



Identifying Primary Biliary Cholangitis: An Old Condition with New Therapy



Final Outcomes Report

Intercept Pharmaceuticals • MED-HEP-674

January 13, 2020



1,145
Participants



2 Activities



962 certificates
issued to date

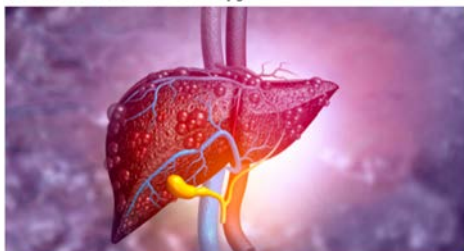
Learning Objectives

- ❖ Review the epidemiology of primary biliary cholangitis (PBC)
- ❖ Describe the pathophysiology of PBC
- ❖ Recognize how to evaluate a patient for PBC
- ❖ Discuss the treatment of PBC, including the treatment of extrahepatic manifestations

2019 Conversations Activity	Date	Participants
Conversations in Primary Care 2019 Episode 3	3/30/19	723
Conversations in Primary Care 2019 Episode 4	5/18/19	422
Total		1,145

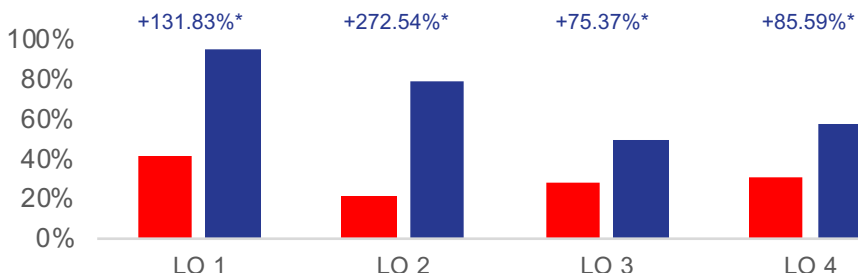
Enduring CME Webcast

Identifying Primary Biliary Cholangitis: An Old Condition with New Therapy



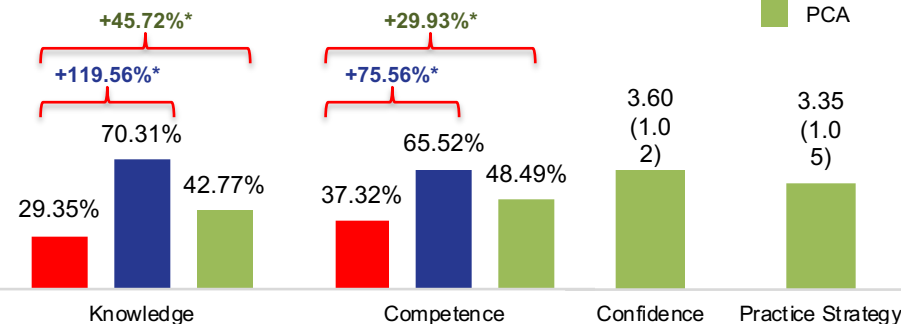
Cost: Free
 Start Date: 06/18/2019
 Expiration Date: 06/18/2020
 Target Audience: Primary Care Providers
 Format: Monograph
 Estimated Time To Complete CME Activity: 1.0 hour
 Credit(s):
 1.0 AMA PRA Category 1 Credit™
 1.0 AANP Contact hour which includes 0.75 pharmacology hours
 Hardware/Software Requirements: Any web browser

Learning Gains Across Objectives



- ❖ **LO 1:** Review the epidemiology of primary biliary cholangitis (PBC)
- ❖ **LO 2:** Describe the pathophysiology of PBC
- ❖ **LO 3:** Recognize how to evaluate a patient for PBC
- ❖ **LO 4:** Discuss the treatment of PBC, including the treatment of extrahepatic manifestations

Learning Domain Analysis



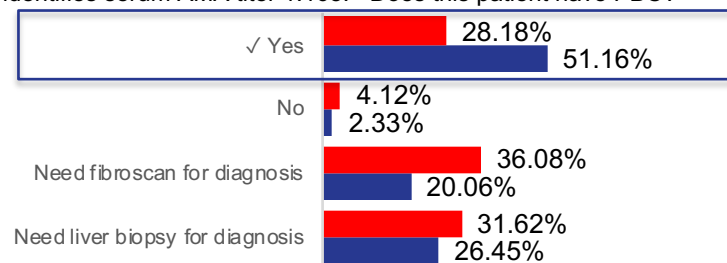
- ❖ Learners demonstrated strong and significant improvements from Pre- to Post-Test in Knowledge and Competence
 - ❖ Low Competence scores were driven by a case-based question where learners struggled to identify that a PBC diagnosis could be made without fibroscan or liver biopsy
- ❖ Knowledge and Competence scores also improved significantly from Pre-Test to follow-up, after some slippage from Post-Test

Persistent Learning Gaps/Needs

Diagnosis of PBC without use of biopsy or fibroscan

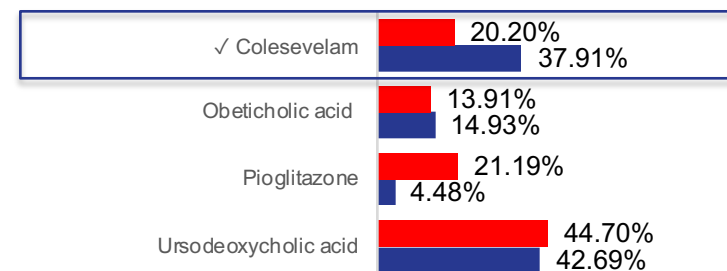
On a Competence item presenting a patient with a history of fatigue, pruritis, and elevated LFTs, learners still struggled at Post-Test to diagnose her with PBC with only the information given, instead indicating the necessity of a fibroscan or liver biopsy to confirm.

A 50-year-old obese woman presents with a 3-year history of fatigue, pruritis, and elevated LFTs (ALP ~3x ULN for last year). She does not use alcohol or drugs. Workup rules out viral hepatitis, biliary obstruction, and other common causes of liver disease. Blood test identifies serum AMA titer 1:168. Does this patient have PBC?



Treatment of PBC-related pruritis

On a Knowledge item where learners were asked to identify which agent had been demonstrated to be effective in the treatment of PBC-related pruritis, learners struggled to correctly identify "Colesevelam" at Post-Test, selecting "Ursodeoxycholic acid" at a higher rate.



Grant ID: MED-HEP-674



Activity Planning Committee

Gregg Sherman, MD

Michelle Frisch, MPH, CHCP

Sandy Bihlmeyer, M.Ed.

Daniela Hiedra

Joshua F. Kilbridge

Faculty

Kalyan Ram Bhamidimarri, MD, MPH

Transplant Hepatologist, University of Miami

Medical Director of Small Bowel & Multi-visceral Transplantation

Miami Transplant Institute

Miami, FL

K.Rajender Reddy, MD

Ruimy Family President's Distinguished Professor of Medicine

Professor of Medicine in Surgery

Director of Hepatology

Director, Viral Hepatitis Center

Medical Director, Liver Transplantation

University of Pennsylvania

Philadelphia, PA



NACE *Conversations* in Primary Care

Commercial Support

The *Conversations in Primary Care: 2019* series of CME activities were supported through educational grants or donations from the following companies:

- ❖ Lilly USA, LLC
- ❖ Amgen, Inc.
- ❖ Sanofi Genzyme and Regeneron Pharmaceuticals
- ❖ Sanofi US and Regeneron Pharmaceuticals
- ❖ Takeda Pharmaceuticals U.S.A., Inc. and Lundbeck
- ❖ Intercept Pharmaceuticals, Inc.
- ❖ Actelion Pharmaceuticals US, Inc.
- ❖ Shire
- ❖ Avanir Pharmaceuticals
- ❖ Eisai
- ❖ Galderma

Learning Objectives

- ❖ Review the epidemiology of primary biliary cholangitis (PBC)
- ❖ Describe the pathophysiology of PBC
- ❖ Recognize how to evaluate a patient for PBC
- ❖ Discuss the treatment of PBC, including the treatment of extrahepatic manifestations

Overview

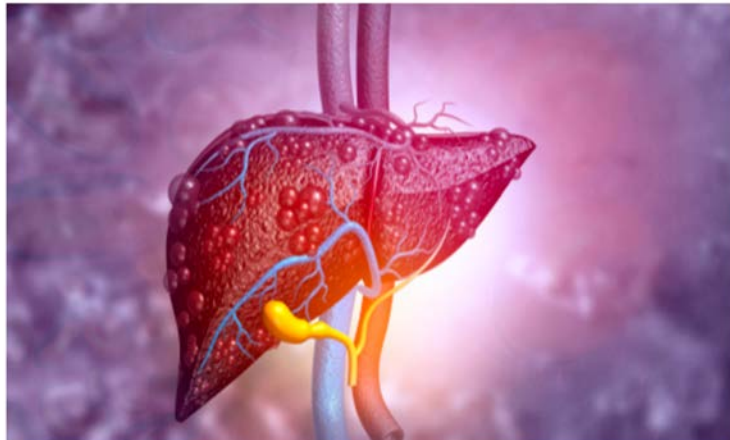


Three Live Virtual CME Symposia



Enduring CME Symposium Webcast

Identifying Primary Biliary Cholangitis: An Old Condition with New Therapy



Cost: Free
 Start Date: 06/18/2019
 Expiration Date: 06/18/2020
 Target Audience: Primary Care Providers
 Format: Monograph
 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

Clinical Highlights eMonograph

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

CONVERSATIONS IN PRIMARY CARE

Live Virtual Conferences

2019 Clinical Highlights

Identifying Primary Biliary Cholangitis: An Old Condition with New Therapy

Faculty

Kalyan Ram Bhamidimarri, MD, MPH
 Transplant Hepatologist, University of Miami
 Medical Director of Small Bowel & Multi-visceral Transplantation
 Miami Transplant Institute
 Miami, FL

K. Rajender Reddy, MD
 Ruimy Family President's Distinguished

- Primary Biliary Cholangitis (PBC) is an autoimmune chronic cholestatic liver disease.
- PBC is characterized by chronic T-cell mediated destruction of small/medium interlobular bile ducts.
- PBC is most common among middle-aged women; prevalence is 30-50 per 100,000 or 1 in 1000 women over the age of 40 years.
- The trigger for pathogenesis is unclear but a combination of environmental triggers plus genetic predisposition is postulated.
- Diagnostic criteria for PBC (must have 2 out of 3):
 - Serum alkaline phosphatase > 1.5 x ULN for > 24 weeks
 - Serum AMA > 1:40 (or PBC specific ANA ie, GP210 or SP100)



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

2019 Conversations Activity	Date	Participants
Conversations in Primary Care 2019 Episode 3	3/30/19	723
Conversations in Primary Care 2019 Episode 4	5/18/19	422
Total		1,145



Participation



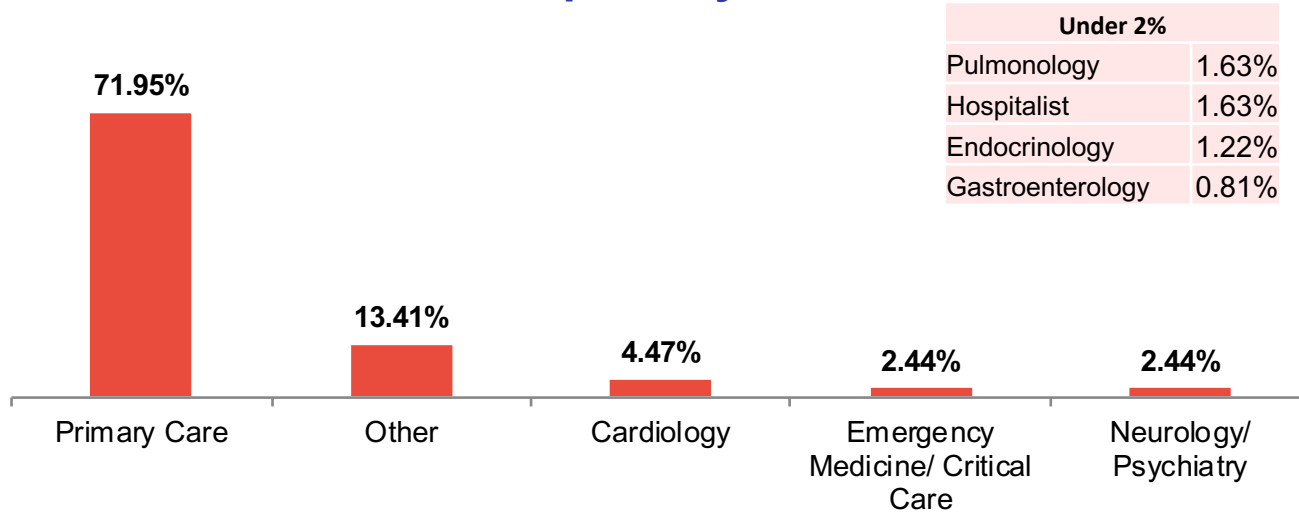
1,145
Total Attendees



2 Sessions

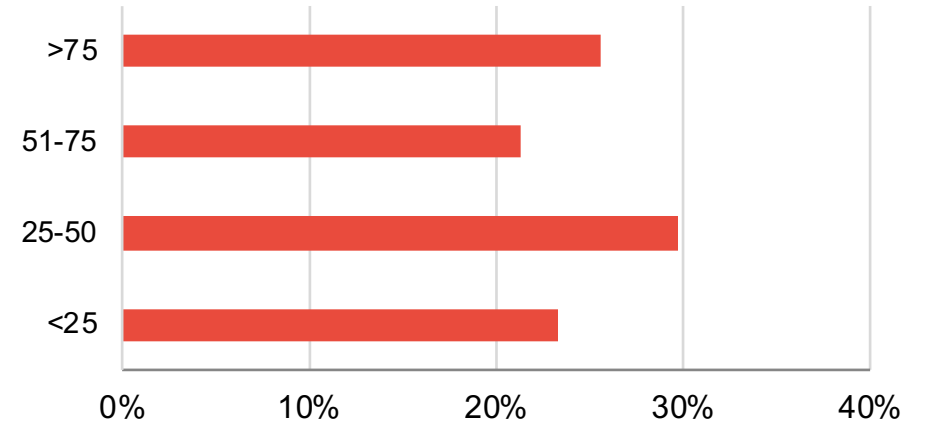
Level 1: Demographics and Patient Reach

Specialty



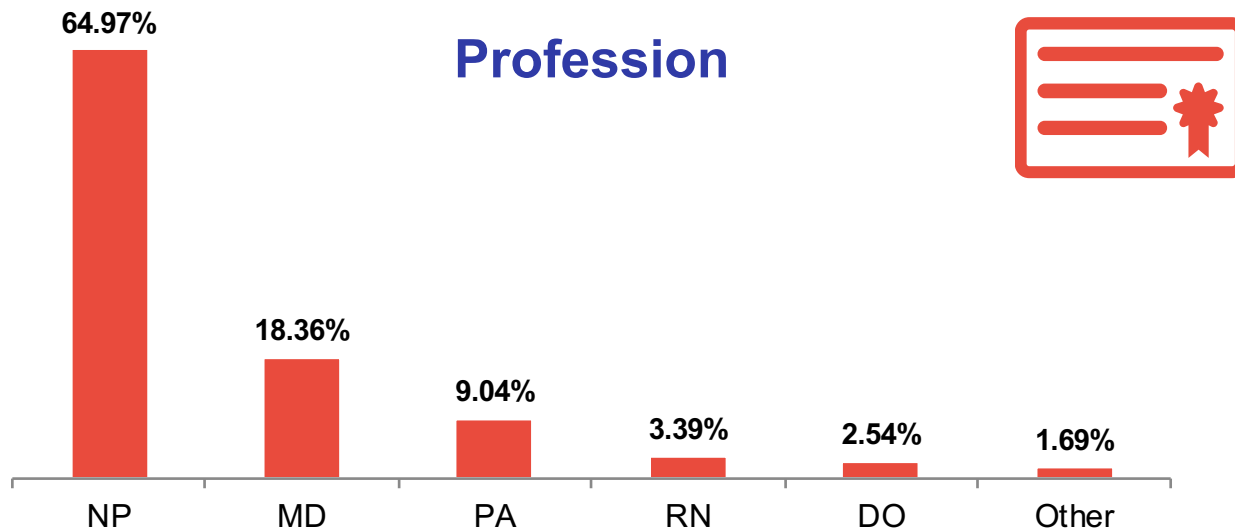
Patient Care Focus: 91%

Patients seen each week, in any clinical setting:

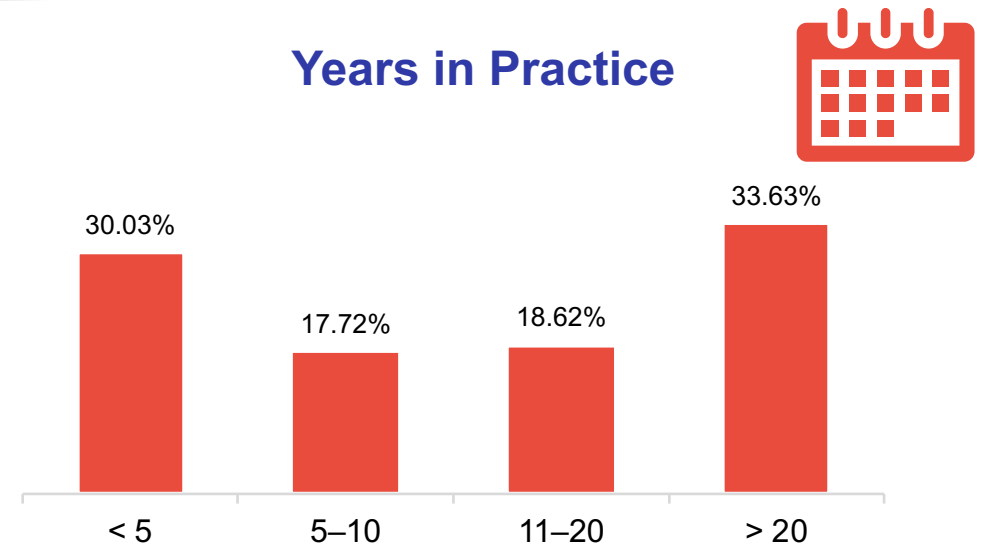


Average number of patients seen each week per clinician: 50

Profession



Years in Practice

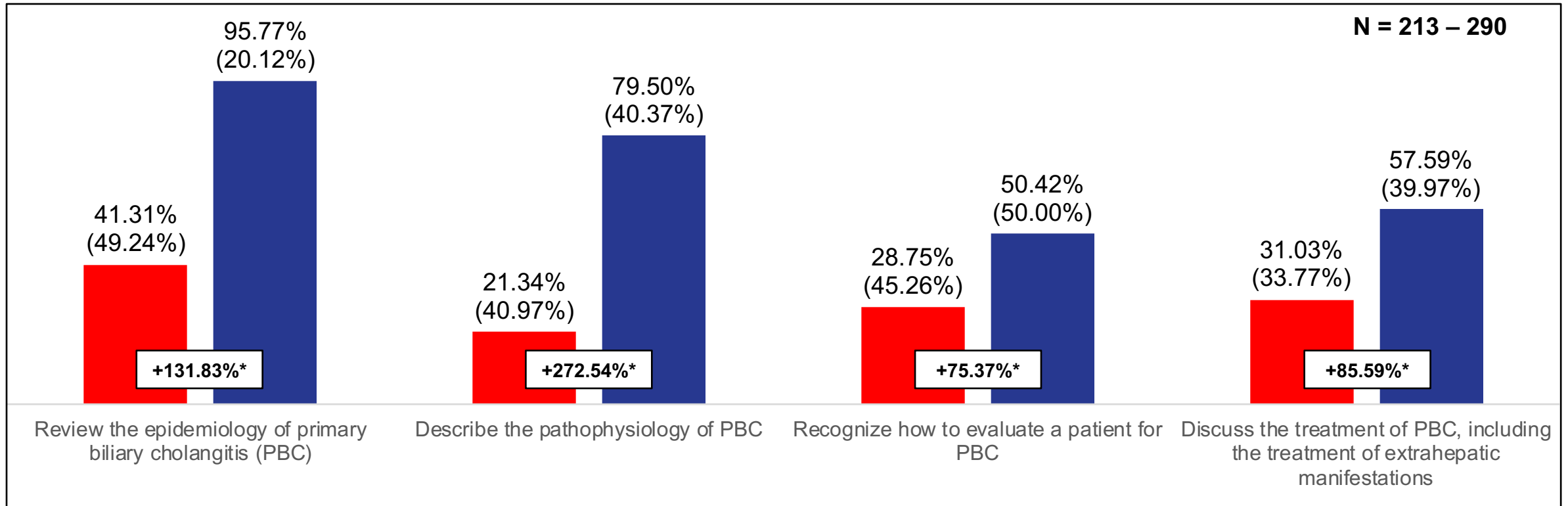




**Level 2-5:
Outcomes Metrics**

Learning Objectives Analysis

Pre-Test
Post-Test

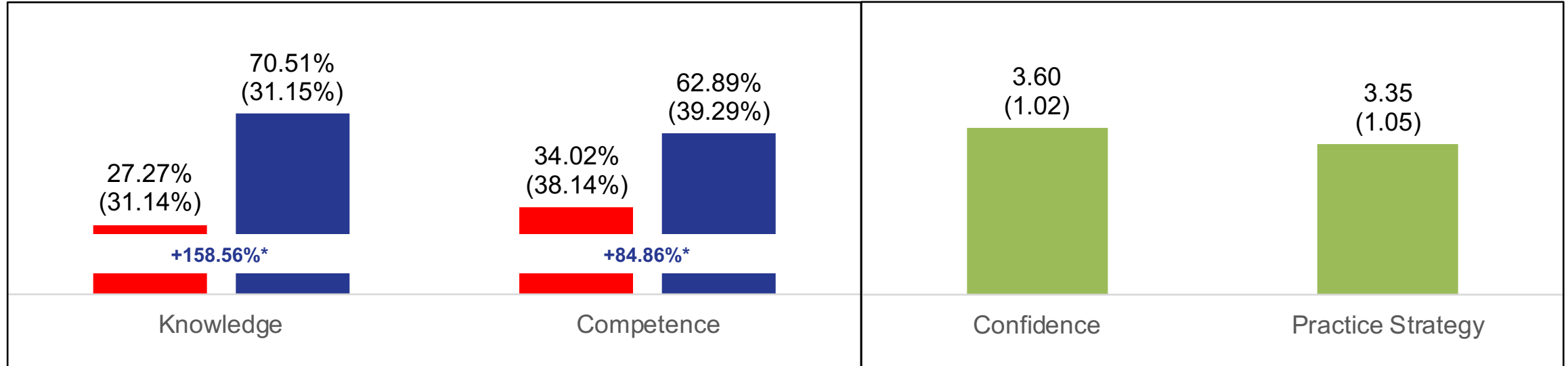


- ❖ Substantial and significant gains, ranging from 75% to 273%, were observed across all four curriculum learning objectives
- ❖ Pre-Test scores were low on all Learning Objectives (21% to 41%)
- ❖ The strongest increases in score, and highest scores at Post-Test, were observed on the Learning Objectives related to the epidemiology and pathophysiology of PBC
- ❖ Learners failed to achieve high Pre- or Post-Test scores on the Objectives related to evaluation and treatment for PBC

Learning Domain Analysis

■ Pre-Test ■ Post-Test ■ PCA

(N = 349–548)



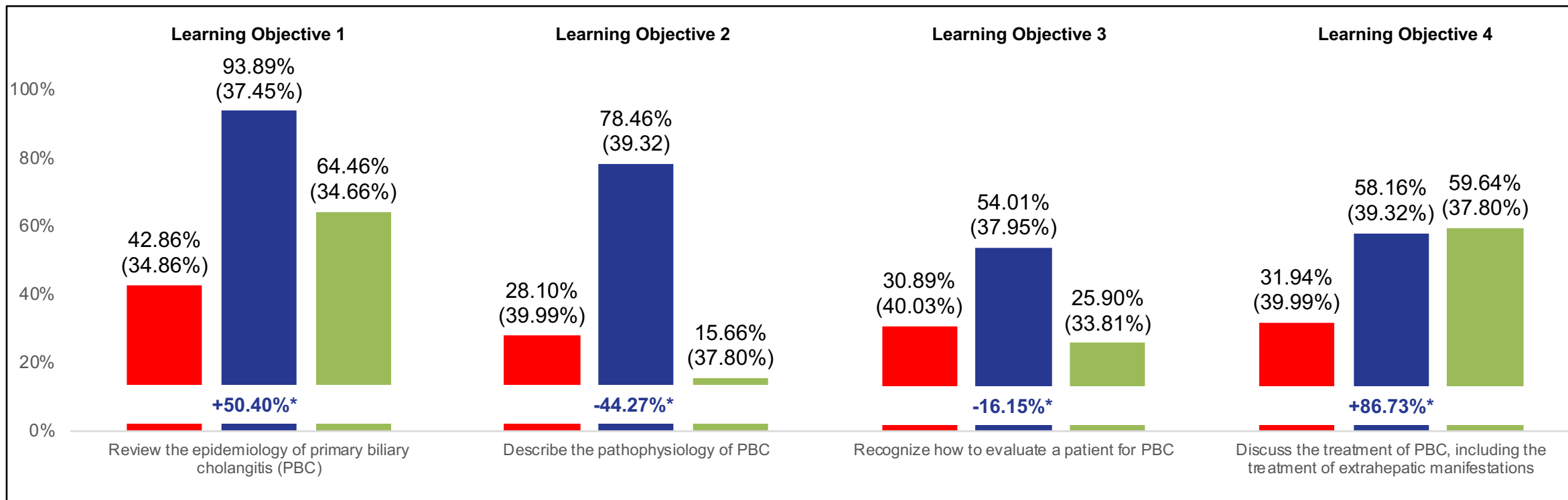
- ❖ Learners demonstrated strong and significant improvements from Pre- to Post-Test in Knowledge and Competence
 - ❖ Low Competence scores were driven by a case-based question where learners struggled to identify that a PBC diagnosis could be made without fibroscan or liver biopsy
- ❖ In Confidence and practice strategy, which were measured at 4 week follow-up only, moderate scores were observed. Learners indicated an increased testing for antimitochondrial antibodies and antinuclear antibodies in patients with sustained elevations in ALP, more likely to recommend Ursodeoxycholic Acid (UDCA) for patients diagnosed with Primary Biliary Cholangitis (PBC), and greater confidence in understanding how to evaluate a patient with possible Primary Biliary Cholangitis (PBC).

*significant at the $p \leq 0.05$ level, matched data

Learning Objectives Retention Analysis

Pre-Test Post-Test PCA

(N = 166–429)

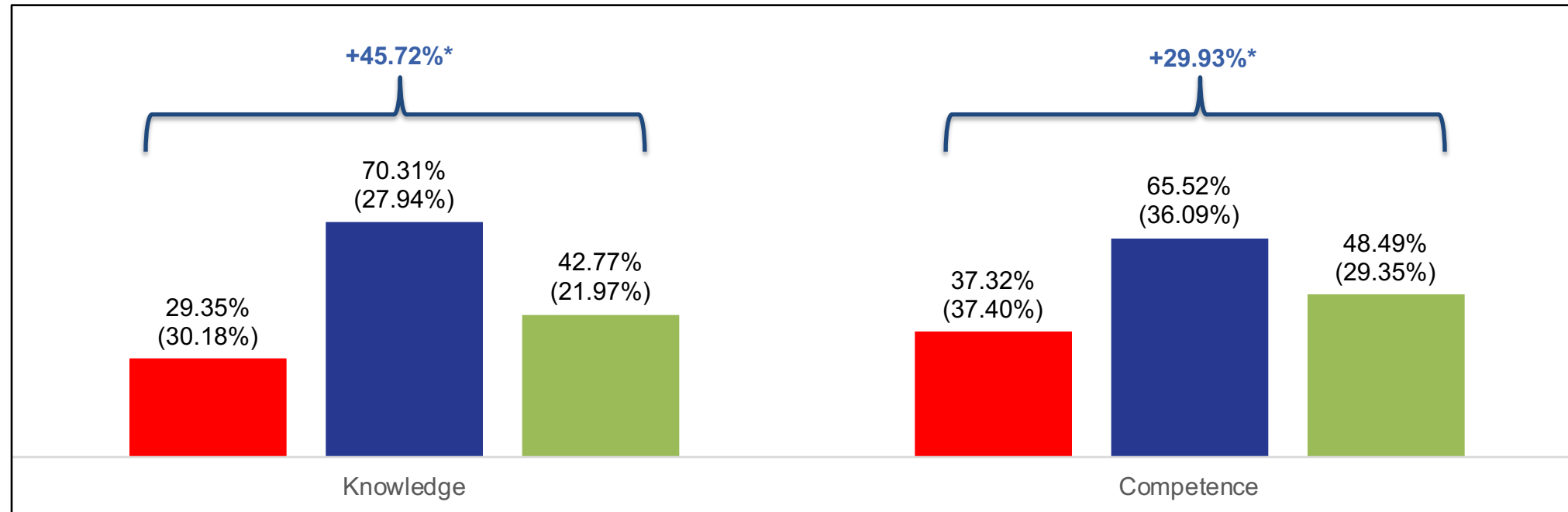


- ❖ Substantial and significant gains, of 50% and 87%, were retained on the learning objectives related to the epidemiology and treatment of PBC
- ❖ On the learning objectives related to the pathophysiology and evaluation of PBC, learners struggled to retain strong score increases on the PCA
 - ❖ Learners scored low at PCA on a case based question asking whether PBC could be diagnosed without liver biopsy or fibroscan, and on a Knowledge question asking which agent has demonstrated efficacy in the treatment of PBC-related pruritis (Colesevelam)

Learning Domains Retention Analysis

Pre-Test Post-Test PCA

(N = 349 – 429)



At follow-up:

- ❖ In addition to collecting Confidence and Practice data for the curriculum, the Post Curriculum Assessment (PCA) repeated questions from the Knowledge and Competence domains
- ❖ A statistically significant net gain was measured from Pre-Test to the Post Curriculum Assessment (PCA) in both Knowledge (46%) and Competence (30%)
- ❖ In both Knowledge and Competence, some decrease in score was measured between Post-Test and PCA, reflecting a need for further reinforcement of both declarative and case-based content

Curriculum/Activity Intervention Effect

Learning Domain	Effect Size*	% Non-Overlap
Knowledge	0.804	51.25%
Competence	0.493	29.09%

Effect Size Definition: This is a standardized measure of the strength/magnitude of the change in scores, irrespective of sample size. This metric quantifies the association between outcome and exposure to education, in a way which makes meta-analysis possible. There exist many types of effect size measures, each appropriate in different situations. We select Cohen's d for this analysis, which is a standardized difference in mean. Most commonly, d ranges from 0–1: $d < 0.2$ is a small effect, $d = 0.2–0.8$ is a medium effect, and $d > 0.8$ is a large effect.

Cohort Comparison by Profession: Learning Objectives

Learning Objective	Nurse Practitioners				Physicians			
	N	Pre-Test	Post-Test	% Change	N	Pre-Test	Post-Test	% Change
Review the epidemiology of primary biliary cholangitis (PBC)	91	40.66% (49.12%)	96.70% (17.86%)	+137.83%*	38	47.37% (49.93%)	97.37% (16.01%)	+105.55%*
Describe the pathophysiology of PBC	98	14.29% (34.99%)	82.65% (37.87%)	+478.38%*	38	39.47% (48.88%)	81.58% (38.77%)	+106.69%*
Recognize how to evaluate a patient for PBC	97	27.84% (44.82%)	55.67% (49.68%)	+99.96%*	40	45.00% (49.75%)	60.00% (48.99%)	+33.33%*
Discuss the treatment of PBC, including the treatment of extrahepatic manifestations	118	27.54% (30.25%)	58.47% (37.57%)	+112.31%*	45	33.33% (31.62%)	62.22% (38.23%)	+86.68%*

- ❖ Both nurse practitioners and physicians achieved substantial and significant improvements across all curriculum learning objectives from Pre- to Post-Test
- ❖ For all learning objectives, physicians had higher or similar Post-Test scores, compared to nurse practitioners
- ❖ For both nurse practitioners and physicians, low scores at Pre- and Post-Test were observed on the Learning Objective on treatment of PBC

Cohort Comparison by Profession: Learning Domains

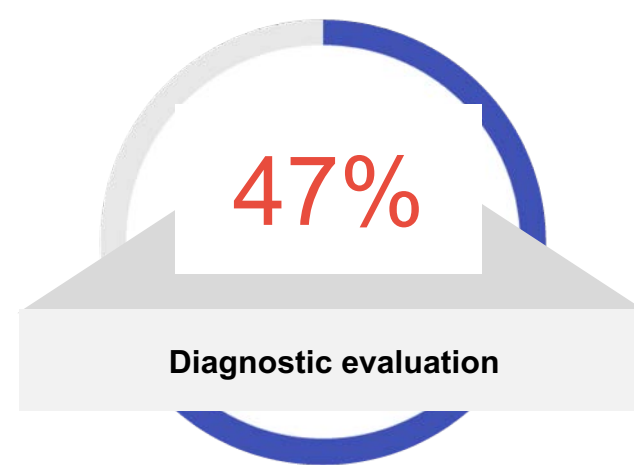
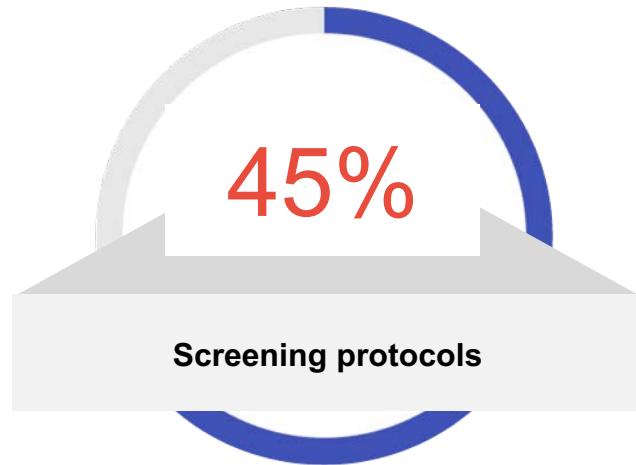
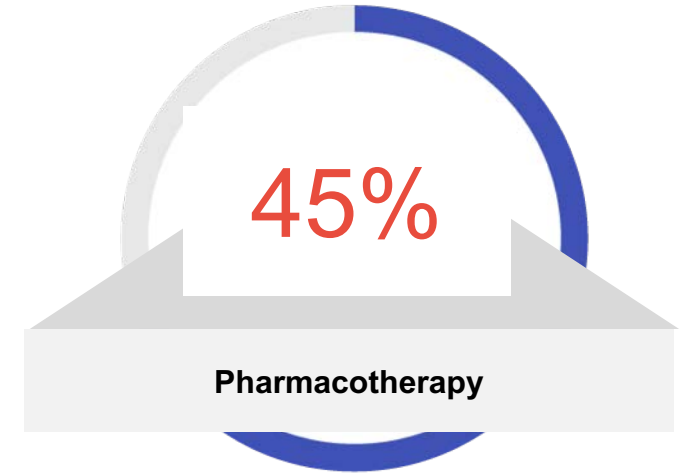
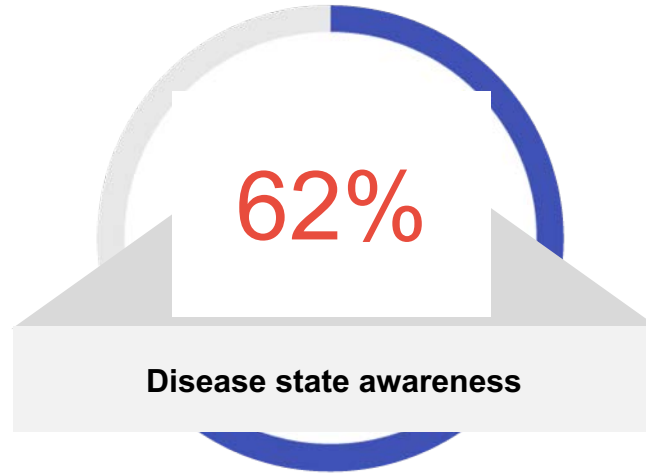
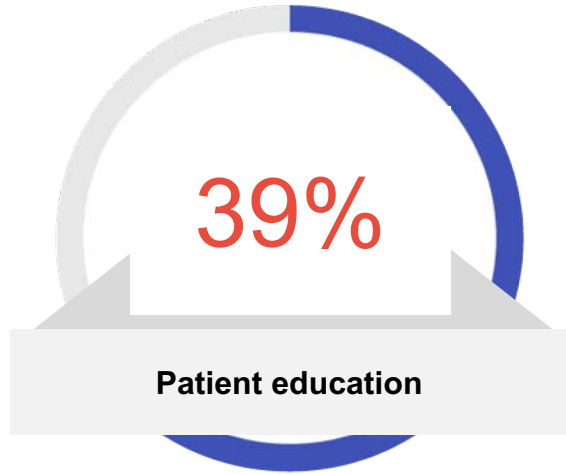
Learning Domain	Nurse practitioners				Physicians			
	<i>N</i>	Pre-Test	Post-Test	% Change	<i>N</i>	Pre-Test	Post-Test	% Change
Knowledge	116	23.99% (29.22%)	70.98% (29.86%)	+195.87%*	45	31.48% (29.02%)	75.19% (29.32%)	+138.85%*
Competence	117	32.05% (36.08%)	65.38% (37.25%)	+103.99%*	47	52.13% (42.47%)	71.28% (36.82%)	+36.74%*

- ❖ Both nurse practitioners and physicians achieved substantial and significant improvements in both Knowledge and Competence, from Pre- to Post-Test
- ❖ Physicians demonstrated higher Pre- and Post-Test scores in both Knowledge and Competence, compared to Nurse Practitioners
- ❖ For both nurse practitioners and physicians, lower scores at Post-Test were measured in Competence, compared to Knowledge

(4-week Post Assessment)

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

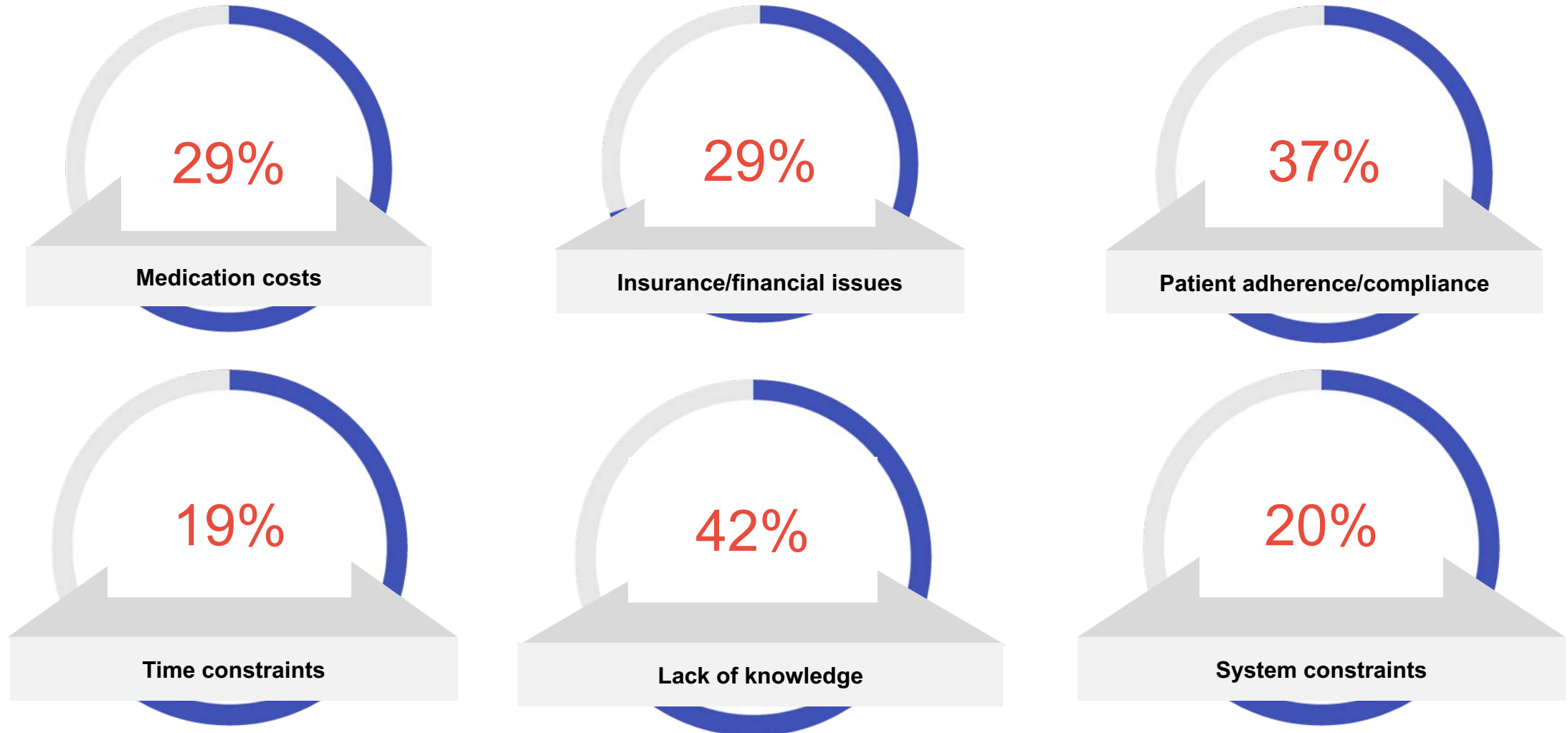
N=349



(4-week Post Assessment)

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

N=349



Identified Learning Gap 1 of 2:

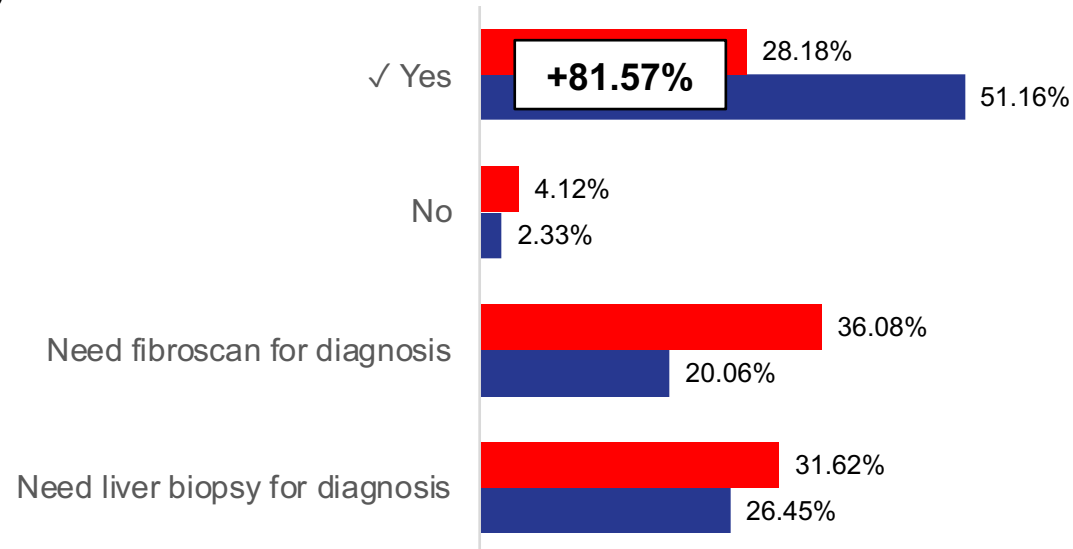
Diagnosis of PBC without use of biopsy or fibroscan

On a Competence item presenting a patient with a history of fatigue, pruritis, and elevated LFTs, learners still struggled at Post-Test to diagnose her with PBC with only the information given, instead indicating the necessity of a fibroscan or liver biopsy to confirm.

Competence: A 50-year-old obese woman presents with a 3-year history of fatigue, pruritis, and elevated LFTs (ALP ~3x ULN for last year). She does not use alcohol or drugs. Workup rules out viral hepatitis, biliary obstruction, and other common causes of liver disease. Blood test identifies serum AMA titer 1:168. Does this patient have PBC?

Results:

- At Post-Test, 51% of learners correctly answered: "Yes"



Identified Learning Gap 2 of 2:

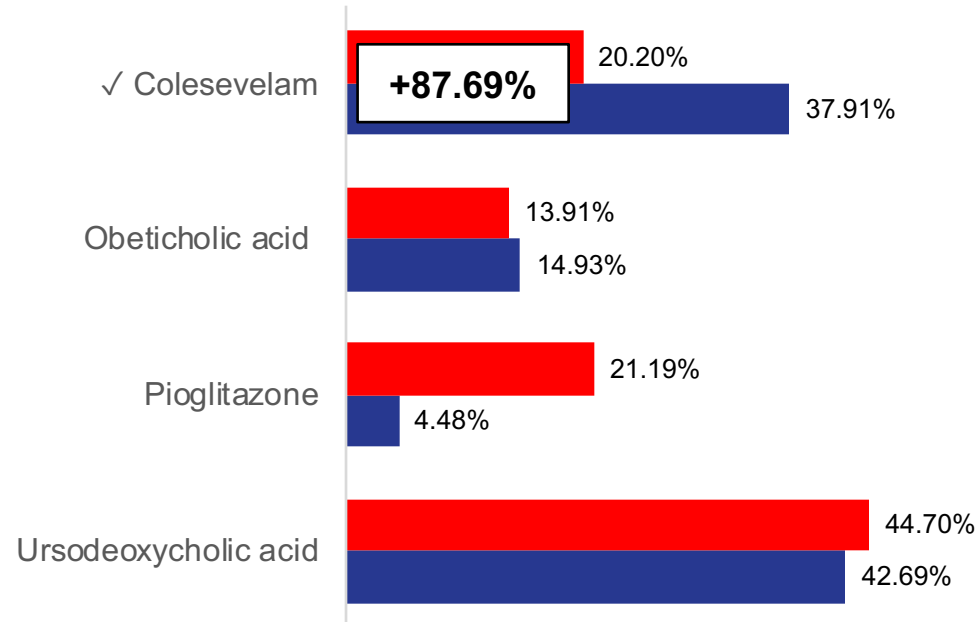
Treatment of PBC-related pruritis

On a Knowledge item where learners were asked to identify which agent had been demonstrated to be effective in the treatment of PBC-related pruritis, learners struggled to correctly identify “Colesevelam” at Post-Test, selecting “Ursodeoxycholic acid” at a higher rate.

Knowledge: Which of the following agents has demonstrated efficacy in the treatment of PBC-related pruritis?

Results:

- At Post-Test, 38% of learners correctly answered: “Colesevelam”



Overall Educational Impact

- ❖ Significant and substantial improvements (of 159% and 87%) were seen in both learner Knowledge and Competence
 - Moderate Post-Test scores (74% and 63%) were measured in Knowledge and Competence, following lower (27% and 34%) Pre-Test scores
 - Final scores on Confidence and practice strategy questions were moderate (3.60 and 3.35)
- ❖ Substantial and significant improvements ranging from 75% to 273% were measured across all Learning Objectives, from Pre-Test to Post-Test. The strongest increases, from very low Pre-Test scores, were on Objectives related to the epidemiology and pathophysiology of PBC
 - Learners achieved near mastery (96%) at Post-Test on their understanding of the epidemiology of PBC
 - Post-Test scores on the other three Learning Objectives were between 50% and 80%, highlighting opportunities for further education
- ❖ The analysis of the Knowledge and Competence domains identified two **persistent learning gaps related to PBC diagnosis without biopsy or fibroscan, and to the treatment of PBC-related pruritis**
 - Pre- and Post-Test scores (28% and 51%) were low on a Competence item presenting a patient with a history of fatigue, pruritis, and LFTs, where they were asked whether a fibroscan or liver biopsy were necessary to confirm a diagnosis of PBC
 - On a Knowledge item which asked about effective agents for treating PBC-related pruritis, learners struggled to identify Colesevelam at Pre-Test (20%) and Post-Test (38%)

Overall Educational Impact – Future Directions

- ❖ Participants in this activity demonstrated low pre-test scores across all learning objectives. As a result of this program, learners are more aware of how to recognize, diagnose, and treat Primary Biliary Cholangitis. 4 weeks after the activity, learners indicated an increased testing for antimitochondrial antibodies and antinuclear antibodies in patients with sustained elevations in ALP, being more likely to recommend Ursodeoxycholic Acid (UDCA) for patients diagnosed with Primary Biliary Cholangitis (PBC), and having greater confidence in understanding how to evaluate a patient with possible Primary Biliary Cholangitis (PBC).
- ❖ Future activities should be designed to help primary care clinicians improve their ability to evaluate patients with elevated alkaline phosphatase, and manage PBC-related pruritis.

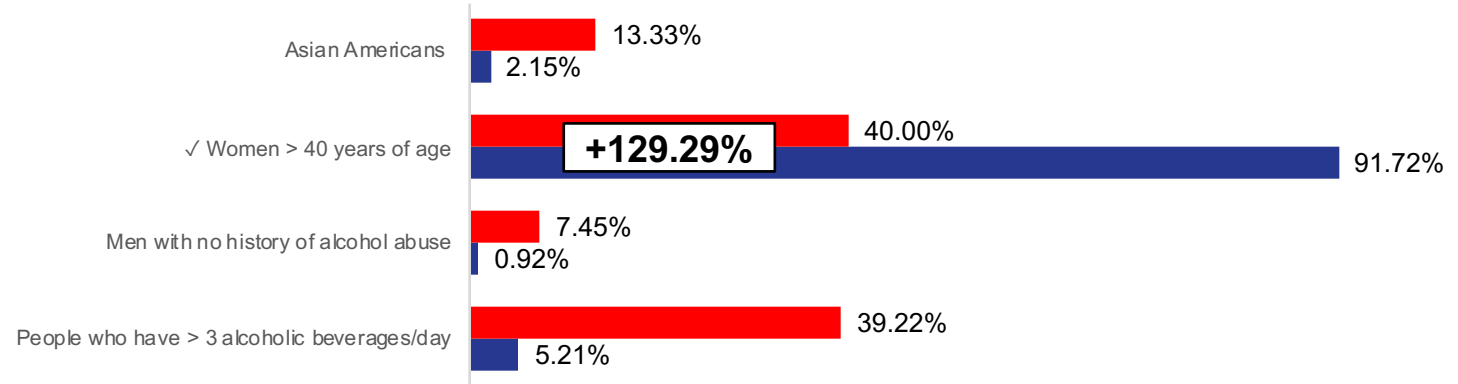
Appendix

Knowledge Items

Pre-Test
Post-Test

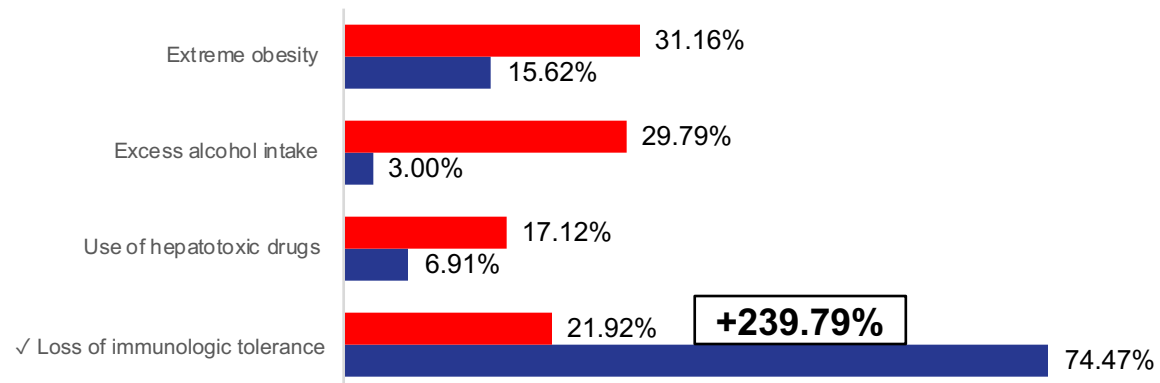
PBC is most common in which of the following groups?

N = 255 – 326



Which of the following is a key pathophysiologic mechanism of PBC?

N = 292 – 333

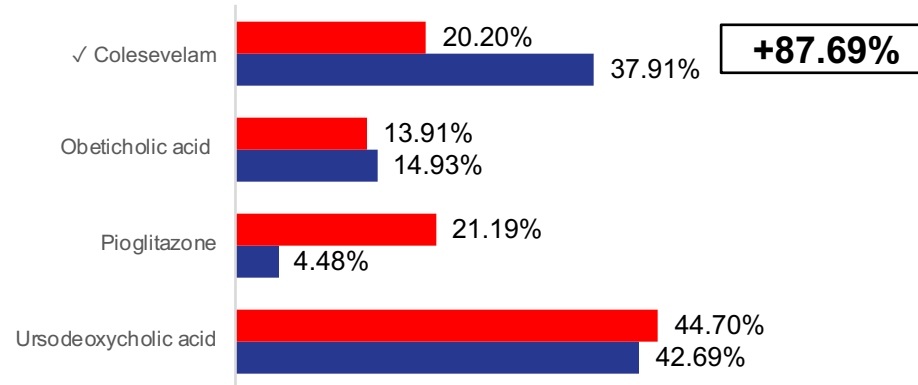


Knowledge Items

Pre-Test
Post-Test

Which of the following agents has demonstrated efficacy in the treatment of PBC-related pruritis?

N = 302 – 335

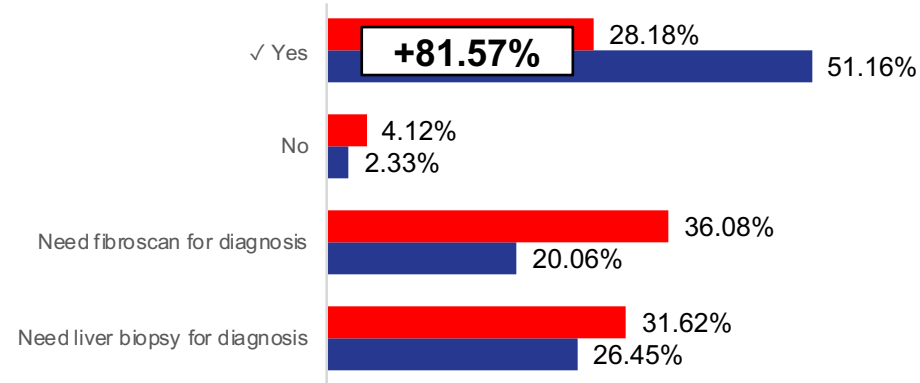


Competence Items

Pre-Test
Post-Test

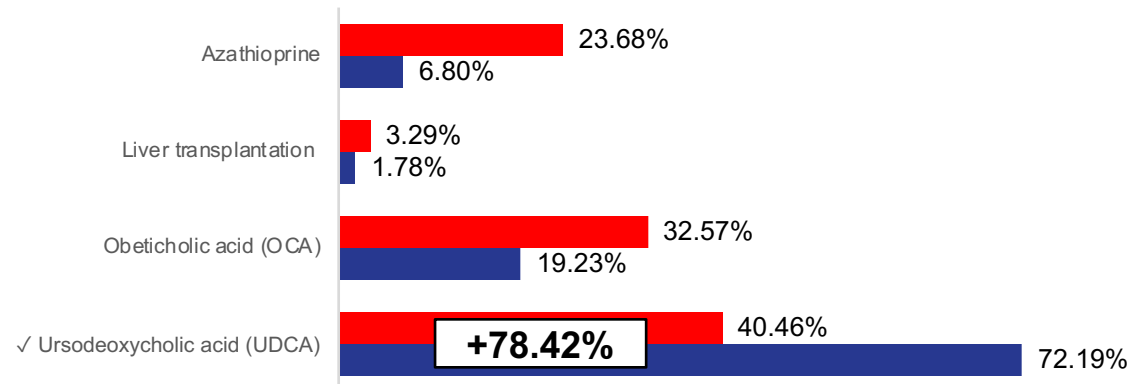
A 50-year-old obese woman presents with a 3-year history of fatigue, pruritis, and elevated LFTs (ALP ~3x ULN for last year). She does not use alcohol or drugs. Workup rules out viral hepatitis, biliary obstruction, and other common causes of liver disease. Blood test identifies serum AMA titer 1:168. Does this patient have PBC?

N = 291 – 344



A 56-year-old overweight woman with a history of fatigue, pruritis, and elevated LFTs is diagnosed with PBC. She also has a history of osteoporosis, treated with bisphosphonates, and hypertension, treated with lisinopril. What is an appropriate first-line treatment for this patient?

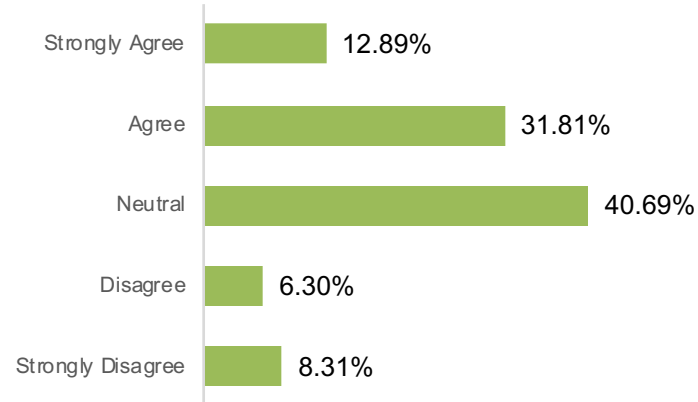
N = 304 – 338



Practice Strategy Items (given at follow-up)

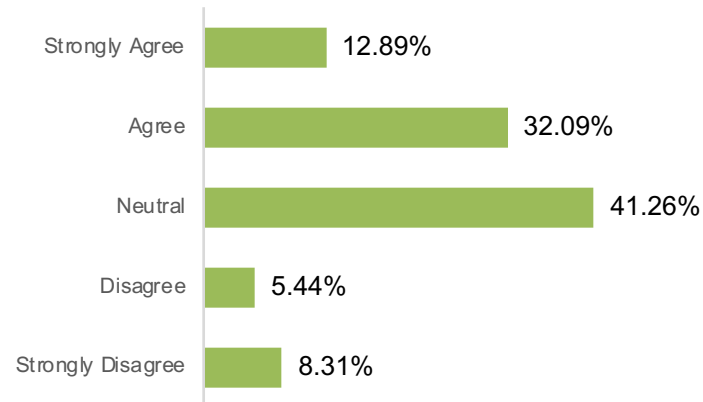
Please rate your level of agreement with the following statement: "I have increased testing for antimitochondrial antibodies and antinuclear antibodies in patients with sustained elevations in ALP."

N = 349



Please rate your level of agreement with the following statement: "I more often recommend Ursodeoxycholic Acid (UDCA) for patients diagnosed with Primary Biliary Cholangitis (PBC)."

N = 349



Confidence Item (given at follow-up)

Please rate your level of agreement with the following statement: "I am much more confident in understanding how to evaluate a patient with possible Primary Biliary Cholangitis (PBC)."

N = 349

