Mass General Brigham

Severe Asthma, the Biologics, and Population Health Management

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March 2026

COI: I have no relevant conflicts to disclose

Objectives

To:

- Highlight the impact of biologics in asthma
- Identify population health challenges in optimizing biologics use
- Discuss system-level management issues/strategies

Severe asthma bears a disproportionate share of asthma burden

Severe asthma (~5–10%)
Majority of hospitalizations & cost

Moderate asthma
Frequent exacerbations

Mild asthma
Largest population
but lower cost

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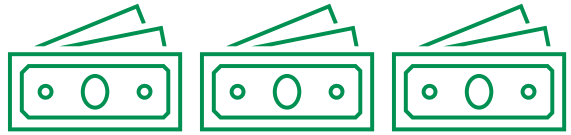

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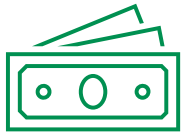
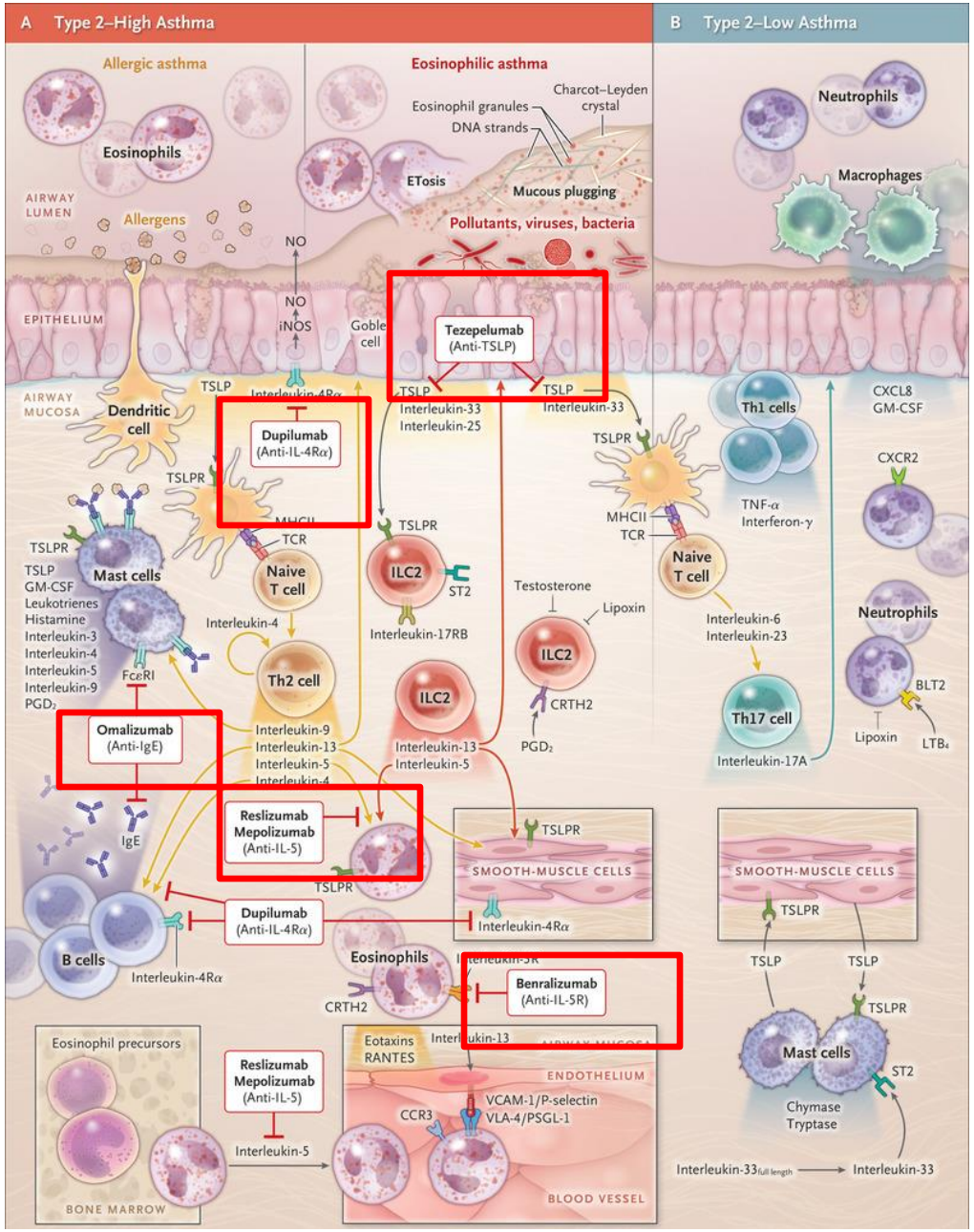
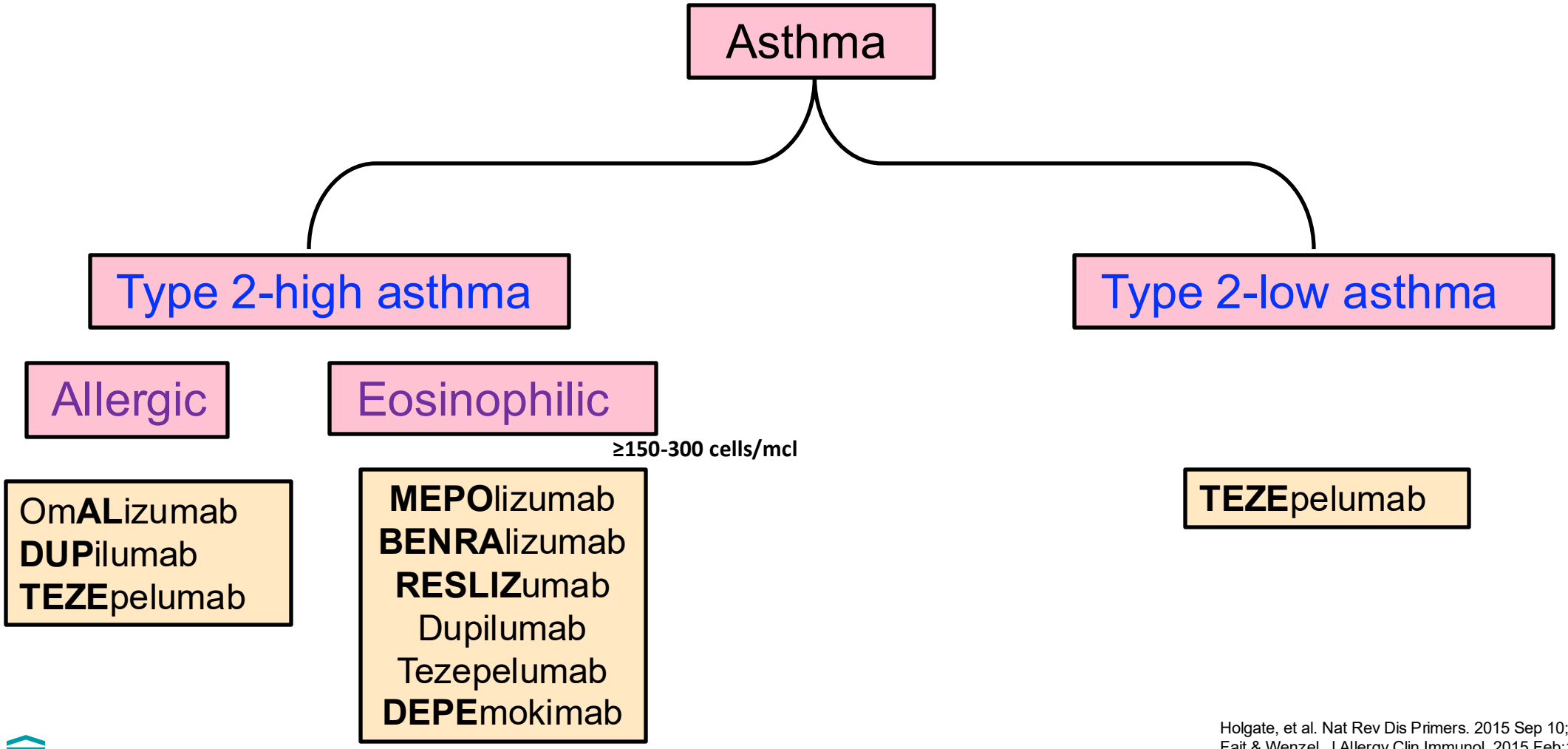


~~Six~~ Seven monoclonal antibodies are now approved for asthma



Seven biologics are currently approved for asthma

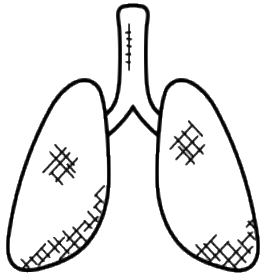
Most are approved for the T2-high endotype



Holgate, et al. Nat Rev Dis Primers. 2015 Sep 10;1(1):15025.
Fajt & Wenzel, J Allergy Clin Immunol. 2015 Feb;135(2):299-310;

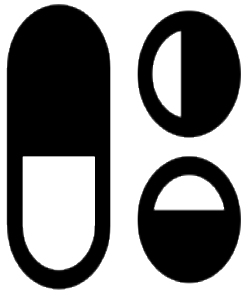
These biologics all worked relatively well in randomized trials

Reduced exacerbations (30 - 70%)



Improved lung function (FEV1) (~90-200 milliliters, ~5-10% increase)

Improved quality of life (modest improvements)

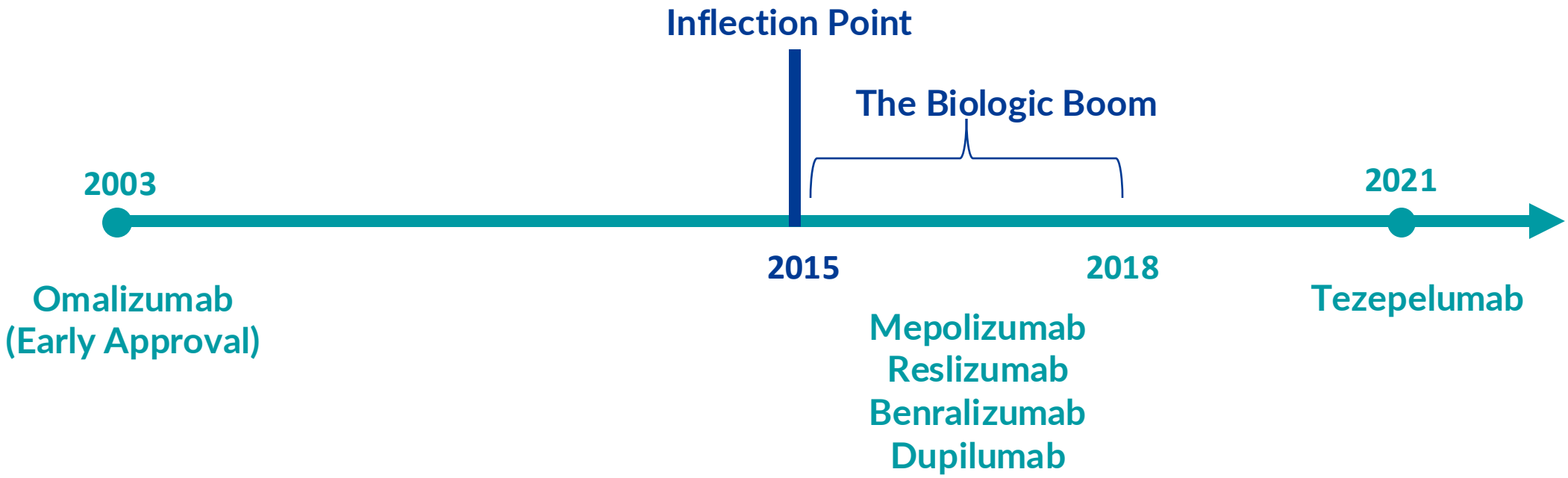


Steroid-sparing (Halving of dose to complete elimination)

MENSA, NEJM 2014
MUSCA, LancetResp 2017
SIROCCO, Lancet 2016
CALIMA, Lancet 2016
Wenzel, Castro et al, Lancet 2016
Castro, Corren et al, NEJM 2018
Akenroye et al., JACI. 2022 Nov;
Nopospon et al, JACI. 2023 Mar;
Akenroye et al. JACI Pract. 2024 Feb

Research question:
What has been the population-level impact of biologic therapies in asthma?

The 2015 "Respiratory Biologic Boom"

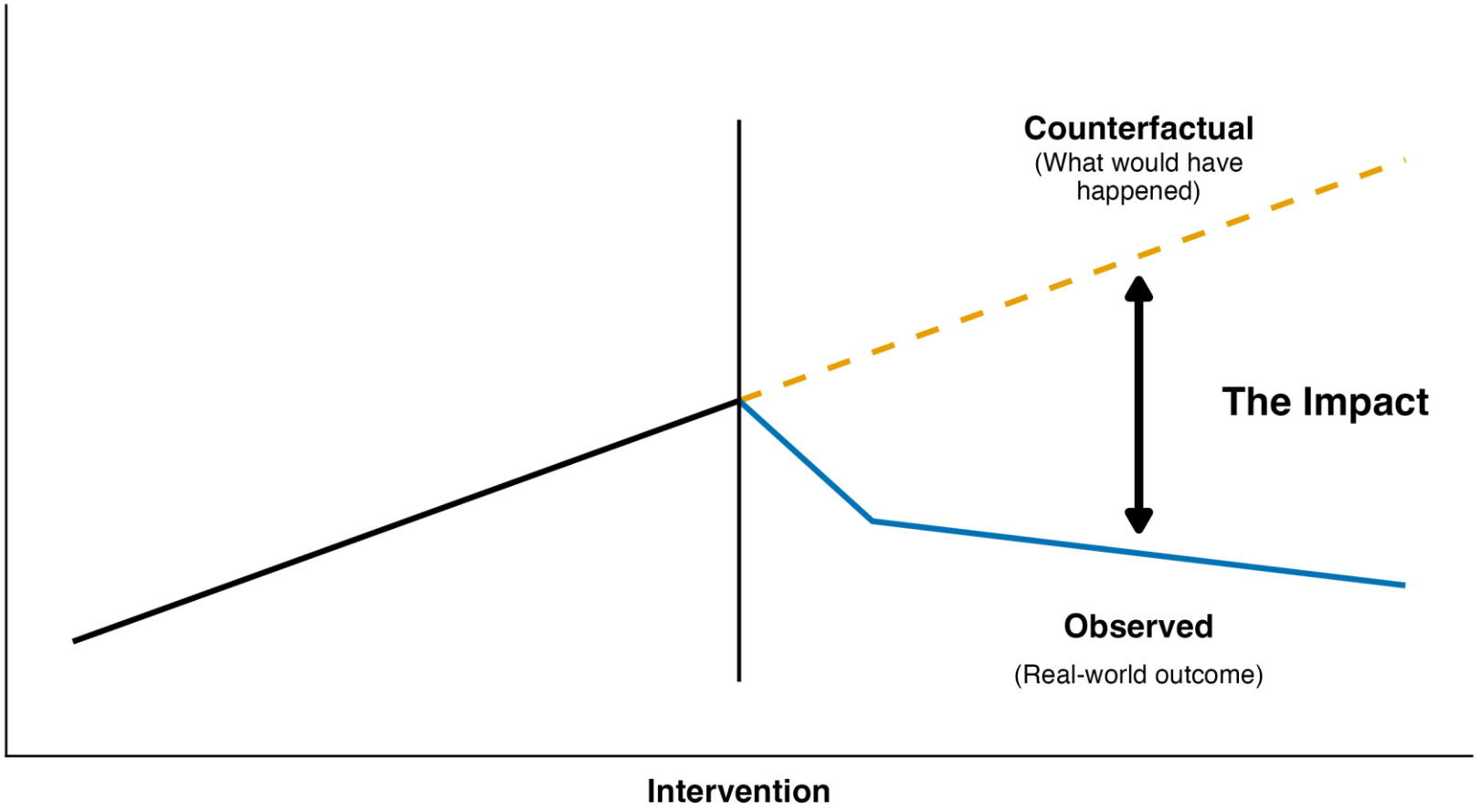


Precision targeting of eosinophilic inflammation
Shifting from symptom management to root-cause treatment
Research question: Have these changes improved asthma outcomes, in general, at the population level?

Tu et al. under review.

Study Design: Interrupted Time Series Analysis

Population: 5,318 adults (≥18 years) with asthma.
Window: January 2006 – May 2025
Concept: Comparing observed reality vs. counterfactual projection.

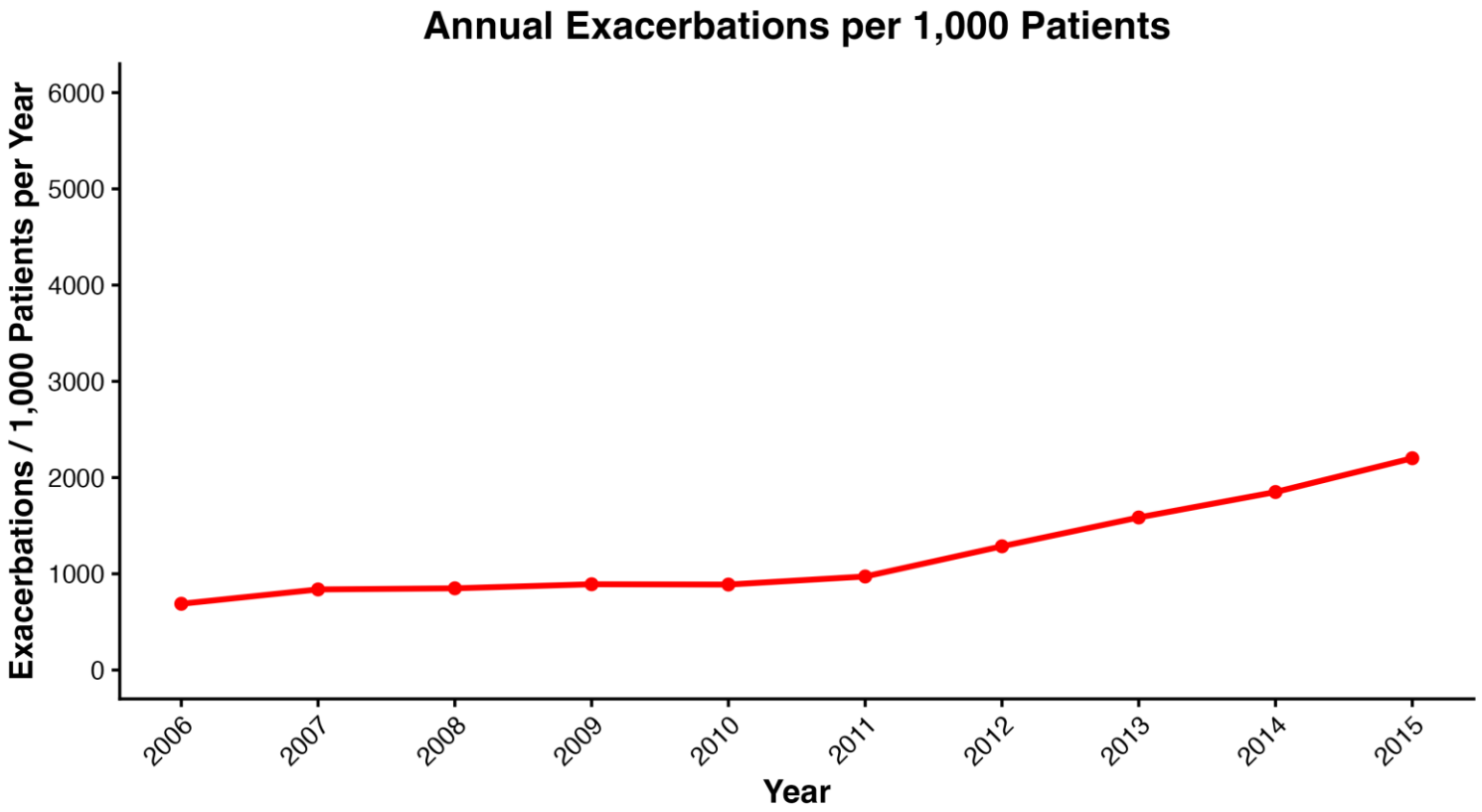


The Pre-2015 Landscape : A Rising Burden

Prior to 2015, asthma control was worsening at the population level.

Standard therapies (ICS, LABA) were insufficient for severe phenotypes.

Result: +155 exacerbation events per 1,000 patients/year (p<0.001).



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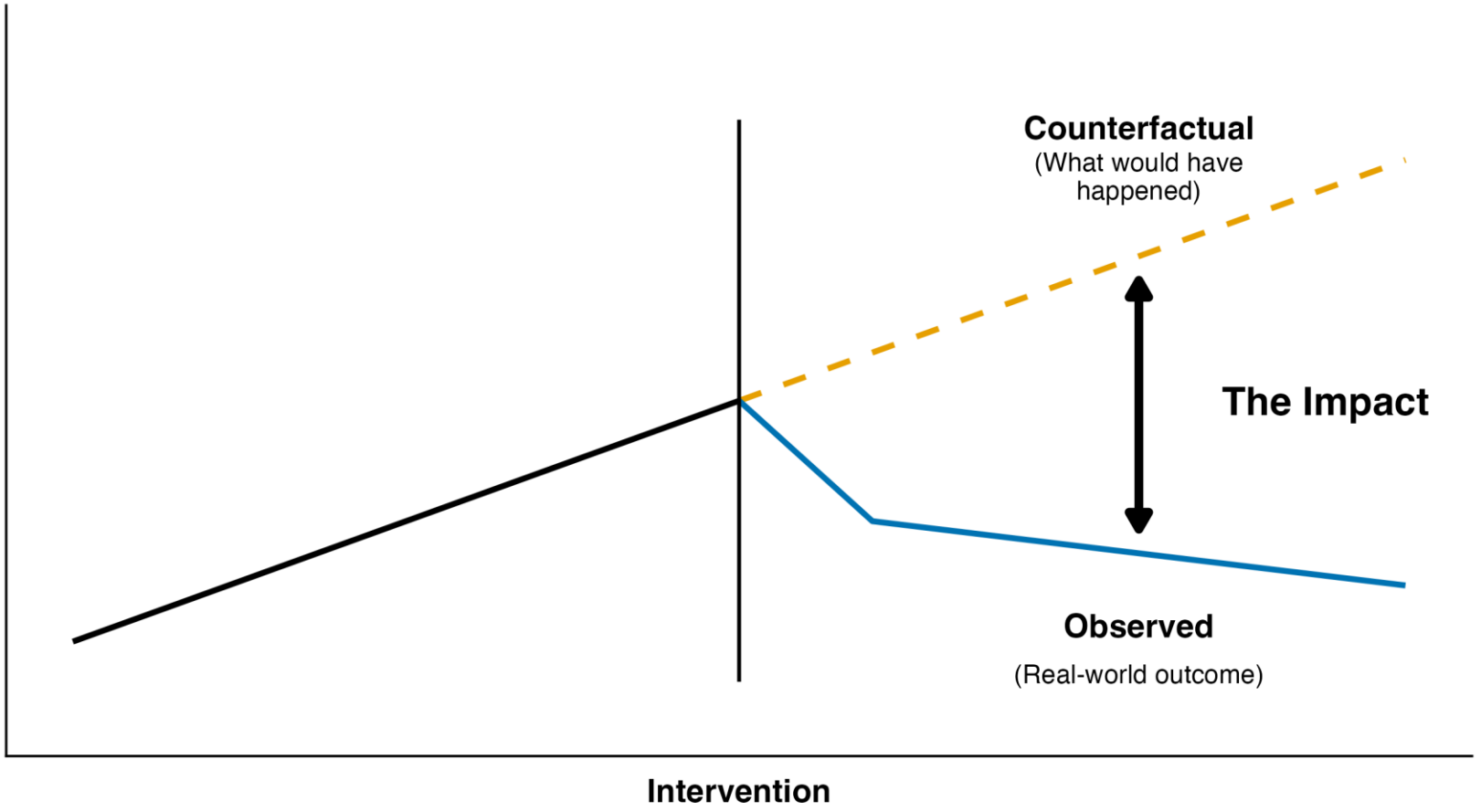
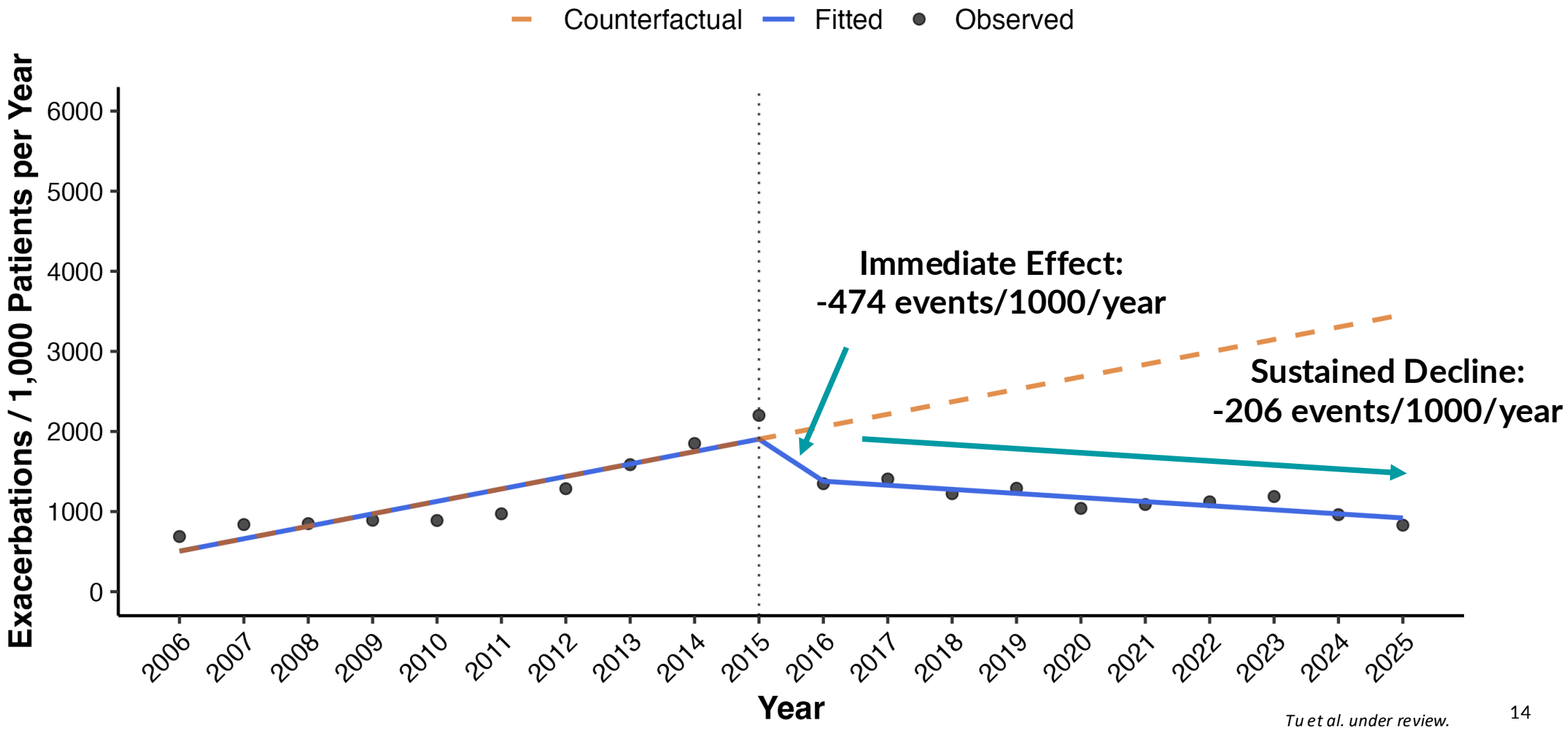
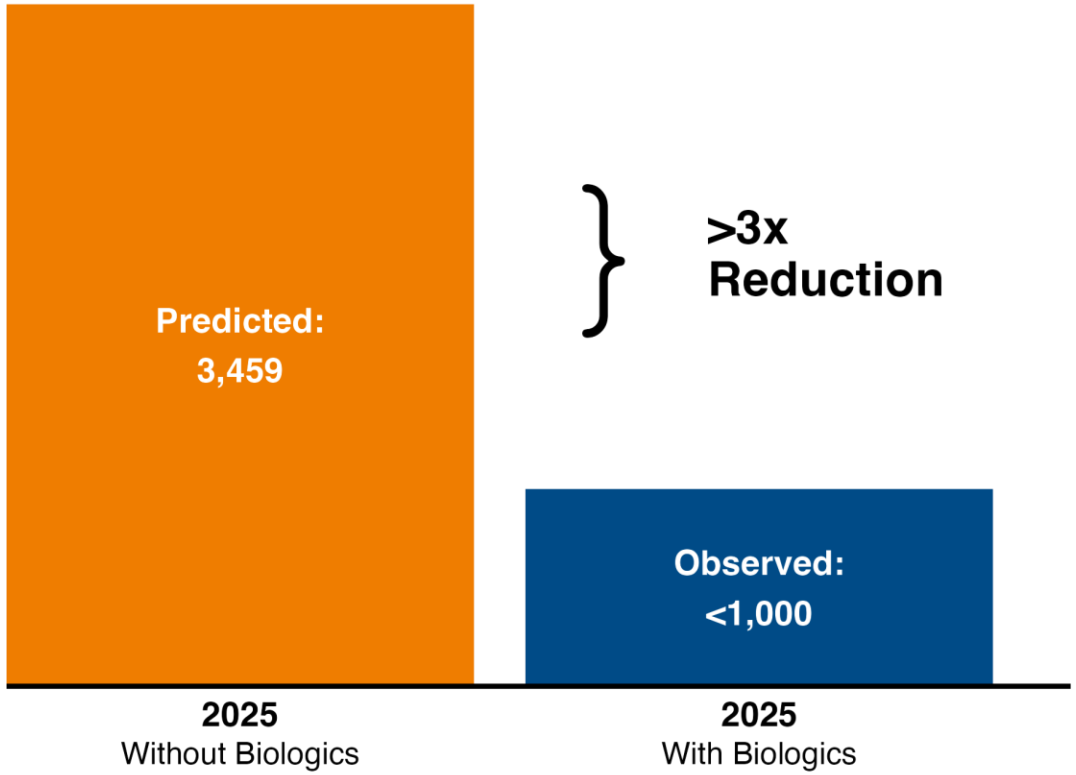


There were immediate and sustained gains



Tu et al. under review.

The 2025 Outlook: A significant reduction in morbidity (exacerbation counts)

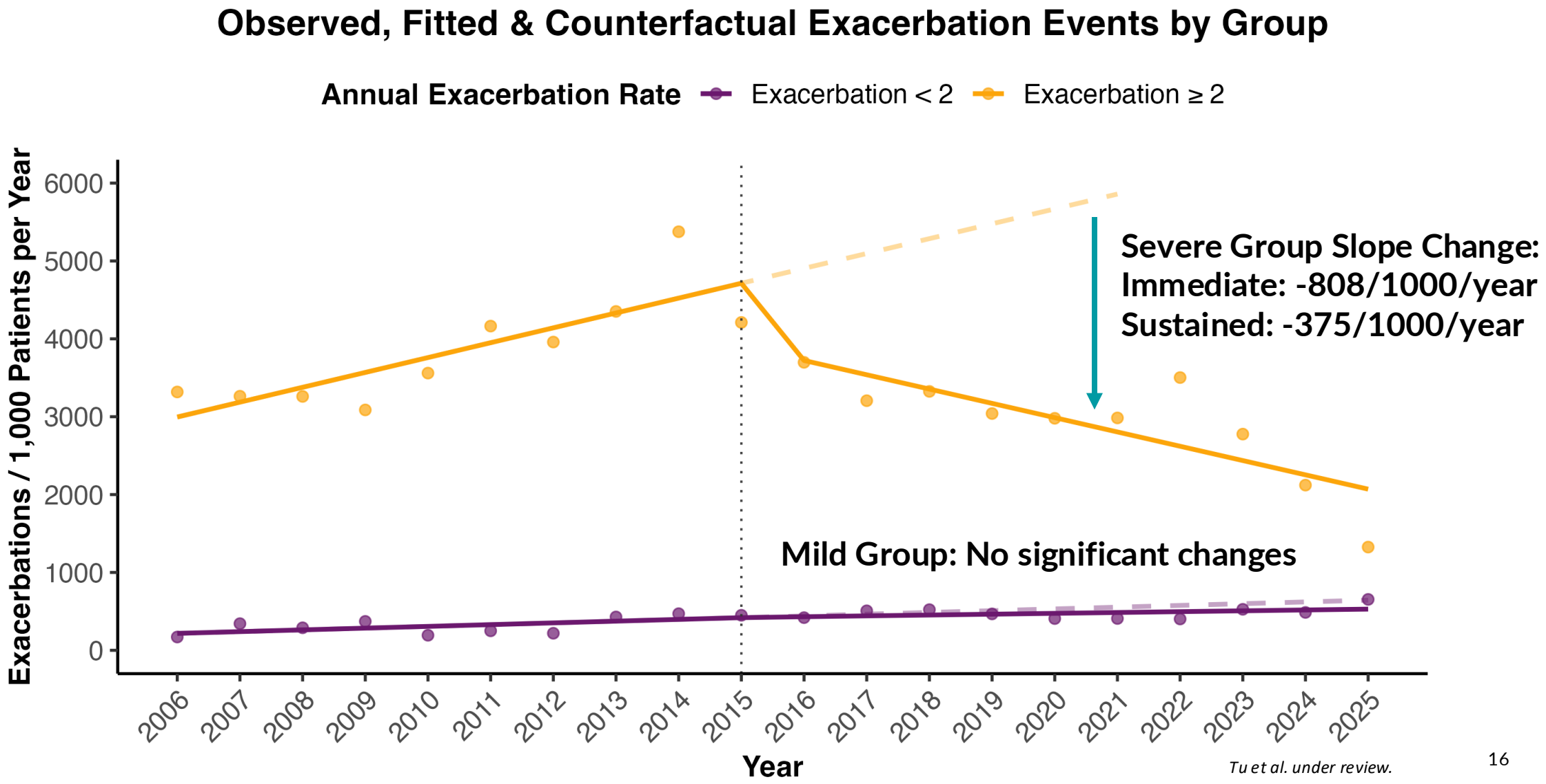


By 2025, the gap between the pre-biologic trajectory and the current reality represents thousands of prevented exacerbations

This translates to a significant reduction in hospitalizations, ER visits and patient burden.

Tu et al. under review.

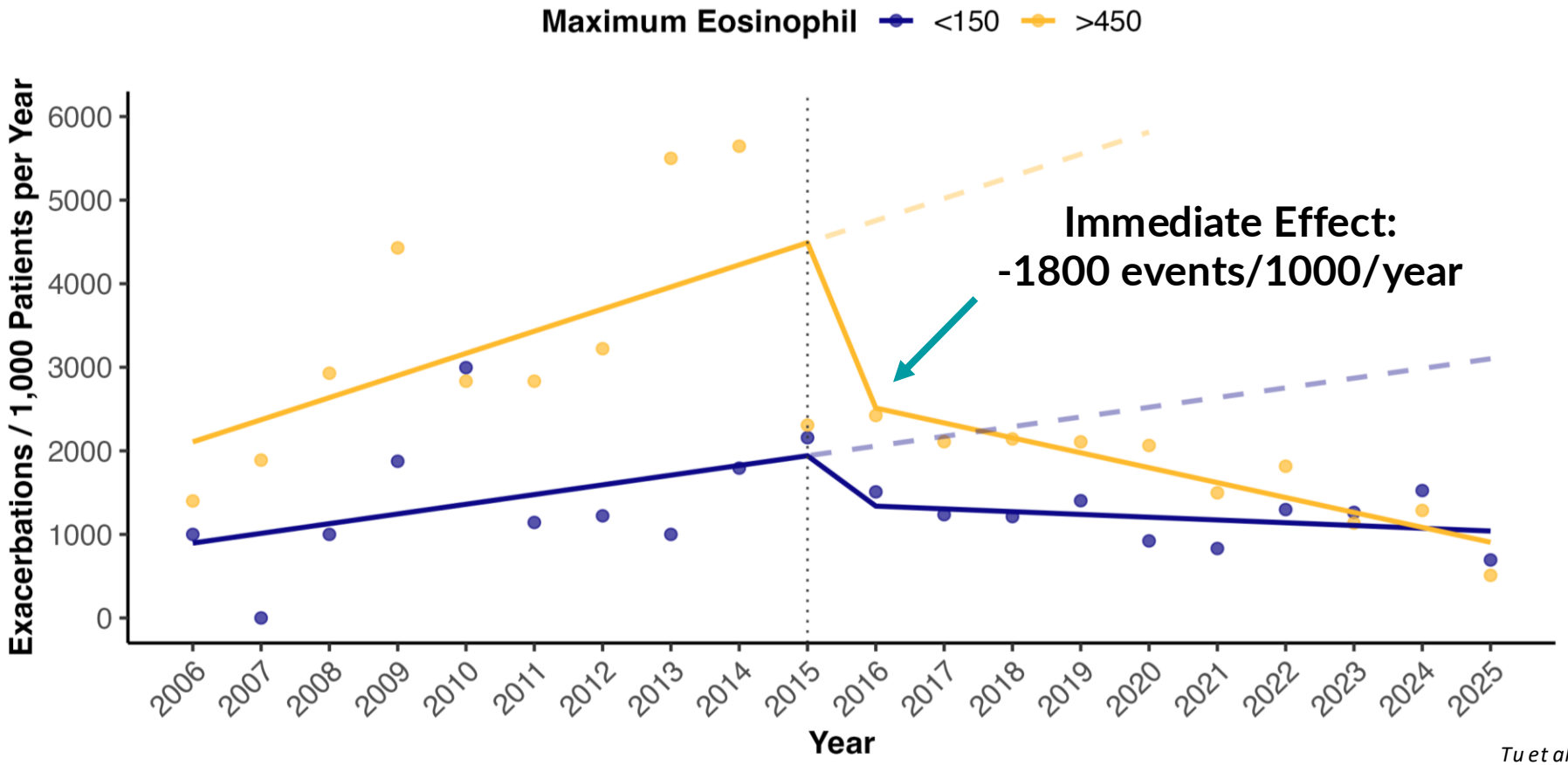
Closing the Outcome Gap for Patients with Severe Diseases



Tu et al. under review.

Greatest reduction was in the subgroup with eosinophilic asthma

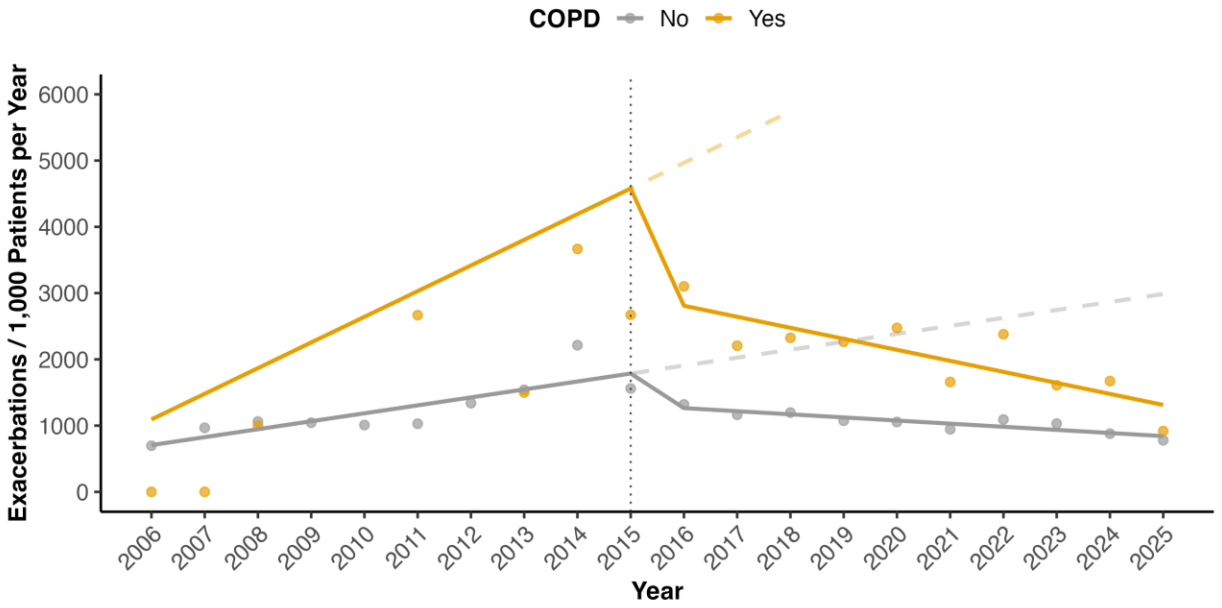
Comparing the lowest eosinophil group vs. the highest group

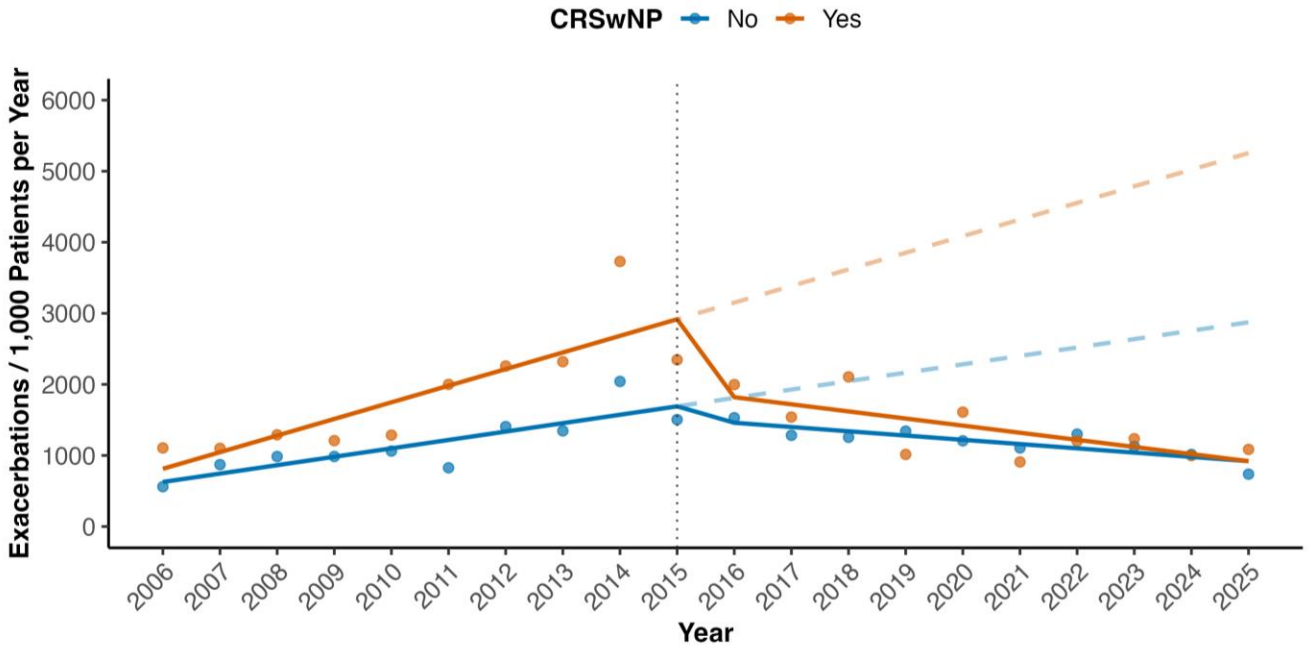


Tu et al. under review.

Shared Benefits: COPD & CRS with nasal polyposis

Patients with 'difficult to treat' overlapping airway diseases derived the greatest relative benefit from biologic therapy.
Biologics attenuated/closed the outcome gap- not so much for COPD

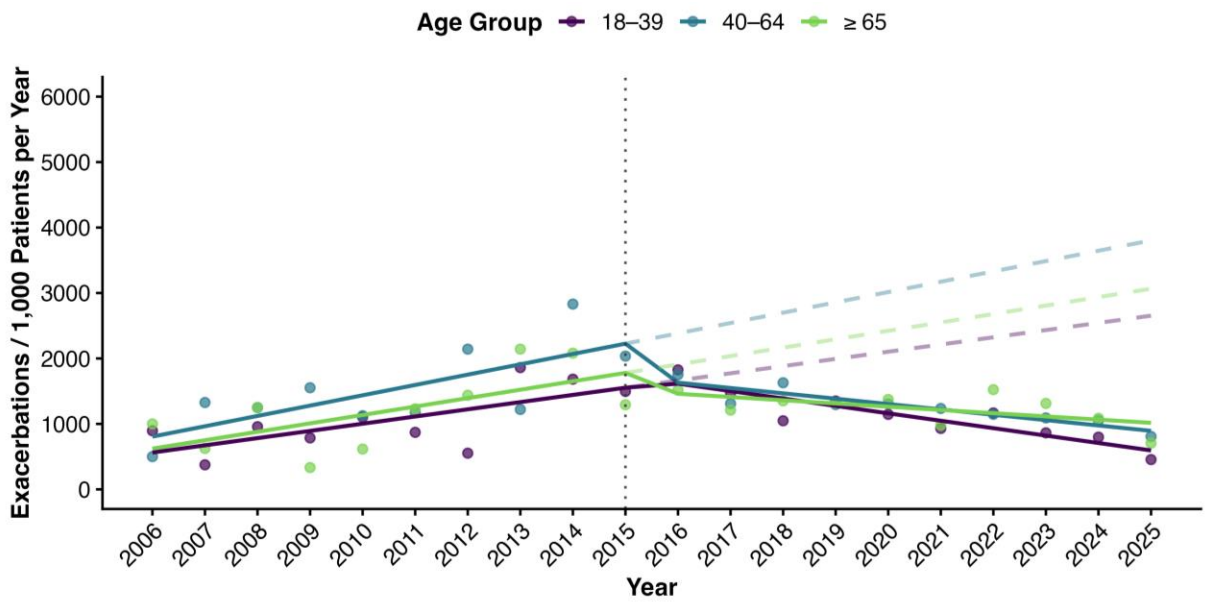




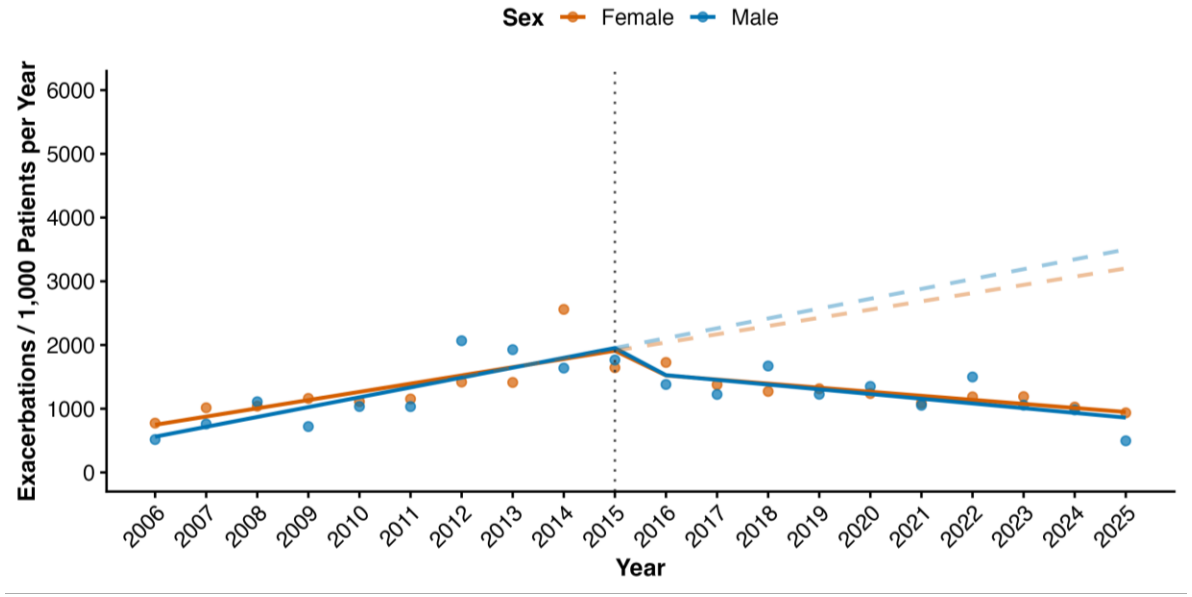
Tu et al. under review.

Universal Benefits across demographic groups

✓**Age Groups** (18-39, 40-64, 65+)



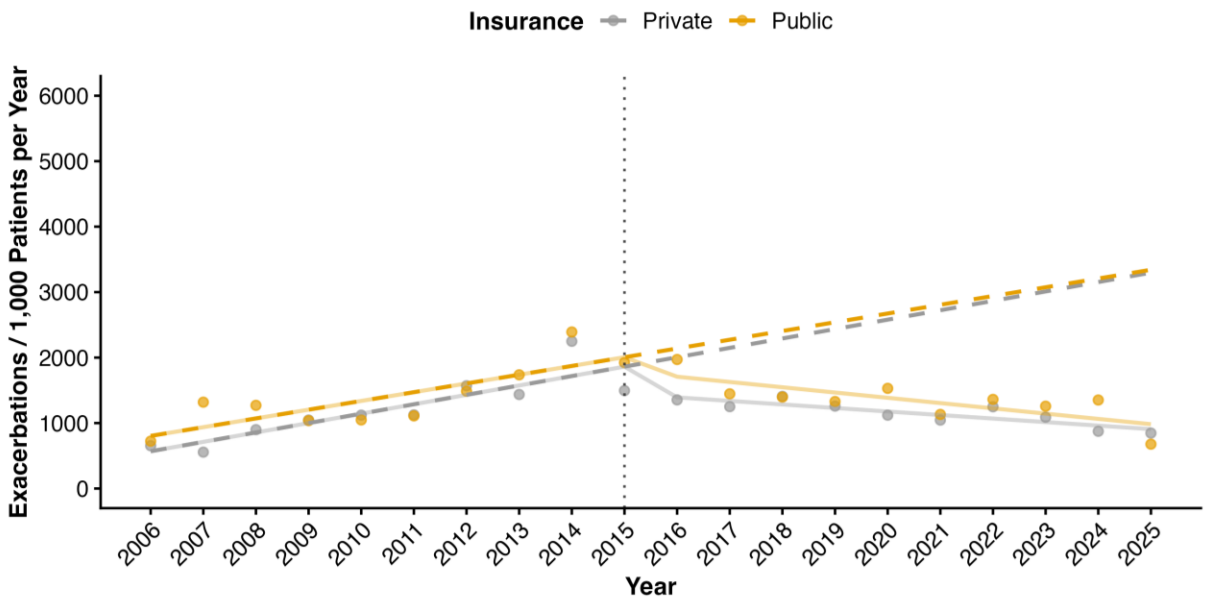
✓**Sex** (Male & Female)



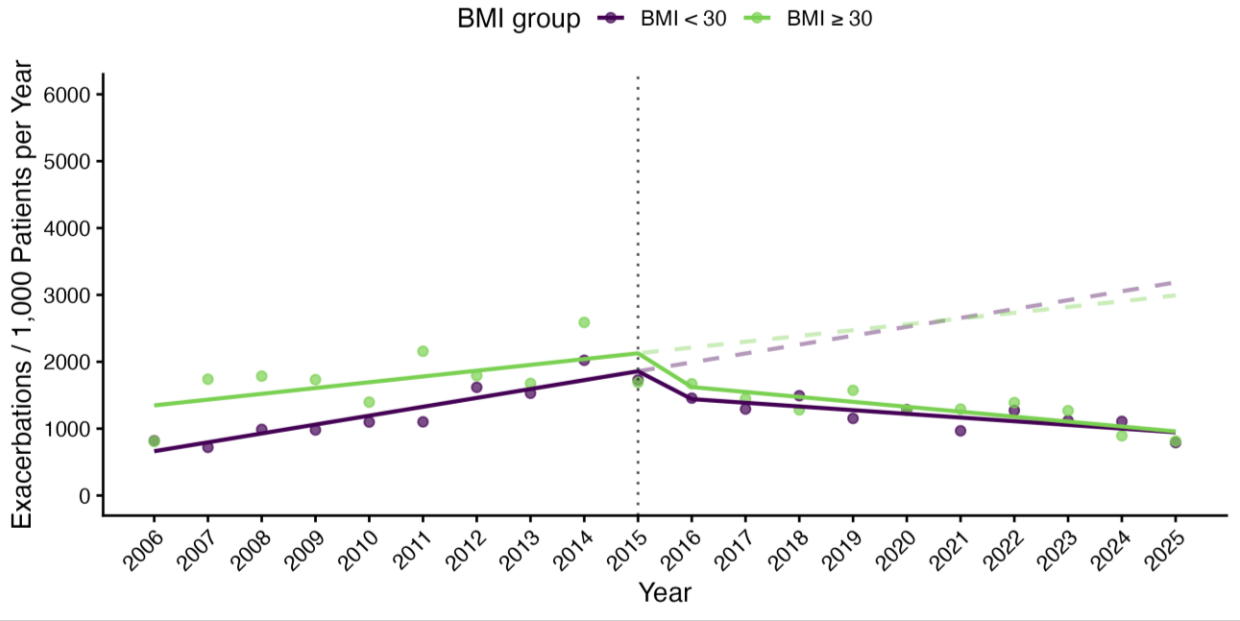
Tu et al. under review.

Universal Benefits across demographic groups

✓**Insurance** (Public & Private)



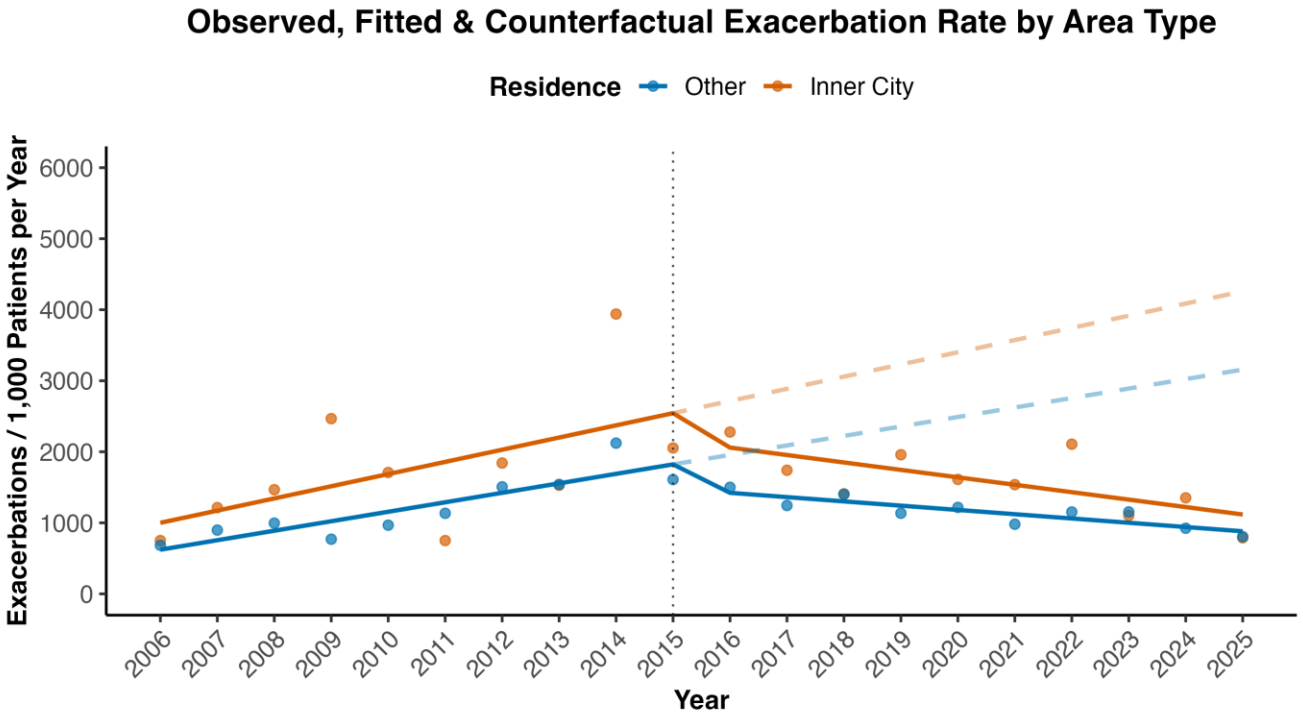
✓**Obesity** (BMI ≥30, BMI <30)



Tu et al. under review.

Persistent disparities with Environmental Determinants

The Inner-City Gap



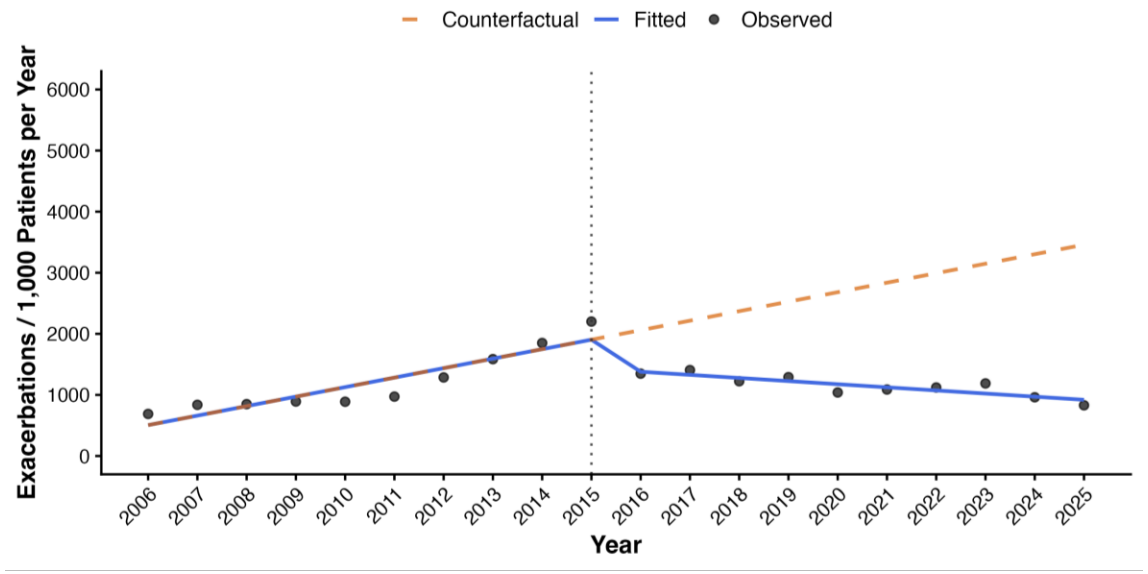
✓Observed benefits derived from patients with:

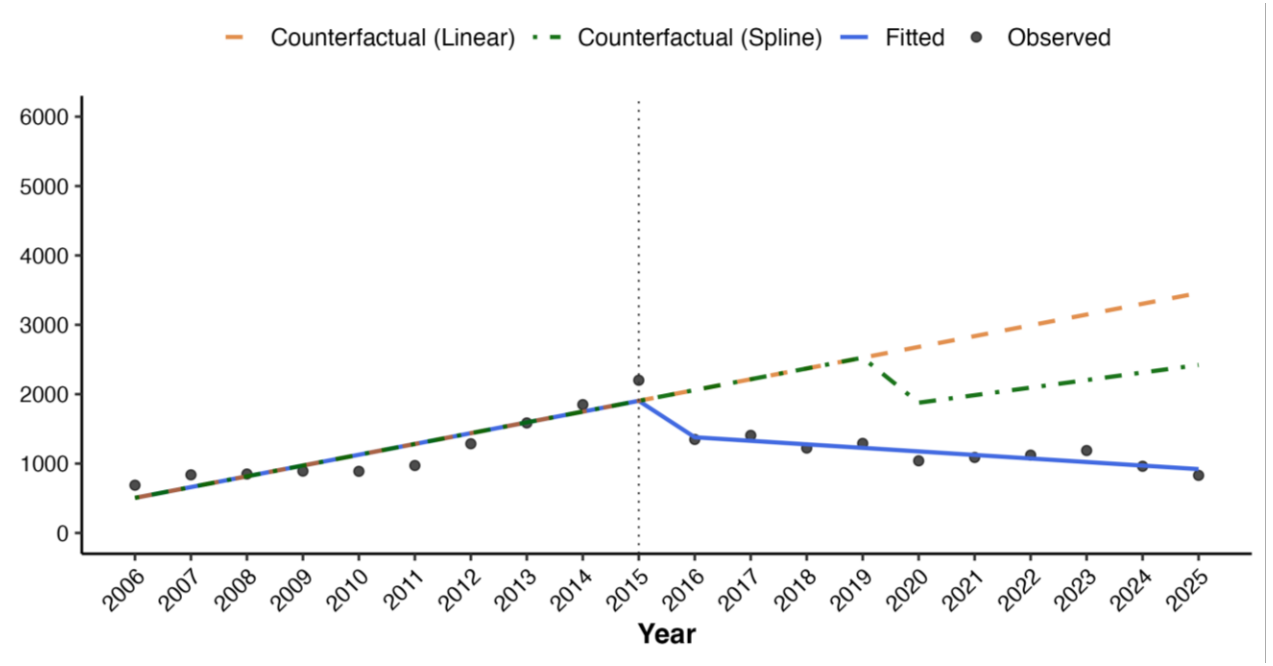
- severe symptoms
- eosinophilic phenotypes
- comorbid airway conditions

✓Biologics reduced exacerbations for all, but some gap remains based on where patients live.

Tu et al. under review.

Robustness of Findings: Adjusted for COVID-19 Impact





- After reducing counterfactual predictions by 30% (2020-2025), the observed rate (920/1,000) remained significantly lower than predicted (2,421/1,000).

- Conclusion: The signal is unlikely to be an artifact of the pandemic.

Tu et al. under review.

Study limitations

✓An extrinsic event that coincided with biologics introduction may have led to these effects

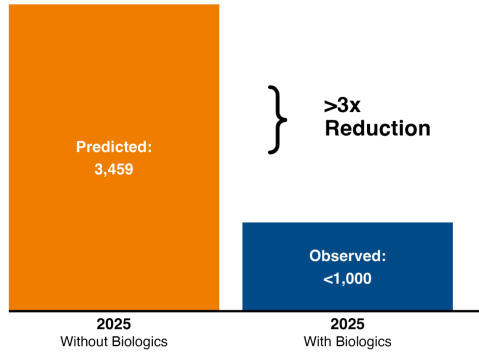
- ✓ Subgroup analyses with mild vs. severe; eosinophilic vs non-eosinophilic, etc., suggest this is less likely.

✓Single center study

- ✓ Most patients are privately insured

Tu et al. under review.

Redefining Severe Asthma Care



The **Biologic Boom** has fundamentally transformed the trajectory of severe asthma care.

We are **bridging the outcome gap** between severe and mild asthma in a real-world setting.

We still need to close the gap for patients with **COPD** and those living in the **inner-city**.

Tu et al. under review.

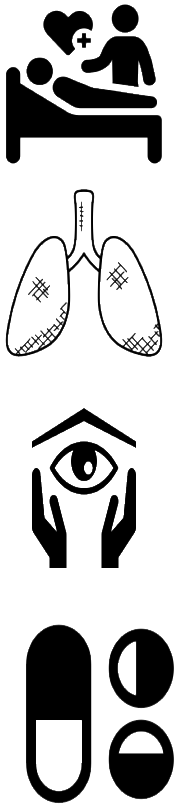
~~Six~~ Seven monoclonal antibodies are now approved for asthma

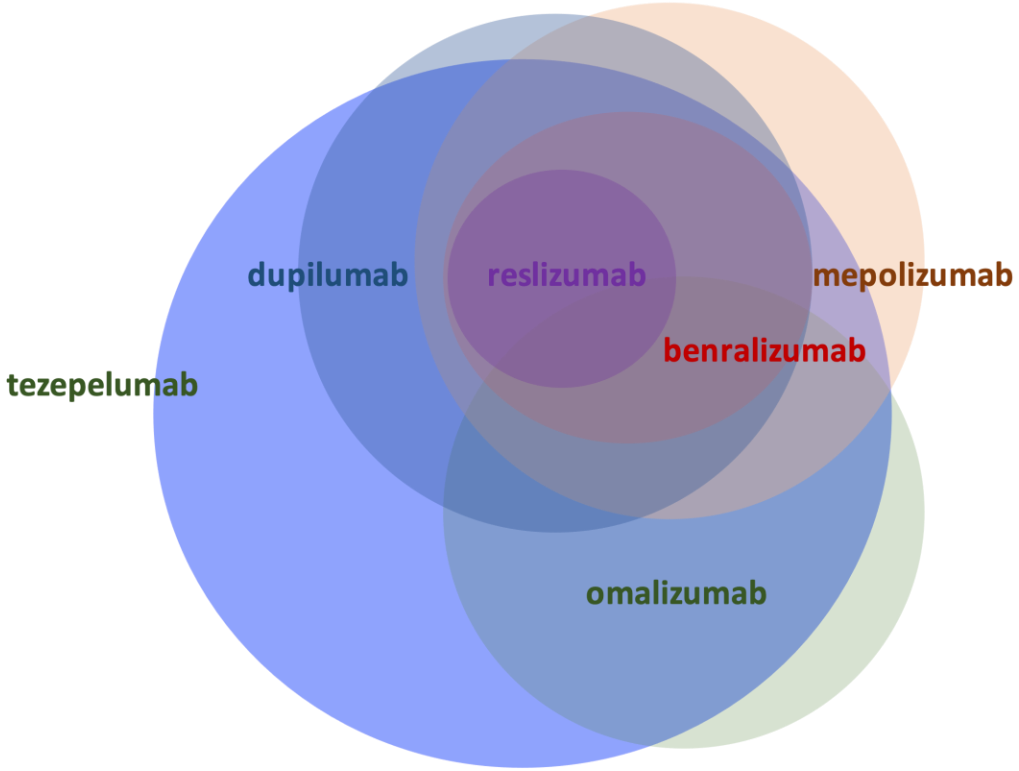
Biologics are effective only if used!

Challenges with managing asthma in the age of biologics

Challenge #1: Limited options for T2-low asthma.
Challenge #2: Suboptimal therapy selection in T2 asthma
Challenge #3: Biomarkers have limited predictive accuracy
Challenge #4: Cost and access barriers
Challenge #5: Diminishing long-term effectiveness?
Challenge #6: When should we start therapy?
Challenge #7: Can we combine or cycle respiratory biologics?
Challenge #8: When do we conclude its not working?
Challenge #9: Biologics do not fix socioeconomic issues

Biologics are effective, but not in distinct patients

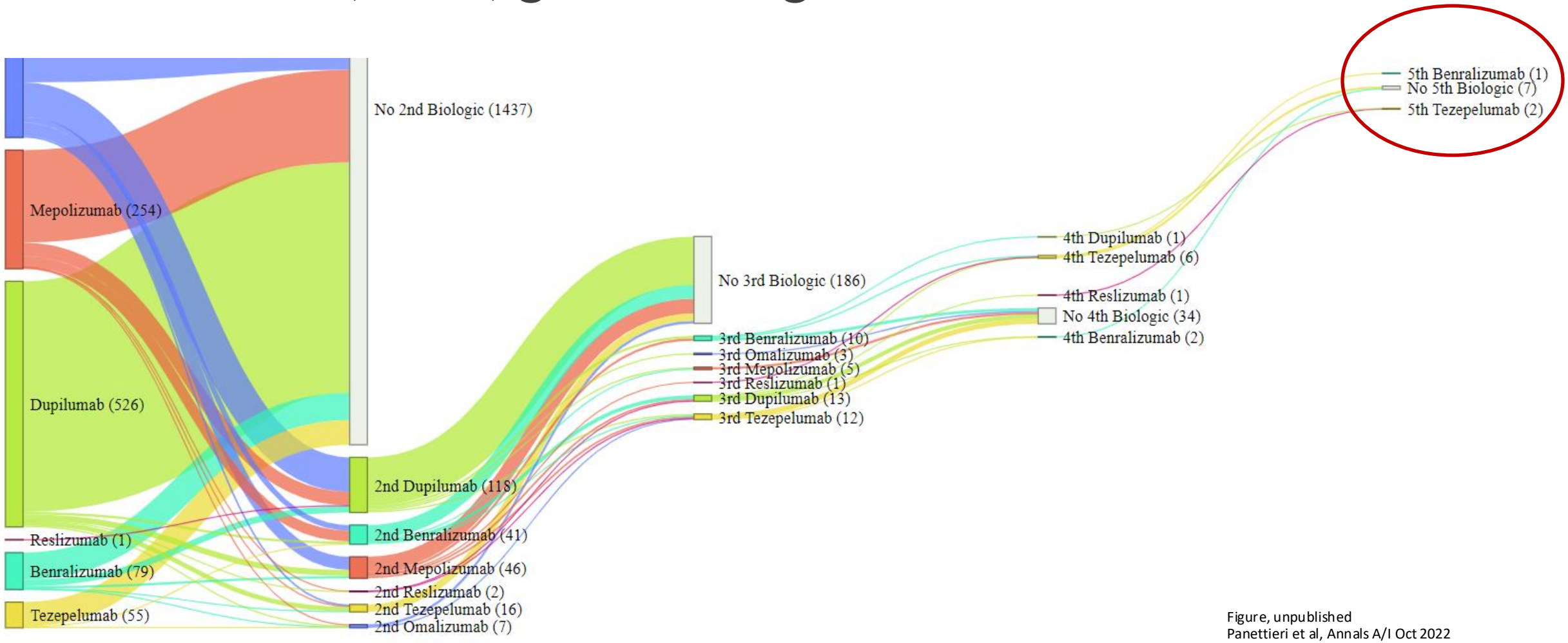




Adopted, Akenroye et al., JACI Apr 2020

Challenge #2: Suboptimal therapy selection in T2 asthma

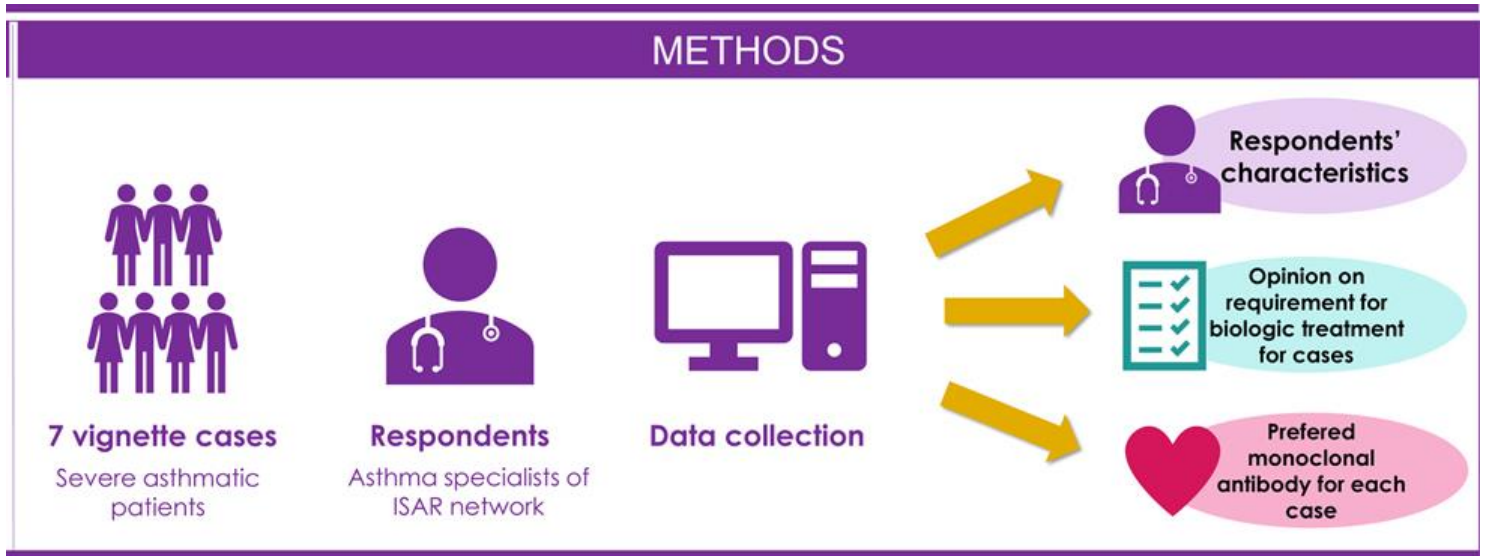
We sometimes (often) get it wrong

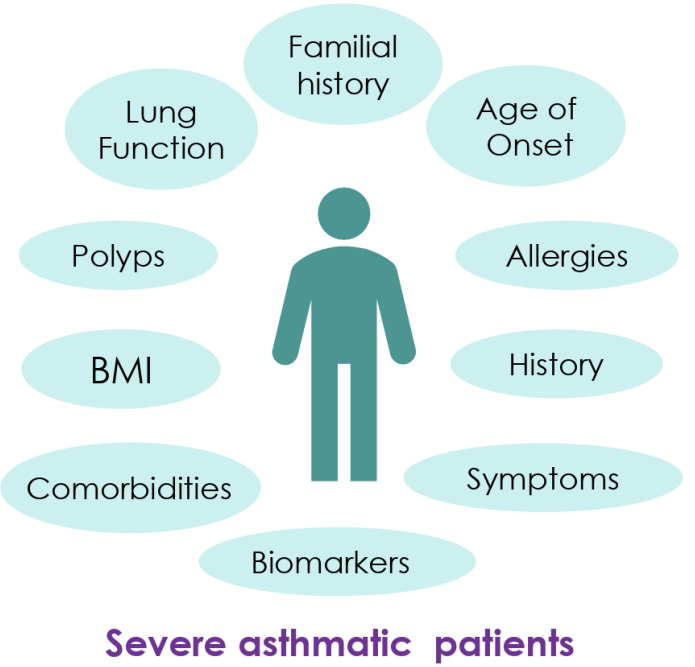


Figure, unpublished
Panettieri et al, Annals A/I Oct 2022
Akenroye et al, JACIIP Nov 2022
Akenroye et al, Allergy Apr 2023

Challenge #2: Suboptimal therapy selection in T2 asthma

Therapy selection is overly provider-dependent





Gwet's Agreement Coefficient (AC1): poor-slight (≤0.20), fair (0.21-0.40); moderate (0.41-0.60); substantial (0.61-0.80); excellent (≥0.80)

Côté, Beaulé et al, JACIIP, Jan 2025

Challenge #2: Suboptimal therapy selection in T2 asthma

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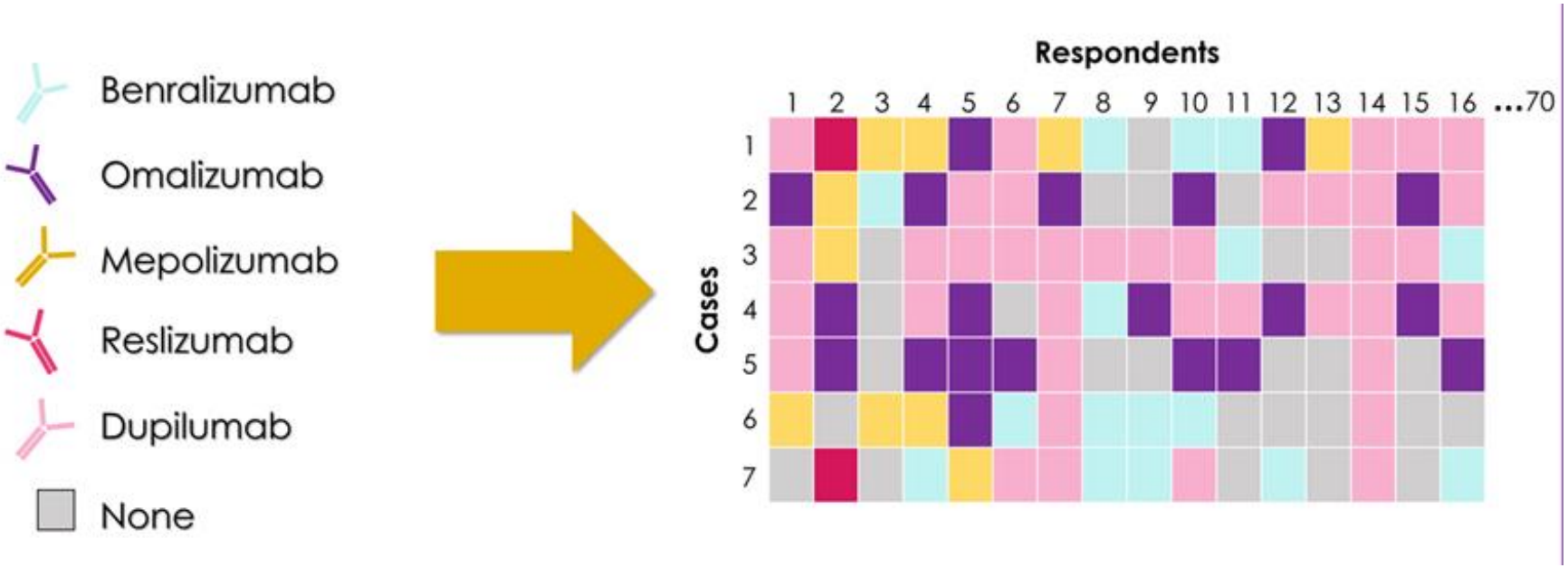

Agreement on the choice of treatment was fair in both the pilot and in the international survey

Côté, Beaulé et al, JACIIP, Jan 2025

Challenge #2: Suboptimal therapy selection in T2 asthma

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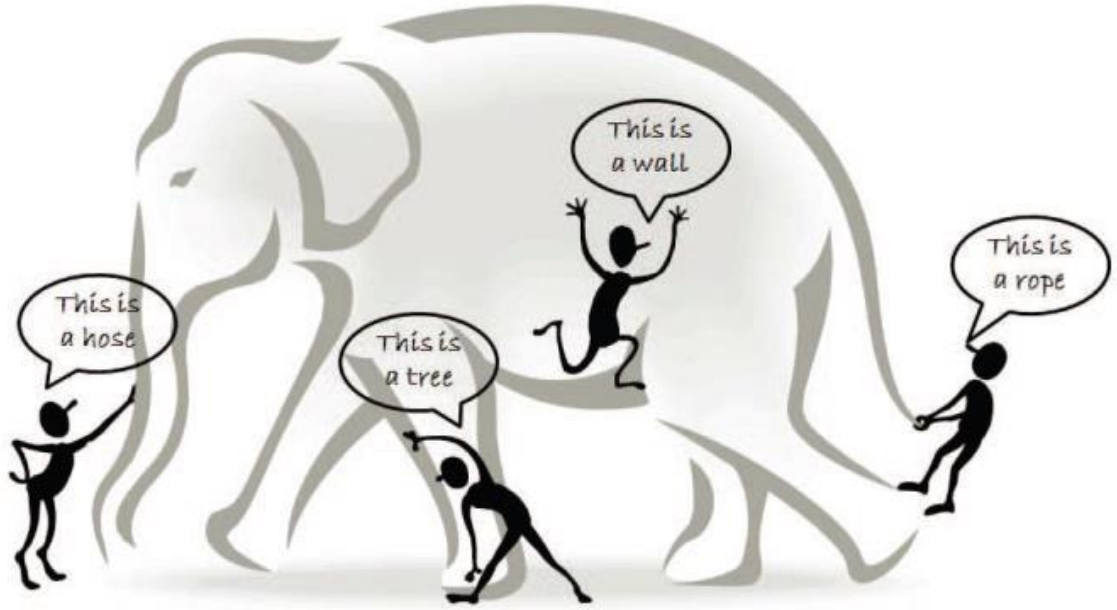

“The justification for therapeutic choice varied widely between specialists.”

Côté, Beaulé et al, JACIIP, Jan 2025
Gupta. & El Taeib; JMEST, March 2015

Challenge #4: Cost and access barriers

TABLE 2 Health Care Sector Cost-Effectiveness Results for the Biologics

	Annual Price, $[a]	Cost per QALY, $
Omalizumab	28,900	325,000
Mepolizumab	29,500	344,000
Reslizumab	28,900	391,000
Benralizumab	27,800	371,000
Dupilumab	31,000	351,000

[a]*Average annual price of each treatment, net of discounts and rebates, as reported to ICER by each manufacturer.*

ICER = Institute for Clinical and Economic Review; QALY = quality-adjusted life-year.

Tice, et al., J Managed Care Spec Pharm May 2019

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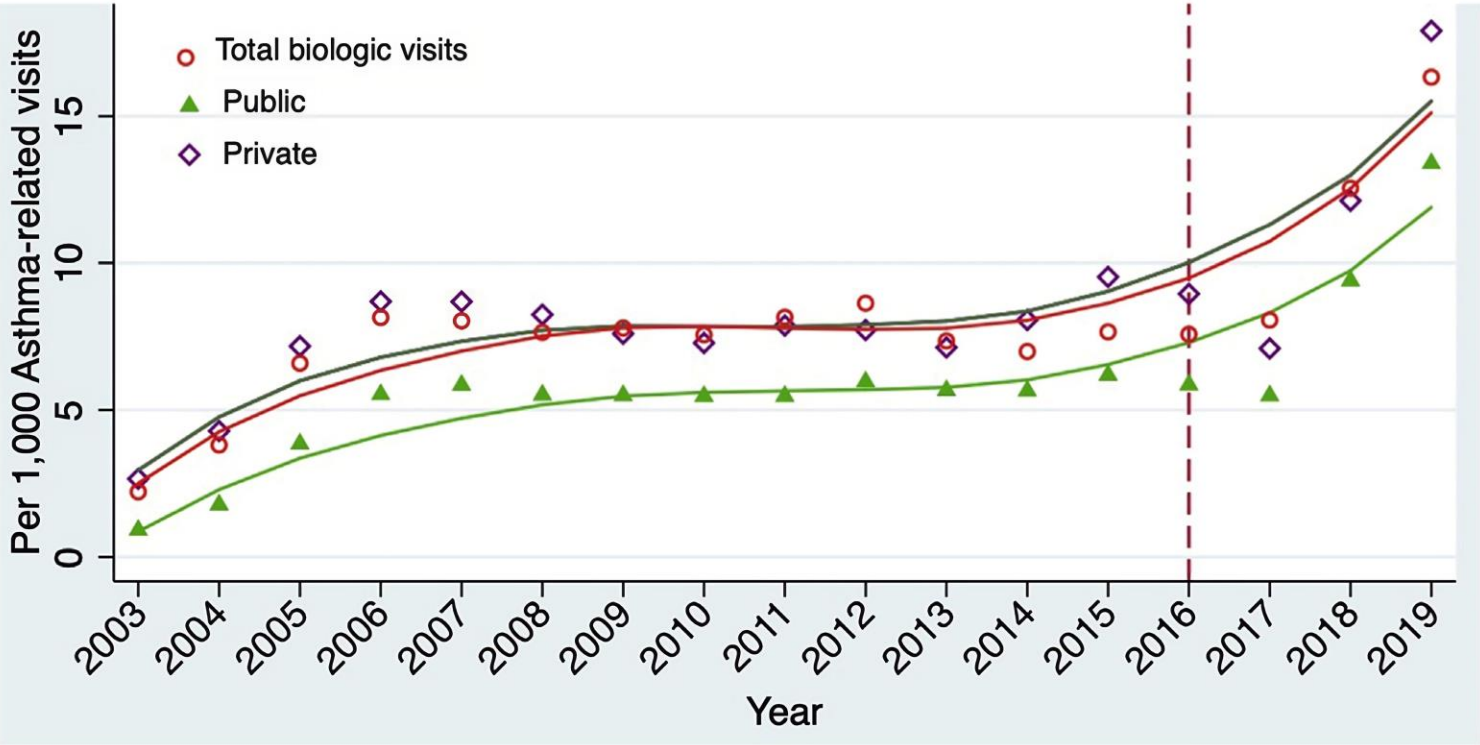
Intervention	Annual Price at $50,000 per QALY	Annual Price at $100,000 per QALY	Annual Price at $150,000 per QALY
Omalizumab	$4,700	$9,000	$13,300
Mepolizumab	$5,100	$9,200	$13,400
Reslizumab	$2,900	$6,500	$10,400
Benralizumab	$4,700	$8,300	$11,900
Dupilumab	$5,500	$9,400	$13,300

Tice, et al., J Managed Care Spec Pharm May 2019

Challenge #4: Cost impacts access, exacerbates inequities

Black and publicly insured patients less likely to use biologics



Akenroye et al, JACI Nov 2021

Challenge #4: Cost impacts access, exacerbates inequities

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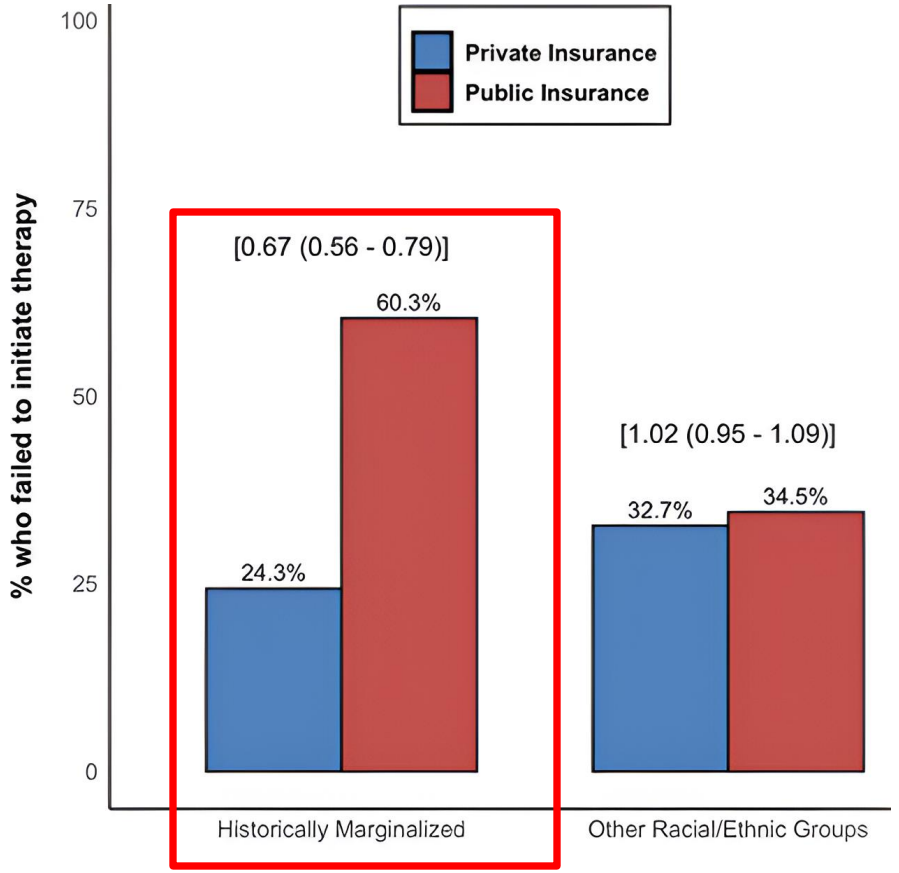
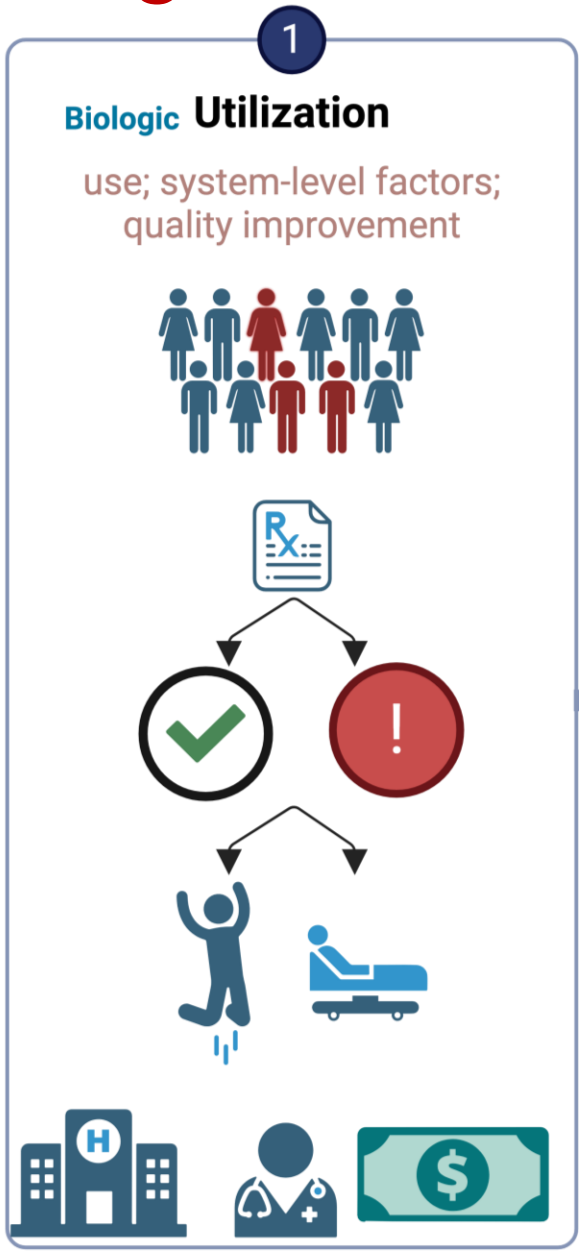


Akenroye et al, JACI Nov 2021
Gleeson et al, JACIIP Jun 2023

Challenge #9: Biologics do not fix socioeconomic issues

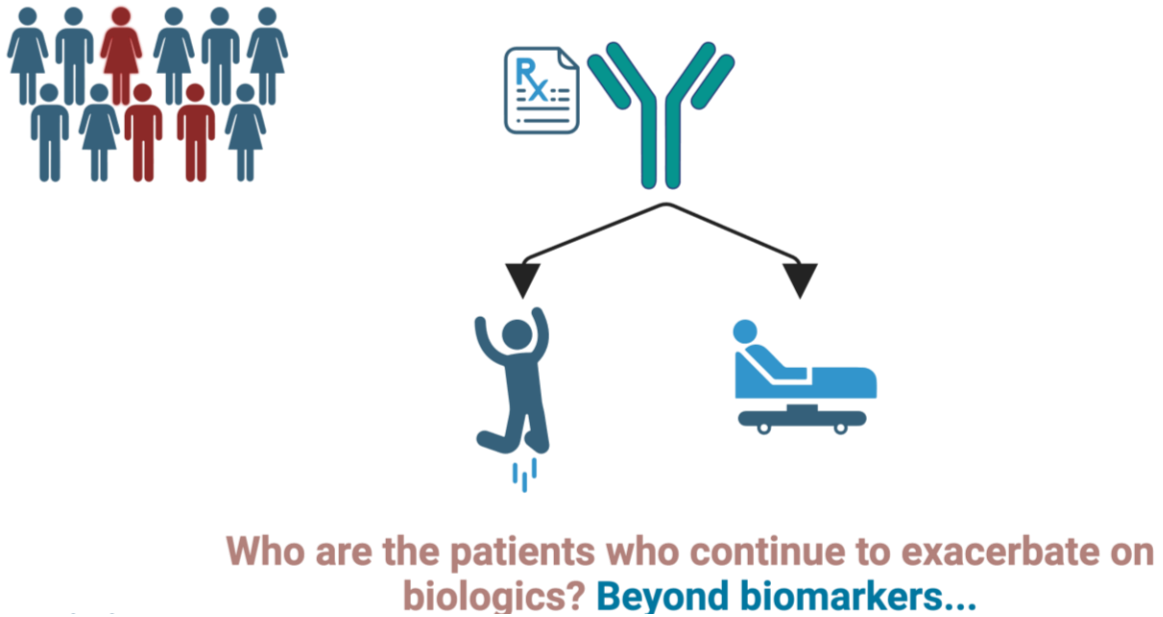


Why do some patients continue to exacerbate on biologics?

What system-level or patient-level factors may be contributing?

Characterize who these “high exacerbators” are in to identify and personalize quality improvement initiatives to improve their care and reduce the rate of exacerbations

Who continues to exacerbate despite biologic therapy?



Some patients continue to have exacerbations

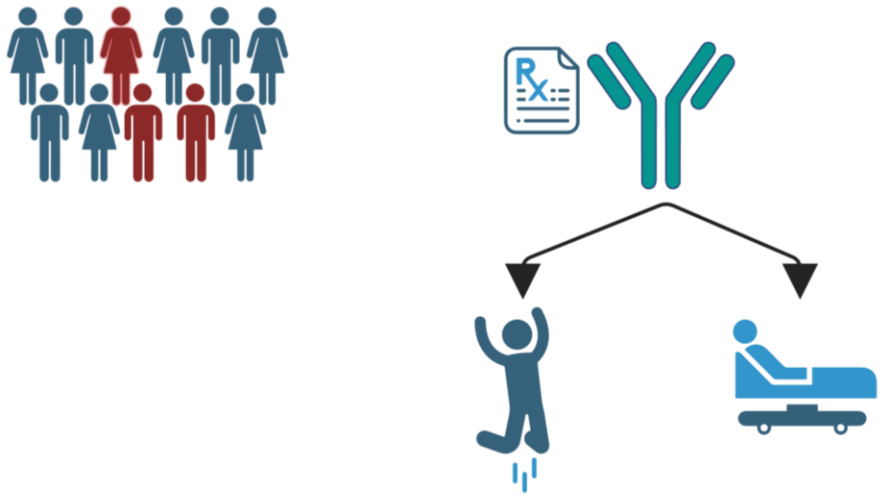
- Despite great selection for therapy
- Socio-economic variables have been shown as associated with severe asthma.

We sought to evaluate factors associated with:

- Continued exacerbations or admissions despite biologic initiation

- Likelihood that a patient in the 'high-frequency' group (≥2 exacerbations at baseline) would transition to the low-frequency group or not in the year following initiation.

Methods



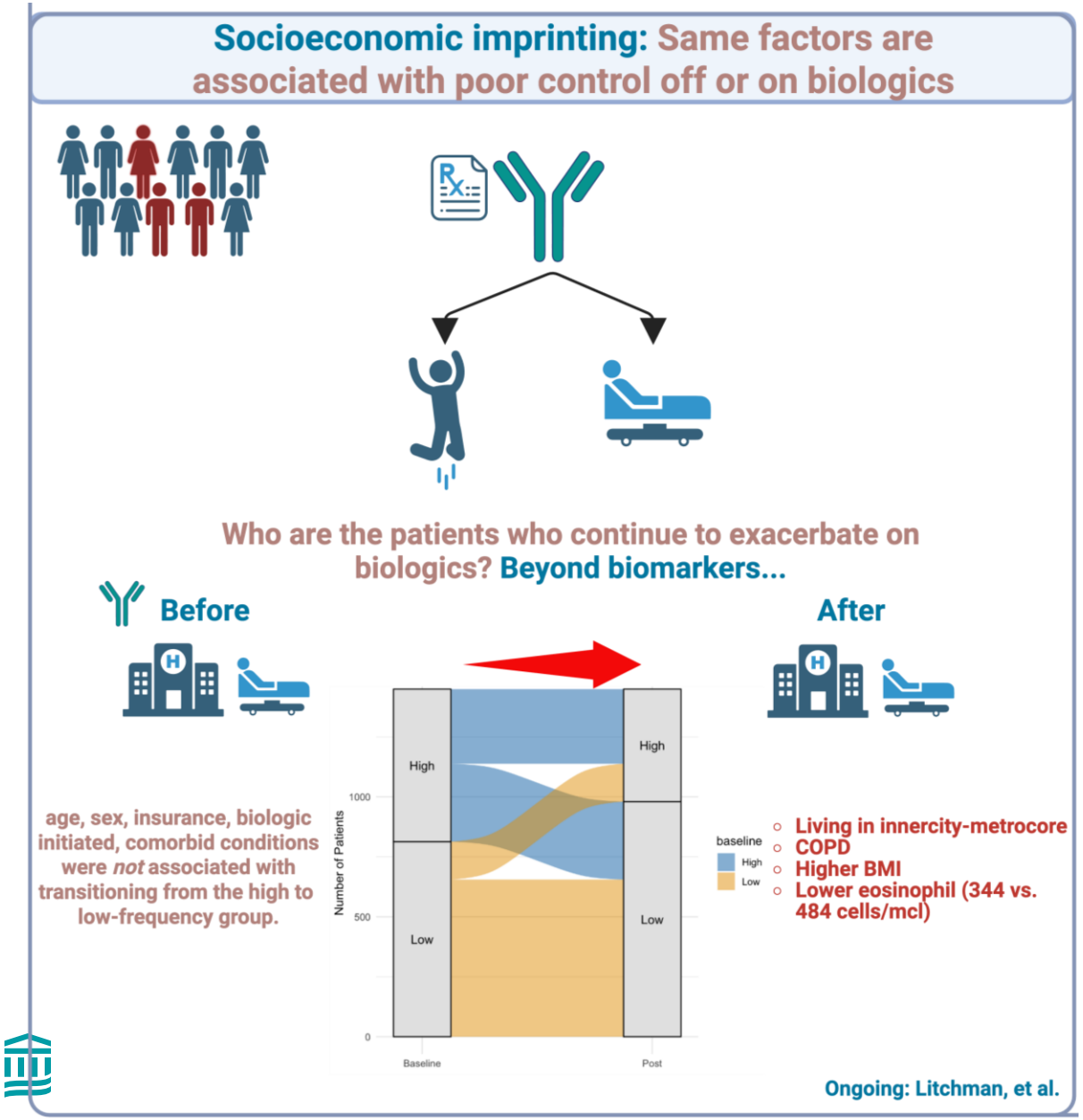
1,449 MGB patients with :

- Moderate-to-severe asthma
- Prescribed biologics
- 2015-2025

Methods:

- Evaluated baseline characteristics before therapy initiation
- Compared features of high-frequency exacerbators who transitioned to the low-frequency group vs not.

Results



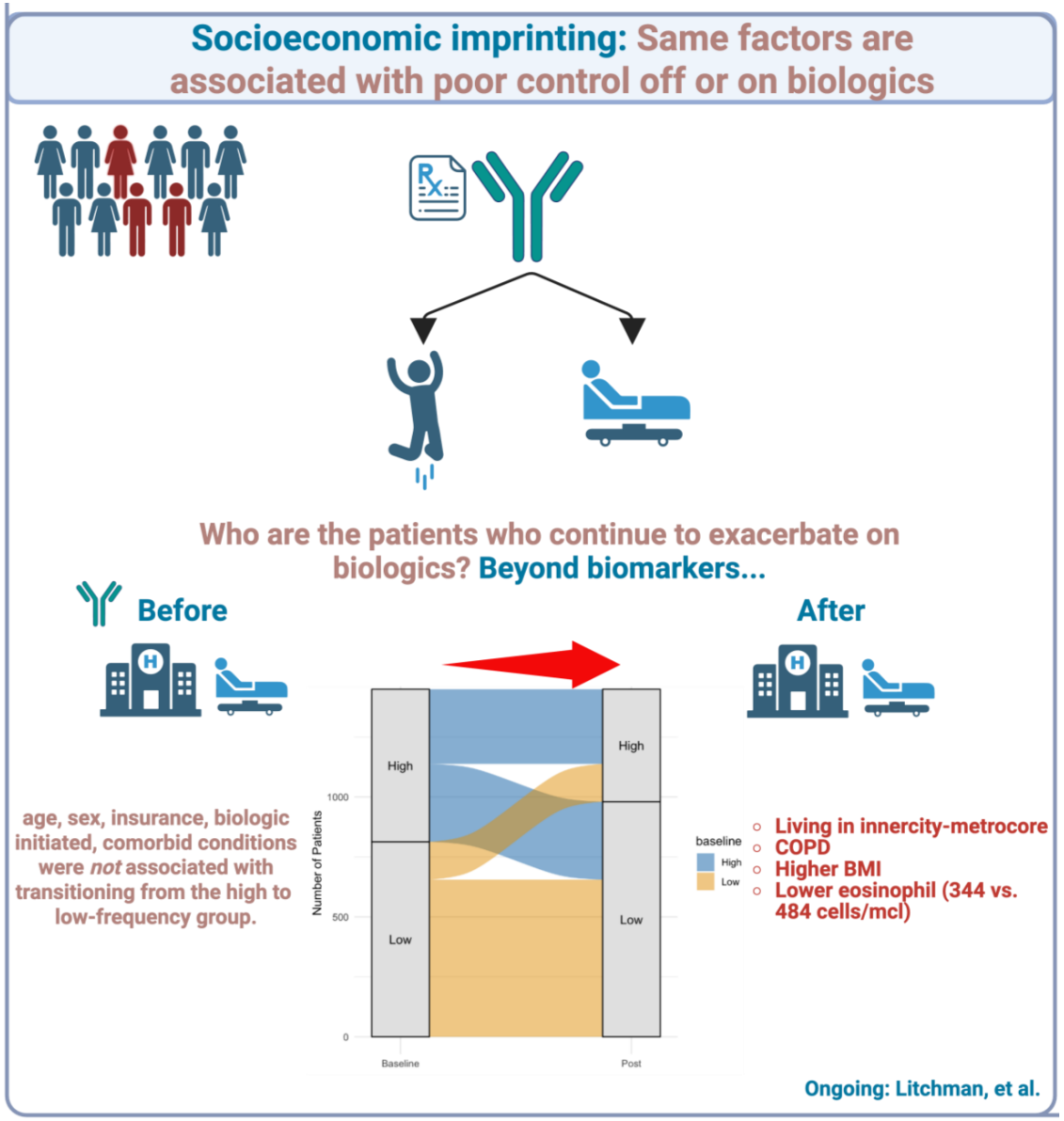
Patients who remained high-frequency exacerbators despite treatment were more likely to be:

- **Hispanic** (5.5% vs. 3.8%, p=0.05)
- **Urban-dwelling** (23.7% vs 13.6%, p<0.001)
- Have **public insurance** (37.5% vs 30.7%, p = 0.012)
- Have **comorbid COPD** (9.6% vs 22.6%, p<0.001)
- **Lower baseline eosinophil counts** (344 vs 484 cells/mcl).

Patients with high-frequency exacerbations requiring **admissions (≥2)** after initiating biologic therapy were more likely to be:

- **urban-dwelling**
- **BMI ≥30, Black**
- **Comorbid COPD**

Study limitations



- 'Prescription' not 'use'

"Inner city":

- Multiple zip codes
- Composite of many factors: pollution, environmental exposures, socioeconomic variables and other SDOH.

Key Take-Home Messages

- Severe asthma drives disproportionate cost and morbidity
- Biologics transform outcomes at the population level
- Multiple challenges in optimizing outcomes remain, including cost, access, selection, etc.
- Biologics will not fix socioeconomic issues- We need to treat the ‘whole’ patient

Thank you!

https://druguselab.bwh.harvard.edu/
Email: aakenroye@bwh.harvard.edu