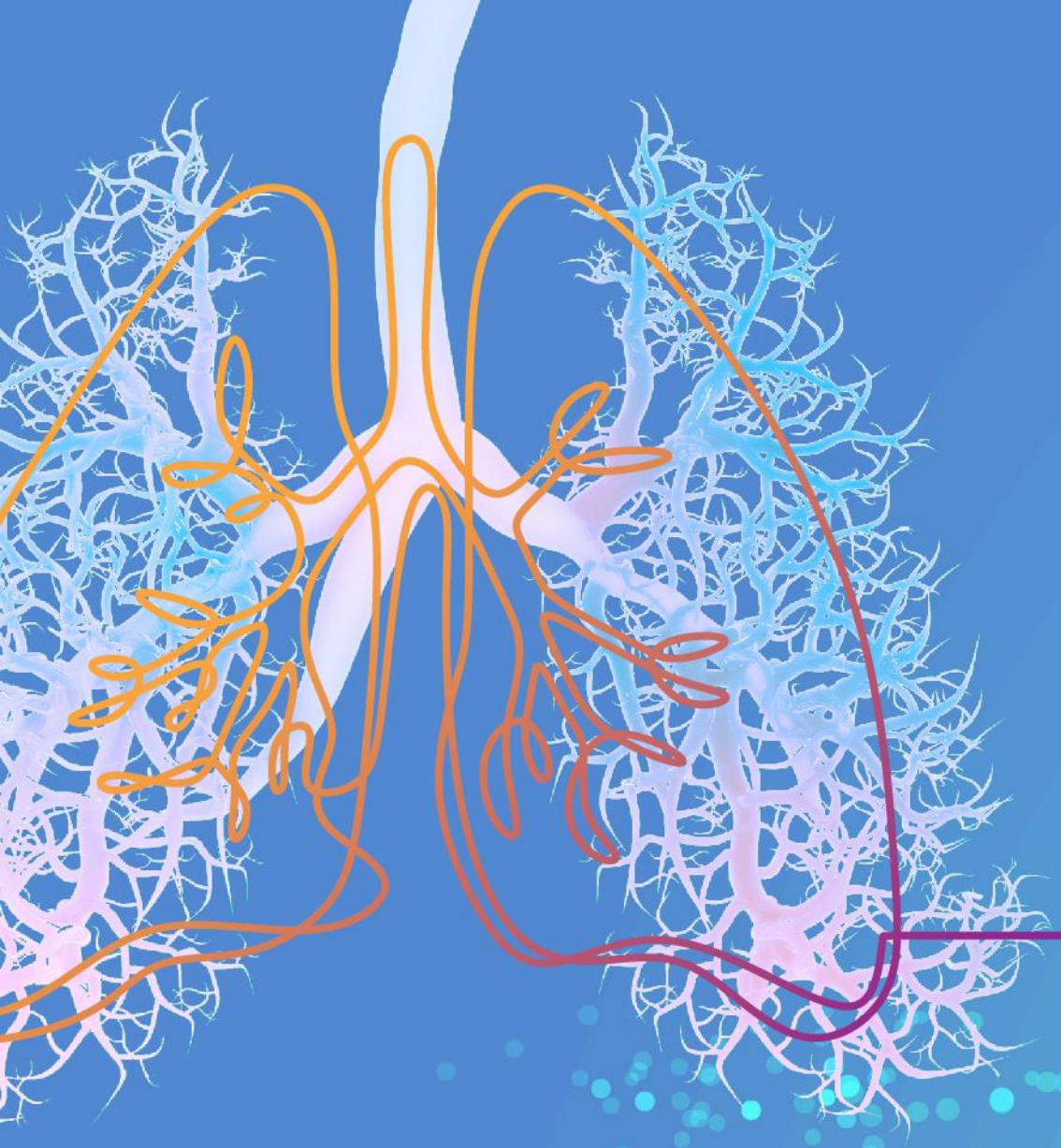

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Unraveling the Complexity of Severe Asthma Treatment

OCTOBER 16, 2022 | NASHVILLE, TN

Final Outcomes Summary
Live Program and Online Enduring
(Online Data from 11/30/22 – 11/30/23)
Grant ID: 72885703

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Final Outcomes Summary – Online Outcomes and Live Program

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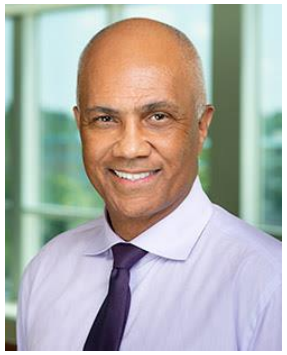
Executive Summary

Final Outcomes Summary – Online Outcomes and Live Program



Ronald Balkissoon, MD, MSc, DIH, FRCPC
Denver, CO

Program Overview

Summary:

This activity was presented as a live CME Satellite Symposium on October 16, 2022 during the American College of CHEST Physicians Annual Meeting (CHEST 2022) in Nashville, TN. The activity unraveled the complexity of severe asthma treatment by providing expert insights into the new paradigm of treatments, providing case examples with interactive polling, and offering a clinical reference aid to illuminate treatment options. Whiteboard animations were also used to illustrate the pathophysiology of severe asthma and treatment targets.

Flavia Cecilia Lega Hoyte, MD
Denver, CO

Learning Objectives

Learning Objectives:

- Describe the role of the airway epithelium in asthma.
- Define the epithelial alarmins and their impact on T2 and non-T2 airway inflammation, remodeling, and hyper responsiveness in severe asthma.
- Evaluate the results of clinical trials of current and emerging therapies that target the epithelial alarmins in severe asthma.
- Match clinical characteristics and phenotypes to treatment targets.

Monica Kraft, MD
New York, NY

Target Audience & Accreditation

Target Audience: Pulmonologists who treat patients with severe asthma.

National Jewish Health designates the live and enduring activities for a maximum of 1.0 *AMA PRA Category 1 Credit*™.

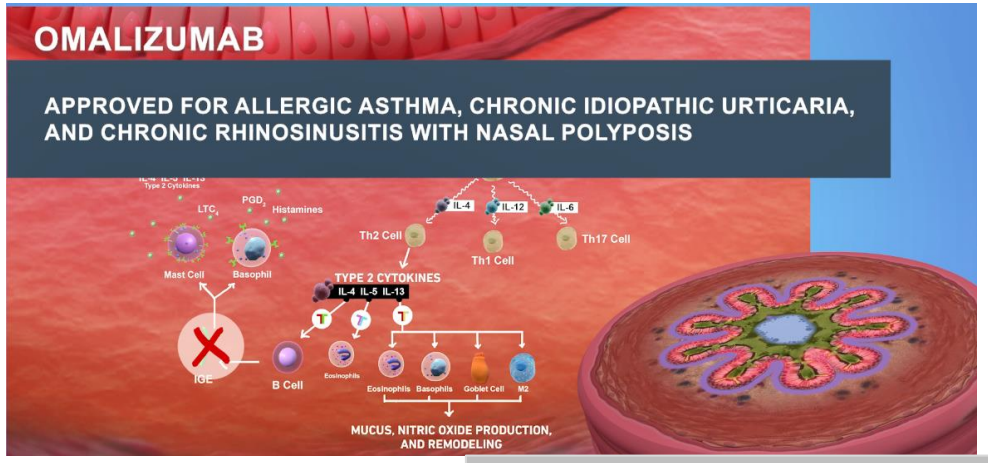
Live activity: October 16, 2022
Location: Omni Nashville Hotel
Nashville, TN 37203

Enduring activity: November 30, 2022 – November 30, 2023
Medscape: https://www.medscape.org/viewarticle/984543
FreeCME: https://www.freecme.com/products/unraveling-the-complexity-of-severe-asthma-treatment

Program Features

Final Outcomes Summary – Online Outcomes and Live Program

Whiteboard Animations



95%

evaluation respondents in the live and online activities reported they are likely to use the clinical reference aid in practice

N=1799

Patient Case Scenarios with Interactive Polling and Faculty Discussion

CASE 3

- 47-year-old obese female
- Diagnosed with asthma at age 42
- Was initially having 3-4 steroid-requiring exacerbations per year
- Started on daily OCS 2 years ago; since then, still having daily symptoms and 1-2 exacerbations per year
- Has tried omalizumab and mepolizumab without any benefit, so both were discontinued

MEDICATIONS:

- High dose ICS/LABA, LAMA, prednisone 10mg daily, albuterol prn

TESTING:

- Total IgE 15
- Absolute Eosinophil Count 100
- Exhaled Nitric Oxide 9
- ACT score 12
- Sputum cell count showed few cells, no specific cell type predominar
- FEV1%: 75% predicted, reversibility: 6%

Which of the following treatments is the most appropriate next step for this patient?

Omalizumab	
Dupilumab	
Reslizumab	
Tezepelumab	

Clinical Reference Aid

Unraveling the Complexity of Severe Asthma Treatment

TYPE 2 ASTHMA

Type 2 asthma is associated with Type 2 inflammation, characterized by:

- Th2 cells
- ILC2s
- Eosinophils
- Mast cells
- Cytokines like IL-4, IL-5, and IL-13

Type 2 asthma includes allergic asthma and eosinophilic asthma.

NON-TYPE 2 ASTHMA

Non-type 2 asthma lacks the features of Type 2 asthma.

Some patients with non-type 2 asthma will have inflammation driven by:

- Th1 cells
- Th17 cells
- Neutrophils
- Macrophages
- Cytokines like IFN-γ

Others have no cellular inflammation identifiable in the airway (pauci-cellular subtype).

CONNECTING INFLAMMATORY PATHWAYS TO TREATMENT OPTIONS

Treatment Target	Biologic Agent	Current and Emerging Treatment Options
TSLP	Tezepelumab	FDA approved ☑ for severe asthma regardless of phenotype or endotype
IL-4Rα (IL-4, IL-13)	Dupilumab	FDA approved ☑ for severe asthma with eosinophilic phenotype or for steroid-dependent asthma
IL-5	Mepolizumab, Reslizumab	FDA approved ☑ for severe asthma with eosinophilic phenotype
IgE	Omalizumab	FDA approved ☑ for allergic asthma, chronic idiopathic urticaria, and chronic rhinosinusitis with nasal polyposis
IL-5Rα	Benralizumab	FDA approved ☑ for severe asthma with eosinophilic phenotype
IL-33	Itepekimab	Not yet approved, currently in phase 2 and 3 trials
IL-33	Tozorakimab	Not yet approved, currently in phase 2 trials
IL-33 (Anti ST2)	Astegolimab	Not yet approved, currently in phase 2 trials
IL-25	None- No human studies	No human studies to date

☑ FDA approved

THE INFLAMMATORY CASCADE OF ASTHMA

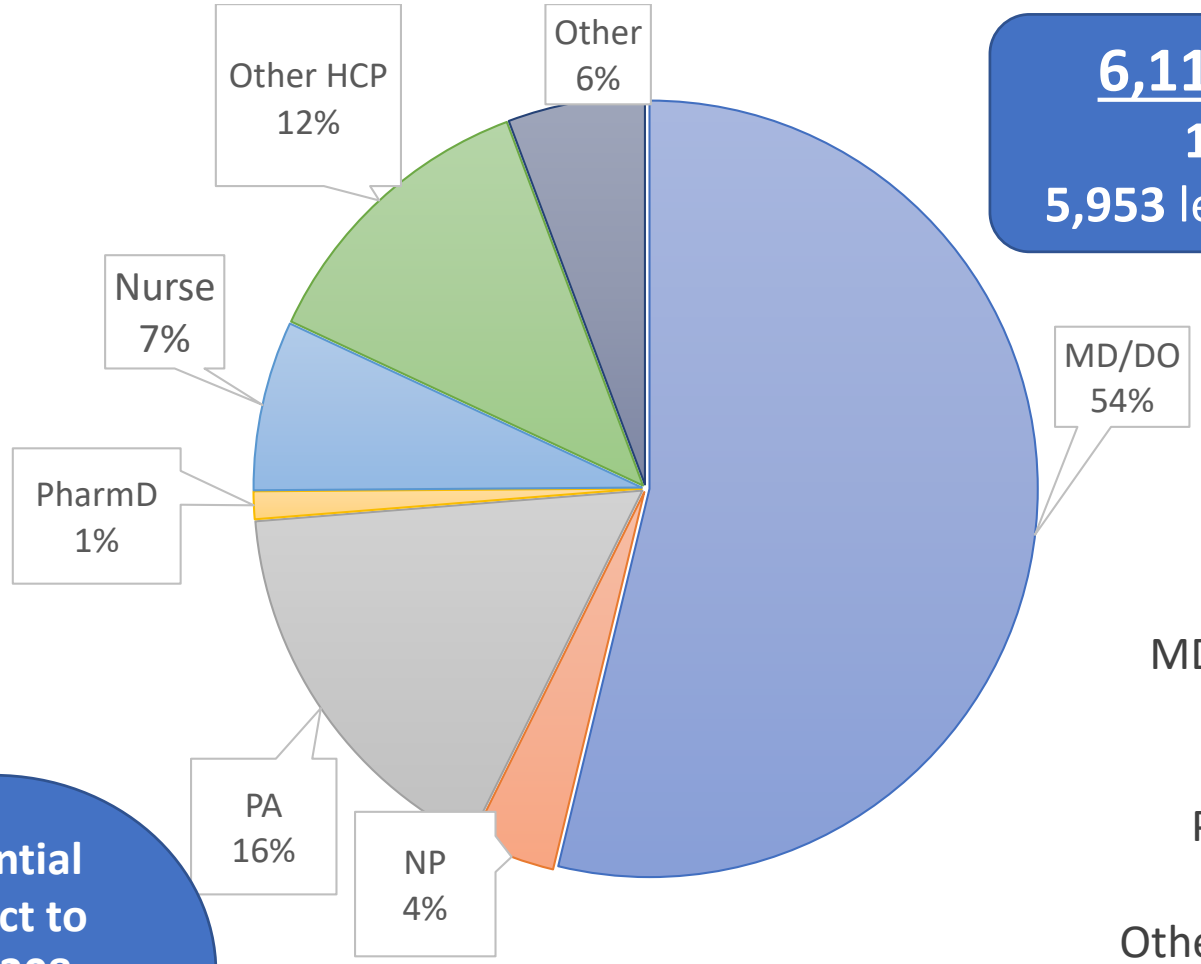
The inflammatory cascade of asthma is thought to begin at the airway epithelium. Once a trigger such as allergens, parasites, fungi, viruses, proteases, or other irritants is introduced:

1. Epithelial alarmins are released.
2. Innate Lymphoid Cells are triggered.
3. T cells are activated. T cells are then stimulated by cytokines and differentiate into Th1, Th2, or Th17 cells.

4A. Triggering of ILC2 or Th2 cells leads to type 2 inflammation and the release of type 2 cytokines.
or
4B. Triggering of Th1 or Th17 cells leads to release of interferon-gamma and other cytokines that lead to non-type 2 inflammation.

Overall Program Impact

Final Outcomes Summary – Online Outcomes and Live Program



Potential impact to 637,208 patient visits this year*

6,112 Learners and 1,999 Completers Total

159 learners/completers in the live program

5,953 learners and **1840** completers in the online activity

MD/DO: 1075
NP: 71
PA: 328
PharmD: 23
Nurse: 141
Other HCP: 247
Other: 114
Total completers = 1,999

"Appreciate your effort in putting up such seminars - and allowing us time away from the Main Convention hustle bustle
- Live learner

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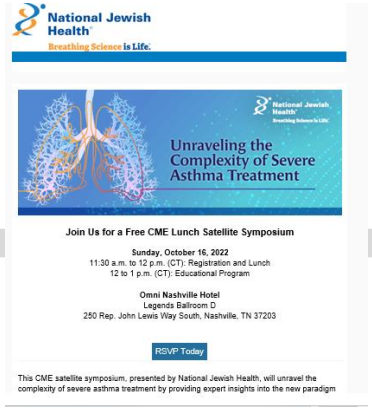
*Note: This estimate is based on total patient visits, not unique patients seen.

Audience Generation

Final Outcomes Summary - Online Outcomes and Live Program

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).

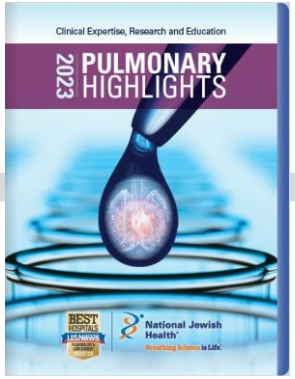
Personalized emails and e-newsletters sent to CHEST registrants & NJH faculty



Digital and print ads on CHEST website and Welcome Back Edition magazine

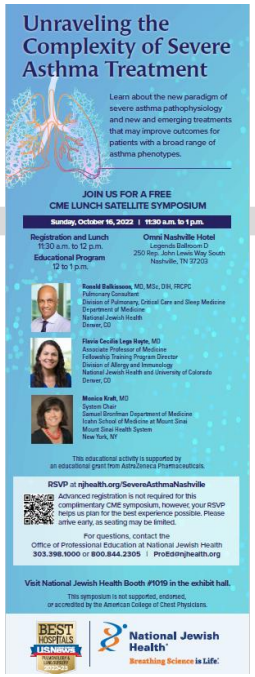
Social media ads and posts

Brochure mailed to CHEST registrants



Online activity featured in 2023 *Pulmonary Highlights* publication

Dedicated landing page on NJH website



Featured Event Listing on CHESTDailyNews.org

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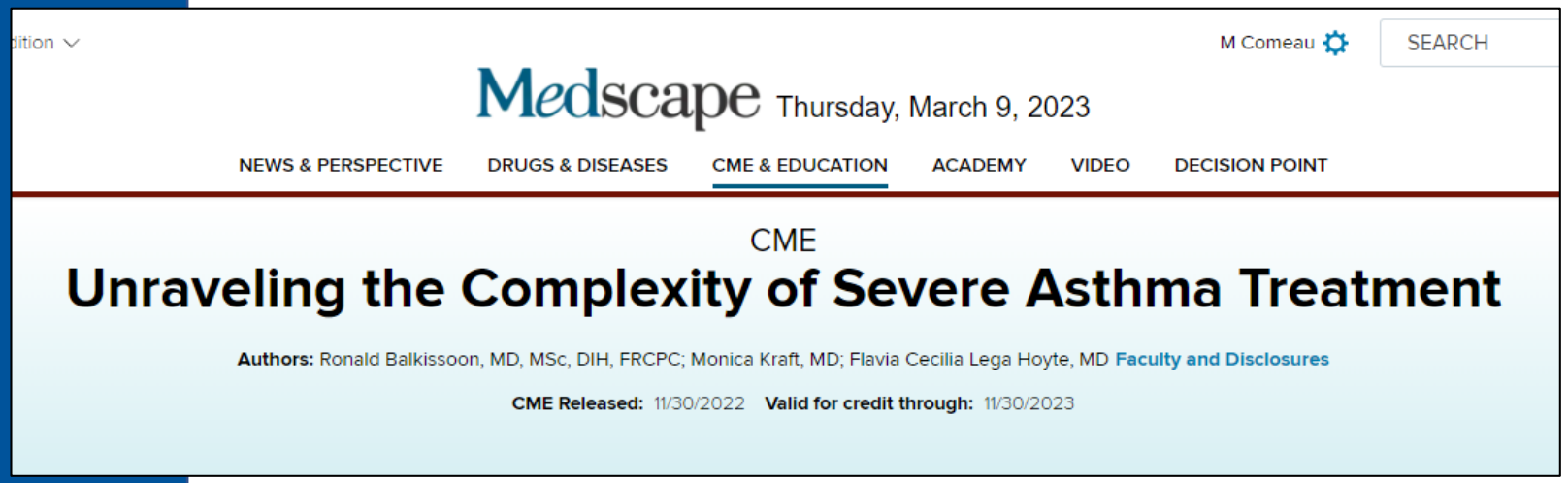
Online Enduring Program

Final Outcomes Summary - Online Outcomes

FreeCME and Medscape
11/30/2022 – 11/30/2023

https://www.freecme.com/products/unraveling-the-complexity-of-severe-asthma-treatment



https://www.medscape.org/viewarticle/984543

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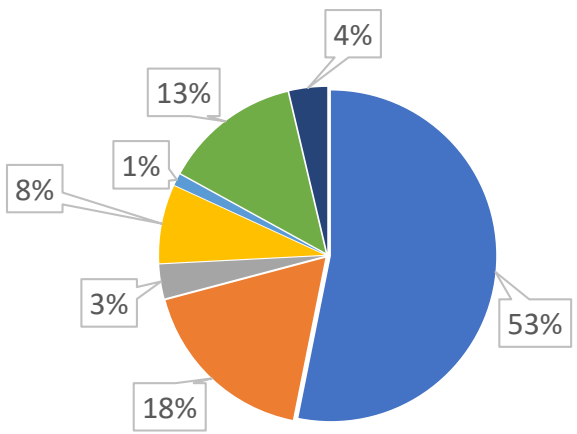
Educational Impact Summary

Final Outcomes Summary – Online Outcomes

Participation



MD/DO=978
PA=326
NP=61
Nurses: 141
PharmD: 21
Other HCP: 245
Other=68
Total Completers = 1840

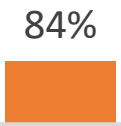
Learner Guarantee	Learner Actual
1,800	5,953

Exceeded learner guarantee for the online enduring by **over 4,000 learners!**

Potential Impact To 623,636 Patient Visits This Year

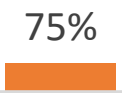
Learning Gain Across Objectives

Overall Knowledge Gain

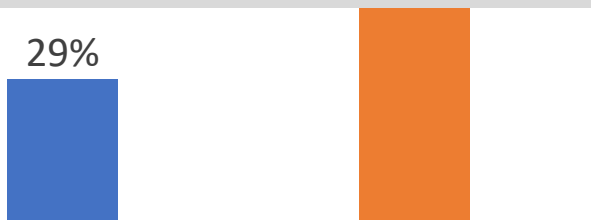


200% relative gain in knowledge
56% absolute gain in knowledge

Overall Confidence Gain



159% relative gain in knowledge
46% absolute gain in knowledge



Evaluation

Met their educational needs **(93%)**

Reinforced or improved current skills **(93%)**

Improved ability to treat patients **(93%)**

N=1903

91%

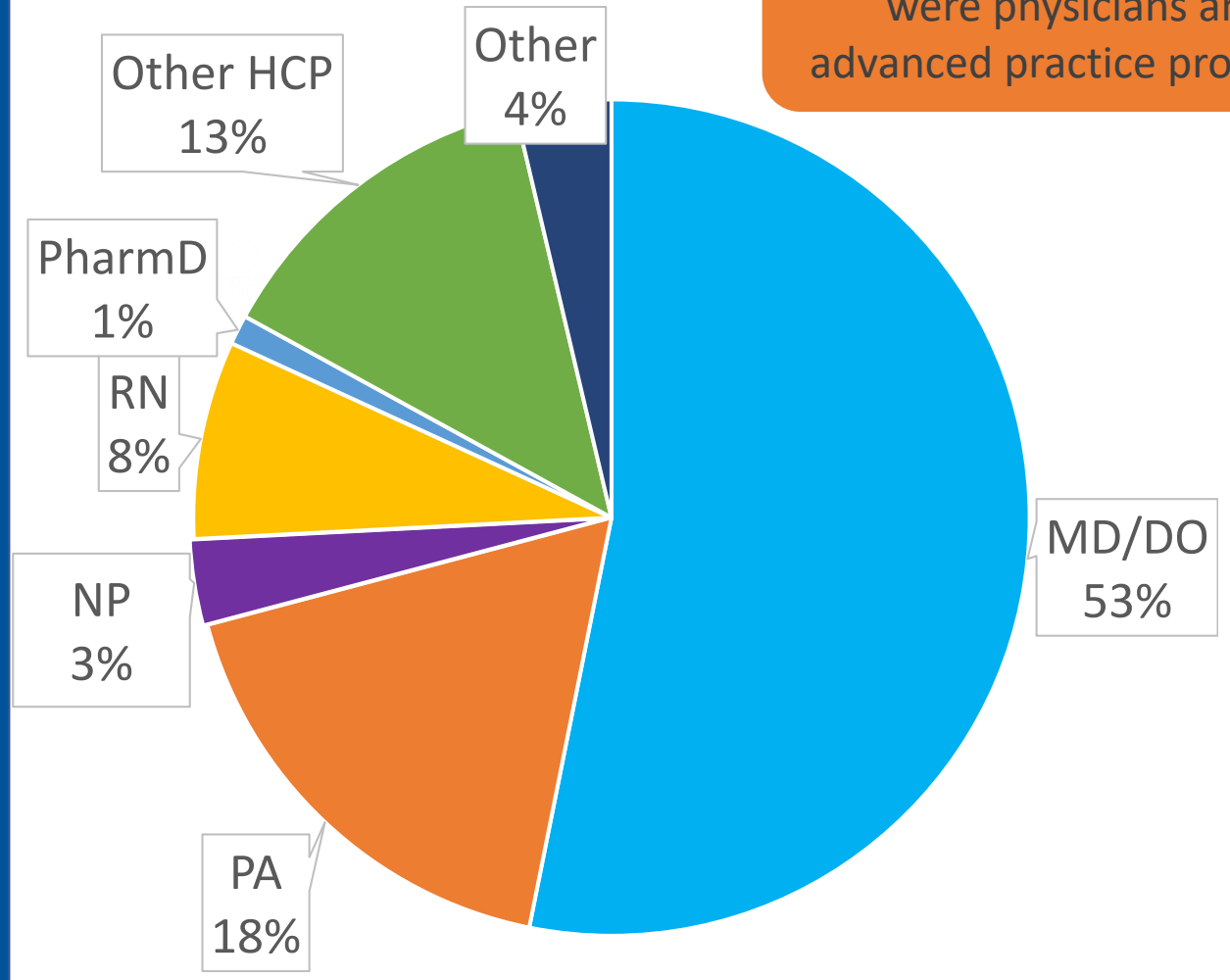
N=1669

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

Level (1) Outcomes: Participation (Degree)

Final Outcomes Summary – Online Outcomes

74% of completers were physicians and advanced practice providers

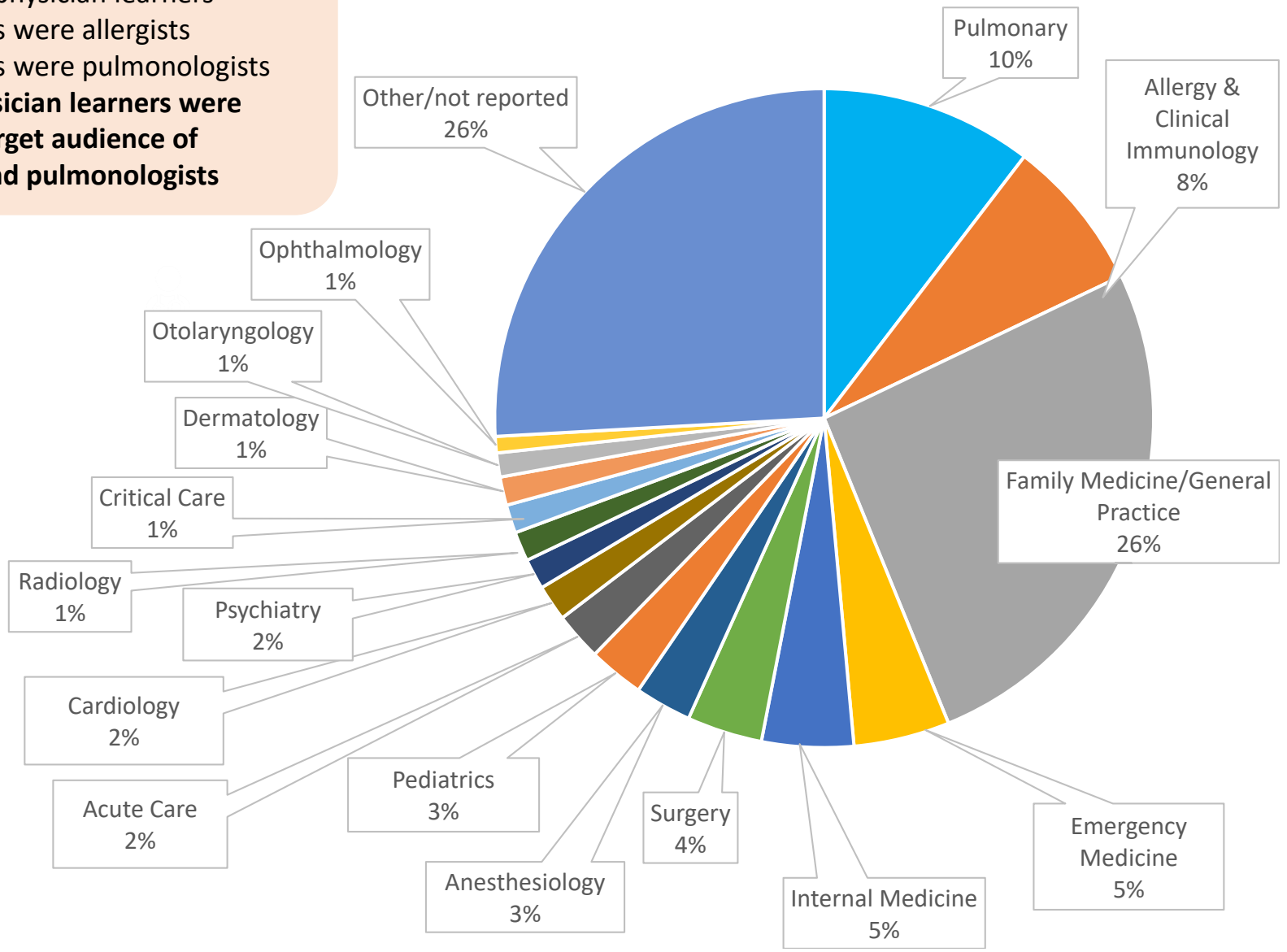


Degree	Total
MD/DO	978
PA	326
NP	61
Nurse	141
PharmD	21
Other Healthcare Provider	245
Other (Case Manager, Business Admin, Medical Student)	68
Total Completers	**1840**

Level (1) Outcomes: Participation (Specialty)

Final Outcomes Summary – Online Outcomes

- 3,566 total physician learners
- 351 learners were allergists
- 981 learners were pulmonologists
- **37% of physician learners were from the target audience of allergists and pulmonologists**

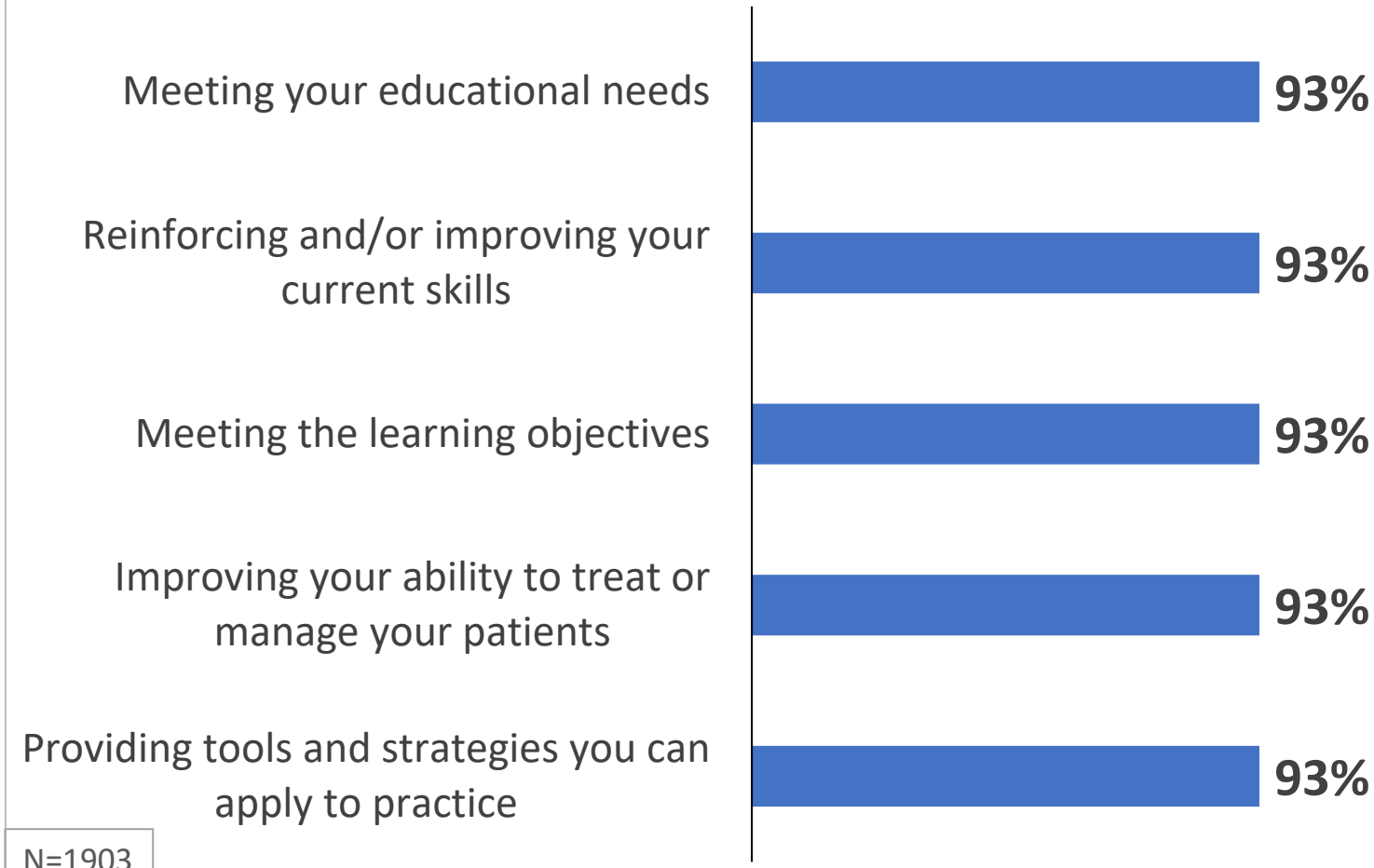


Specialty	Total
Pulmonary	194
Allergy & Clinical Immunology	140
Family Medicine/General Practice	484
Emergency Medicine	88
Internal Medicine	84
Surgery	69
Anesthesiology	52
Pediatrics	51
Acute Care	44
Cardiology	33
Psychiatry	28
Critical Care	27
Radiology	26
Dermatology	26
Otolaryngology	22
Ophthalmology	15
Other/not reported	457
Total Completers	**1840**

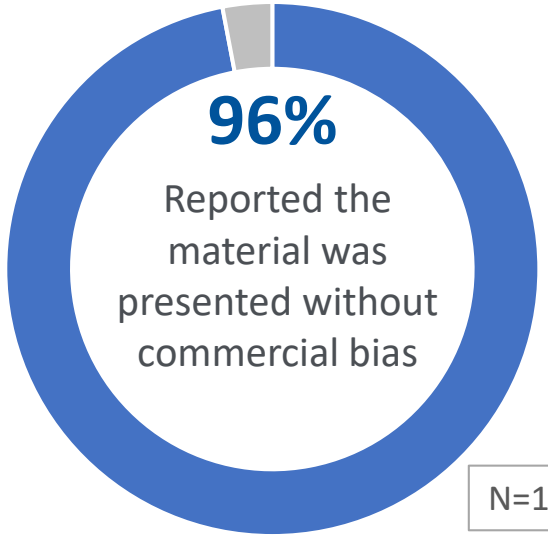
Level (2) Outcomes: Satisfaction

Final Outcomes Summary - Online Outcomes

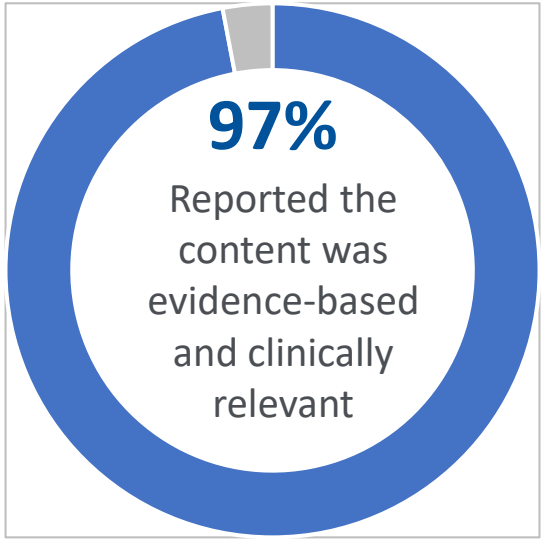
Evaluation respondents rated the activity "Excellent" to "Good" at:



N=1903



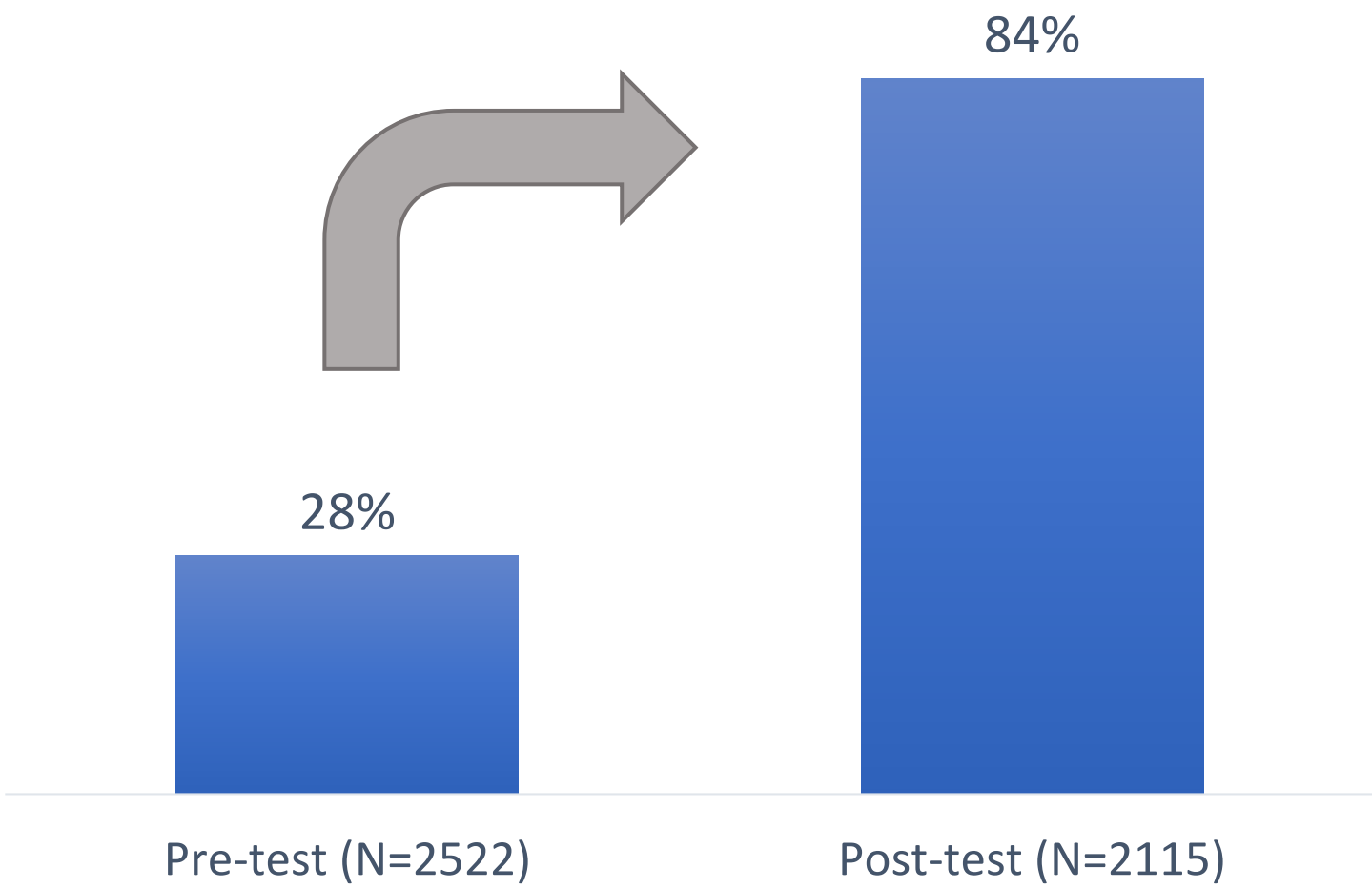
N=1903



Level (3 & 4) Outcomes: Knowledge & Competence

Final Outcomes Summary - Online Outcomes

Overall Knowledge Gain across Learning Objectives



200% Overall Relative Knowledge Gain

56% Overall Absolute Knowledge Gain

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Level (3 & 4) Outcomes: Knowledge & Competence

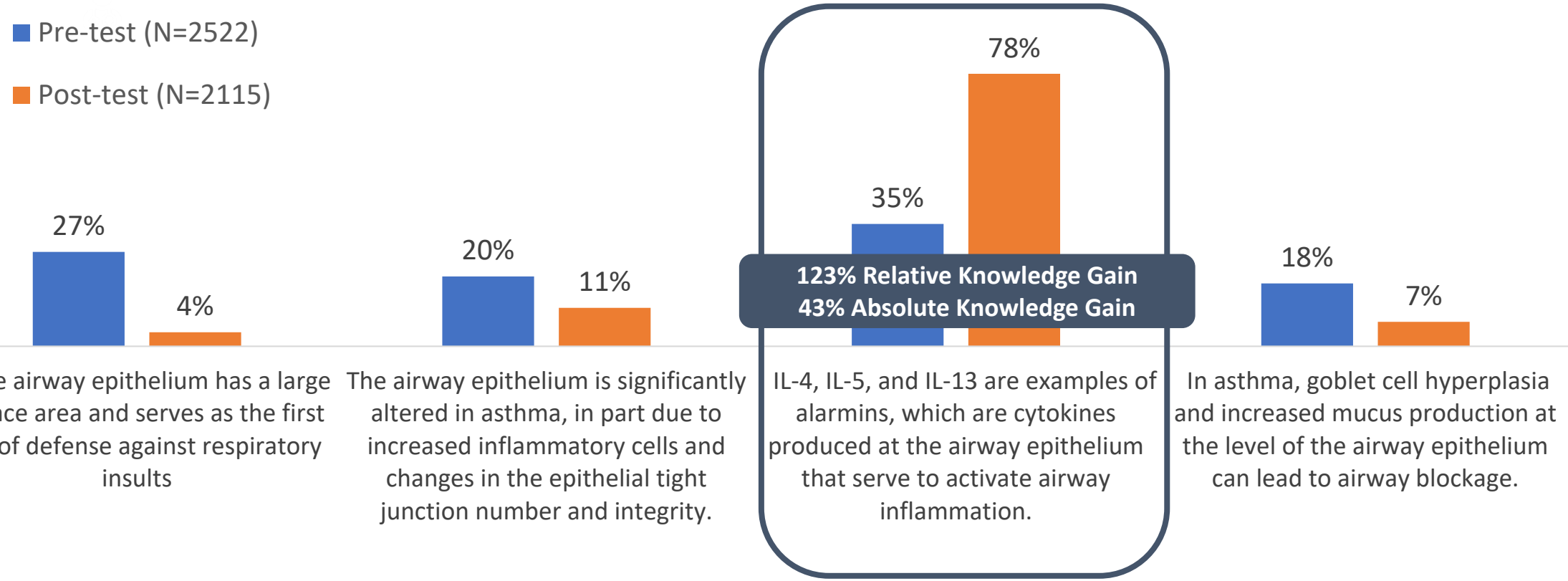
National Jewish Health

Final Outcomes Summary - Online Outcomes

Learning Objective: Describe the role of the airway epithelium in asthma.

Question 1: Which of the following is **INCORRECT** about the role of the airway epithelium?

Clinical Rationale:
The statement "IL-4, IL-5, and IL-13 are examples of alarmins" incorrectly describes the role of the airway epithelium because IL-4, IL-5 and IL-13 are not alarmins. TSLP, IL-33, and IL-25 are examples of alarmins, which are cytokines produced at the airway epithelium that serve to activate airway inflammation. All other statements correctly describe the role of the airway epithelium.



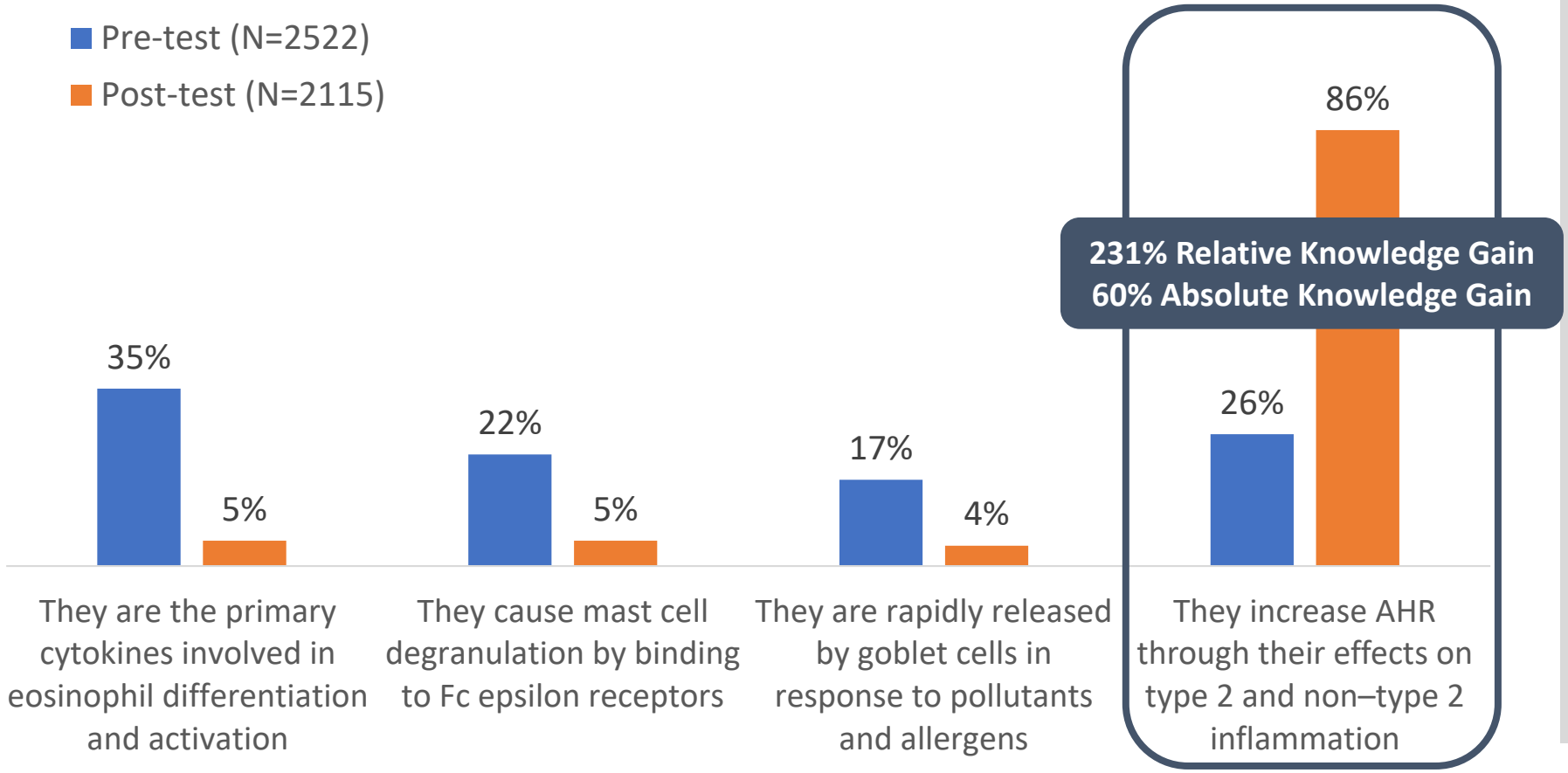
Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Outcomes

Learning Objective: Define the epithelial alarmins and their impact on T2 and non-T2 airway inflammation, remodeling, and hyper responsiveness in severe asthma.

Question 2: Which of the following is true about the alarmins and their role in airway hyperresponsiveness (AHR) in asthma?



Clinical Rationale:

Airway hyperresponsiveness (AHR) is in part caused by type 2 (particularly IL-13) and non-type 2 inflammation which have direct effects upon airway smooth muscle. Alarmins are produced by the airway epithelium in response to insults such as viruses, bacteria, allergens and pollutants to initiate the cascade which leads to either T2 or non-T2 inflammation, depending upon the insult. Therefore, alarmins increase AHR through their effects upon T2 and non-T2 inflammation.

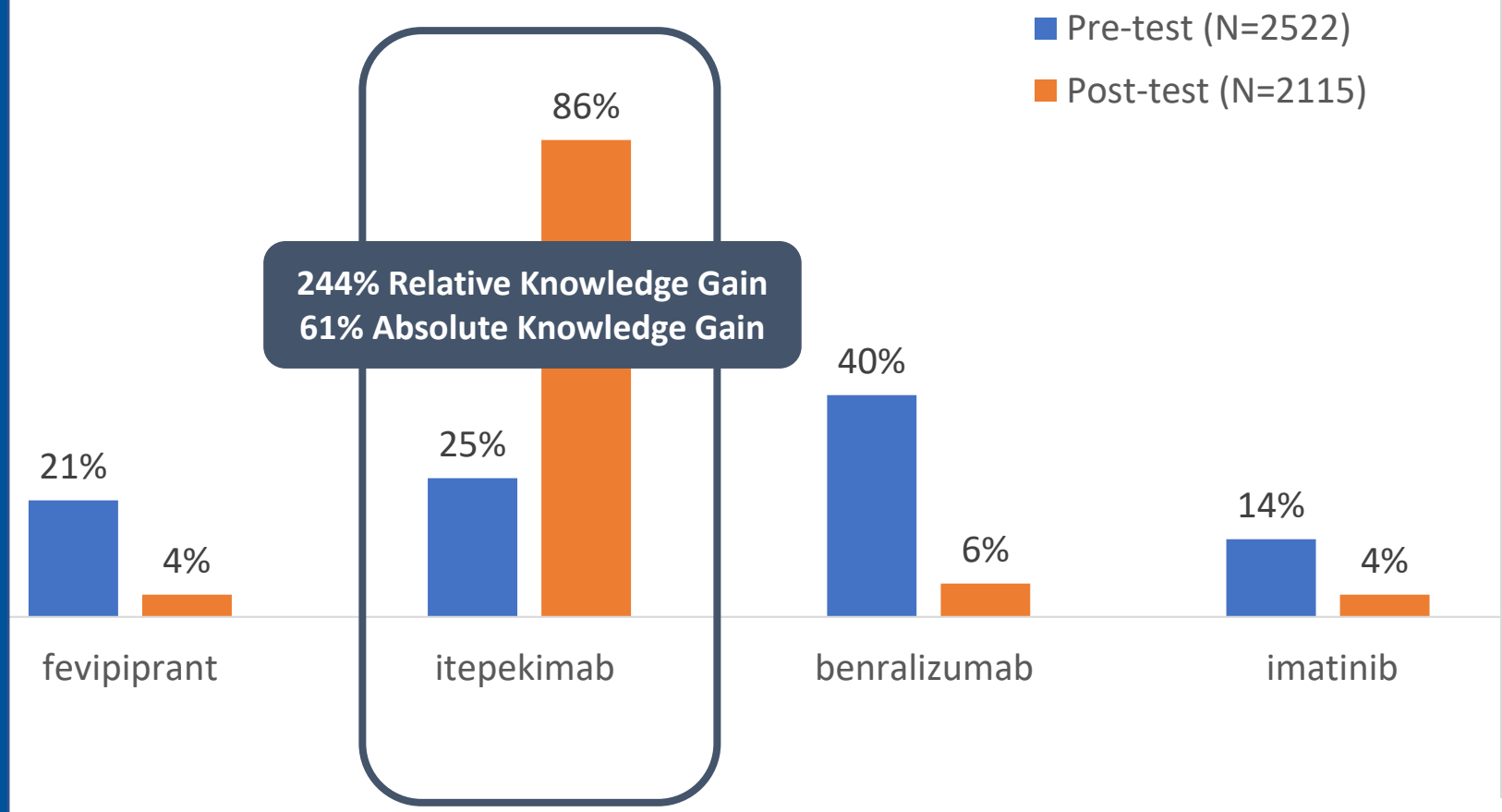
Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Outcomes

Learning Objective: Evaluate the results of clinical trials of current and emerging therapies that target the epithelial alarmins in severe asthma.

Question 3: Which of the following therapies is a monoclonal antibody against an epithelial alarmin, currently being studied for asthma?



Clinical Rationale:

Itepekimab is a monoclonal anti-body that targets the IL-33 ligand that is part of the alarmin group of cytokines (e.g., IL-33, IL-25 and thymic stromal lymphopoietin (TSLP)). These cytokines are released by bronchial epithelial cells in response to exogenous agents such as allergens, microbes, air pollutants and other environmental triggers binding to various pattern recognition receptors on bronchial epithelial cells. The alarmins have been shown to induce downstream production of both T-2 and non-T-2 cytokines and play a pivotal role in the underlying pathogenesis of asthma.

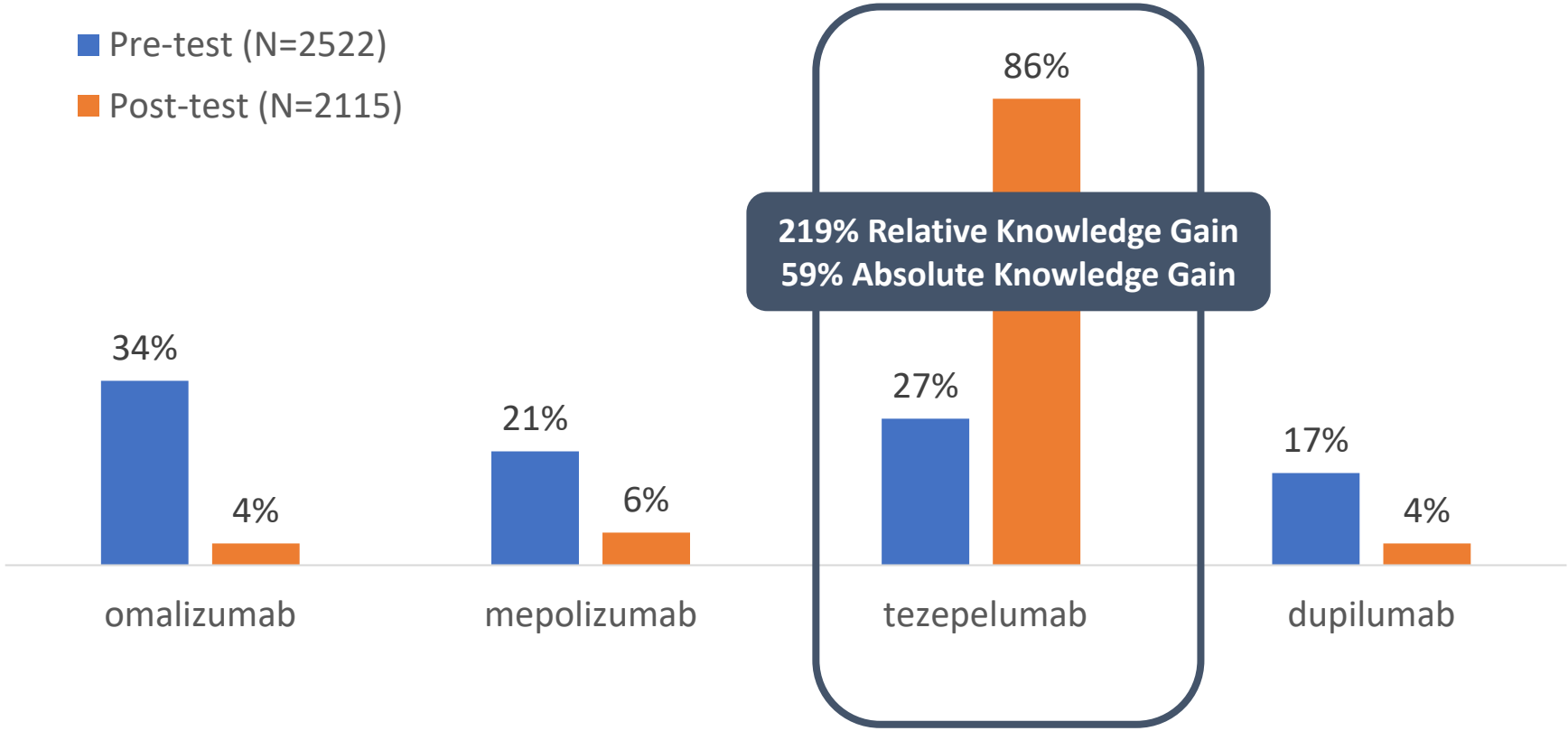
Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary – Online Outcomes

Learning Objective: Match clinical characteristics and phenotypes to treatment targets.

Question 4: Sarah is a 47-year-old female patient with adult-onset asthma, her main triggers being wildfire smoke and viral infections. She is non-atopic (negative allergy skin testing) and has normal eosinophil counts, exhaled nitric oxide, and total IgE levels on testing. Which of the following biologics would be most appropriate to prescribe if she is having 2 corticosteroid-requiring exacerbations per year despite high-dose ICS/LABA therapy?

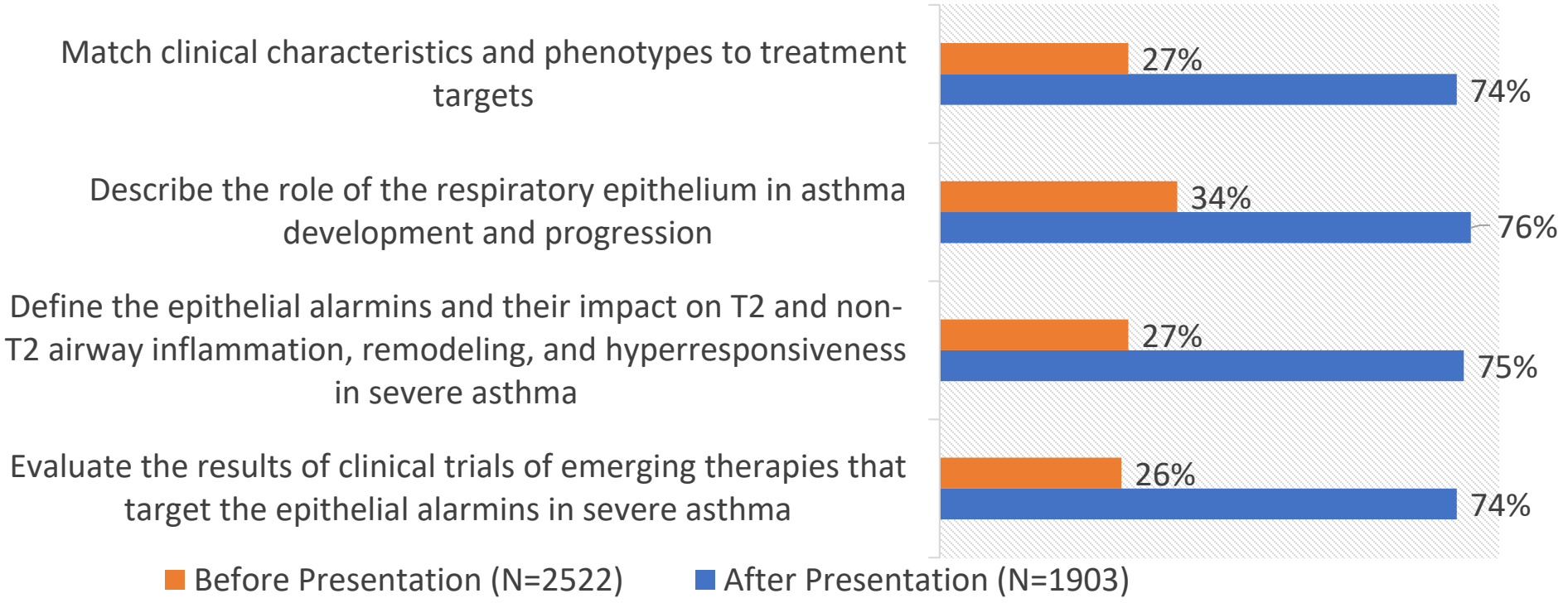


Clinical Rationale:
The patient described in this vignette has non-type 2 asthma. Of the biologic agents listed, tezepelumab is the only one approved for asthma regardless of phenotype. The other answer choices are approved for allergic asthma, eosinophilic asthma, or steroid-dependent asthma, none of which apply to this patient.

Level (4) Outcomes: Competence

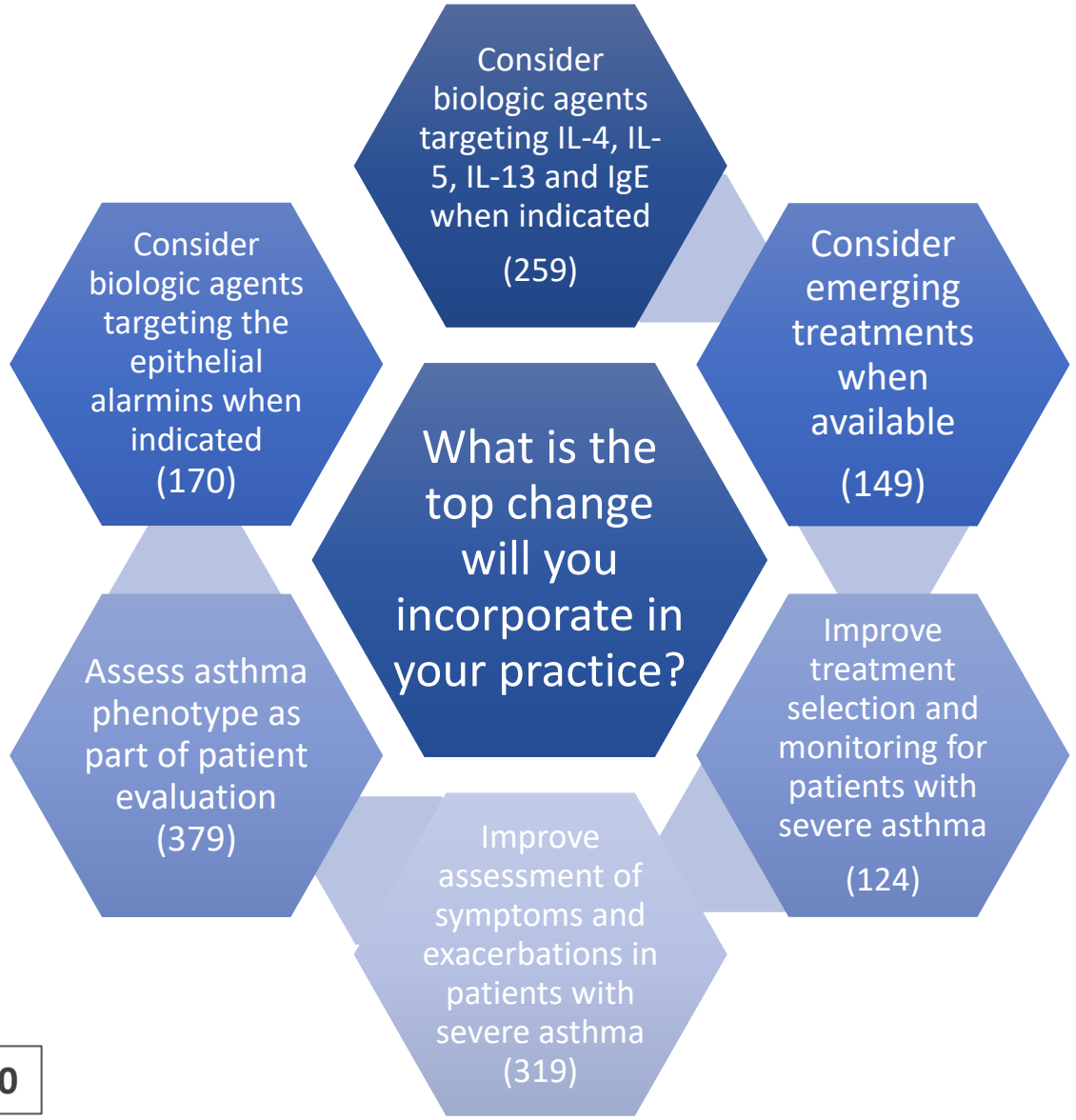
Final Outcomes Summary - Online Outcomes

Evaluation respondents reported their confidence as it relates to the learning objectives before and after the activity (Very confident – confident)



Level (4) Outcomes: Competence

Final Outcomes Summary - Online Outcomes



N=1400

91%

N=1669

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

Evaluation Survey Results

Final Outcomes Summary - Online Outcomes

National Jewish Health

Key Takeaways

- New drugs in the pipeline
- Different indications for the various biologics
- Multiple new asthma treatments
- Understanding the phenotype and endotype
- Phenotype evaluation is more important than I thought
- There is a role for biologics in those who do not have a phenotype with hypereosinophilia or elevated IgE
- Improving understanding about developments in asthma inflammatory pathways
- How to treat asthma patients based on evidence-based medicine
- Proper assessment of clinical characteristics and phenotypes to improve treatment
- Differentiation between biologic drugs
- Consider recent biologics in asthma
- Severe asthma can be very complex in its evaluation and treatment

Barriers the Activity will Help to Address

- Improved communication with patients
- Cost
- Access to care
- Improved referrals
- Fear of using biologics
- Treatment
- Insurance formularies are a huge problem to accessing these meds
- Examining patient in context of home environment

"Thank you for wonderful education."

-Online participant

Live Program

Final Outcomes Summary

CHEST 2022 Annual Meeting l CME Lunch Symposium

October 16, 2022

Nashville, Tennessee

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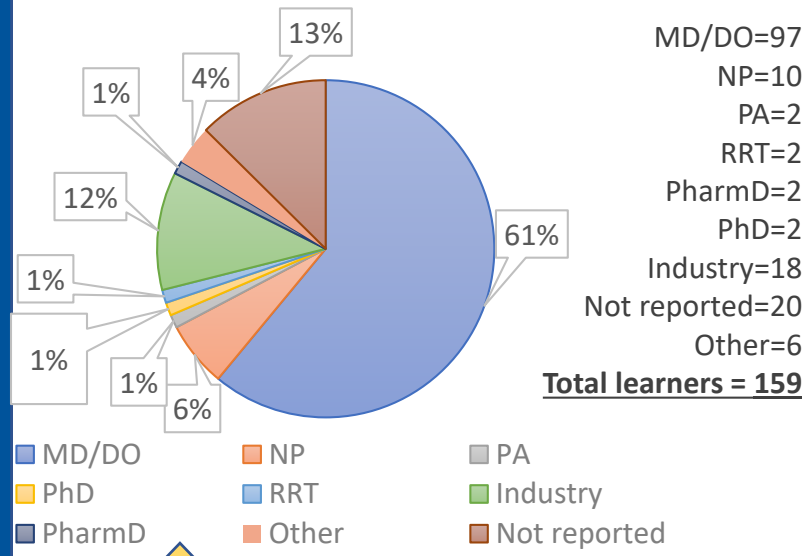
Educational Impact Summary

Final Outcomes Summary - Live program

Participation



MD/DO=97
NP=10
PA=2
RRT=2
PharmD=2
PhD=2
Industry=18
Not reported=20
Other=6
Total learners = 159

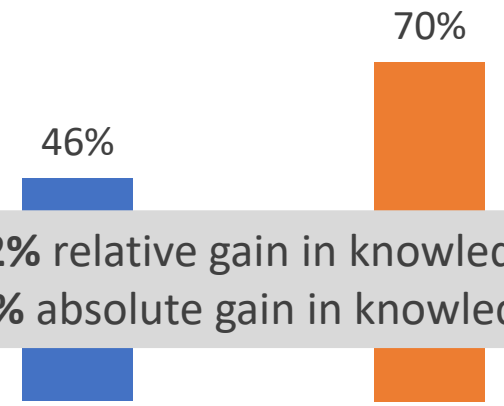
Exceeded learner guarantee for the live program!

Learner Guarantee	Learner Actual
150	159

Potential Impact To 13,572 Patient Visits This Year

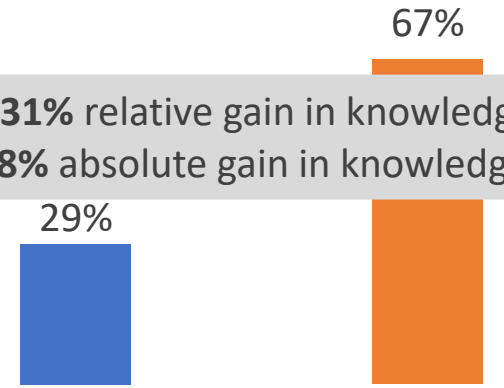
Learning Gain Across Objectives

Overall Knowledge Gain



52% relative gain in knowledge
24% absolute gain in knowledge

Overall Confidence Gain



131% relative gain in knowledge
38% absolute gain in knowledge

Evaluation

Met their educational needs **(91%)**

Reinforced or improved current skills **(91%)**

Improved ability to treat patients **(91%)**

N=43

95%

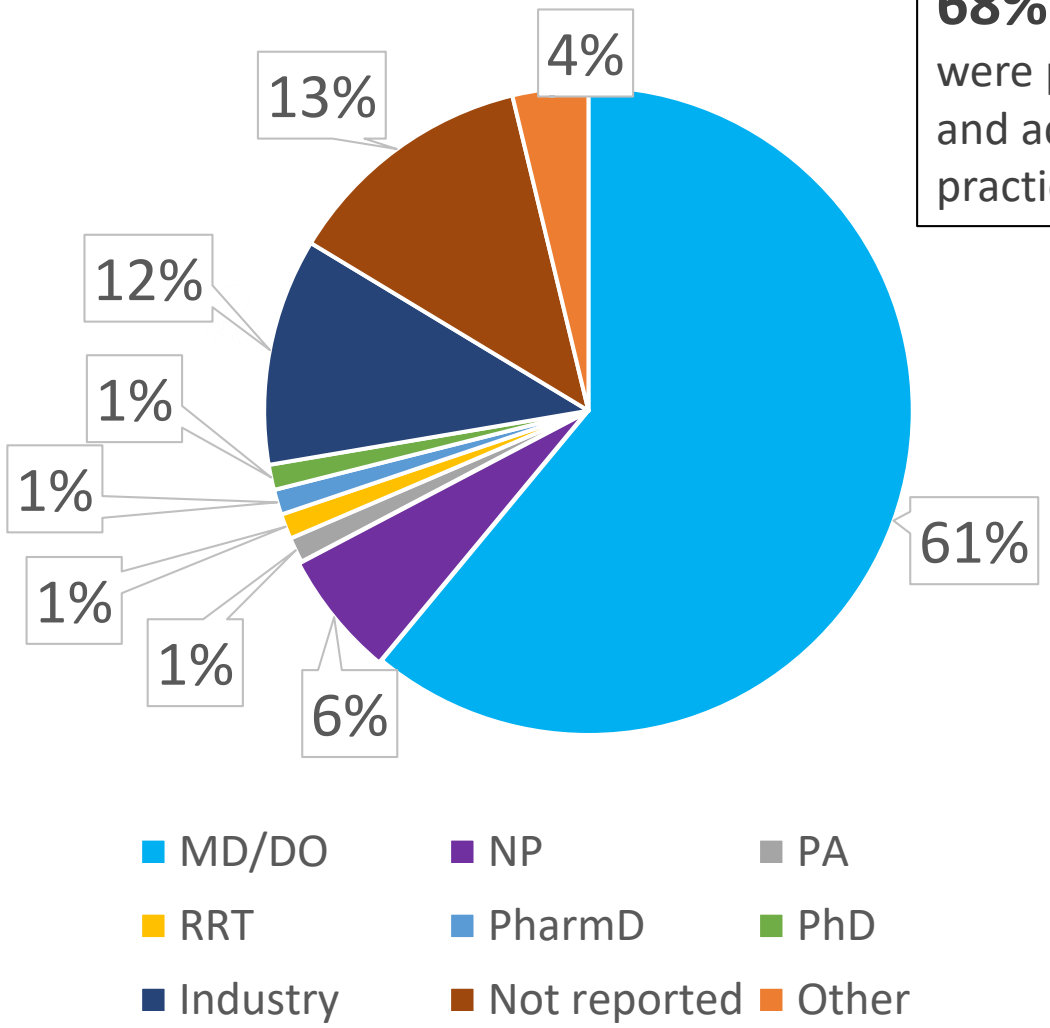
N=43

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

Level (1) Outcomes: Participation (Degree)

Final Outcomes Summary – Live Program

National Jewish Health

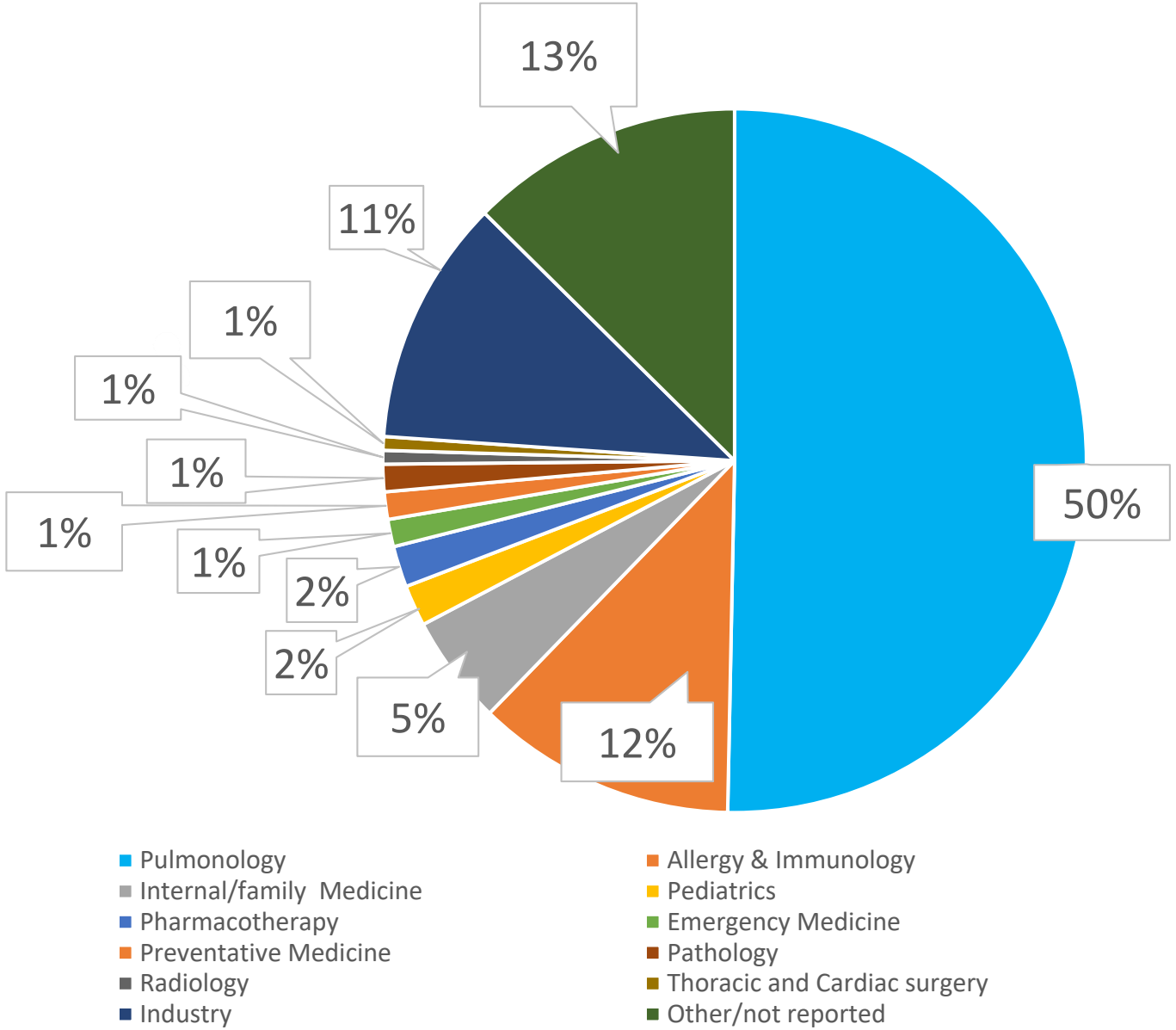


68% of learners were physicians and advanced practice providers

Degree	Total
MD/DO	97
NP	10
PA	2
RRT	2
PhD	2
PharmD	2
Industry	18
Not reported	20
Other	6
Total Learners	**159**

Level (1) Outcomes: Participation (Specialty)

Final Outcomes Summary – Live Program

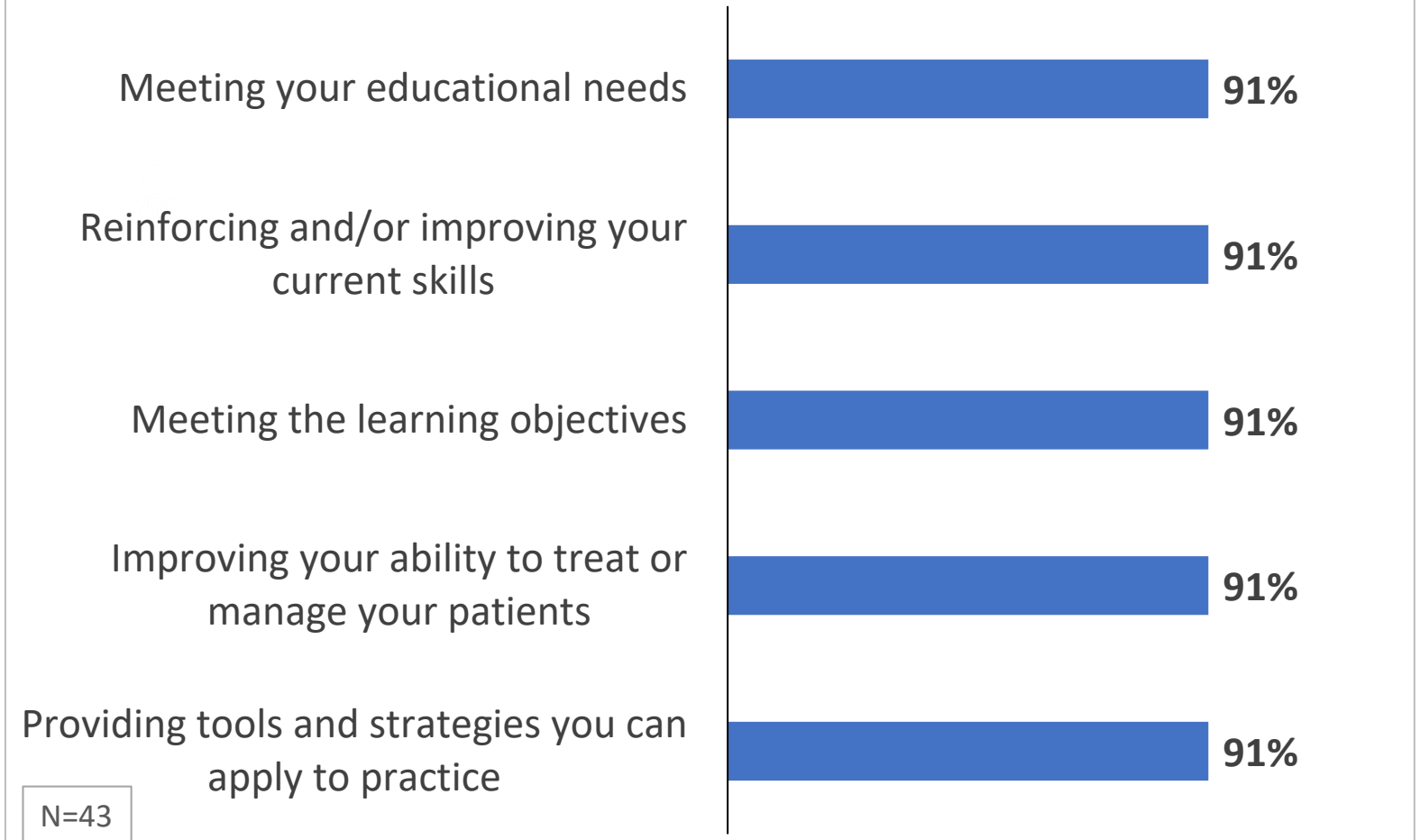


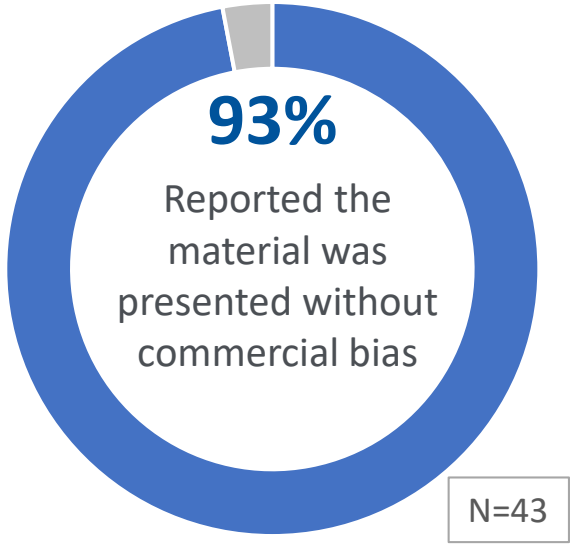
Specialty	Total
Pulmonary	80
Allergy/ Immunology	19
Internal medicine/family medicine	8
Pediatrics	3
Pharmacotherapy	3
Emergency Medicine	2
Preventative Medicine	2
Pathology	2
Radiology	1
Thoracic and Cardiac Surgery	1
Industry	18
Other/not reported	20
Total Learners	**159**

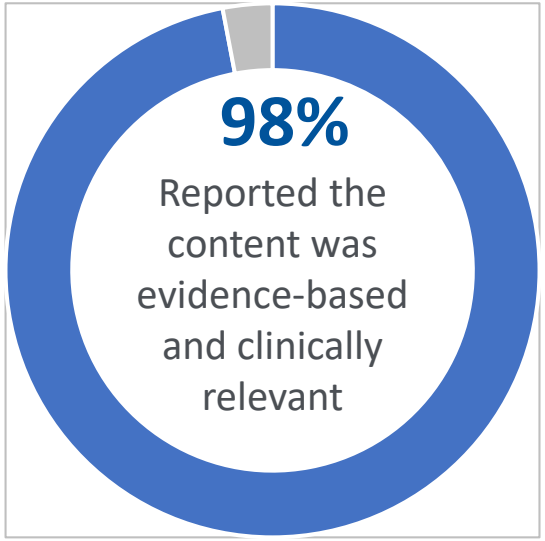
Level (2) Outcomes: Satisfaction

Final Outcomes Summary: Live Program

Evaluation respondents rated the activity "Excellent" to "Good" at:



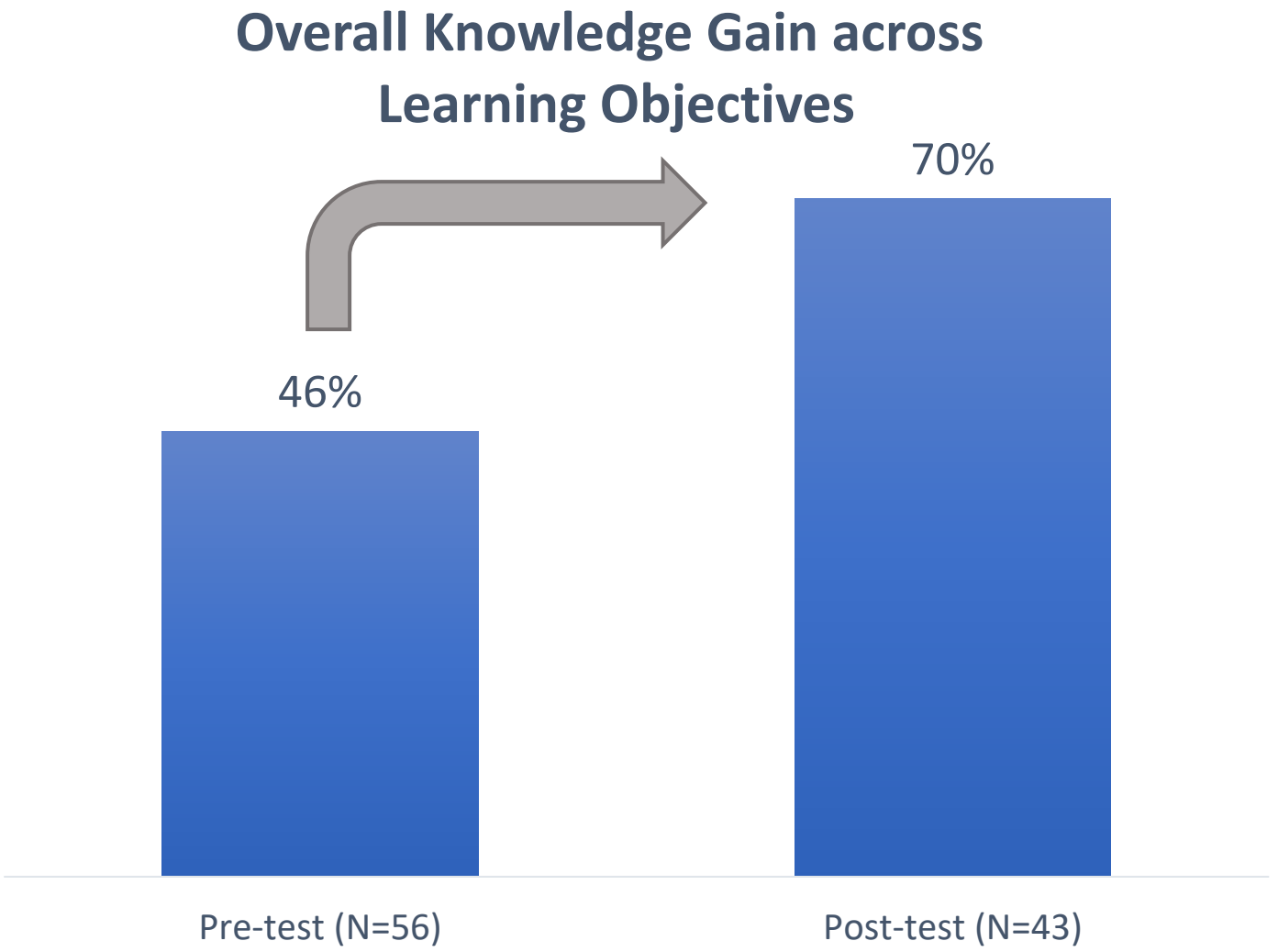




Level (3 & 4) Outcomes: Knowledge & Competence

Final Outcomes Summary: Live Program

National Jewish Health



52% Overall Relative Knowledge Gain

24% Overall Absolute Knowledge Gain

Level (3 & 4) Outcomes: Knowledge & Competence

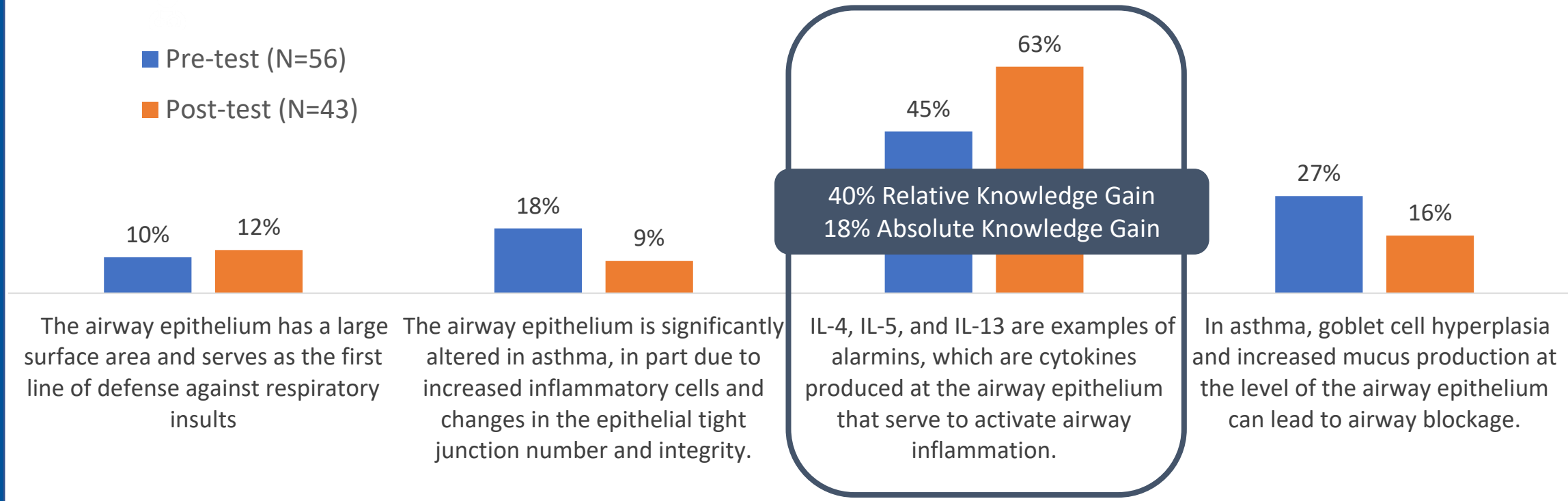
Final Outcomes Summary: Live Program

National Jewish Health

Learning Objective: Describe the role of the airway epithelium in asthma.

Question 1: Which of the following is **INCORRECT** about the role of the airway epithelium?

Clinical Rationale:
The statement "IL-4, IL-5, and IL-13 are examples of alarmins" incorrectly describes the role of the airway epithelium because IL-4, IL-5 and IL-13 are not alarmins. TSLP, IL-33, and IL-25 are examples of alarmins, which are cytokines produced at the airway epithelium that serve to activate airway inflammation. All other statements correctly describe the role of the airway epithelium.



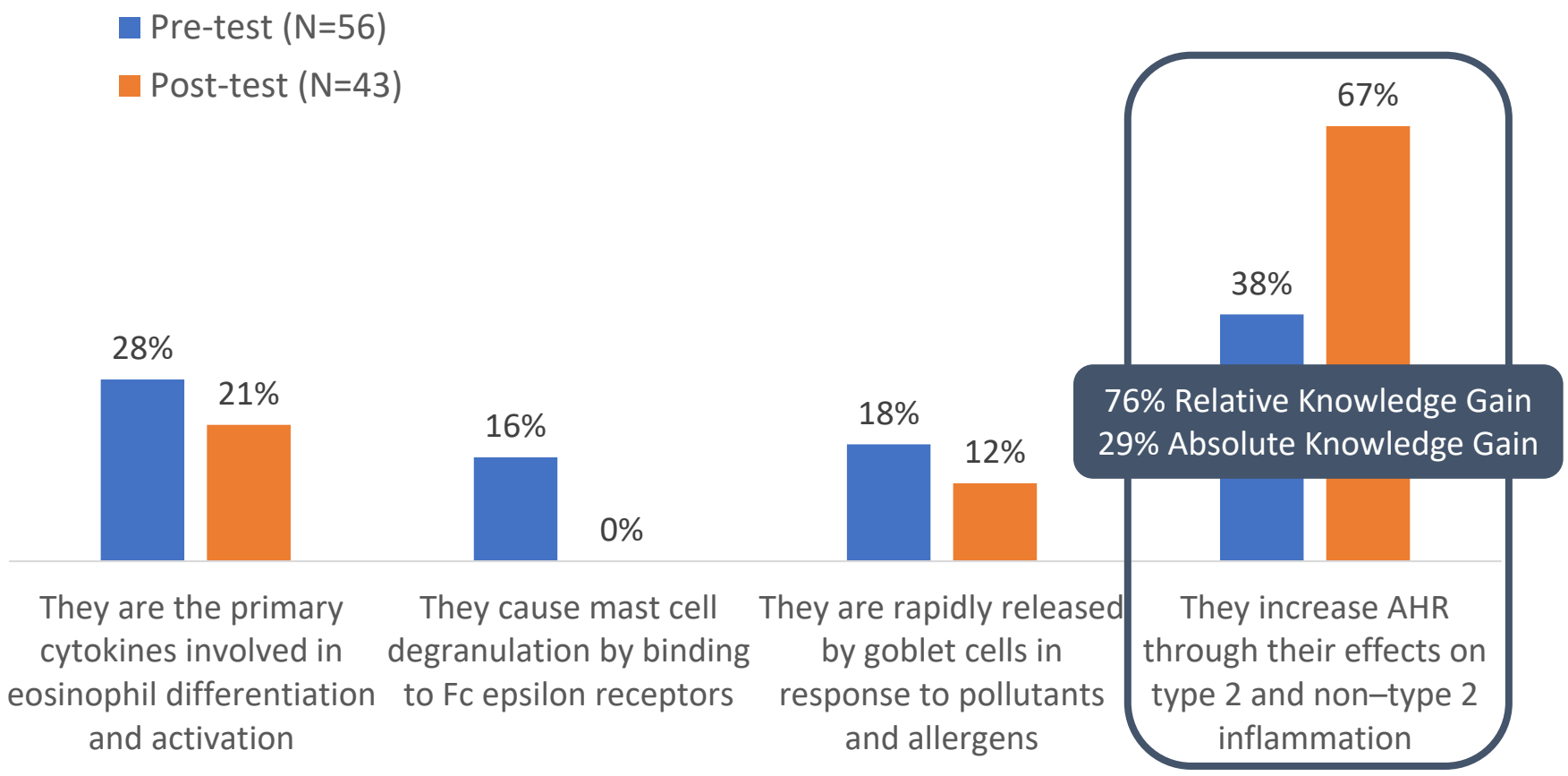
Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary: Live Program

Learning Objective: Define the epithelial alarmins and their impact on T2 and non-T2 airway inflammation, remodeling, and hyper responsiveness in severe asthma.

Question 2: Which of the following is true about the alarmins and their role in airway hyperresponsiveness (AHR) in asthma?



Clinical Rationale:

Airway hyperresponsiveness (AHR) is in part caused by type 2 (particularly IL-13) and non-type 2 inflammation which have direct effects upon airway smooth muscle. Alarmins are produced by the airway epithelium in response to insults such as viruses, bacteria, allergens and pollutants to initiate the cascade which leads to either T2 or non-T2 inflammation, depending upon the insult. Therefore, alarmins increase AHR through their effects upon T2 and non-T2 inflammation.

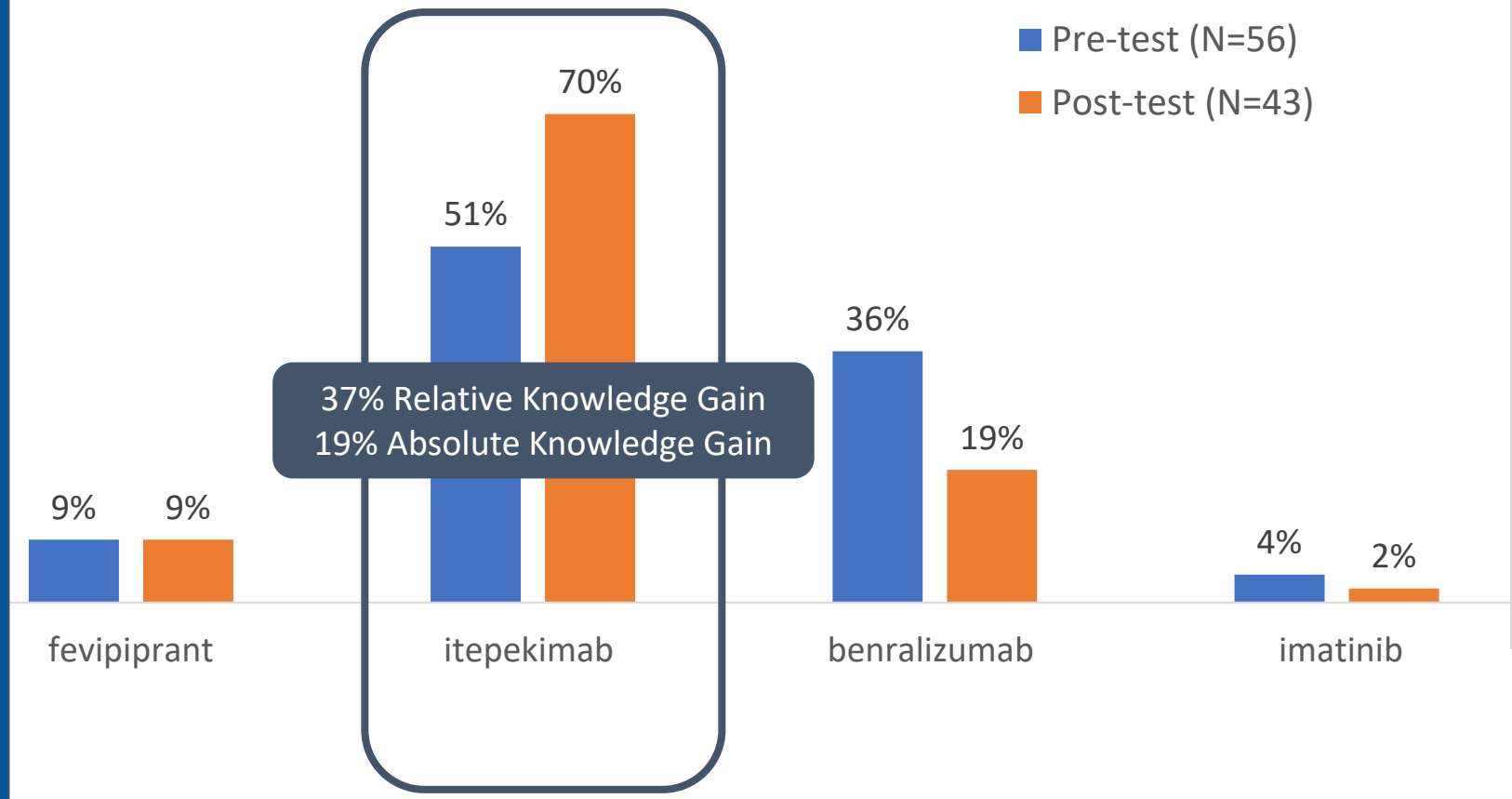
Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary: Live Program

Learning Objective: Evaluate the results of clinical trials of current and emerging therapies that target the epithelial alarmins in severe asthma.

Question 3: Which of the following therapies is a monoclonal antibody against an epithelial alarmin, currently being studied for asthma?



Clinical Rationale:

Itepekimab is a monoclonal anti-body that targets the IL-33 ligand that is part of the alarmin group of cytokines (e.g., IL-33, IL-25 and thymic stromal lymphopoietin (TSLP)). These cytokines are released by bronchial epithelial cells in response to exogenous agents such as allergens, microbes, air pollutants and other environmental triggers binding to various pattern recognition receptors on bronchial epithelial cells. The alarmins have been shown to induce downstream production of both T-2 and non-T-2 cytokines and play a pivotal role in the underlying pathogenesis of asthma.

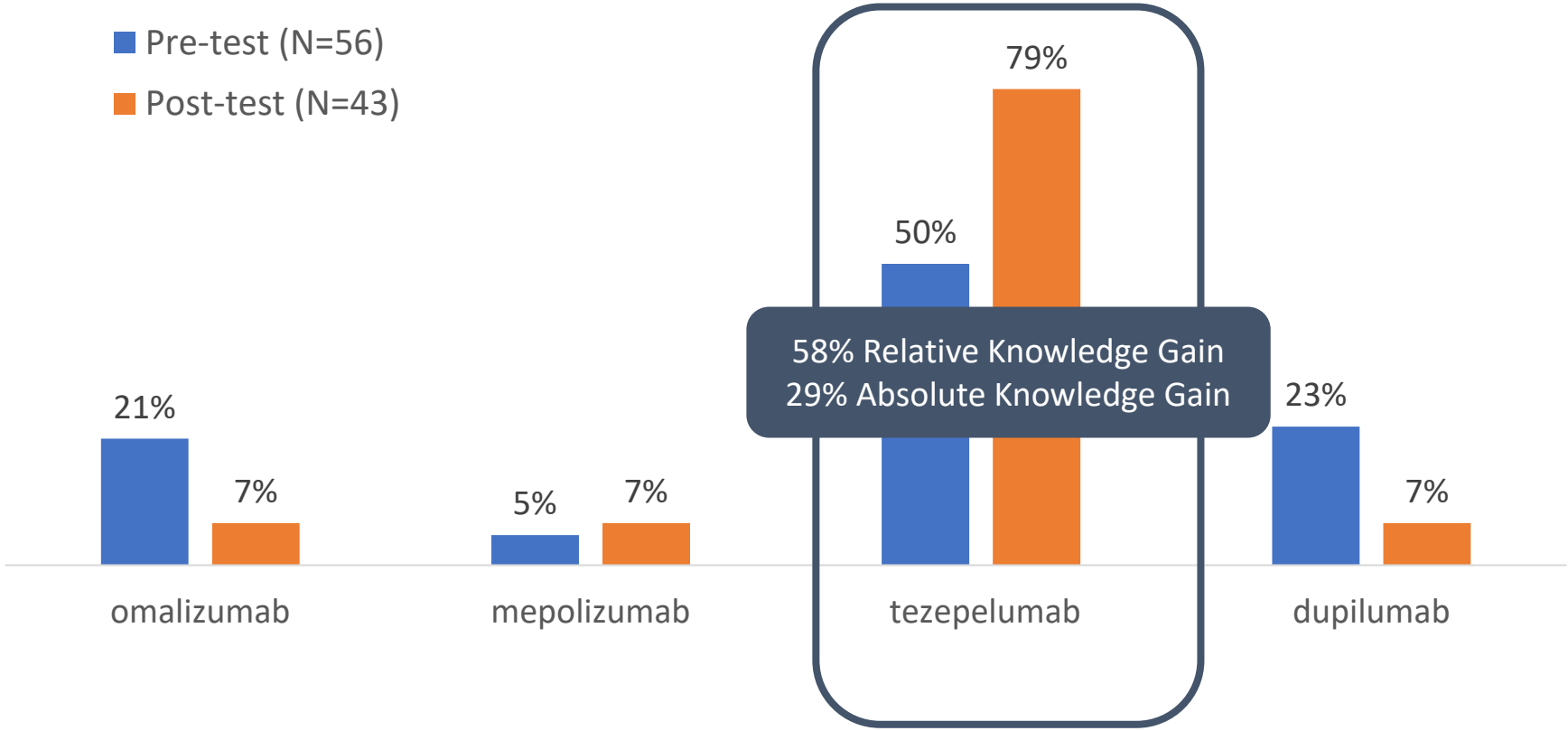
Level (3 & 4) Outcomes: Knowledge & Competence

National Jewish Health

Final Outcomes Summary: Live Program

Learning Objective: Match clinical characteristics and phenotypes to treatment targets.

Question 4: Sarah is a 47-year-old female patient with adult-onset asthma, her main triggers being wildfire smoke and viral infections. She is non-atopic (negative allergy skin testing) and has normal eosinophil counts, exhaled nitric oxide, and total IgE levels on testing. Which of the following biologics would be most appropriate to prescribe if she is having 2 corticosteroid-requiring exacerbations per year despite high-dose ICS/LABA therapy?

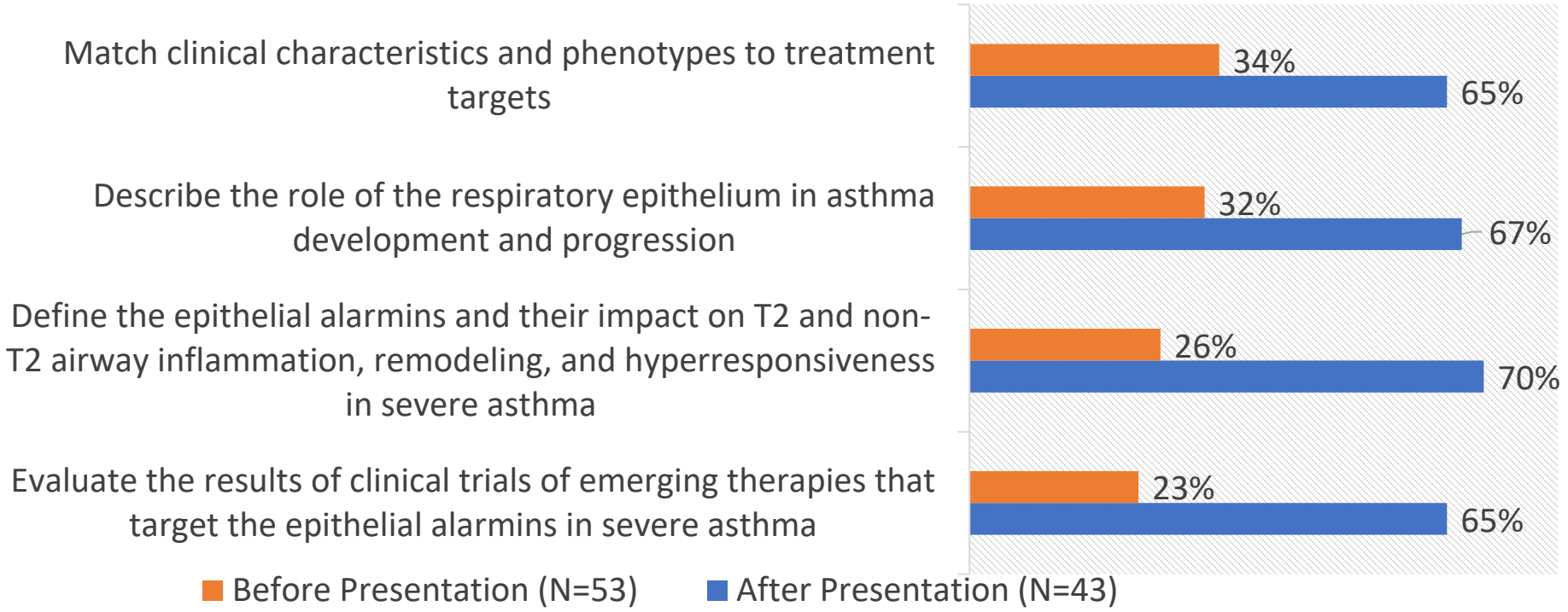


Clinical Rationale:
The patient described in this vignette has non-type 2 asthma. Of the biologic agents listed, Tezepelumab is the only one approved for asthma regardless of phenotype. The other answer choices are approved for allergic asthma, eosinophilic asthma, or steroid-dependent asthma, none of which apply to this patient.

Level (4) Outcomes: Competence

Final Outcomes Summary: Live Program

Evaluation respondents reported their confidence as it relates to the learning objectives before and after the activity (Very confident – confident)



Level (4) Outcomes: Competence

Final Outcomes Summary: Live Program

N=40

95%

N=43

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

Evaluation Survey Results

Final Outcomes Summary: Live Program

National Jewish Health

Key Takeaways

- New drugs in the pipeline
- Different indications for the various biologics
- Multiple new asthma treatments
- Understanding the phenotype and endotype
- There is a role for biologics in those who do not have a phenotype with hypereosinophilia or elevated igE
- Improving understanding about developments in asthma inflammatory pathways

Future Topics

- Biologics
- Atypical cases of asthma
- Use of thermoplasty
- Signs and symptoms that qualify patient as severe, testing required and treatment options

"Nice to appreciate indications from national experts in the field."

-Live participant

Accreditation Details

Final Outcomes Summary: Online Outcomes and Live Program

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.

National Jewish Health designates the live activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™.

National Jewish Health designates the enduring material for a maximum of 1.0 *AMA PRA Category 1 Credit*™.