# Eosinophilic Esophagitis Management

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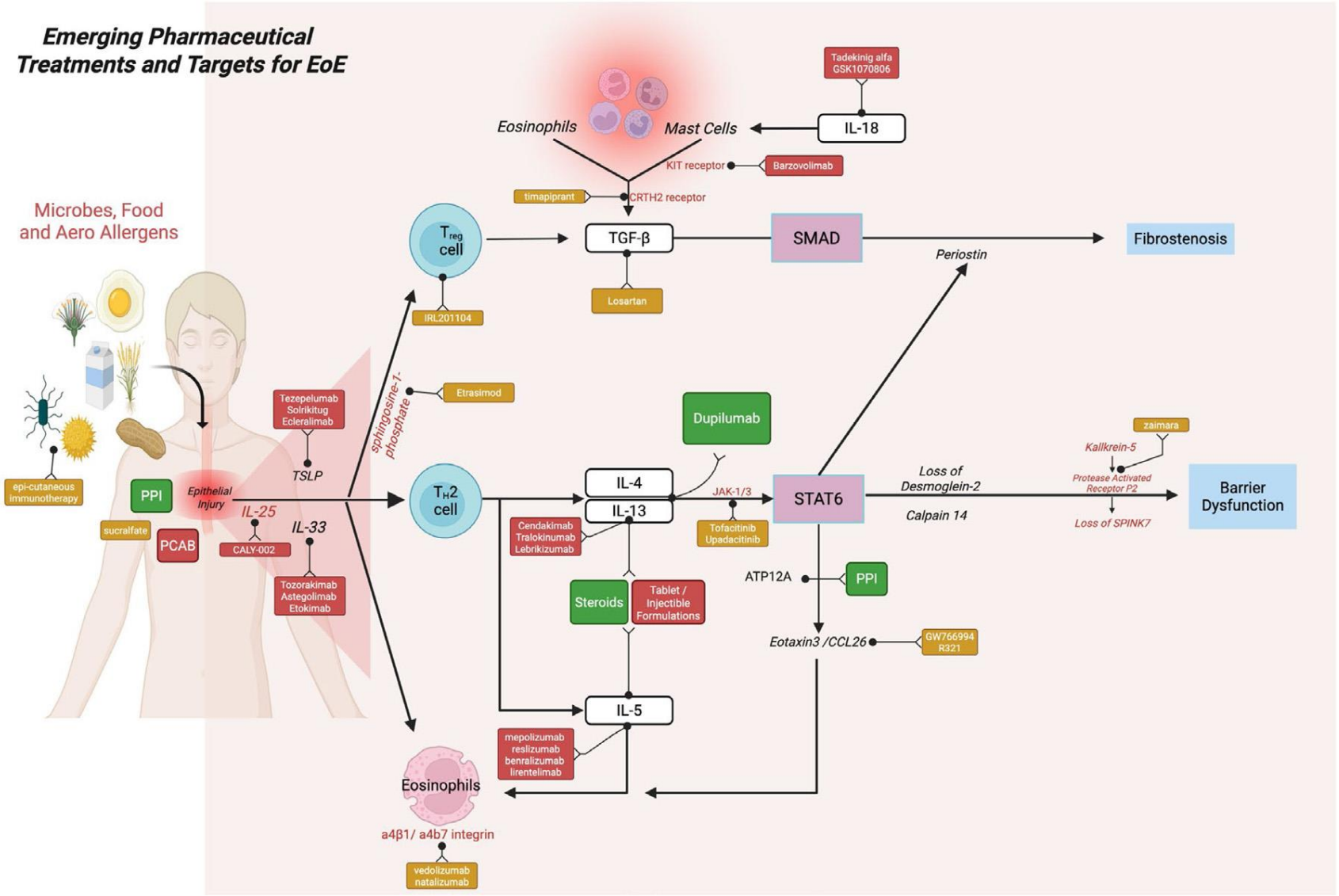
# Learning Objectives

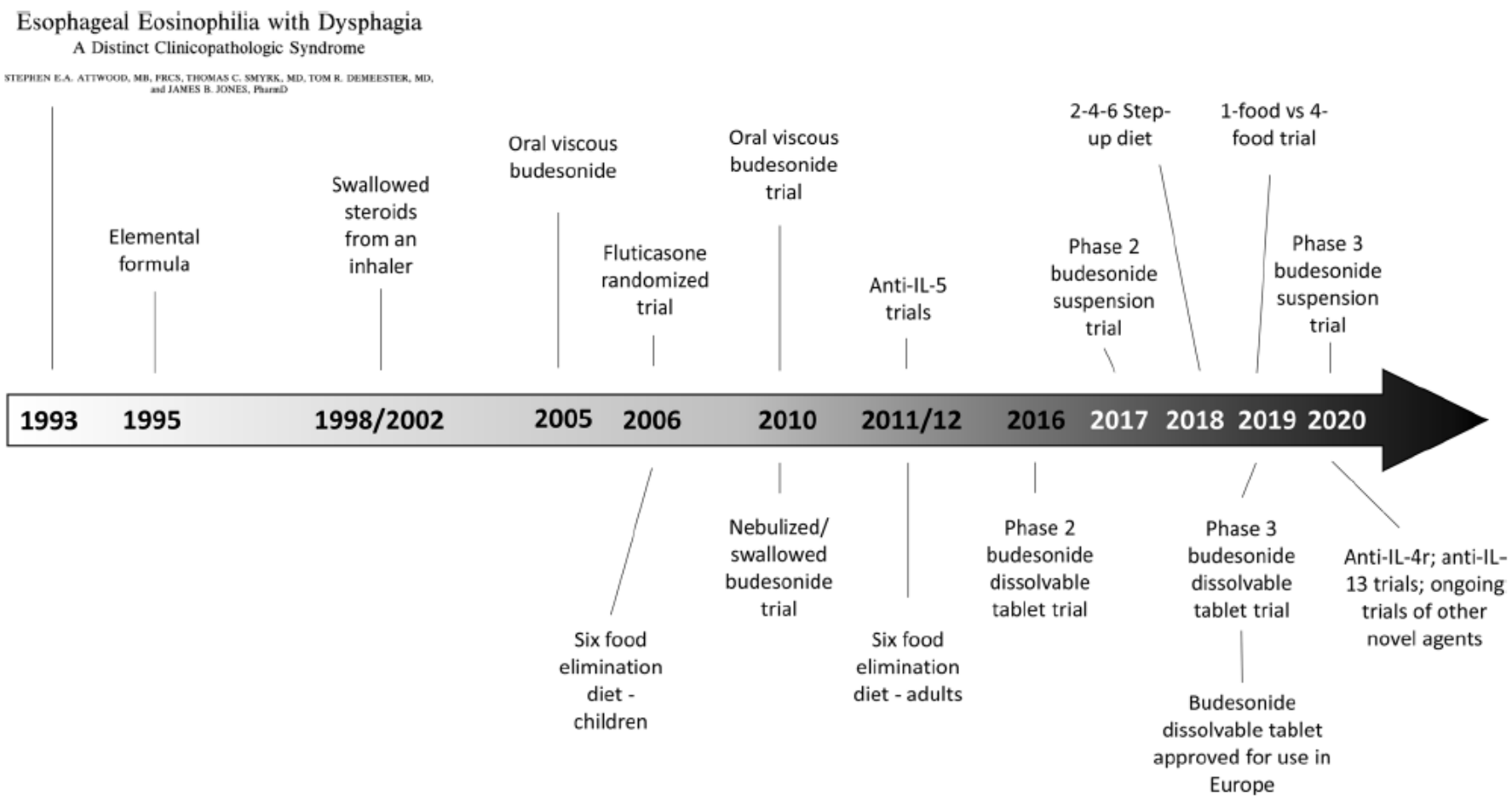
- Review the evidence and guideline recommendations for treating EoE
- Describe the current and emerging treatment options for EoE
- Understand the approach to tailoring therapy and shared decision-making in choice of EoE therapy

# T2 Pathophysiology = Multiple Potential Treatments




Dickerson et al Ann Allergy Asthma Immunol135(2025)143−154

# Evolution of EoE Treatment Choices




Dellon ES. Digestive Diseases and Sciences 2020; 65: 3434-47

# What Do the ACG Guidelines "Suggest"

## Treatment for Eosinophilic Esophagitis

**Shared Decision Making**

Use shared decision making to select first line dietary (empiric elimination) or pharmacologic (PPI or topical steroids) therapy.

**Dietary Elimination**

An empiric food elimination diet is suggested for treatment of EoE.

- Consider starting with a less restrictive empiric elimination (1FED or 2FED) initially

Allergy testing to direct food elimination diets is not currently suggested

Trials show that 1FED has similar response rates to more restrictive diets

**Endoscopic Dilation**

Esophageal dilation should be used in parallel with anti-inflammatory therapy in patients with esophageal strictures and dysphagia, and not used as monotherapy.

### PHARMACOLOGIC THERAPY

**Proton Pump Inhibitors**

- Adults: Omeprazole 20 mg BID or 40 mg daily or equivalent
- Children: 2mg/kg/day (or 1mg/kg twice daily)

**Swallowed Topical Steroids**

**Budesonide**
- Adults: 2-4 mg/day
- Children: 1-2 mg/day

**Fluticasone**
- Adults: 1760 mcg/day in a divided dose
- Children 110-880mcg/day in a divided dose

A trial comparing budesonide to fluticasone showed similar efficacy; choice of topical steroid depends on local availability and patient/provider preference

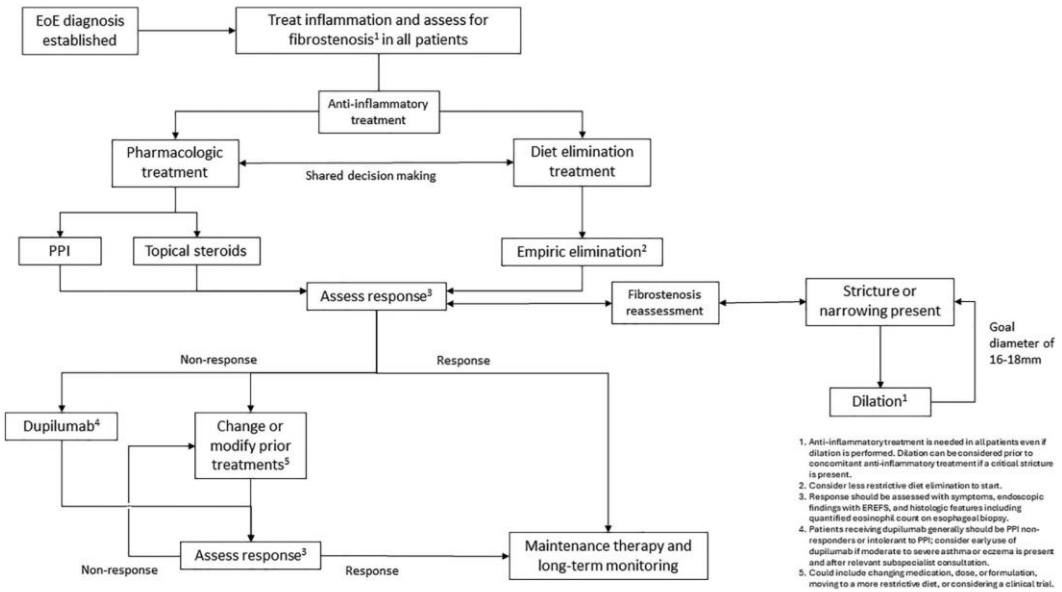
**Dupilumab:** Consider for patients who are non-responsive to PPI treatment and for step-up therapy in most cases.

- ≥40 kg: 300 mg subq every week
- 30 to <40 kg: 300 mg subq every other week
- 15 to <30 kg: 200 mg subq every other week

Dellon et al *Am J Gastroenterol 2025;120:31–59.*

# ACG Algorithm—Do Allergists Agree?

| Treatment | | |
|---|---|---|
| *PPIs* | | |
| 5. We suggest PPIs as a treatment for EoE | Low | Conditional |
| *Topical steroids* | | |
| 6. We recommend the use of swallowed topical steroids as a treatment for EoE | Moderate | Strong |
| 7. We suggest the use of either fluticasone propionate or budesonide in patients with EoE being treated with topical steroids | Low | Conditional |
| *Dietary elimination* | | |
| 8. We suggest an empiric food elimination diet as a treatment for EoE | Low | Conditional |
| 9. We do not suggest currently available allergy testing to direct food elimination diets for treatment of EoE | Very low | Conditional |
| *Biologics* | | |
| 10. We suggest dupilumab as a treatment for EoE in individuals 12 years of age or older who are nonresponsive to PPI therapy | Moderate | Conditional |
| 11. We suggest dupilumab as a treatment for EoE in pediatric patients (ages 1–11 years) who are nonresponsive to PPI therapy | Low | Conditional |
| 12. We cannot make a recommendation for or against cendakimab, benralizumab, lirentelimab, mepolizumab, or reslizumab as a treatment for EoE | — | — |
| 13. We suggest against using omalizumab as a treatment for EoE | Low | Conditional |
| *Small molecules* | | |
| 14. We suggest against the use of cromolyn and montelukast as a treatment for EoE | Very low | Conditional |




- There may be a fundamental disconnect in how an allergist vs. gastroenterologist approaches treatment
- Allergists are probably unlikely to rely or offer PPI-monotherapy and more likely to offer biologic therapy

Dellon et al *Am J Gastroenterol 2025;120:31–59.*

# The Role of Food Allergens

- Kelly et al—removal of food via elemental diet showed improvement in symptoms/histology
  - Multiple other observational studies have supported role for 3 possible forms of diet elimination
- Entopy has been shown in the esophagus
- Allergen/Allergy are terms that take on different context in IgE vs EoE
  - SFED and targeted approaches identify milk, egg, soy, wheat as common triggers
  - Not all elimination success corresponds to allergen sensitization, or reported difficulty with such foods
- While removal of trigger food may (eventually) leads to biopsy normalization, the efficacy of approaches has not been directly compared, or compared with results for patients on steroid vs. diet

Spergel J and Aceeves S. J Allergy Clin Immunol. 2018 July ; 142(1): 1–8.
Rank MA et al. *Gastroenterology*. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
Hirano I et al.. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

# Testing Data

**TABLE III.** Comparison of food prick skin testing and atopy patch testing precision in patients with eosinophilic esophagitis

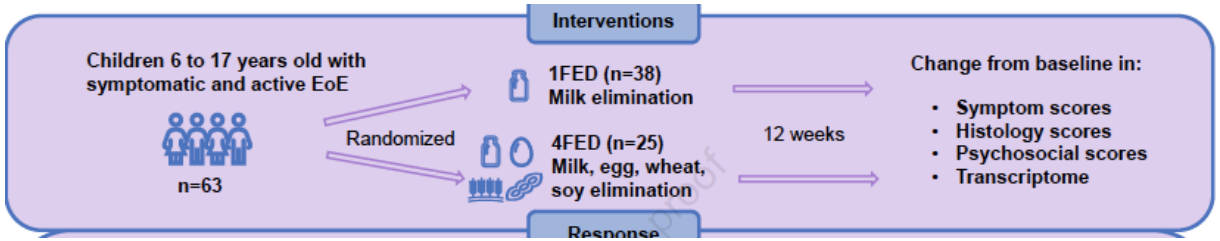
| | Prick skin testing precision | | | | Atopy patch testing precision | | | |
|---|---|---|---|---|---|---|---|---|
| **Food** | **Sensitivity** | **Specificity** | **NLR*** | **PLR*** | **Sensitivity** | **Specificity** | **NLR*** | **PLR*** |
| Milk | 26.6 | 87.8 | 0.84 | 2.18 | 29.9 | 87.0 | 0.81 | 2.30 |
| Egg | 70.0 | 85.8 | 0.35 | 4.92 | 48.8 | 91.4 | 0.56 | **5.70** |
| Soy | 40.4 | 82.1 | 0.73 | 2.25 | 52.5 | 86.7 | 0.55 | 3.95 |
| Wheat | 18.1 | 87.4 | 0.94 | 1.44 | 57.1 | 81.8 | 0.52 | 3.14 |
| Peanut | 88.2 | 88.4 | **0.13** | **7.61** | 60.0 | 92.6 | 0.43 | **8.15** |
| Corn | 30.6 | 91.5 | 0.76 | 3.60 | 92.1 | 86.7 | **0.09** | **6.91** |
| Beef | 45.7 | 92.3 | 0.59 | **5.90** | 55.6 | 89.1 | 0.50 | **5.11** |
| Chicken | 55.9 | 89.5 | 0.49 | **5.31** | 68.0 | 88.0 | 0.36 | **5.67** |
| Rice | 13.3 | 97.5 | 0.89 | **5.32** | 86.7 | 87.5 | **0.15** | **6.93** |
| Potato | 42.1 | 97.0 | 0.60 | **14.00** | 69.2 | 91.3 | 0.34 | **7.93** |
| Pork | 29.4 | 95.4 | 0.74 | **6.34** | 47.1 | 89.6 | 0.59 | 4.51 |

- CHOP data--tested by skin/patch, any positive food eliminated, then had repeat endoscopy. 112/120 had resolution on directed diet at 6-8 weeks, 39/112 had immediate relapse with reintroduction
- APT appears to have overall strong +LR, though mixed in terms of strong +LR vs. -LR for the same food
- Other centers have tried but did not replicate the methods/ages studied and got different results
- Empiric elimination has succeeded with foods that were negative on testing, which casts some doubt on if we are using the right modality for testing
- 2020 JTF guidelines and 2025 ACG guidelines are dissuasive of test-based elimination

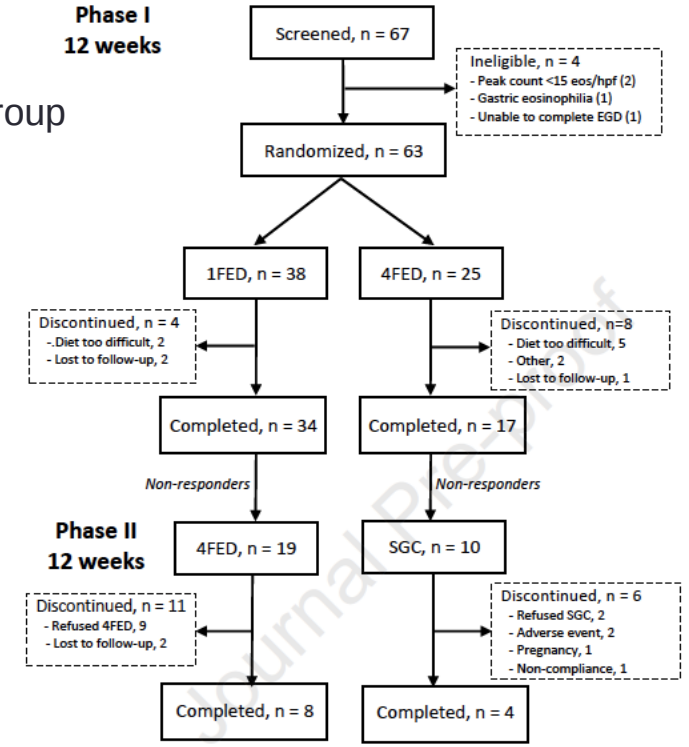
Spergel et al J Allergy Clin Imunol 2012; 130: 461-7
Henderson et al. J Allergy Clin Immunol 2012; 129: 1570-8
Molina Infante et al J Allergy Clin Immunol 2012: 129: 1200-2
Rank MA et al. *Gastroenterology*. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
Hirano I et al.. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038
Dellon et al *Am J Gastroenterol 2025;120:31–59.*

# What About The 1FED GI Insists Works "Just As Well"?

- 6-17yr, histologically active and symptomatic EoE randomized 1:1 to 1FED or 4FED for 12 weeks.
- Primary endpoint was symptom improvement by PEESSv2.0. Secondary endpoints were % histologic remission (<15/hpf); change in HSS and EREFS, transcriptome, QoL score
- Study staff and participants were not blinded to diet assignment (admittedly, this would be hard)
- 1FED excluded milk
- 4FED excluded milk, egg, wheat, and soy
  - 1FED non-responders were assigned to 12-week 4FED, and 4FED non-responders were assigned to 12-week swallowed Flovent, with both undergoing final EGD
- 10 centers in the CEGIR consortium

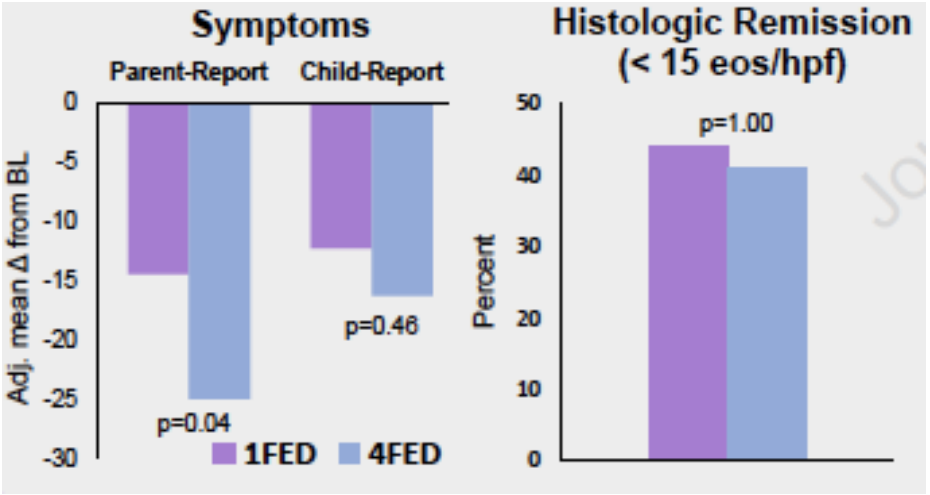


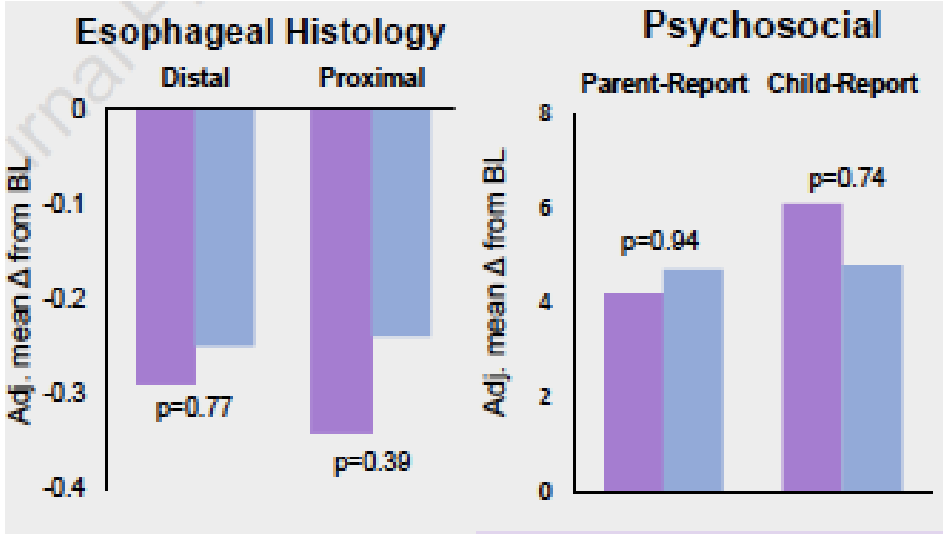

N=131 per group to show 80% power



# Did Either 1FED and 4FED Actually Work?

- The study was underpowered, critically
- 3-fold higher withdrawal rate in the 4FED arm
- 4FED sx response > 1FED (p=0.04), met primary endpoint
- Sx response only significant and different for the proxy-report
- No other marker significantly different between arms
- PedsQL EoE child/proxy scores NS improved in both arms
- Histologic improvement seen in only 41% (4FED) and 44% (1FED) of patients—no difference between approach
- Proxy PEESS in histologic non-responders to 4FED was about twice that of 1FED, but PEES change did not correlate overall with histologic changes
- EREF scores were not different between groups
- Only 12.5% on 4FED and 50% on salvage steroids achieved histologic remission in Phase II
- Adherence was good in both arms



# 1FED vs 4FED Take Home Messages

1. Their conclusion is that 1FED and 4FED were equally as effective.
2. My conclusion is that neither diet worked well (>55% didn't respond to either), and only the 4FED addressed symptoms and histology (to meet remission criteria). If neither worked well, then maybe perhaps it doesn't matter which you use for failed efficacy….
3. Best remission was getting steroids AFTER failing 4FED, and the question we should be asking is why are we continuing to treat EoE like eczema in the late 1990's
4. This used <15 eos/HPF—very weak remission criteria and still barely worked.
5. This was fatally underpowered—therefore can't really make any conclusions
6. Were the right foods chosen?  1FED did not vary the single food
7. We need to stop pretending (and stop GI from saying) 1FED is effective—it isn't, and this may be mistreating patients by withholding better treatments

# Current Dietary Recommendations

- **JTF/AGA:**
  - **In patients with EoE, the AGA/JTF suggests using elemental diet over no treatment (***conditional recommendation, moderate quality evidence).*
  - **In patient with EoE the AGA/JTF suggests using an empiric six-food elimination diet over no treatment** *(conditional recommendation, low quality evidence).*
  - **In patients with EoE, the AGA/JTF suggests allergy testing-based elimination diet over no treatment** *(conditional recommendation, very low quality evidence).*

**ACG:**

- **We suggest an empiric FED as a treatment for EoE (quality of evidence: low; strength of recommendation: conditional).**
- **We do not suggest currently available allergy testing to direct FEDs for treatment of EoE (quality of evidence: very low; strength of recommendation: conditional)**

**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] | — |

Rank MA et al. Gastroenterology. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
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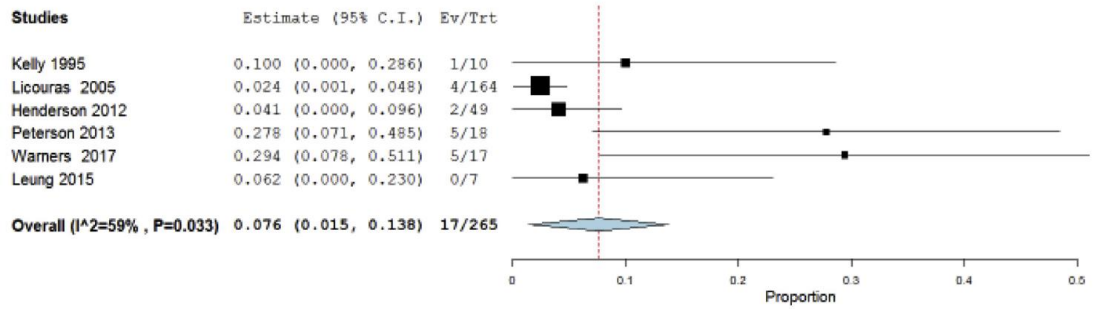
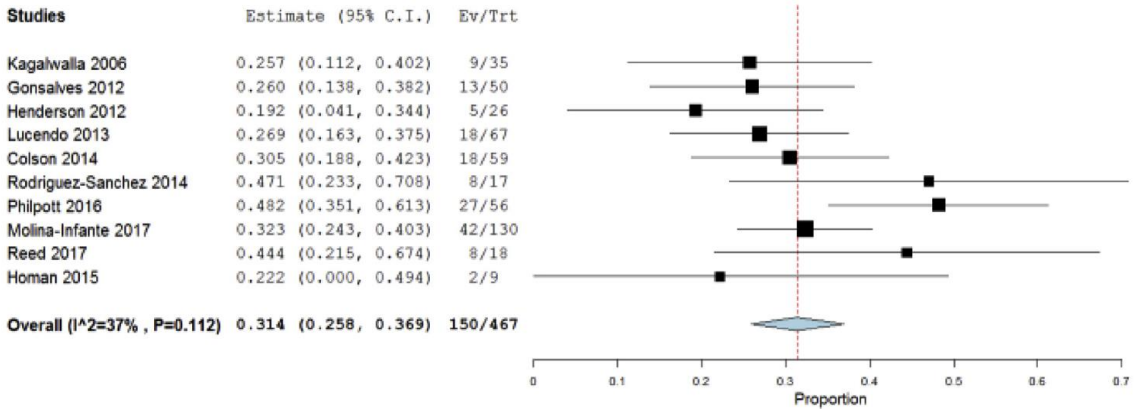
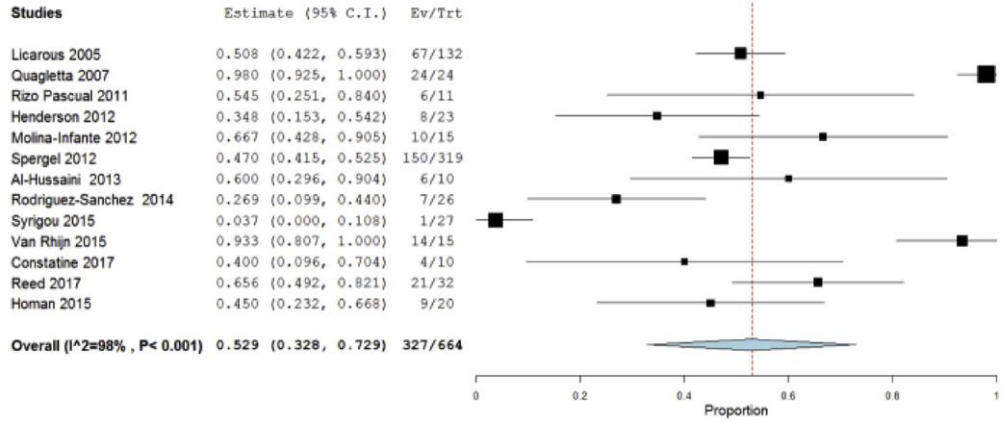
Dellon et al Am J Gastroenterol 2025;120:31–59.

# JTF Evidenece Profiles: Diet Therapy




Elemental diets compared to placebo for the management of EoE

| Outcomes and follow-up | No. of participants (studies)[56–61] | Certainty of the evidence (GRADE) | Relative effect, RR (95% CI) | Anticipated absolute effects: Risk with placebo | Anticipated absolute effects: Risk difference with elemental diets |
|---|---|---|---|---|---|
| Not achieving histologic remission (eos <15/hpf) follow-up: mean 8 wk | 431 (6 observational studies)[b,c,d] | ⊕⊕⊕◯ MODERATE[e] | 0.07 (0.05–0.12) | 880 per 1000 | 807 fewer per 1000 (824 fewer to 763 fewer) |

SFED compared to placebo for the management of EoE

| Outcomes | No. of participants (studies), follow-up[62–69] | Certainty of the evidence (GRADE) | Relative effect, RR (95% CI) | Anticipated absolute effects: Risk with placebo | Anticipated absolute effects: Risk difference with SFED |
|---|---|---|---|---|---|
| Failure to achieve histologic remission (proportion) assessed with: esophageal eosinophils <5/hpf follow-up: mean 6 wk | 633 (9 observational studies)[b,c,d,e,f,g,h,i,j] | ⊕⊕◯◯ LOW[k] | 0.38 (0.32–0.43) | 880 per 1000 | 550 fewer per 1000 (600 fewer to 500 fewer) |

Allergy-based elimination diets compared to placebo for management of EoE

| Outcomes and follow-up | No. of participants (studies)[57,64,66,68,69,74–81] | Certainty of the evidence (GRADE) | Relative effect, RR (95% CI) | Anticipated absolute effects: Risk with placebo | Anticipated absolute effects: Risk difference with allergy-based elimination diets |
|---|---|---|---|---|---|
| Not achieving histologic response assessed with: <15 eos/hpf, follow-up: 8 wk | 830 (11 observational studies)[b,c,d,e,f] | ⊕◯◯◯ VERY LOW[g] | 0.57 (0.33–0.73) | 880 per 1000[h] | 373 fewer per 1000 (581 fewer to 234 fewer) |

# Which Diet Choice is Best?

- Know your audience—easy in theory, difficult in execution, response not always rapid
- Elemental diets had highest reported “efficacy” of responders
  - Single arm, not directly compared, histologic response only, fewest studies
- 4 types of empiric diets considered (6,4,2,1 food elimination)
  - SFED had 10 studies, with 3,2, and 2 studies of the other types of elimination, foods not uniform
  - Don’t buy hype of 1FED being “similar”—it worked < 50%, and that’s just not OK (terrible study, TBH)
- Testing methods and foods tested in these studies were heterogeneous
- Widespread elimination has harm/risk and this is why recommendations are conditional
- Bottom line—if someone really wants this, and understands risks/benefits, it can work, but steroids and biologics have much stronger and controlled evidence

Rank MA et al. Gastroenterology. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
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# Why Is Diet Conditional, Low Certainty?

- All diet studies were single arm, observational studies
  - Relative effect sizes were calculated by using the control group from the steroid studies as a comparator, but may not reflect a similar comparator population that would receive diet
- Testing based diet had the most number of studies, but higher % rate failing to respond
- Adult and pediatric studies were pooled into one estimate as were different testing methods
- Overall, testing rated very low certainty of evidence, downgraded more than the other diets
- Certainty of evidence and strength of recommendation for any diet still lower than steroid
- QoL and other effects were not assessed

Rank MA et al. *Gastroenterology*. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
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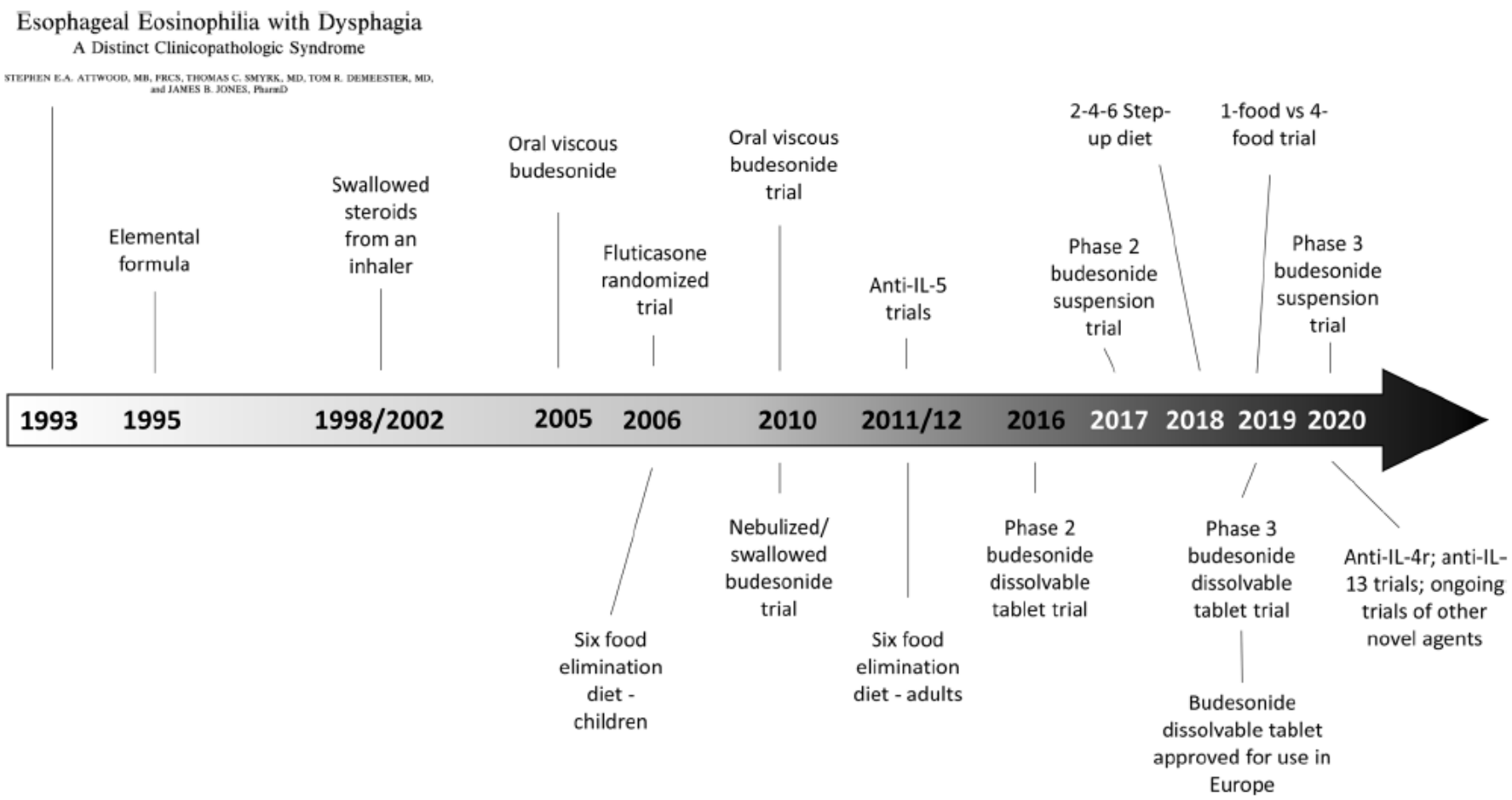
Dellon et al *Am J Gastroenterol 2025;120:31–59.*

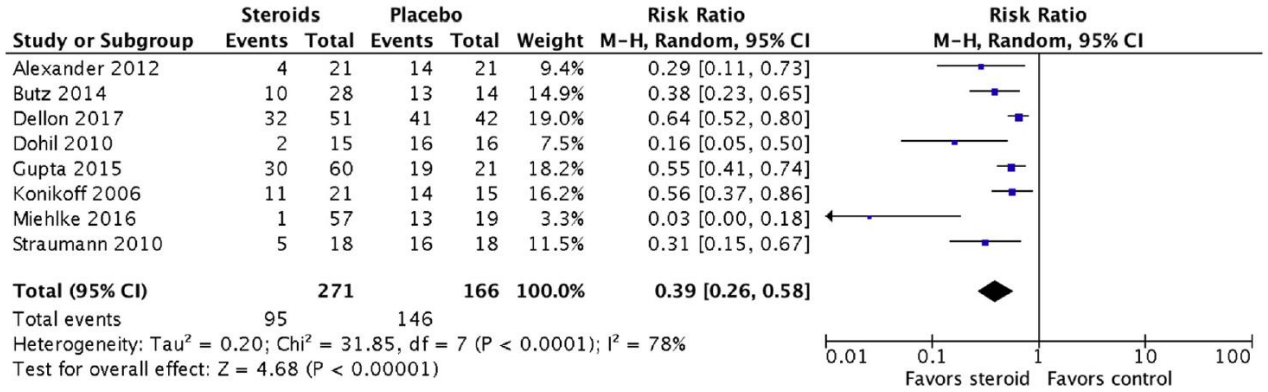
# Evolution of EoE Treatment Choices




Dellon ES. Digestive Diseases and Sciences 2020; 65: 3434-47

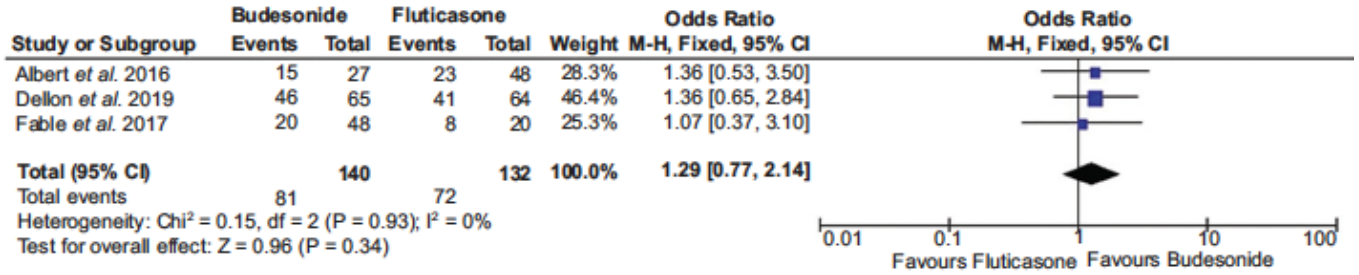
# JTF/AGA Topical/Swallowed Steroid Treatment

- **In patients with EoE, the AGA/JTF recommends topical glucocorticosteroids over no treatment *(Strong recommendation, moderate quality evidence)***
  - Topical swallowed steroids (HFA or liquid) are a first line therapy (RR 0.39, CI 0.26-0.58)
  - Studies mainly included PPI poorly responsive subjects
  - All studies had a direct placebo comparator, but didn't parse type of topical steroid as there was no agent effect
  - These are based on short term (~3mo) studies to a histologic endpoint of <15 Eos/HPF
  - No evidence of increased risk of adverse events
  - Recent updated meta-analysis of budesonide vs fluticasone reinforced no significant difference in steroid type




Systemic glucocorticosteroid compared to topical glucocorticosteroid for EoE

| Outcomes and follow-up | No. of participants (studies)[50] | Certainty of the evidence (GRADE) | Relative effect, RR (95% CI) | Anticipated absolute effects: Risk with topical steroid | Anticipated absolute effects: Risk difference with systemic steroid |
|---|---|---|---|---|---|
| Not achieving histologic remission (<15 eos/hpf); follow-up: mean 8 wk | 80 (1 RCT) | ⊕⊕⊕◯ MODERATE[b,c,d] | R0.79 (0.41–1.52) | 350 per 1000[e] | 73 fewer per 1000 (207 fewer to 182 more) |





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Numan Ann Gastroenterol 2023; 36 (5): 511-16

# Role of Swallowed Steroids

- This is the treatment with the highest certainty of evidence and confidence in that evidence
  - A strong recommendation implies this should be done and that there is minimal impact that shared decision making can do in influencing the decision
- No difference in formulation noted
- Efficacy primarily tested in patients unresponsive to PPI therapy with GERD excluded
- Highest strength/certainty, though still is a  preference-sensitive choice
- Therapy is still off-label technically but an approved formulation available in Europe
- If using budesonide, multiple suitable agents to thicken
  - Aim to make it into a thick slurry that has slower esophageal surface transit

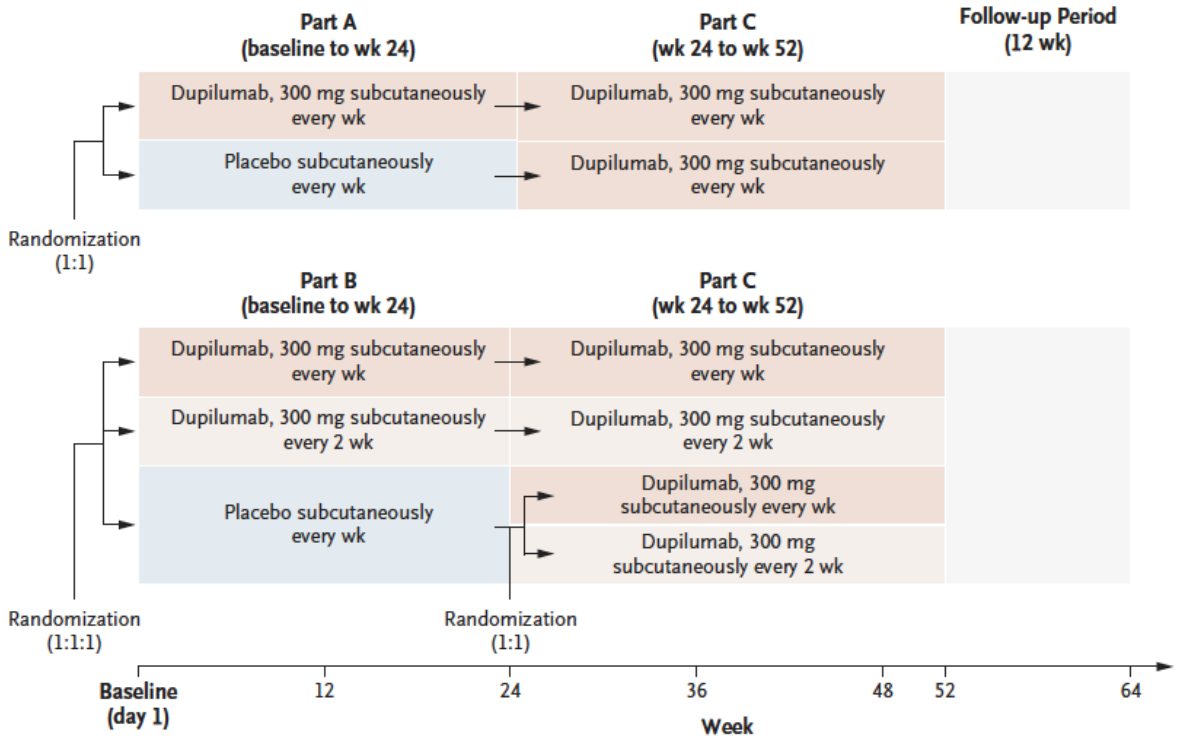
Rank MA et al. *Gastroenterology*. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
Hirano I et al.. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038
Numan Ann Gastroenterol 2023; 36 (5): 511-16

# JTF/AGA Biologics/Emerging Therapies Evidence (in 2020)

- Biologic therapies: **Anti-IgE**
  - Recommendation: In patients with EoE, AGA/JTFPP suggests against use of anti-IgE therapy (conditional recommendation; very low-quality evidence). In 2025 this remains unchanged.
- Biologic therapies: **Anti-IL-5**
  - Recommendation: In patients with EoE, AGA/JTFPP recommends using anti-IL-5 therapy only in context of a clinical trial (no recommendation; knowledge gap). In 2025 this remains unchanged.
- Miscellaneous therapies: **Montelukast, cromolyn, immunomodulator, anti-TNF**
  - Recommendation: In patients with EoE the AGA/JTFPP suggest using montelukast, cromolyn sodium, immunomodulators, and anti-TNF only in the context of a clinical trial (no recommendation; knowledge gap)
- Biologic therapies: **Anti-IL-13. THIS IS BEING UPDATED**
  - Recommendation: In patients with EoE, AGA/JTFPP recommends using anti-IL-13 or anti-IL-4 receptor alpha therapy only in context of a clinical trial (no recommendation; knowledge gap).

Hirano I, et al. *Gastroenterology*. 2020;158:1776-1786. Rank MA, et al. *Gastroenterology*. 2020;158:1789-1810.e15. Hirano I, et al. *Ann Allergy Asthma Immunol*. 2020;124:416-423. Rank MA, et al. *Ann Allergy Asthma Immunol*. 2020;124:424-440.e17.

# Dupilumab Adult Data



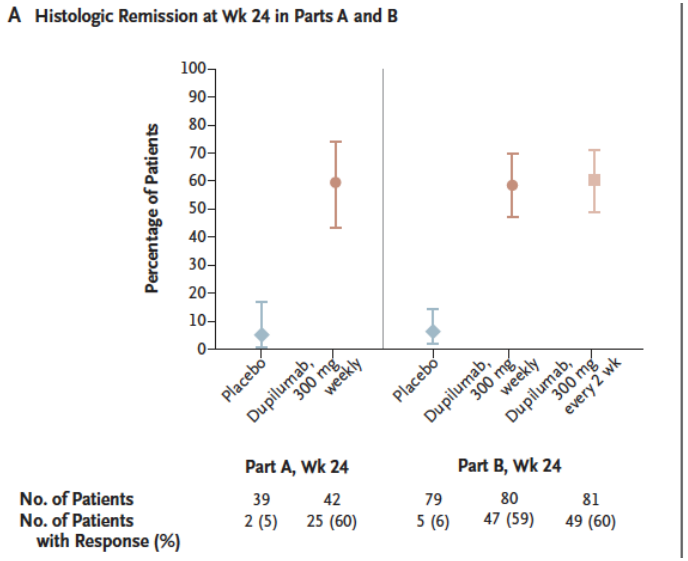

Histologic remission considered ≤6 eosinophils per high-power field

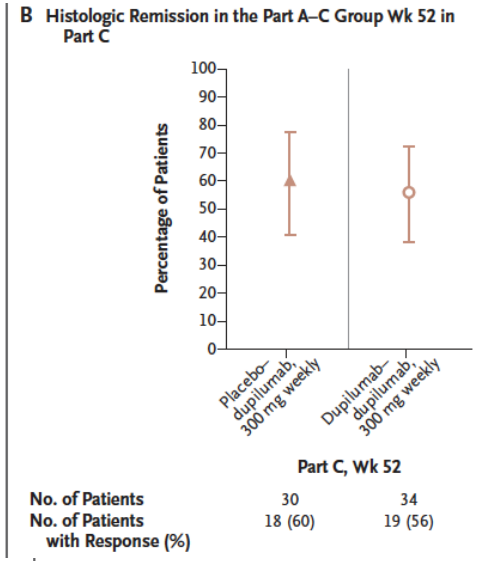
Higher DSQ score means worse symptoms

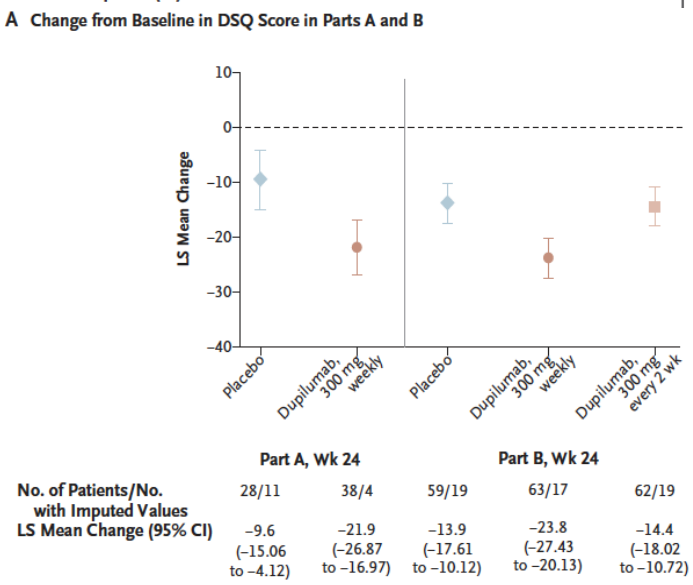
- 3 part trial—part A & B were independent trials, rolling over into part c long term follow up
- >12 years with documented EoE on biopsy despite 8 wks PPI, DSQ score ≥10
- 96 sites across Australia, Canada, Europe, and the US
- 1:1 randomization to weekly 300 mg dose vs placebo placebo (Part A) or 1:1:1 ratio to receive 300 mg either weekly or every 2 weeks vs weekly placebo (Part B) for 24 weeks.
- In part C, part A continued weekly doses, and part B continued their assigned dose, with placebo randomized 1:1 to weekly vs every 2 week dose
- Could continue PPI but not start PPI; could continue stable food elimination; could not start or continue steroids

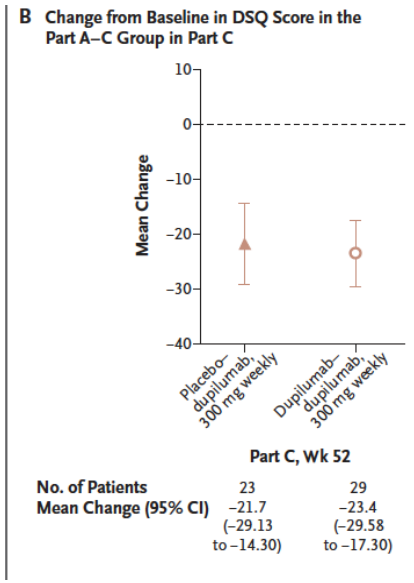
Dellon et al N Engl J Med. 2022 Dec 22;387(25):2317-2330.

# Results




## Histologic End Points

- Part A: 25/42 (60%) vs. 2/39 (5%) receiving placebo met histologic end point
- Part B: 47/80 (59%) on weekly vs 49/8 (60%) on every 2 weeks vs 5/79 (6%) on placebo met histologic end point

## Symptom End Points

- Part A: DSQ scores significantly improved with weekly dupilumab vs placebo by –12.32
- Part B: DSQ scores significantly improved with weekly dupilumab by –9.92 Part B (both P<0.001) but with dupilumab every 2 weeks only improved by –0.51 (NS)

## Demographics

- Mean EoE duration of 5-5.6yr, mean DSQ 33.6 36.7, mean Eos count 87.1-89.3, mean EREFS 6.3-7.2
- *Most had prior treatment*

Dellon et al N Engl J Med. 2022 Dec 22;387(25):2317-2330.

# Safety

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

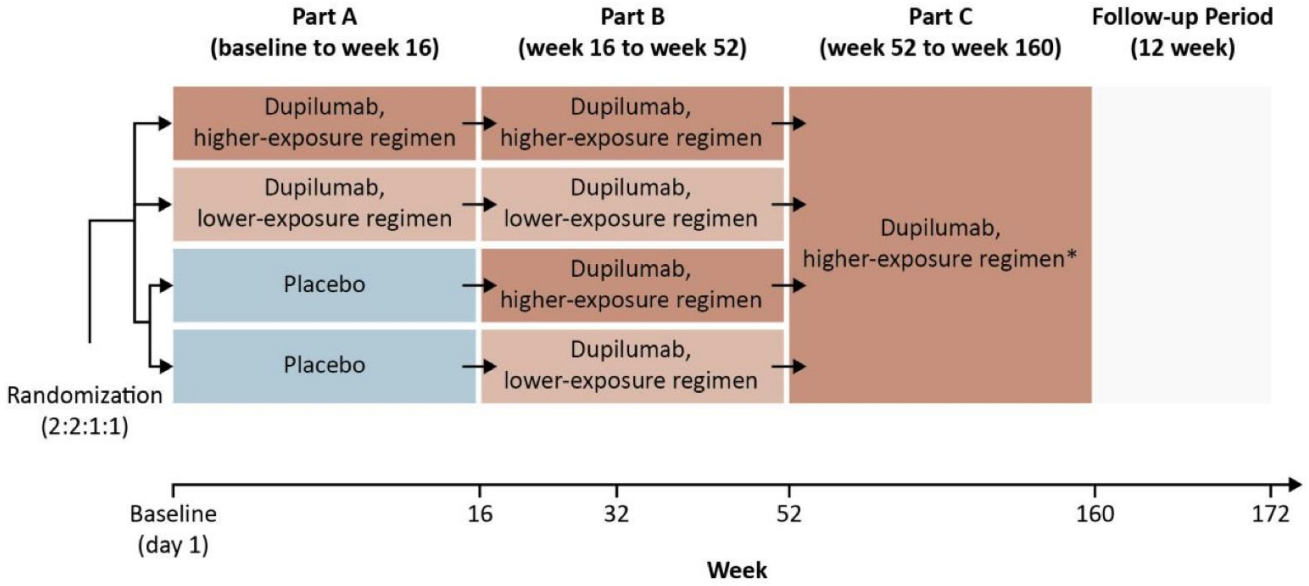
| Event | Part A | | Part B | | | Part A–C Group in Part C | |
|---|---|---|---|---|---|---|---|
| | Dupilumab, 300 mg weekly (N=42) | Placebo (N=39) | Dupilumab, 300 mg weekly (N=80) | Dupilumab, 300 mg every 2 wk (N=81) | Placebo (N=78) | Dupilumab–dupilumab (N=40) | Placebo–dupilumab (N=37) |
| | *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 |

- Serious adverse events occurred in 9 patients during the Part A or B treatment period (7q week,  1 q2 weeks, 1 placebo) and in 1 patient in part A–C group crossing over from part A placebo
- No fatalities
- Most frequently reported adverse event in the dupilumab groups was injection-site reaction
- Only 7 had adverse events leading to discontinuation

Dellon et al N Engl J Med. 2022;387(25):2317-2330

# Pediatric Data-Methods

- Part A is 16-week, randomized DBPC. If completed Part A, continued to Part B, 36-week extended active treatment phase, pt aware of active tx but not their regimen. Part C is ongoing 108-week OLE not being reported.
- 1 to 11y, active EoE with sx in past month, PPI refractory
- High dose (100mg q2, 200mg q2,300mg q2) vs low dose (200mg q4, 300mg q4, 200mg q2) weight based
- Endpoint was % with histologic remission at 16 w (<6/hpf).
- Patients received 100 mg every 2 weeks (q2w) if they weighed ≥5 kg to <15 kg, 200 mg q2w if they weighed ≥15 kg to <30 kg, and 300 mg q2w if they weighed ≥30 kg to <60 kg; respective weight-tiered dosing in the lower-exposure regimen group was 200 mg every 4 weeks (q4w), 300 mg q4w, and 200 mg q2w




| Study | Dupilumab Regimen | Patient Weight* | | | | | |
|---|---|---|---|---|---|---|---|
| | | ≥5 kg to <15 kg | ≥15 kg to <30 kg | ≥30 kg to <60 kg | ≥60 kg (Part B Only) | ≥30 kg to <40 kg | ≥40 kg |
| Part A and Part B | Higher-exposure regimen | 100 mg q2w | 200 mg q2w | 300 mg q2w | 300 mg qw | — | — |
| Part A and Part B | Lower-exposure regimen | 200 mg q4w | 300 mg q4w | 200 mg q2w | 300 mg q2w | — | — |
| Part C | Higher-exposure regimen | 200 mg q3w | 200 mg q2w | — | — | 300 mg q2w | 300 mg qw |

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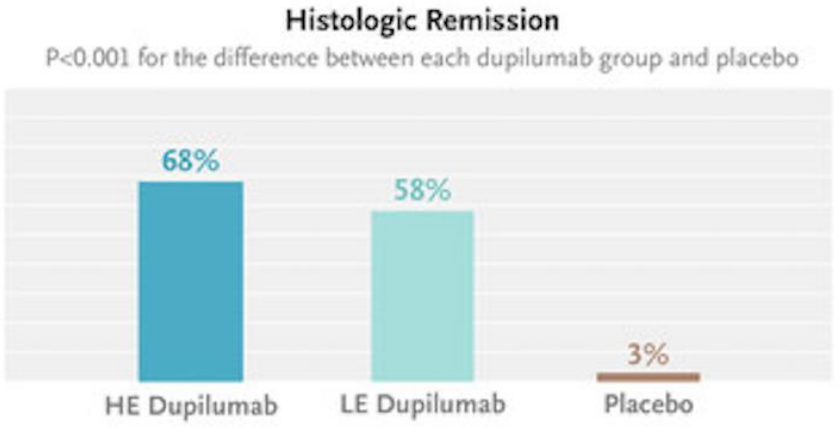
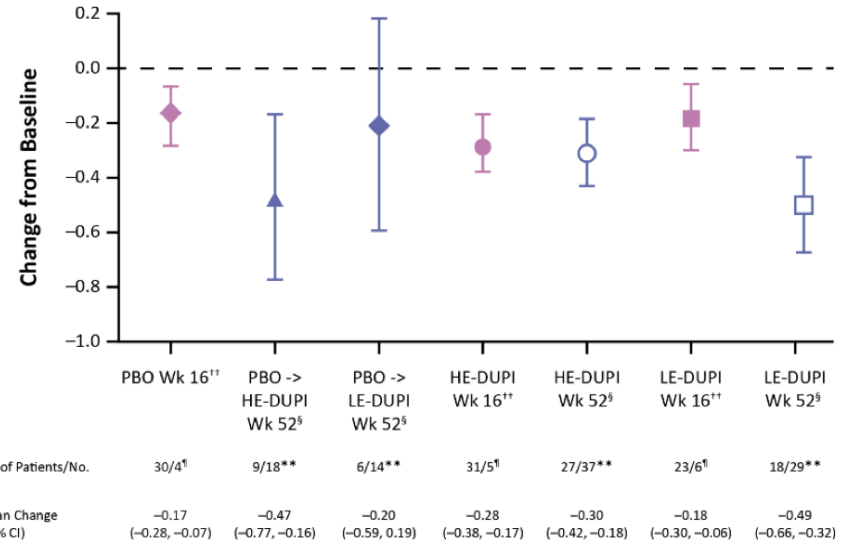
# Pediatric Part A Results

- Histologic remission in 25/37 high dose (68%), 18/31 patients (58%) low dose, 1/34 placebo patients (3%) (all P<0.001).
  - Only the high dose could be analyzed due to the hierarchical plan (one high-dose analysis was NS)
- High dose led to significant improvements in histologic, endoscopic, and transcriptomic measures as compared vs placebo.
  - Histologic, endoscopic, and transcriptomic measures between at week 52 were similar to the improvements at week 16 in Part A.
  - In Part A, the incidence of COVID, nausea, injection-site pain, and headache was at least 10% higher among all dose strengths vs placebo.
  - SAE's were reported in 3 patients who received dupilumab during Part A and in 6 patients overall during Part B.
- Days with caregiver assessed symptoms not able to be assessed due to the hierarchy being broken




**Change from Baseline in Proportion of Days with 1 or More EoE Signs/Symptoms at Week 16 in Part A and Week 52 in Part B**




Chehade et al N Engl J Med 2024 390;24

# Dupilumab Take Home Messages

1. Dupilumab found to have efficacy in treating EoE histology down to age 1 (no sx endpoint) and histology and symptoms in adults
2. It makes no sense that this is given q2wks in children and q1week in adults.
3. The label very clearly states this is a first line agent (e.g., not for EoE refractory to….), and we need to put aside obtuse arguments about “patient selection in trials” as a reason to make this 3rd tier
4. Safety established down to age 1
5. Long-term follow up in both age groups lacking but patients seem to really respond to this treatment, FWIW

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# Treatment Pipeline

| Currently under study: | Targets | Clinical trial notes | |
|---|---|---|---|
| Tezepelumab | TSLP | Phase 3 | NA |
| Solrikitug | TSLP | Phase 2 | NA |
| Barzolvolimab | KIT | Phase 2 | NA |
| CALY-002 | IL-15 | Phase 1a/b trial completed | NA |
| APT-1011 (fluticasone tablet) | Glucocorticoid receptors | Phase 3 | NA |
| Injectable fluticasone | Glucocorticoid receptors | Phase 2a | NA |
| Losartan | TGF-β | Phase 2a completed | NA |
| IRL201104 | | Phase 2a completed | NA |
| Etrasimod | S1P | Phase 2 completed | NA |
| Potassium competitive acid blockers | H+/K+ ATPase transporter | Phase 2 planned | NA |
| Zaimara | α-1-proteinase | Phase 2 | NA |
| Sucralfate | NA | Phase 1 completed | NA |

- Main issue with pipeline is that the symptom end-point (DSQ score) missed, not histologic endpoint
- Tezepelumab is deep into a phase 3 expected to complete with data in 20206-7
- Anti-IL-5 development has stopped for now but are intriguing post-hoc data suggesting effect
- Current budesonide ODT remains approved in Europe only
- Fluticasone ODT completed 24-week phase 3 study in 2024 (NCT 05634746)

Dickerson et al Ann Allergy Asthma Immunol135(2025)143−154

# Dosing for Medical Therapies

**Table 6. Medication dosing for initial treatment**

| 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) |
| Topical steroids | |
| Budesonide[a] | |
| Children | 1–2 mg/d (depending on age, height, and weight; can be divided twice daily) |
| Adults | 2–4 mg/d[b] (can be divided twice daily) |
| Fluticasone[c] | |
| Children | 110–880 μg/d (depending on age, height, weight) in a divided dose |
| Adults | 1760 μg/d in a divided dose |
| Dupilumab | |
| 15–<30 kg | 200 mg subcutaneously every other week |
| 30–<40 kg | 300 mg subcutaneously every other week |
| ≥40 kg | 300 mg subcutaneously every week |

Dellon et al Am J Gastroenterol 2025;120:31–59.

# Tailoring a Treatment Plan

- Many, though no superior option—all studies have flaws and real-world considerations
  - Many different therapies can result in remission, so this gives you options
- Age and lifestyle are chief considerations dictating choice
  - Elemental diets or more widespread elimination are more appropriate in particular ages
  - Swallowed steroids may be easier for certain populations than others
  - Testing for diet may not have any advantage over empiric elimination
  - Biologic therapy is indicated 1$^{st}$ line agent may have distinct advantages over a daily therapy
- Determine your patient/family goals and preferences first
  - Understand risks and benefits of each therapy, discuss this in a way that allows values to be clarified

Hirano I et al.. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

# Placeholder Slide(s) for EoE Network Meta-Analysis Data

- One to three additional slides anticipated, if possible, detailing data from the ongoing JTF food allergy parameter that is finalizing a network meta-analysis of EoE treatments
- If this is available for the conference I will present it
- If not, this slide will be deleted

# Tailoring Therapy: Evidence Hierarchy

**Table 1**
Summary of Effectiveness of EoE Therapies

| Therapy | Relative risk for histologic remission of EoE (95% CI) | Ability for normalization of histology | Practical considerations |
|---|---|---|---|
| Elemental diet | 0.07 (0.05-0.12) | 93% | Inconsistent coverage by insurance, poor adherence, multiple endoscopies |
| Six-food group elimination diet | 0.38 (0.32-0.43) | 62% | Poor adherence, multiple endoscopies |
| Topical corticosteroids | 0.39 (0.26-0.58) | 61% | Inconsistent coverage by insurance, candida |
| Four-food group elimination diet | 0.49 (0.42-0.57) | 51% | Poor adherence, multiple endoscopies |
| Single-food elimination diet | 0.52 (0.37-0.74) | 48% | Variable efficacy |
| Allergy testing elimination diet | 0.57 (0.33-0.73) | 43% | Multiple endoscopies |
| Two-food group elimination diet | 0.66 (0.57-0.77) | 34% | Variable efficacy |
| PPI | 0.66 (0.61-0.72) | 34% | Variable efficacy |
| Cromolyn | 0.89 (0.71-1.12) | 21% | Lack of efficacy |
| Anti-IL5 | 0.92 (0.84-1.00) | 8% | Lack of efficacy |
| Anti-IL13 | 0.94 (0.67-1.30) | 6% | Lack of efficacy |
| Esophageal dilation, montelukast | No data | — | Lack of efficacy on histology |

Abbreviations: CI, confidence interval; EoE, eosinophilic esophagitis; PPI, proton pump inhibitor; RR, relative risk.

- Steroid data are the only truly randomized, controlled data—diet data were approximated vs. historical control
- Diet efficacy ranges from very high to moderate, depending on choice
- Elemental diets are a very mixed bag, rife with many considerations regarding adherence and QoL
- Diet was not homogeneous among any of the trials—definitions varied considerably in what was avoided

Spergel J, Aceeves S, Greenhawt M. Ann Allergy Asthma Immunol 2020; 124: 411-41
Rank MA et al. *Gastroenterology*. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039
Hirano I et al.. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

# Considerations for Trade-offs in Treating EoE

Example Tradeoff Matrix in Considering EoE Therapies in a Shared Decision-Making Paradigm

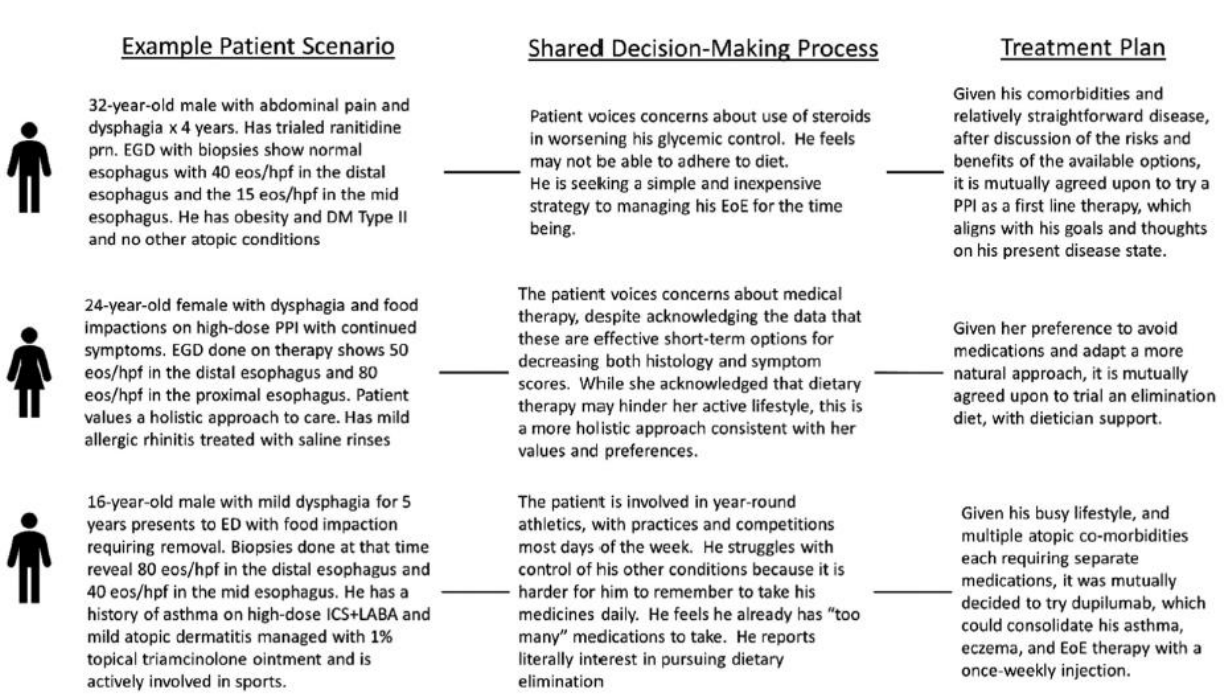
| Outcome | Swallowed topical steroids | PPI | Dietary therapy | Dupilumab |
|---|---|---|---|---|
| **Efficacy** | High. Strong recommendation with moderate certainty evidence from a recent meta-analysis. Backed by multiple placebo-controlled studies, No difference by agent used (liquid or inhaler) | Potentially inconsistent. Overall works for less than 50% of patients in most series. Conditional recommendation with very low-quality evidence from recent meta-analysis. | Considered high, and highest for elemental diet vs empirical elimination or tailored elimination. Conditional recommendations with moderate to very low-quality evidence from recent meta-analysis. | High. Effective in treating both esophageal inflammation (histology) endoscopy, and symptoms using objective measures. No GRADE rating is available yet. |
| **Adverse effects** | In isolation, at the doses and routes used in EoE, this is the least bioavailable form, and these are considered low doses that are safe in asthma. AGA-JTF analysis noted no increased risk of adverse effects. As a general class, there are concerns for thrush, adrenal suppression, and growth effects. Many of these are quite limited when used as a swallowed therapy | Concerns for renal and other adverse effects with long-term use though on the basis of lower quality observational data, which were not confirmed in a large RCT, though there may be a slight increased risk of enteric infections with prolonged use. | Nutritional deficiencies. Anxiety, poor quality of life. Frustration. | Conjunctivitis is a major concern with use in other disease states (although not reported yet in EoE). Very low risk of anaphylaxis. Injection site reactions occur. Cytokine block is broad and may have unintended effects that could be both beneficial (eg, will treat other allergic disease) and detrimental (unclear long-term safety). |
| **Monitoring** | Need for periodic endoscopy to monitor response. For persons on other long-term steroid use, may need to monitor cortisol levels to check for adrenal suppression | Need for periodic endoscopy to monitor response. No evidence supporting serologic monitoring for adverse events. | High need to monitor for overall nutritional and growth status with any dietary elimination. Need for frequent endoscopy to monitor response to stop therapy and reintroduce food. Some centers will do in-office reintroduction if there is a concern for IgE-mediated symptom emergence after elimination. | Need for periodic endoscopy to monitor response. |
| **Lifestyle** | Must be taken daily or twice daily. Some potential for inconvenience. Must be mixed which can decrease adherence | Must be taken daily or twice daily. Some potential for inconvenience. | Potential to affect the patient and family at every meal. Can be quite disruptive to some families. Prolonged avoidance is associated with poor QoL in IgE-mediated food allergy. | Must be injected on a weekly basis. Potential for inconvenience or dislike of injection. Can be done at home. |
| **Price** | Varies on the basis of coverage. There are generic fluticasone and budesonide forms available, but these can be expensive for some plans. Branded forms are expensive. Newer oral agents not yet available in the United States may be expensive when these are available | Over-the-counter availability for many agents. Generally, less expensive though some prescription forms may still be very expensive. | Can be expensive to buy replacement foods or special formula. | Extremely expensive. Coverage variable and being defined. |

Abbreviations: AGA, American Gastroenterological Association; EoE, eosinophilic esophagitis; GRADE, Grading of Recommendations, Assessment, Development, and Evaluations; IgE, immunoglobulin E; JTF, the Joint Task Force on Allergy–Immunology Practice Parameters; PPI, proton pump inhibitor; QoL, quality of life.

NOTE. This table is meant to serve as an example of considerations for discussion with patients and families in a shared decision-making discussion. It is not a formal decision-support tool or is intended to have comprehensive detail on each consideration. The clinician engaging in shared decision-making should research the primary eosinophilic esophagitis treatment literature to help frame the discussion according to their own interpretations of these data.

Aceeves et al Ann Allergy Asthma Immunol 130 (2023) 371−378

# Engaging Shared Decision-Making In EoE




| Treatment | |
|---|---|
| *PPIs* | |
| We advise "high-dose" PPI use for EoE treatment | |
| We advise providers to counsel patients as to the rationale for PPI use in EoE | Patients without heartburn or reflux symptoms could be confused as to why a PPI is prescribed without this explanation |
| *Topical steroids* | |
| We advise that induction with swallowed topical steroids with budesonide and fluticasone improve symptoms, histology, and endoscopic disease activity in adolescents and adults with EoE | Options for swallowed topical steroids include the EMA-approved budesonide orodispersible tablet and FDA-approved budesonide oral suspension as well as off-label use of asthma preparations adapted for esophageal delivery |
| We advise administration of topical steroids after meals or before bedtime with nothing to eat or drink after 30–60 minutes to help maximize medication dwell time in the esophagus | If patients drink or eat right after medication administration, the medication will be cleared from the esophagus and will be less effective |
| In young children, providers should consider use of a slurry or suspension, rather than an inhaler device | Inhaler devices can be difficult for young children to use correctly |
| *Diet elimination* | |
| Providers may consider starting with a less-restrictive empiric elimination (i.e., 1FED or 2FED) as the initial diet therapy choice | Patient preference for diet selection should be incorporated in a shared decision-making process |
| We advise providers to collaborate with a dietician or nutritionist for patients undergoing dietary elimination | Dieticians can help with education, label reading and contaminant avoidance, food substitutions, meal planning, and other activities to help maximize success and adherence |
| After an initial response to dietary elimination, we advise a structured food reintroduction process | A food reintroduction process is needed to identify food triggers |
| Symptoms should not be used in isolation to determine food triggers | Endoscopy with biopsy is required after each food is reintroduced to assess whether eosinophilia has recured |

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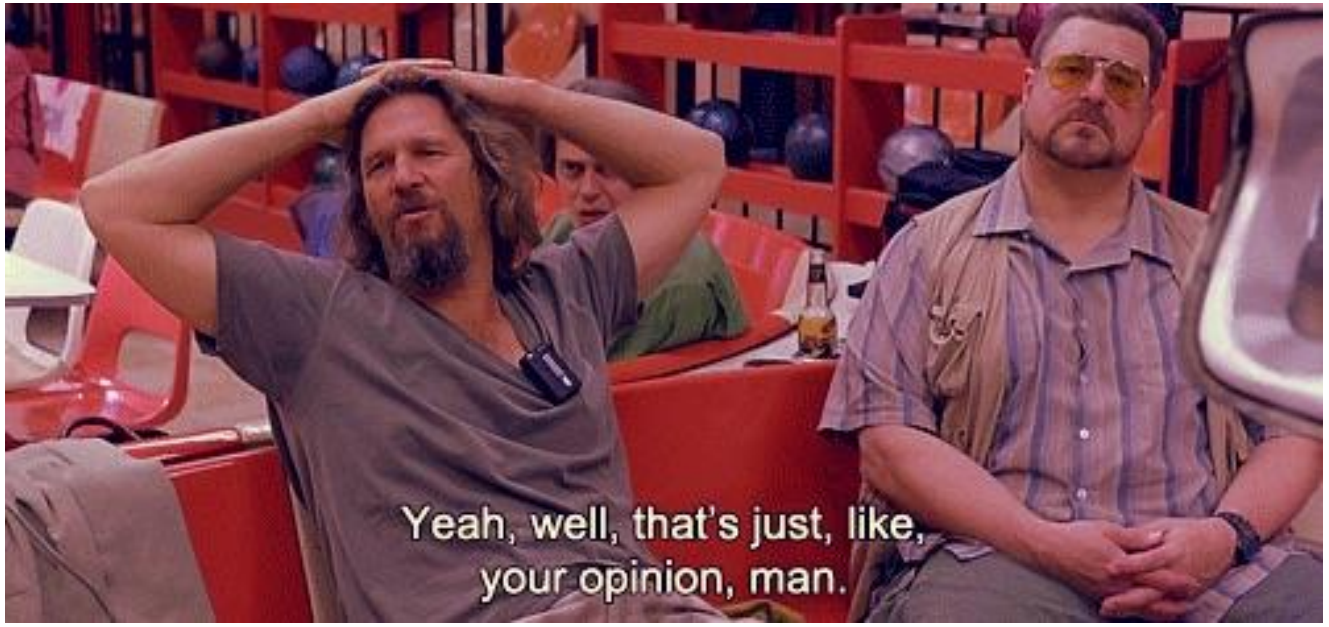
# Any Questions?





So you have no frame of reference here, Donny. You're like a child who wanders into the middle of a movie and wants to know...