Use of GLP-1s should be considered in asthmatics with comorbid obesity

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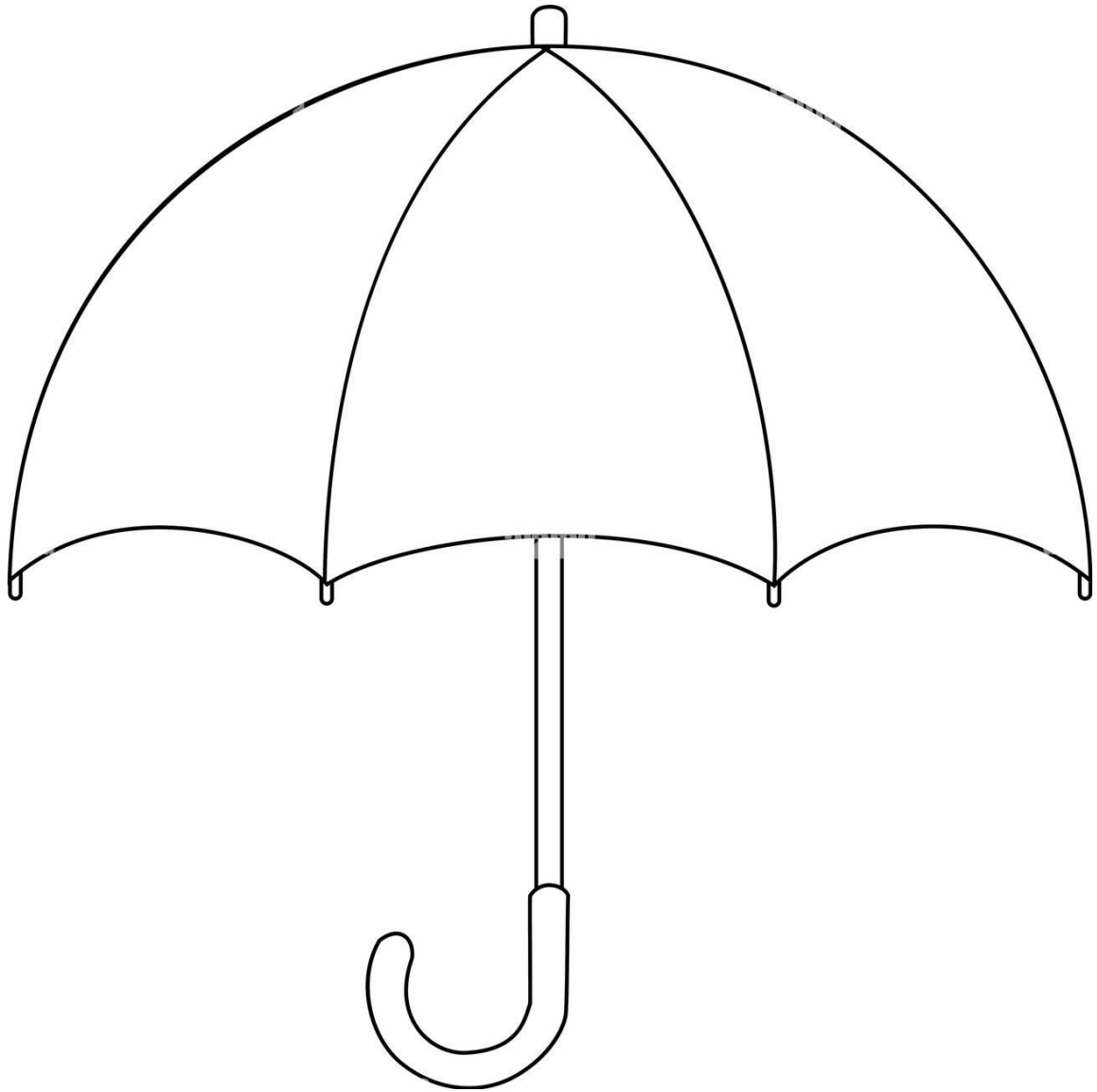
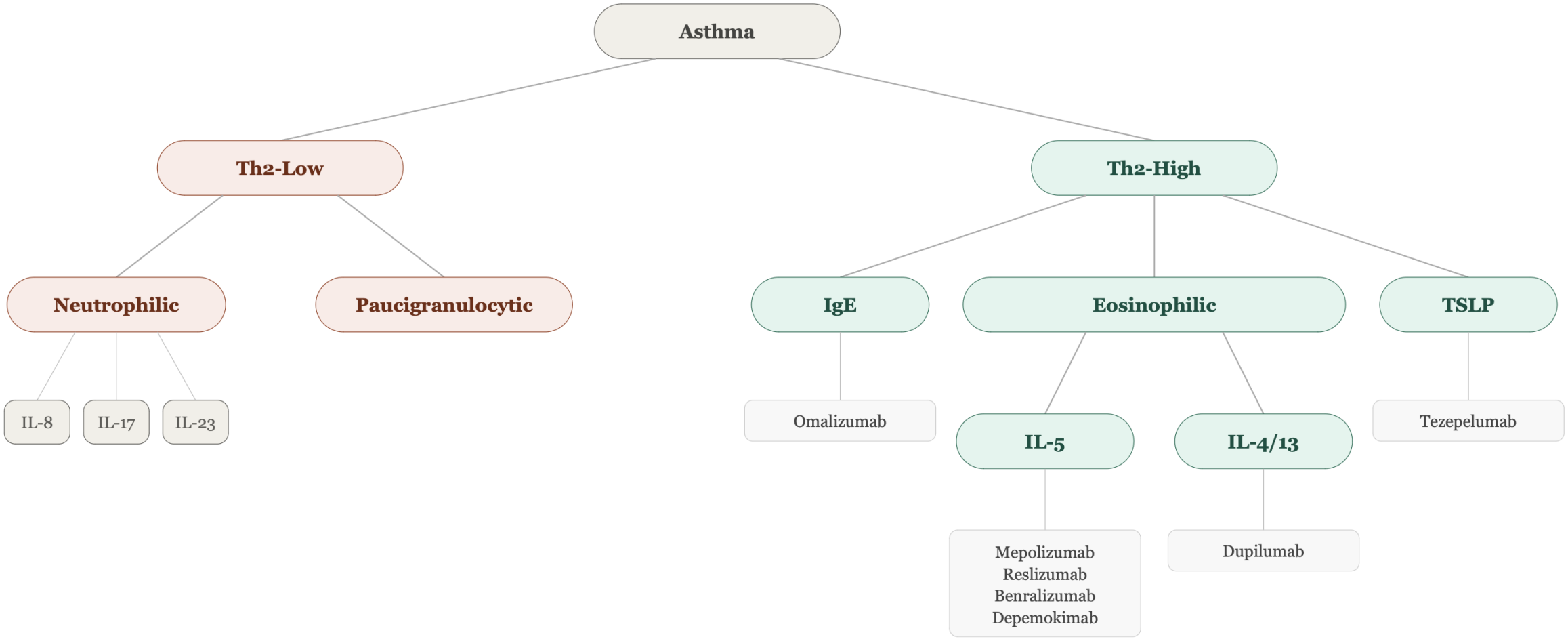
Outline

1. Asthma is not one disease
2. In the right patient, GLP-1s can be a tool
3. GLP-1s are:
   - ✓Mechanistically sound
   - ✓Clinically promising
   - ✓Cost effective

Asthma: one diagnosis, multiple phenotypes



There are multiple biologic targets for T2 high asthma



Tezepelumab has the greatest reduction in asthma exacerbations in patients with an AEC >300

GRADE recommendation			
High certainty	Definitely more beneficial than standard care	Definitely more harmful than standard care	Definitely no different than standard care
Moderate certainty	Probably more beneficial than standard care	Probably more harmful than standard care	Probably no different than standard care
Low certainty	May be more beneficial than standard care	May be more harmful than standard care	May be no different than standard care
Very low certainty	We are very uncertain	We are very uncertain	We are very uncertain

Drug	Asthma exacerbations		ACQ		FEV1 (L)		Hospital admissions	Corticosteroid sparing	Adverse events leading to discont.
Eosinophils	*≥ 300*	*< 300*	*≥ 300*	*< 300*	*≥ 300*	*< 300*	NA	NA	NA
Baseline risk	*470 per 1000*		*NA*		*NA*		*137 per 1000*	*560 per 1000*	*19 per 1000*
MCID/MID	*20%*		*-0.5*		*0.1 L*		*5%*	*20%*	*10%*
Tezepelumab	-329 (-366.6 to -272.6)	-173.9 (-277.3 to -23.5)‡	-0.4 (-0.61 to -0.19)‡	-0.23 (-0.36 to -0.09)	0.24 (0.16 to 0.32)	0.1 (0 to 0.19)¶	-110.97 (-120.56 to -94.53)‡	33.6 (-72.8 to 168)¶	-6.08 (-12.54 to 6.65)
Dupilumab	-319.6 (-357.2 to -272.6)	-112.8 (-225.6 to 51.7)‡	-0.73 (-0.98 to -0.48)‡	-0.2 (-0.42 to 0.02)	0.25 (0.21 to 0.29)	0.1 (0 to 0.2)¶	-97.27 (-124.67 to -4.11)‡	274.4 (123.2 to 464.8)¶	0.57 (-10.26 to 24.7)
Mepolizumab	-211.5 (-258.5 to -155.1)‡		-0.33 (-0.51 to -0.15)‡	0.49 (0.01 to 0.97)‡	0.1 (0.04 to 0.15)‡			341.6 (39.2 to 789.6)‡	-6.65 (-12.16 to 3.04)
Reslizumab	-230.3 (-282 to -164.5)‡	371.3 (-188 to 2002.2)¶††	-0.28 (-0.44 to -0.11)	0.12 (-0.09 to 0.33)	0.19 (0.12 to 0.25)	0.09 (-0.04 to 0.22)¶		128.8 (-84 to 436.8)¶	-6.65 (-11.21 to 0.38)
Benralizumab	-230.3 (-277.3 to -173.9)‡	-145.7 (-263.2 to 37.6)‡	-0.3 (-0.44 to -0.16)	-0.23 (-0.41 to -0.06)	0.14 (0.11 to 0.18)‡	0.04 (-0.05 to 0.13)‡	-17.81 (-41.1 to 10.96)	431.2 (162.4 to 800.8)‡	12.35 (-3.99 to 46.55)
Omalizumab	-225.6 (-296.1 to -131.6)‡	-9.4 (-192.7 to 296.1)¶	-0.25 (-0.5 to 0.01)‡*		0.09 (0.02 to 0.16)‡*		-84.94 (-105.49 to -47.95)‡	179.2 (84 to 285.6)‡	3.8 (-3.8 to 15.39)‡

Pitre T, Jassal T, Angjeli A, Jarabana V, Nannapaneni S, Umair A, Hussain M, Leung G, Kirsh S, Su J, Desai K, Coyne J, Mohan S, Zeraatkar D. A comparison of the effectiveness of biologic therapies for asthma: A systematic review and network meta-analysis. Ann Allergy Asthma Immunol. 2023 May;130(5):595-606. doi: 10.1016/j.anai.2022.12.018. Epub 2022 Dec 20. PMID: 36563746.

Should GLP-1s be **considered** in the treatment of asthma with comorbid obesity?

Should GLP-1s be **considered** in the treatment of asthma with comorbid obesity?

Yes, in the appropriate patient, they should be considered.

As allergists, it’s our job to treat the patient in front of us.

GLP-1s are a tool that can be used for patients who are not benefiting from our available therapies.

Case 1: T2 Low + Obesity

52 yo female with severe uncontrolled asthma. Her BMI is 38. She's on maximum dose ICS-LABA (budesonide-formoterol), LAMA (tiotropium), and azithromycin TIW. She has no history of atopy.

FEV1: 58%

FeNO: 12

AEC: 135

IgE: 45

Required oral steroids x4 this year, without much benefit

Case 2: T2 High + Obesity

44 yo female with severe uncontrolled asthma, GERD, OSA. BMI is 35.

FEV1: 64%

FeNO: 58

AEC: 580

IgE: 280

On Dupixent but continues to have 2-3 exacerbations per year

Case 3: Asthma as a weight related co-morbidity

38 yo male with history of moderate persistent asthma and OSA. He is on Symbicort 80-4.5 mcg 2 puffs BID, and PRN up to 12 puffs (SMART). BMI is 29.

FEV1: 78%

FeNO: 18

AEC: 135

IgE: 35

AHI: 22

Required short course of oral steroids x1 this year

The right patient for a GLP-1

T2 low + obesity

GLP-1s may be the primary disease-modifying option

T2 high + obesity

GLP-1s may be an adjunctive therapy to a biologic

Asthma as a weight-related comorbidity

Adults with BMI >=27, pediatric patients with BMI >95th percentile

GLP-1s are mechanistically sound

1) **Mechanical:** improved FRC, GERD, and OSA

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2) **Metabolic:**
   - Decreased systemic inflammation (IL-6, TNF-alpha)[1]
   - Decreased leptin (Leptin, in particular, promotes neutrophilic airway inflammation and suppresses regulatory T-cell function)[1]
   - Less insulin resistance (less airway smooth muscle hypertrophy and hyper-responsiveness)[2]

1. Ren Y *et al.* GLP-1 receptor agonists and inflammatory markers in type 2 diabetes: systematic review/meta-analysis. *Diabetes Obes Metab.* 2025;27(7):3607–3626.
2. Wu TD. Diabetes, insulin resistance, and asthma: potential links. *Curr Opin Pulm Med.* 2021;27(1):29–36.

GLP-1s are mechanistically sound

1) Mechanical: improved FRC, GERD, and OSA
2) Metabolic:
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   - Less insulin resistance (less airway smooth muscle hypertrophy and hyper-responsiveness)[2]
3) **Airway:** direct GLP-1R effects via receptors on bronchial smooth muscle (reduced bronchial hyper-responsiveness)[3]

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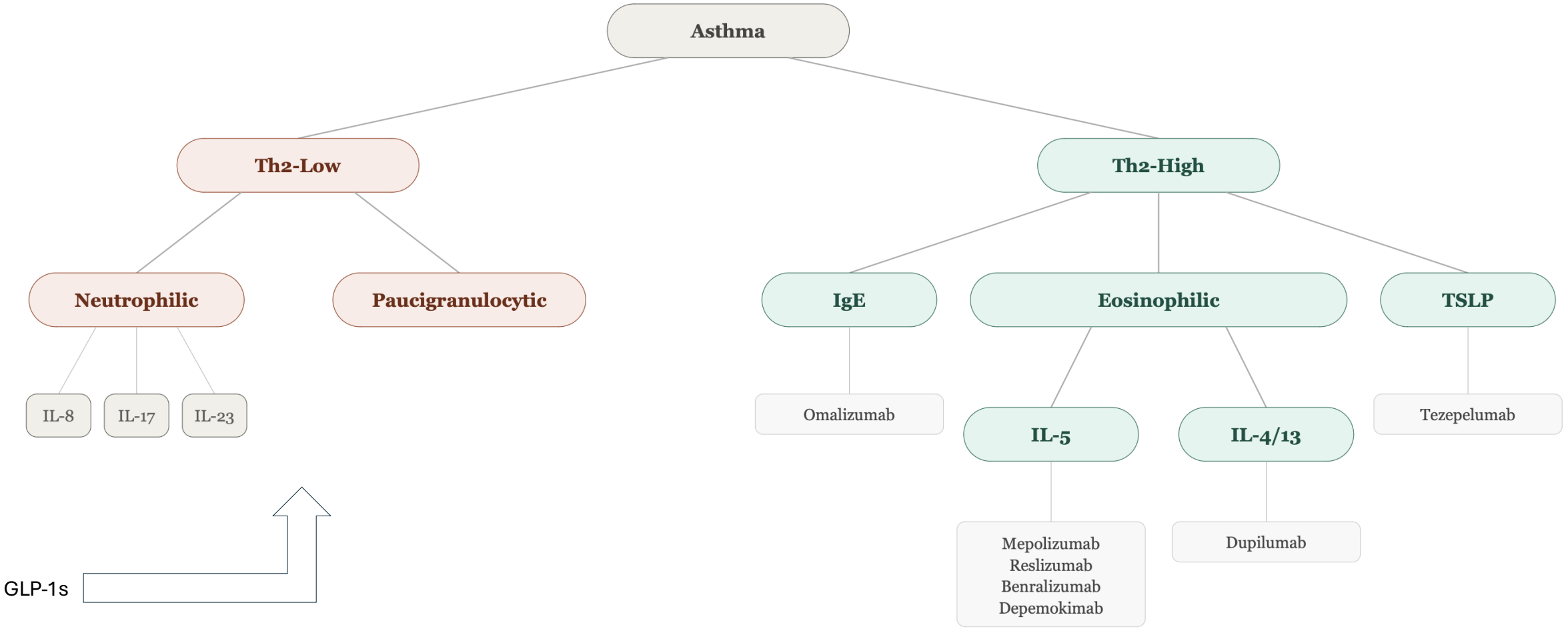
2. Wu TD. Diabetes, insulin resistance, and asthma: potential links. *Curr Opin Pulm Med.* 2021;27(1):29–36.
3. Rogliani P *et al.* GLP-1 receptor as a target for bronchial hyperresponsiveness. *Am J Respir Cell Mol Biol.*2016;55(6):804–814.

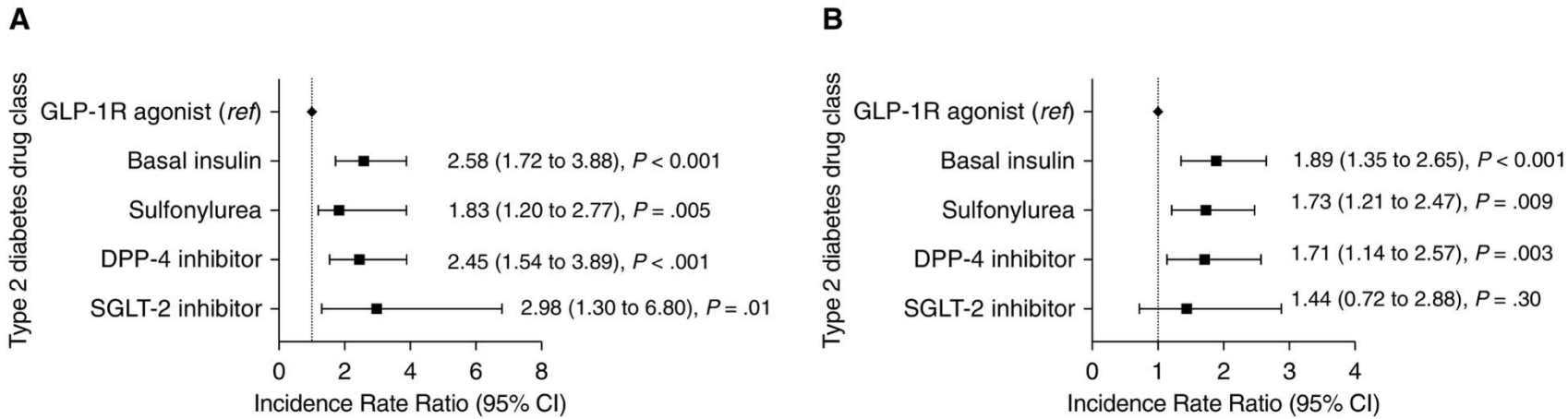

Asthma
Th2-Low
Th2-High
Neutrophilic
Paucigranulocytic
IgE
Eosinophilic
TSLP
IL-8
IL-17
IL-23
Omalizumab
IL-5
IL-4/13
Tezepelumab
Mepolizumab
Reslizumab
Benralizumab
Depemokimab
Dupilumab
GLP-1s

GLP-1s are clinically promising

In a study of 448 patients with T2DM and asthma, those initiating GLP-1 receptor agonists had significantly lower asthma exacerbations at 6 months compared to those starting other diabetes medications.

The **risk reduction** was significant.

2-3 fold lower rates compared to: SGLT-2 inhibitors (IRR 2.98, 95% CI 1.30-6.80), DPP-4 inhibitors (IRR 2.45, 95% CI 1.54-3.89), sulfonylureas (IRR 1.83, 95% CI 1.20-2.77), and basal insulin (IRR 2.58, 95% CI 1.72-3.88)



Foer D *et al.* Asthma exacerbations in T2D patients on GLP-1 receptor agonists. *Am J Respir Crit Care Med.*2021;203(7):831–840

GLP-1s are clinically promising

In a study published in JAMA of 4278 patients in a self-controlled case series and 8424 patients in a propensity-weighted cohort, found that metformin resulted in fewer asthma attacks and GLP-1 receptor agonists provided **additive** benefit (IRR 0.60, 95% CI 0.49-0.73).[4]

This was independent of glycemic control or weight loss and **occurred across asthma phenotypes,** including those with and without blood eosinophilia and across all levels of asthma severity

4. Lee B, Man KKC, Wong E, Tan T, Sheikh A, Bloom CI. Antidiabetic Medication and Asthma Attacks. *JAMA Intern Med.* 2025;185(1):16–25. doi:10.1001/jamainternmed.2024.5982

GLP-1s are cost effective

Total annual cost of asthma in the US equaled **$89.1 billion** in 2013[5]

Hospital admission for asthma: $17,756[6]

ICU admission for asthma: $20,000-28,000[6]

Total annual cost of obesity in the US equaled **$261-481** billion in 2016 in the US[7]

GLP-1: $15,000-16,000/year

5. Kang HR *et al.* Trends in asthma hospitalization, costs, and mortality after biologics (US). *J Manag Care Spec Pharm.*2023;29(7):721–731.
6. Zghebi SS *et al.* Trends in asthma hospitalizations and outcomes in the US. *PLoS One.* 2022;17(12):e0276731.
7. GBD 2021 US Obesity Collaborators. Overweight/obesity prevalence and forecasts in the US, 1990–2050. *Lancet.*2024;404:2278–2298.

Conclusion

1. Asthma is a disease with multiple phenotypes.
2. In the right patient, GLP-1s can be a tool.
   - ➢T2 low asthma + obesity
   - ➢T2 high asthma + obesity
   - ➢Asthma as a weight-related co-morbidity
3. GLP-1s are:
   - ✓Mechanistically sound
   - ✓Clinically promising
   - ✓Cost effective

AAAAI Podcast: Conversations from the World of Allergy

The Potential Role for GLP-1 Agonists in Asthma Treatment

March 03, 2026 •

The American Academy of Allergy, Asthma & Immunology (AAAAI)

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Show Notes Transcript

GLP-1 agonists have been blockbuster medications in diabetes and obesity but they may also have a surprising role in the treatment of asthma. Join the conversation as Katherine Cahill, MD, FAAAAI, discusses how GLP-1 agonists may improve asthma control and reduce airway inflammation.

Rebuttal

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Adverse effects can be safely managed

- Common side effects with GLP-1s:
  - GI side effects (nausea, vomiting, diarrhea)
  - Pancreatitis and gallbladder disease → real but rare, 0.2%
  - Gastroparesis → manageable risk with dose titration and frequent small meals
  - Thyroid cancer in mice → no association seen in humans
  - Aspiration risk under anesthesia → safely managed by current pre-operative preparation, which includes holding for up to 1 week prior to surgery
- Partner with PCPs to prescribe and monitor for safety
- As allergists, we are adept at working with a multidisciplinary team (i.e. Dermatology, ENT)

No end point for treatment…like most of the conditions we treat

Weight gain after discontinuation has been noted.

However, asthma is also a chronic disease. As allergists, we are used to managing chronic conditions and safely follow many patients on biologics for years.

Access to GLP-1s is improving

- Generic liraglutide received tentative FDA approval in 2024
- Oral semaglutide approved in December 2025
- Increased indications mean better coverage for patients who already qualify or could benefit from a medication
- Limitations are system issues, not a reason to limit care

Is it really the GLP-1, or is it the weight loss? It's both!

- GLP-1s are superior to other weight loss medications → 2-4x the weight loss of other therapies[8] → improved **mechanical obstruction**
- They also act on the **metabolic** (systemic inflammation, leptin pathway, insulin resistance) and **airway** (bronchial smooth muscle) axes

8. Yanovski SZ *et al.* Approach to obesity treatment in primary care: a review. *JAMA Intern Med.* 2024;184(7):818–829.

But there aren’t enough RCTs…

Let’s run some! But in the meantime, let’s not withhold a medication that is safe and many of our patients are eligible for.

Questions or thoughts?

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