The Role of Type 2 Inflammation in Severe Asthma: Integrating Biologic Therapy to Optimize Outcomes

Final Outcomes Report

Prepared for: AstraZeneca Pharmaceuticals

Grant ID: 38096395

October 22, 2018

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Executive Summary

- This curriculum focused on utilizing emerging biologic therapies to address severe asthma and type 2 inflammation.
- Significant improvements were seen across all learning domains within the curriculum, ranging from 31%–74%.

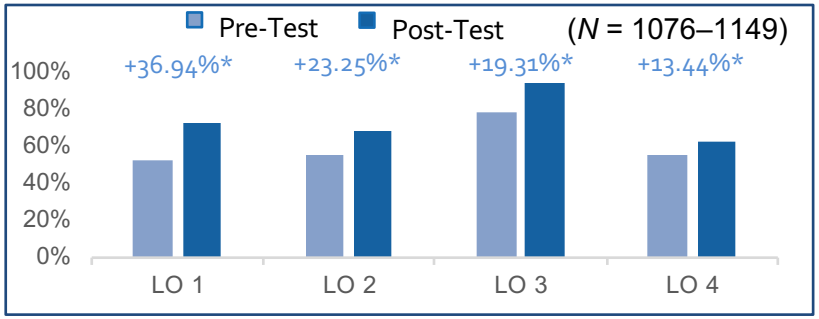
2,250* Total Attendees

5 Cities

927* On Site

1,323* Simulcast / Virtual Symposium

Pre to Post Test Results By Learning Objective



- **37% Improvement**: Describe newer concepts in the pathophysiology of asthma and type 2 inflammation and the implications of biologic therapies in the era of precision medicine.
- **23% Improvement**: Determine the utility of simple biomarkers to identify patients who are candidates for targeted biologic therapies and appropriate referral.
- **19% Improvement**: Discuss the impact of comorbid conditions on asthma control and the evidence-based approach to their treatment.
- **13% Improvement**: Discuss the paradigms of multidisciplinary care in asthma with an emphasis on patient and provider education, to improve adherence to inhalers and emerging biologic therapies in asthma.

Impact

- 2,313 attendees in multiple professional specialties were reached via both online and live formats, with significant gains observed across cohorts and modalities. The size and significance of the net gains from Pre-Test to the PCA highlight the curriculum's long term impact on learners' proficiency.
- Despite these improvements, a persistent learning gap on the asthma phenotypes which benefit from Anti-IL-5 agents could impede the ability of clinicians to optimally utilize such emerging therapies. Learners also remained challenged on when to refer patients to asthma specialists.

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*These numbers represent the total number of attendees, irrespective of assessment participation

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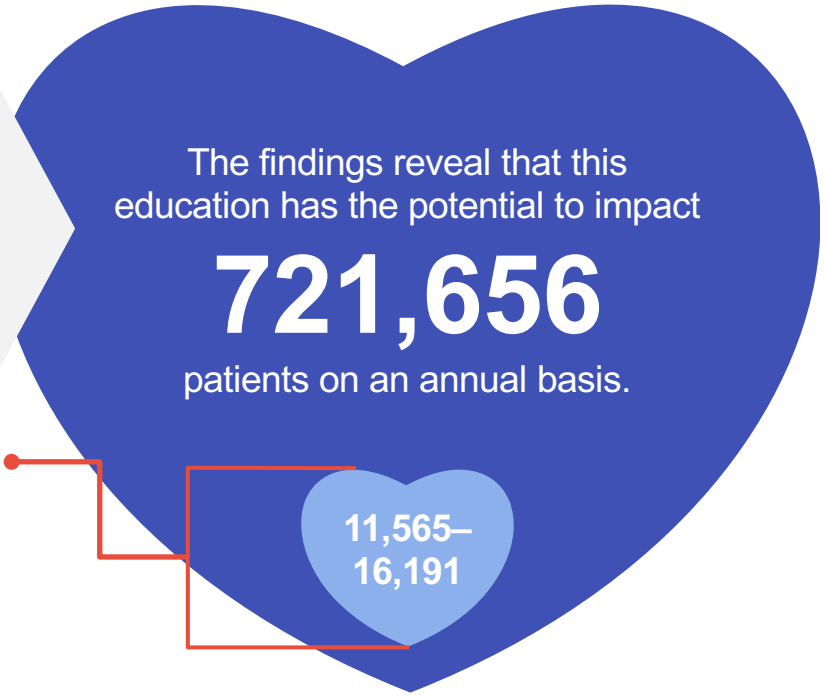
Curriculum Patient Impact

In the evaluation, learners (N = 2,250) were asked to report how many patients with asthma they see in any clinical setting per week by selecting a range. The resulting distribution of learner responses was then extrapolated to reflect the total number of learners who have attended the onsite and online meetings.



11,565–16,191 patients on a weekly basis

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Course Director

Diego J. Maselli, MD, FCCP
Assistant Professor of Medicine
Division of Pulmonary Diseases & Critical Care
University of Texas Health Science Center at San Antonio
Director, Respiratory Care, University Health System
Director, Severe Asthma Program, University Health System
San Antonio, TX

Activity Planning Committee

Gregg Sherman, MD

Michelle Frisch, MPH, CCMEP

Stephen Webber

Sandy Bihlmeyer M.Ed

Alan Goodstat, LCSW

Sheila Lucas, CWEP

Faculty

Sandra G. Adams, MD, MS
Professor, Division of Pulmonary Diseases and Critical Care Medicine
UT Health San Antonio
Staff Physician, The South Texas Veterans Health Care System
Founder, President
WipeDiseases Foundation
San Antonio, TX

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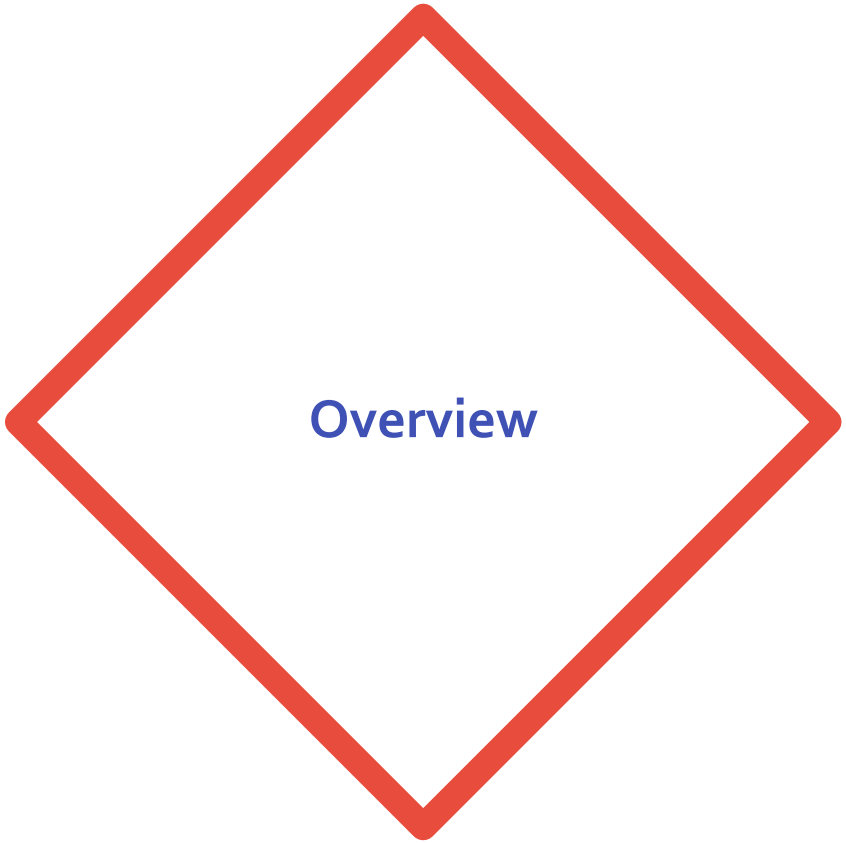
Director, Respiratory Care, University Health System
Director, Severe Asthma Program, University Health System
San Antonio, TX

Commercial Support

The Emerging Challenges in Primary Care: 2018 series of CME activities were supported through educational grants or donations from the following companies:

- Actelion Pharmaceuticals US, Inc
- AstraZeneca Pharmaceuticals LP
- ER/LA Opioid Analgesic REMS Program Companies
- Lilly USA
- Novo Nordisk Inc
- Sanofi Genzyme and Regeneron Pharmaceuticals


Overview

Emerging Challenges in Primary Care 2018
17th Annual Regional and Online CME Conference Series

8 Accredited Live Regional Symposia

April 28, 2018 – August 11, 2018

1 Accredited Live Virtual Symposium:

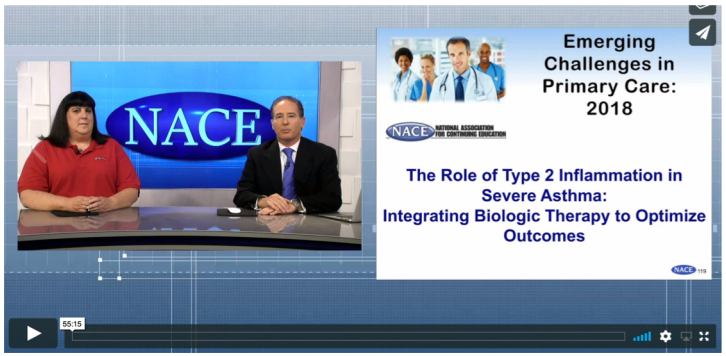
June 23, 2018

Enduring CME Symposium Webcast

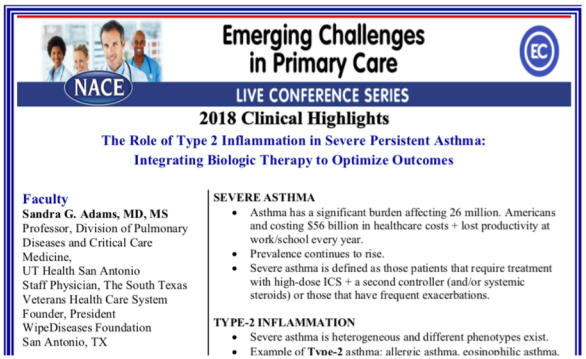
Launch Date: August 15, 2018

End Date: August 14, 2019

Available at http://bit.ly/NACE2018ECASTHMA



Clinical Highlights eMonograph - eMonograph containing key teaching points from the CME Activity was distributed 1 week after the meeting to all attendees.


Emerging Challenges in Primary Care

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LIVE CONFERENCE SERIES

2018 Clinical Highlights

The Role of Type 2 Inflammation in Severe Persistent Asthma: Integrating Biologic Therapy to Optimize Outcomes

Faculty

Sandra G. Adams, MD, MS
Professor, Division of Pulmonary Diseases and Critical Care Medicine,
UT Health San Antonio
Staff Physician, The South Texas Veterans Health Care System
Founder, President
WipeDiseases Foundation
San Antonio, TX

SEVERE ASTHMA

- Asthma has a significant burden affecting 26 million. Americans and costing $56 billion in healthcare costs + lost productivity at work/school every year.
- Prevalence continues to rise.
- Severe asthma is defined as those patients that require treatment with high-dose ICS + a second controller (and/or systemic steroids) or those that have frequent exacerbations.

TYPE-2 INFLAMMATION

- Severe asthma is heterogeneous and different phenotypes exist.
- Example of Type-2 asthma: allergic asthma, eosinophilic asthma,

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Learning Objectives

- Describe newer concepts in the pathophysiology of asthma and type 2 inflammation and the implications of biologic therapies in the era of precision medicine.
- Determine the utility of simple biomarkers to identify patients who are candidates for targeted biologic therapies and appropriate referral.
- Discuss the impact of comorbid conditions on asthma control and the evidence-based approach to their treatment.
- Discuss the paradigms of multidisciplinary care in asthma, with an emphasis on patient and provider education, to improve adherence to inhalers and emerging biologic therapies in asthma.

Outcomes Methodology

Learning outcomes were measured using matched Pre-Test and Post-Test scores for four learning domains (Knowledge, Competence, Confidence, and Practice Strategy) and across all of the curriculum's Learning Objectives.

Outcomes Metric	Definition	Application
Percentage change	This is how the score changes resulting from the education are measured. The change is analyzed as a relative percentage difference by taking into account the magnitude of the Pre-Test average.	Differences between Pre-Test, Post-Test, and PCA score averages
P value (p)	This is the measure of the statistical significance of a difference in scores. It is calculated using dependent or independent samples t-tests to assess the difference between scores, taking into account sample size and score dispersion. Differences are considered significant for when $p \leq .05$.	Significance of differences between Pre-Test, Post-Test, and PCA scores and among cohorts; significance of drivers in predictive modeling
Effect size (d)	This is a measure of the strength/magnitude of the change in scores (irrespective of sample size). It is calculated using Cohen's d formula, with the most common ranges of d from 0-1: d < .2 is a small effect, d=.2-.8 is a medium effect, and d > .8 is a large effect.	Differences between Pre-Test, Post-Test, and PCA score averages
Power	This is the probability (from 0 to 1) that the "null hypothesis" (no change) will be appropriately rejected. It is the probability of detecting a difference (not seeing a false negative) when there is an effect that is dependent on the significance (p), effect size (d), and sample size (N).	Differences between Pre-Test, Post-Test, and PCA score averages
Percentage non-overlap	This is the percentage of data points at the end of an intervention that surpass the highest scores prior to the intervention. In this report, it will reflect the percentage of learners at Post-Test who exceed the highest Pre-Test scores.	Differences between Pre-Test, Post-Test, and PCA score averages

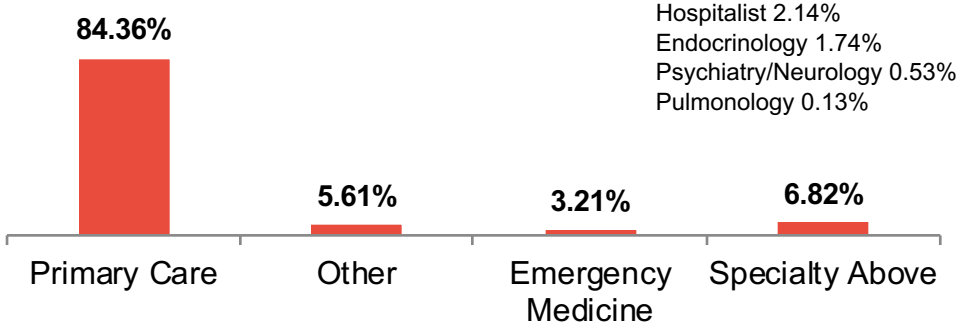
Participation

2018 Meeting/Simulcast	Date	Attendees
Miami, FL	4/28/18	179
Baltimore, MD	5/5/18	218
Baltimore, MD Simulcast	5/5/18	372
St. Louis, MO	5/12/18	129
Atlanta, GA	6/2/18	233
Atlanta, GA Simulcast	6/2/18	296
Raleigh, NC	6/16/18	168
Virtual Symposium	6/23/18	655
		2250


Level 1:
Demographics & Patient Reach

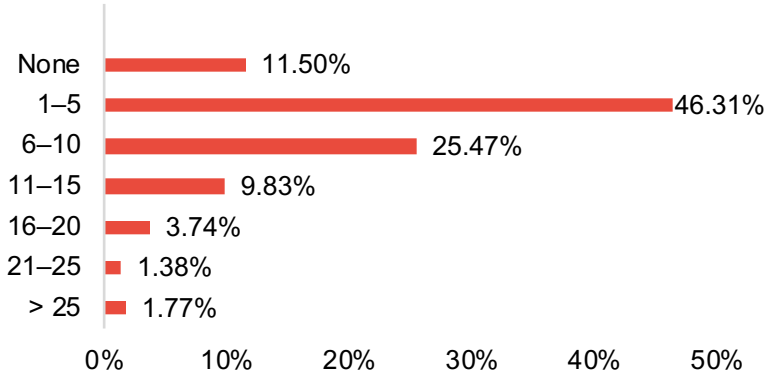
Level 1: Participation

Specialty



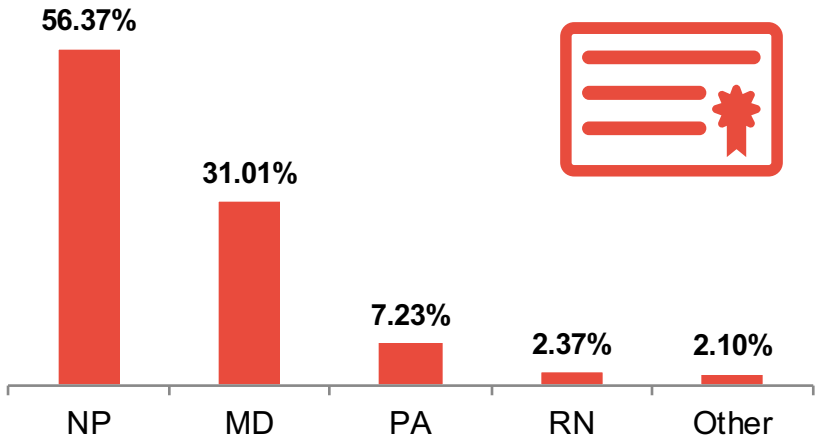
Specialists:
Cardiology 2.27%
Hospitalist 2.14%
Endocrinology 1.74%
Psychiatry/Neurology 0.53%
Pulmonology 0.13%

Patients with asthma seen each week, in any clinical setting:



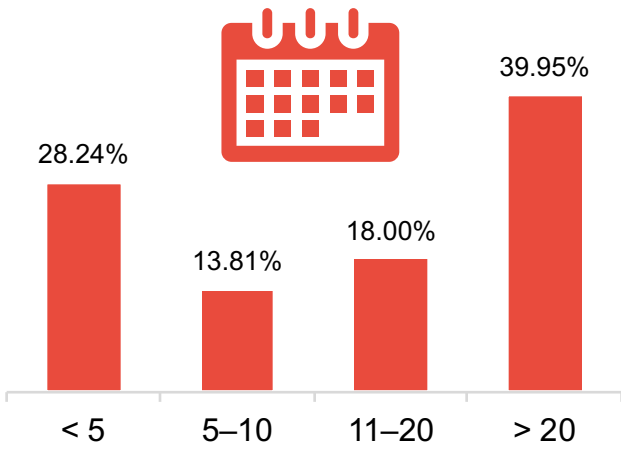
Patient Care Focus: 93%

Profession



Patients with asthma seen per week: 6 per clinician

Years in Practice



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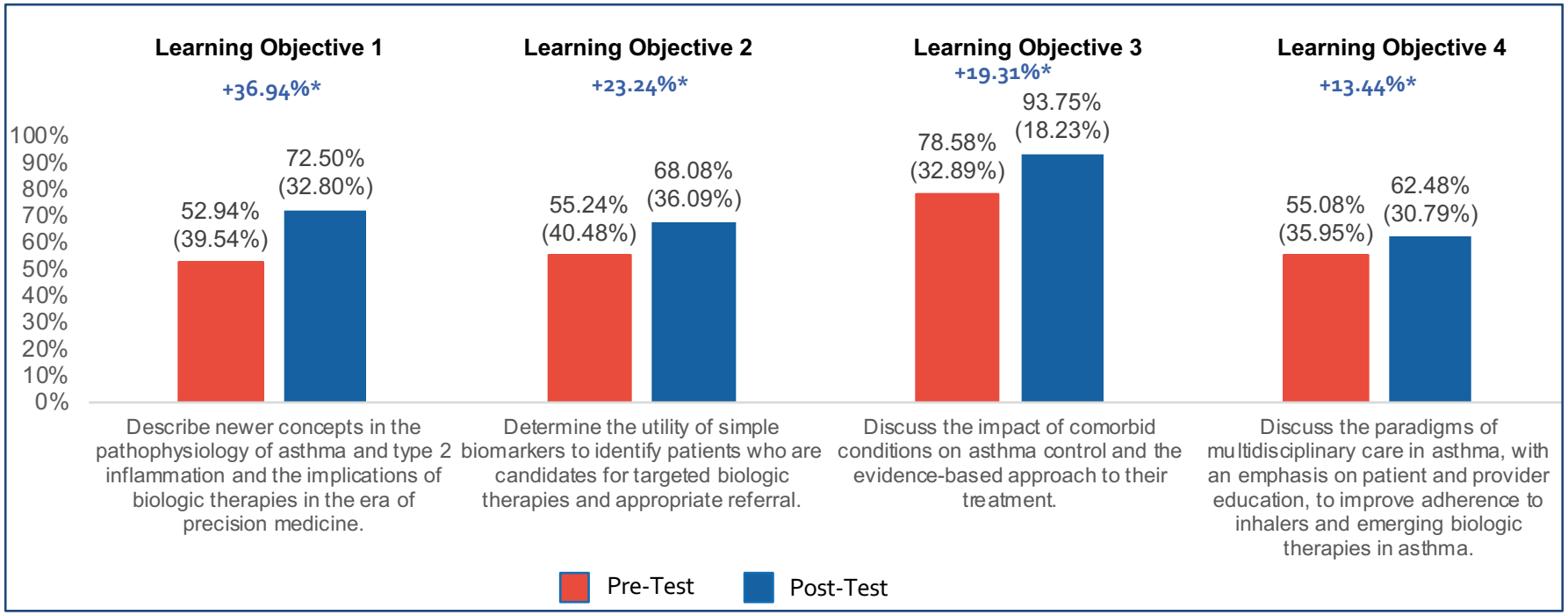
Level 2-5:
Outcomes Metrics

Learning Objectives Analysis



(*N* = 1076–1149)

significant at the p ≤ 0.05 level

- Substantial and significant gains (ranging from 13% to 37%) were achieved on all Learning Objectives.
- Learning Objectives 2 and 4 demonstrated low Post-Test scores (68% and 62%).
  - Learners had difficulty with the utility and interpretation of serum IgE and eosinophil levels, specifically on how they might impact treatment selection with Anti-IL-5 agents.
  - Learners also demonstrated difficulty recognizing when referral of a patient to an asthma specialist is most appropriate.

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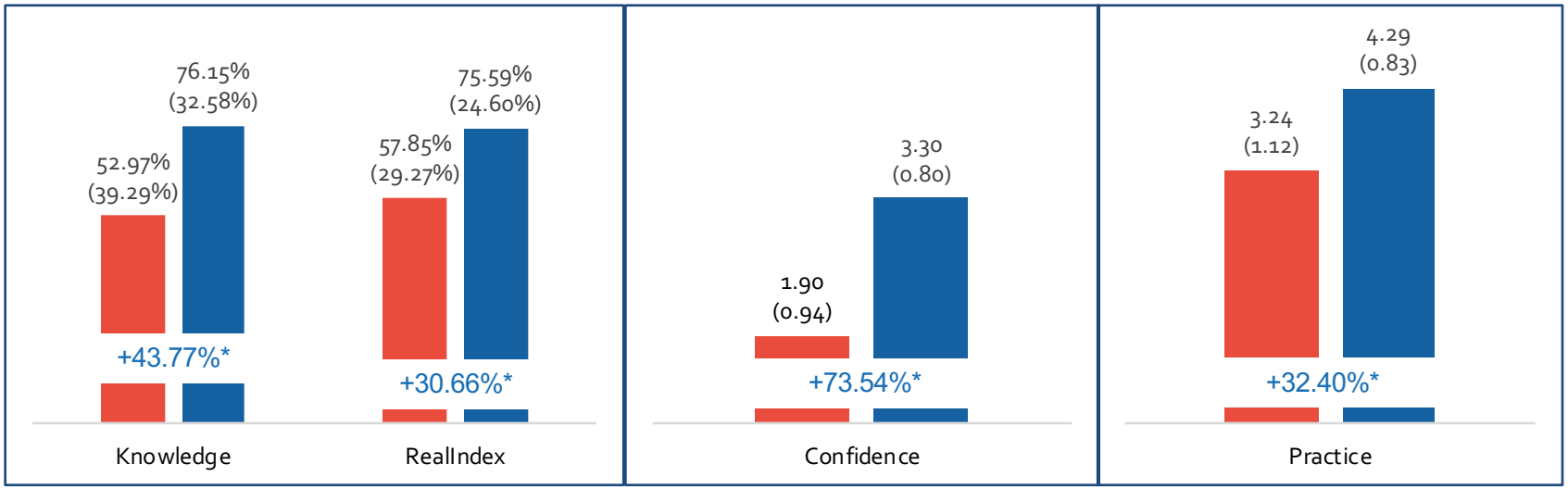
Learning Domain Analysis



- Significant gains (31%–74%) were achieved in all learner domains.
- The increase in Knowledge from Pre- to Post-Test was exclusively driven by one of the two questions related to examples of type-2 asthma; in contrast, the average score on the question about Anti-IL-5 agents showed a modest decrease.
- Learners substantially (74%) increased their reported Confidence in their ability to differentiate phenotypes of asthma. The Post-Test average rating, however, remained low.
- There was a substantial (32%) increase in their reported intent to treat comorbidities to improve asthma control.

Learning Domain by Professional Cohort

Learning Domain	Nurse Practitioner				Physician			
	N	Pre Test	Post Test	% Change	*N*	Pre Test	Post Test	% Change
Knowledge	260	55.58% (37.19%)	81.10% (28.95%)	**+45.92%***	156	51.42% (38.35%)	71.29% (33.56%)	**+38.65%***
Confidence	267	1.70 (0.81)	3.22 (0.76)	**+89.43%***	167	2.19 (1.03)	3.50 (0.87)	**+60.00%***
Practice	268	3.02 (1.14)	4.30 (0.85)	**+42.52%***	170	3.42 (1.10)	4.42 (0.76)	**+29.26%***
RealIndex	228	54.79% (28.26%)	78.41% (23.07%)	**+43.12%***	137	61.15% (28.86%)	74.04% (23.63%)	**+21.08%***

significant at the p≤.05 level

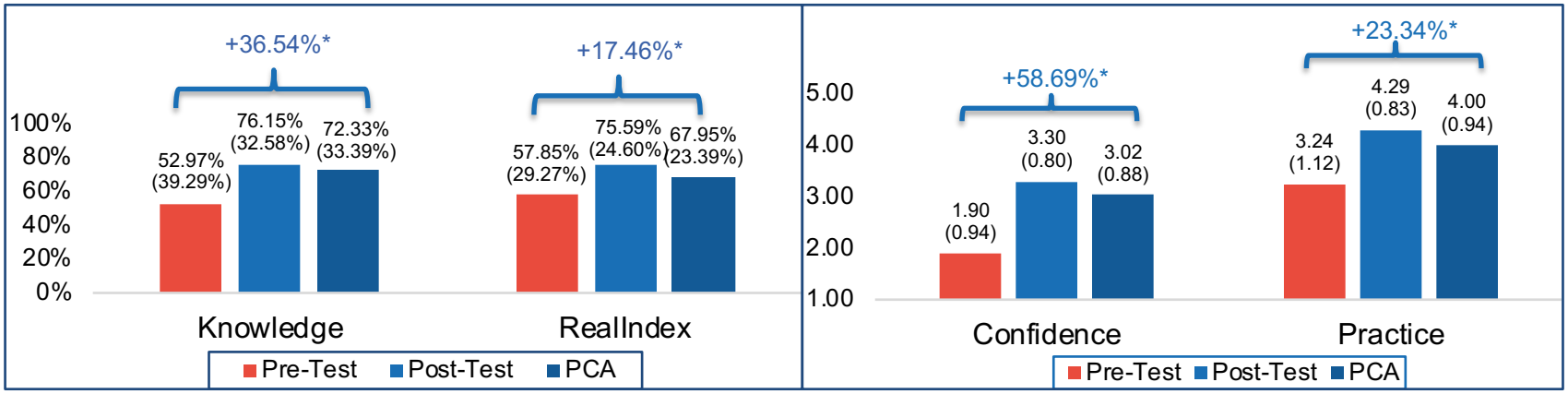
- Nurse practitioners (NPs) and physicians demonstrated statistically significant gains in all learning domains.
- NPs achieved greater gains and higher Post-Test scores on the two scored domains (Knowledge and RealIndex), compared to physicians.
- On the Confidence and practice strategy ratings, NPs again demonstrated the greatest increases; however, their Post-Test averages remained lower than those of physicians.

Curriculum/Activity Intervention Effect

Learning Domain	Effect Size*	% Non-Overlap
Knowledge	0.578	35.11%
RealIndex	0.468	23.94%

Effect Size Definition: This is a measure of the strength/magnitude of the change in scores (irrespective of sample size). It is calculated using Cohen's d formula, with the most common ranges of d from 0-1: d < .2 is a small effect, d=.2-.8 is a medium effect, and d > .8 is a large effect.

4 Week Retention Analysis



significant at the p ≤ 0.05 level

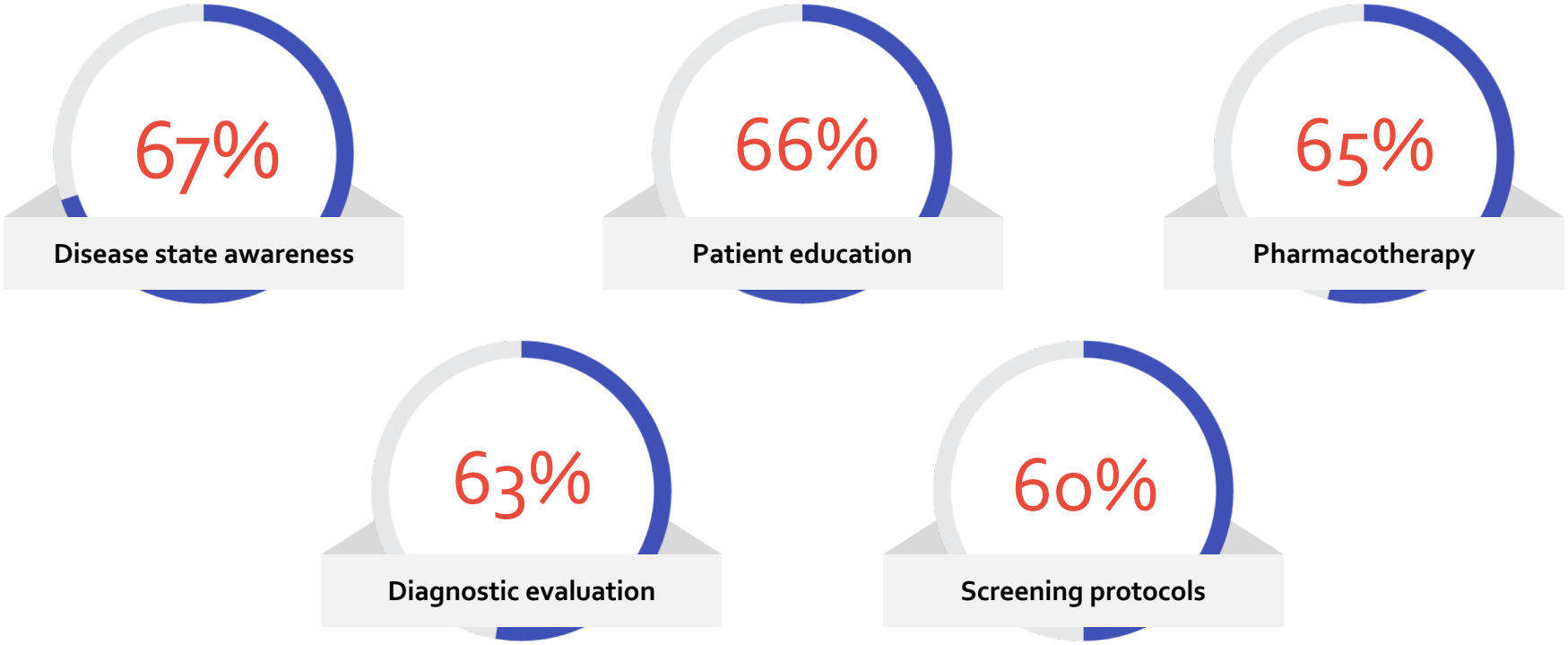
At follow-up (N = 533):

- Statistically significant net gains were measured from Pre-Test to the Post Curriculum Assessment (PCA) in all learning domains.
- The greatest net increases were observed in the Knowledge and Confidence domains.
- Some score slippage was observed in all domains from Post-Test to PCA. However, this slippage was modest compared to the net gains from Pre-Test to the PCA.

(4-week Post Assessment)

Please select the specific areas of skills, or practice behaviors, you have improved regarding the treatment of patients with asthma since this CME activity. (Select all that apply.)

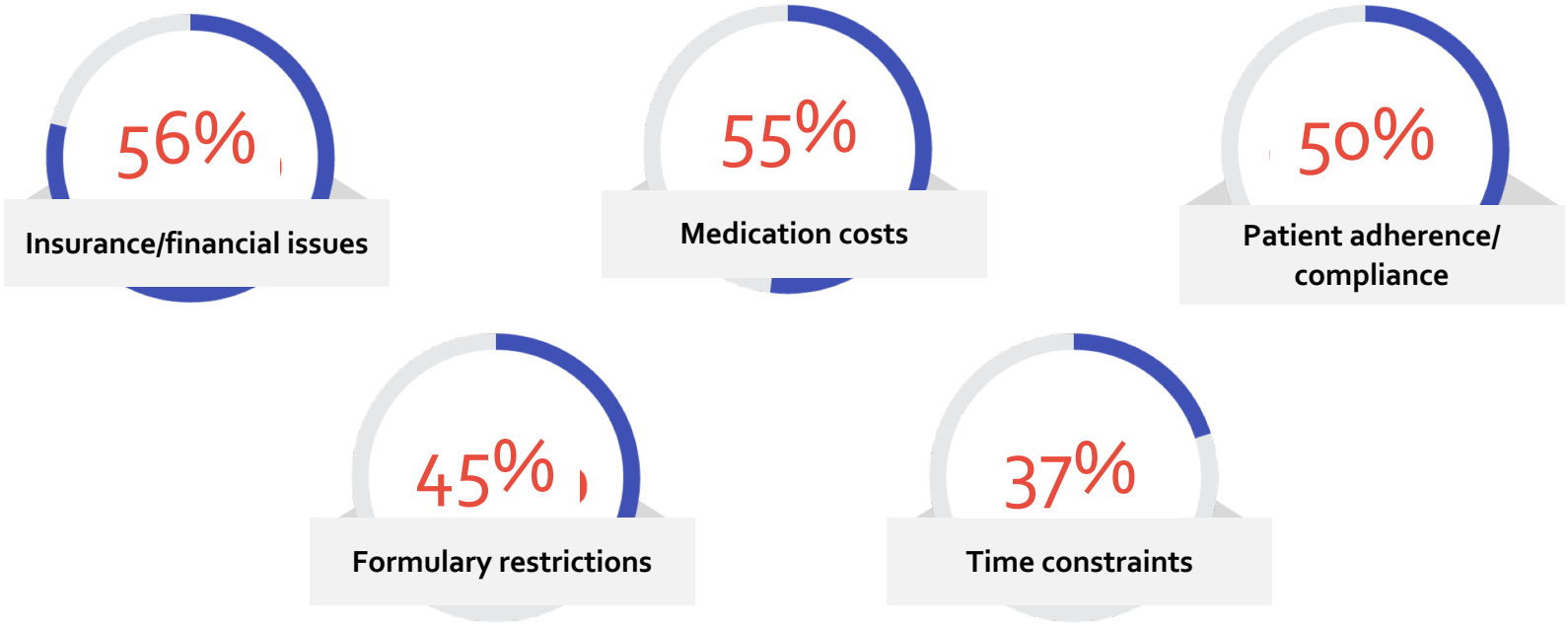
N=516



(4-week Post Assessment)

What specific barriers have you encountered that may have prevented you from successfully implementing strategies for patients with asthma since this CME activity? (Select all that apply)

N=516



Identified Learning Gaps:

Asthma phenotypes which benefit from Anti-IL-5 agents

A low scoring question in the Knowledge domain related to the benefit of Anti-IL-5 therapy for patients with the eosinophilic asthma phenotype.

Knowledge Question:

Which of the following suggests potential benefits to use of an Anti-IL-5 agent (i.e. mepolizumab, reslizumab, benralizumab) for the patient with allergic asthma?

Results:

- At Post-Test, 61% of learners correctly answered: “Serum eosinophils > 400 cells/mcL”.
- At Post-Test, 36% of learners incorrectly answered “Serum IgE 30-700 IU/mL”.

When to refer patients to asthma specialists

A low scoring RealIndex statement addressed whether asthmatic patients should be managed under primary or specialty care.

RealIndex Question:

A 38-year-old obese man (BMI 30.3 kg/m2) with 10 year history of asthma and 5-year history of GERD presents for a checkup. He reports 2 acute asthma exacerbations in the last year and notes that his asthma is often worse after supper. Current medications include high-dose inhaled steroids, long-acting beta agonist (LABA), and an H2 receptor blocker. After reviewing the brief scenario above, please rate each of the statements as consistent with or not consistent with your clinical practice.

Results:

- At Post-Test, 31% of learners correctly categorized “Refer to asthma specialist” as: “No, it is not consistent.”

Overall Educational Impact

- This curriculum focused on the utilization of emerging biologic therapies in the treatment of asthma and type 2 inflammation.
- Significant improvements (ranging from 31% – 74%) were seen across all learning domains.
  - The cohort analysis of professions showed that NPs demonstrated greater gains in all learning domains and achieved higher scores in Knowledge and Performance, compared to physicians. Physicians demonstrated higher averages on the Confidence and practice strategy ratings.
  - Mostly comparable scores and gains were demonstrated by live meeting and online participants.
- Significant improvements were seen across all Learning Objectives, ranging from 13%-37%.
  - Live meeting learners demonstrated greater improvements, resulting in modestly higher Post-Test scores on all Learning Objectives.
- The analysis of the Knowledge and Competence domains identified a **persistent learning gap related asthma phenotypes that benefit from Anti-IL-5 agents and when to refer patients to asthma specialists.**
  - The Knowledge question concerning the cases which benefit from Anti-IL-5 showed a score decrease from Pre-Test to Post-Test. On this question, 61% of learners correctly selected an eosinophilic phenotype, with a large proportion of learners incorrectly selecting serum IgE 30-700.
  - On the RealIndex item addressing when to refer an asthmatic patient to specialty care, only 31% of learners correctly categorized it as “not consistent”, suggesting that learners require guidance on when referrals are needed and when patients can be managed in the primary care setting.

Appendix

Learning Objectives Analysis – Live Onsite vs. Live Online Audience

- "Live onsite learners" include only those attending in-person meetings.
- "Live online learners" include those from both the Simulcast and Virtual Symposium.

Learning Objective	Live Onsite Learners				Live Online Learners			
	N	Pre-Test	Post-Test	% Change	*N*	Pre-Test	Post-Test	% Change
Describe newer concepts in the pathophysiology of asthma and type 2 inflammation and the implications of biologic therapies in the era of precision medicine.	645	51.47% (38.60%)	74.47% (31.27%)	**+44.69%***	443	55.08% (40.76%)	69.77% (34.61%)	**26.68%***
Determine the utility of simple biomarkers to identify patients who are candidates for targeted biologic therapies and appropriate referral.	648	53.86% (38.40%)	69.19% (33.68%)	**+28.47%***	431	57.31% (43.34%)	66.52% (39.17%)	**+16.08%***
Discuss the impact of comorbid conditions on asthma control and the evidence-based approach to their treatment.	630	77.74% (33.00%)	94.76% (16.80%)	**+21.89%***	429	79.84% (32.68%)	92.41% (19.90%)	**+15.74%***
Discuss the paradigms of multidisciplinary care in asthma, with an emphasis on patient and provider education, to improve adherence to inhalers and emerging biologic therapies in asthma.	634	57.18% (35.84%)	65.46% (29.55%)	**+14.48%***	458	52.07% (35.91%)	58.64% (31.90%)	**+12.61%***

significant at the $p \leq 0.05$ level

Learning Domain Analysis - Live Onsite vs. Live Online Audience

- "Live onsite learners" include only those attending in-person meetings.
- "Live online learners" include those from both the Simulcast and Virtual Symposium.

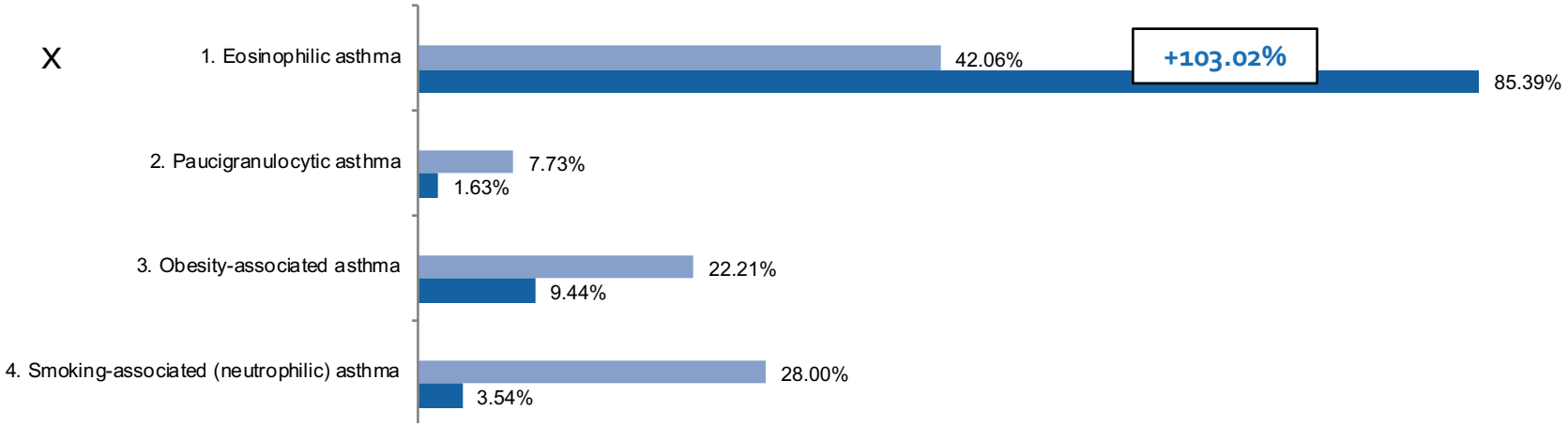
Learning Domain	Live Onsite Learners				Live Online Learners			
	N	Pre Test	Post Test	% Change	*N*	Pre Test	Post Test	% Change
Knowledge	523	51.91% (38.72%)	75.95% (32.83%)	+46.32%*	298	54.80% (40.07%)	76.49% (32.13%)	+39.58%*
Confidence	522	1.97 (0.99)	3.42 (0.83)	+73.60%*	296	1.79 (0.83)	3.10 (0.70)	+73.18%*
Practice	519	3.24 (1.16)	4.33 (0.85)	+33.72%*	320	3.23 (1.06)	4.21 (0.79)	+30.24%*
RealIndex	486	58.55% (28.78%)	76.75% (22.93%)	+31.09%*	240	56.71% (29.95%)	73.68% (26.65%)	+29.93%*

**significant at the $p \leq 0.05$ level*

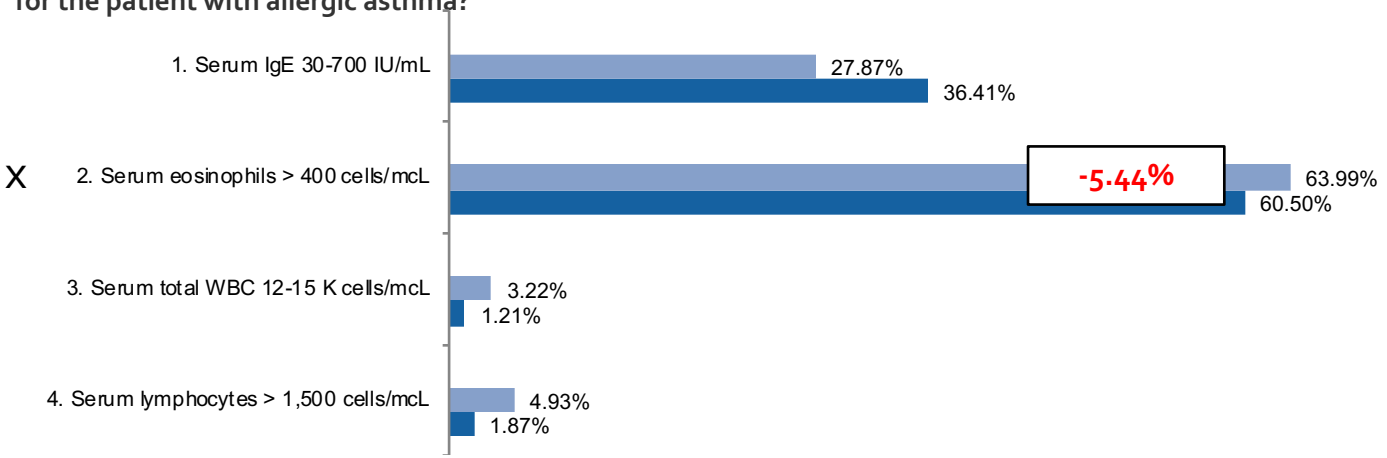
Knowledge Questions

N = (932–1102)

Which of the following is an example of type-2 asthma?



Which of the following suggests potential benefits to use of an Anti-IL-5 agent (i.e. mepolizumab, reslizumab, benralizumab) for the patient with allergic asthma?



Pre-Test Post-Test

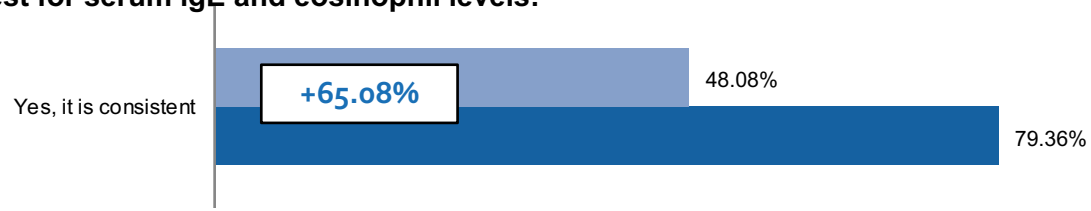
Note: Data is unmatched

RealIndex Questions

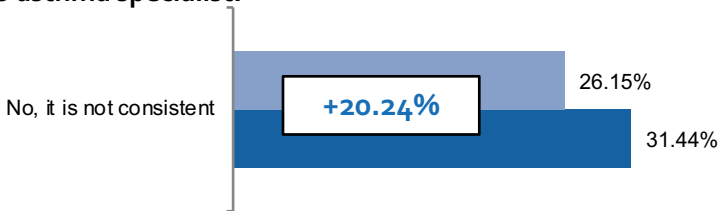
N = (934–1041)

A 38-year-old obese man (BMI 30.3 kg/m2) with 10 year history of asthma and 5-year history of GERD presents for a checkup. He reports 2 acute asthma exacerbations in the last year and notes that his asthma is often worse after supper. Current medications include high-dose inhaled steroids, long-acting beta agonist (LABA), and an H2 receptor blocker. After reviewing the brief scenario above, please rate each of the statements as consistent with or not consistent with your clinical practice:

Order test for serum IgE and eosinophil levels:

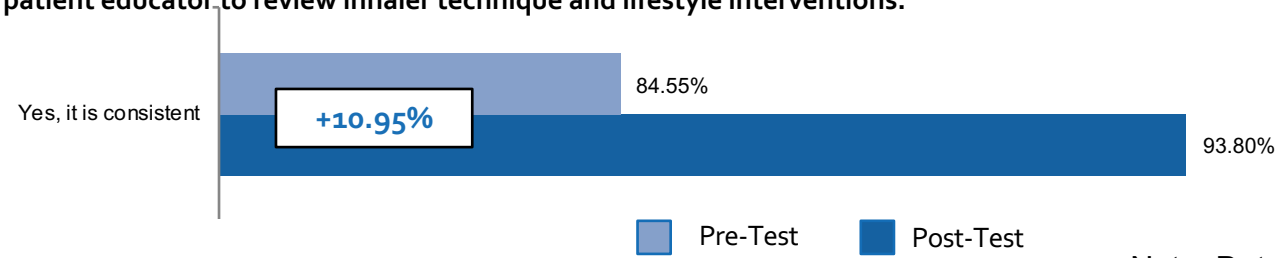


Refer to asthma specialist:



Discontinue H2 blocker and start proton pump inhibitor:

Refer to patient educator to review inhaler technique and lifestyle interventions:



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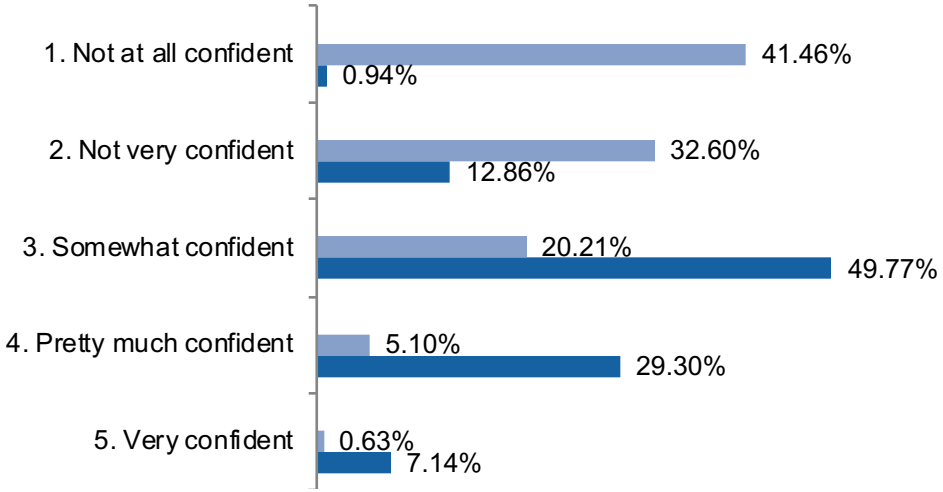
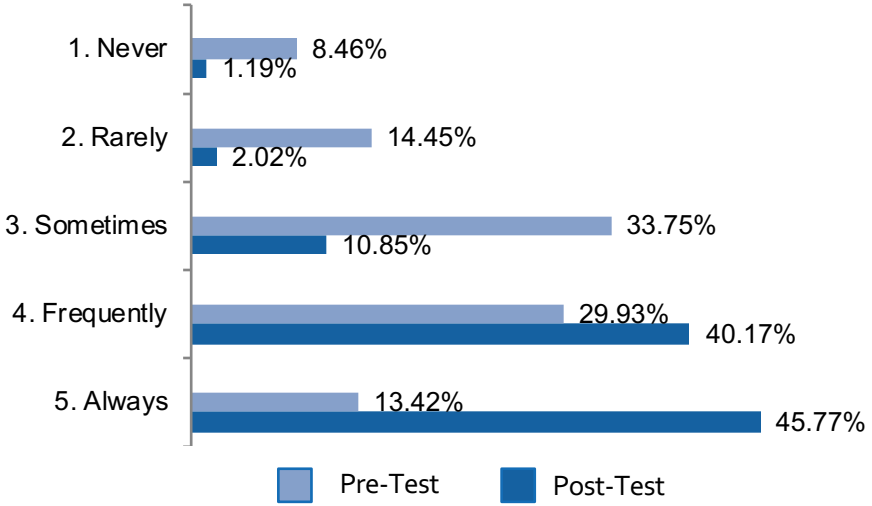
Confidence & Practice Questions

N = (960–969)

Confidence Question:
How confident are you in your ability to differentiate phenotypes of asthma?



Practice Question:
How often do you treat comorbidities to improve asthma control?



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