

# EoE

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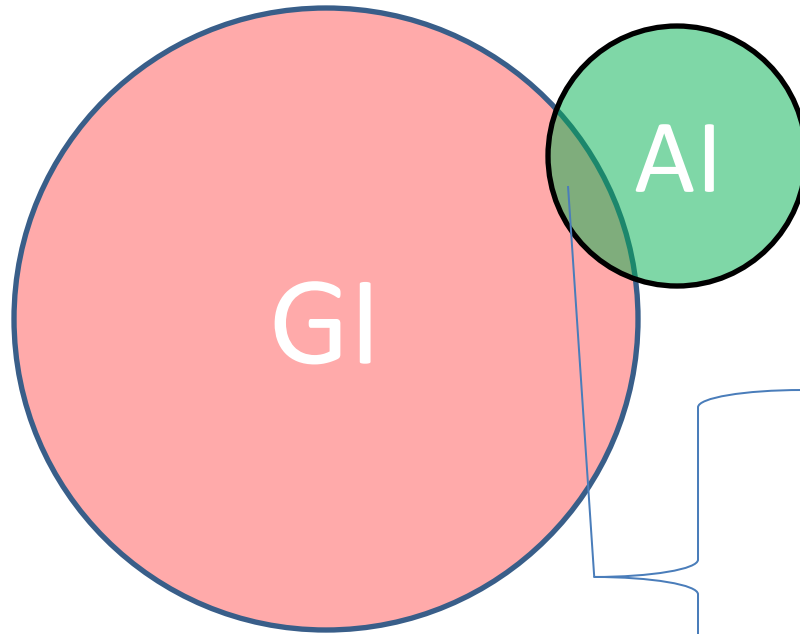


**Boston  
Specialists**  
Dr. John Leung

# Disclosure

<b>Advisory boards:</b>	Sanoli, Regeneron, American Gastroenterology Association
<b>Clinical trials:</b>	ALK, AstraZeneca, Allakos, BMS, Ellodi, Revolo, Regeneron, Sanofi, Takeda
<b>Speaker Bureau:</b>	Sanoli, Regeneron, Abbvie

# Clinical interests



- Food intolerance/allergy
- EoE, EGID
- Celiac/NCGS
- Mast cell related GI disorders
- Misc enteropathy (Lichen planus, lymphocytic, autoimmune enteropathy, CVID)

# Learning Objectives

- Basics of EoE
- Discuss latest treatment guideline EoE (2020)
- Bridge knowledge gaps with experience

# A case study

- 27 yo M with AR, AC, moderate eczema
- Dysphagia to solid food 3x/week for 5 months
- No particular food triggers
- Outside EGD showed only 5 eos/HPF in the distal esophagus
- Tried OTC PPI and it feels 50% better

# What do you recommend?

1. Continue PPI as he feels better
2. Barium swallow study and manometry
3. Repeat EGD
4. Review outside pathology report

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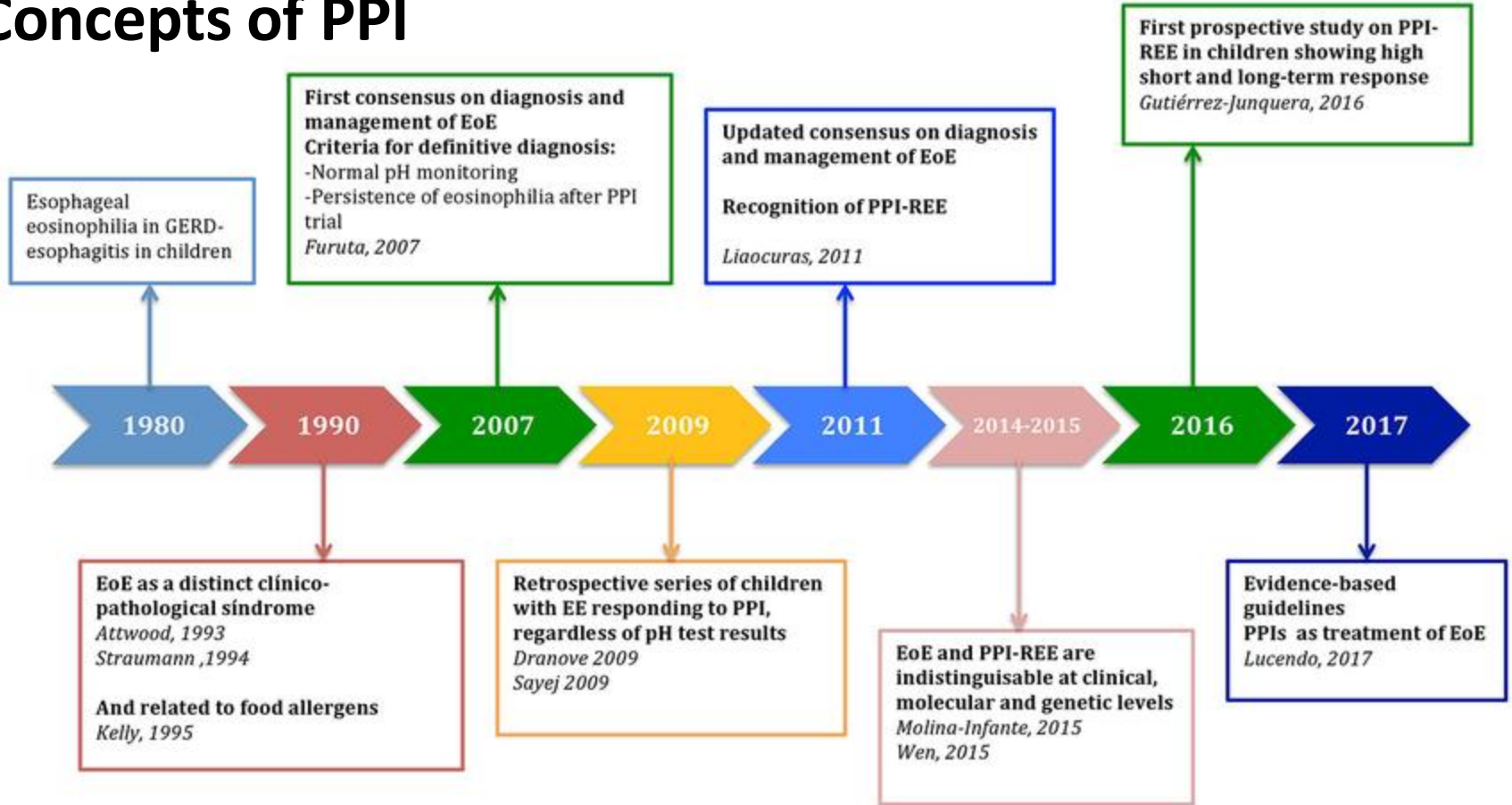
1 biopsy of the esophagus will miss half the case of EoE

# Definition & background

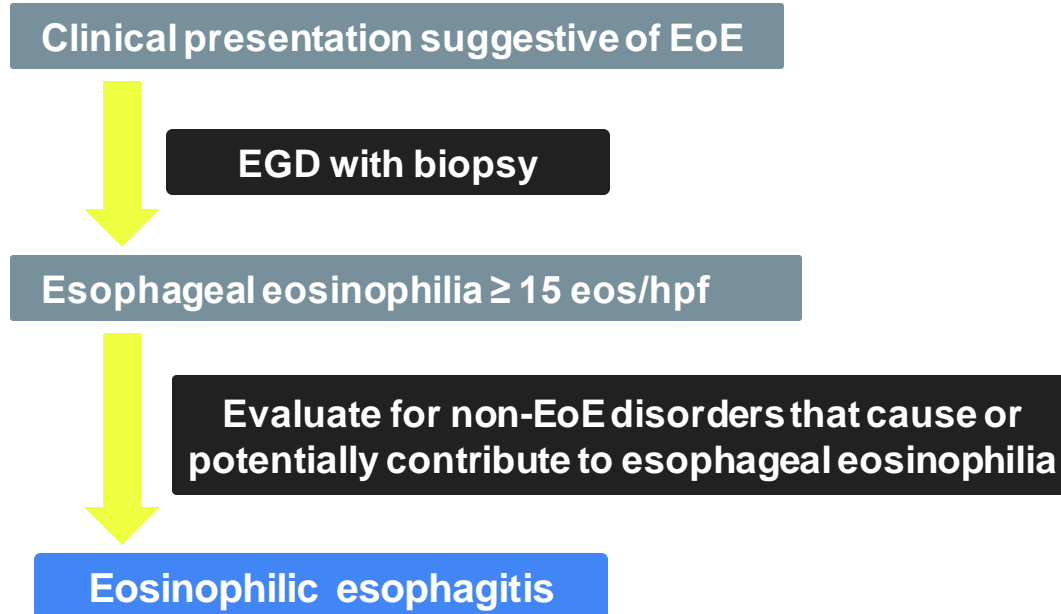
- A **chronic & progressive**, immune/antigen mediated, esophageal disease characterized clinically by symptoms related to **esophageal dysfunction** and histologically by **eosinophil-predominant** > 15 eos/hpf
- EoE is a rare disease, 1 in 2000, ~ FPIES
- First case was reported in 1977
- The leading cause of dysphagia and food impaction in children and young adults
- > 50% of cases of food impaction that present to the emergency department
- First consensus published in **2007, then 2011, 2013, 2014, and 2020**



# Concepts of PPI



# EoE Diagnostic Algorithm



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# History of EoE



eosinophilic esophagitis



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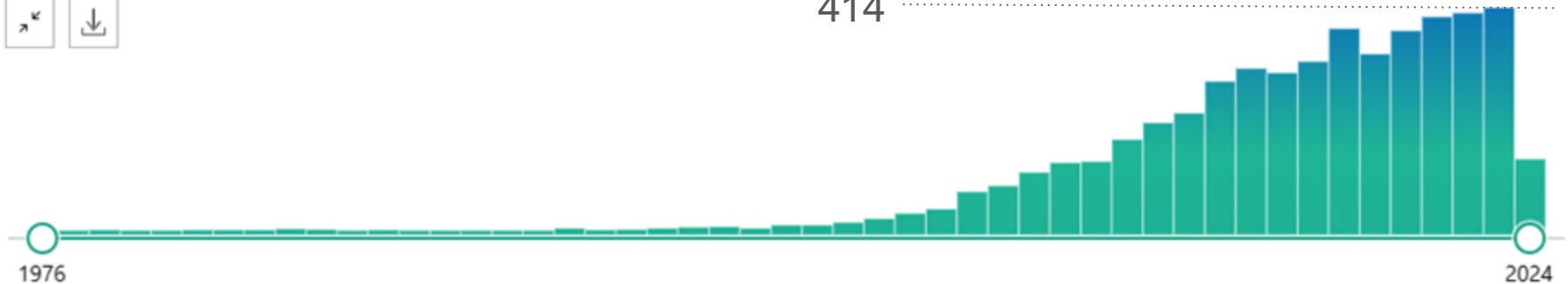
RESULTS BY YEAR

4,197 results

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# Prevalence of EoE

- Prevalence in US = 0.51%

## Global incidence and prevalence of eosinophilic esophagitis (EoE), 1976-2022

### Systematic review Meta-analysis



288 million  
participants

147,668 patients  
with EoE

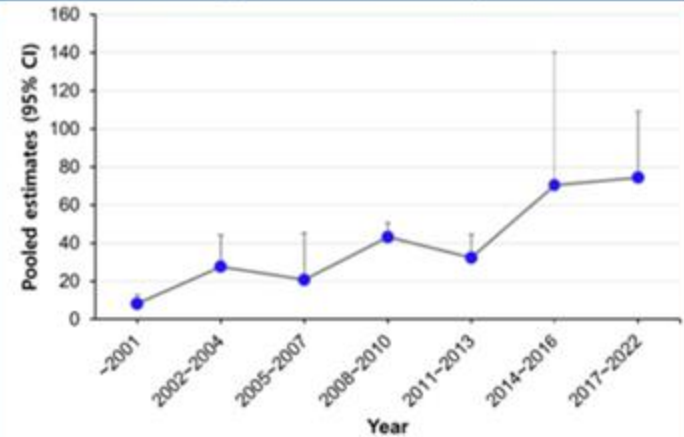
### Global map

15 countries across the five continents



### Time trends of prevalence of EoE

cases per 100,000 inhabitant-years



- Global incidence of EoE: 5.31 (95% CI, 3.98–6.63) cases per 100,000 inhabitant-years
- Global prevalence of EoE: 40.04 (95% CI, 31.10–48.98) cases per 100,000 inhabitant-years

Clinical Gastroenterology  
and Hepatology

Hahn CGH 2022

# Prevalence of EoE

**Increase in recognition or true increase?**



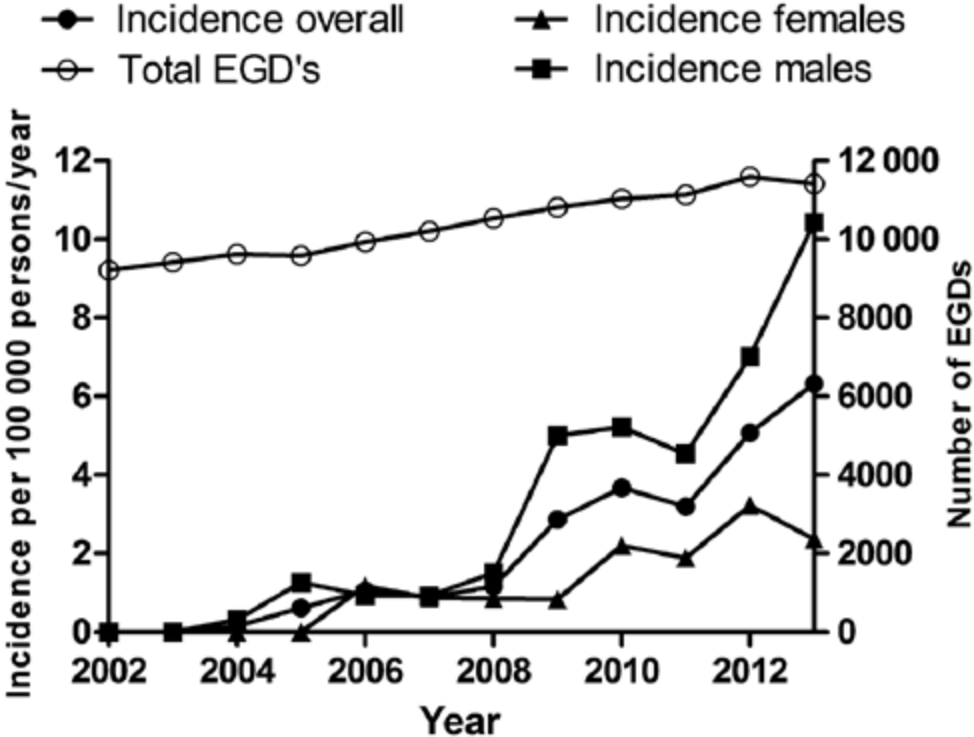
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Canton of Vaud, Switzerland.

“geographically and socioeconomically defined indicator area”

Giriens et al. Allergy 2015

# Prevalence of EoE



# The Majority of Cases in EoE are Seen in Young Males



Peak Age at  
Diagnosis  
**<50 years old**



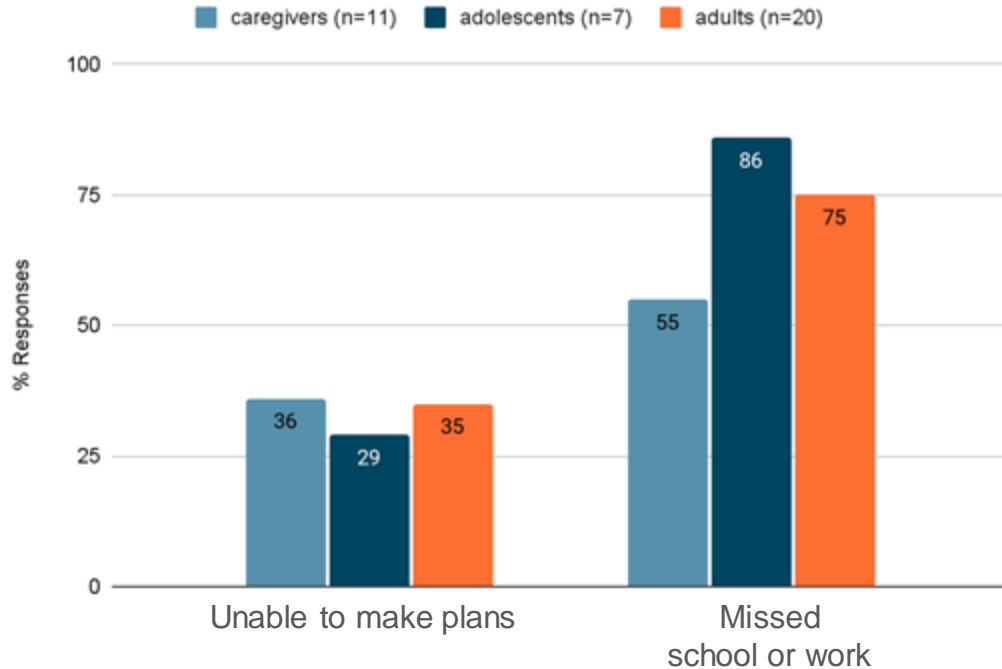
Male to female  
risk ratio  
**3:1**



Racial  
Predominance  
**>80% White**

EoE affects all races, ethnicities, and genders, and assessment should be performed in all suspected cases, regardless of the population

# EoE Contributes to Significant Patient and Caregiver Burden and Impacts Quality of Life



**65%**  
concerned about  
disease impact on  
social relationships

**28%**  
have anxiety or  
depression



# Association with other type 2 disease

**70%**  
allergic  
rhinitis

**36%**  
asthma

**24%**  
food allergy

**14%**  
Eczema

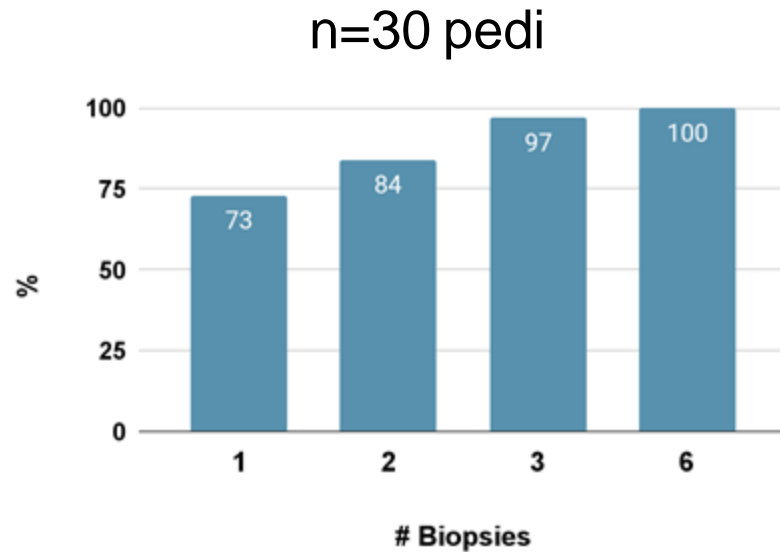
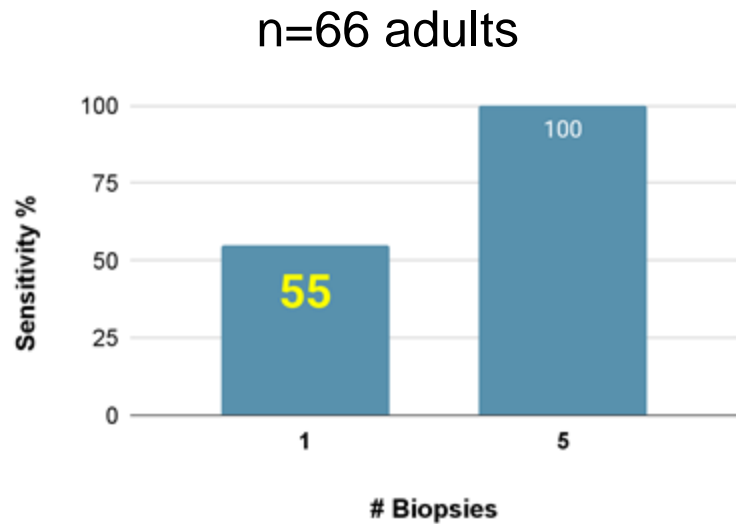
# Varying Symptoms Across Age Groups

	<b>Children (≤ 11 years)</b>	<b>Adults/Adolescents (≥ 12 years)</b>
<b>Most Common Symptoms</b>	<ul style="list-style-type: none"><li>● Regurgitation</li><li>● Vomiting</li><li>● Food Refusal</li><li>● Abdominal Pain</li><li>● Failure to Thrive</li></ul>	<ul style="list-style-type: none"><li>● Dysphagia</li><li>● Food Impaction</li><li>● Non-swallowing chest pain</li><li>● Regurgitation</li><li>● Heartburn</li></ul>

# 2022 ASGE Consensus Statement

- 6 esophageal bx (distal and mid/proximal esophagus)
- +/- bx from stomach and duodenum at diagnostic EGD
- In suspected EoE, bx should be obtained regardless of endoscopic appearance
- Bx should be obtained at the time of food impaction
- Bx is needed to monitor response to a change of treatment

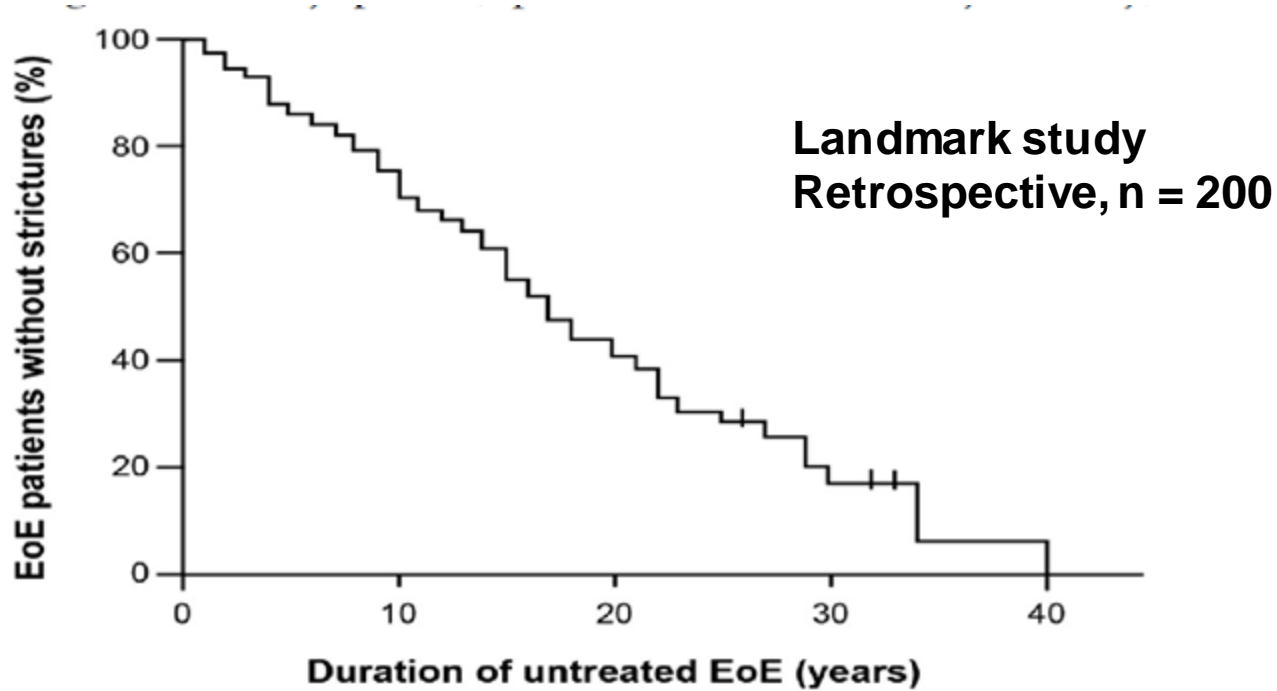
# EoE is a Patchy Disease



# What is the odd to find EoE during EGD?

<b>Reason for EGD</b>	<b>Percent of EoE</b>
<b>Food impaction</b>	<b>50%</b>
<b>Dysphagia</b>	<b>23%</b>
Refractory GERD	8%
Non-cardiac chest pain	6%
Abdominal pain	4%
Refractory Aero-digestive sx	4%

# Progression of EoE



# Diagnosis is often missed

1. Delayed in diagnosis is 6 yo in 2013
2. EGD with biopsy is needed →
  - a. Young patients: parents/MD may be reluctant
  - b. Older patients: cost, invasive nature, assess, misconception, coping

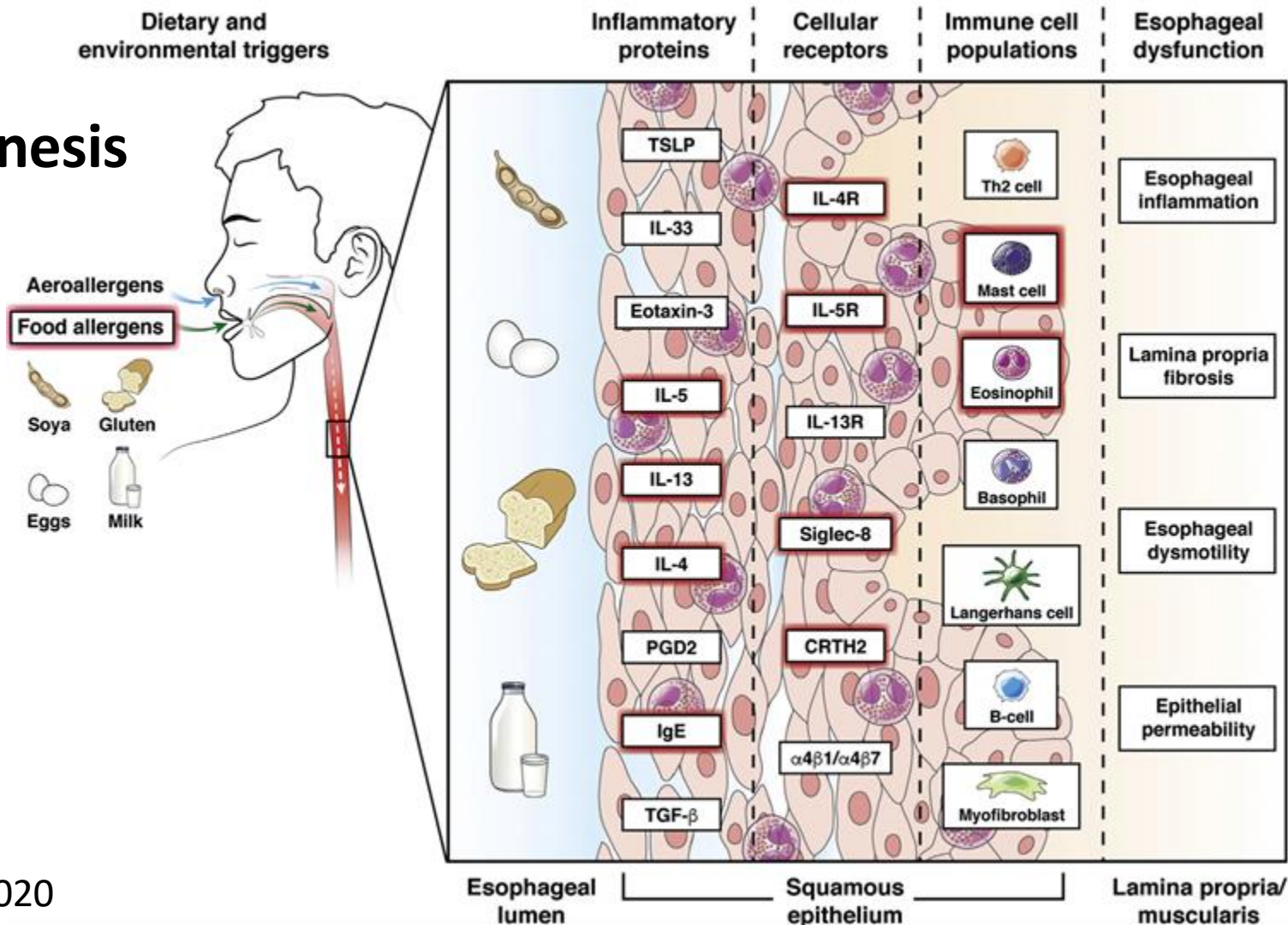
# Diagnosis is often missed



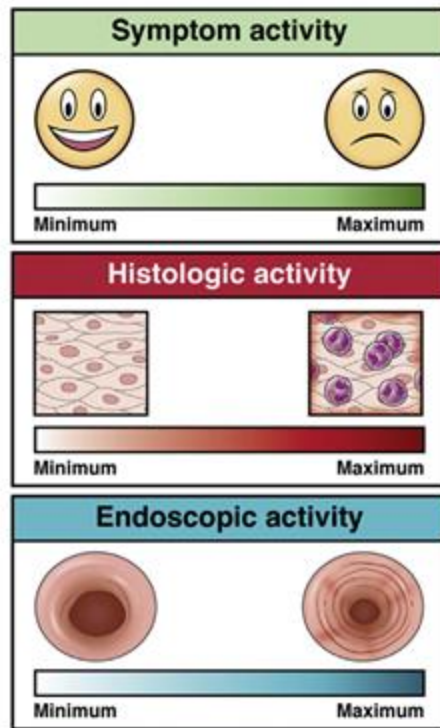
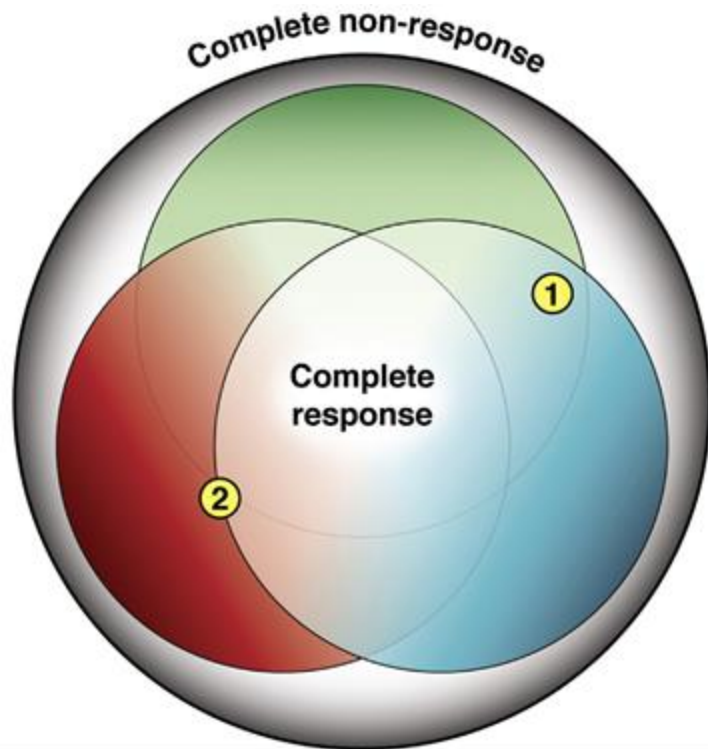
- I mbibe fluids with meals
- M odify food (cutting into small pieces, pureeing)
- P rolong mealtimes
- A void hard-texture foods
- C hew excessively
- T urn away tablets/pills



# Pathogenesis



# Goals of management



# Half-time summary

- EoE is progressive and chronic, >15 eos
- Six biopsies are needed +/- stomach and duodenum bx
- PPI is not required in the diagnosis. It is one of the Rx option
- It is a rare disease, 1 in 2000, prevalence is increasing, 3:1 M:F, >80% white
- EoE is #1 reason for food impaction in ED
- 1/3 have anxiety/depression, 2/3 negative social relationship
- AR, FA, AD, asthma are common
- Sx alone cannot be used to monitor response, bx is needed
- Dysphagia to solid food in adult <> children
- 10% esophagus can be normal endoscopically
- Remission = sx + histology + endoscopic



# 2020 Guideline on the Management of EoE

Gastroenterology 2020;158:1776-1786

## **CLINICAL PRACTICE GUIDELINES**

AGA Institute and the Joint Task Force on Allergy-Immunology  
Practice Parameters Clinical Guidelines for the Management of  
Eosinophilic Esophagitis

Ann Allergy Asthma Immunol 2020; 124: 416-423

## Practice Parameter

AGA institute and the joint task force on allergy-immunology  
practice parameters clinical guidelines for the management of  
eosinophilic esophagitis

- Collaborate effort between AGA and Joint Task Force for Allergy-Immunology Practice Parameters
- JTF = AAAAI + ACAAI
- Collaborative guideline reflects the interdisciplinary nature of EoE

# Current treatment guidelines 2020

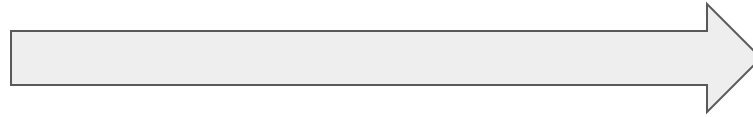
Effective	Questionable	Ineffective
<ul style="list-style-type: none"><li>★ PPI 42%</li><li>★ Topical steroids 65%</li><li>★ FED<ul style="list-style-type: none"><li>○ elemental diet 94%</li><li>○ 6 FED 68%</li><li>○ SPT-based FED 50%</li></ul></li><li>★ Dilations 0%</li></ul>	IL-5, IL13, montelukast, cromlyn, immunomodulators, Anti-TNF	Xolair

1. Maintenance Rx is needed for topical steroids
2. EGD with bx is a must to evaluate response to rx
3. Topical steroids > oral steroids

# Current treatment guidelines 2020

## Effective

- ★ PPI
- ★ Topical steroids
- ★ FED
  - elemental diet,
  - 6 FED,
  - SPT-based FED,
- ★ Dilations



Updated 2024  
approach

PPI - dementia  
Eohilia approval  
Dupixent approval  
Milk-only FED  
FED Adherence

# Cumulative Use of Proton Pump Inhibitors and Risk of Dementia

People who have used PPIs for more than 4.4 years have a 33% higher risk of developing dementia in later life.

FDA has issued warning for: **C diff, fractures of hip wrist and spine, CKD, Vit B12 deficiency, Low magnesium**

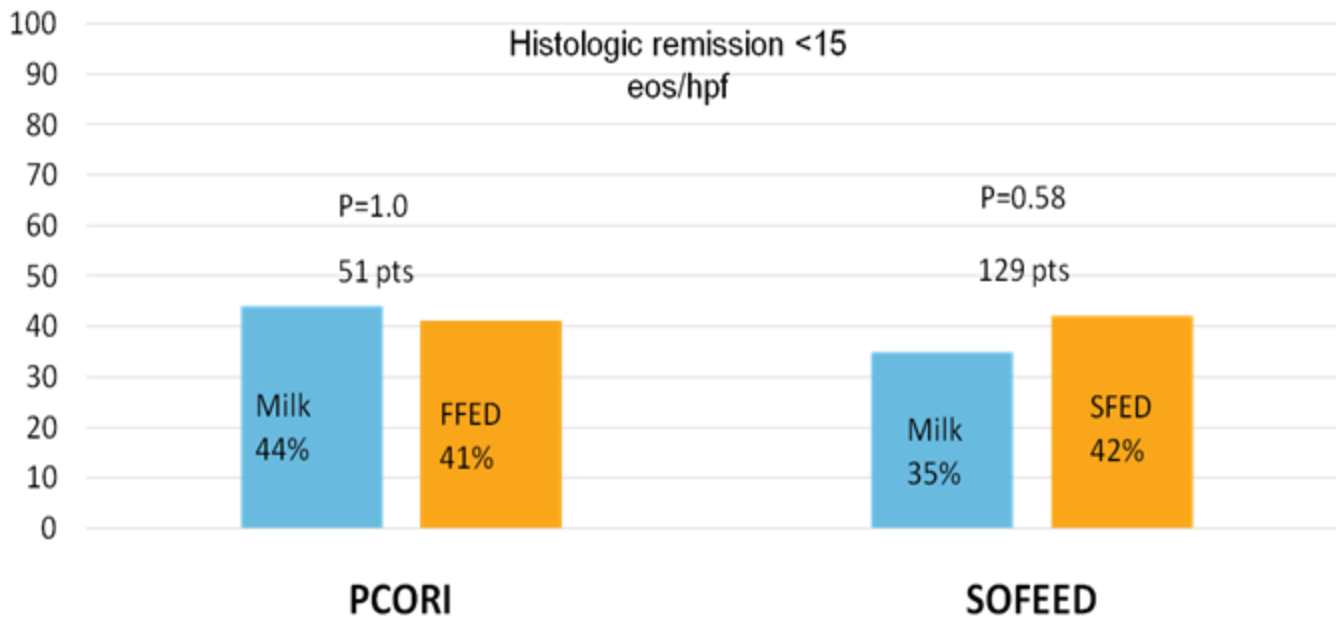
# FDA approved medication for EoE since the guideline

	Route	Indication	Note
Eohilia	PO	> 11 yo	Approved for only 12 weeks
Dupixent	SQ	> 1 yo	



# Single milk FED ~ 4 or 6 FED

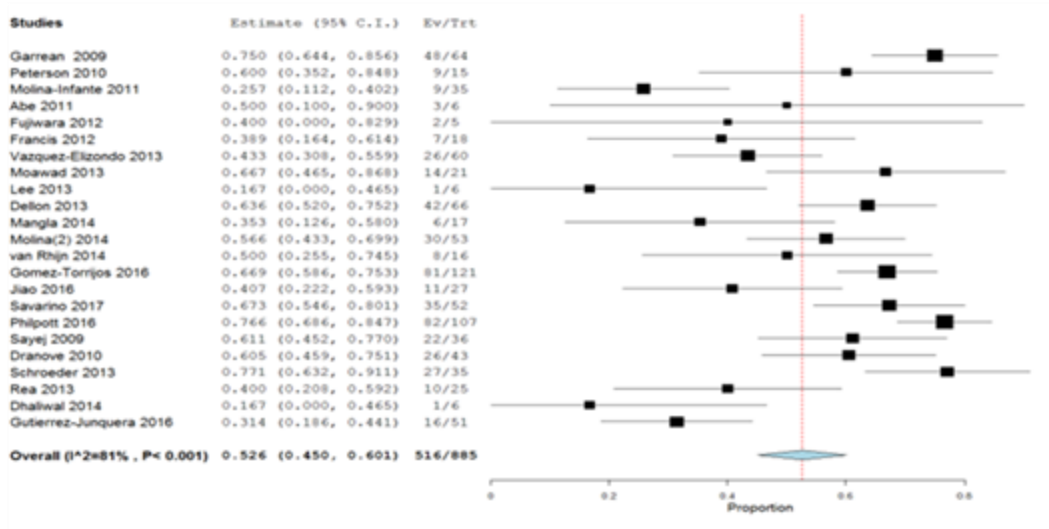
## Histologic Response in PCORI and SOFEED



# Understanding Factors Affecting Adherence/Compliance

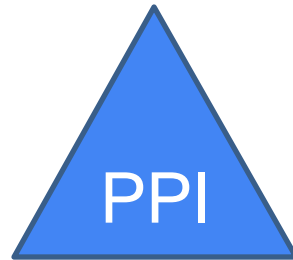
- Survey Study Assessing Factors influencing adherence
- 57% who completed SFED were active on Maintenance
- Factors Affecting Adherence
  - Diet effectiveness at reducing symptoms
  - Social situations
  - Diet related anxiety
- Most recommend diet to other EoE patients

# Treatment of EoE - PPI key player

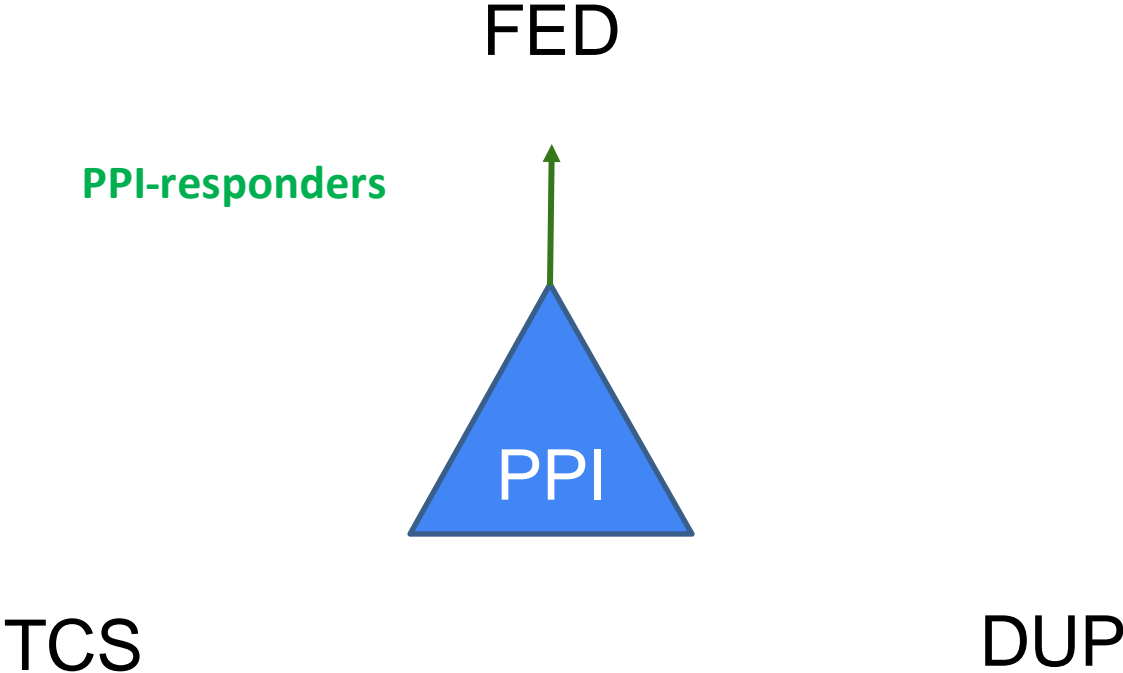


- PPI **42%** histological response
- Cheap and safe, few resistance
- Acid-independent anti-eos

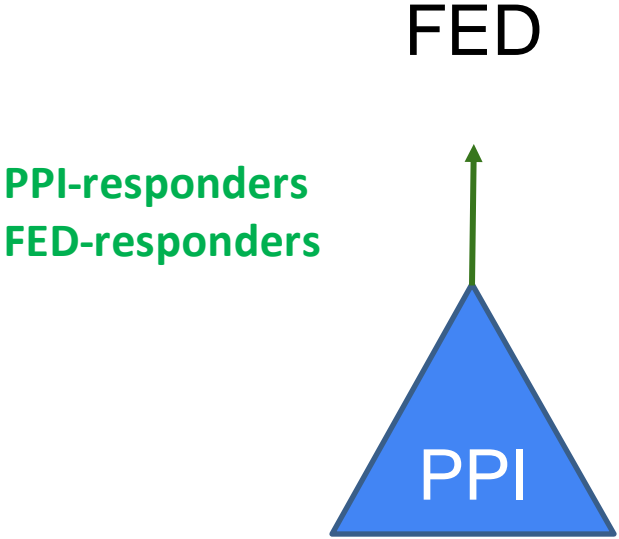
# Treatment of EoE



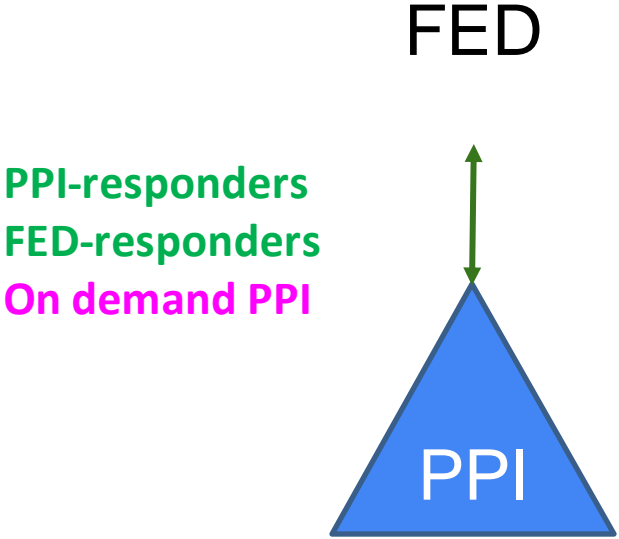
# Treatment of EoE



# Treatment of EoE



# Treatment of EoE



# Food elimination diet is a viable alternative therapy for eosinophilic esophagitis responsive to proton pump inhibitors



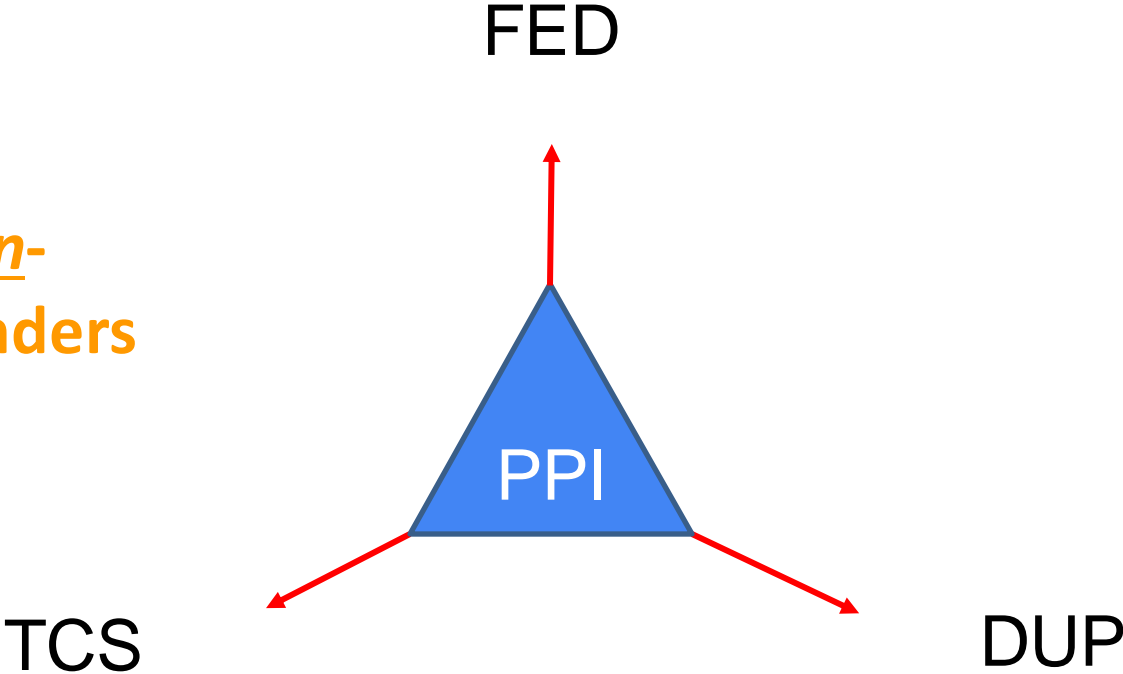
All reported **improved quality of life**





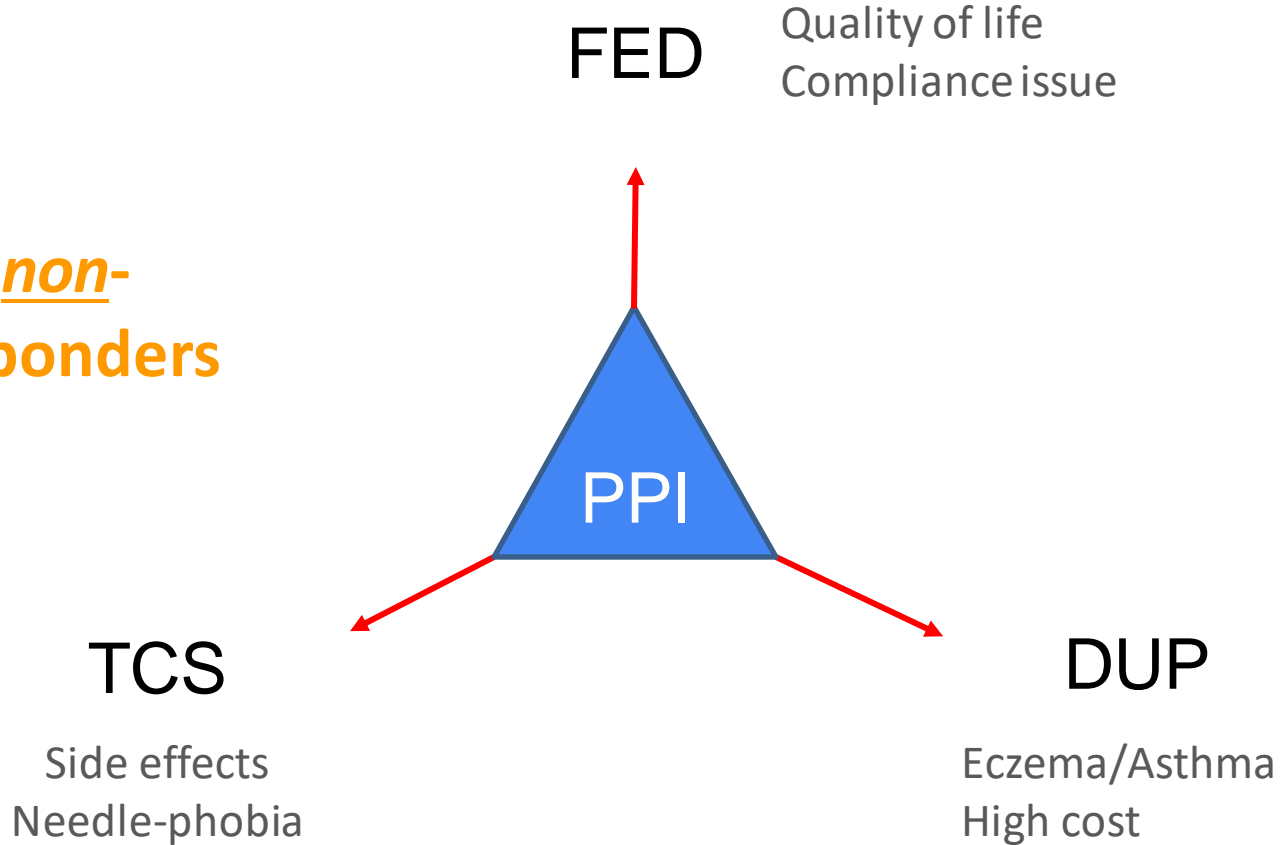
# Treatment of EoE

*PPI non-responders*



# Treatment of EoE

**PPI non-  
responders**

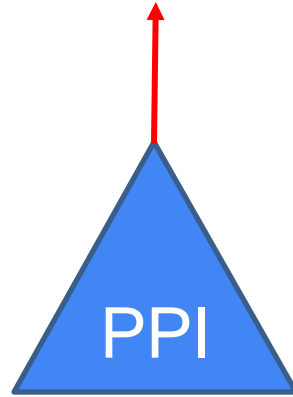


# Case studies

# Treatment of EoE

FED

14 yo fails PPI,  
does not want meds,  
no other atopic diseases



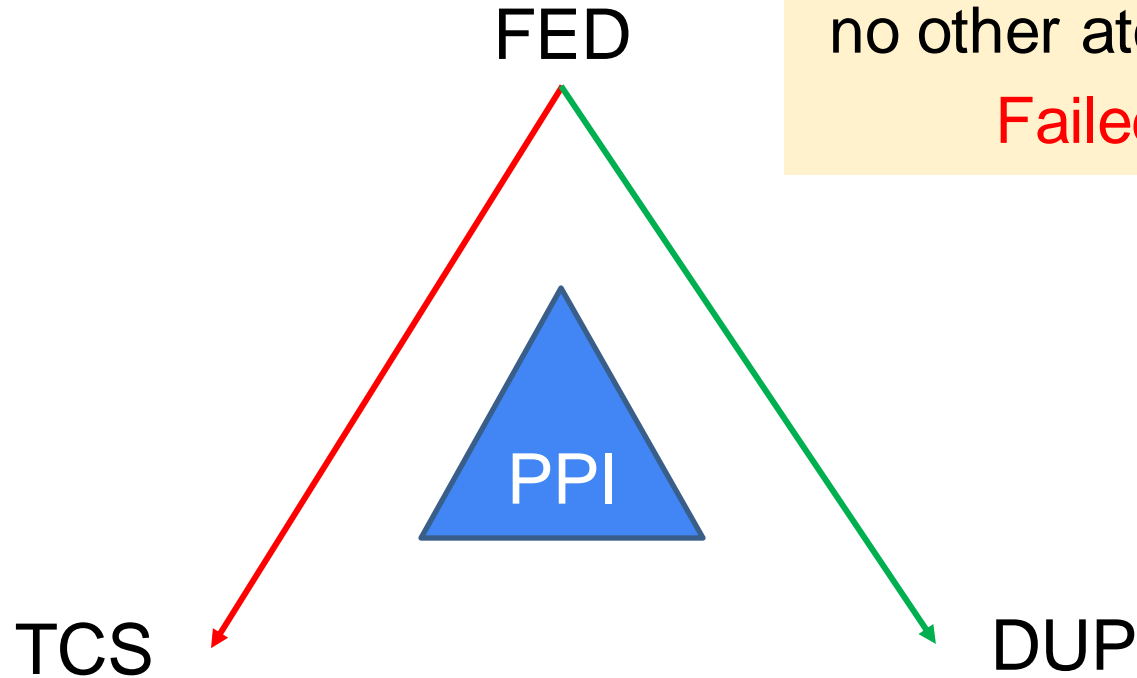
TCS

DUP



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# Treatment of EoE



**Case 1:** 14 yo fails PPI,  
does not want meds,  
no other atopic diseases

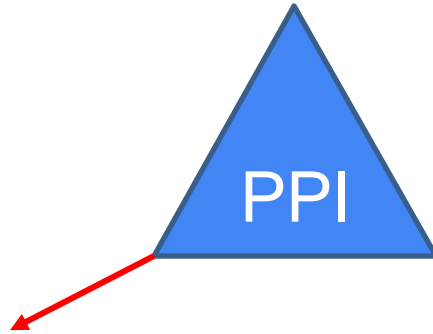
**Failed 6FED**



# Treatment of EoE

FED

**Case 2:** 44 yo fails PPI,  
Not thrilled about diet  
restriction or needles



TCS

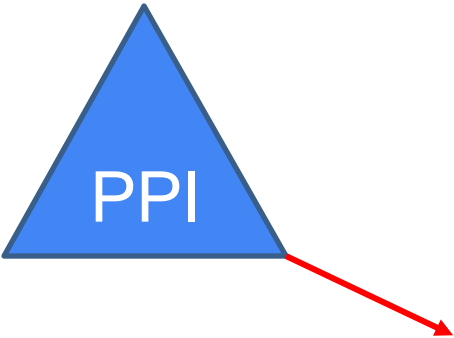
DUP



# Treatment of EoE

**Case 3:** 8 yo fails PPI,  
Severe asthma + eczema

FED

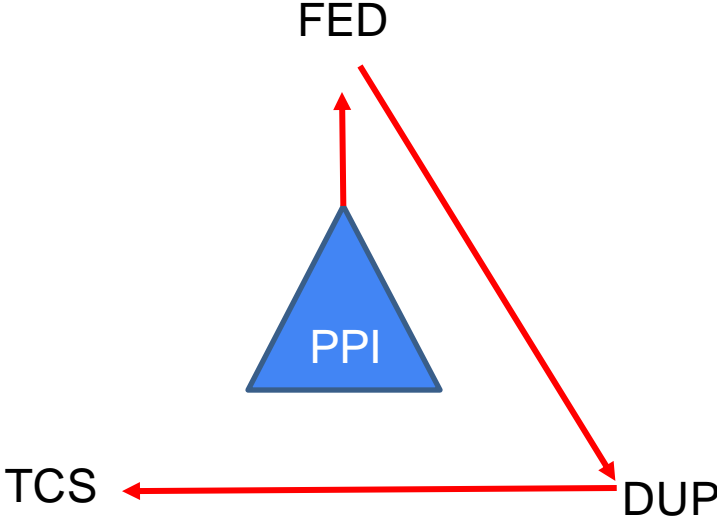
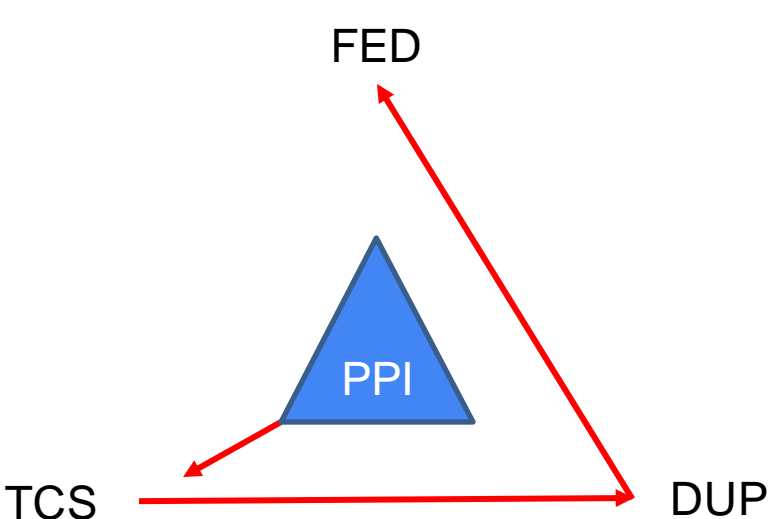


TCS

DUP

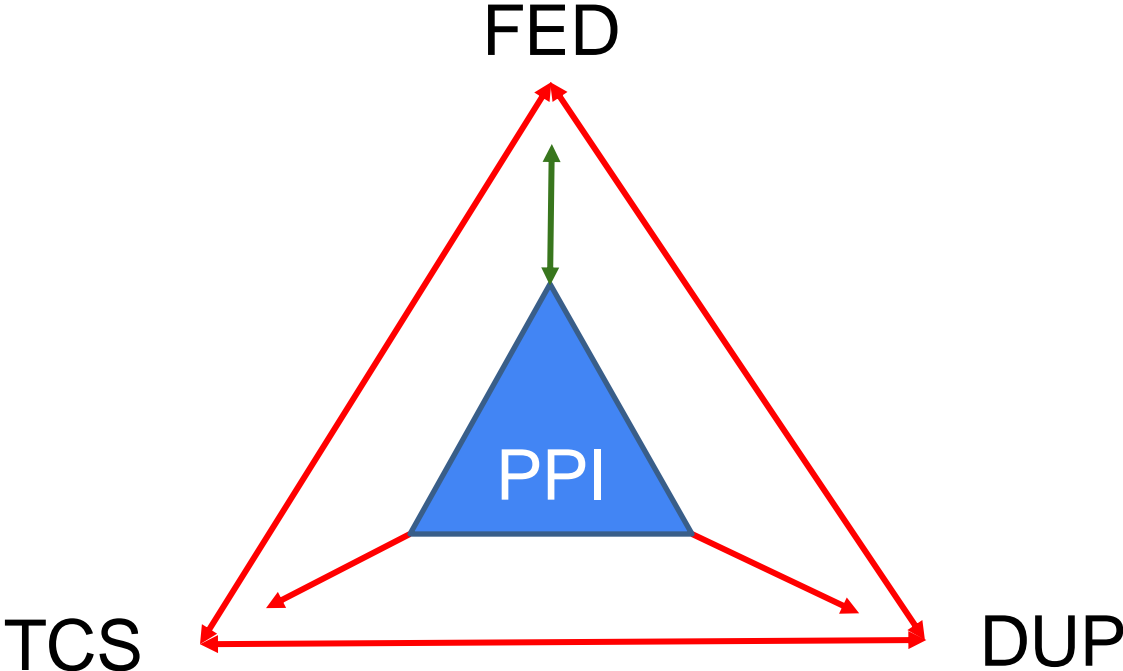


# Treatment of EoE

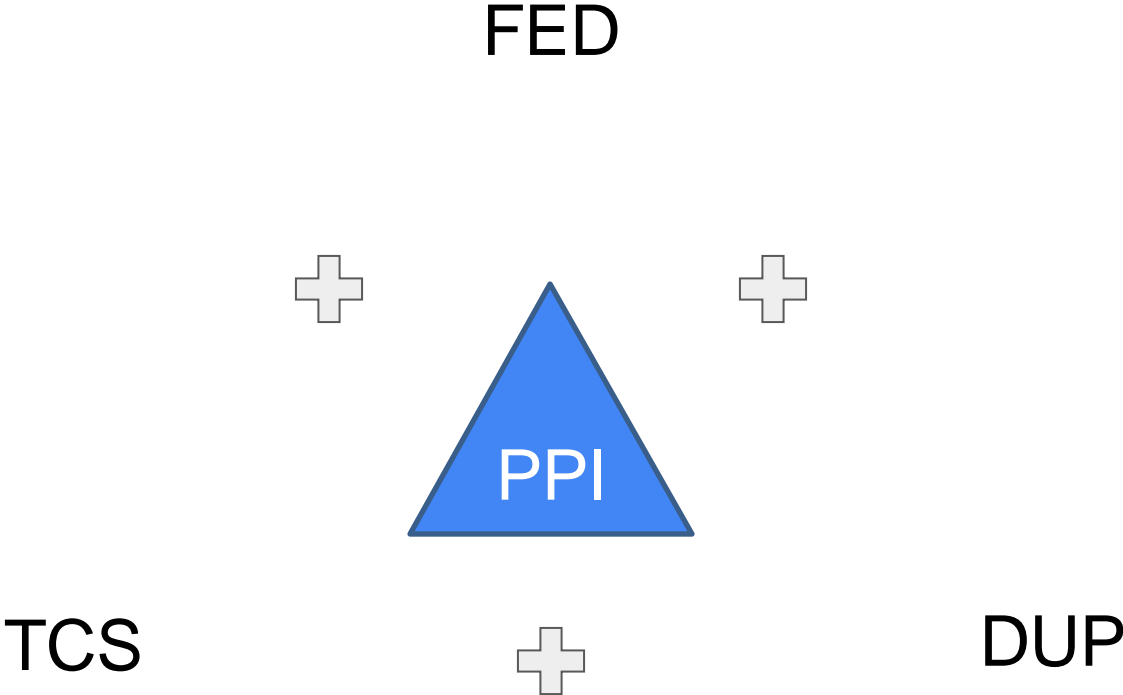




# Treatment of EoE

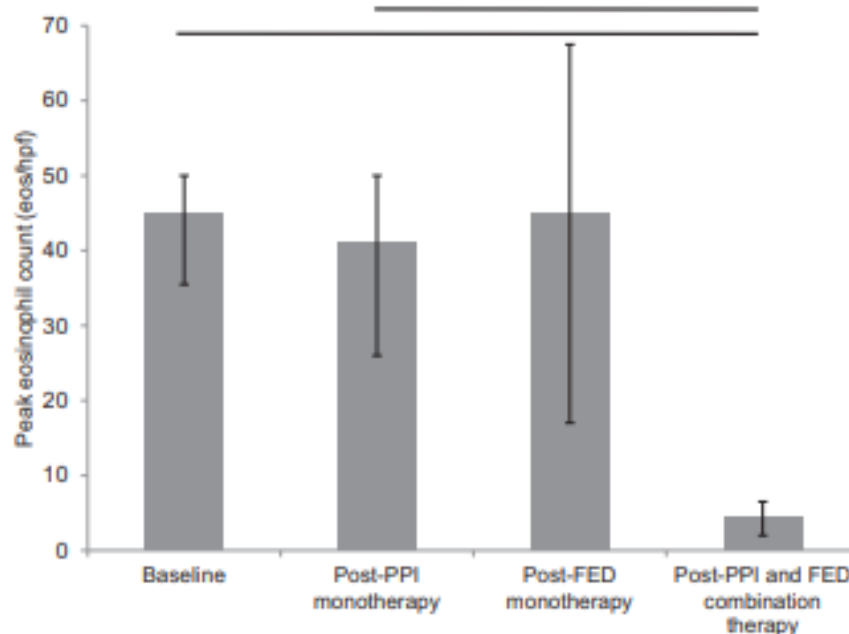


# Treatment of EoE



## ORIGINAL RESEARCH—CLINICAL

### Combination of Proton Pump Inhibitors and Food Elimination Diet for Eosinophilic Esophagitis Refractory to Monotherapy



#### Combination therapy

- Omeprazole 40 mg twice daily & 2FED
- Omeprazole 40 mg twice daily & milk FED
- Omeprazole 40 mg twice daily & raw milk FED
- Omeprazole 40 mg twice daily & milk, wheat, soy, egg, lentil, bean, chickpea FED
- Omeprazole 20 mg twice daily & 2FED
- Omeprazole 20 mg twice daily & milk, wheat, soy, egg, coconut FED
- Esomeprazole 20 mg twice daily & milk, wheat, corn FED
- Omeprazole 10 mg twice daily & 4FED

# The End

## Completed enrollment:

- Cendakimab (Anti-IL 13)
- APT-011 (Fluticasone tablets)
- Etrasimod (S1P)

## Upcoming

- Budesonide tablets

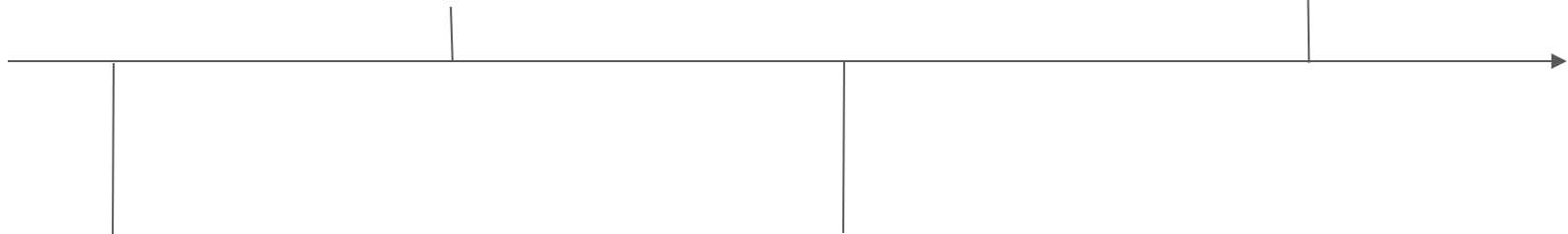
## Current enrolling EoE patients:

- Barzolovimab (Anti-KIT)
- Tezepelumab (Anti-TSLP)

## Past clinical trials

### resulted in FDA-approved

- Dupixent (Anti-IL4Ra receptor)
- Eohilia (budesonide slurry)





# Practical Considerations for PPI Therapy in EoE

- PPIs are no longer required for the diagnosis of EoE
- Histologic benefits of PPIs = 30-50%
- Mechanism = improvement in epithelial barrier function and an acid-independent anti-inflammatory effect
- Effectiveness, widespread availability, ease of administration and safety position PPIs as a popular first line treatment option
- **Loss of therapeutic benefit with prolonged use reported but uncommon**



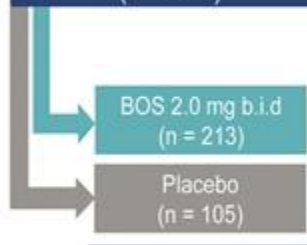
# Novel Potential Therapeutics for EoE

- Barzolovimab (Anti-KIT)
- Tezepelumab (Anti-TSLP)

# Budesonide Oral Suspension improves outcomes in EoE

Patients with eosinophilic esophagitis and dysphagia (11–55 years old) were randomized 2:1 to receive either **budesonide oral suspension (BOS)** or placebo

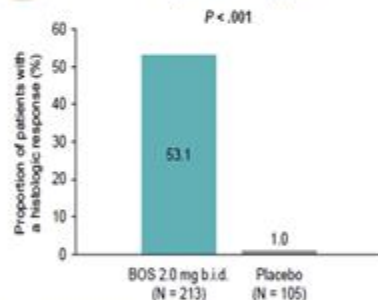
Randomization (2:1)  
(N = 318)



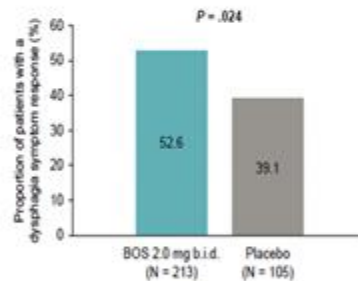
12 weeks



Stringent histologic response  
( $\leq 6$  eos/hpf)<sup>a</sup>



Dysphagia symptom response  
( $\geq 30\%$  reduction in DSQ score)<sup>b</sup>



b.i.d. twice daily; DSQ, Dysphagia Symptom Questionnaire; eos/hpf, eosinophils per high-power field

<sup>a</sup>Stringent histologic response defined as  $\leq 6$  eos/hpf at week 12 of therapy. <sup>b</sup>Dysphagia symptom response defined as  $\geq 30\%$  reduction in DSQ score at week 12 of therapy

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## Elimination Diets: What to Eliminate

	6-Food (SFED)	4-Food (FFED)	2-Food	1-Food
Cow's milk	✓	✓	✓	✓
Wheat	✓	✓	✓	
Egg	✓	✓		
Soy	✓	✓		
Peanut/tree nut	✓			
Fish/Seafood	✓			



# Restrictive Dietary Therapy Approaches

Approach	Relative risk (95% CI) of <b>not achieving</b> histologic remission <sup>a,b</sup>	Number of participants (studies)
Empiric elimination diet: Avoidance of foods that most commonly cause immediate hypersensitivity	6-food: 0.38 (0.32-0.43)	633 (9 observational studies)
	4-food: 0.49 (0.42-0.57)	426 (3 observational studies)
	2-food: 0.66 (0.57-0.77)	311 (2 observational studies)
	Single food: 0.52 (0.37-0.74)	203 (2 observational studies)
Elemental diet: Amino acid-based (elemental) formula to eliminate all potential food allergens	0.07 (0.05-0.12)	431 (6 observational studies)
Testing-directed elimination diet: Skin prick testing and atopy testing to identify food allergies and subsequently avoid	0.57 (0.33-0.73)	830 (11 observational studies)

<sup>a</sup>Relative effect compared to placebo; Histologic remission defined as <15 eos/hpf CI

<sup>b</sup>Rank MA, et al. *Ann Allergy Asthma Immunol.* 2020;124:424-440.



# Practical Approach to use of Diet Therapy

- Diet therapies are effective first-line options for children and adults with EoE
- Empiric elimination diets have advantages over elemental and allergy testing directed diets
- Shared decision making is important in the selection of available options for empiric diet therapies (i.e. 1, 2, 4, 6 FED, step up or step down)
- Consultation with a dietician
- Food reintroduction is essential to identify specific food trigger(s)



## Practical Challenges to Diet Therapy in EoE

- Elemental diets can be costly, have limited palatability for many patients and require prolonged period for reintroduction
- Allergy testing directed diets are limited by low sensitivity and specificity for IgE testing and lack of standardization of atopy patch testing
- Empiric elimination diets require repeated endoscopic exams during food reintroduction. Increasing application of office-based testing may improve utilization
- Concerns for reduced quality of life with imposed restrictions
- Better understanding of obstacles to prolonged adherence is needed



# Dupixent RCT Phase 3 – 52 wk

- Histological = 60% vs 5%
  - Endoscopic = 49% vs 5%
  - Symptoms = 68 vs 27%
- 
- ✓ First and only FDA approved for EoE (SQ qweek)
  - ✓ 12 or older, weighing 40 Kg or more
  - ✓ No need for baseline or monitoring labs
  - ✓ Injection site reaction, URI, joint pain, and Herpes viral



# Percent of patients maintaining diet over time

