Mass General Brigham

Obesity, Type 2 Diabetes, and Asthma

Severe Asthma CME Course March 2026

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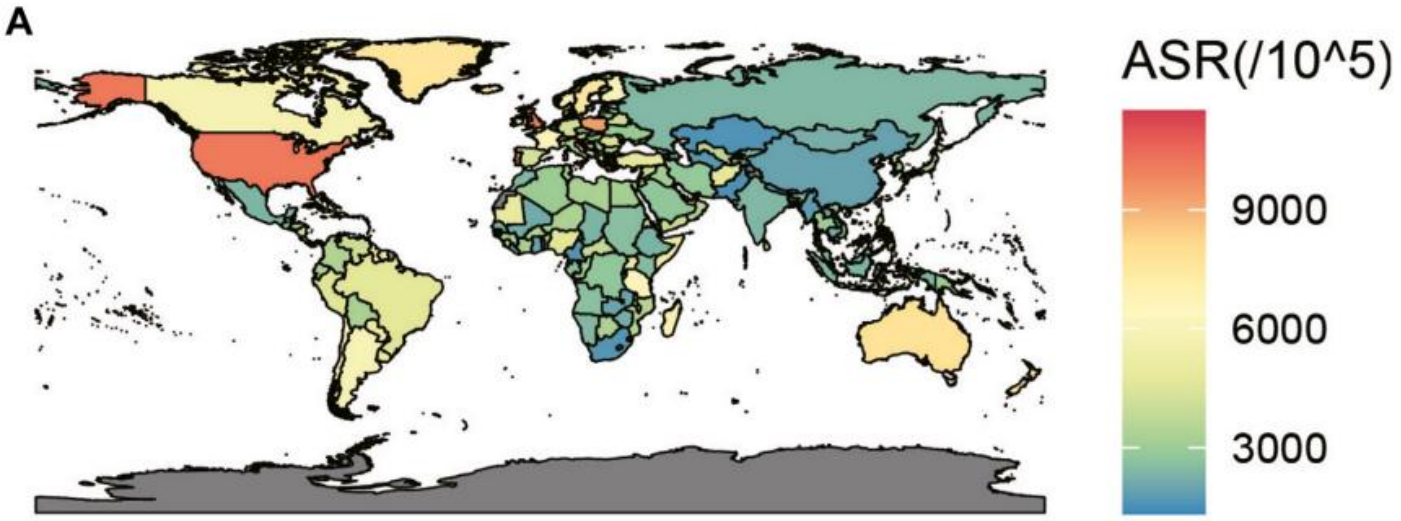
RELEVANT DISCLOSURES

- Eli Lilly & Co.: Advisory boards; site PI NCT07219173

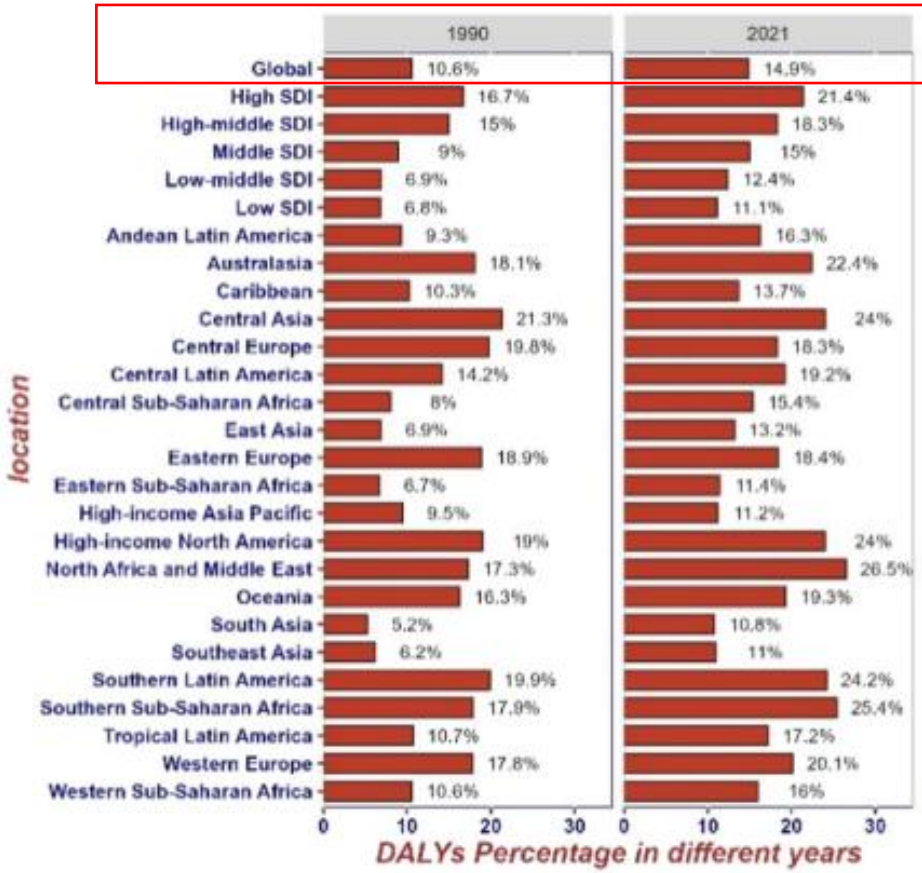
BMI as a leading global risk factor for asthma morbidity.

Age standardized prevalence rates of asthma (2021)



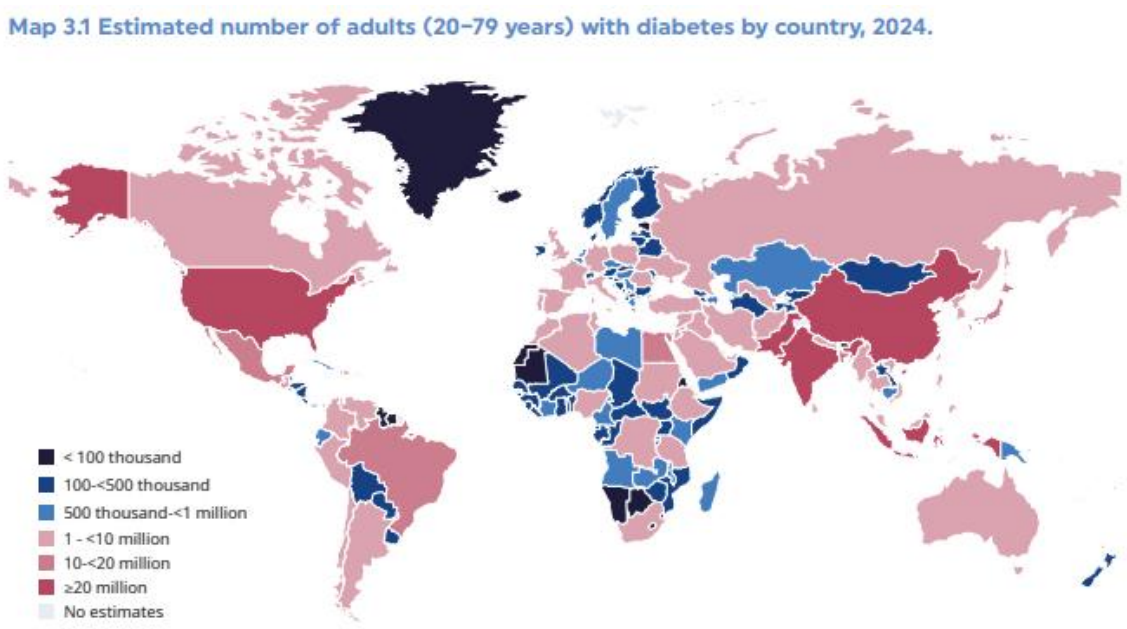
Yuan, *Lancet*, 2025
ASR=age-standardized prevalence rates [of asthma];

Proportion of asthma DALYs caused by high BMI by region (1990, 2021)



DALY=disability-adjusted life years

Global risk of obesity, type 2 diabetes heightens implications for asthma.



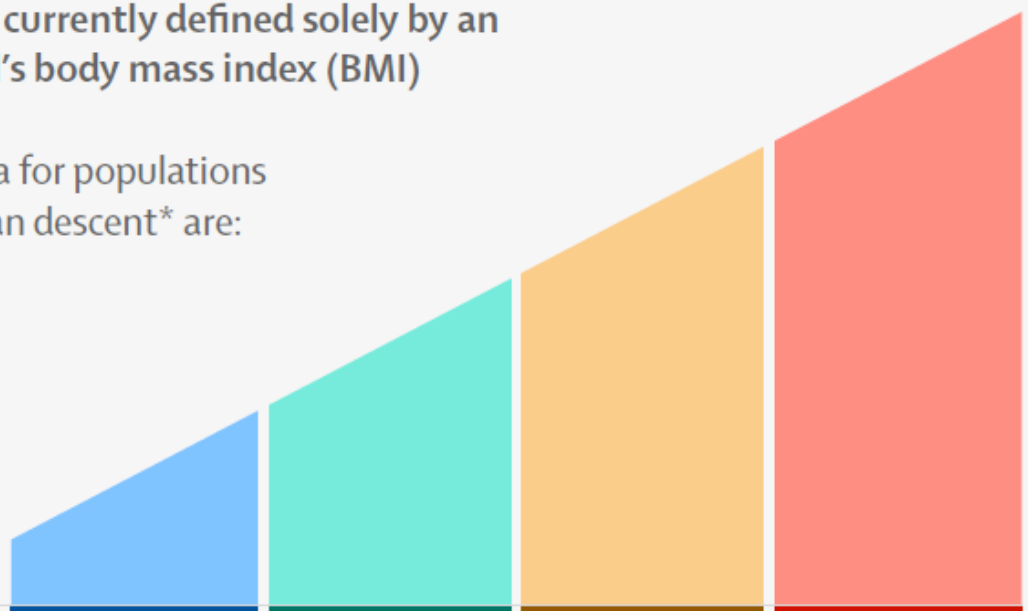
World Obesity Federation, *https://www.ncdrisc.org/data-downloads-adiposity.html*; International Diabetes Federation, Atlas, 2025.

Acknowledging fundamentals.

Limitations of the current definition of obesity

Obesity is currently defined solely by an individual's body mass index (BMI)

The criteria for populations of European descent* are:



Diagnosis	Underweight	Normal	Overweight	Obesity
BMI (kg/m²)	Under 18.5	18.5 to 24.9	25 to 29.9	30 and over

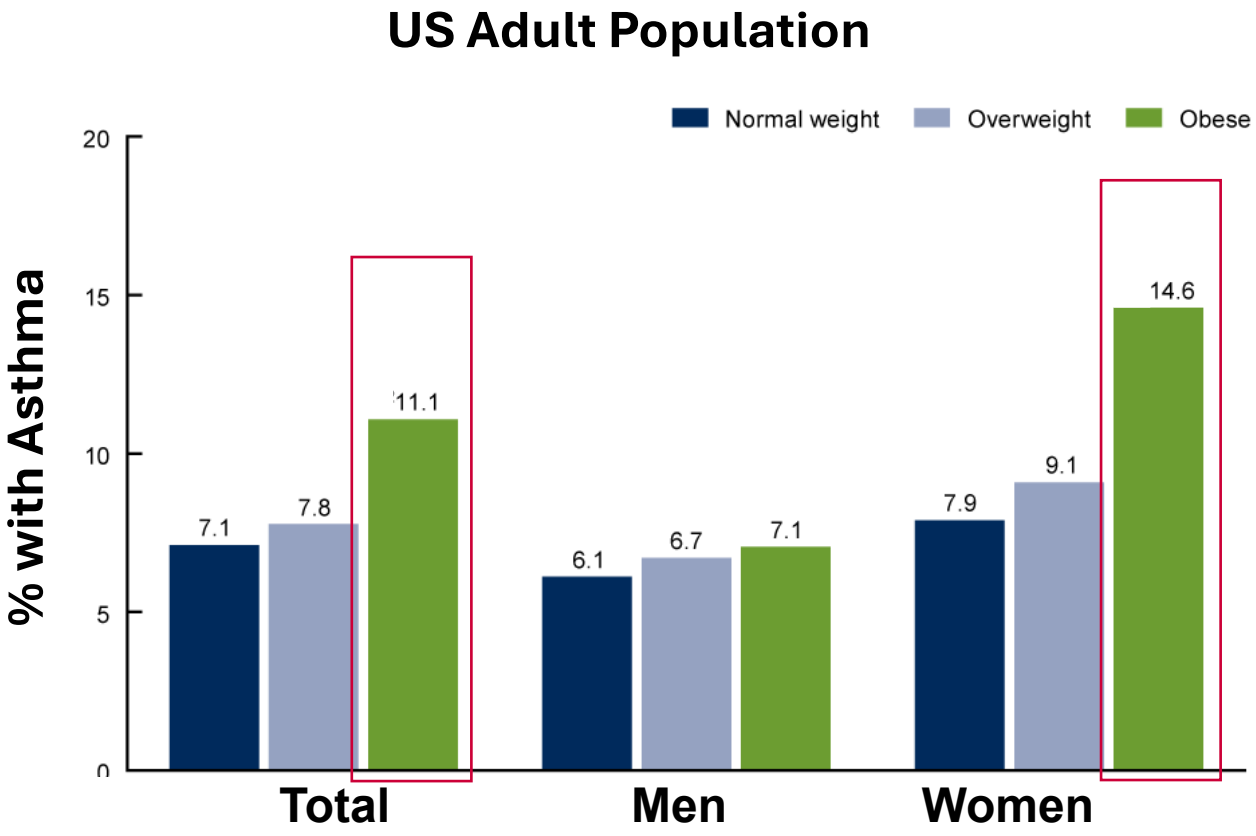
*Criteria for other ethnic groups are different

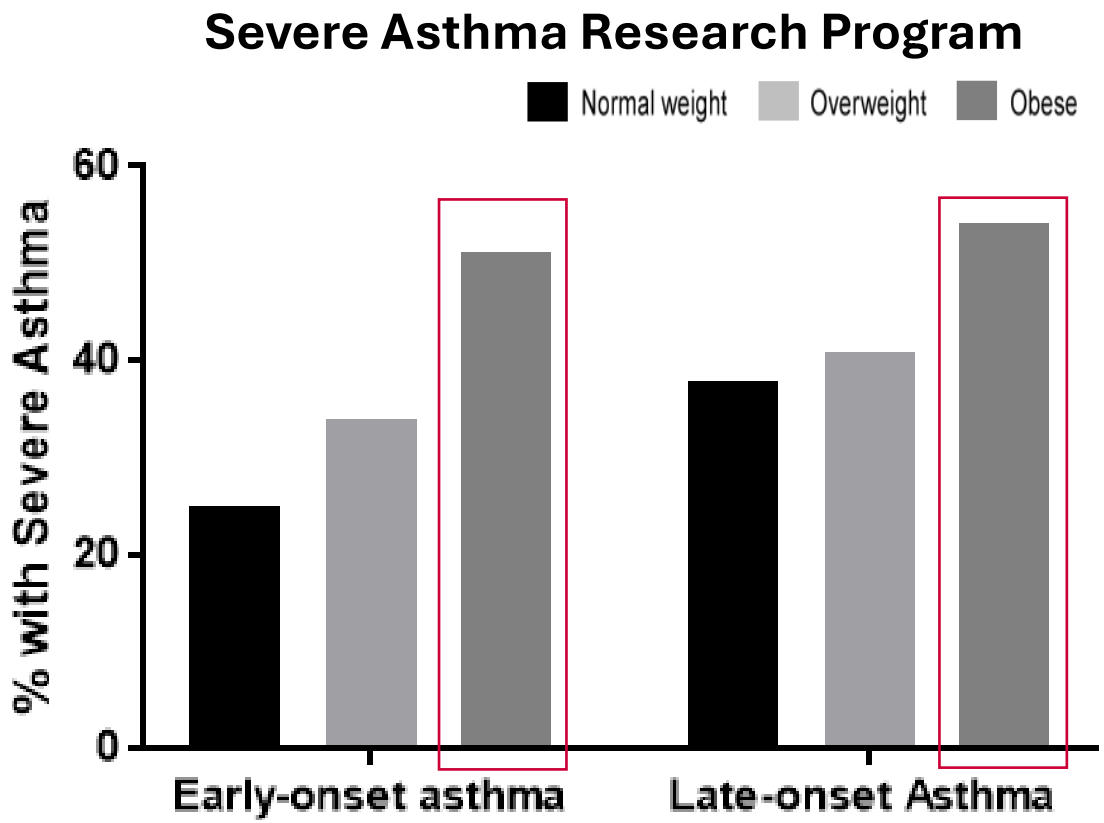
- ✓ Although BMI is **useful** for identifying individuals at increased risk of health consequences...
- ✗ It **is not** a direct measure of fat
- ✗ It **does not** establish the distribution of fat around the body
- ✗ It **cannot** determine when excess body fat is a health problem

Lancet Diabetes & Endocrinology Commission, 2025

POPULATION LEVEL EVIDENCE

Asthma prevalence, severity associated with obesity.





>60% with comorbid obesity

http://www.cdc.gov/nchs/databriefs/db239_table.pdf#1
Adapted from Holguin R et al. *JACI,* 2011
Boulet et al. *Eur Respir J.* 2007

Obesity associated with worse clinical asthma outcomes.

	Non-overweight (BMI <25) (mean (95% CI))	Overweight (25 ⩽ BMI<30) (mean (95% CI))	Obese (BMI ⩾30) (mean (95% CI))	p Value
Respondents (weighted†)	1 940 176 (35)	1 887 938 (34)	1 706 849 (31)	
GINA severity class (%)				
Remission	18.2 (14.7–21.8)	10.5 (8.1–12.9)	10.6 (8.0–13.1)	
I (Mild intermittent)	46.6 (42.4–50.7)	53.0 (48.9–58.2)	44.2 (39.9–48.5)	
II (Mild persistent)	11.3 (8.9–13.7)	12.4 (9.8–15.1)	10.3 (7.8–12.8)	
III (Moderate persistent)	8.8 (6.3–11.2)	6.9 (4.8–9.0)	10.7 (8.0–13.4)	
IV (Severe persistent)	15.1 (12.2–18.0)	17.2 (14.2–20.1)	24.2 (20.5–27.9)	<0.01
Symptoms				
Days with asthma symptoms in the past 30 days	4.4 (3.7–5.0)	4.3 (3.7–4.9)	5.0 (4.3–5.7)	0.01
Nights with asthma symptoms in the past 30 days	2.7 (2.2–3.2)	2.6 (2.1–3.2)	4.6 (3.7–5.4)	<0.01
Asthma attacks in the past 90 days	3.1 (2.3–3.8)	3.6 (2.6–4.6)	4.1 (3.0–5.3)	0.01
Healthcare utilisation				
ER/urgent care visits				
Proportion with at least 1 ER visit in the past 12 months (%)	11.2 (8.3–14.1)	11.6 (9.1–14.2)	17.9 (14.3–21.4)	0.01
Average number of ER visits in the past 12 months (only those with ⩾1 visit)	2.1 (1.6–2.5)	1.8 (1.5–2.2)	2.5 (2.1–3.0)	0.04
Average number of urgent visits to PCP in the past 12 months	0.9 (0.7–1.0)	0.9 (0.7–1.1)	1.3 (1.0–1.6)	<0.01
Missed work days in the past 12 months	2.7 (2.1–3.3)	3.4 (2.6–4.2)	4.1 (3.3–4.8)	<0.01

Obesity associated with reduced quality of life measures in severe asthma cohort

Odds of asthma hospitalizations >2x in patients with severe asthma and obesity compared with patients with healthy weight

Taylor et al, *Thorax*, 2008
Holguin et al, *JACI*, 2011
Moore et al, *AJRCCM*, 2010

Type 2 diabetes increases odds of incident asthma diagnosis.

Sensitivity analysis: association (odds ratios) of metabolic syndrome and its components with incident asthma on medication

Metabolic components	Total n	Incident asthma on medication[#]	Model 1[§] OR (95% CI)	Model 2[+] OR (95% CI)	Model 3[§] OR (95% CI)
Waist circumference ≥88 cm in females, ≥102 cm in males	2 563	119	1.80 (1.46–2.23)	1.66 (1.34–2.06)	1.55 (1.23–1.95)
Triglycerides ≥1.7 mmol·L^{-1}	6401	195	1.30 (1.08–1.57)	1.21 (1.01–1.46)	1.05 (0.86–1.29)
HDL cholesterol <1.3 mmol·L^{-1} in females, <1.0 mmol·L^{-1} in males	4106	150	1.39 (1.15–1.69)	1.30 (1.07–1.58)	1.18 (0.96–1.46)
Elevated blood pressure[f] or use of anti-hypertensive medication	9859	269	1.10 (0.92–1.31)	1.07 (0.89–1.28)	0.99 (0.82–1.19)
Elevated glucose[##] or diabetes	501	24	1.87 (1.23–2.85)	1.76 (1.15–2.68)	1.64 (1.07–2.52)
Metabolic syndrome[¶¶] ≥3 components	2413	95	1.55 (1.23–1.94)	1.42 (1.13–1.79)	NA

Total n = 20 155. HDL: high-density lipoprotein; NA: not applicable. [#]: incident asthma definition requires use of an asthma medication at follow-up and excludes those with wheezing from at-risk group at baseline and follow-up. [¶]: adjusted for age, sex and family history of asthma. [+]: adjusted for age, sex, family history of asthma, smoking, physical activity, education, social benefit and economic difficulties at baseline. [§]: adjusted for all covariates and other metabolic risk factors. [f]: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg. [##]: elevated glucose was ≥5.6 mmol·L^{-1} and ≥4 h since last meal. [¶¶]: metabolic syndrome was defined according to the Joint Interim Statement clinical criteria including alternate indicators anti-hypertensive medication and diabetes; glucose was nonfasting and ≥4 h since last meal.

Brumpton et al, *ERJ*, 2013

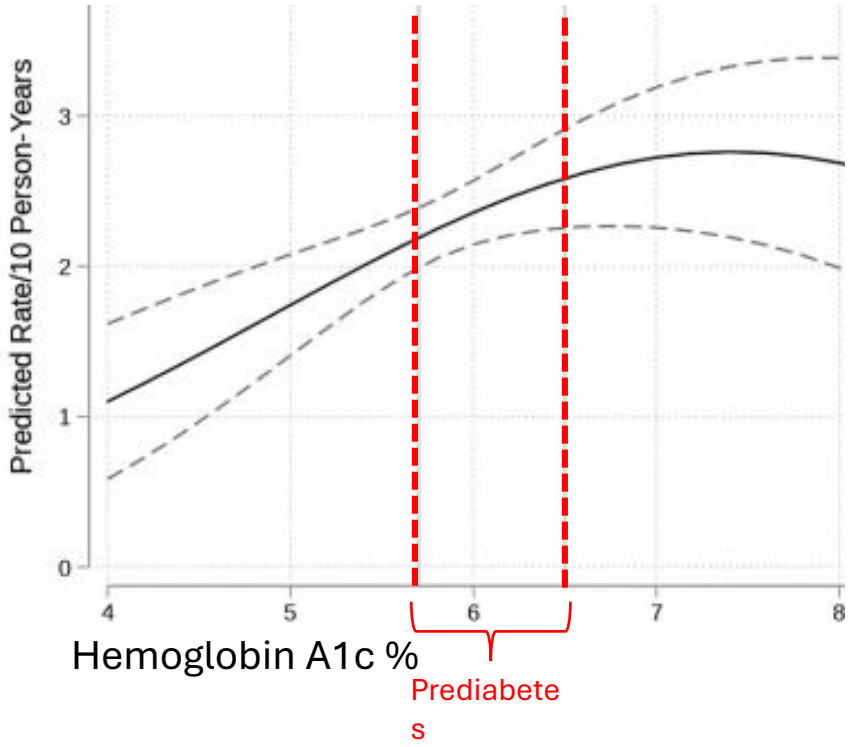
Hemoglobin A1c predicts clinical asthma outcomes.

Predictor of asthma hospitalizations (UK Biobank)

Exposure	Odds ratio (95% CI) Unadjusted analysis	Adjusted analysis*
HbA_{1c} level (per each mmol/mol increment)	1.02 (1.02-1.03)†	1.03 (1.01-1.04)†
Normal HbA_{1c} level (<42 mmol/mol) (N = 45,286)	1.0	1.0
Prediabetes/diabetes range (≥42 mmol/mol) (N = 2,320)	1.61 (1.33-1.94)†	1.68 (1.18-2.41)†

- Asthma hospitalization risk increases with HbA1c
- Odds ratio higher starting in the prediabetes range

Predictor of Asthma Exacerbations

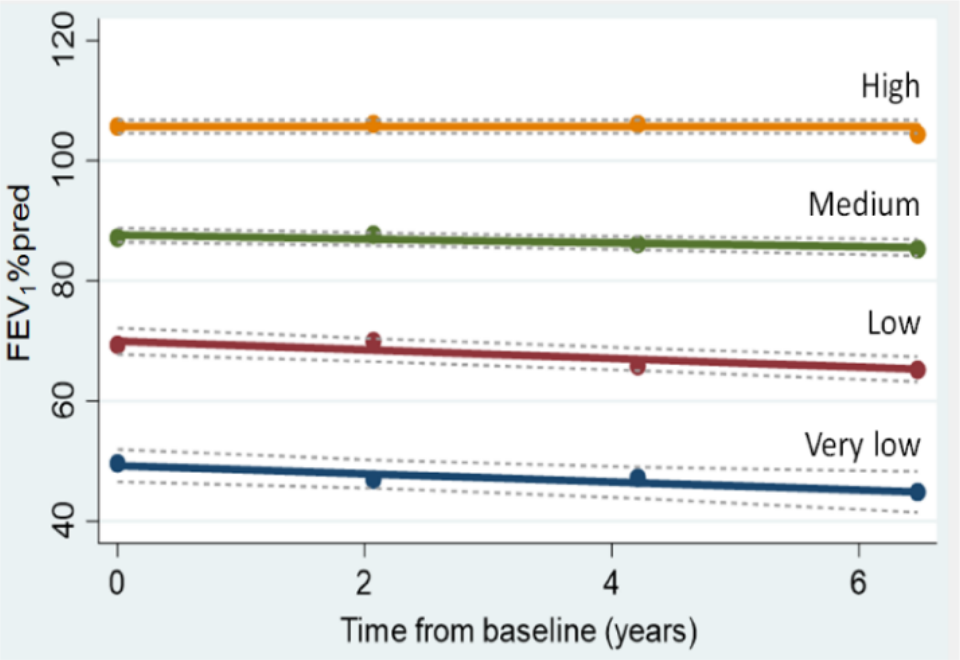


- Diabetes: 33% higher exacerbation risk
- Prediabetes: 27% higher exacerbation risk than with normal A1c

Wu TD et al. *JACI:IP,* 2019; Yang, *JACI:IP*, 2020; Zhang, *JACI:IP*, 2020

High Hba1c predicts lower lung function trajectories (in population-level study).

Trajectory modelling identified four participant groups in the Fremantle Diabetes Study Phase II with ≥2 biennial measurements of FEV1 as a % of predicted (FEV_1%pred) over 6 years.

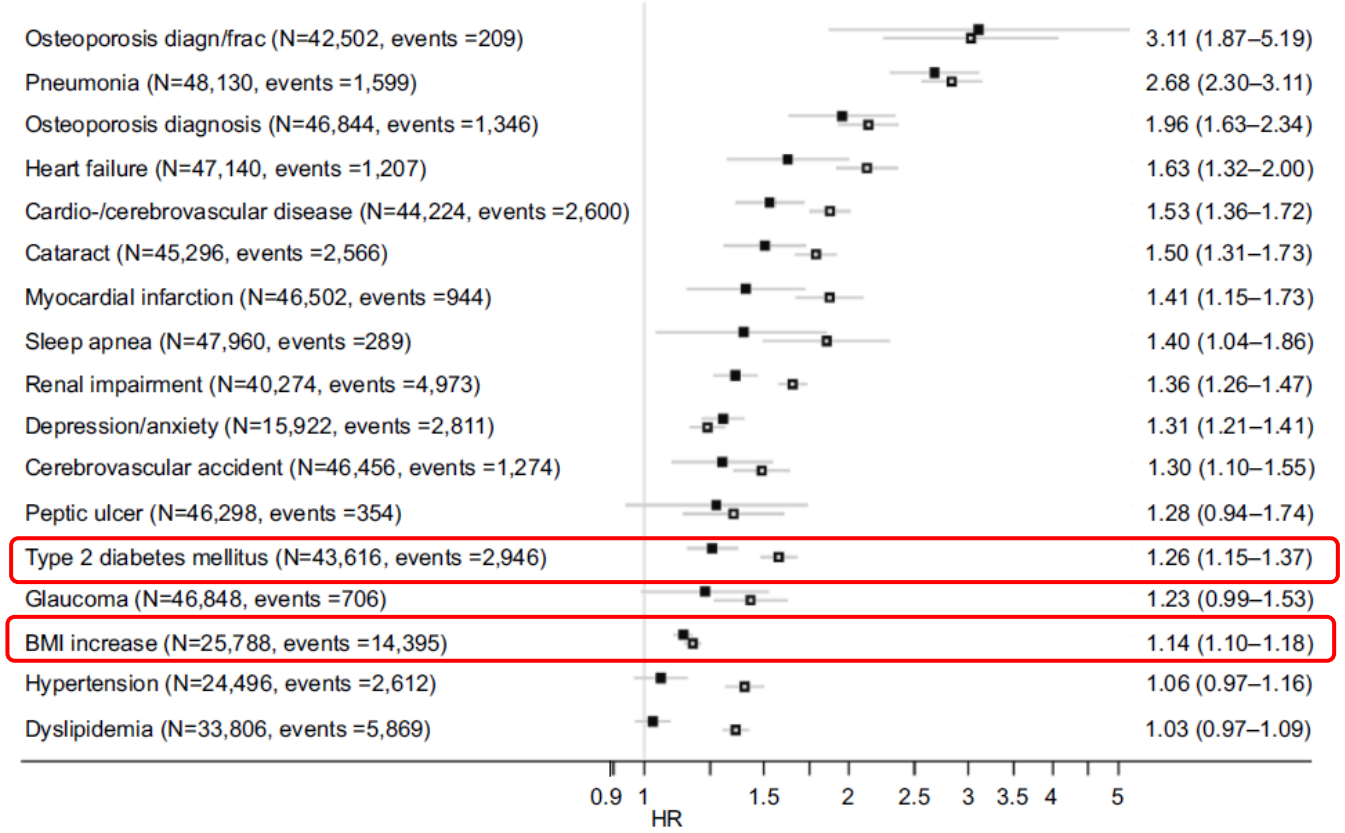


- T2D associated with lower FEV1, lower FVC, and normal/slightly impaired FEV1/FVC, depending on the study
- Metanalysis suggests long-term lower FVC
  - Independent of sex, smoking, BMI
- Patients with higher HbA1cs have lower lung function over time with a graded increase in mortality

Diez-Manglano et al, *ERJ Open*, 2022; Davis et al, *Diabetes Care*, 2023

Core asthma therapies contribute to obesity and metabolic disease.

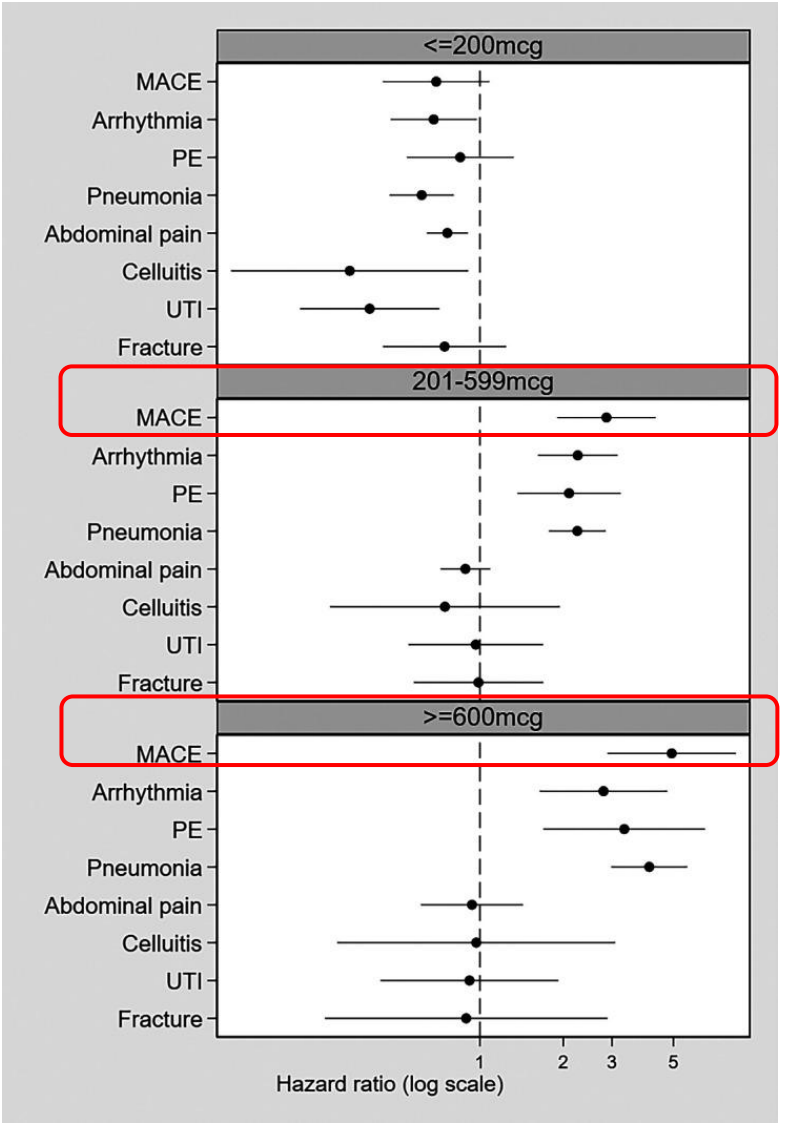
Adverse outcomes in asthmatic systemic corticosteroid users versus asthmatic non-users



ıre 2 HR (95% CI) for each adverse outcome in the SCS arms (vs non-SCS arms). The open squares represent unadjusted, and the closed squares, adjusted results. The ıted HRs (95% CIs) are shown on the right. See Table S3 for list of confounders.

Price et al, 2018; Bloom et al, 2024

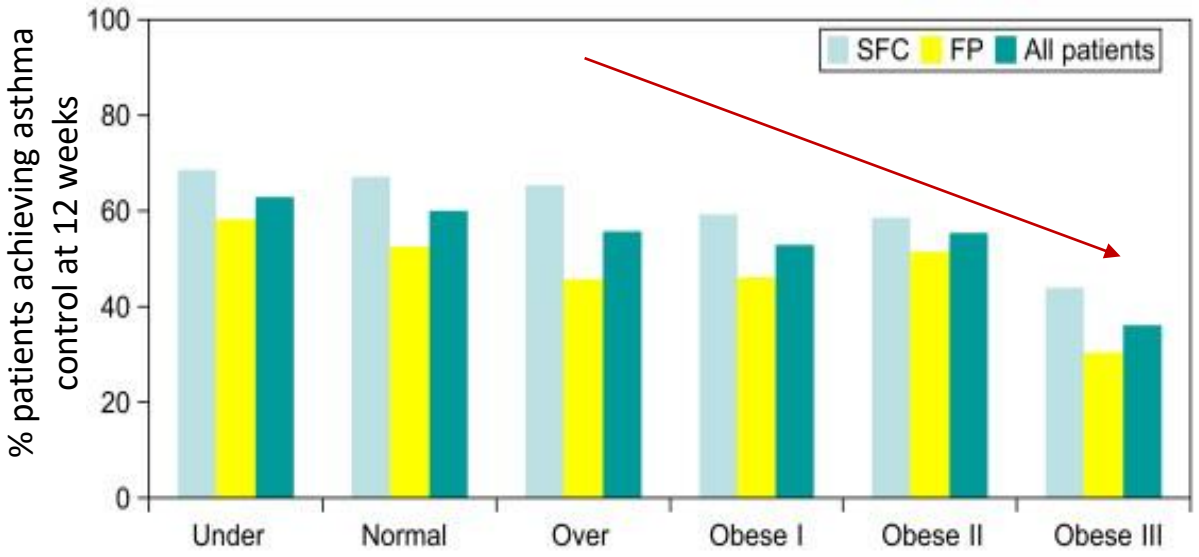
Association between ICS use and outcomes, categorized by average daily ICS dose



MACE=Major adverse cardiac event

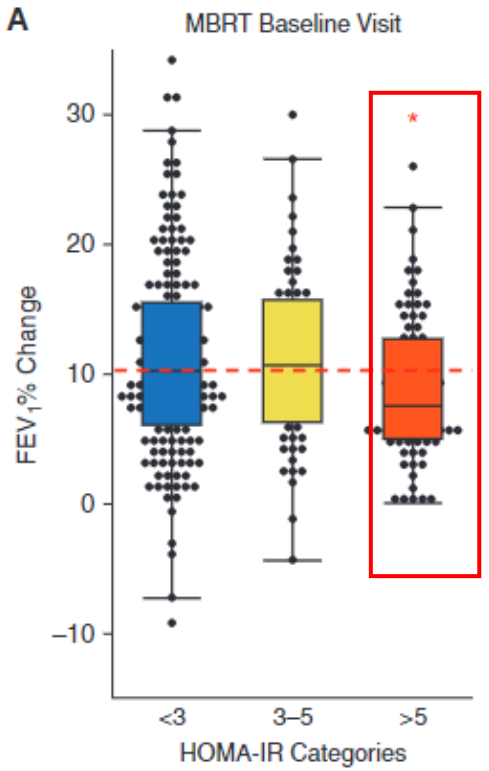
Obesity and metabolic dysregulation decrease response to standard asthma medications.

Asthma control on ICS (fluticasone/FP) versus ICS+LABA (salmeterol+fluticasone/SFC)

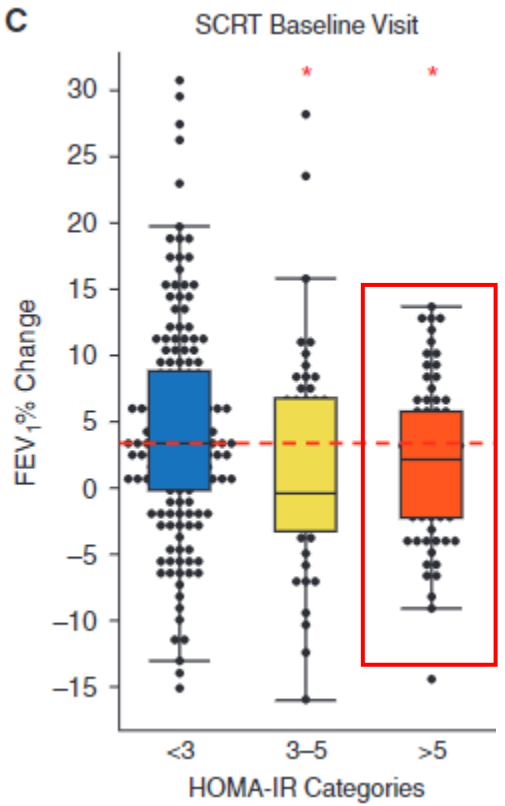


Peters-Golden M et al. *ERJ*. 2006;
Peters et al, *AJRCCM*, 2022

β-adrenergic agonist response

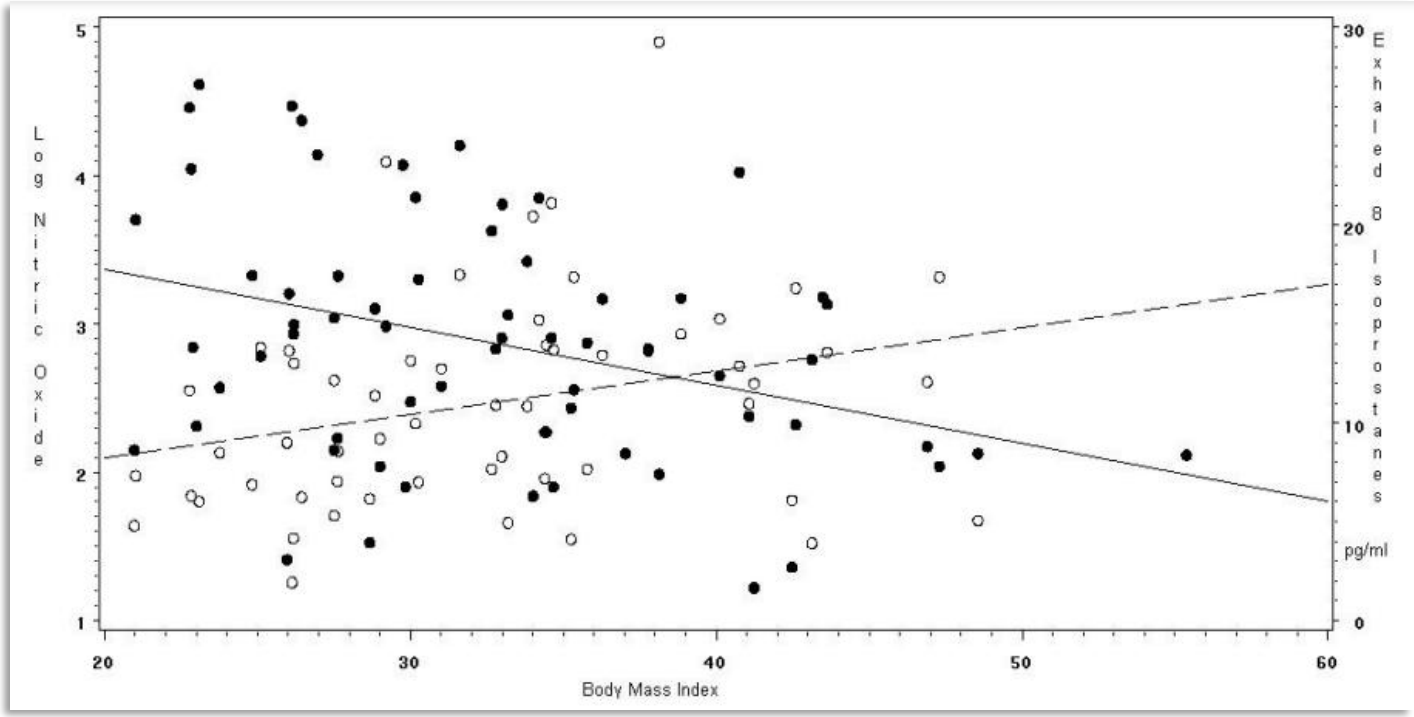


Intramuscular triamcinolone response



HOMA-IR=Marker of insulin resistance, higher score is worse (more glycemic dysfunction).
MBRT=Maximal bronchodilator reversibility testing.
Dashed red line=median value in participants without insulin resistance

BMI-associated reductions in exhaled nitric oxide: Implications for FeNO interpretation?



- In adults with moderate-to-severe asthma, BMI associated with reduced exhaled NO

  +*increased oxidative stress marker (8-isoprostanes) in airway*

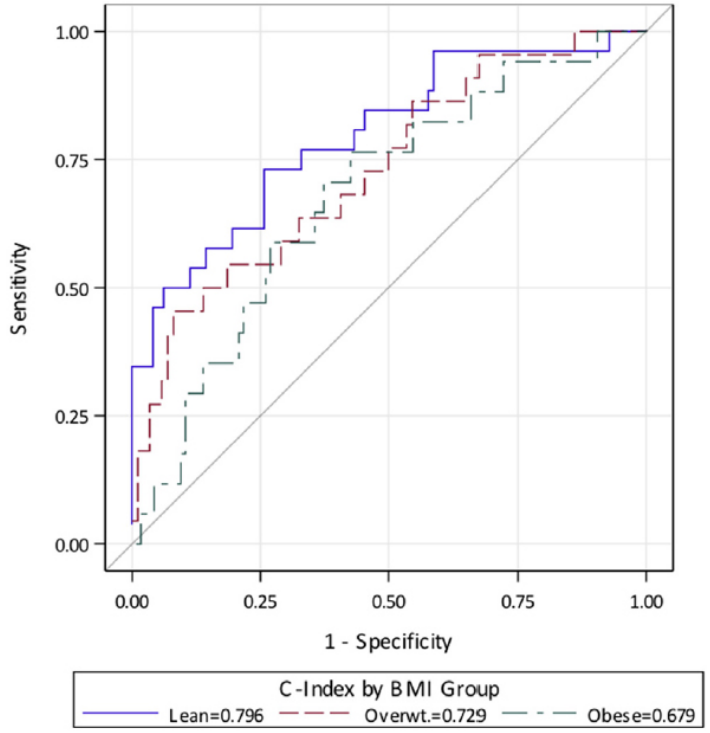
- Oxidative may ↓ endogenous nitric oxide (NO) bioavailability

→ Loss of bronchodilation

Komakula, *Respir Res*, 2007; Peters MC et al. *Lancet Respir Med* 2016.

Limitations of current asthma biomarkers by BMI.

Diagnostic accuracy of biomarkers to predict high sputum eosinophils (>2%)



		Maximize AUC		
Biomarker	BMI Category	Cut Point	SENS	SPEC
Log(IgE)	Overall	268	0.46	0.73
	Lean	277	0.43	0.75
	Overweight	605	0.35	0.88
	Obese	268	0.53	0.76
Log(FeNO)	Overall	17.1	0.78	0.43
	Lean	17.1	0.93	0.44
	Overweight	31.2	0.42	0.78
	Obese	14.5	0.79	0.42
Log(Blood Eosinophils)	Overall	195	0.70	0.57
	Lean	195	0.75	0.66
	Overweight	400	0.36	0.95
	Obese	96	0.25	0.85

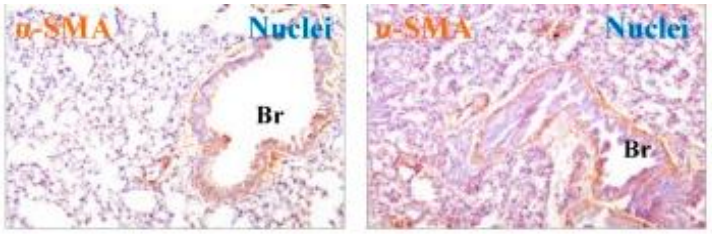
Suggests lower cut-offs for T2 Inflammation:
IgE 268 IU
FeNO 14.5 ppb
Eos 96 cells/µl

Increasing BMI decreases ability of IgE, FeNO, and blood eosinophils to predict high sputum eosinophils

Lugogo, *JACI*, 2018

How do obesity and/or type 2 diabetes impact the lung? Multiple mechanistic hypotheses...*little consensus*.

-Insulin potentiates airway hyperresponsiveness and contractility, increases airway smooth muscles and collagen



-Impaired viral response

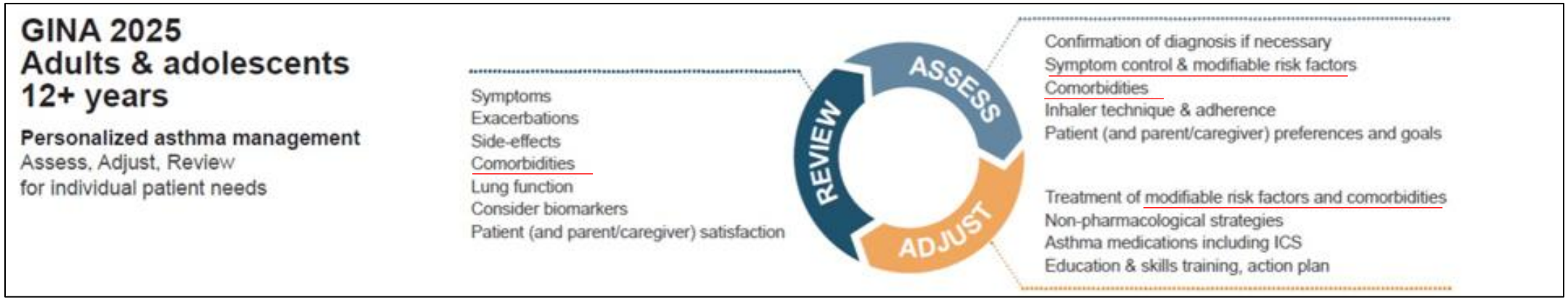
-Impaired respiratory neuromuscular function related to diabetic polyneuropathy

-Hyperglycemia

- Increases oxidative stress
- Favors growth of bacterial organisms
  – Observational associations with greater risk of respiratory infection
- Microvascular damage, non-enzymatic glycation (analogous to retinopathy, neuropathy, nephropathy)
- Thickening of alveolar epithelial and pulmonary capillary basal laminae
- Drives mucus metaplasia

COMORBIDITY MANAGEMENT IN CLINICAL CARE

GINA guidelines recognize role of weight reduction, recently increase emphasis on comorbidities

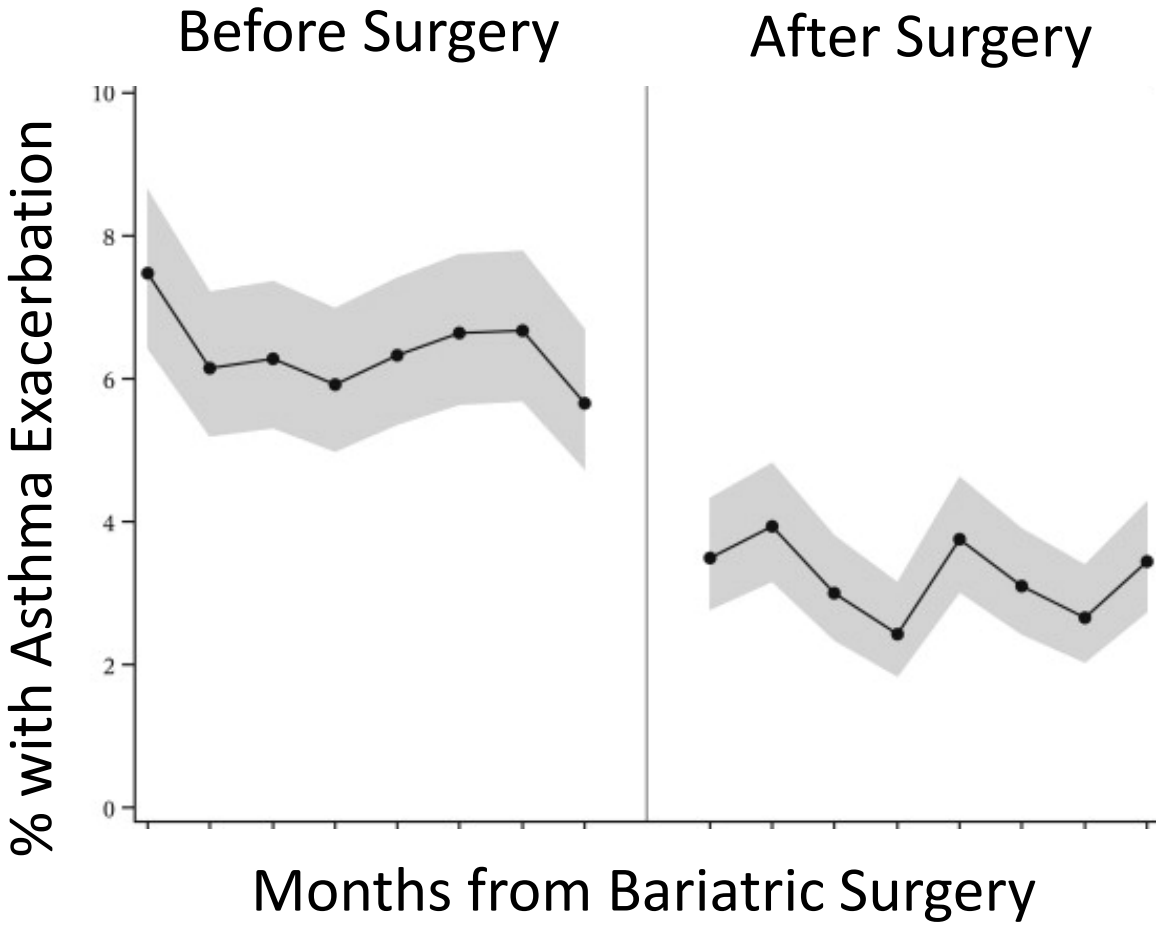


Management

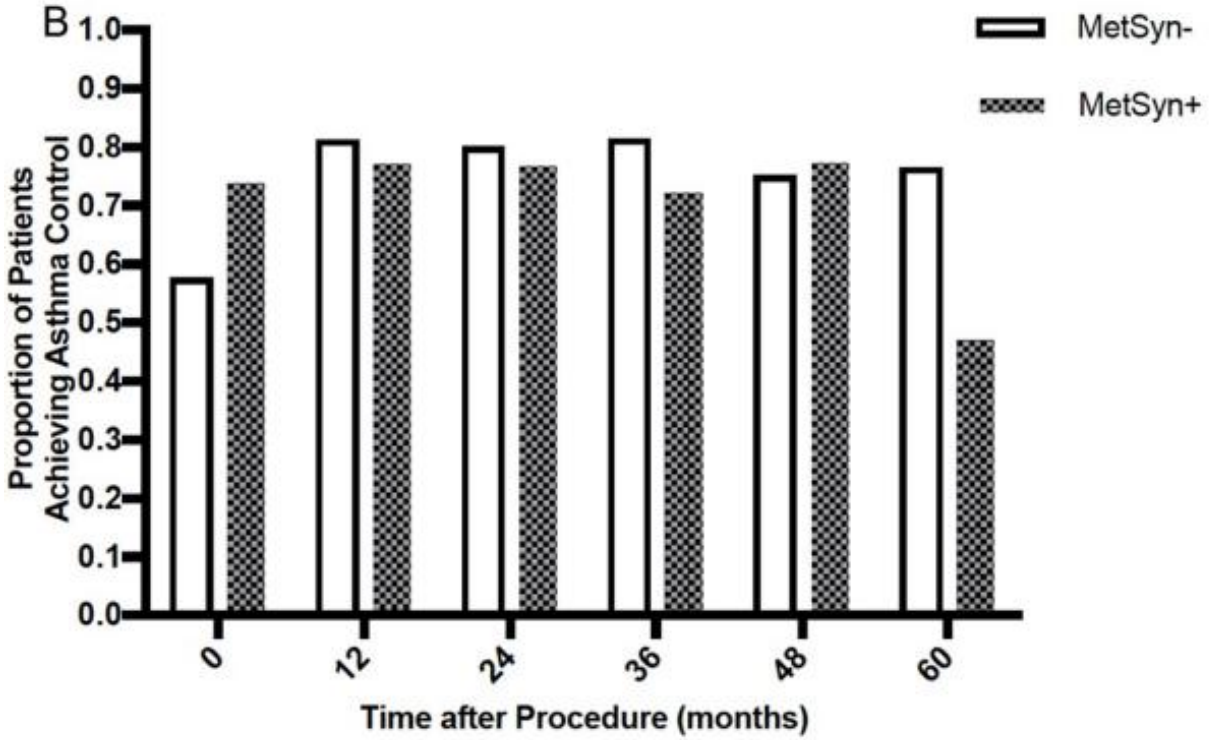
As for other patients with asthma, ICS are the mainstay of treatment in obese patients (Evidence B), although their response may be reduced.[398] Weight reduction should be included in the treatment plan for obese patients with asthma (Evidence B). Increased exercise alone appears to be insufficient (Evidence B).[404] Weight loss can improve asthma control, lung function, health status and reduces medication needs in obese patients,[400,401] but the studies have generally been small, quality of some studies is poor, and the interventions and results have been variable.[399] The most striking results have been observed after bariatric surgery,[402,403,484] but even 5–10% weight loss can lead to improved

Non-pharmacologic strategies include smoking cessation, physical activity, pulmonary rehabilitation, weight reduction, vaccinations (see text for more)
Allergen immunotherapy, e.g. HDM SLIT: consider for patients with clinically relevant sensitization and not well-controlled (but stable) asthma See text for further information and safety advice
Additional controller options (e.g., add-on LAMA at Step 4, add-on LTRA) have less evidence for efficacy or for safety than Tracks 1 or 2 (see text). Maintenance OCS should only ever be used as last resort.

Weight is a known, modifiable asthma risk factor.



Forno et al, *PLoS ONE*, 2019



"Achieving asthma control"=ACT >19
"MetSyn"= Metabolic syndrome= ≥ 3 of:
abdominal obesity; high serum triglycerides;
low serum HDL; hypertension; hyperglycemia

RCTs of physical activity on asthma outcomes

	LUNG FUNCTION	ASTHMA CONTROL	HEALTH-RELATED QUALITY OF LIFE
Abd El-Kader et al. (2016)			
Arandelovic et al. (2007)	+*		
Bacon et al. (2015)	N	+*	
Boyd et al. (2012)	N	N	
Evaristo et al (2020)	N	+*	+*
Franca-Pinto et al. (2015)	N	+*	+*
Freitas et al. (2017)	N	+*	+
Hass et al. (1987)	N		
Ma et al. (2015)	N	N	+
Mendes et al. (2010)	N	+*	+*
Meyer et al. (2015)	N	N	N
Paul et al. (2013)	+		
Razavi et al. (2011)	+*		
Refaat et al. (2015)	+*		+*
Schichilone et al. (2012)	N		
Scott et al. (2013)	+*	N	N
Shaw et al. (2010)	+*		
Toennesen et al. (2018)	N	+*	+*
Turk et al. (2017)		+*	
Turner et al. (2011)	N	N	+*

- No worsening of asthma control
- No studies for longer than one year
- Supervised activity may not be accessible/feasible to others
- Serologic markers varied in choice and response; IL-6 decreased in 3 studies
- Only 3 studies in patients with obesity and moderate to severe asthma
- Diet + exercise> exercise alone in overweight/obesity populations with asthma (Scott, *Clin Exp All*, 2013)

Kuder et al, *JACIIP*, 2022

Rigorous, diet-based approach reduces weight, but fails primary asthma endpoints.

Counterweight-Plus program (CWP)

-12 wk total diet replacement phase (Liquid formula ~850 kcal/d)

~6 wk food reintroduction phase of stepwise calorie-controlled meals with reducing formula

~34 wk weight maintenance phase of tailored calorie-controlled meals with dietitian review

TABLE 2 Intention-to-Treat Analysis Comparing Asthma-Related and Anthropomorphic Outcomes Over 1 Year Between CWP and UC

Variable	Group	N	Mean (95% CI)/Median (IQR)			Repeated Measures ANOVA/Friedman Test		V1-V3	
			V1	V2	V3	*P* Value	Effect Size	Change in Variable	*P* Value
ACQ-6	CWP	17	2.6 (2.1, 3.2)	2.2 (1.5, 2.8)	2.2 (1.6, 2.8)	.168	0.105	−0.5 (−1.1, 0.2)	
	UC	16	2.7 (2.2, 3.3)	2.9 (2.3, 3.6)	2.6 (2.0, 3.3)	.465	0.050	−0.1 (−0.7, 0.6)	.409
AQLQ	CWP	17	3.9 (3.3, 4.5)	4.7 (4.2, 5.3)	4.5 (3.9, 5.1)	**.016**	0.227	0.6 (−0.1, 1.2)	
	UC	16	3.8 (3.2, 4.5)	3.9 (3.4, 4.5)	3.9 (3.3, 4.6)	.914	0.006	0.1 (−0.5, 0.7)	.254
AQLQ symptom domain	CWP	17	3.8 (3.2, 4.5)	4.8 (4.3, 5.4)	4.5 (3.8, 5.1)	**.010**	0.249	0.6 (−0.1, 1.4)	
	UC	16	3.9 (3.2, 4.6)	4.1 (3.6, 4.7)	4.2 (3.5, 4.9)	.315	0.074	0.4 (−0.3, 1.0)	.595
AQLQ activity domain	CWP	17	4.0 (3.4, 4.5)	4.5 (3.9, 5.1)	4.3 (3.7, 5.0)	.149	0.112	0.4 (−0.3, 1.0)	
	UC	16	3.7 (3.0, 4.3)	3.5 (2.9, 4.2)	3.6 (2.9, 4.3)	.916	0.006	−0.1 (−0.7, 0.6)	.370
AQLQ emotional domain	CWP	17	3.7 (2.9, 4.6)	5.2 (4.4, 5.9)	4.5 (3.8, 5.2)	**.004**	0.289	0.8 (−0.1, 1.7)	
	UC	16	3.9 (3.0, 4.8)	4.6 (3.9, 5.2)	4.3 (3.5, 5.0)	**.039**	0.195	0.3 (−0.2, 0.8)	.357
AQLQ environmental domain	CWP	17	4.1 (3.4, 4.8)	4.6 (3.8, 5.4)	4.8 (3.9, 5.6)	.157	0.109	0.7 (−0.1, 1.4)	
	UC	16	4.2 (3.4, 5.0)	3.7 (2.9, 4.5)	3.7 (2.8, 4.6)	.432	0.054	−0.5 (−1.5, 0.5)	**.047**
Weight, kg[a]	CWP	9	101.7 (95.5 to 112.0)	88.8 (82.0 to 90.7)	87.1 (85.9 to 93.3)	**.001**	0.778	−14.0 (−14.8 to −9.2)[b]	
	UC	8	106.0 (80.9 to 128.0)	105.6 (80.9 to 124.9)	108.6 (87.1 to 145.5)	.417	0.109	1.9 (−7.3 to 7.9)[b]	**.015**
BMI, kg/m^2[a]	CWP	9	37.5 (35.6 to 41.8)	32.6 (30.1 to 35.1)	33.1 (31.4 to 37.6)	**.004**	0.613	−4.2 (−6.4, −2.0)	
	UC	8	37.1 (31.5 to 47.8)	37.2 (31.0 to 47.0)	37.5 (32.6 to 54.4)	.417	0.109	−0.1 (−3.6, 3.4)	**.036**
Annualized prednisolone courses[a]	CWP	17	4 (2 to 5)	0 (0 to 5)	0 (0 to 2)	**.001**	0.435	−3 (−5, −1)	
	UC	16	3 (2 to 5)	3 (0 to 6)	2 (1 to 4)	.824	0.012	−1 (−3, 1)	.109

Sharma et al, *CHEST*, 2024

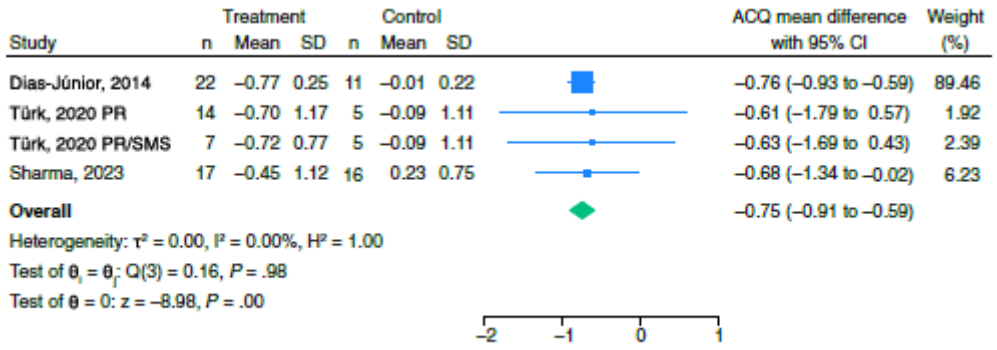
Nonsurgical weight loss interventions warrant further study to demonstrate long-term asthma benefit.

- 6 studies, N=522 pts
- 1 pharmacotherapy intervention (orlistat, sibutramine)
- Improvements by 12-24 wks; weaker by 1 yr
- Benefits at 10% TBW threshold
- Exacerbations understudied
- Predominantly female populations, av age mid-40s

TABLE II. Outcomes assessment in analyzed studies

Study	Timing	Intervention group Ibody weight reduction from baseline|, %	Control group Ibody weight reduction from baseline|, %	ACQ	ACT	AQLQ	miniAQLQ	SGRQ	FEV_1
Dias-Júnior, 2014[24]	24 wk	−13.3	−1.2	↓	↔	n/a	n/a	↔	↔
Mu, 2015[11]	24 wk	−5.0	−1.3	↔	↔	n/a	↔	n/a	↔
Mu, 2015[11]	52 wk	−4.1	−2.1	↔	↔	n/a	↔	n/a	↔
Ozbey, 2020[25]	10 wk	−5.3	0.0	n/a	↑	↑	n/a	n/a	↑
Türk, 2020 PR[26]	12 wk	−5.0	0.7	↓	n/a	↔	n/a	n/a	↔
Türk, 2020 PR/SMS[26]	12 wk	−12.0	0.7	↓	n/a	↔	n/a	n/a	↔
Türk, 2020 PR[26]	52 wk	−5.9	2.2	↓	n/a	↔	n/a	n/a	↔
Türk, 2020 PR/SMS[26]	52 wk	−13.3	2.2	↓	n/a	↔	n/a	n/a	↔
Sharma, 2023[27]	16 wk	−12.3	−1.2	↓	n/a	↑	n/a	n/a	↔
Sharma, 2025[28]	52 wk	−11.2	-0.3	↔	n/a	↑	n/a	n/a	↔

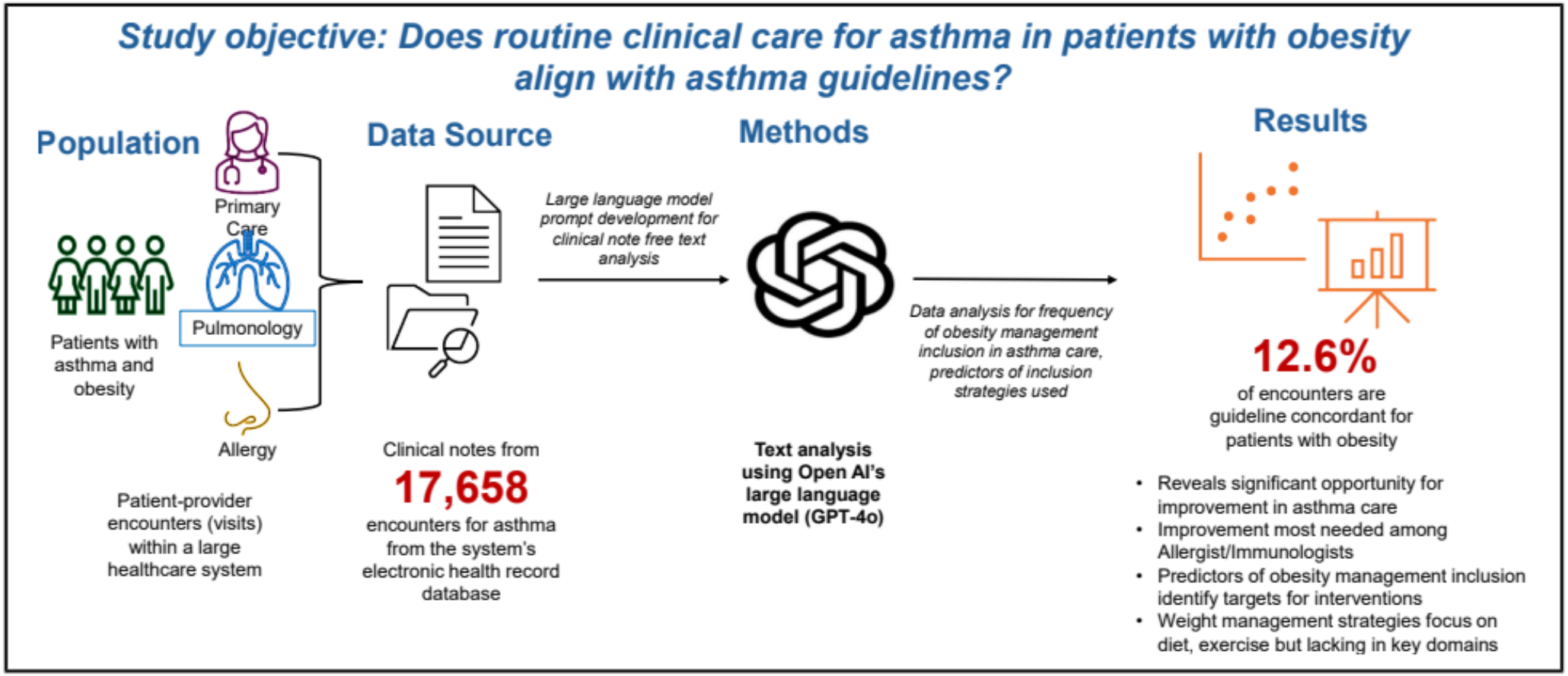
n/a, Not available; *PR*, pulmonary rehabilitation; *SMS*, use of an Internet-based self-management support; ↓, decrease; ↔, no change; ↑, increase.



Asthma control in ACQ score at 12—24 wks

Rybka-Fraczek, *J Allergy Clin Immunol Pract*, 2025

Identifying/quantifying gaps in care as a prerequisite to improvement.



Olayiwola, *J Allergy Clin Immunol Pract*, 2025

~12% of visits for asthma in patients with obesity include obesity management as part of asthma care.

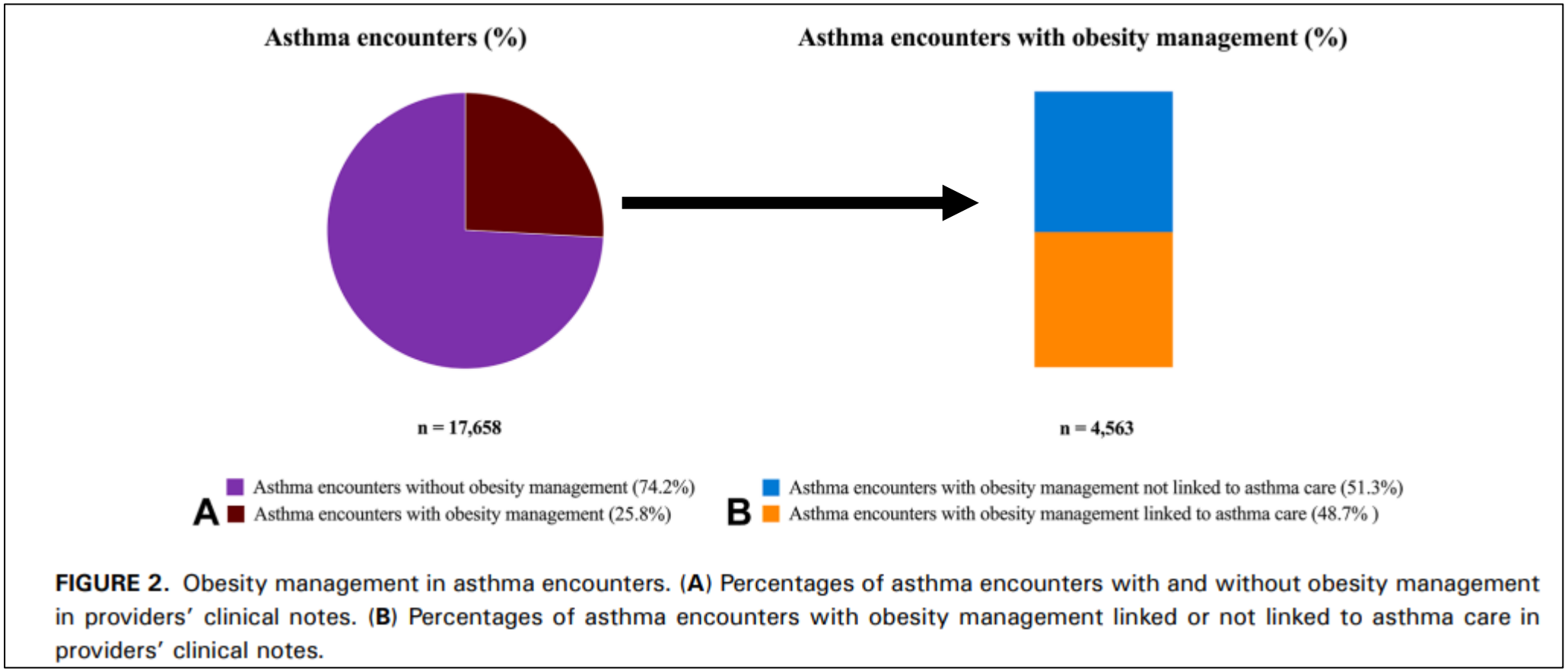
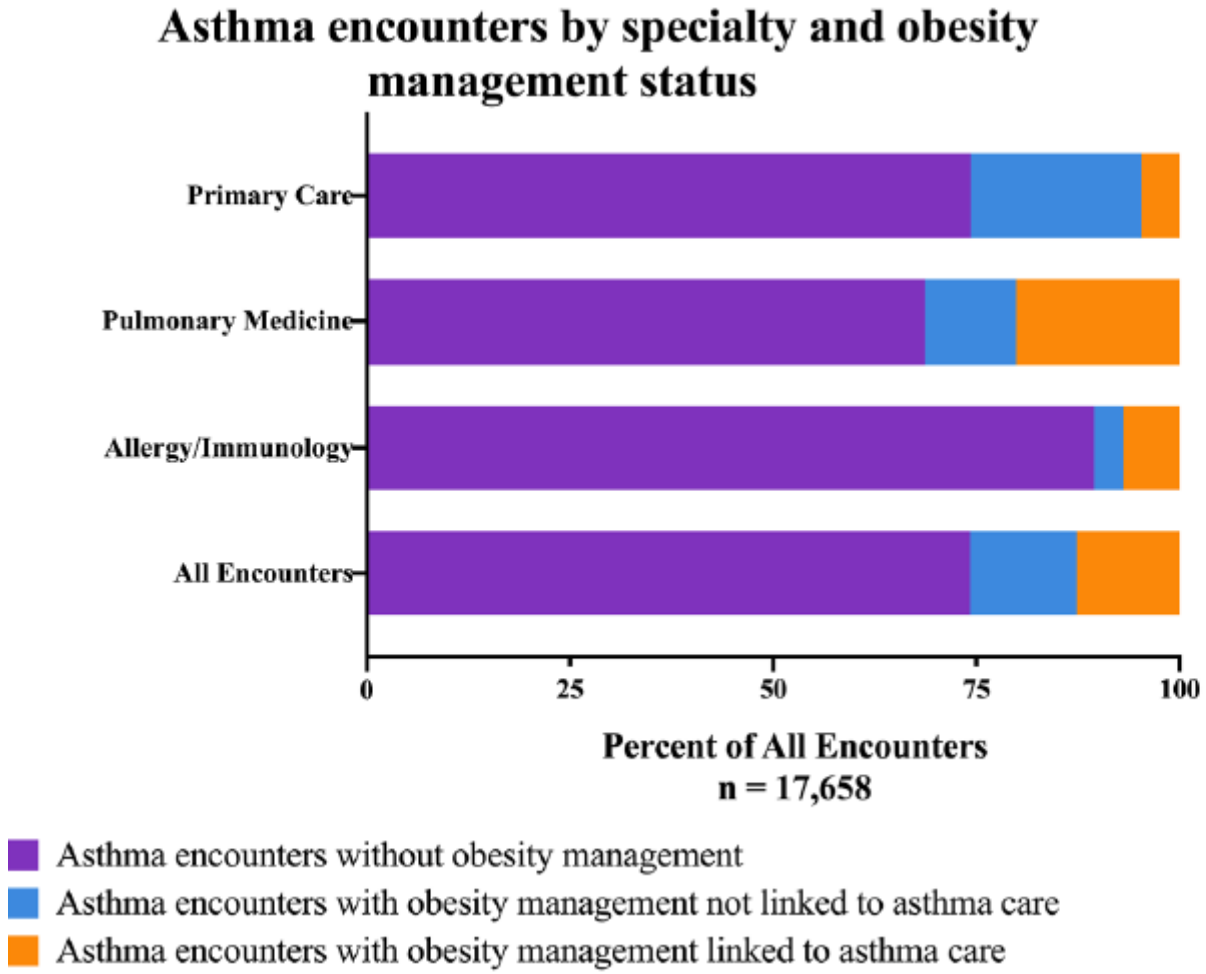


FIGURE 2. Obesity management in asthma encounters. (**A**) Percentages of asthma encounters with and without obesity management in providers' clinical notes. (**B**) Percentages of asthma encounters with obesity management linked or not linked to asthma care in providers' clinical notes.

Olayiwola, *J Allergy Clin Immunol Pract*, 2025

Pulmonologist outperforming allergist/ immunologists.



Olayiwola, *J Allergy Clin Immunol Pract*, 2025

INSIGHTS FROM ONGOING PHARMACOLOGIC CLINICAL TRIALS

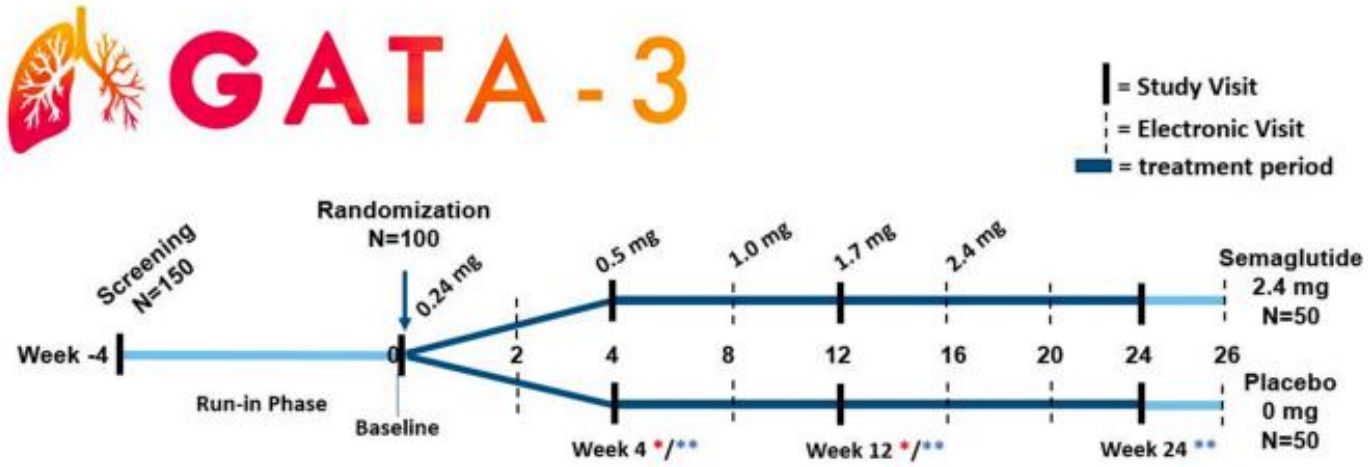
Metformin IN Asthma for Overweight and Obese Individuals (MINA)

- NIH funded
- 2 sites, United States
- Adults
- BMI≥25
- Physician diagnosed asthma
- ACT score <20, or at least one asthma exacerbation requiring corticosteroids in the prior 12 months
- Baseline ICS use
- Telemedicine visits
- Excludes overt T2D

Outcome Measure	Measure Description	Time Frame
Asthma control as assessed by the Asthma Control Test (ACT) score	Difference in Asthma Control Test (ACT) score at week 24; range is from 5-25 with higher being better asthma control	Baseline to week 24
Change in Asthma exacerbations rate	Change in (annualized) asthma exacerbations rate at week 24	Baseline to week 24
Pre-bronchodilator lung function	Difference in volume of air exhaled in the first second during spirometry (FEV1) at week 24	Baseline to week 24
Fractional exhaled nitric oxide (FeNO)	Difference in FeNO between baseline and week 24	Baseline to week 24
Airways hyperresponsiveness	Difference in cumulative dose of mannitol required to precipitate a significant decrement in FEV1 between baseline at week 24	Baseline to week 24

https://clinicaltrials.gov/study/NCT06273072; PIs: Drs Tianshi David Wu and Meredith McCormack

GLP-1R **A**gonists in the **T**reatment of **A**dult, **S**ymptomatic, **O**besity-related **A**sthma



*Primary Outcomes
**Secondary & Exploratory Outcomes

TABLE I. GATA-3 clinical and mechanistic outcomes

Outcome	Outcome measure	Measure description
Primary	Efficacy of semaglutide on ACQ-7 score in subjects with symptomatic, persistent asthma and obesity at week 12	Primary clinical outcome is difference between treatment and placebo groups in change from baseline in ACQ-7 score to week 12
	Effect of semaglutide once weekly on serum periostin in subjects with symptomatic, persistent asthma and obesity at week 4	Primary mechanistic outcome is difference between treatment and placebo groups in change from baseline in serum periostin at week 4
Secondary	Effect of semaglutide on weight loss to week 24	Change from baseline in weight to week 24
	Efficacy of semaglutide once weekly on ACQ-6 score in subjects with symptomatic, persistent asthma and obesity to week 12	Change from baseline in ACQ-6 score to week 12
	Maximal dose of semaglutide tolerated in persistent asthma with obesity to week 24	Maximum tolerated dose of investigational product at week 24
	Change in exhaled nitric oxide from semaglutide to week 12	Change from baseline in exhaled nitric oxide at weeks 4 and 12
	Change in serum periostin from semaglutide to week 12	Change from baseline in serum periostin at week 12

Tomasello…Cahill, *JACI Global*, 2026;
PI: Dr. Katherine Cahill NCT05254314

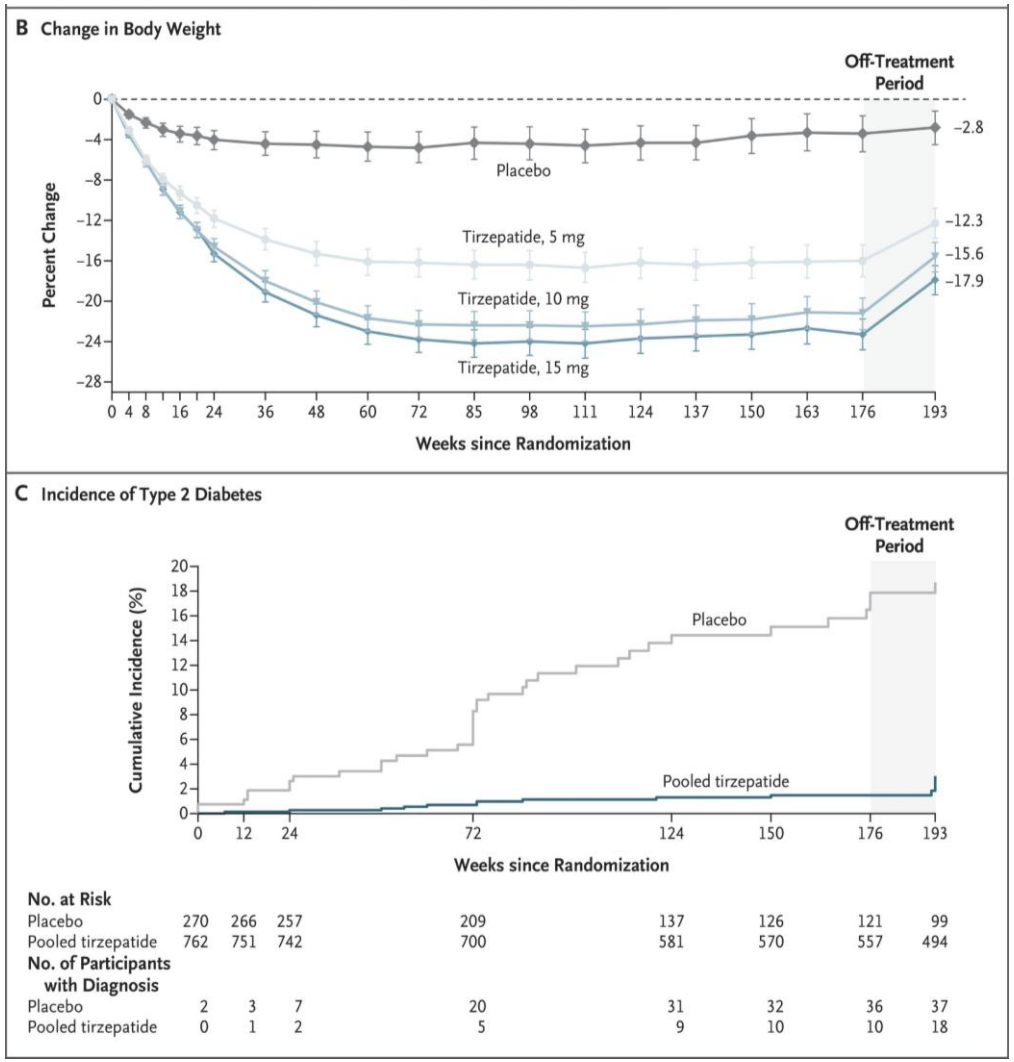
A Phase 2, Multicenter, Randomized, Double-blind, 52-week Study, to Investigate the Efficacy and Safety of Brenipatide Compared With Placebo for the Treatment of Adult Participants With Uncontrolled Moderate to Severe Asthma

- Industry sponsored (Eli Lilly & Co.)
- Global, multi-site Phase II
- Physician-diagnosed asthma on ICS
- ACQ-6 score of ≥1.5 on 2 out of 3 visits before randomization
- History of 1 severe asthma exacerbation in past 12 months
- Primary outcome measure: Annualized Asthma Exacerbation Rate Over 52 Weeks of Treatment
- Secondary outcomes: pharmacokinetics, spirometry, PROs etc.

https://clinicaltrials.gov/study, NCT07219173;
https://rally.massgeneralbrigham.org/study/gzmr

While the trials recruit…

Weight AND insulin resistance now medically modifiable to an unprecedented degree.



Jastreboff et al, SURMOUNT-1 Investigators, *NEJM*, 2024

Table. Annual Prescription Trends for OMDs and GLP-1RAs With Weight Loss Effects Between 2018 and 2023, IQVIA National Prescription Audit (January 2018 to December 2023)

	No. of prescriptions (annual percent change)			
Year	OMDs[a]	Semaglutide (Wegovy, Ozempic, Rybelsus)	Tirzepatide (Mounjaro, Zepbound)	GLP-1RAs with weight loss effects[b]
2018	9 060 679	347 128	0	4 599 064
2019	8 926 721 (−1.5)	2 192 863 (531.7)	0	6 160 831 (34.0)
2020	8 688 979 (−2.7)	4 883 081 (122.7)	0	8 375 377 (35.9)
2021	9 654 487 (11.1)	8 630 164 (76.7)	0	11 259 455 (34.4)
2022	10 337 271 (7.1)	15 147 512 (75.5)	2 482 961[c] (June 2022-December 2022)	19 113 488 (69.8)
2023	15 164 706 (46.7)	29 931 933 (97.6)	5 696 709 (January 2023-July 2023) (129.4)[c]; 11 035 526 (January 2023-December 2023)	37 968 969 (98.7)

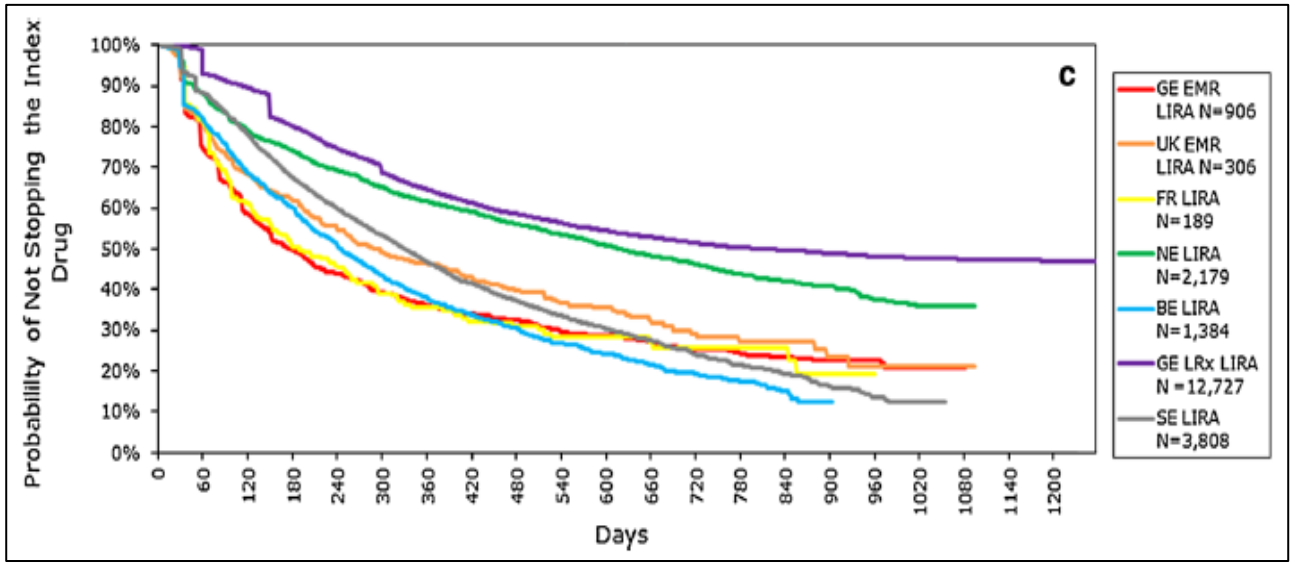
Abbreviations: GLP-1RA, glucagon-like peptide 1 receptor agonist; OMD, obesity management drug.

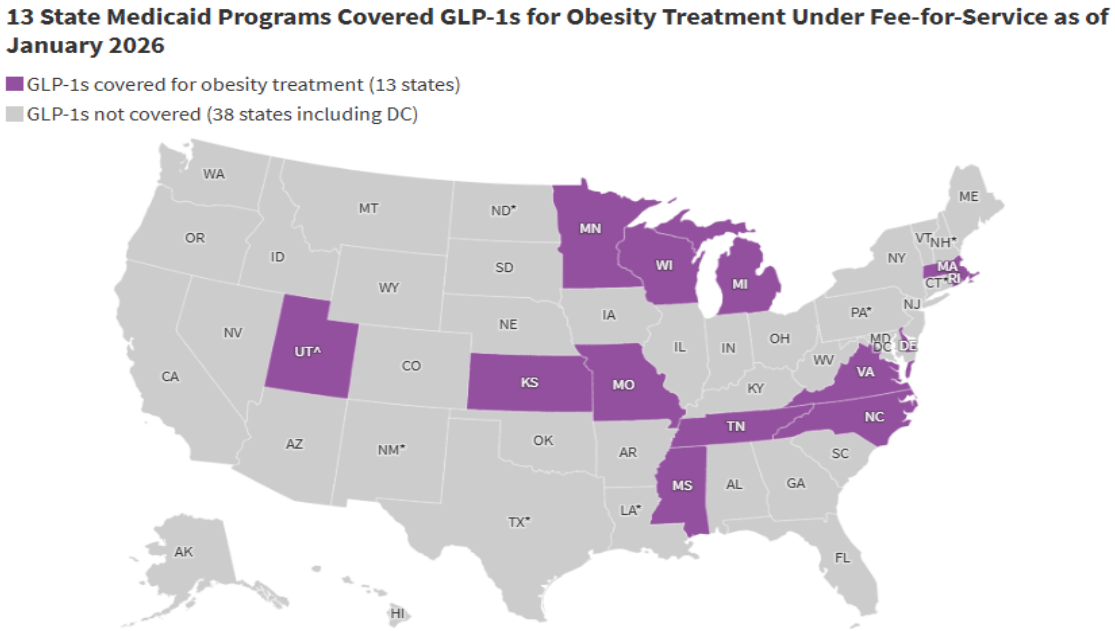
Berning, *JAMA Network Open*, 2025

Words of caution about the “GLP-1 era”

Blue Cross Blue Shield of Massachusetts will stop covering popular drugs for weight loss. Here's why.

- Overall, about one in four (26%) adults say they or someone in their household had problems paying for prescription drugs in the past year. The shares are higher among uninsured adults (41%), Hispanic adults (33%), Black adults (32%), and those with annual household incomes below $40,000 (33%).





Divino, *Diabetes Ther*, 2014; Essien et al, *JAMA Network Open*, 2023; KFF.org, last accessed Feb 2026; Source: KFF analysis of FDA website, accessed January 2026

Little known about dietary supplements and anti-obesity medications (AOMs) in asthma.

- Few dietary supplements specifically evaluated to improve asthma outcomes in patients with comorbid obesity or diabetes
- Studies limited by small sample size; subsequent evaluation in larger, **randomized clinical trials is underway for several agents**
- Example: L-citrulline, a semiessential amino acid

- FDA- approved AOMs include: phentermine, diethylpropion, benzphetamine (Regimex©), phendimetrazine, naltrexone/bupropion (Contrave©), phentermine/topiramate (Qysmia©), orlistat, setmelanotide (MC4R agonist for monogenetic obesity)
- None of these are approved or indicated specifically for asthma
- **None studied specifically in asthma populations**

Foer, Forno, Holguin, Cahill. *JACI:IP*, 2023

Med review can support interdisciplinary approach to weight loss in asthma.

Weight Effects of Medications by Therapeutic Class

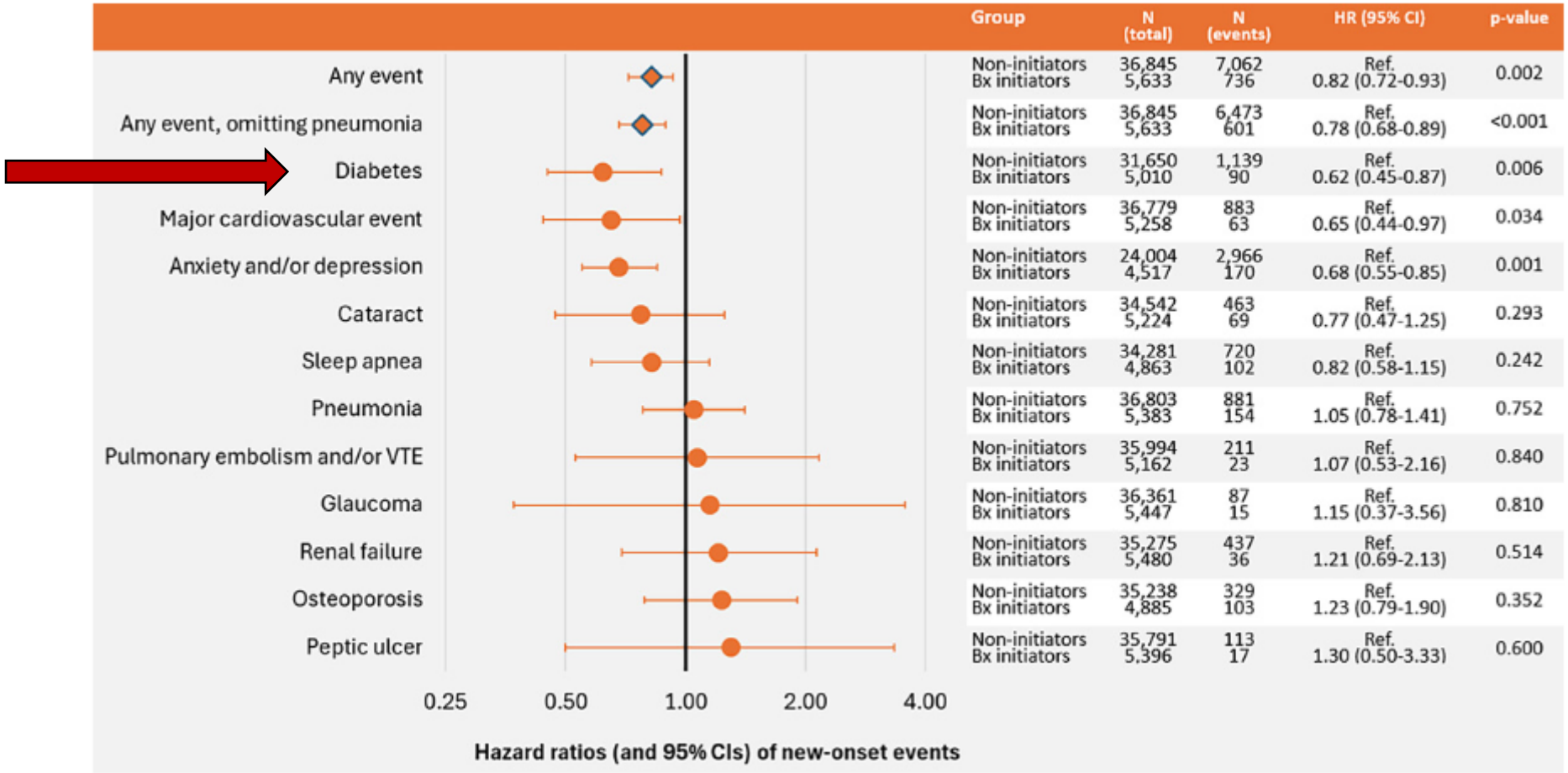
Therapeutic Class	Weight ↓	Weight Neutral	Weight ↑
Hypertension		ACEi, ARB, CCB	Beta blockers (older)
Type 2 Diabetes	Metformin • GLP-1 RAs • SGLT2i	DPP-4 inhibitors	Insulin • Sulfonylureas • TZDs
Antidepressants	Bupropion	SSRIs/SNRIs	Paroxetine • Mirtazapine • TCAs
Anticonvulsants	Topiramate • Zonisamide	Lamotrigine	Valproate • Gabapentin • Pregabalin

- Metformin: Possible asthma benefits
- DPP-4i: No association with asthma benefits
- Thiazolidinediones (TZD): RCTs with no benefit/potential harm in asthma
- Insulin: Potential harm in asthma (bronchoreactivity)

Polverino et al, AJRCCM, 2021;
Wu et al, *Ann Am Thorac. Soc*., 2019
Dixon AE, Holguin F. *Respir Res*. 2015
Ge, Foer, Cahill KN. *Pulmonary Therapy.* 2022
Kaler M et al. *JACI.* 2017

Table generated with ChatGPT (OpenAI, 2026)

Respiratory biologics reduce risk of adverse systemic steroid effects by 5 years.



	Group	N (total)	N (events)	HR (95% CI)	p-value
Any event	Non-initiators	36,845	7,062	Ref.	0.002
	Bx initiators	5,633	736	0.82 (0.72-0.93)	
Any event, omitting pneumonia	Non-initiators	36,845	6,473	Ref.	<0.001
	Bx initiators	5,633	601	0.78 (0.68-0.89)	
Diabetes	Non-initiators	31,650	1,139	Ref.	0.006
	Bx initiators	5,010	90	0.62 (0.45-0.87)	
Major cardiovascular event	Non-initiators	36,779	883	Ref.	0.034
	Bx initiators	5,258	63	0.65 (0.44-0.97)	
Anxiety and/or depression	Non-initiators	24,004	2,966	Ref.	0.001
	Bx initiators	4,517	170	0.68 (0.55-0.85)	
Cataract	Non-initiators	34,542	463	Ref.	0.293
	Bx initiators	5,224	69	0.77 (0.47-1.25)	
Sleep apnea	Non-initiators	34,281	720	Ref.	0.242
	Bx initiators	4,863	102	0.82 (0.58-1.15)	
Pneumonia	Non-initiators	36,803	881	Ref.	0.752
	Bx initiators	5,383	154	1.05 (0.78-1.41)	
Pulmonary embolism and/or VTE	Non-initiators	35,994	211	Ref.	0.840
	Bx initiators	5,162	23	1.07 (0.53-2.16)	
Glaucoma	Non-initiators	36,361	87	Ref.	0.810
	Bx initiators	5,447	15	1.15 (0.37-3.56)	
Renal failure	Non-initiators	35,275	437	Ref.	0.514
	Bx initiators	5,480	36	1.21 (0.69-2.13)	
Osteoporosis	Non-initiators	35,238	329	Ref.	0.352
	Bx initiators	4,885	103	1.23 (0.79-1.90)	
Peptic ulcer	Non-initiators	35,791	113	Ref.	0.600
	Bx initiators	5,396	17	1.30 (0.50-3.33)	

Note: obesity not included as a study outcome

Sadatsafavi, ISAR SOLAR II Working Group, *AJRCCM*, 2025

Existing study of BMI on asthma response varies by individual biologics, study design: most show benefit.

Table 1. Summary of findings from studies examining response to asthma biologic therapies by BMI or obesity

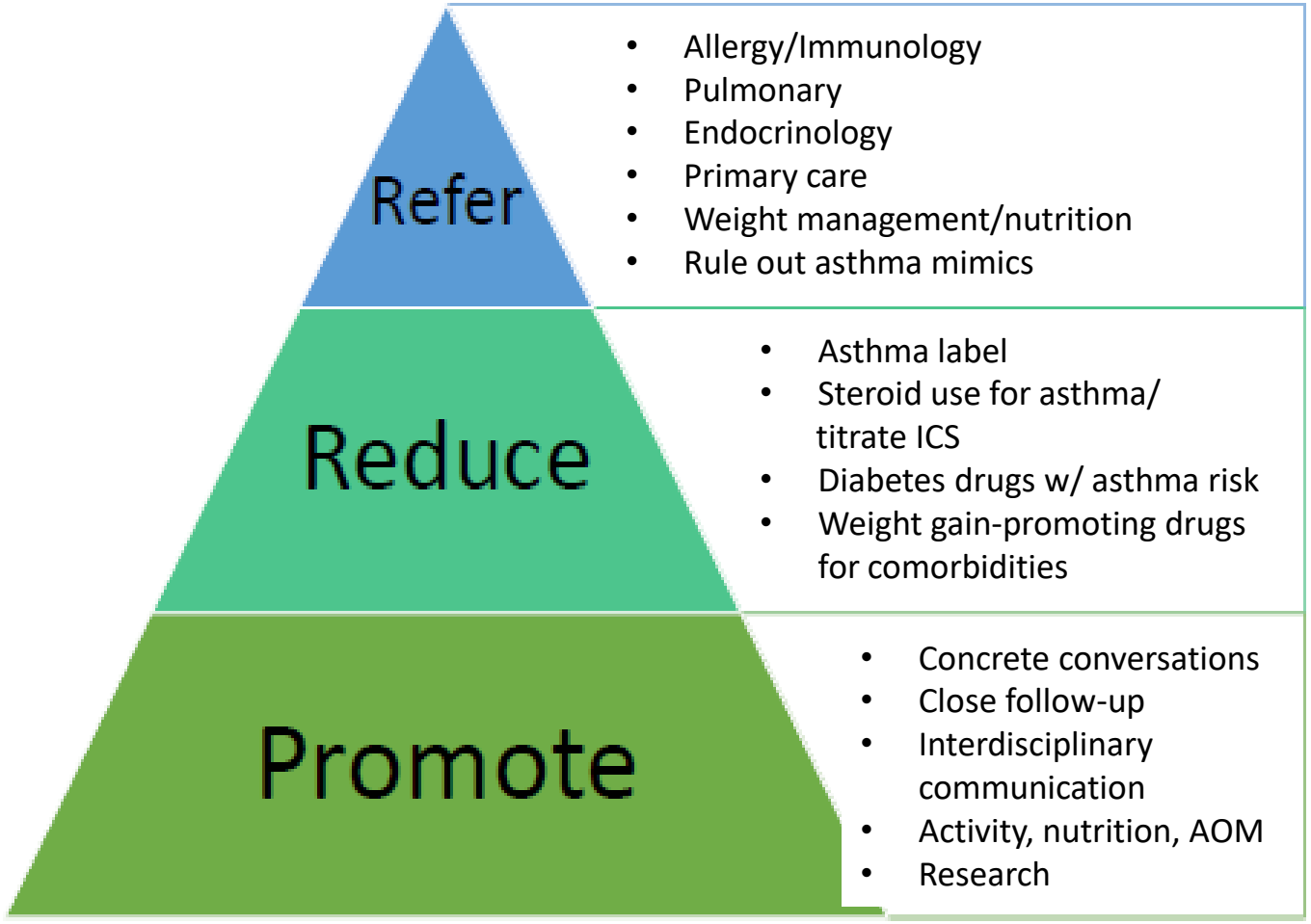
	Impact of BMI on Treatment Response		
Monoclonal Antibody	**Neutral**	**Positive**	**Negative**
Children			
Omalizumab	Asthma control[60] Reduction in ICS dose[60]	Exacerbation rate reduction[60]	
Adults			
Omalizumab	Exacerbations[65,68] FEV1[61,64,68] Asthma control[61,64,65,68] Reduction in ICS dose[61,65]	Exacerbation rate reduction[61] FEV1[63,67] Asthma control[62,63]	Exacerbations[62-64] FEV1[65] Asthma control[66,67]
Dupilumab	Exacerbation rate reduction [69,70] FEV1[69,70]		Asthma control[70*] Clinical remission[72]
Mepolizumab	Exacerbation rate reductions[75,78-80] Asthma control[75,78-80] FEV1[78-80]		Asthma control[82] FEV1[75] Being a "super-responder"^[83]
Reslizumab	Exacerbations[84]		
Benralizumab	Being a "Responder"#[88]		Exacerbation rate reduction[87] FEV1[87]
Tezepelumab	Exacerbations[93,94]		

Althoff et al, *AJRCCM*, 2024; Gonem et al, *JACIIP,* 2025; Foer… Akenroye*, JACIIP*, 2026

Metabolic Asthma Clinic

Mission: The Metabolic Asthma Clinic (MAC), within Mass General Brigham's Allergy/Clinical Immunology Clinic, serves patients with asthma and comorbid obesity, prediabetes, and/or type 2 diabetes. By intentionally integrating metabolic comorbidity considerations into asthma management, MAC aims to provide guideline-informed asthma care, improve clinical asthma outcomes, advance research in metabolic asthma, and facilitate education for trainees.

Early framework for re-thinking asthma management in obesity and T2D.



Adapted from Foer, Forno, Holguin, Cahill. *JACI:IP*, 2023

Thank you.

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Vinik, Kaye and Karol families

Jeff and Penny Vinik
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