Reframing the Significance of Airway Hyperresponsiveness in Severe Asthma

Grant ID: 71024551
Final Online Enduring Outcomes Summary
5/27/2022-5/27/2023

Table of Contents

Final Outcomes Summary –Online Enduring Outcomes

National Jewish Health

Executive Summary

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

Program Overview

This program was designed to engage specialty health care practitioners in pulmonology and allergy in the topic of airway hyperresponsiveness (AHR), with three activities endured on Peer Audience, which excels at reaching specialists:

- Two 15-minute video-based activities to help learners understand airway hyperresponsiveness, its clinical significance, and emerging treatments; these incorporate micro-learning to deliver a high-impact, accessible message that is sensitive to health care providers' time constraints.
- One certified text-based monograph activity encompassing the content of the two video-based activities that will convey the nuances of airway hyperresponsiveness and appropriate therapies. This activity appeals to health care providers' strong preference for text-based learning.

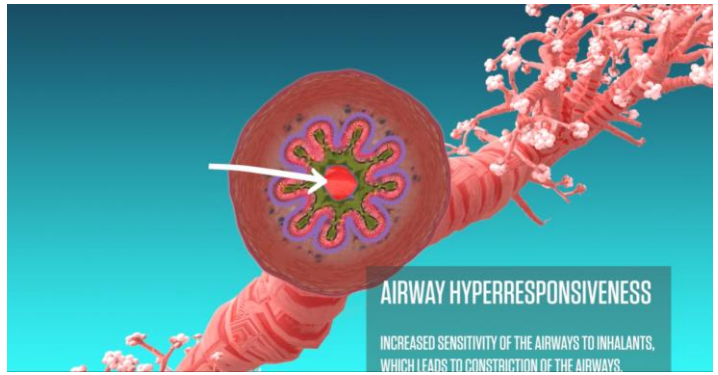
The video-based activities also incorporate presentation of case scenarios and 2D/3D animation clips to illustrate and demystify the complexity of our new understanding of severe asthma pathophysiology, the inflammatory cascade, and hyperresponsiveness.

Online Enduring Dates:
May 27, 2022 – May 27, 2023 (Peer Audience)

Program Faculty

Michael E. Wechsler, MD, MMSc
Director of The Cohen Family Asthma Institute and Professor of Medicine
Division of Pulmonary, Critical Care, & Sleep Medicine
Department of Medicine
National Jewish Health
Denver, Colorado

Flavia Cecilia Lega Hoyte, MD
Associate Professor
Fellowship Training Program Director
Division of Allergy & Clinical Immunology
Department of Medicine
National Jewish Health
Denver, Colorado



Learning Objectives

- Define AHR and its relationship to epithelial cell function, inflammation, and airway remodeling in asthma
- Evaluate the role of bronchoprovocation challenge testing in asthma diagnosis and management
- Discuss the implications of AHR for treatment selection in severe asthma
- Compare the effects of current and emerging biologic therapies on AHR in clinical studies

Target Audience & Accreditation

Target Audience: Pulmonologists, Allergists, and Nurse Practitioners and Physician Assistants in those specialties who treat severe asthma.

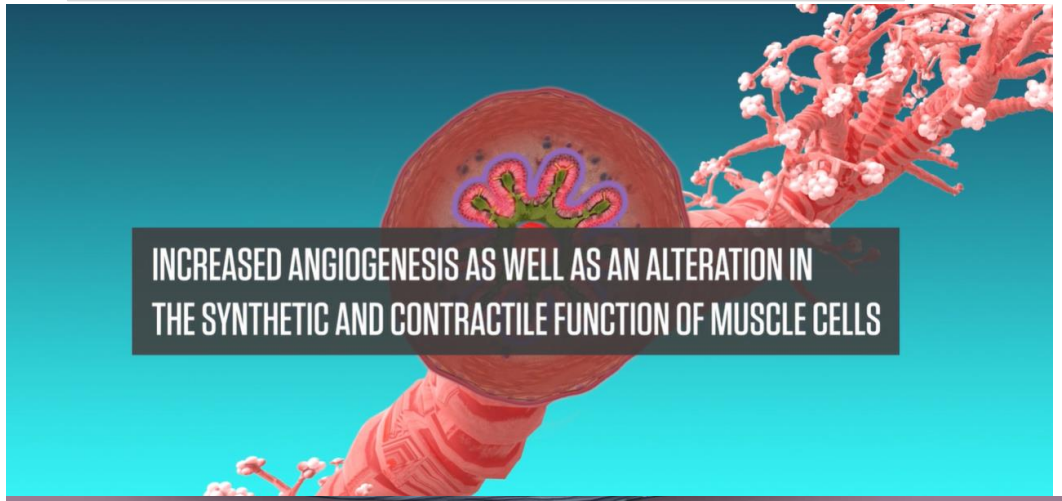
National Jewish Health designates each video-based activity for a maximum of 0.25 *AMA PRA Category 1 Credit*™ and the monograph activity for 0.5 *AMA PRA Category 1 Credit*™

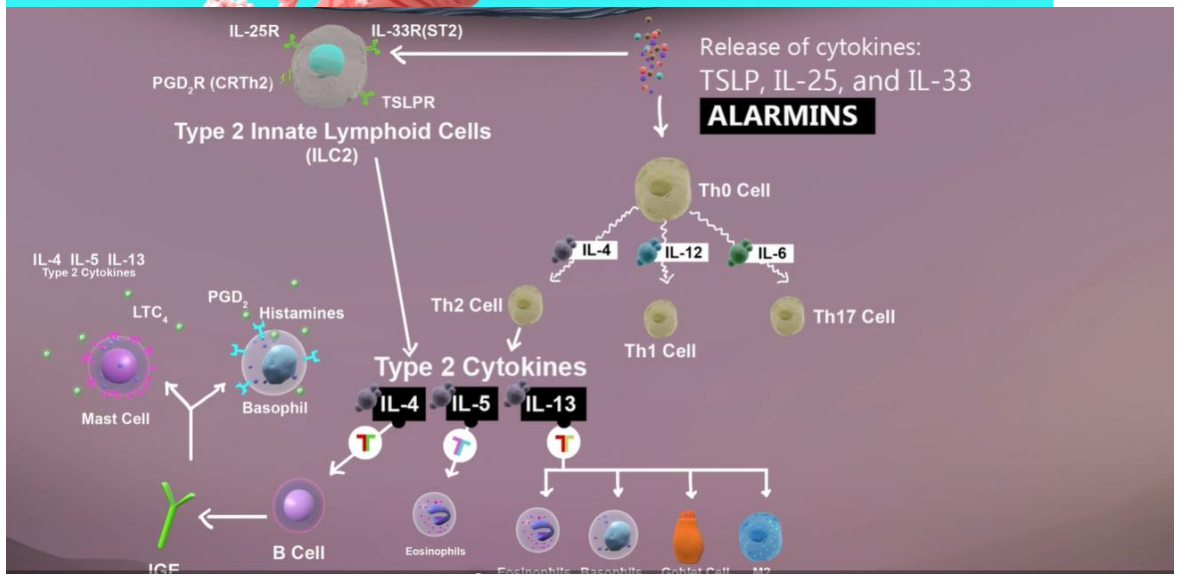
Program Features

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

Animation Clips





Patient Case Scenarios

Case 2

- 42-year-old woman
- Severe refractory eosinophilic asthma despite ICS/LABA
- Anti IL-5 therapy with history of eosinophilia to 450
- Despite Eos now reduced to 0, she continues to have coughing and wheezing, particularly in response to exposure to smoke and perfumes, or on high ozone days

National Jewish Health

Monograph

Introduction

Asthma affects over 25 million people in the United States and is characterized by wheezing, cough, and chest tightness.[1] Asthma symptoms are brought forth by airway inflammation, bronchoconstriction, and airway hyperresponsiveness (AHR), which is sometimes described as airway "twitchiness." AHR is underappreciated by most clinicians. However, AHR affects patients with asthma daily and is an important asthma feature to consider when optimizing management.

Asthma involves narrowing of the airways.[2] Airway narrowing is caused primarily by the constriction of smooth muscle that surrounds the airway. Airway narrowing results in the symptoms of cough, shortness of breath, chest tightness, and wheezing. Airway smooth muscle constriction, airway inflammation, and mucus plugging increase alveolar gas trapping. In patients experiencing an asthma attack, airway narrowing is particularly pronounced and severe.

Definition and clinical significance of AHR

AHR reflects the predisposition of the airways of individuals with asthma to narrow excessively in response to stimuli that would produce little or no effect in healthy subjects. AHR is a heightened bronchoconstrictive response to either direct or indirect stimuli that can be demonstrated in patients with either episodic or active symptomatic asthma.[2,3] Understanding the factors that contribute to AHR provides an opportunity to improve asthma control and reduce disease progression.[2]

AHR is a cardinal feature of asthma that is associated with reduced lung function.[4,5] AHR is also associated with increased wheezing[6] and asthma severity,[7] a higher risk for asthma development,[4] and suboptimal responsiveness to asthma therapies, including inhaled corticosteroids (ICS).[6,9] In patients with severe asthma, AHR is associated with the occurrence of asthma exacerbations and can be accentuated during exacerbations.

Measurement of AHR with bronchoprovocation testing (BPT) can be used to establish a diagnosis of asthma, characterize the type of asthma, and classify asthma severity. Assessing AHR provides an opportunity to improve asthma control and lung function and to reduce disease progression by identifying treatments that ameliorate AHR and symptoms, particularly in patients who respond poorly to treatment with ICS.

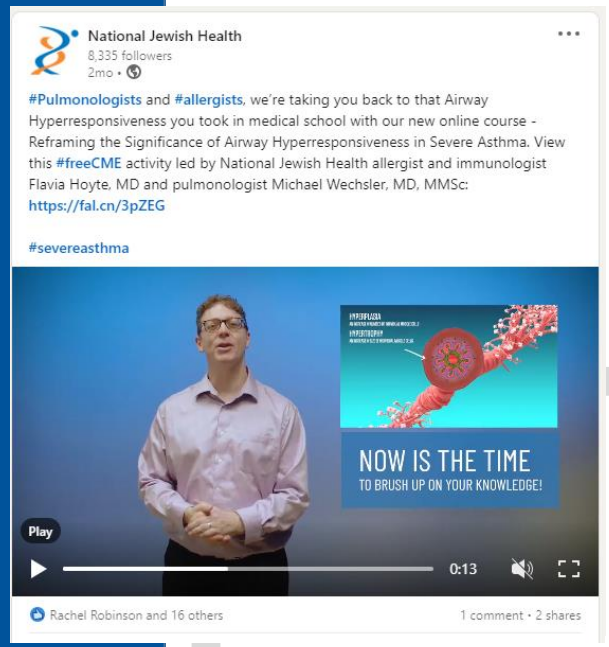
Role of the epithelial alarmins in AHR

In susceptible individuals, AHR may increase after inhalational exposure to different types of stimuli that include respiratory pathogens (eg, viruses, bacteria), aeroallergens (eg, dust mites, cockroaches, animal dander, molds, pollen), and air pollutants (eg, smoke, dust, chemicals, particulates).[10-12]

Audience Generation

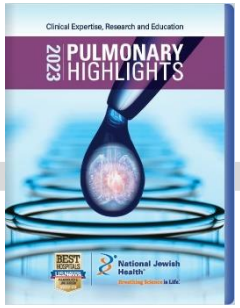
Final Outcomes Summary – Online Enduring Outcomes

Personalized targeting tools across numerous tactics reach HCPs by leveraging demographic data (such as location, profession, specialty) and behavioral data (such as learner participation history, areas of interest).



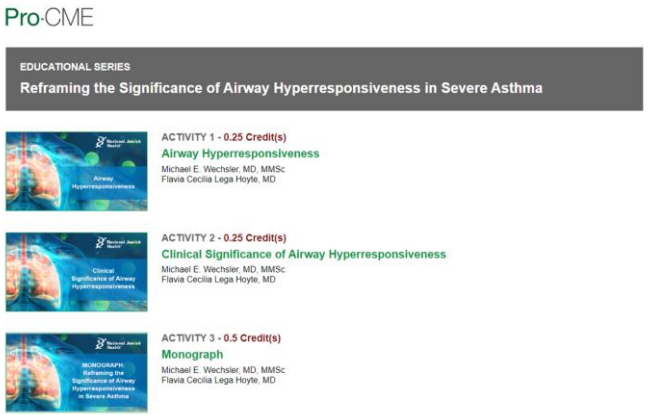
Promotional video clip on social media platforms

Featured in Pulmonary Highlights publication



Social media ads and posts

Dedicated landing page on NJH website



PeerAudience recruitment: emails, network marketing, social media, search engine advertising, dedicated landing page

Course spotlight in emails to NJH database

Online Enduring Program

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

PeerAudience

5/27/2022 – 5/27/2023

https://www.pro-c.me/180200652?Promocode=800

Pro-CME

EDUCATIONAL SERIES

Reframing the Significance of Airway Hyperresponsiveness in Severe Asthma

ACTIVITY 1 - 0.25 Credit(s)

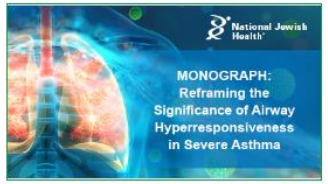
Airway Hyperresponsiveness

Michael E. Wechsler, MD, MMSc
Flavia Cecilia Lega Hoyte, MD

ACTIVITY 2 - 0.25 Credit(s)

Clinical Significance of Airway Hyperresponsiveness

Michael E. Wechsler, MD, MMSc
Flavia Cecilia Lega Hoyte, MD



ACTIVITY 3 - 0.5 Credit(s)

Monograph

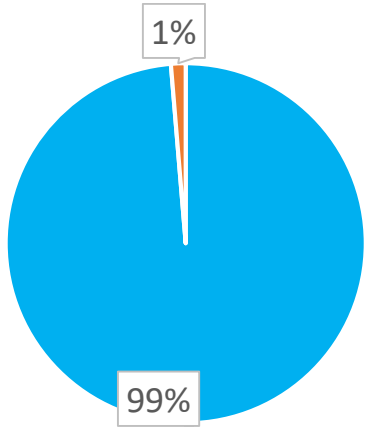
Michael E. Wechsler, MD, MMSc
Flavia Cecilia Lega Hoyte, MD

Educational Impact Summary (Across 3 Activities)

Final Outcomes Summary – Online Enduring Outcomes

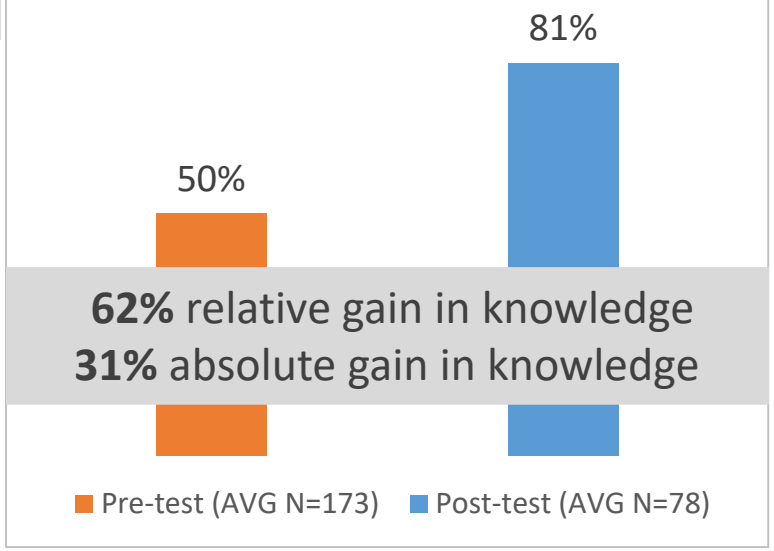
National Jewish Health

Participation



MD/DO=2,097
Other=28
Total Learners=2,125

99% of learners were physicians



Evaluation N=228

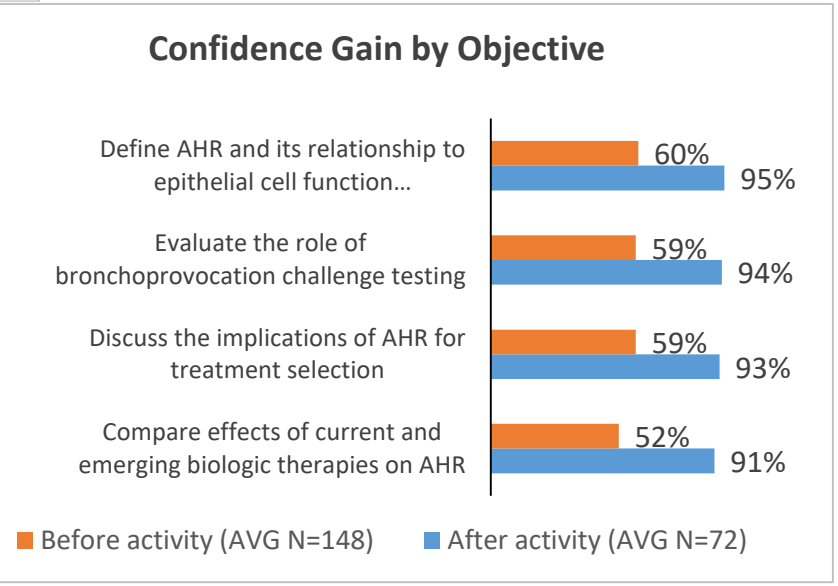
Met their educational needs **(98%)**

Reinforced or improved current skills **(98%)**

Improved ability to treat patients **(96%)**

Learner Guarantee	Learner Actuals
1,400 • 400 allergy • 1,000 pulmonology	**2,125** • **888 allergy** • **1209 pulmonology**

Potential Impact To 99,892 Patient Visits This Year



92% N=226

Evaluation respondents intend to make changes to practice as a result of the activity

Educational Impact Summary (Across 3 Activities)

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

Patient Impact	Educational Impact	Practice Change
224 evaluation respondents	**71%** relative knowledge gain seen from learners in defining AHR and its relationship to epithelial cell function, inflammation, and airway remodeling in asthma (AVG N=78)	**92%** intend to make changes in practice as a result of what they learned (N=226)
Who see **1,921** severe asthma patients weekly	**51%** relative knowledge gain in evaluating the role of bronchoprovocation challenge testing in asthma diagnosis and management (AVG N=78)	**97%** indicated the activity gave tools and strategies to apply in practice (N=228)
Which translates to **99,892** potential patient visits annually	**54%** relative knowledge gain seen from learners in discussing the implications of AHR for treatment selection in severe asthma (AVG N=78)	**60%** relative gain in confidence across learning objectives (AVG N=72)
	89% relative knowledge gain in comparing effects of current and emerging biologic therapies on AHR in clinical studies (AVG N=78)	

Program Insights (Across 3 Activities)

Final Outcomes Summary – Online Enduring Outcomes

- Learner reach for this activity was 52% higher than expected, and 99% of learners were in the target audience, indicating significant interest in the topic of airway hyperresponsiveness among pulmonologists and allergists.

- Knowledge gains were highest among allergists, at 82% overall relative knowledge gain vs. 48% overall relative knowledge gain among pulmonologists (across all learning objectives and all 3 activities).

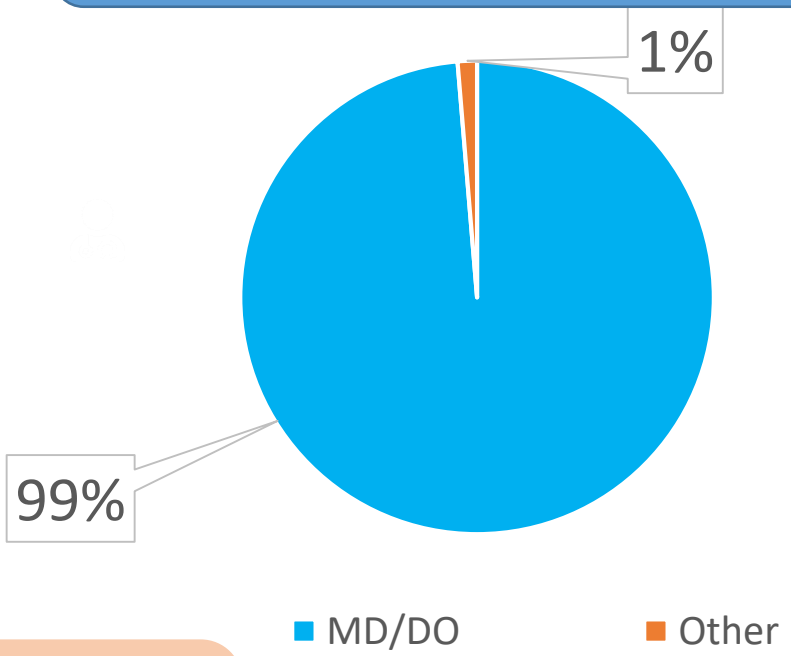
    - Pulmonologists, however, had higher baseline knowledge across all learning objectives as demonstrated by pre-test scores.

- A gap may still exist with regard to the effects of current and emerging biologic therapies on AHR, as an average of 32% of learners were unable to answer correctly at post-test.

Level (1) Outcomes: Participation (Degree)

Final Outcomes Summary – Online Enduring Outcomes

Total Learners (across the 3 activities): 2,125



99% of learners were physicians

Learners = individuals who entered the digital interface

Video 1: AHR	
MD/DO	737
Other	15
TOTAL LEARNERS	**752**

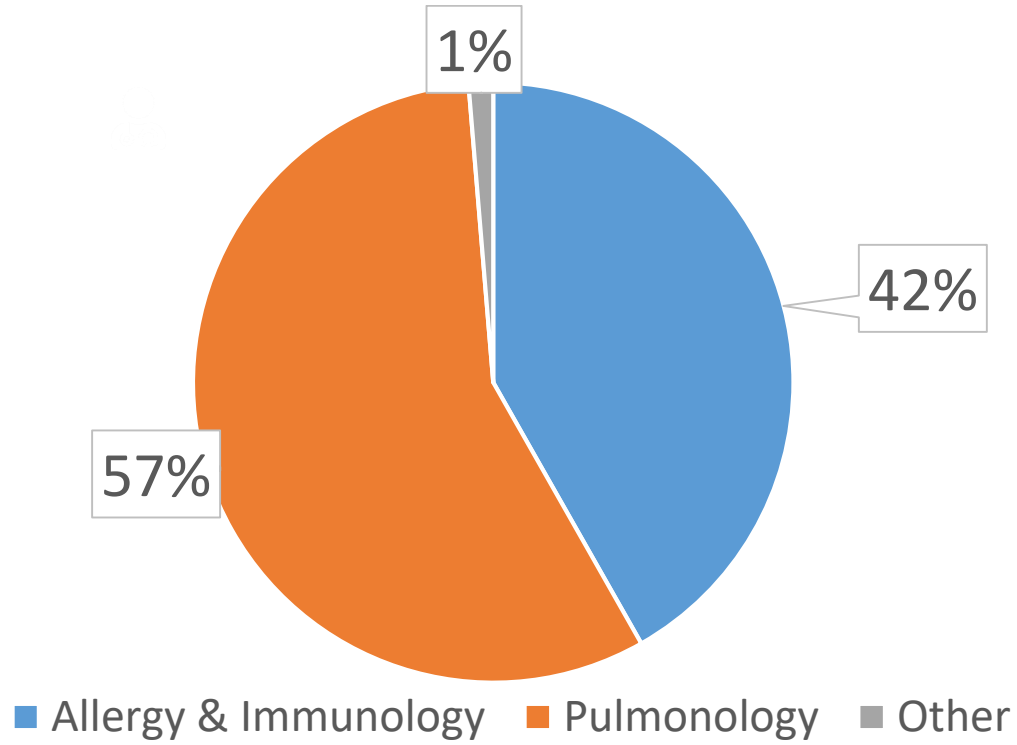
Video 2: Clinical Significance of AHR	
MD/DO	696
Other	2
TOTAL LEARNERS	**698**

Monograph	
MD/DO	664
Other	11
TOTAL LEARNERS	**675**

Level (1) Outcomes: Participation (Specialty)

Final Outcomes Summary – Online Enduring Outcomes

99% of learners across the 3 activities were in the target audience



N=2,125

Video 1: AHR	
Allergy/Immunology	276
Pulmonology	461
Other	15
TOTAL LEARNERS	**752**

Video 2: Clinical Significance of AHR	
Allergy/Immunology	322
Pulmonology	374
Other	2
TOTAL LEARNERS	**698**

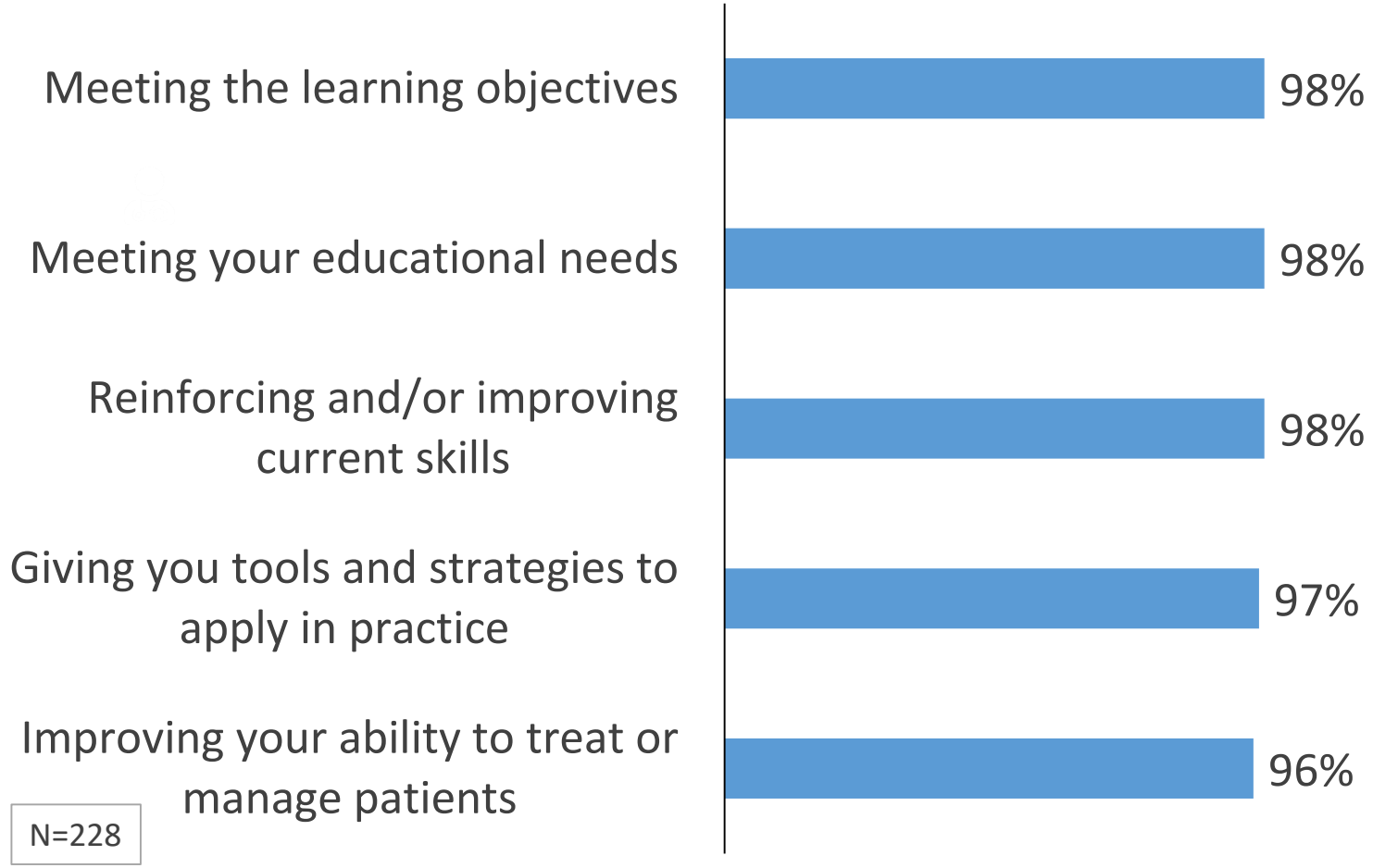
Monograph	
Allergy/Immunology	290
Pulmonology	374
Other	11
TOTAL LEARNERS	**675**

Level (2) Outcomes: Satisfaction (Across 3 Activities)

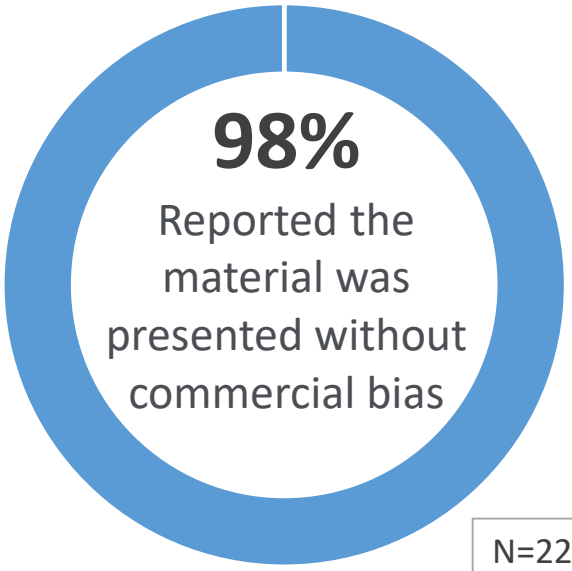
Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

Evaluation respondents report the activity was "Excellent" to "Good" at:



N=228



N=224

N=224

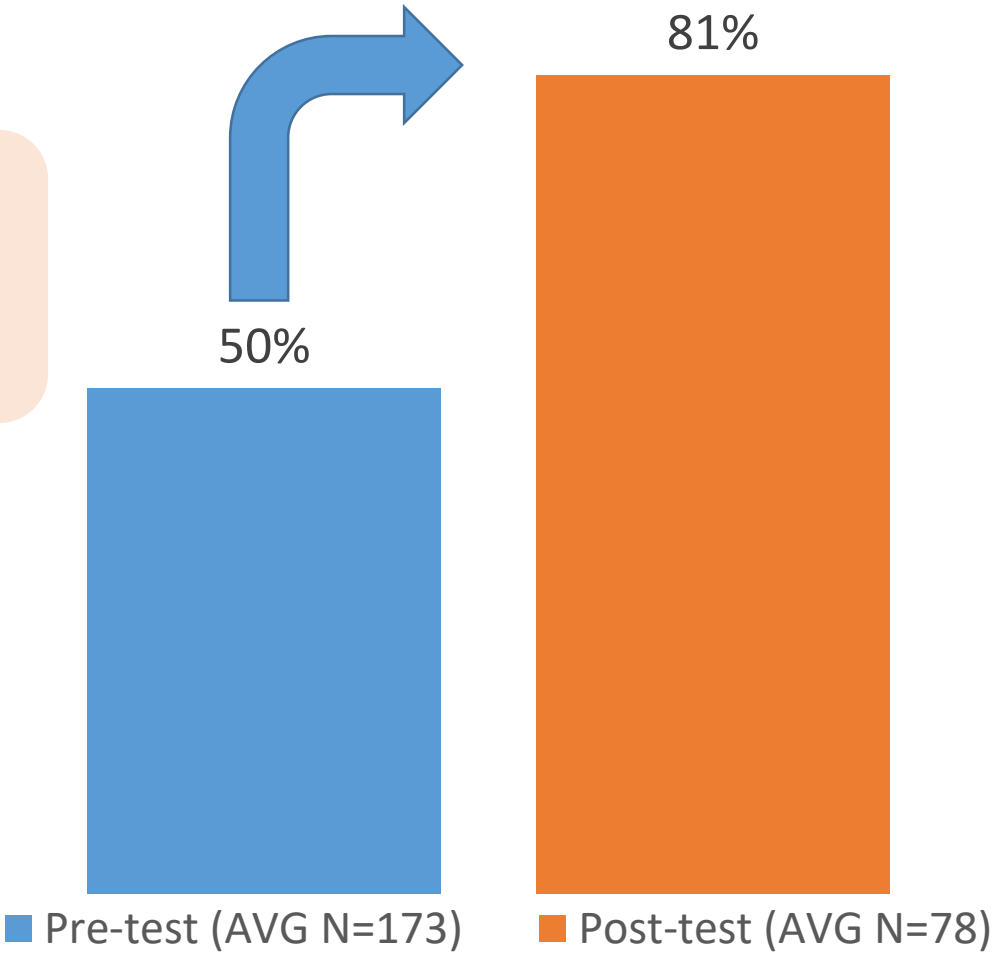
Level (3 & 4) Outcomes: Knowledge & Competence

Final Outcomes Summary – Online Enduring Outcomes

Overall Knowledge Gain across Learning Objectives Across All 3 Activities

62% Relative Knowledge Gain

31% Absolute Knowledge Gain

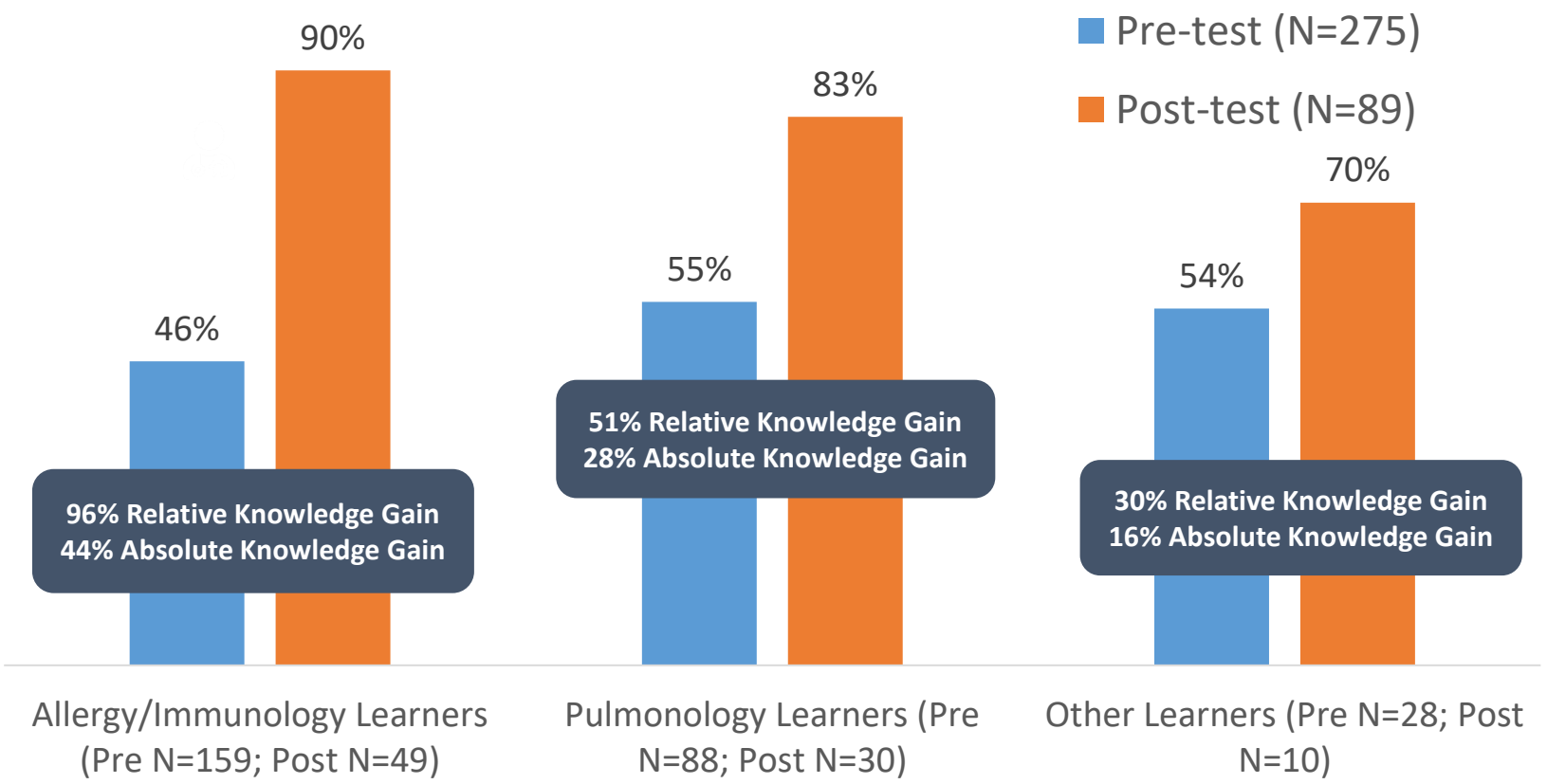


Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Define AHR and its relationship to epithelial cell function, inflammation, and airway remodeling in asthma***



Question 1 (Video 1): Which of the following is least likely to be involved in airway hyperresponsiveness in asthma?

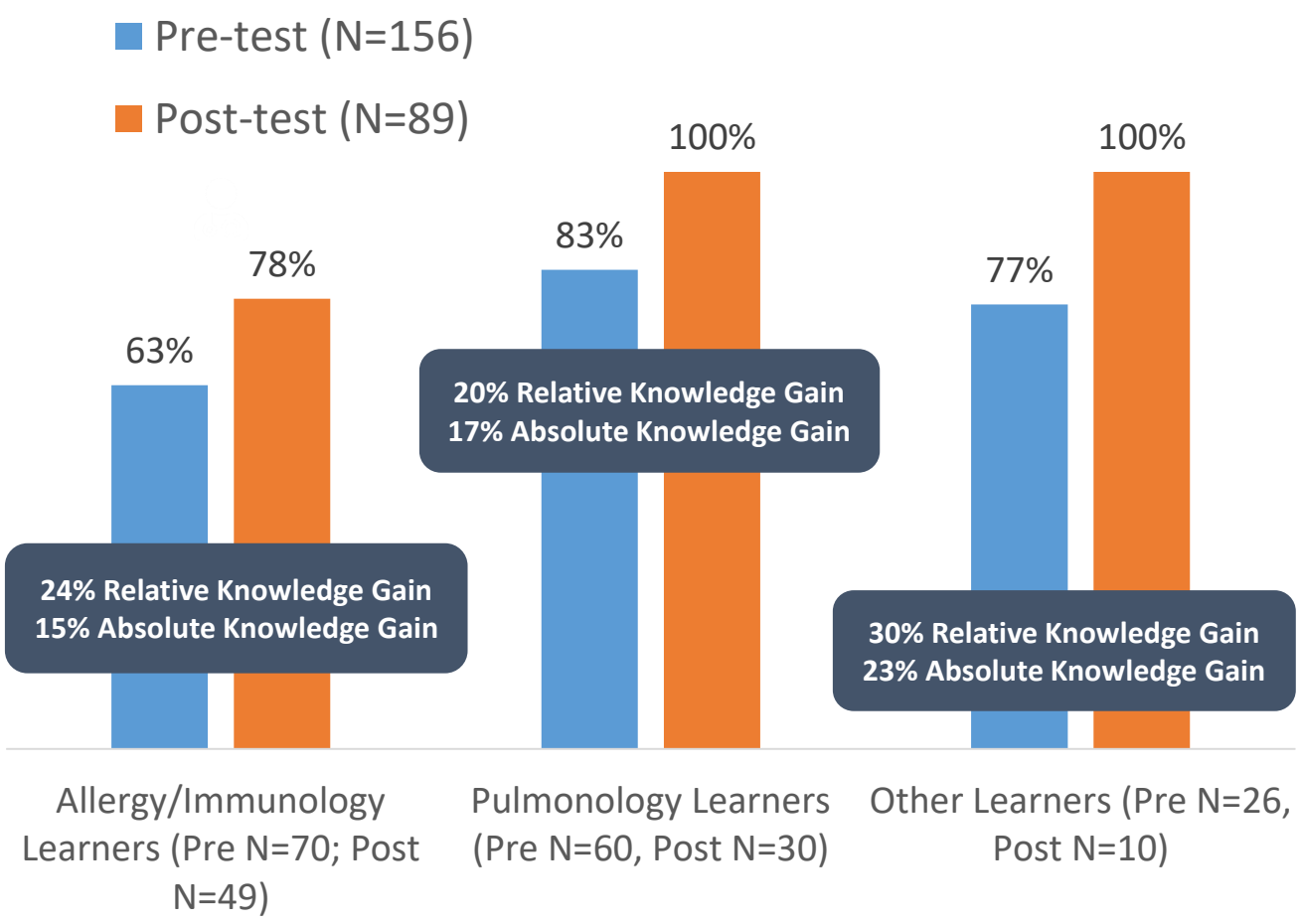
a. Airway epithelium
b. Mast cells
c. Airway smooth muscle
d. Neutrophils
e. TH2 cells

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Evaluate the role of bronchoprovocation challenge testing in asthma diagnosis and management.***



Question 2 (Video 1): Manny is an 18-year-old male who states that he has coughing and wheezing whenever he is around his friend's dogs and prolonged cough whenever he gets a cold. He has no pets at home since he is known to be allergic to dogs based on skin testing performed about 5 years ago. He is feeling well today. On pulmonary testing today, he has a normal exhaled nitric oxide and normal lung function, without bronchodilator reversibility. You decide to use a bronchial provocation test (BPT) to help understand his respiratory symptoms given his normal pulmonary testing thus far. Which of the following is an example of a direct BPT used commonly in clinical practice to assess for airway hyperresponsiveness?

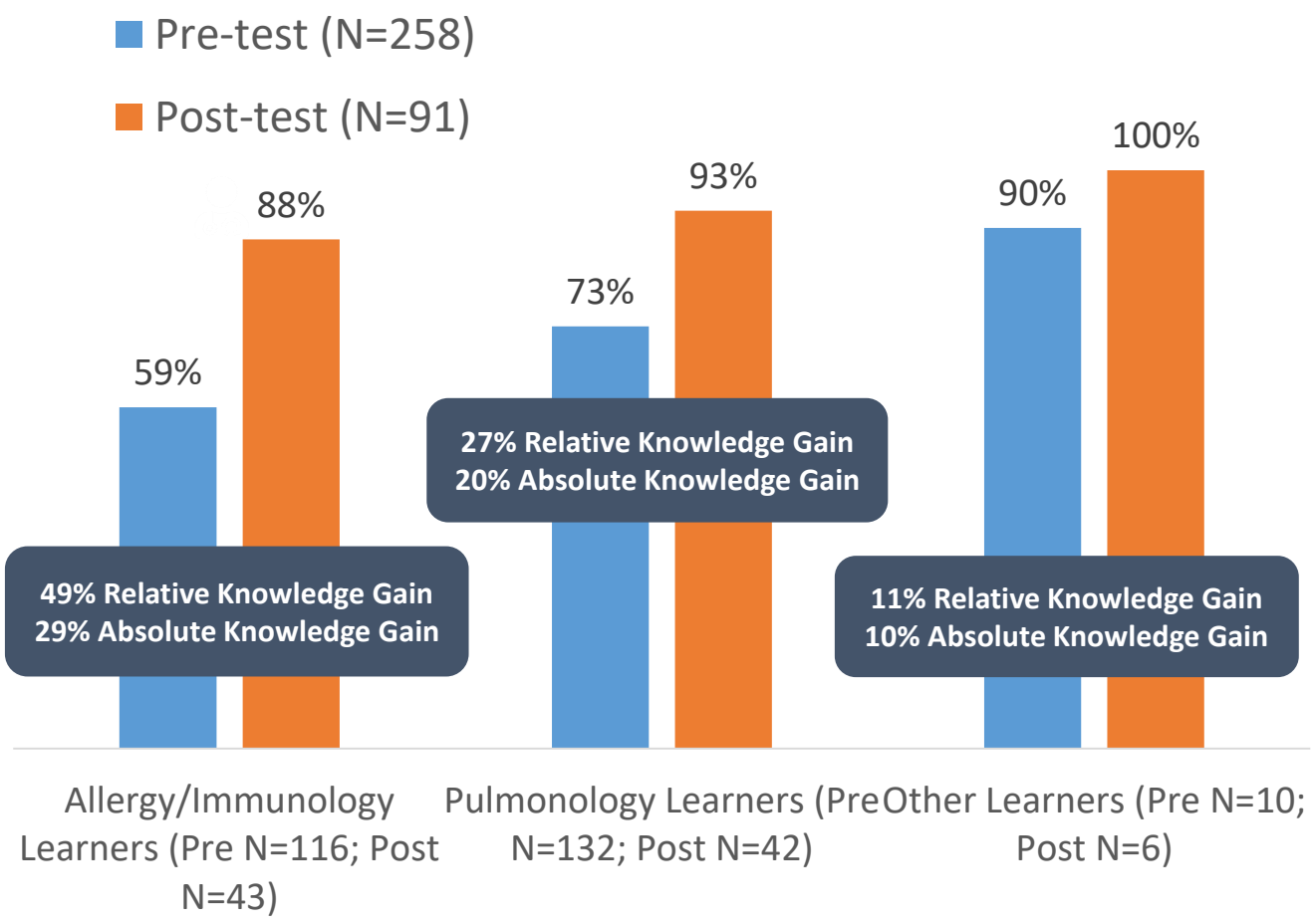
a. Histamine challenge
b. Methacholine challenge
c. Mannitol challenge
d. Allergen challenge

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Discuss the implications of AHR for treatment selection in severe asthma.***



Question 3 (Video 2): Cassie is a 26-year-old female with severe persistent asthma. Her exhaled nitric oxide, total IgE level, and circulating eosinophil counts are all elevated. She continues to require her rescue inhaler 4-5 times a week and have occasional nighttime awakening despite being on high-dose ICS/LABA/LAMA therapy. Prior to starting therapy, she was noted to have significant airway hyperresponsiveness on methacholine challenge, with a PC-20 of 0.25. Repeat methacholine challenge now demonstrates a PC-20 of 3.2mg/ml. Which would be your next intervention?

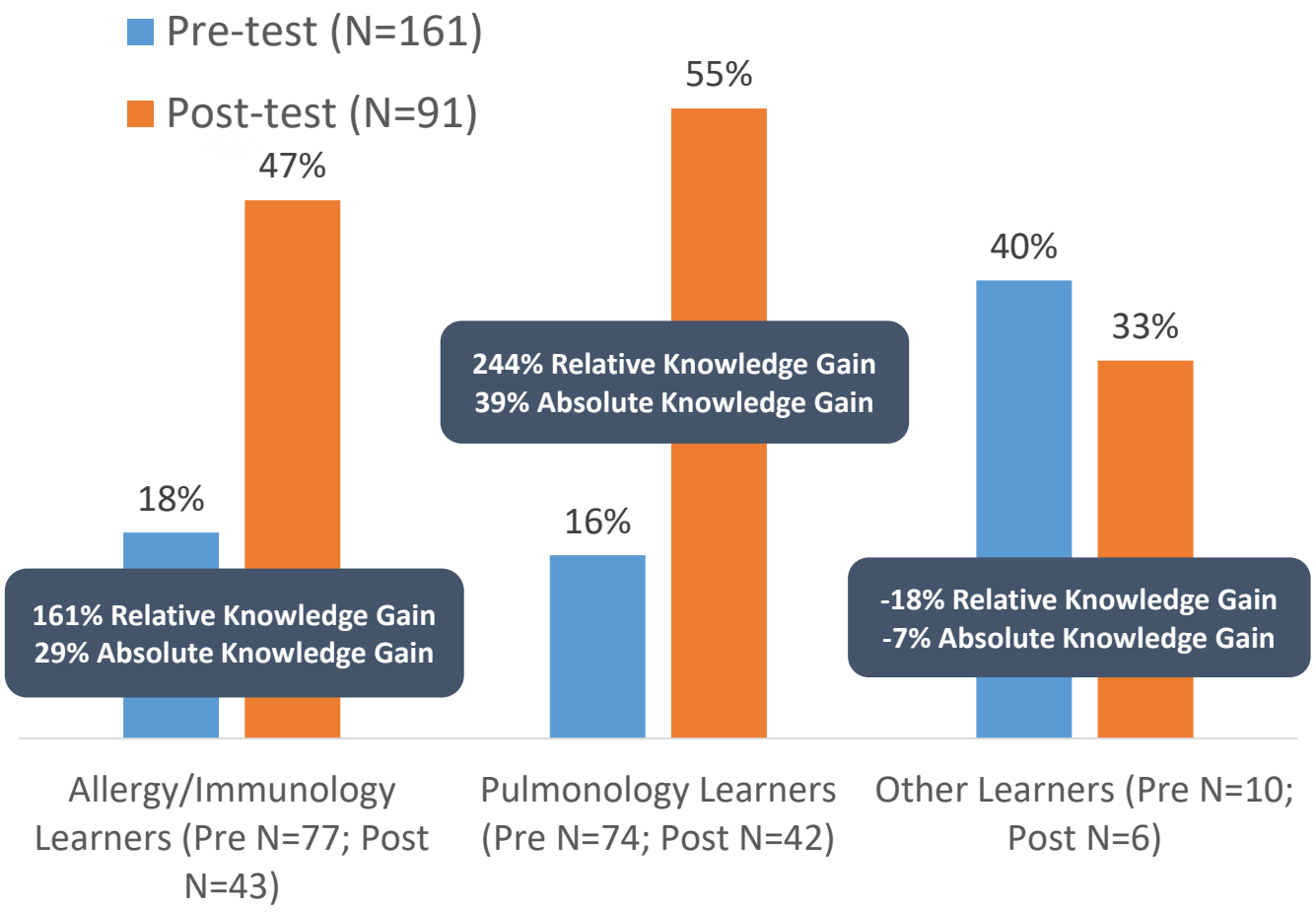
a. No further intervention as her AHR has improved so much after starting ICS/LABA/LAMA therapy
b. Add a biologic agent such as tezepelumab for continued poor control of her severe persistent asthma and continued AHR
c. Switch to a different ICS/LABA/LAMA inhaler as the current one does not seem to be fully controlling her asthma
d. Prescribe imatinib for her asthma

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Compare the effects of current and emerging biologic therapies on AHR in clinical studies***



Question 4 (Video 2): Which of the following therapies has been shown to consistently reduce airway hyperresponsiveness?

a. Tyrosine kinase inhibition with imatinib
b. Anti-IgE therapy with omalizumab
c. Anti-TSLP therapy with tezepelumab
d. Anti-IL-5 therapy with reslizumab
e. A and C
f. B and C

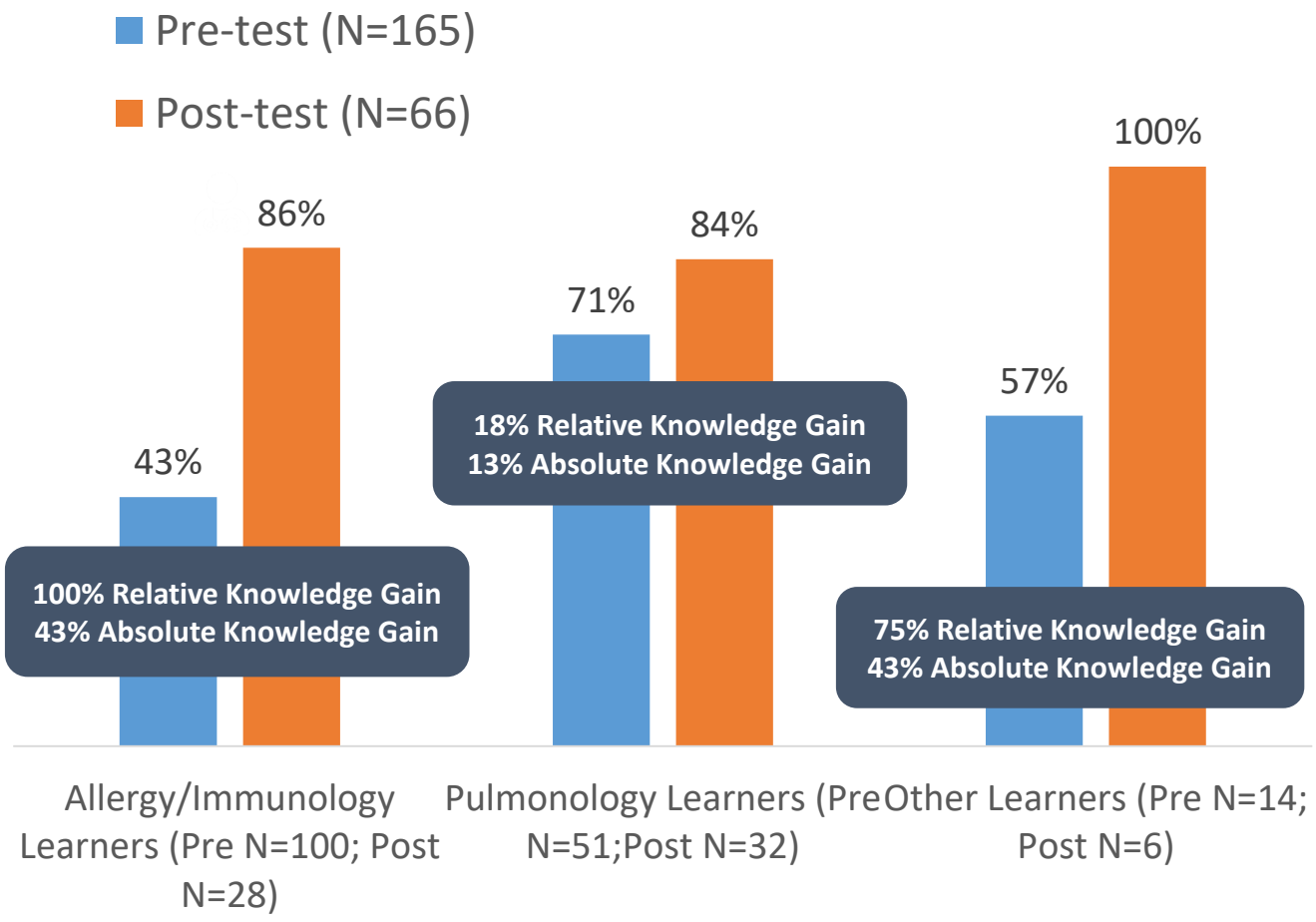
Of note, "other" learners demonstrated a knowledge decrease with regard to comparing the effects of biologics on AHR in clinical studies. However, because allergists and pulmonologists demonstrated significant gains, faculty determined it was not necessary to revise the question.

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Define AHR and its relationship to epithelial cell function, inflammation, and airway remodeling in asthma***



Question 5 (Monograph): Which of the following is true about the alarmins and their role in airway hyperresponsiveness (AHR) in asthma?

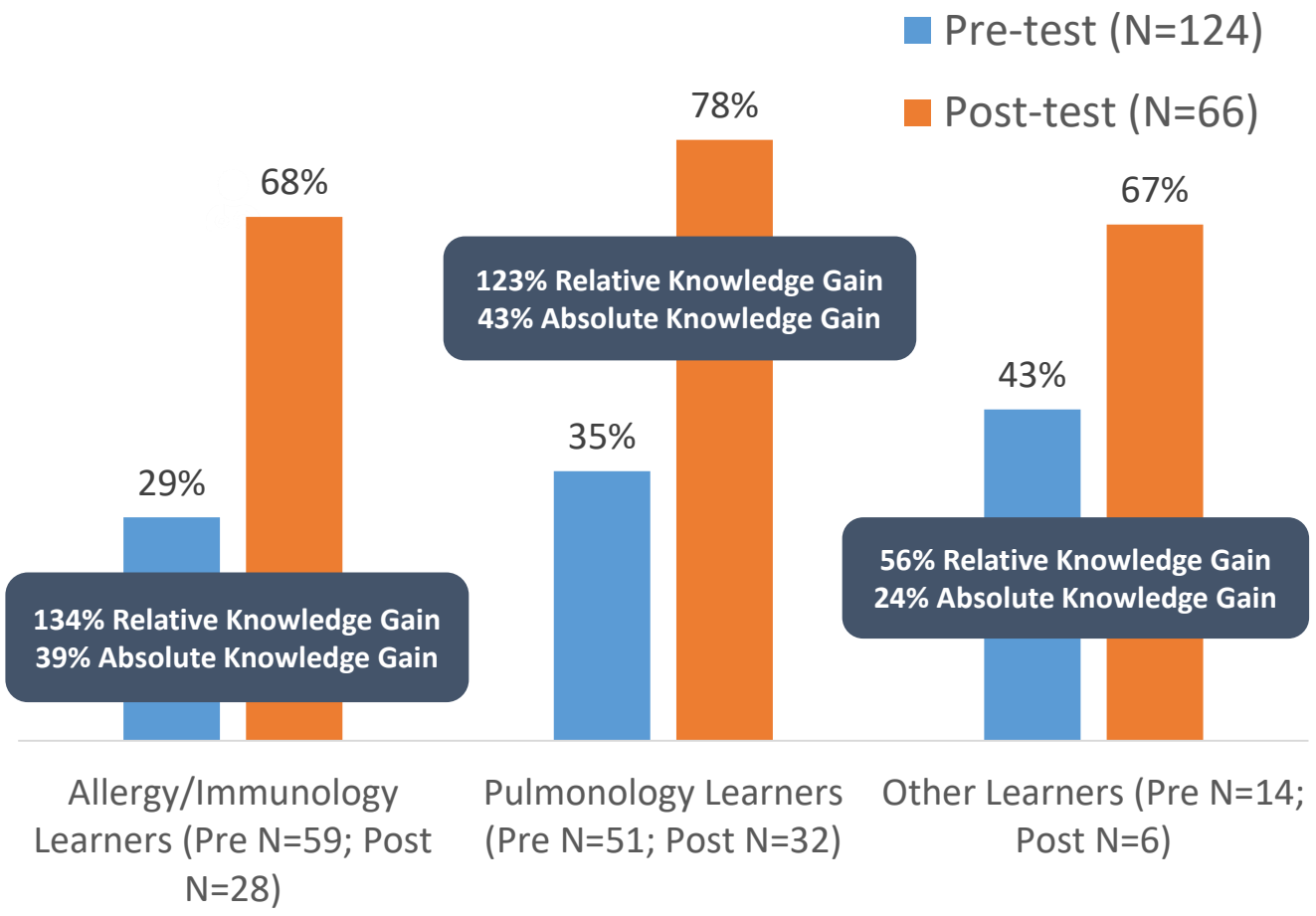
a. They are the primary cytokines involved in eosinophil differentiation and activation
b. They cause mast cell degranulation by binding to Fc epsilon receptors
c. They increase AHR through their effects on type 2 and non-type 2 inflammation
d. They are rapidly released by goblet cells in response to pollutants and allergens

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Evaluate the role of bronchoprovocation challenge testing in asthma diagnosis and management***



Question 6 (Monograph): A 40-year-old woman has severe uncontrolled asthma despite treatment with an inhaled corticosteroid, a long-acting beta-2 agonist, and a long-acting muscarinic antagonist. Her peripheral blood eosinophil count is 200 cells/µl. You decide that bronchoprovocation testing could provide insight into whether type 2 airway inflammation is driving her symptoms. The results of which of the following bronchoprovocation tests has been shown to correlate closely with the presence of biomarkers of type 2 airway inflammation?

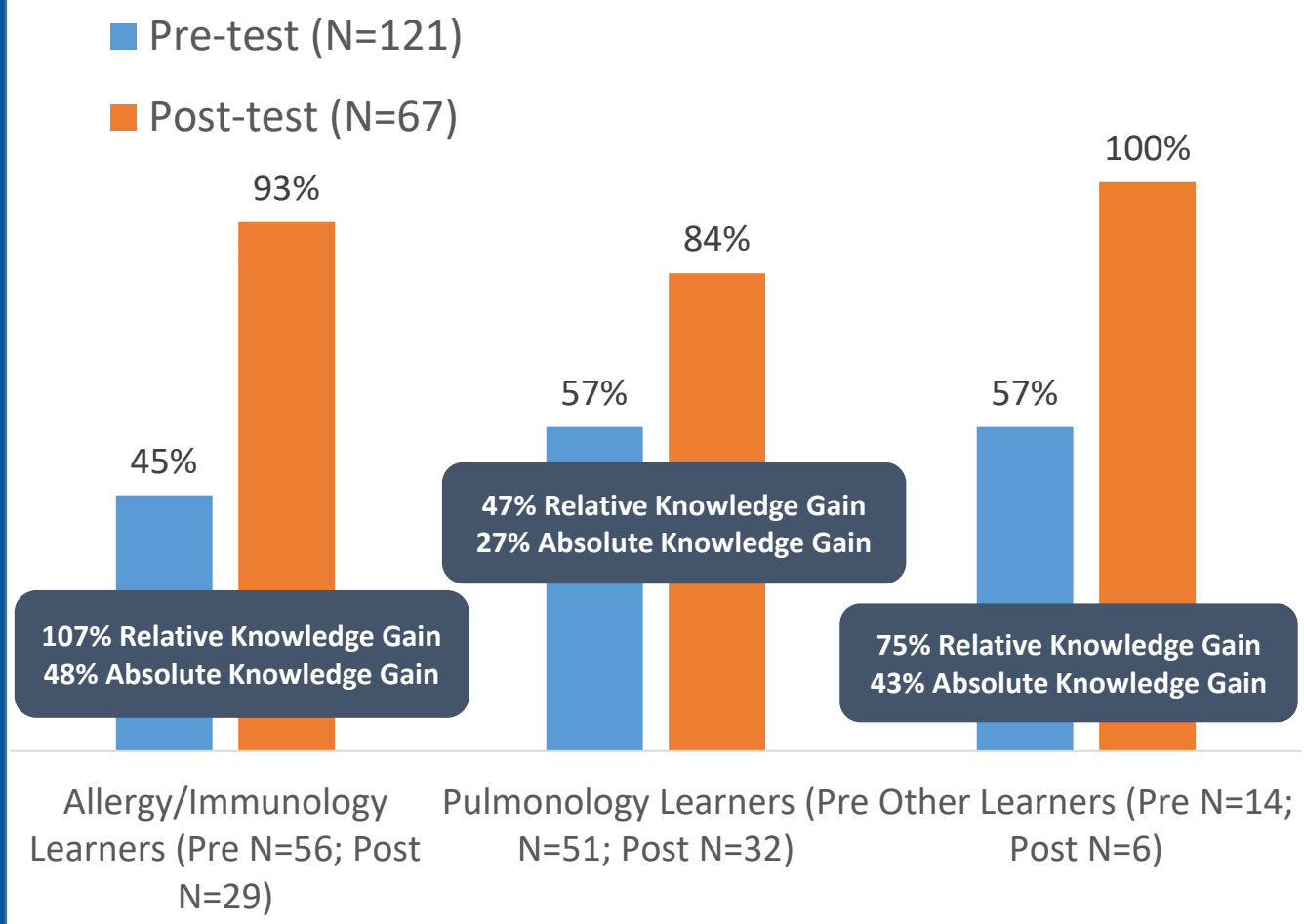
a. **Mannitol challenge**
b. Adenosine monophosphate (AMP) challenge
c. Histamine challenge
d. Eucapnic voluntary hyperventilation challenge

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: *Discuss the implications of AHR for treatment selection in severe asthma*



Question 7 (Monograph): 32-year-old man with severe asthma has uncontrolled symptoms despite treatment with 8 months of an anti–IL-5 biologic, in addition to a high-dose inhaled corticosteroid, a long-acting beta-2 agonist, and a long-acting muscarinic antagonist. His peripheral blood eosinophil count decreased from 475 cells/µl to 250 cells/µl on an anti–IL-5 therapy. His methacholine PC20 is 1.8 mg/mL (normal > 16 mg/mL) and unchanged. His FEV1 is unchanged. He has no history of atopy, and skin prick testing to common aeroallergens is negative. You stop the anti-IL-5 biologic because the clinical response was insufficient. He will continue his inhaled medications. Which of the following represents the next best treatment step?

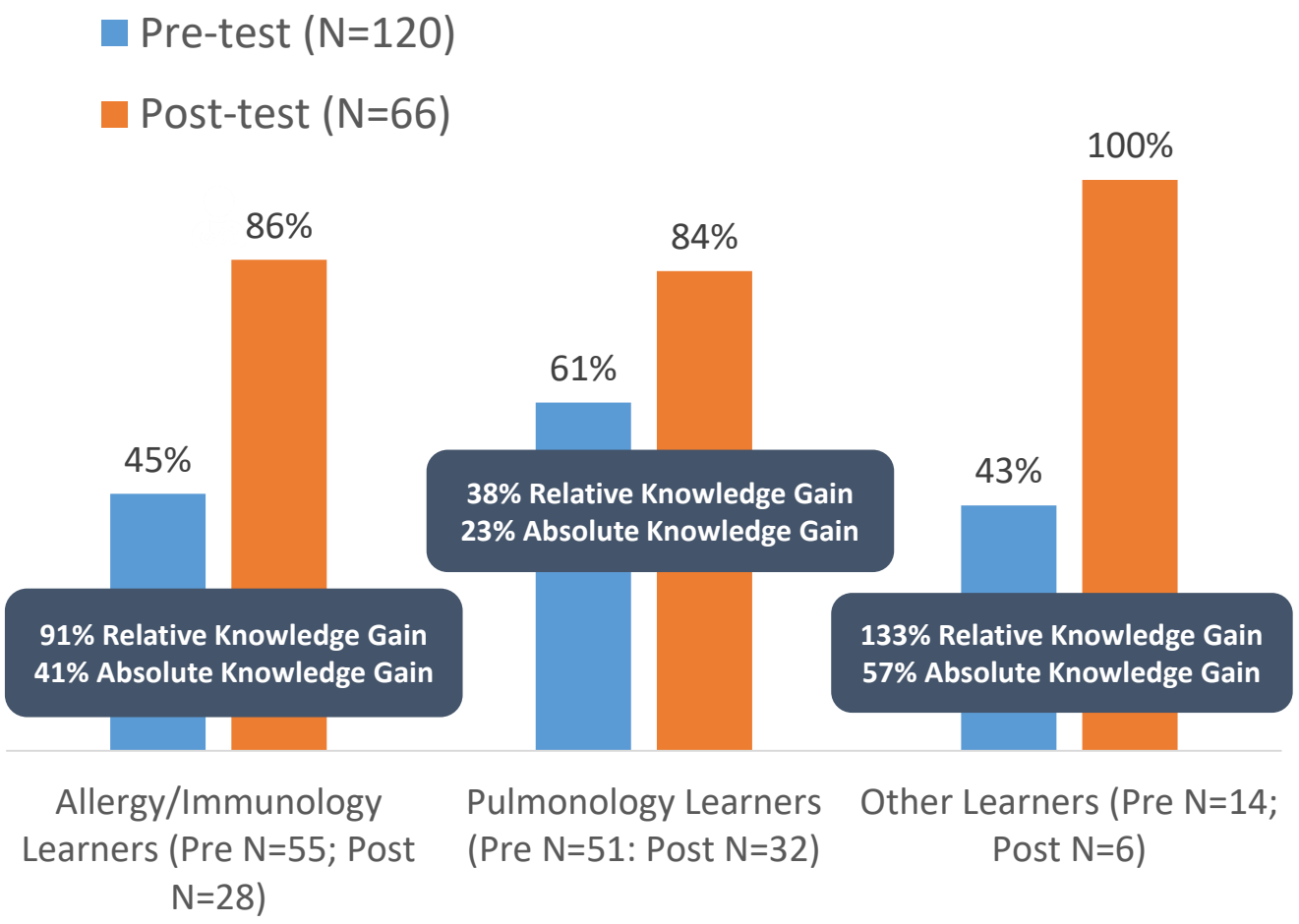
a. Begin a 3-week oral corticosteroid taper
b. Begin a 12-week trial of an oral macrolide antibiotic
c. Begin a biologic therapy that targets immunoglobulin E
d. Begin a biologic therapy that targets thymic stromal lymphopoietin

Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Enduring Outcomes

Learning Objective: ***Compare the effects of current and emerging biologic therapies on AHR in clinical studies***

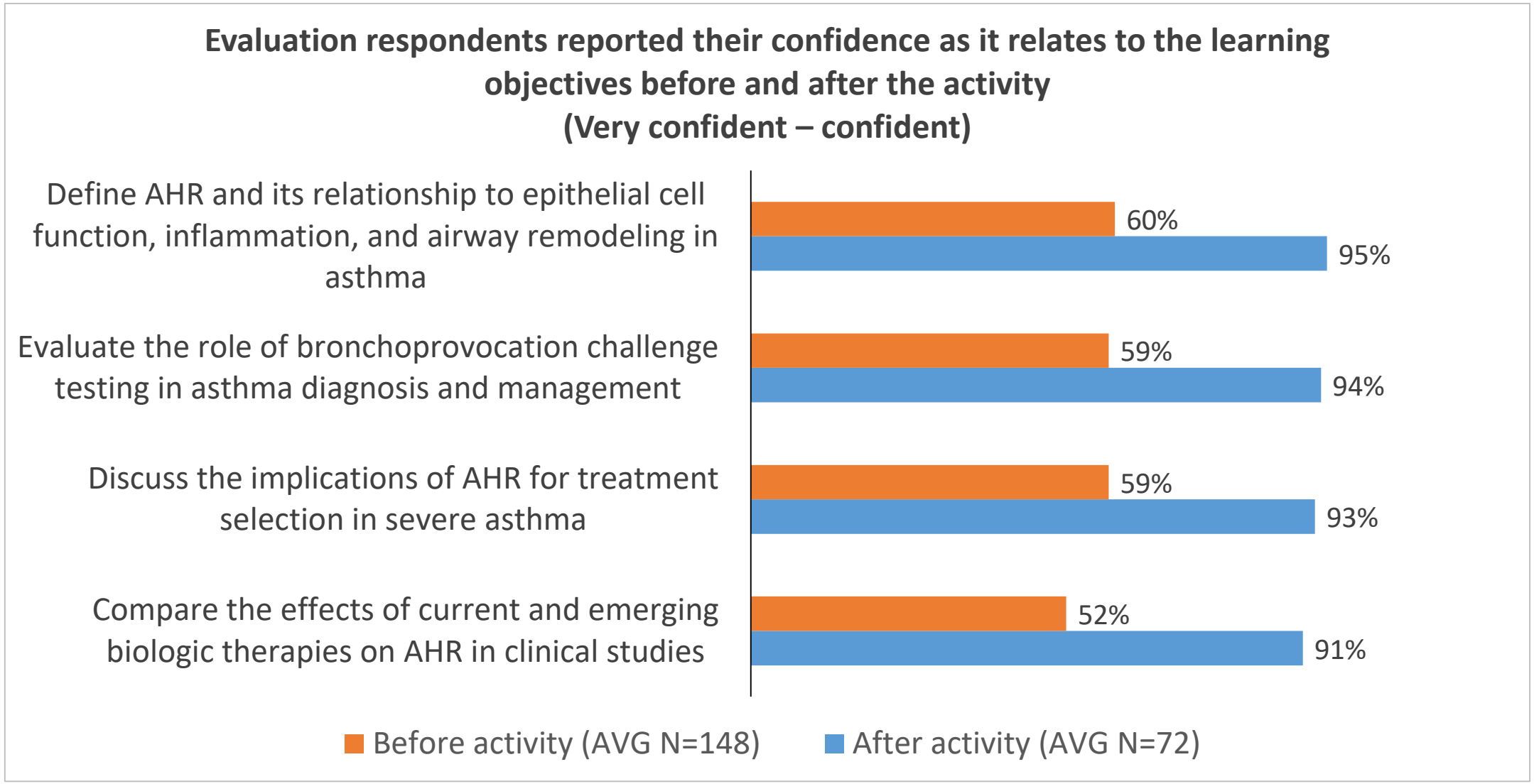


Question 8 (Monograph): A 53-year-old woman has severe asthma. Her peripheral blood eosinophil count has always been normal. Despite treatment with a high-dose inhaled corticosteroid, a long-acting beta-2 agonist, and a long-acting muscarinic antagonist, she continues to have intense bouts of coughing and shortness of breath, particularly on high-pollution days and with respiratory viral infections. Severe airway hyperresponsiveness is present; her methacholine PC20 is 0.12 mg/mL (normal > 16 mg/mL). Treatment with which of the following biologic therapies has been shown in clinical trials to reduce airway hyperresponsiveness in individuals with severe asthma?

a. Mepolizumab
b. Dupilumab
c. Benralizumab
d. Tezepelumab

Level (4) Outcomes: Competence (Across 3 Activities)

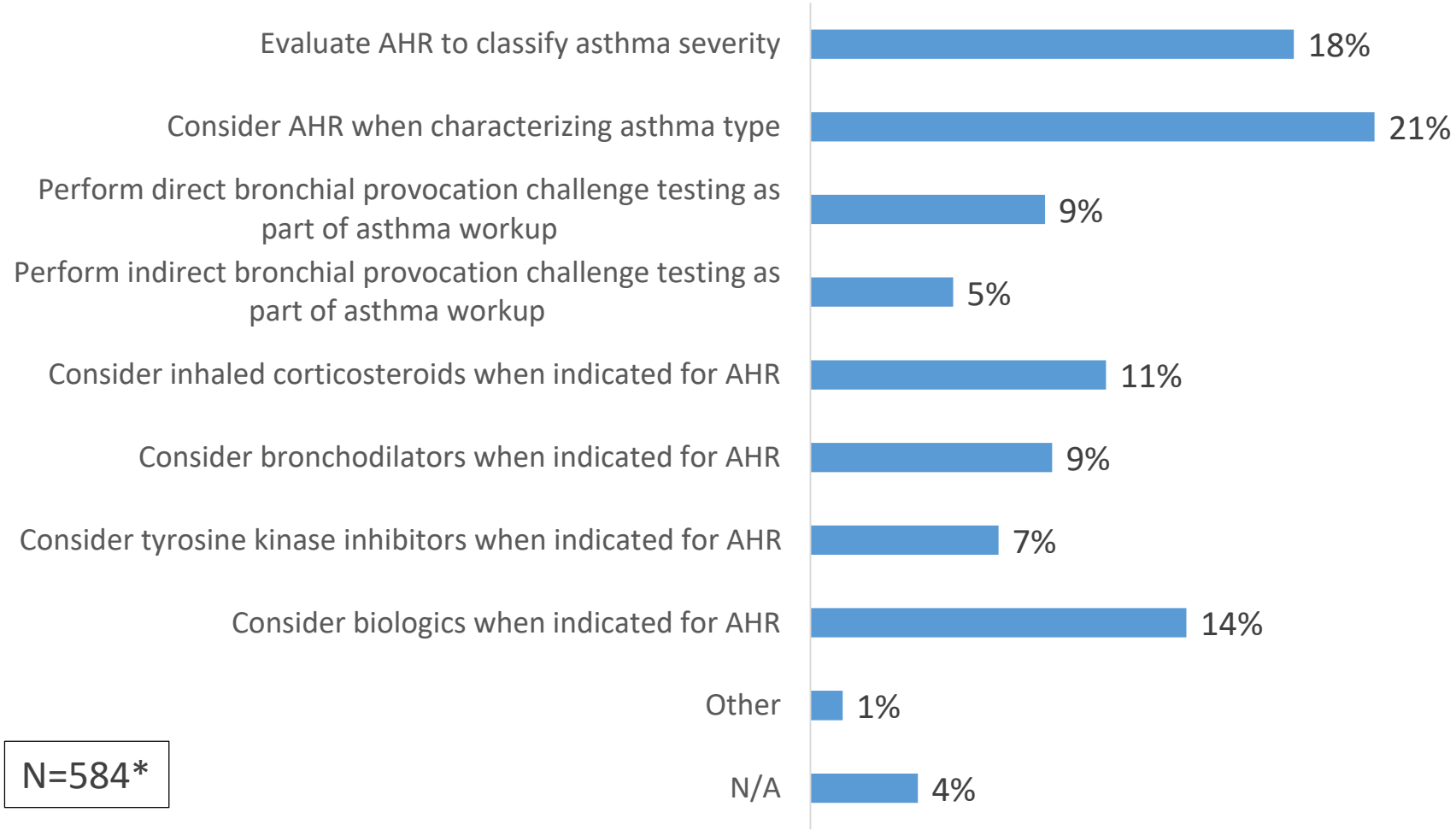
Final Outcomes Summary – Online Enduring Outcomes



Level (4) Outcomes: Competence (Across 3 Activities)

Final Outcomes Summary – Online Enduring Outcomes

What change will you incorporate into your practice as a result of the knowledge acquired during the activity?



N=584*

92%

N=226

Evaluation respondents intend to make changes in practice as a result of the activity

**Evaluation respondents were able to select more than one answer*

Evaluation Survey Results

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

What barriers will the education provided help to address?

- Accurate diagnosis and treatment
- Allergy referrals
- Better management strategies
- Best options for continued care
- Clarification around clinical practice guidelines
- Hesitancy in constructing a BPT in those with occupational asthma
- Improved understanding of various biologics and when to use each one
- Insurance payments and cost
- Lack of time
- Patient cooperation

What barriers to optimal patient care are you facing that were not addressed in this activity?

- Availability of resources
- Cannot do EVH or mannitol here
- Cost of biologics
- Insurance coverage
- Medication coverage
- Reimbursement and prior authorization
- Resource availability
- Time and cost

Evaluation Survey Results

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

Key Takeaways

- Already implemented what was presented
- Assessing AHR in patients with normal PFTs
- Asthma is very complicated!
- Better information about tezepelumab
- Consider different phenotypes for the management of severe persistent asthma with the use of new biologics
- Importance of screening asthma patients
- Multifaceted disease
- Multiplicity of AHR causes and mechanisms
- Pulmonology consultation is valuable
- Receptor mediated responsiveness
- TSLP therapy treats higher up in cascade
- Use of methacholine
- Using AHR assessment tools to guide selection of therapy options
- Understanding of the pathways and contributors to airway hyperresponsiveness
- Value of BPT as aid in management
- When to think about switching biologics
- Which biologics target certain inflammatory agents

Future Topics

- Adequate control of asthma symptoms
- Association with sinusitis and allergic rhinitis
- Biologic therapies
- Bronchial thermoplasty
- Combination biologic therapies
- Direct treatment
- Discussion on mucosal microenvironment
- Impact of new therapies
- New emerging agents for treatment of AHR
- Occupational asthma
- Pediatric asthma
- Relation to sleep
- Role of FeNO
- TH2 cell types

"It was very well presented and personally I learned a lot about newer diagnostic and treatment therapies."

– Online enduring learner

Accreditation Details

Final Outcomes Summary – Online Enduring Outcomes

National Jewish Health

National Jewish Health is accredited with Commendation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The NJH Office of Professional Education produced and accredited this program and adhered to the updated ACCME guidelines.

Video Activities

NJH designates each enduring material for a maximum of 0.25 *AMA PRA Category 1 Credit*™.

Monograph

NJH designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credit*™.

ACCME™
ACCREDITED WITH COMMENDATION