Emerging Challenges in Primary Care: 2020

Statin Intolerance and Cardiovascular Risk – Strategies for Improving Outcomes

Esperion Therapeutics, Inc Grant 2020-1374

October 15, 2020

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Emerging Challenges in Primary Care 2020

This curriculum focused on management of patients with hyperlipidemia, statin intolerance and cardiovascular risk.

Participation

12,728*
Total Attendees

9 Virtual Sessions

4,382 certificates issued to date

This education has the potential to impact
6,823,515
Hyperlipidemia patients on an annual basis.

121,033 – 141,409
Patients Weekly

2020 Session	Date	Attendees
Emerging Challenges in Primary Care, Episode 1 *Miami: Florida, Georgia, Alabama, Mississippi, South Carolina*	4/25/20	1,834
Emerging Challenges in Primary Care, Episode 2 Baltimore: Maryland, Pennsylvania, Virginia, West Virginia, Delaware, Ohio	5/2/20	1,741
Emerging Challenges in Primary Care, Episode 3 *Tampa: Florida, Georgia, Alabama, Mississippi, South Carolina*	5/9/20	1,068
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Emerging Challenges in Primary Care, Episode 7 *St. Louis: Missouri, Iowa, Nebraska, Kansas, Oklahoma, Arkansas, Illinois*	6/20/20	743
Emerging Challenges in Primary Care, Episode 8 *Virtual: National audience*	6/27/20	1,323
Emerging Challenges Episode 8, Rebroadcast	7/11/20	258
Total		**12,728**

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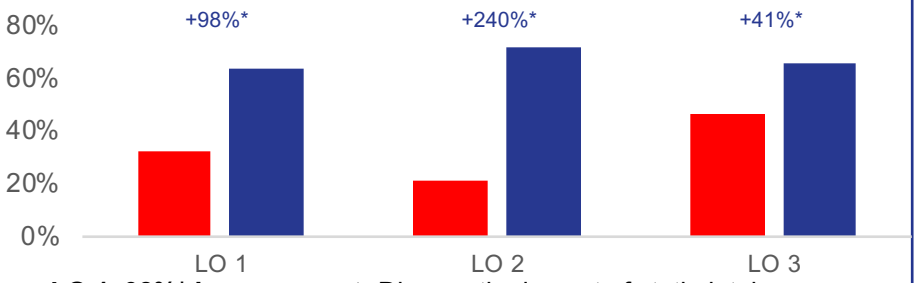
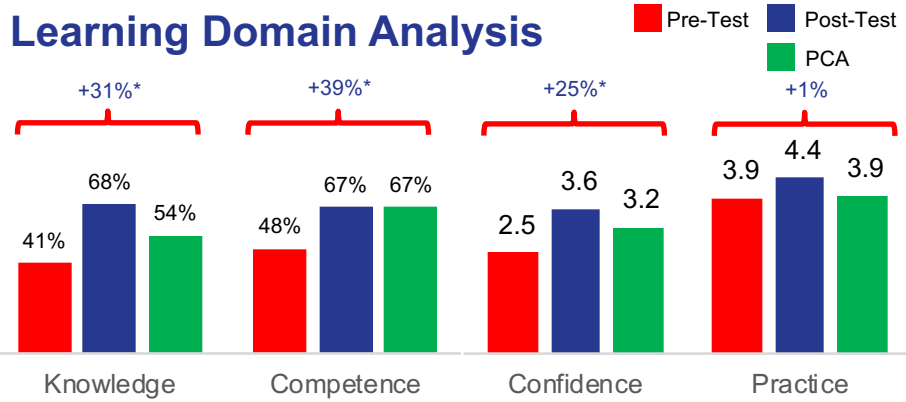
Learning Gains Across Objectives



- **LO 1, 98%* Improvement:** Discuss the impact of statin intolerance on ASCVD event risk
- **LO 2, 240%* Improvement:** Recognize the ways in which the unique mechanisms of action for current and emerging non-statin therapies can be useful for hypercholesteremia management
- **LO 3, 41%* Improvement:** Incorporate strategies to reduce cardiovascular risk in statin-intolerant patients, utilizing therapeutic combinations and lifestyle modification

Learning Domain Analysis

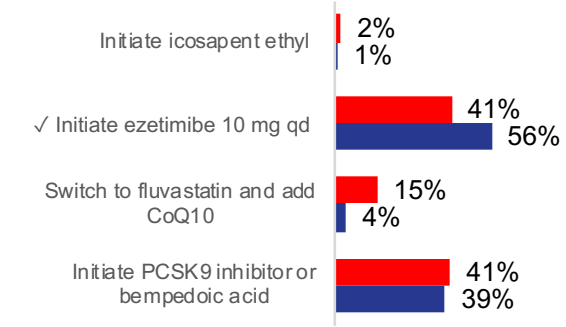


- In each of the four curriculum learning domains, substantial and significant gains were achieved from Pre- to Post-Test
- The strongest improvements, from lowest Pre-Test scores, were measured in Knowledge, where gains were driven by an item on results of a study of Medicare beneficiaries who started statin therapy after a myocardial infarction
- Low Pre- and Post-Test Confidence despite gains indicates possible learner awareness of gaps in Knowledge and Competence
- Practice strategy ratings, on assessment of adherence to and tolerance of statin therapy, were high

Persistent Learning Gaps/Needs

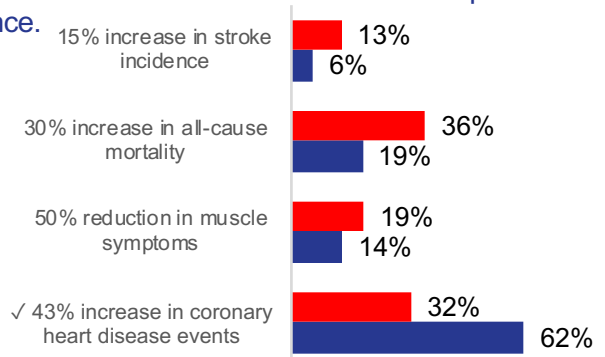
Selecting between statin and non-statin therapies

Despite improvements in score on a Competence item presenting the case of a patient in need of therapy modification, learners struggled at Post-Test to correctly identify the most appropriate non-statin agent to add



Impact of adherence to statin therapy on rate of cardiovascular events

Despite improvements in score on a Knowledge item on a study of outcomes for patients with high statin adherence and those with statin intolerance, low scores were measured at Post-Test indicating underappreciation of the increased cardiovascular risk associated with poor adherence.



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Curriculum Patient Impact

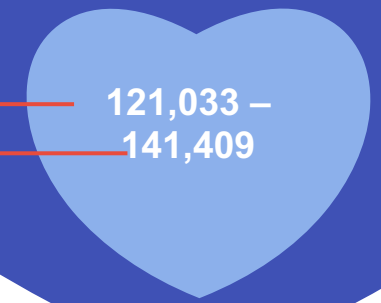
In the Post-Test, learners (N = 4,846) were asked to report how many patients with hyperlipidemia they see per week in any clinical setting by selecting a range. The resulting distribution of learner responses was then extrapolated to reflect the total number of learners who have attended the sessions.

The findings reveal that this education has the potential to impact

6,823,515

patients on an annual basis.

121,033 – 141,409 patients on a weekly basis



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Commercial Support

The Emerging Challenges in Primary Care: 2020 series of CME activities were supported through educational grants or donations from the following companies:

- Amgen
- Astellas Pharma Global Development, Inc.
- AstraZeneca Pharmaceuticals LP
- Bayer Healthcare Pharmaceuticals Inc.
- Esperion Therapeutics, Inc.
- Ferring Pharmaceuticals, Inc.
- Gilead Sciences, Inc.
- Kaneka Pharma America LLC
- Lilly
- Novo Nordisk, Inc.
- Takeda Pharmaceuticals U.S.A., Inc.

Overview

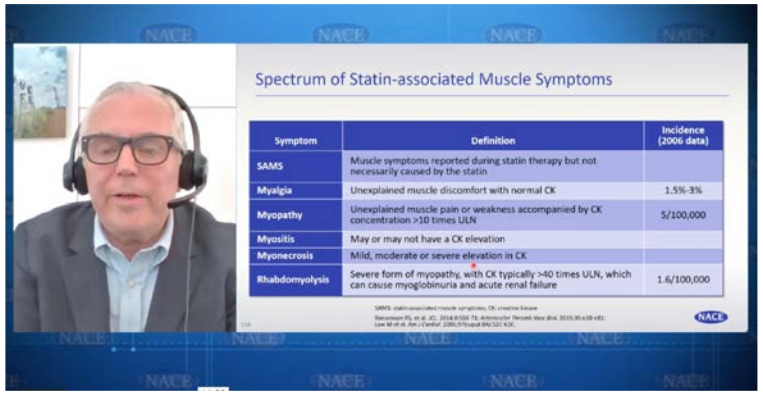
Learning Objectives

- Discuss the impact of statin intolerance on ASCVD event risk
- Recognize the ways in which the unique mechanisms of action for current and emerging non-statin therapies can be useful for hypercholesterolemia management
- Incorporate strategies to reduce cardiovascular risk in statin-intolerant patients, utilizing therapeutic combinations and lifestyle modification

Curriculum Overview

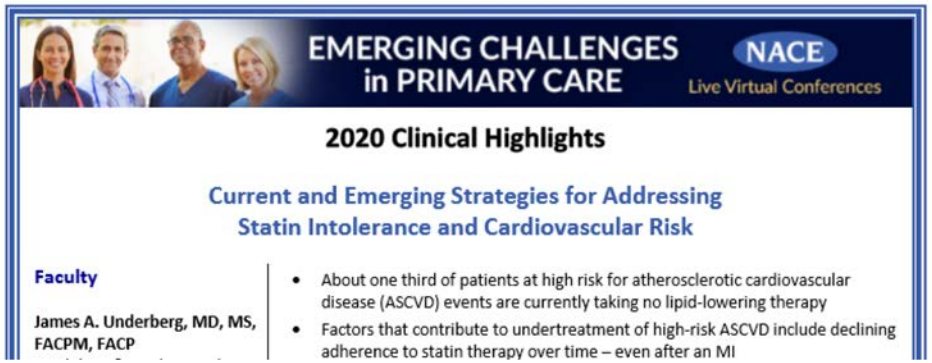
8 Accredited Live Virtual Symposia with

1 Rebroadcast: April – July 2020



Clinical Highlights eMonograph

eMonograph, containing key teaching points from the CME activity, was distributed 1 week after the meeting to all attendees.



Podcast

The NACE Clinical Highlights Show

Statin Intolerance and Cardiovascular Risk – Strategies for Improving Outcomes
Launch: June 15, 2020

Enduring CME Symposium Webcast

Available at:
https://www.naceonline.com/courses/statin-intolerance-and-cardiovascular-risk-strategies-for-improving-outcomes

Statin Intolerance and Cardiovascular Risk – Strategies for Improving Outcomes

COURSE SUMMARY

Cost: Free

Start Date: 06/30/2020

Expiration Date: 06/29/2021

Target Audience: Primary Care Providers

Format: Webcast

Estimated Time To Complete CME Activity: 1.0 hour

Credit(s):
1.0 *AMA PRA Category 1 Credit*™
1.0 AANP Contact hour which includes 0.75 pharmacology hours

Hardware/Software Requirements: Any web browser

Speaker

Daniel Soffer, MD, FNLA
University of Pennsylvania Health System
Internal Medicine/Clinical Lipidology
Philadelphia, PA

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Outcomes Methodology

Learning outcomes were measured using matched Pre-Test and Post-Test scores for Knowledge, Performance, 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
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 and Post-Test 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 and Post-Test 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 and Post-Test score averages

Participation

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Total		**12,728**

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Participation

Level 1
Participation
Demographics
Patient Reach

12,728*
Total Attendees

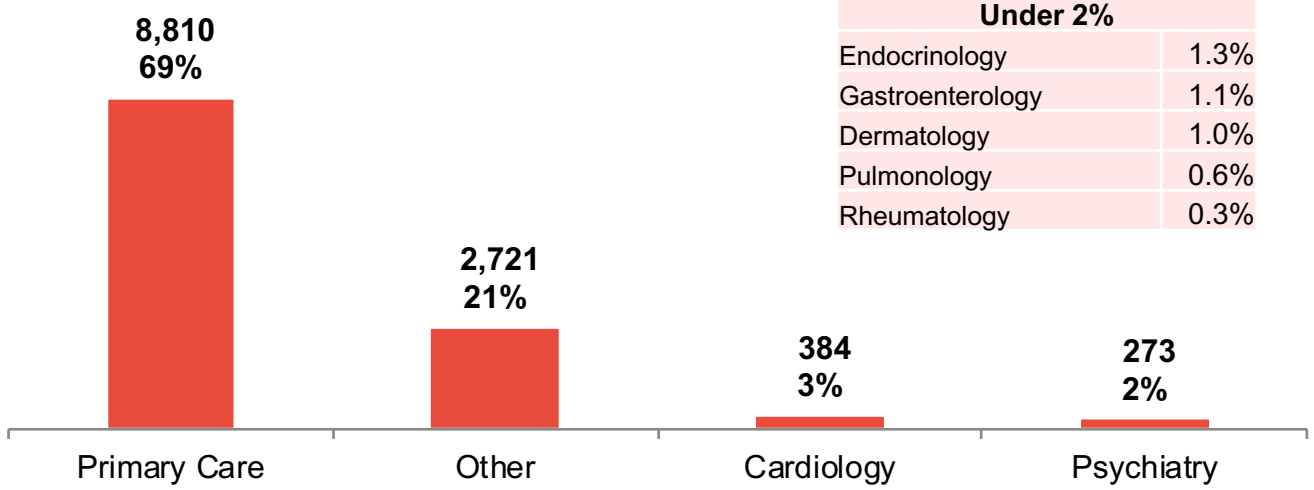
9 Virtual Sessions

3,483 Follow-up Participants
27% Rate of follow-up engagement

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

Level 1: Demographics and Patient Reach

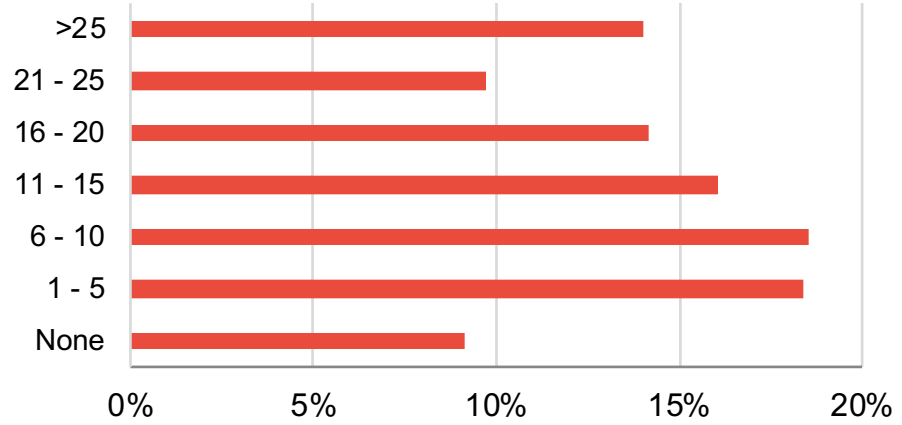
Specialty



Under 2%	
Endocrinology	1.3%
Gastroenterology	1.1%
Dermatology	1.0%
Pulmonology	0.6%
Rheumatology	0.3%

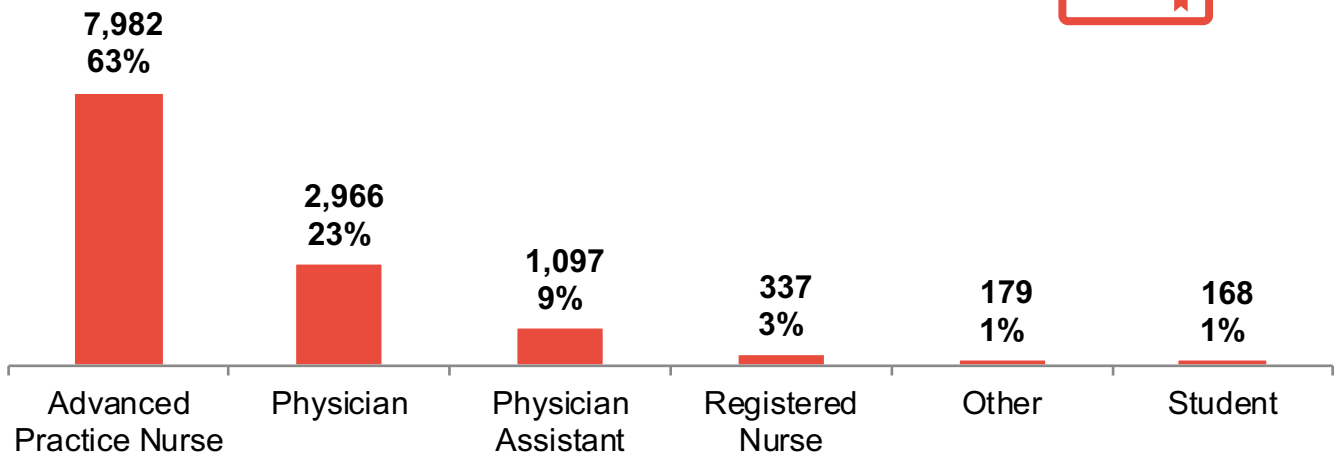
Patient Care Focus: 91%

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

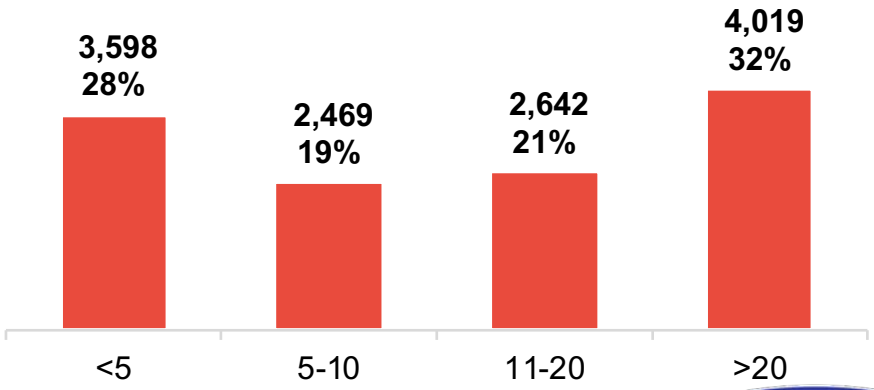


Average number of hyperlipidemia patients seen each week per clinician: 13

Profession



Years in Practice



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Level 2-5:
Outcomes Metrics

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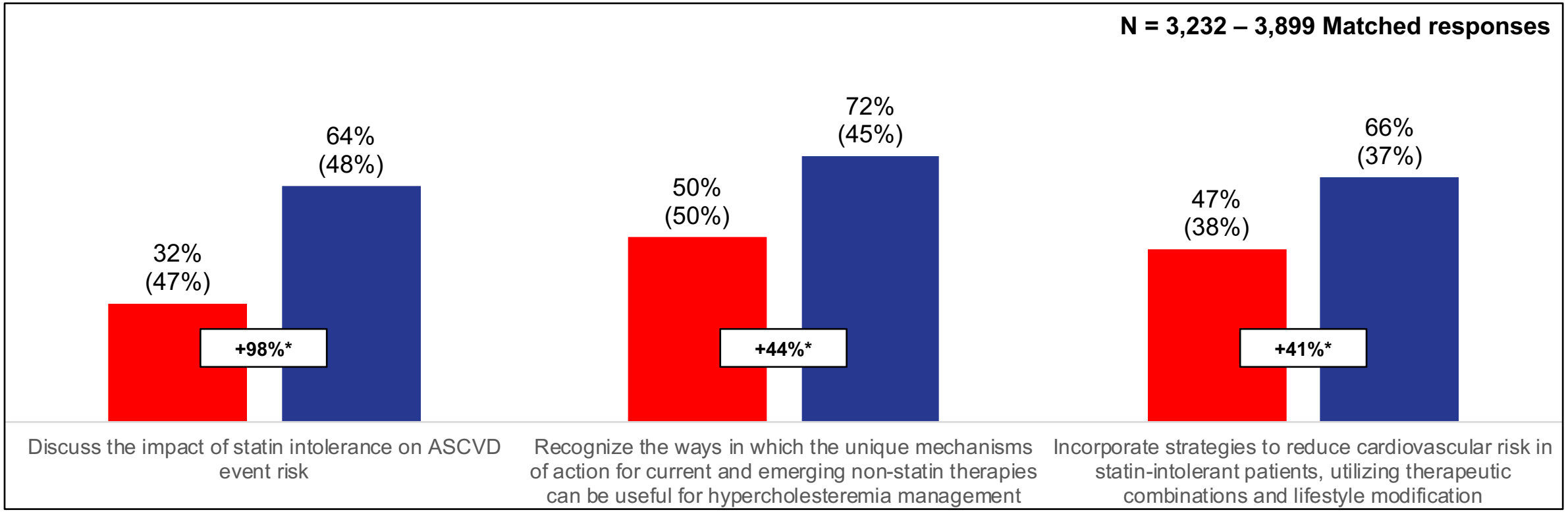
Learning Objective Analysis



- Across all three curriculum Learning Objectives, substantial and statistically significant improvements were measured from Pre- to Post-Test
- The strongest gains were measured on discussing the impact of statin intolerance on ASCVD event risk
- Highest scores at Pre- and Post-Test (50% and 72%) were measured on recognizing ways in which mechanisms of action for non-statin therapies can be useful for hypercholesteremia management
- Despite these improvements, low to moderate Post-Test scores across all three Objectives (64% to 72%) highlight opportunities for further education in this area

RealCME * indicates significance, $p < 0.05$

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Learning Objective Analysis

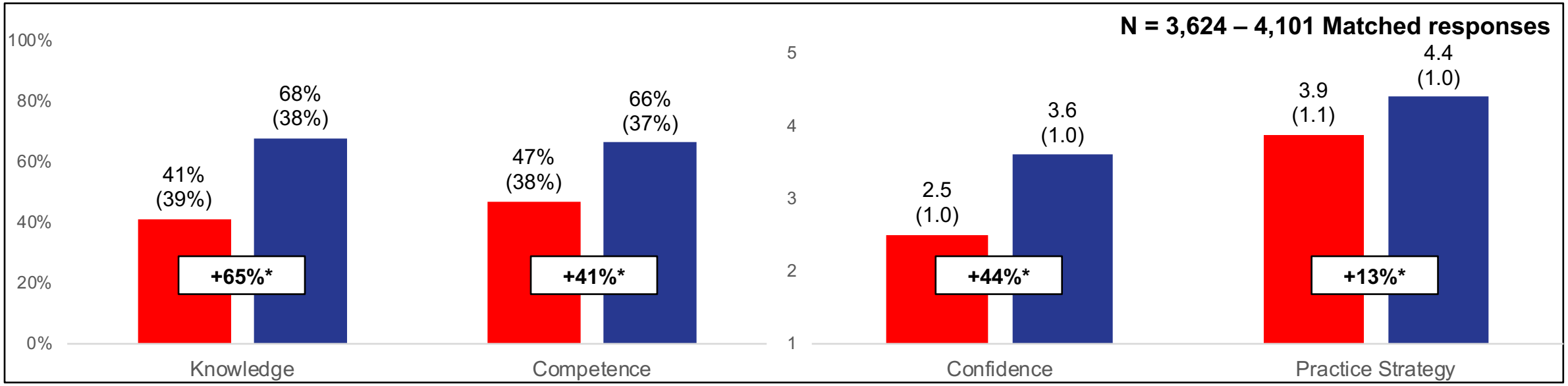
Cohort comparison by profession

Matched data, * indicates significance, $p < 0.05$

Learning Objective	Advanced Practice Nurses				Physicians			
	N	Pre-Test	Post-Test	Change	*N*	Pre-Test	Post-Test	Change
Discuss the impact of statin intolerance on ASCVD event risk	1,166	30% (46%)	64% (48%)	+111%*	406	33% (47%)	70% (46%)	+117%*
Recognize the ways in which the unique mechanisms of action for current and emerging non-statin therapies can be useful for hypercholesteremia management	1,200	48% (50%)	70% (46%)	+44%*	424	53% (50%)	79% (41%)	+47%*
Incorporate strategies to reduce cardiovascular risk in statin-intolerant patients, utilizing therapeutic combinations and lifestyle modification	1,359	43% (37%)	66% (38%)	+53%*	497	51% (36%)	69% (34%)	+35%*

- For both advanced practice nurses and physicians, significant gains were measured from Pre- to Post-Test on each of the three curriculum Learning Objectives
- On all three Learning Objectives, physicians achieved somewhat higher scores at Pre- and Post-Test compared to advanced practice nurses
- For both groups, highest Pre- and Post-Test scores were measured on recognizing the ways in which mechanisms of action for non-statin therapies can be useful for hypercholesteremia management

Learning Domain Analysis



- In each of the four curriculum learning domains, substantial and significant gains were achieved from Pre- to Post-Test
- The strongest improvements, from lowest Pre-Test scores, were measured in Knowledge, where gains were driven by an item on results of a study of Medicare beneficiaries who started statin therapy after a myocardial infarction
- Low Pre- and Post-Test Confidence despite gains indicates possible learner awareness of gaps in Knowledge and Competence
- Practice strategy ratings, on assessment of adherence to and tolerance of statin therapy, increased to a high average value at Post-Test (4.5)

* indicates significance, $p < 0.05$

Learning Domain Analysis

Cohort comparison by profession

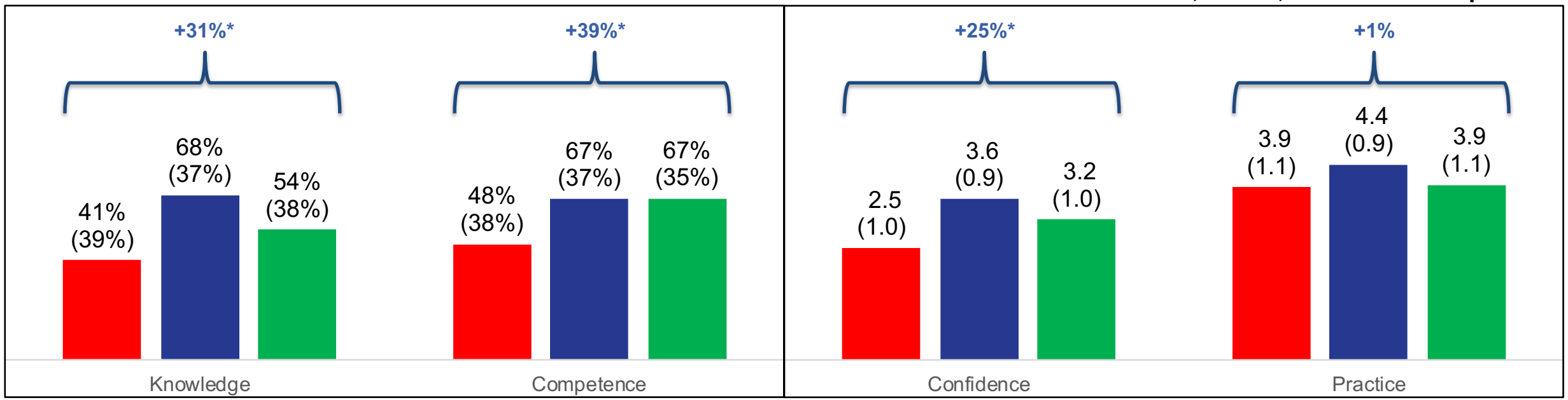
Matched data, * indicates significance, $p < 0.05$

Learning Domain	Advanced practice nurses				Physicians			
	N	Pre-Test	Post-Test	% Change	*N*	Pre-Test	Post-Test	% Change
Knowledge	1,300	39% (38%)	66% (38%)	+70%*	458	43% (40%)	75% (36%)	+72%*
Competence	1,359	43% (37%)	66% (38%)	+53%*	497	51% (36%)	69% (34%)	+35%*
Confidence	1,448	2.4 (1.0)	3.6 (0.9)	+48%*	508	2.6 (1.0)	3.7 (0.9)	+43%*
Practice	1,285	3.9 (1.1)	4.4 (0.9)	+13%*	481	3.9 (1.1)	4.4 (0.9)	+13%*

- When comparing the scores of advanced practice nurses and physicians by learning domain, both groups achieved statistically significant gains from Pre- to Post-Test, across all four domains
- In Knowledge and Competence, higher Pre- and Post-Test scores were measured for physicians, compared to advanced practice nurses
  - In Knowledge, physicians had slightly stronger gains, while advanced practice nurses had stronger gains in Competence
- Similar Confidence and practice strategy ratings were given by advanced practice nurses and physicians

4-Week Retention Analysis

By Learning Domain



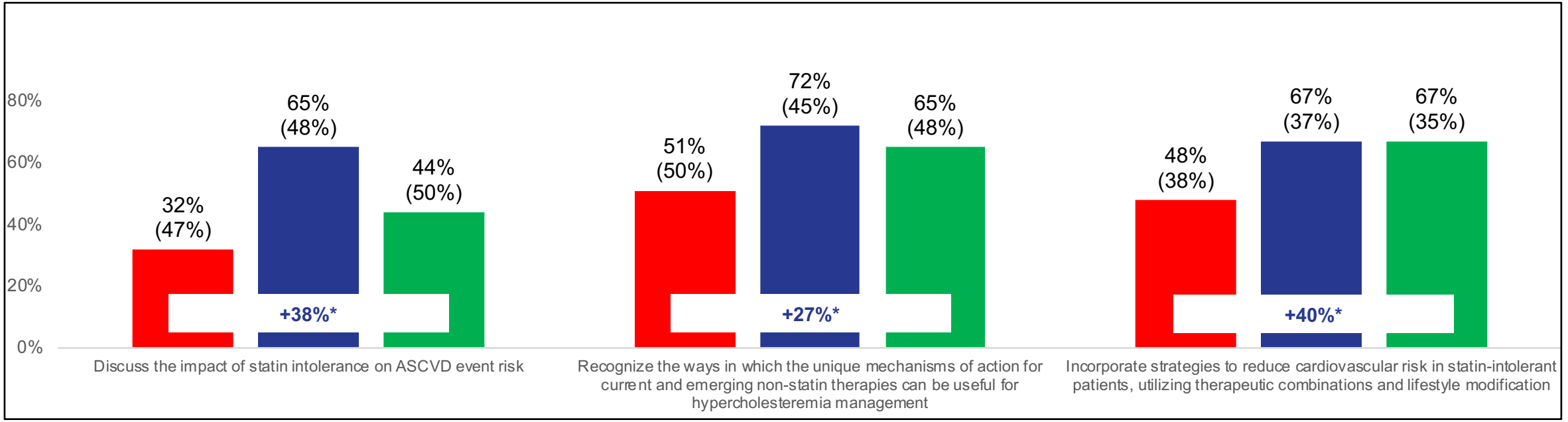
- Four to six weeks following their engagement in one of the curriculum sessions, learners were prompted to complete a brief Post Curriculum Assessment (PCA), which repeated items from each of the four curriculum learning domains
- In each of the four curriculum learning domains except practice strategy, substantial and significant net gains were achieved from Pre-Test to PCA measurements
  - Despite these gains, some score slippage was seen from Post-Test to PCA in Knowledge, Confidence, and practice strategy
- In Competence, proficiency was well retained, with no change in score from Post-Test to PCA measurements

* indicates significance, $p < 0.05$

4-Week Retention Analysis

By Learning Objective

N = 1,427 – 1,661 Matched responses



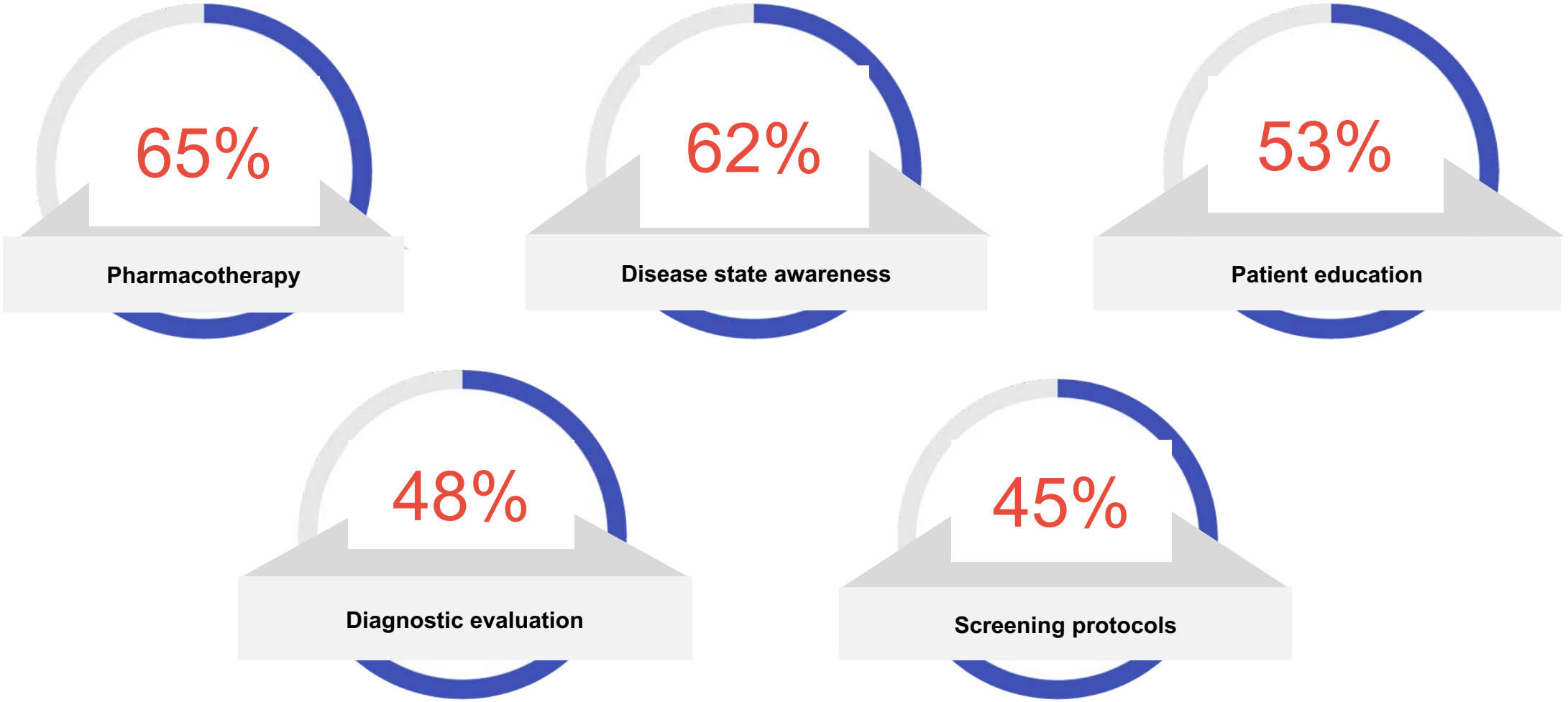
- When examining results by Learning Objective, substantial and significant net gains were achieved from Pre-Test to PCA measurements on each of the three Objectives
- On incorporating strategies to reduce cardiovascular risk in statin-intolerant patients, gains from Pre- to Post-Test were retained on the PCA, with no change measured between Post-Test and PCA assessment

* indicates significance, $p < 0.05$

(4-week Post Assessment)

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

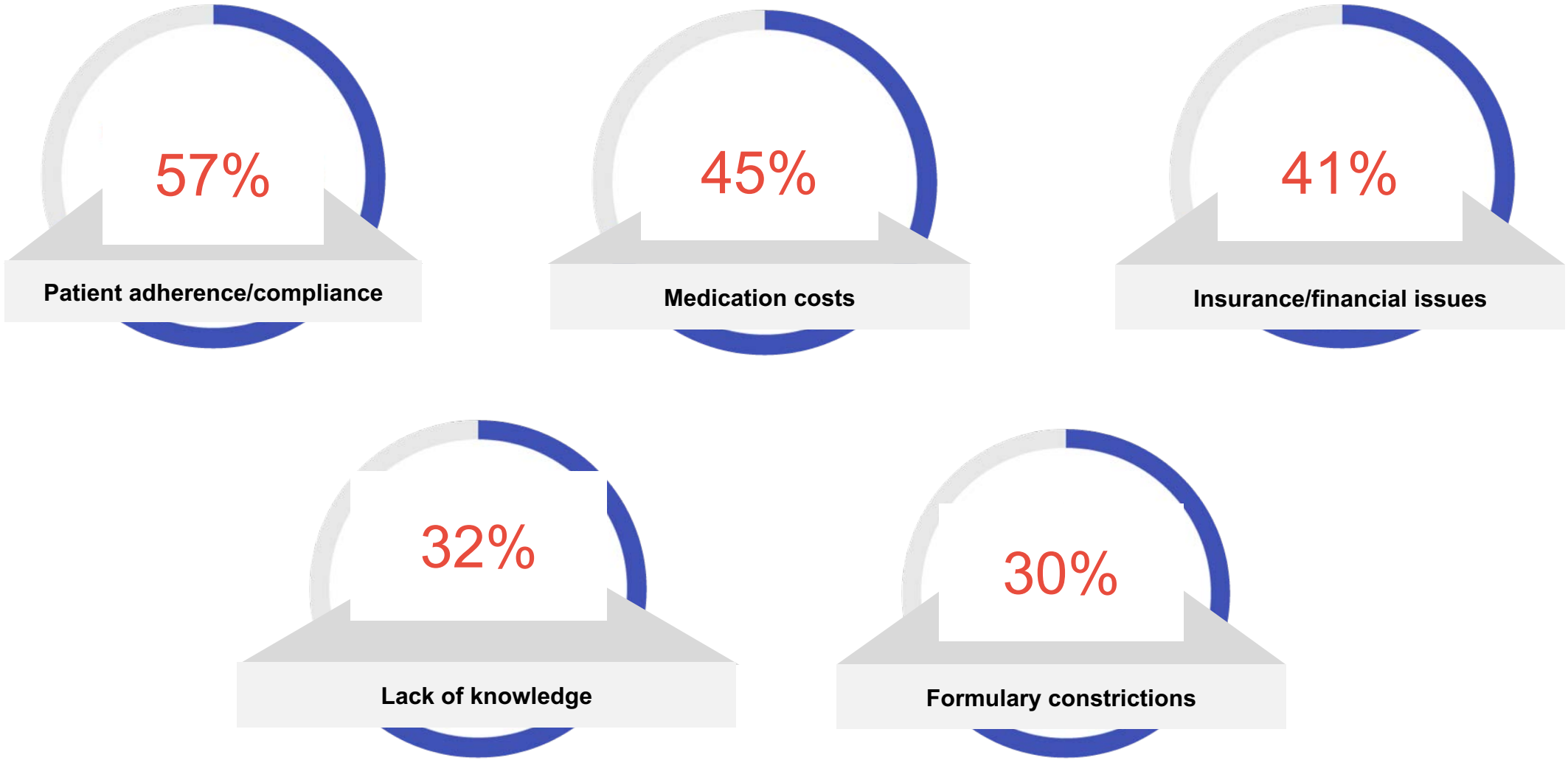
N = 3,483



(4-week Post Assessment)

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

N = 3,483



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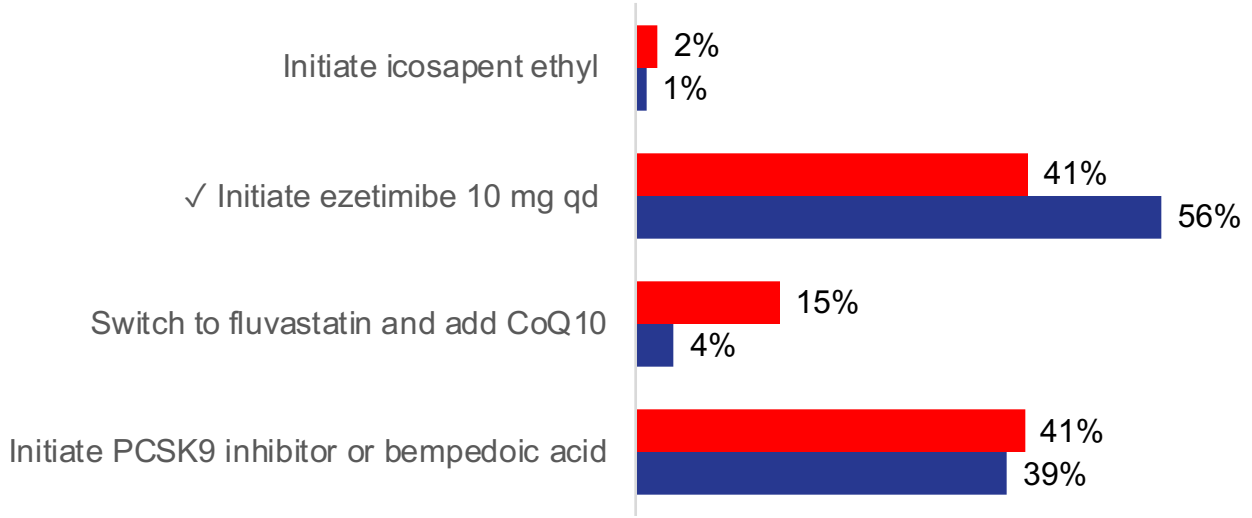
Identified Learning Gap, 1 of 2:
Selecting between statin and non-statin therapies

Despite improvements in score on a Competence item presenting the case of a patient in need of therapy modification, learners struggled at Post-Test to correctly identify ezetimibe as the most appropriate agent.

60 y/o woman with history of T2D and hypertension Hospitalized for NSTEMI 3 months ago LDL-C at MI: 145 mg/dL Atorvastatin 80 mg started Stopped atorvastatin after onset of muscle pain 3 weeks later Muscle symptoms persisted when dose reduced to 20 mg/qd and after trying two daily low-dose statins and once-a-week dosing of rosuvastatin What might be appropriate for this patient at this time?

- At Post-Test, 56% of learners correctly answered: “Initiate ezetimibe 10 mg qd”



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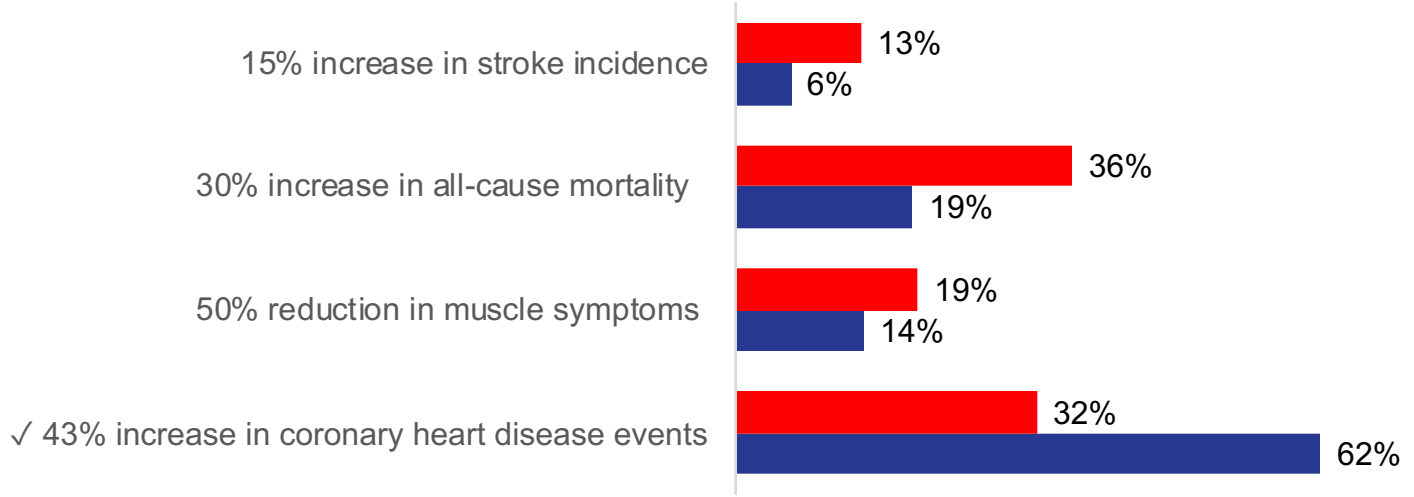
Identified Learning Gap, 2 of 2:
Impact of adherence to statin therapy on rate of cardiovascular events

Despite improvements in score on a Knowledge item on a study of outcomes for patients with high statin adherence and those with statin intolerance, low scores were measured at Post-Test.

A study of Medicare beneficiaries who started statin therapy after a myocardial infarction reported which of the following outcomes among patients with statin intolerance, compared to patients with high statin adherence?

Results:

- At Post-Test, 62% of learners correctly answered: “43% increase in coronary heart disease events”



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Overall Educational Impact

- Substantial, significant improvements were seen across all four curriculum learning domains, from Pre- to Post-Test (Knowledge, Competence, Confidence, and practice strategy)
    - These gains were stronger for advanced practice nurses compared to physicians in Competence and Confidence, though physicians achieved similar or higher scores in all learning domains
    - These gains were seen across all individual Knowledge and Competence items, with improvements ranging from 38% to 98%
- Significant improvements ranging from 41% to 98% were measured across all Learning Objectives, with Post-Test scores between 64% and 72%
- The analysis of the Knowledge and Competence domains identified two **opportunities for further education on selecting between statin and non-statin therapies and the impact of adherence to statin therapy on rate of cardiovascular events**
    - Despite improvements in score on a Competence item presenting the case of a patient in need of therapy modification, learners struggled at Post-Test to correctly identify the most appropriate non-statin agent to add.
    - Despite improvements in score on a Knowledge item, on a study of outcomes for patients with high statin adherence and those with statin intolerance, low scores were measured at Post-Test indicating underappreciation of the increased cardiovascular risk associated with poor adherence.

Appendix

Slides 26 – 28: Pre-Test to Post-Test matched item responses

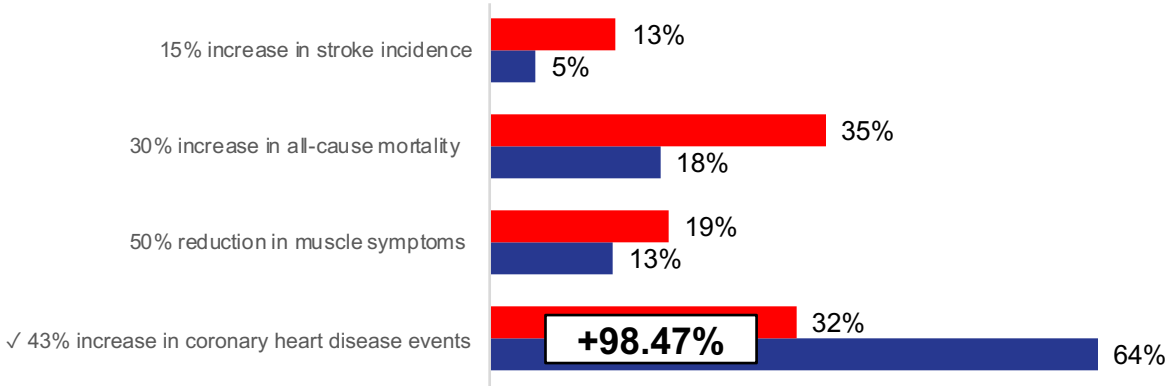
Slides 29 – 31: Pre-Test, Post-Test, and PCA matched item responses*

*Both sets of response distributions are included due to the smaller sample size of matched PCA respondents

Knowledge Items

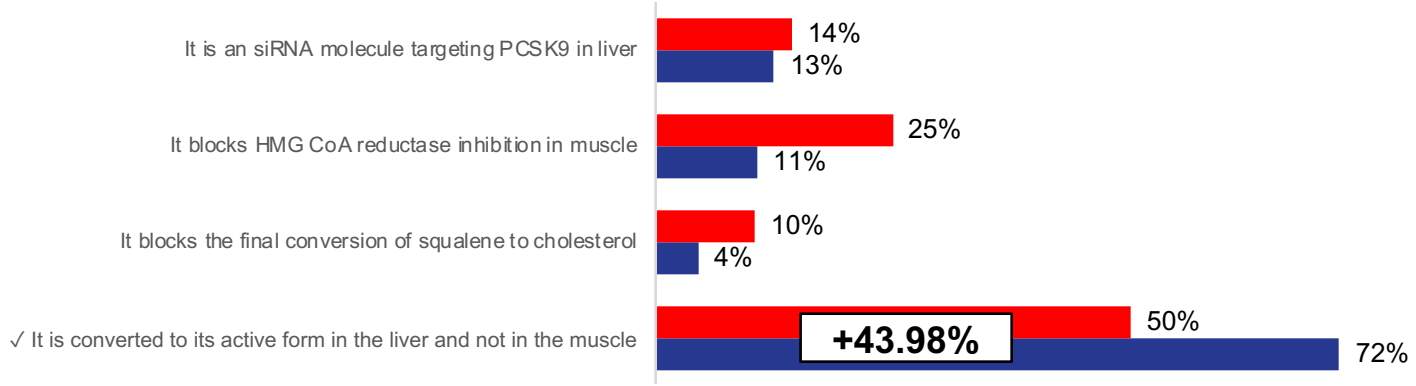
A study of Medicare beneficiaries who started statin therapy after a myocardial infarction reported which of the following outcomes among patients with statin intolerance, compared to patients with high statin adherence?

N = 3,232 Matched responses



Bempedoic acid is unlikely to cause myalgias as it promotes lipid lowering because?

N = 3,312 Matched responses



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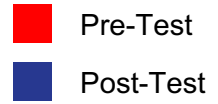
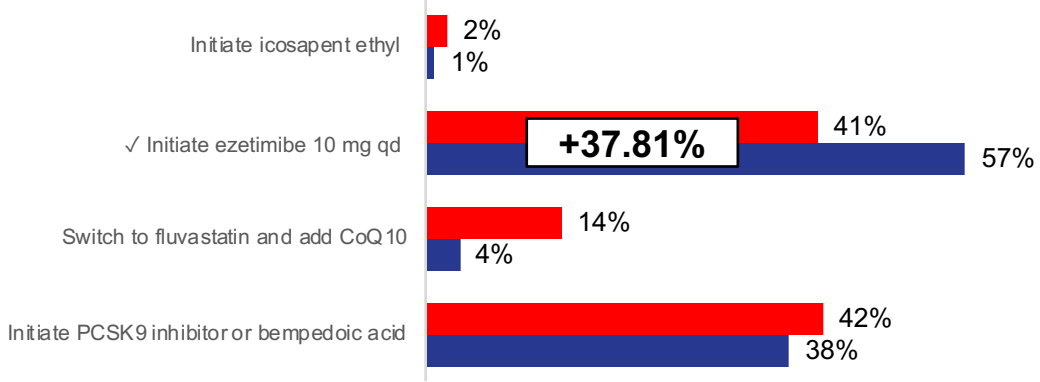
Competence Items



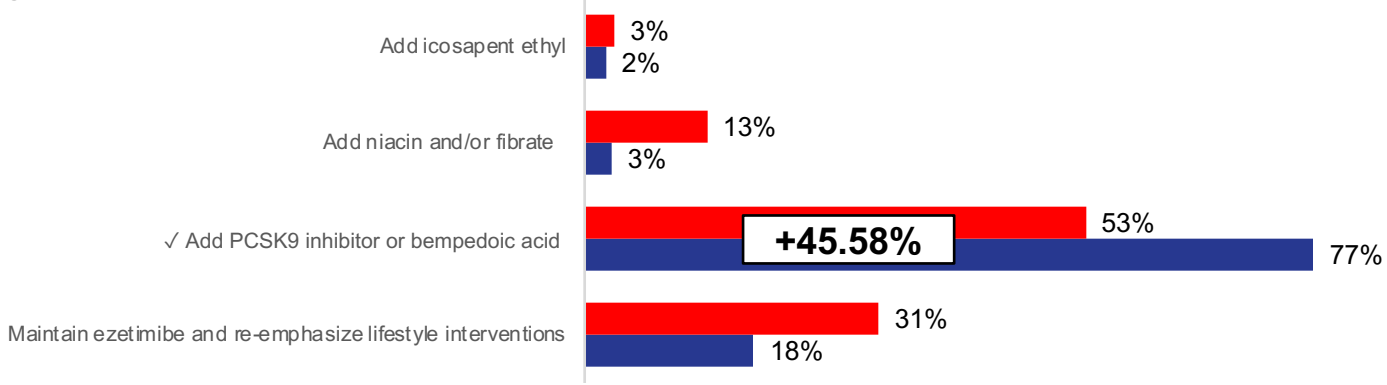
60 y/o woman with history of T2D and hypertension. Hospitalized for NSTEMI 3 months ago. LDL-C at MI: 145 mg/dL Atorvastatin 80 mg started. Stopped atorvastatin after onset of muscle pain 3 weeks later. Muscle symptoms persisted when dose reduced to 20 mg/qd and after trying two daily low-dose statins and once-a-week dosing of rosuvastatin. Which of the following medications would be the most reasonable next step for this patient for LDL-C lowering?

N = 3,558 Matched responses



59 y/o man with history of hypertension, obesity, and prediabetes. Hospitalized for NSTEMI 6 months ago; atorvastatin 80 mg initiated At time of MI, LDL-C 138 mg/dL, TG 110 mg/dL (no lipid-lowering therapy). Counseled on lifestyle interventions. Experienced muscle symptoms, which persisted after trying two daily low-dose statins and once-a-week dosing of rosuvastatin. Ezetimibe 10 mg qd added; 12 weeks later, LDL-C 112 mg/dL. What might be appropriate for this patient at this time?

N = 3,572 Matched responses



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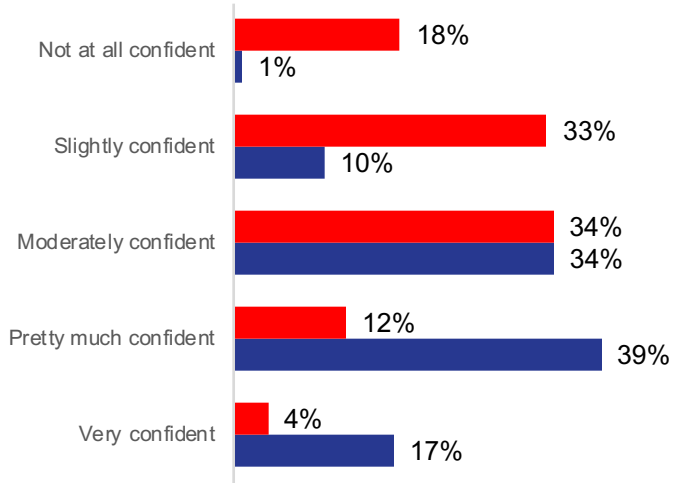
Confidence and Practice Strategy Items

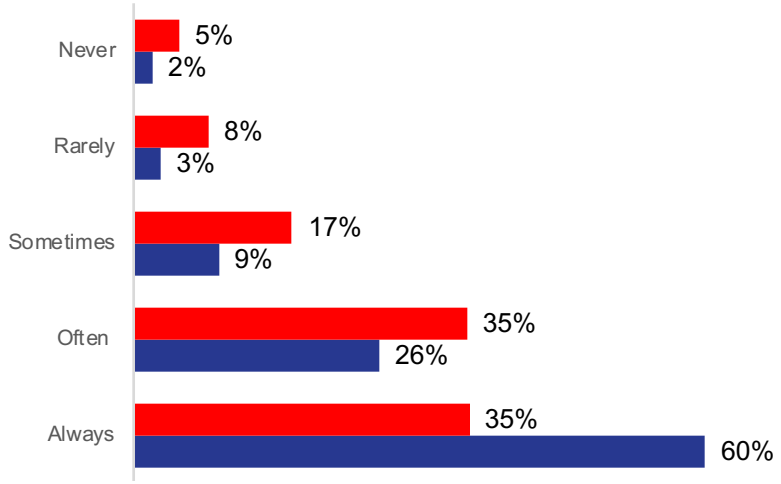
How confident are you in your ability to select non-statin lipid-lowering therapy to manage ASCVD risk in patients who do not tolerate statins?

N = 4,101 Matched responses



How often do you assess patients' adherence to, and tolerance of, statin therapy?

N = 3,631 Matched responses



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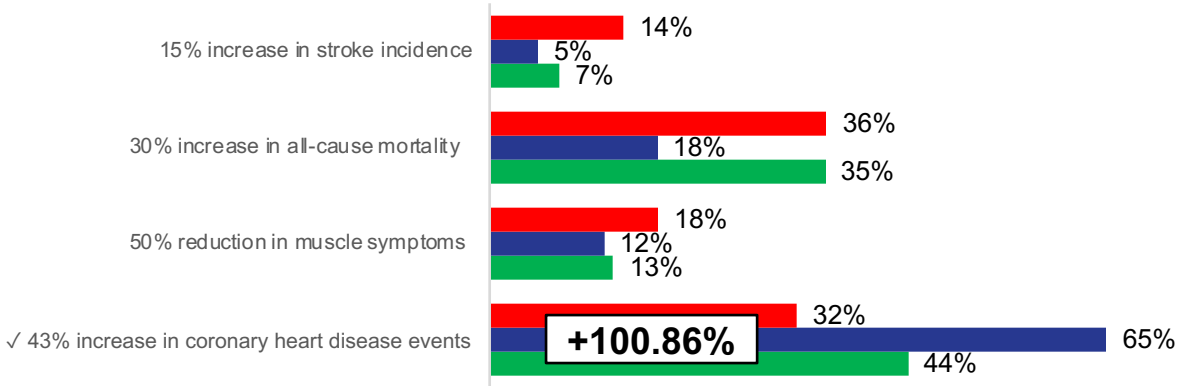
Knowledge Items

Post Curriculum Assessment (PCA)

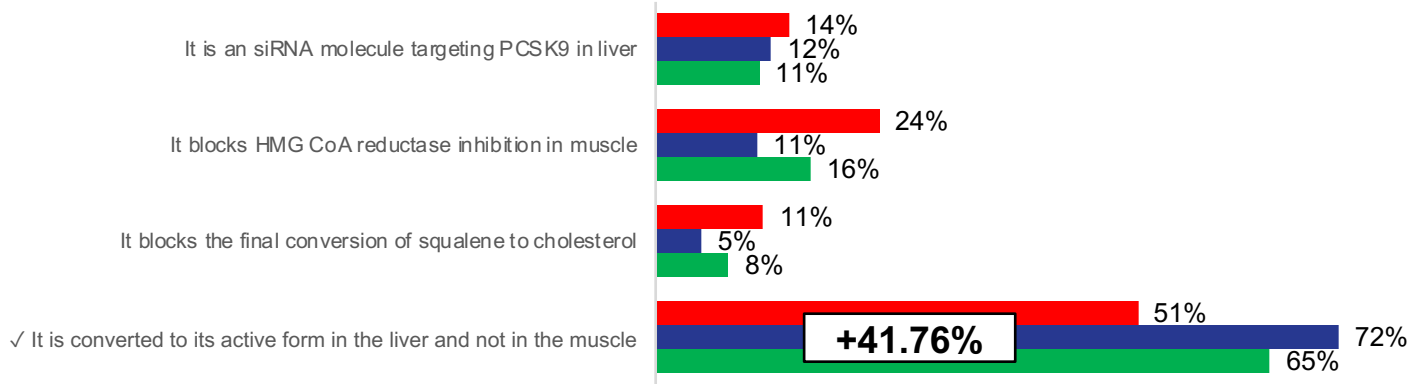
A study of Medicare beneficiaries who started statin therapy after a myocardial infarction reported which of the following outcomes among patients with statin intolerance, compared to patients with high statin adherence?

N = 1,427 Matched responses



Bempedoic acid is unlikely to cause myalgias as it promotes lipid lowering because?

N = 1,454 Matched responses



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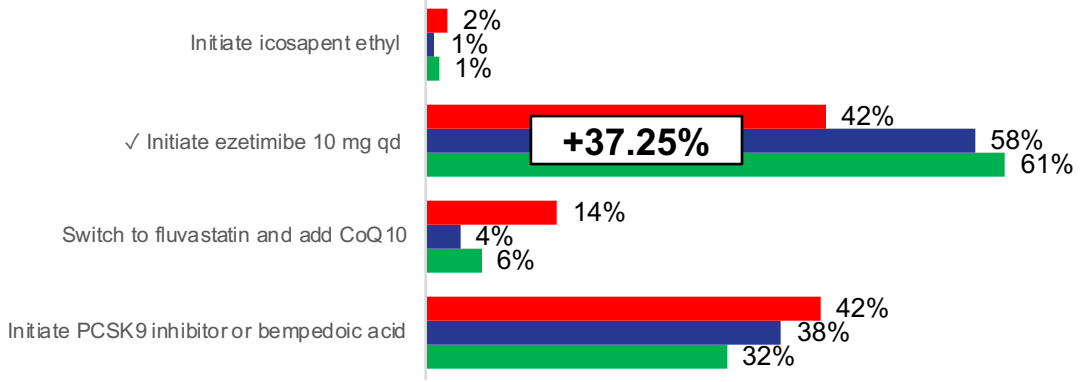
Competence Items

Post Curriculum Assessment (PCA)

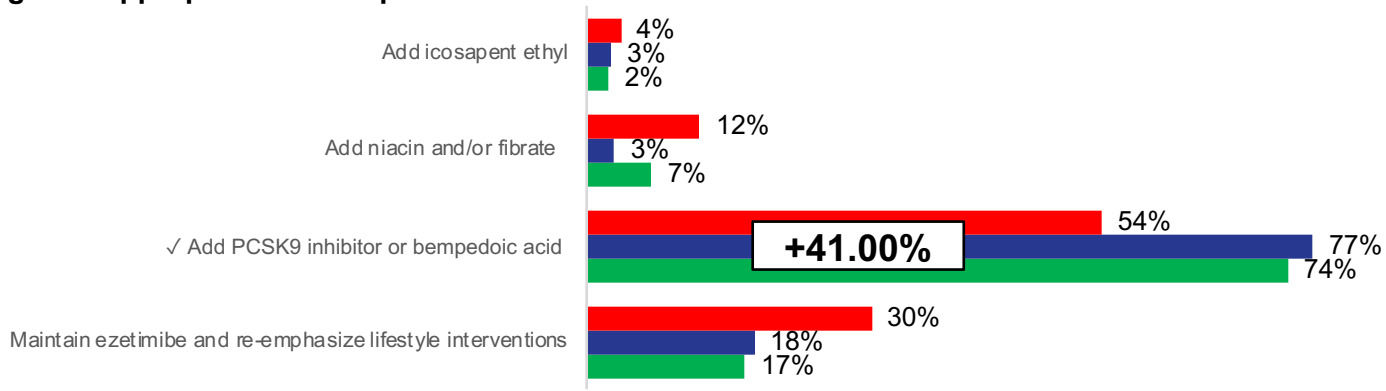
60 y/o woman with history of T2D and hypertension. Hospitalized for NSTEMI 3 months ago. LDL-C at MI: 145 mg/dL Atorvastatin 80 mg started. Stopped atorvastatin after onset of muscle pain 3 weeks later. Muscle symptoms persisted when dose reduced to 20 mg/qd and after trying two daily low-dose statins and once-a-week dosing of rosuvastatin. Which of the following medications would be the most reasonable next step for this patient for LDL-C lowering?

N = 1,532 Matched responses



59 y/o man with history of hypertension, obesity, and prediabetes. Hospitalized for NSTEMI 6 months ago; atorvastatin 80 mg initiated At time of MI, LDL-C 138 mg/dL, TG 110 mg/dL (no lipid-lowering therapy). Counseled on lifestyle interventions. Experienced muscle symptoms, which persisted after trying two daily low-dose statins and once-a-week dosing of rosuvastatin. Ezetimibe 10 mg qd added; 12 weeks later, LDL-C 112 mg/dL. What might be appropriate for this patient at this time?

N = 1,542 Matched responses



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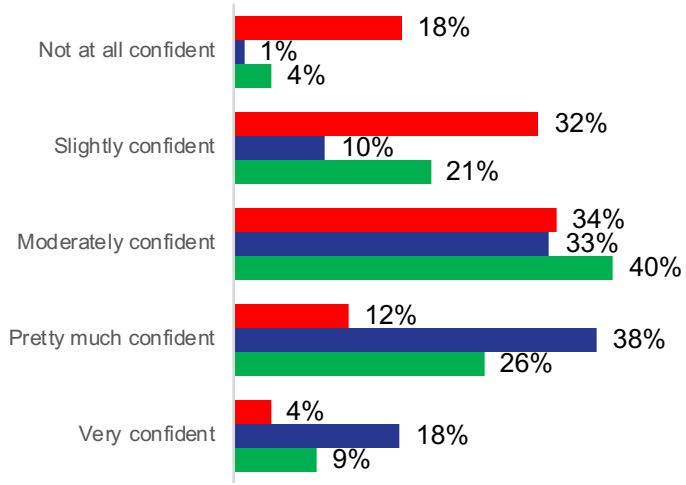
Confidence and Practice Strategy Items

Post Curriculum Assessment (PCA)

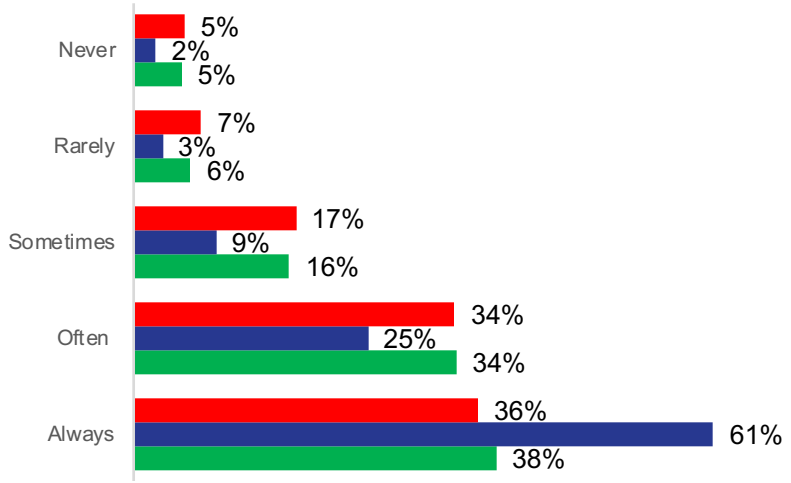
How confident are you in your ability to select non-statin lipid-lowering therapy to manage ASCVD risk in patients who do not tolerate statins?

N = 1,726



How often do you assess patients' adherence to, and tolerance of, statin therapy?

N = 1,534



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