple sessions)

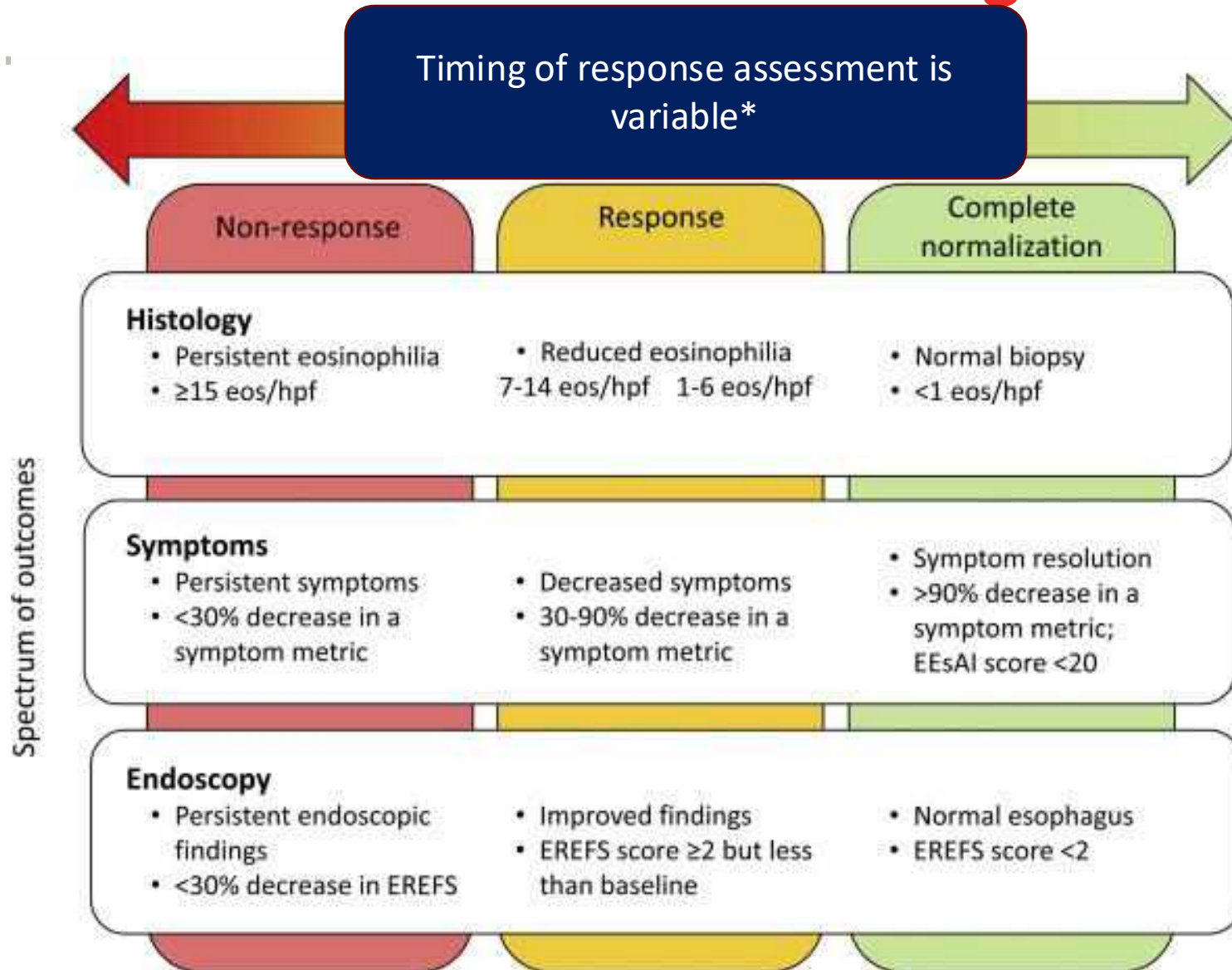
Dilator choice based on stricture morphology

Start low and work up to larger sizes

Use in combination with effective medical therapy

Wherein does the future lie?

The future is now for assessing treatment response



There is discordance between measures but PEC<15 eos/hpf is acceptable for defining histo response

EREFS ≤2 or esophageal diameters ≥16 mm associated with better outcomes



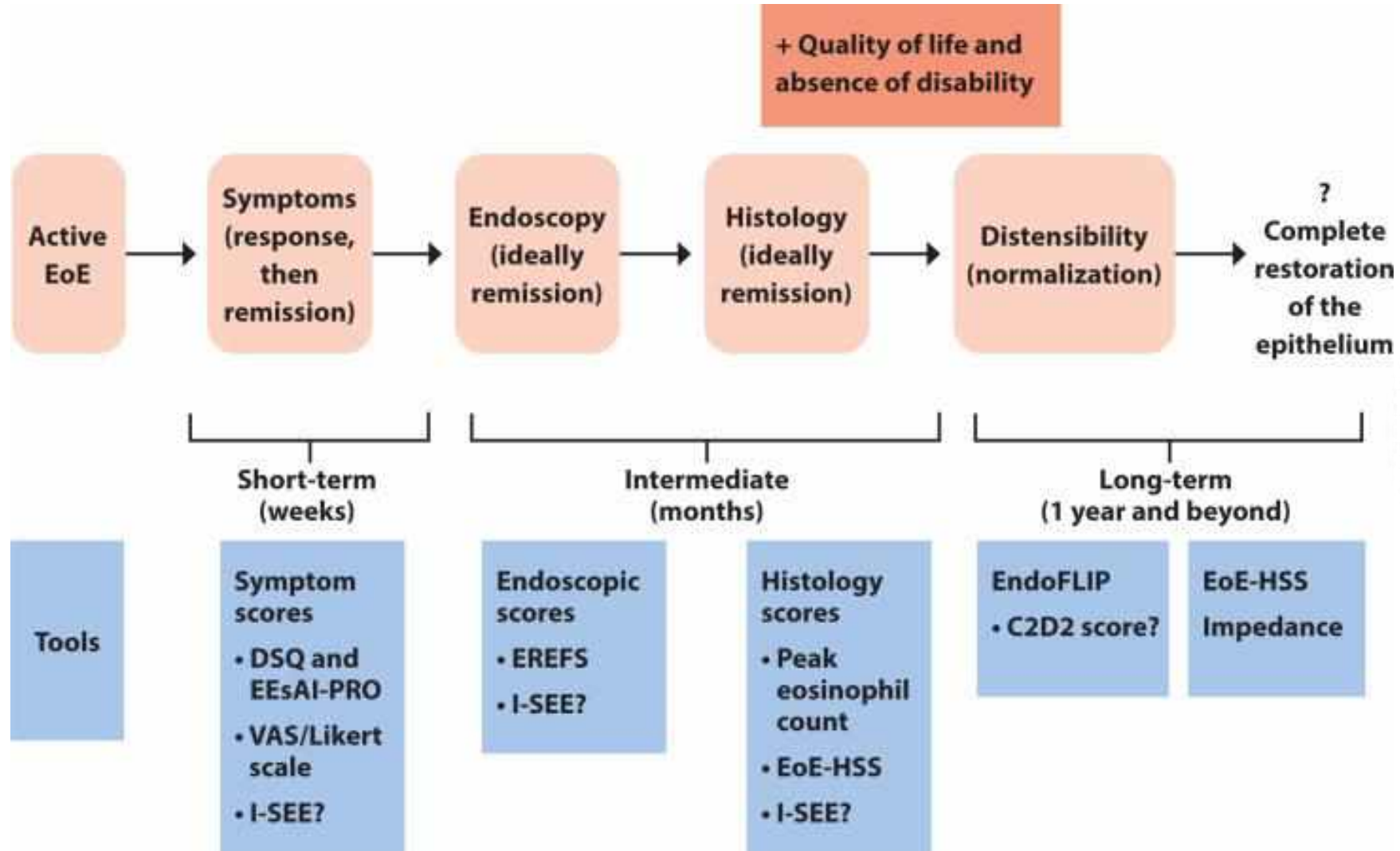
Patients should be counselled on the chronic, relapsing nature of EoE

Consideration of dose de-escalation to lowest effective dose

Disease relapse occurs universally after treatment discontinuation

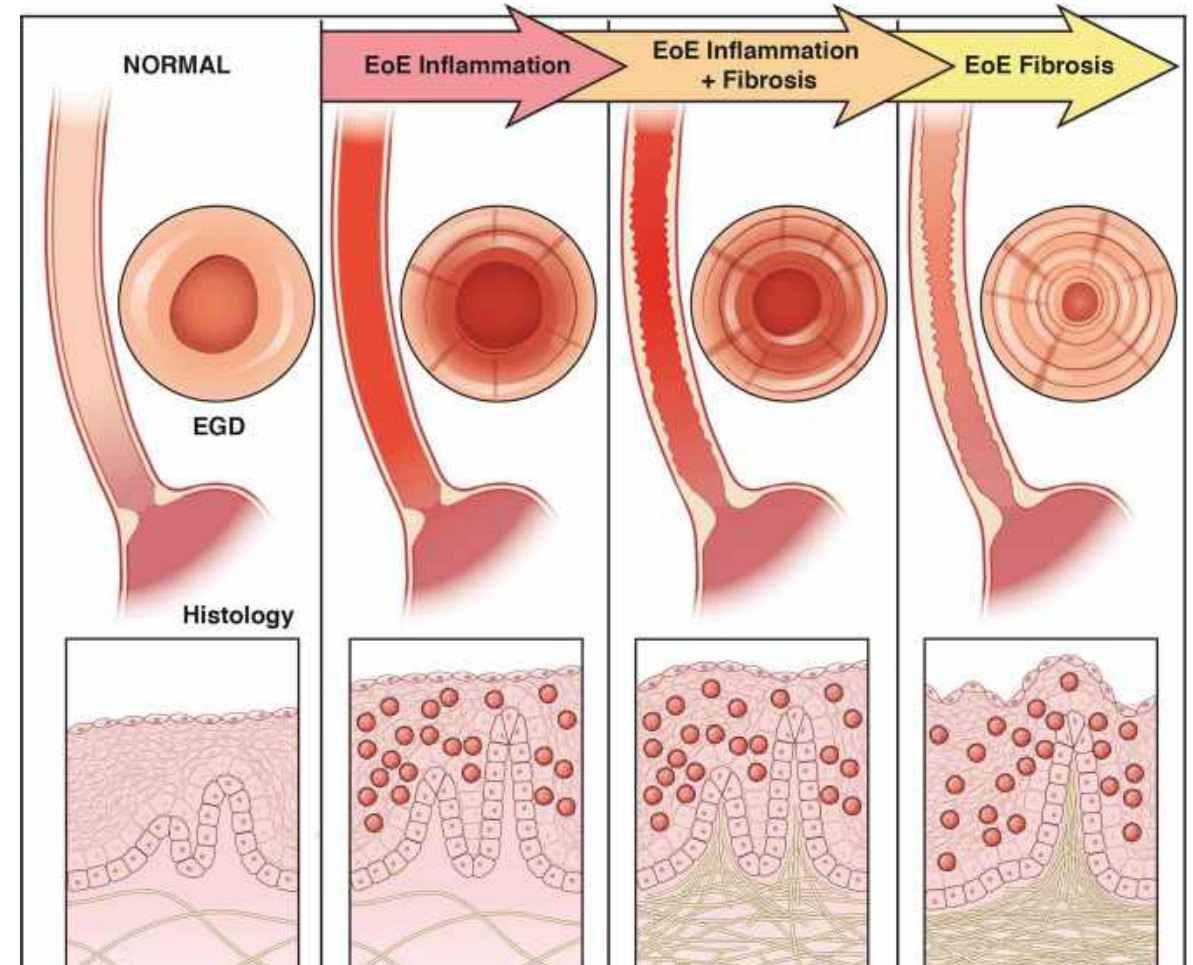
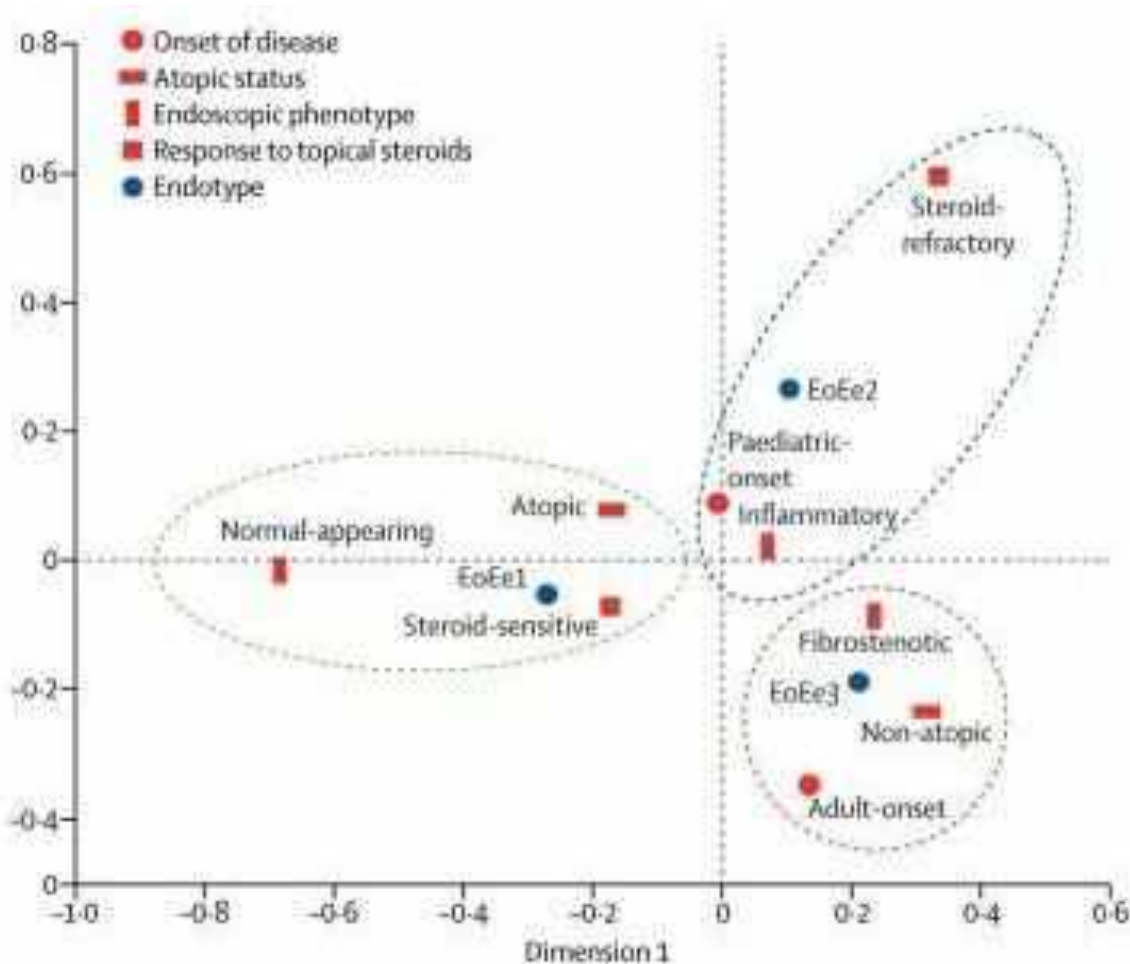
Monitoring response on the basis of symptoms alone

The future is now: how should we shape the use of “maintenance” therapy in EoE



Assumption #1: patients with untreated EoE will progress to complications

Assumption #2: treatment to target *causally* reduces risk of complications



Treating to target – what this means for the future and what innovations are needed to get us there?



- **Improvements in disease understanding**

- Better understanding of epidemiology and natural history
- Better prognostication of disease course
- Better identification of unique endotypes of disease



- **Improvements in treatment toolbox**

- Better treatments for refractory disease
- Better treatment options for stepping up
- Better treatment options for stepping down



- **Improvements in care delivery**

- Better standardization of quality care metrics
- Better sustainability and cost effectiveness for health systems



No one is 100% happy but
we're in it together!

Thank you!

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