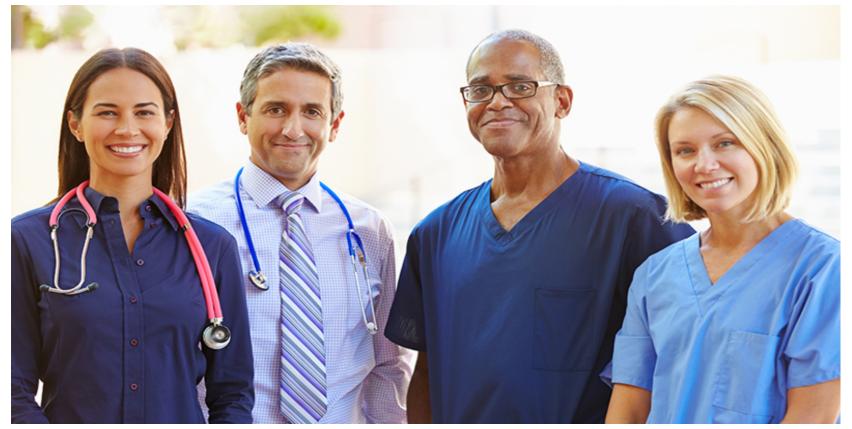
Emerging Challenges in Primary Care: 2020

Moving Ahead in Migraine Management: Translating the Latest Science into Patient Care



November 16, 2020 Amgen GHCCHOPS – IME - 266166

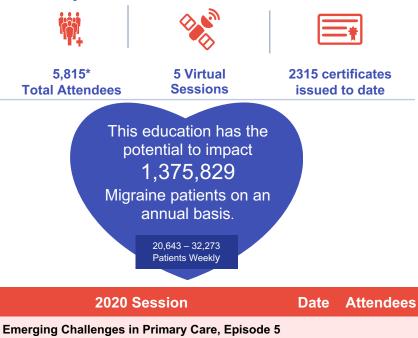




Emerging Challenges in Primary Care: 2020

This curriculum focused on management of patients with migraine

Participation



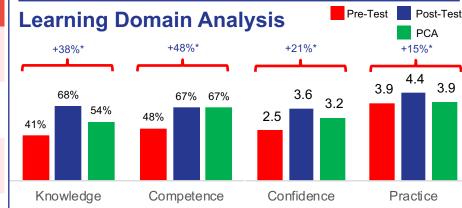
Total		5,815
Emerging Challenges Episode 8, Rebroadcast	7/11/20	258
Emerging Challenges in Primary Care, Episode 8 Virtual: National audience	6/27/20	1,323
Emerging Challenges in Primary Care, Episode 7 St. Louis: Missouri, Iowa, Nebraska, Kansas, Oklahoma, Arkansas, Illinois	6/20/20	743
Emerging Challenges in Primary Care, Episode 6 Atlanta: Georgia, Florida, Alabama, Tennessee, North Carolina, South Carolina, Mississippi	6/13/20	2,235
Raleigh: North Carolina, South Carolina, Tennessee, Kentucky, Virginia, West Virginia, Georgia	6/6/20	1,256



Learning Gains Across Objectives



- LO 1, 34%* Improvement: Recognize migraines as a neurological condition requiring both prophylactic & on-demand treatment strategies
- LO 2, 79%* Improvement: Identify strategies to differentially diagnose episodic & chronic migraines
- LO 3, 69%* Improvement: Compare therapies for migraine prophylaxis, including CGRP antagonists & botulinum toxin
- LO 4, 267%* Improvement: Evaluate newly approved and emerging ondemand treatments for migraines
- LO 5, 91%* Improvement: Propose primary care-driven strategies to develop
 & support migraine management considering heterogeneous patient cases



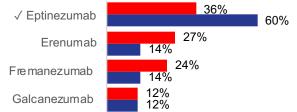
- In each of the four curriculum learning domains, substantial and significant gains were achieved from Pre- to Post-Test
- The strongest improvements, from lowest Pre-Test scores, were measured in Competence, where gains were driven by an item on prescribing oral CGRP antagonist for a patient for whom NSAIDs and acetaminophen have been inadequate in providing relief from pain
- Despite these gains, low Post-Test scores in Knowledge and Competence (62% to 65%)
 reflect opportunities for further education
- Low Pre- and Post-Test Confidence ratings indicate possible learner awareness of gaps in Knowledge and Competence
- Practice strategy ratings, on prescribing preventive drug therapy for patients with chronic or episodic migraine, increased to a moderate average value at Post-Test (3.8)

Persistent Learning Gaps/Needs

Side effects of CGRP inhibitors

Despite improvements in score on a Knowledge item asking about side effects of eptinezumab, learners struggled at Post-Test to associate it with its side effects.

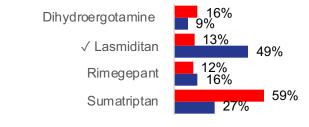
Which of the following CGRP inhibitors for migraine prevention has not been associated with injection site reactions, but may be associated with upper respiratory side effects?



Mechanism of action of novel migraine therapies

Though very strong gains were seen on an item about the mechanism of action of lasmiditan, low scores were measured at Post-Test.

Which of the following acute treatments for migraine acts through agonism of the 5-HT1F receptor only?



Differentiating between chronic and episodic migraine in diagnosis

Despite improvements in score on a Competence item presenting a patient with frequent headaches for which ibuprofen poorly manage his pain, learners struggled at Post-Test to appropriately diagnose episodic migraine.



Curriculum Patient Impact

In the Post-Test, learners (N = 2,384) were asked to report how many patients with migraine 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

1,375,829 patients on an annual basis.

20,643 – _32,273

20,643 – 32,273 patients on a weekly basis





Course Director

Jeff Unger, MD, FAAFP, FACE

Diplomate-American Board of Family Medicine Fellow, American Association of Clinical Endocrinologists Assistant Clinical Professor of Family Medicine UC Riverside School of Medicine Director, Unger Concierge Primary Care Medical Group Director, Metabolic Studies Catalina Research Institute Riverside, CA

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David M. Kaufman, MD (Peer Reviewer)

Professor, The Saul R. Korey Department of Neurology Professor, Department of Psychiatry and Behavioral Sciences Albert Einstein College of Medicine Montefiore Medical Center Bronx, NY





Commercial Support

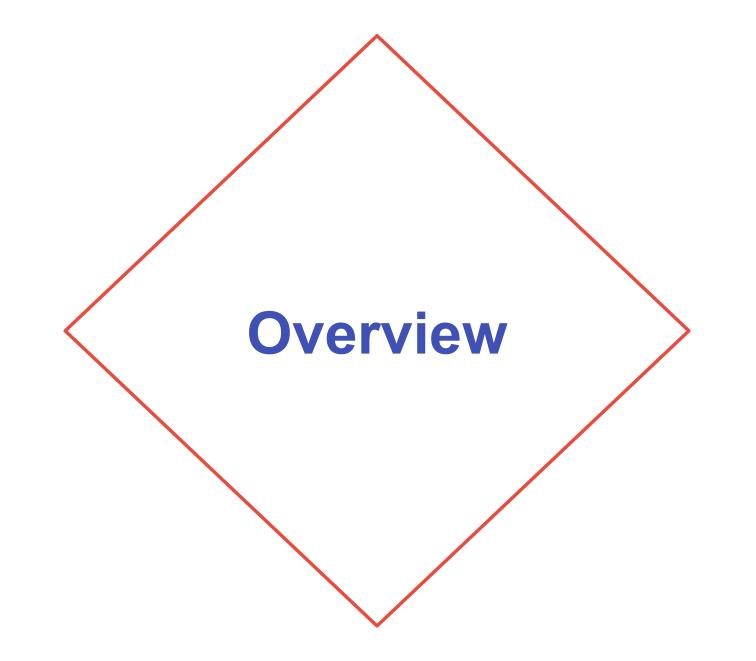
The Emerging Challenges in Primary Care: 2020 series of CME activities were supported through educational grants or donations from the following companies:

- 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.











Learning Objectives

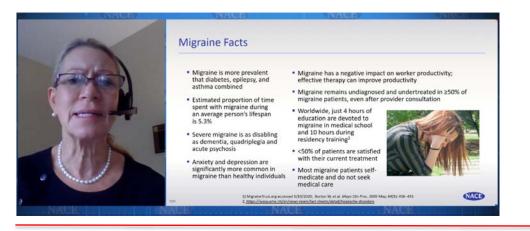
- Recognize migraines as a neurological condition requiring both prophylactic & on-demand treatment strategies
- Identify strategies to differentially diagnose episodic & chronic migraines
- Compare therapies for migraine prophylaxis, including CGRP antagonists & botulinum toxin
- Evaluate newly approved and emerging on-demand treatments for migraines
- Propose primary care-driven strategies to develop & support migraine management considering heterogeneous patient cases





Curriculum Overview

4 Accredited Live Virtual Symposium, with 1 Virtual Rebroadcast: June – July 2020



Enduring CME Symposium Webcast

Available at: <u>https://www.naceonline.com/courses/moving-ahead-in-</u> migraine-management-translating-the-latest-science-into-patientcare

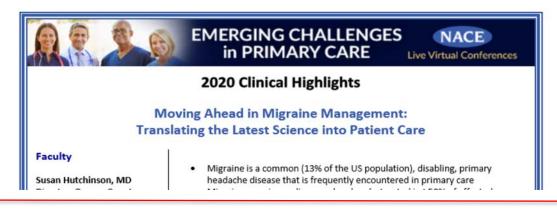
Moving Ahead in Migraine Management: Translating the Latest Science into Patient Care



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Clinical Highlights eMonograph

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



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: 1.5 hours

Credit(s): 1.5 AMA PRA Category 1 CreditsTM 1.5 IPCE Credits 1.5 AANP contact hours which includes 1.0 pharmacology hour

Hardware/Software Requirements: Any web browser

Speakers



Susan Hutchinson, MD Director, Orange County Migraine & Headache Center Diplomate-American Board of Family Medicine UCNS Headache Certified Irvine, CA



Alan M. Rapoport, MD Clinical Professor of Neurology The David Geffen School of Medicine at UCLA Los Angeles, CA Past President The International Headache Society (IHS) Founder and Director-Emeritus The New England Center for Headache Stamford, CT



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 Differences between Pre-Test, Post-Test, and PCA score averages		
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.			
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 $p \le .05$.	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=.28 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		



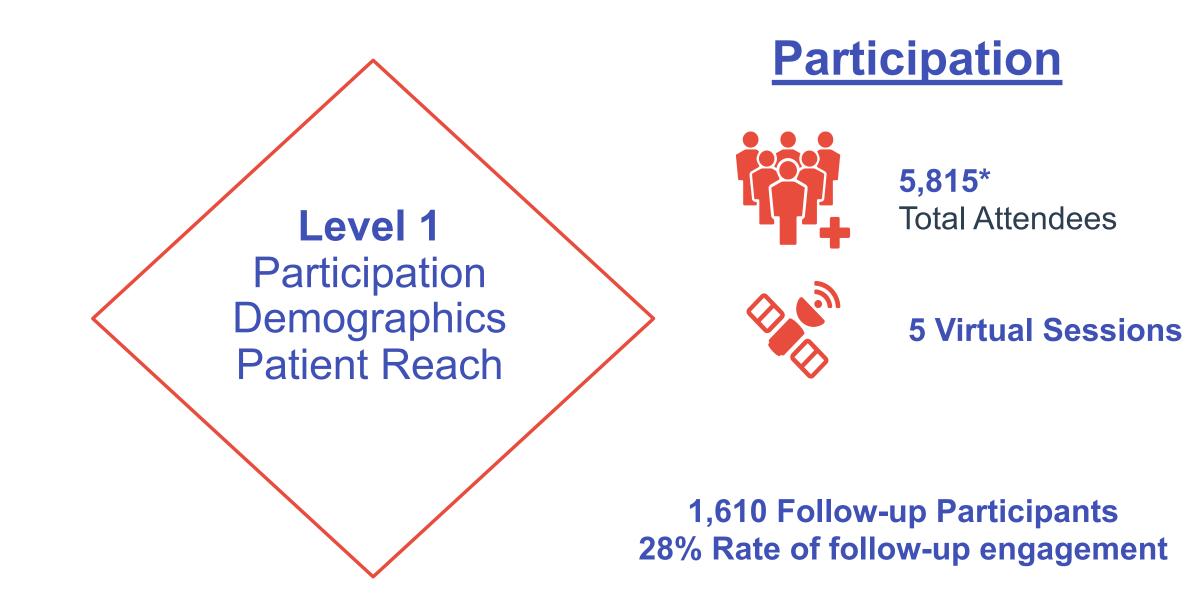


Participation

2020 Session	Date	Attendees
Emerging Challenges in Primary Care, Episode 5 Raleigh: North Carolina, South Carolina, Tennessee, Kentucky, Virginia, West Virginia, Georgia	6/6/20	1,256
Emerging Challenges in Primary Care, Episode 6 Atlanta: Georgia, Florida, Alabama, Tennessee, North Carolina, South Carolina, Mississippi	6/13/20	2,235
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		5,815





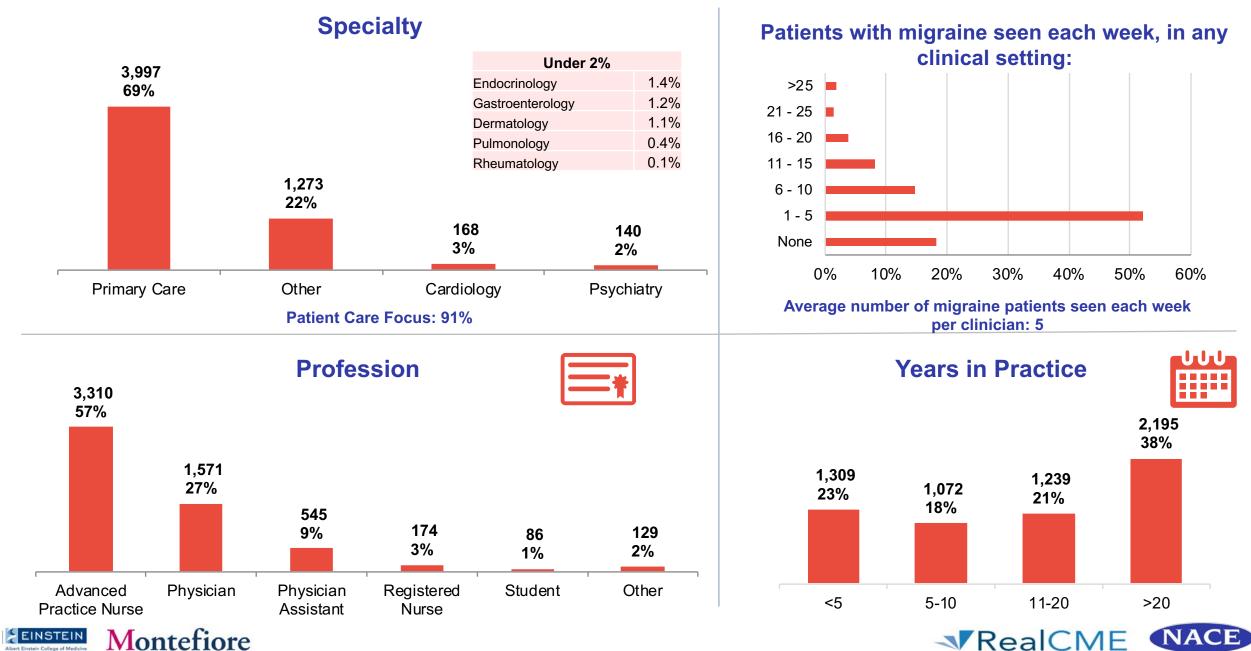


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*These numbers represent the total number of attendees, irrespective of assessment participation VReaICME



Level 1: Demographics and Patient Reach

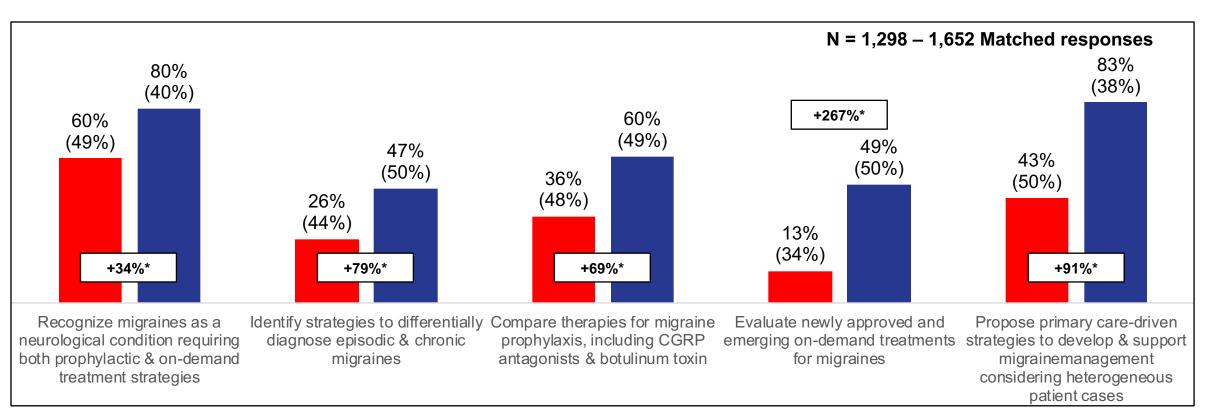








Learning Objective Analysis



- Across all five curriculum Learning Objectives, substantial and statistically significant improvements were measured from Pre- to Post-Test
- Very high gains (+267%) from very low Pre-Test scores (13%) were seen on evaluation of newly approved and emerging on-demand migraine treatments
 - Despite these improvements, low Post-Test scores were seen on this Objective, and on identification of strategies to differentially diagnose episodic and chronic migraines, and comparing therapies for migraine prophylaxis
- Higher Pre- and Post-Test scores were seen in recognizing migraines as a neurological condition requiring both prophylactic and on-demand treatments, and primary care-driven strategies to develop and support migraine management considering heterogeneous patient cases





Pre-Test

Post-Test

Learning Objective Analysis

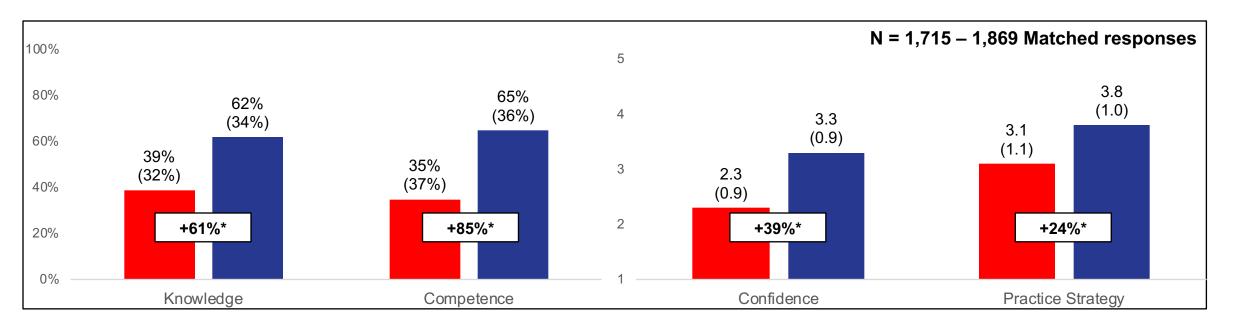
Cohort comparison by profession

Learning Objective		Advanced Practice Nurses				Physicians			
		Pre-Test	Post-Test	Change	N	Pre-Test	Post-Test	Change	
Recognize migraines as a neurological condition requiring both prophylactic & on-demand treatment strategies	559	60% (49%)	80% (40%)	+33%*	324	57% (49%)	81% (40%)	+40%*	
Identify strategies to differentially diagnose episodic & chronic migraines	654	25% (43%)	46% (50%)	+85%*	356	32% (47%)	53% (50%)	+68%*	
Compare therapies for migraine prophylaxis, including CGRP antagonists & botulinum toxin	626	38% (49%)	62% (49%)	+62%*	328	35% (48%)	59% (49%)	+70%*	
Evaluate newly approved and emerging on-demand treatments for migraines	648	11% (31%)	46% (50%)	+317%*	357	15% (36%)	56% (50%)	+277%*	
Propose primary care-driven strategies to develop & support migraine management considering heterogeneous patient cases	664	37% (48%)	81% (39%)	+122%*	376	55% (50%)	88% (33%)	+59%*	

- For both advanced practice nurses and physicians, significant gains were measured from Pre- to Post-Test on each of the five curriculum Learning Objectives
- On evaluating newly approved and emerging on-demand treatments for migraines, and primary care-driven strategies to develop and support migraine management considering heterogeneous patient cases, advanced practice nurses achieved stronger improvements from lower Pre-Test scores compared to physicians
- Scores on the other three Objectives were similar when comparing these groups



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 Competence, where gains were driven by an item on prescribing oral CGRP antagonist for a patient for whom NSAIDs and acetaminophen have been inadequate in providing relief from migraine pain
- Despite these gains, low Post-Test scores in Knowledge and Competence (62% to 65%) reflect opportunities for further education
- Low Pre- and Post-Test Confidence ratings indicate possible learner awareness of gaps in Knowledge and Competence
- Practice strategy ratings, on prescribing preventive drug therapy for patients with chronic or episodic migraine, increased to a moderate average value at Post-Test (3.8)

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* indicates significance, p < 0.05



Pre-Test

Post-Test

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	763	38% (31%)	62% (34%)	+62%*	429	39% (33%)	65% (35%)	+69%*
Competence	730	31% (36%)	63% (36%)	+100%*	410	44% (40%)	71% (35%)	+62%*
Confidence	718	2.2 (0.9)	3.2 (0.8)	+46%*	377	2.6 (0.9)	3.4 (0.8)	+32%*
Practice	721	3.0 (1.1)	3.8 (1.0)	+28%*	394	3.4 (1.0)	4.0 (0.9)	+18%*

- 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 all four domains, somewhat higher Pre- and Post-Test scores were measured for physicians, compared to advanced practice nurses
 - In Knowledge, physicians had stronger gains, while advanced practice nurses had stronger gains in Competence, Confidence, and practice strategy

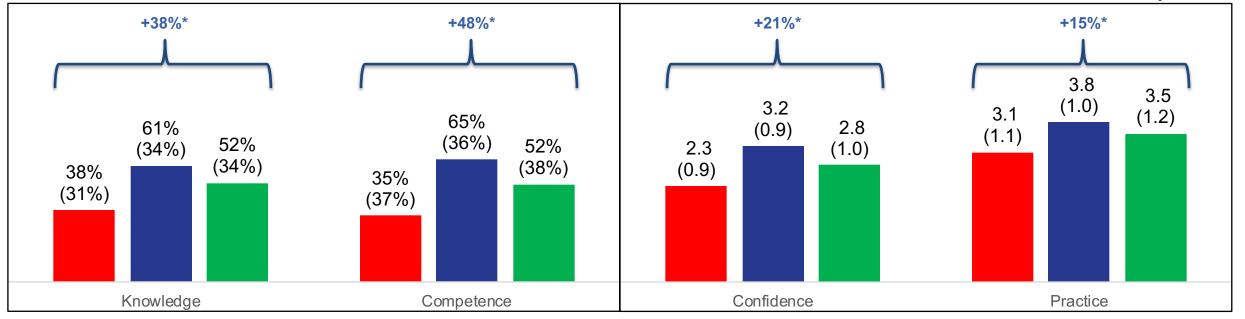




4-Week Retention Analysis

By Learning Domain

N = 698 – 757 Matched responses



- 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 domains, 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 all areas

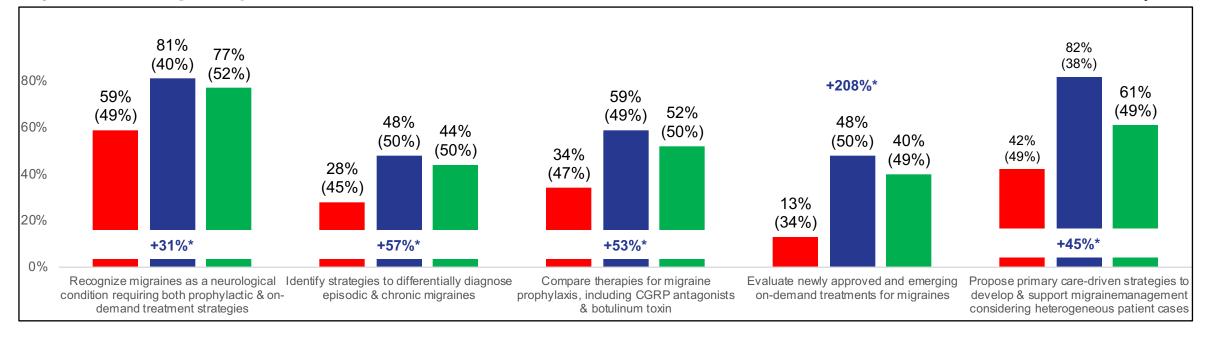




4-Week Retention Analysis

By Learning Objective

N = 514 – 677 Matched responses



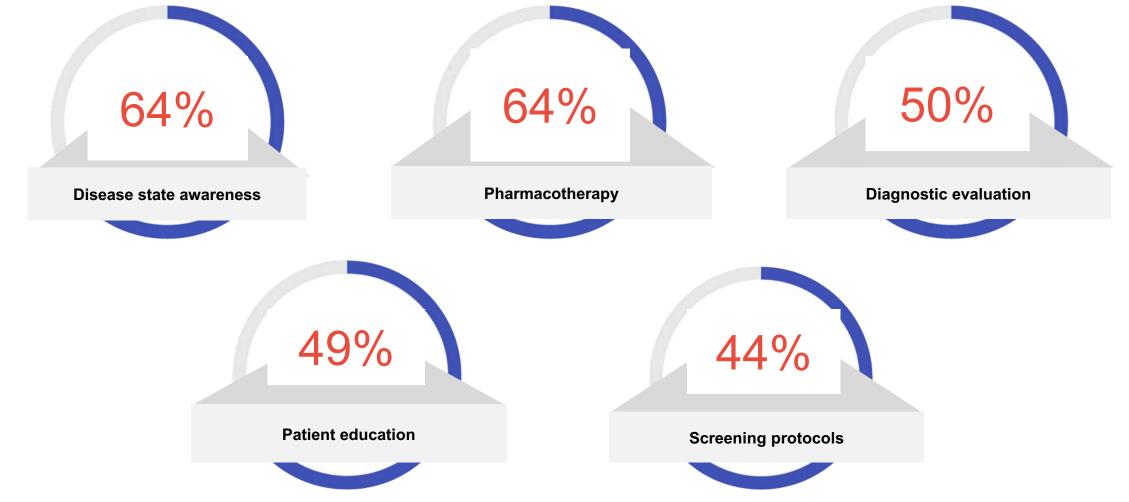
- When examining results by Learning Objective, substantial and significant net gains were achieved from Pre-Test to PCA measurements on each of the five Objectives
- Though some slippage in score was seen across all Objectives, strongest retention was seen in recognition of migraines as a neurological condition requiring both prophylactic and an-demand treatment strategies





(4-week Post Assessment)

Please select the specific areas of *skills, or practice behaviors*, you have improved regarding the treatment of patients with migraine since this CME activity. (Select all that apply.) N = 1,549

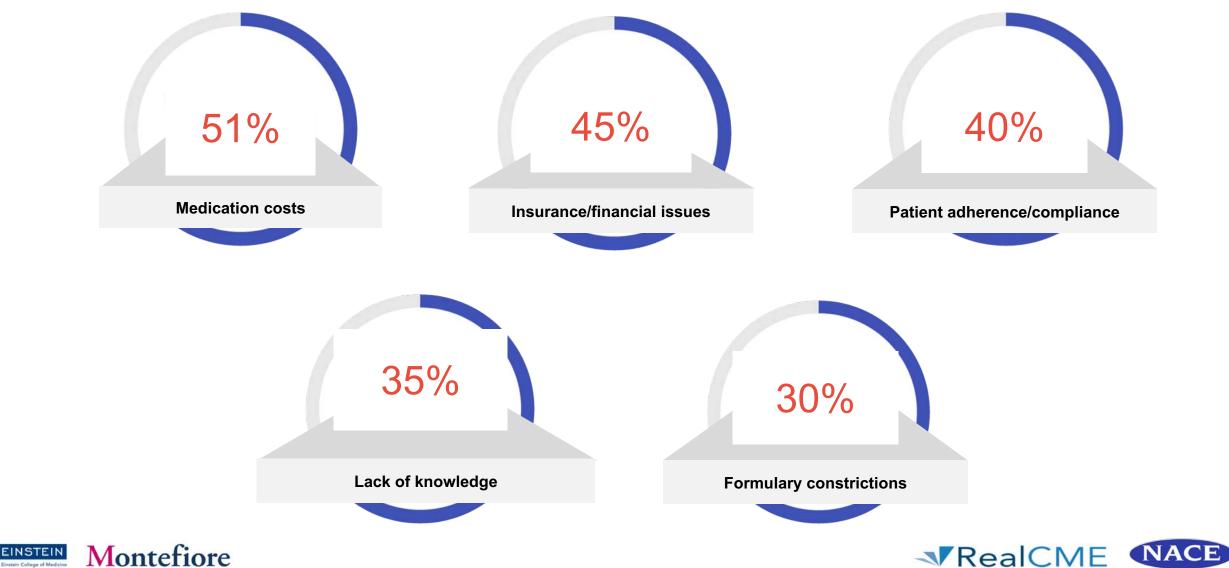






(4-week Post Assessment)

What specific *barriers* have you encountered that may have prevented you from successfully implementing strategies for patients with migraine since this CME activity? (Select all that apply.) N = 1,549



Identified Learning Gap, 1 of 3: *Side effects of CGRP inhibitors*

Despite improvements in score on a Knowledge item asking about side effects of eptinezumab, learners struggled at Post-Test to associate it with its side effects.

Which of the following CGRP inhibitors for migraine prevention has not been associated with injection site reactions, but may be associated with upper respiratory side effects?

- ✓ Eptinezumab36%Erenumab27%14%24%Galcanezumab12%12%
- At Post-Test, 60% of learners correctly answered: "Eptinezumab"

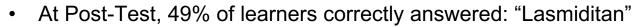


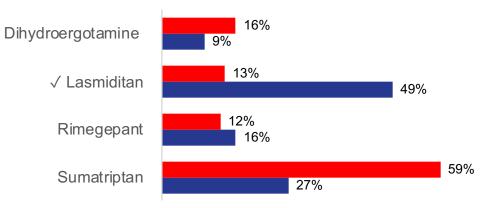


Identified Learning Gap, 2 of 3: *Mechanism of action of novel migraine therapies*

Though very strong gains were seen on an item about the mechanism of action of lasmiditan, low scores were measured at Post-Test.

Which of the following acute treatments for migraine acts through agonism of the 5-HT1F receptor only? Results:









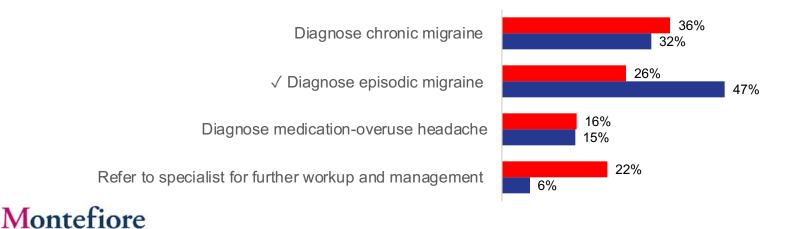
Identified Learning Gap, 3 of 3: Differentiating between chronic and episodic migraine in diagnosis

Despite improvements in score on a Competence item presenting a patient with frequent headaches for which ibuprofen poorly manage his pain, learners struggled at Post-Test to appropriately diagnose episodic migraine.

31 y/o woman presents complaining of frequent, disabling sinus headaches: Has had headaches for >5 years; in last month, had ~10 days with headache. Reports occasional nausea, vertigo, and neck pain when headaches occur. Uses decongestants, antihistamines, and ibuprofen prn, which help "a little". Physical and neurological exams are WNL; lab findings (CBC, ESR, CRP, metabolic panel, thyroid panel) are WNL. What might be an appropriate action at this time?

Results:

• At Post-Test, 47% of learners correctly answered: "Diagnose episodic migraine"





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 all domains except Knowledge
- Statistically significant net gains were also seen in each domain from Pre-Test to a follow-up assessment, indicating strong retention of in-curriculum improvements
- Significant improvements ranging from 34% to 267% were measured across all Learning Objectives, with Post-Test scores between 47% and 83%
 - Highest scores were seen on recognition of migraines as a neurological condition requiring both prophylactic and on-demand treatment strategies, and primary care-driven strategies to develop and support migraine management considering heterogeneous patient cases
- The analysis of the Knowledge and Competence domains identified three opportunities for further education on the management of patients with migraine, specifically related to:
 - Side effects of CGRP inhibitors
 - Mechanism of action of novel migraine therapies
 - Differentiating between chronic and episodic migraine in diagnosis





Slides 27 – 30: Pre-Test to Post-Test matched item responses

Appendix

Slides 31 – 34: 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

Approximately what proportion of migraines are preceded by the focal neurological symptoms of aura, coming from the occipital cortex N = 1,298 Matched responses in the brain?

19%

17%

10%

+34%

60%

80%

Which of the following CGRP inhibitors for migraine prevention has not been associated with injection site reactions, but may be associated with upper respiratory side effects?

10%

√ 30%

50%

70%

5%

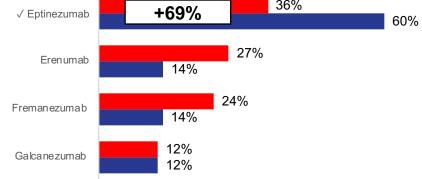
5%

6%

36% +69% ✓ Eptinezumab 60% 27% Erenumab 14% 24% Fremanezumab 14% 12% Galcanezumab 12%

N = 1,513 Matched responses

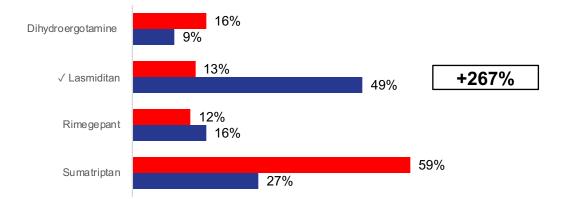






Knowledge Items

Which of the following acute treatments for migraine acts through agonism of the 5-HT1F receptor only?



N = 1,581 Matched responses





Competence Items

Montefiore

31 y/o woman presents complaining of frequent, disabling sinus headaches: Has had headaches for >5 years; in last month, had ~10 days with headache. Reports occasional nausea, vertigo, and neck pain when headaches occur. Uses decongestants, antihistamines, and ibuprofen prn, which help "a little".Physical and neurological exams are WNL; lab findings (CBC, ESR, CRP, metabolic panel,

Diagnose chronic migraine

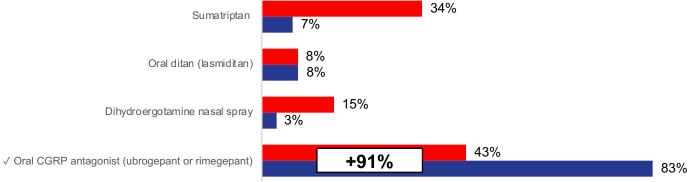
✓ Diagnose episodic migraine

Diagnose medication-overuse headache

Refer to specialist for further workup and management

thyroid panel) are WNL. What might be an appropriate action at this time?

57 y/o man presents with history of 3-5 migraine attacks per month; works as delivery driver: Has tried NSAID and acetaminophen, with little benefit; asks if he can take something at the time of a headache to reduce pain. Med Hx: Hypertension, dyslipidemia, coronary artery disease, NSTEMI 3 years ago. Current Meds: Lisinopril, metoprolol, atorvastatin, aspirin. Which of the following might be most appropriate for acute therapy in this patient?



N = 1,591 Matched responses

N = 1,652 Matched responses



6%

+79%

16%

15%

36%

47%

32%

26%

22%

$d \sim 10$ N = 1.591 Matched respo

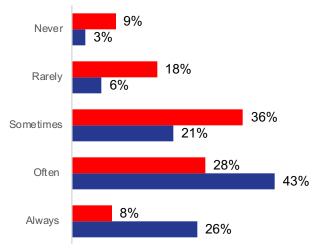
Confidence and Practice Strategy Items



Not at all confident20%Slightly confident37%Moderately confident16%Pretty much confident7%Very confident2%%8%

How confident are you in your ability to diagnose and manage migraine in your patients?

How often do you consider prescribing preventive drug therapy for a patient with chronic or episodic migraine?



N = 1,715 Matched responses

N = 1,730 Matched responses



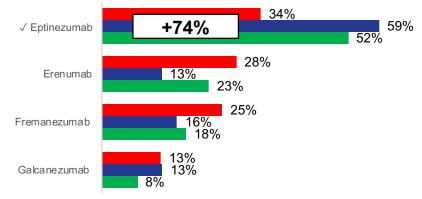


Knowledge Items

Post Curriculum Assessment (PCA)

Approximately what proportion of migraines are preceded by the focal neurological symptoms of aura, coming from the occipital cortex N = 514 Matched responses in the brain?

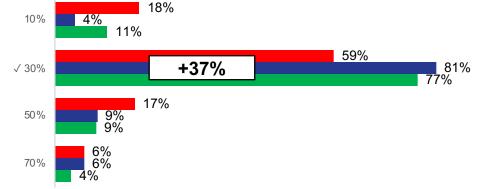
Which of the following CGRP inhibitors for migraine prevention has not been associated with injection site reactions, but may be associated with upper respiratory side effects?



N = 640 Matched responses



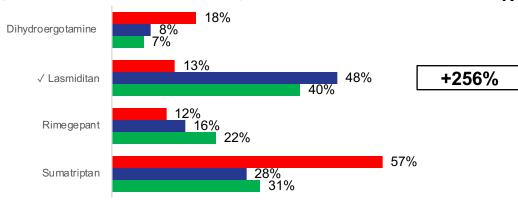






Knowledge Items

Post Curriculum Assessment (PCA)



Which of the following acute treatments for migraine acts through agonism of the 5-HT1F receptor only?





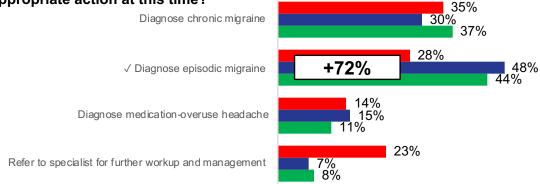


Competence Items

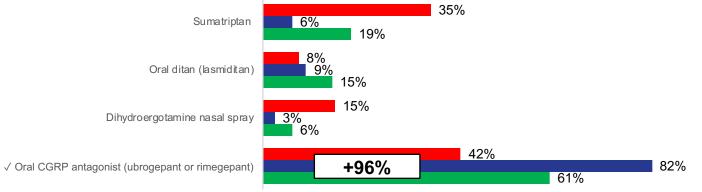
Post Curriculum Assessment (PCA)

31 y/o woman presents complaining of frequent, disabling sinus headaches: Has had headaches for >5 years; in last month, had ~10 days with headache. Reports occasional nausea, vertigo, and neck pain when headaches occur. Uses decongestants, antihistamines, and ibuprofen prn, which help "a little".Physical and neurological exams are WNL; lab findings (CBC, ESR, CRP, metabolic panel,

thyroid panel) are WNL. What might be an appropriate action at this time?



57 y/o man presents with history of 3-5 migraine attacks per month; works as delivery driver: Has tried NSAID and acetaminophen, with little benefit; asks if he can take something at the time of a headache to reduce pain. Med Hx: Hypertension, dyslipidemia, coronary artery disease, NSTEMI 3 years ago. Current Meds: Lisinopril, metoprolol, atorvastatin, aspirin. Which of the following might be most appropriate for acute therapy in this patient?



N = 677 Matched responses

Pre-Test Post-Test PCA

N = 657 Matched responses





Confidence and Practice Strategy Items

Post Curriculum Assessment (PCA)

How confident are you in your ability to diagnose and manage migraine in your patients?

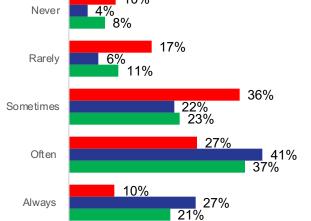
How often do you consider prescribing preventive drug therapy for a patient with chronic or episodic migraine?

10% Never 4% 8% 17% Rarely 6% 11% 36% 22% 23% Sometimes 27% 41% 37% Often 10% 27% Always 21%



N = 713 Matched responses





22%

17%

15%

37%

45%

41%

31% 32%

26%

2%

8%

7%

10%

1%

5%

Not at all confident

Slightly confident

Moderately confident

Pretty much confident

Very confident



