Emerging Challenges in Primary Care
18th Annual Conference Series - 2019

EC

Final Live Outcomes Report

Insulin Therapy and Glycemic Variability:
Strategies for Achieving Diabetes Goals While Minimizing Hypoglycemia

Novo Nordisk • MED-DIA-25664

October 2, 2019

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Emerging Challenges in Primary Care
18th Annual Conference Series - 2019

Insulin Therapy and Glycemic Variability:
Strategies for Achieving Diabetes Goals While Minimizing Hypoglycemia

Participation

1,745 Total Attendees
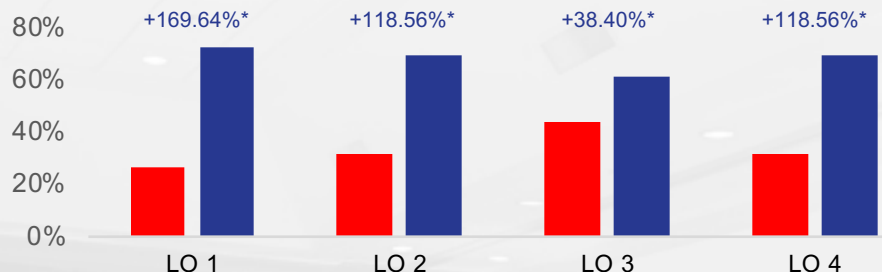
4 Live Activities

450 On Site

1,295 Simulcast & Virtual Symposium

1745 Certificates issued to date

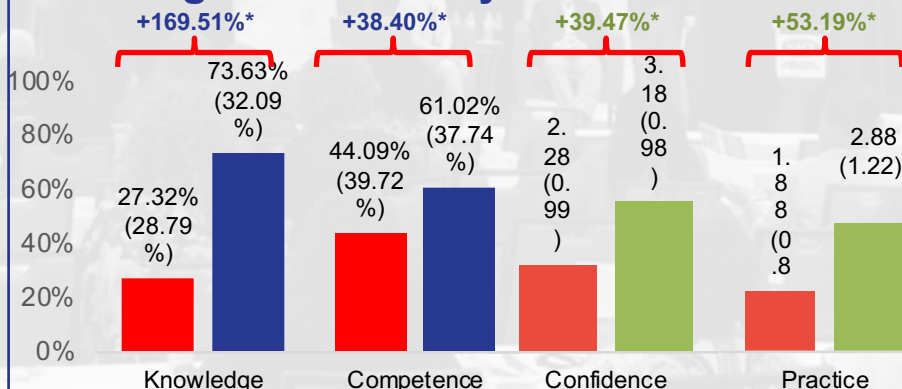This education has the potential to impact 967,288 patients with T2D on an annual basis.

16,742–20,462 per week

2019 Symposium	Date	Attendees
Miami, FL	4/27/19	188
Birmingham, AL	5/4/19	143
Birmingham, AL Simulcast	5/4/19	526
St. Louis, MO	5/11/19	119
Virtual Symposium	6/22/19	769
Total		**1,745**

Learning Gains Across Objectives

+169.64%* +118.56%* +38.40%* +118.56%*

LO 1   LO 2   LO 3   LO 4

- ❖ **LO 1:** Recognize the risk for, and impact of hypoglycemia in patients with diabetes
- ❖ **LO 2:** Describe strategies for reducing the occurrence of glycemic variability
- ❖ **LO 3:** Understand effective SMBG vs. newer CGM in managing diabetes and reducing risk of dysglycemia/hypoglycemia
- ❖ **LO 4:** Differentiate between available insulin preparations and their effects on glycemic variability and hypoglycemic risk

Learning Domain Analysis

+169.51%*   +38.40%*   +39.47%*   +53.19%*

- Knowledge: 27.32% (28.79%) → 73.63% (32.09%)
- Competence: 44.09% (39.72%) → 61.02% (37.74%)
- Confidence: 2.28 (0.99) → 3.18 (0.98)
- Practice: 1.88 (0.8) → 2.88 (1.22)

- ❖ Substantial and significant gains (38% to 170%) were achieved in all learning domains
- ❖ A very low Pre-Test average (27%) in Knowledge was due to uniformly low Pre-Test scores on all three items (15% to 35%), related to T2D pathology and specific insulin formulations
- ❖ Low scores on both Competence items, related to modifying insulin therapy to address episodes of hypoglycemia, drove low averages at Pre- and Post-Test
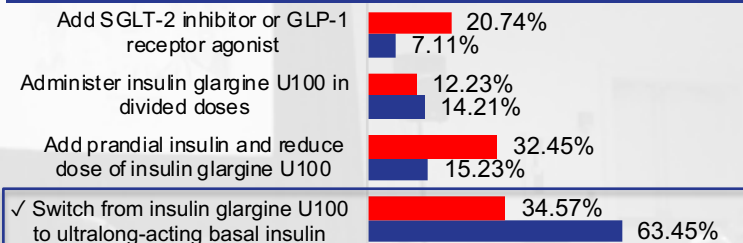
Persistent Learning Gaps/Needs

Appropriate context for use of continuous glucose monitoring
Despite improvements in score on a Competence item presenting the case of a patient with a 9-year history of type 2 diabetes and an A1C of 7.6%, learners struggled at Post-Test to identify continuous glucose monitoring as the most appropriate next step.
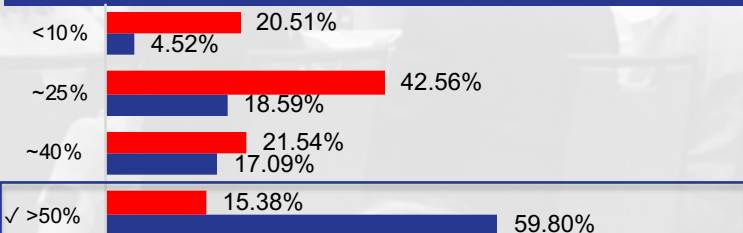
Adjustments to therapy for type 2 diabetic patients with uncontrolled episodes of hypoglycemia
On a Competence item presenting the case of a patient with a 10-year history of type 2 diabetes, currently on both metformin and insulin glargine but with an A1C of 7.6%, learners struggled to correctly identify the most appropriate adjustment in therapy.

- Add SGLT-2 inhibitor or GLP-1 receptor agonist — 20.74% / 7.11%
- Administer insulin glargine U100 in divided doses — 12.23% / 14.21%
- Add prandial insulin and reduce dose of insulin glargine U100 — 32.45% / 15.23%
- ✓ Switch from insulin glargine U100 to ultralong-acting basal insulin — 34.57% / 63.45%

Prevalence of asymptomatic episodes of hypoglycemia in type 2 diabetic patients
Despite improvements in score from a very low (15%) average score at Pre-Test, Post-Test scores remained low on a Knowledge item asking the proportion of T2D patients with asymptomatic hypoglycemic episodes.

- <10% — 20.51% / 4.52%
- ~25% — 42.56% / 18.59%
- ~40% — 21.54% / 17.09%
- ✓ >50% — 15.38% / 59.80%

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Curriculum Patient Impact

In the evaluation, learners (N = 576) were asked to report how many patients with type 2 diabetes they see in any clinical setting per week by selecting a range. The resulting distribution of learner responses was then extrapolated to reflect the total number of learners who have attended the onsite and online meetings.

The findings reveal that this education has the potential to impact

967,288

patients with type 2 diabetes on an annual basis.

16,742–20,462 patients on a weekly basis

16,742–20,462

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Commercial Support

❖ Amgen, Inc.

❖ AstraZeneca Pharmaceuticals LP

❖ Amarin

❖ Avanir Pharmaceuticals

❖ Ferring Pharmaceuticals

❖ Gilead Sciences, Inc.

❖ Grifols

❖ Novo Nordisk

❖ Shire

Overview

Learning Objectives

❖ Recognize the risk for, and impact of hypoglycemia in patients with diabetes

❖ Describe strategies for reducing the occurrence of glycemic variability

❖ Understand effective SMBG vs. newer CGM in managing diabetes and reducing risk of dysglycemia/hypoglycemia

❖ Differentiate between available insulin preparations and their effects on glycemic variability and hypoglycemic risk

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Curriculum Overview

3 Accredited Live Regional Symposia with National Simulcast from One Location: August 27, 2019 – May 11, 2019

One Accredited Live Virtual Symposiums: June 22, 2019

Enduring CME Symposium Webcast

Speaker

Launch Date: July 30, 2019

End Date: July 29, 2020

Available at: https://www.naceonline.com/courses/insulin-therapy-and-glycemic-variability

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East Hills, NY

Insulin Therapy and Glycemic Variability: Strategies for Achieving Diabetes Goals While Minimizing Hypoglycemia

Clinical Highlights eMonograph

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

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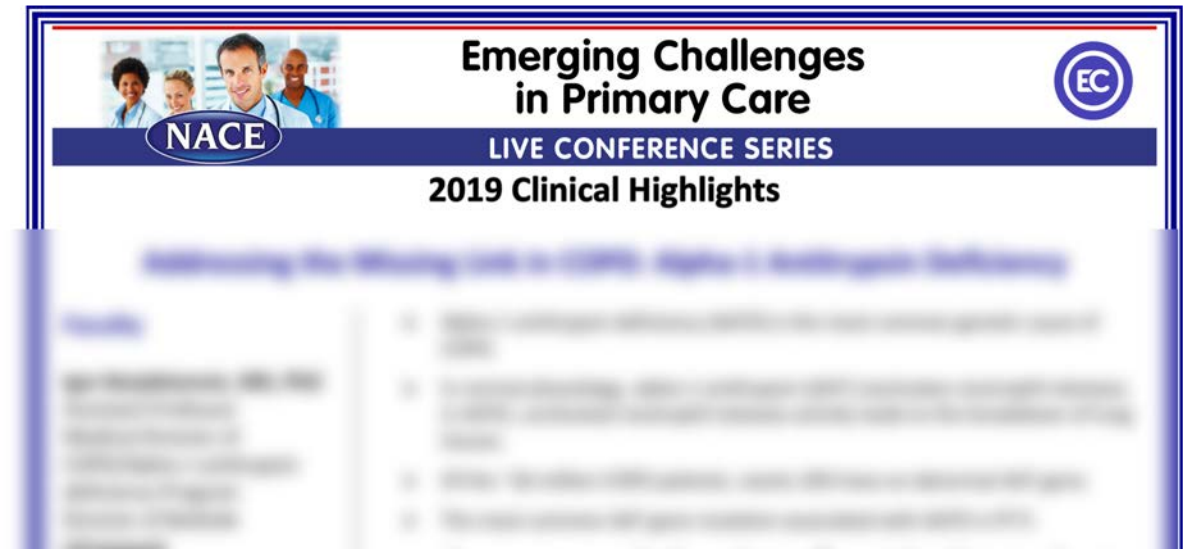
Outcomes Methodology

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.

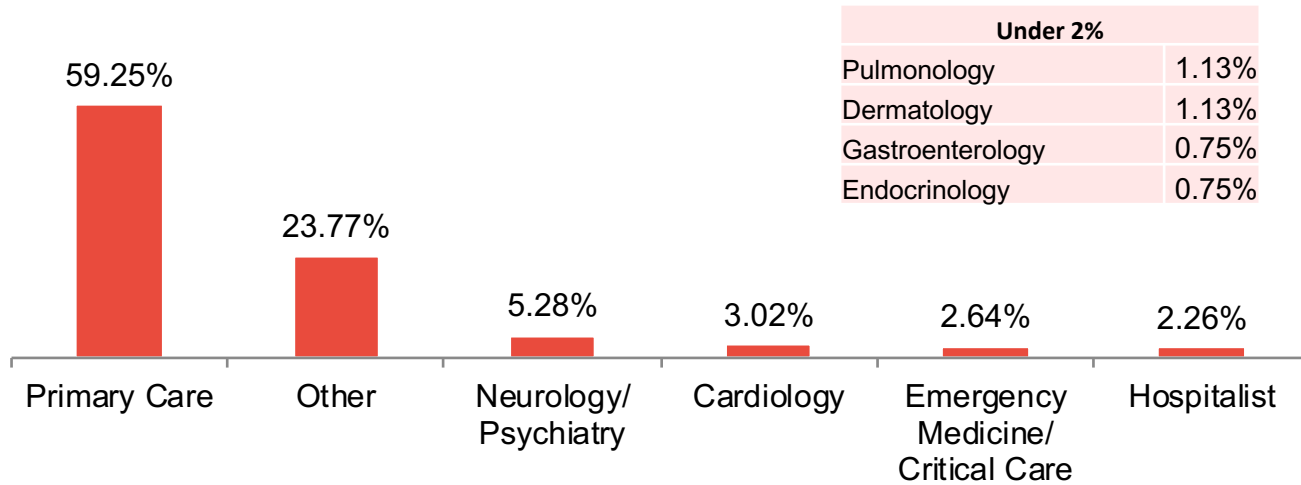| Outcomes Metric	Definition	Application
Percentage change	This is how the score changes resulting from the education are measured. The change is analyzed as a relative percentage difference by taking into account the magnitude of the Pre-Test average.	Differences between Pre-Test, Post-Test, and PCA 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

Level 1
Participation
Demographics
Patient Reach

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

Participation

2019 Meeting/Simulcast	Date	Attendees
Miami, FL	4/27/19	188
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St. Louis, MO	5/11/19	119
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Level 1: Demographics and Patient Reach

Specialty

Under 2%	
Pulmonology	1.13%
Dermatology	1.13%
Gastroenterology	0.75%
Endocrinology	0.75%

- Primary Care: 59.25%
- Other: 23.77%
- Neurology/Psychiatry: 5.28%
- Cardiology: 3.02%
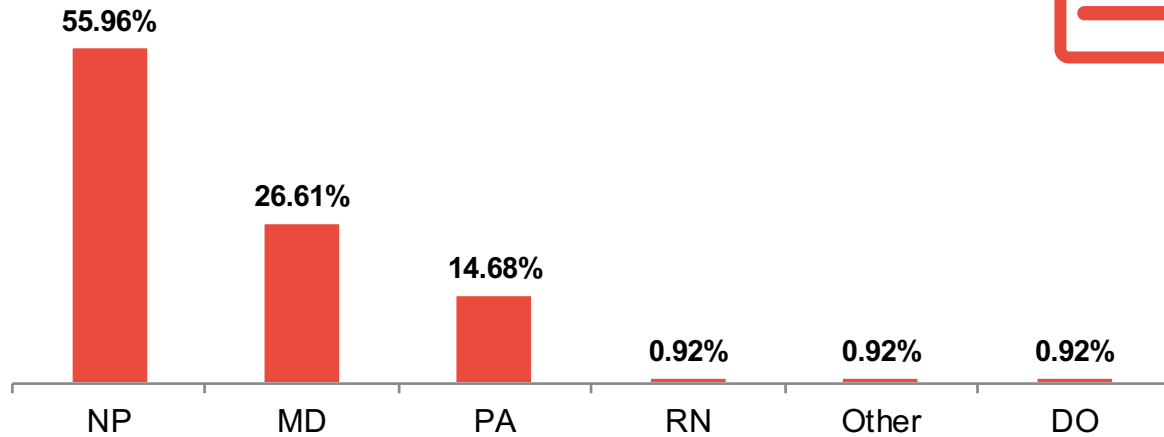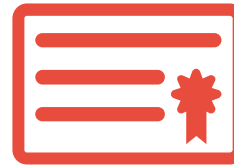- Emergency Medicine/Critical Care: 2.64%
- Hospitalist: 2.26%

Patient Care Focus: 92%

Patients with type 2 diabetes seen each week, in any clinical setting:
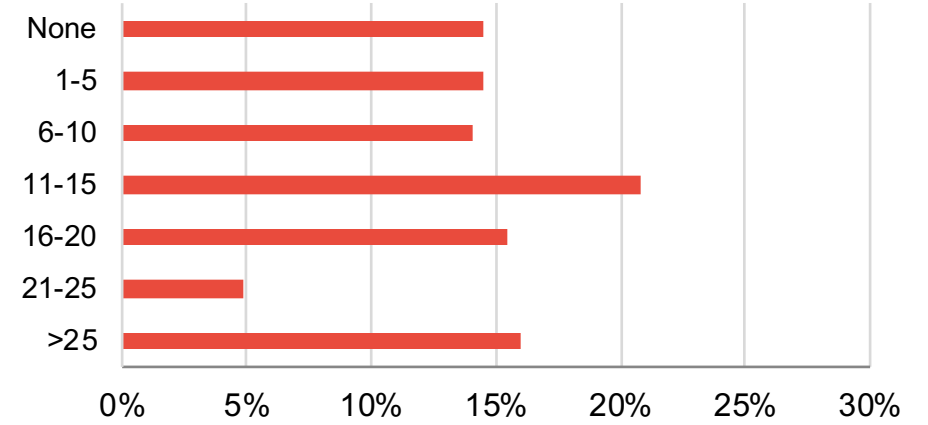
Average number of patients with type 2 diabetes seen each week per clinician: 13
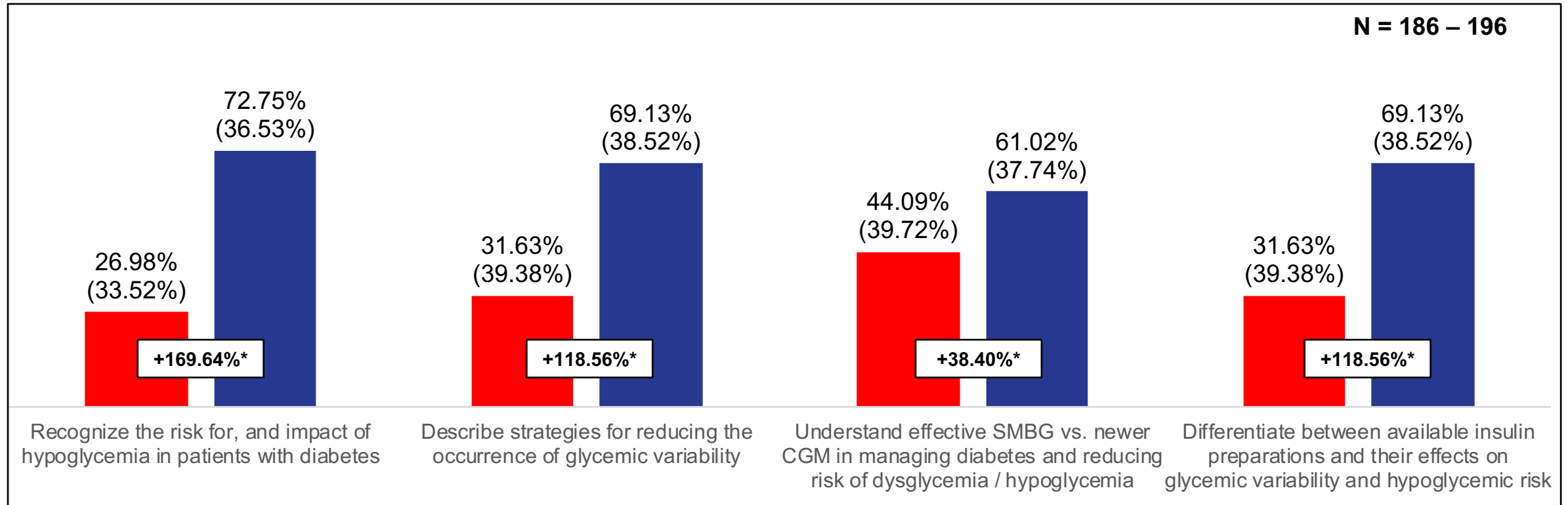
Profession

- NP: 55.96%
- MD: 26.61%
- PA: 14.68%
- RN: 0.92%
- Other: 0.92%
- DO: 0.92%

Years in Practice

- < 5: 28.36%
- 5–10: 20.36%
- 11–20: 20.73%
- > 20: 30.55%

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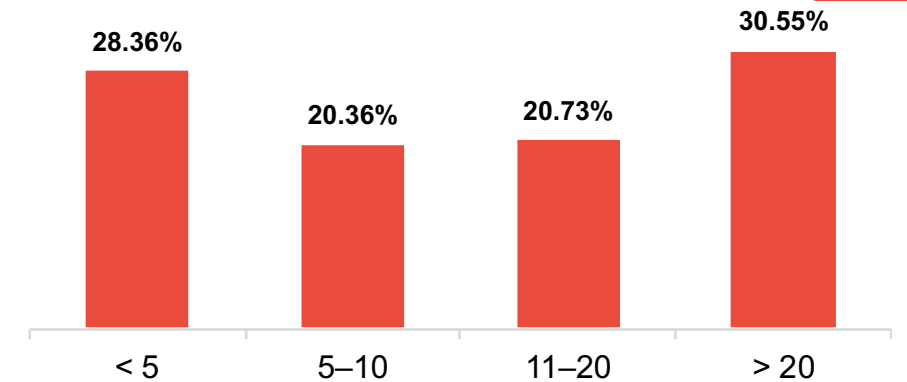
Level 2-5:
Outcomes Metrics

Learning Objective Analysis

N = 186 – 196

Recognize the risk for, and impact of hypoglycemia in patients with diabetes
- 26.98% (33.52%) Pre-Test
- 72.75% (36.53%) Post-Test
- +169.64%*

Describe strategies for reducing the occurrence of glycemic variability
- 31.63% (39.38%) Pre-Test
- 69.13% (38.52%) Post-Test
- +118.56%*

Understand effective SMBG vs. newer CGM in managing diabetes and reducing risk of dysglycemia / hypoglycemia
- 44.09% (39.72%) Pre-Test
- 61.02% (37.74%) Post-Test
- +38.40%*

Differentiate between available insulin preparations and their effects on glycemic variability and hypoglycemic risk
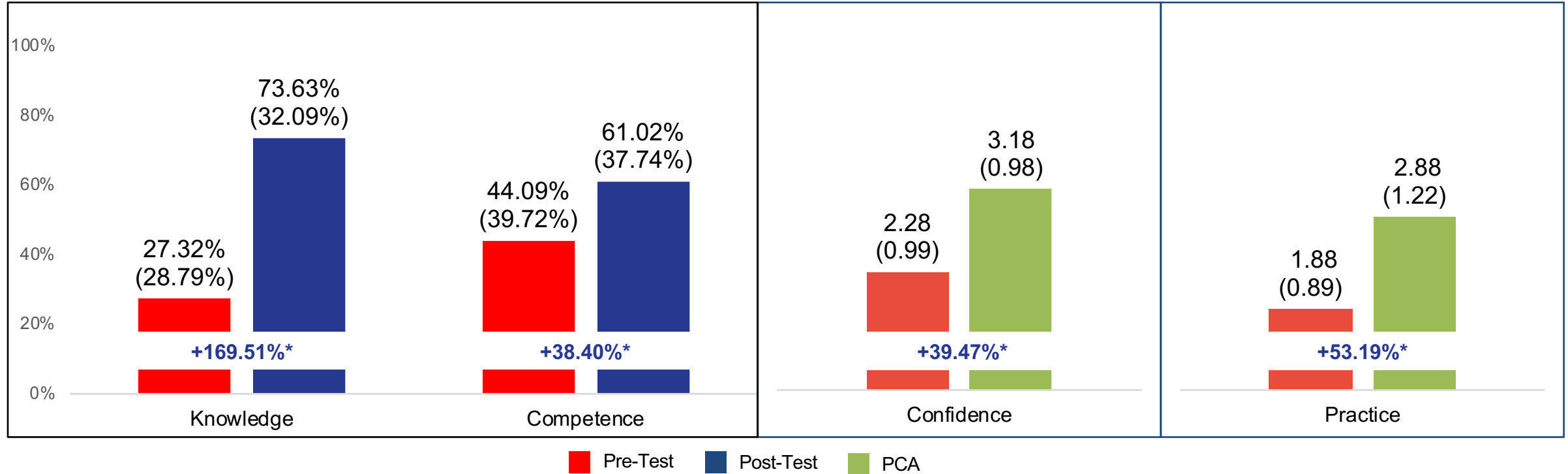- 31.63% (39.38%) Pre-Test
- 69.13% (38.52%) Post-Test
- +118.56%*

- ❖ Substantial and significant gains (38% to 169%) were achieved on all curriculum Learning Objectives
- ❖ Low Post-Test scores (61% to 73%) following very low Pre-Test scores (27% to 44%) were measured across all Learning Objectives
    - ❖ These represent uniformly low and moderate (57% to 75%) Post-Test scores on all curriculum scored questions

Note: data are matched.
* indicates significance, $p < 0.05$.

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Learning Domain Analysis

(*N* = 186—467)

Legend: Pre-Test (red), Post-Test (dark blue), PCA (green)

Knowledge: Pre-Test 27.32% (28.79%), Post-Test 73.63% (32.09%), +169.51%*

Competence: Pre-Test 44.09% (39.72%), Post-Test 61.02% (37.74%), +38.40%*

Confidence: Pre-Test 2.28 (0.99), PCA 3.18 (0.98), +39.47%*

Practice: Pre-Test 1.88 (0.89), PCA 2.88 (1.22), +53.19%*

- ❖ Substantial and significant gains (38% to 170%) were achieved in all learning domains

- ❖ A very low Pre-Test average (27%) in Knowledge was due to uniformly low Pre-Test scores on all three items (15% to 35%), related to T2D pathology and specific insulin formulations

- ❖ Low scores on both Competence items, related to modifying insulin therapy to address episodes of hypoglycemia, drove low averages at Pre- and Post-Test

Note: Knowledge and Competence data are matched; Confidence and practice strategy are not, as these domains are collected at follow-up.
* indicates significance, $p < 0.05$.

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Learning Objectives by Professional Cohort

Learning Domain	Nurse Practitioners				Physicians			
	N	Pre-Test	Post-Test	% Change	N	Pre-Test	Post-Test	% Change
Recognize the risk for, and impact of hypoglycemia in patients with diabetes	119	31.09% (37.23%)	69.33% (37.30%)	+123.00%*	89	24.72% (31.02%)	72.47% (35.17%)	+193.16%*
Describe strategies for reducing the occurrence of glycemic variability	126	28.17% (38.06%)	69.44% (37.78%)	+146.50%*	92	40.22% (39.18%)	66.85% (39.89%)	+66.21%*
Understand effective SMBG vs. newer CGM in managing diabetes and reducing risk of dysglycemia / hypoglycemia	120	37.50% (37.22%)	56.25% (36.26%)	+50.00%*	90	51.67% (37.60%)	61.11% (37.84%)	+18.27%*
Differentiate between available insulin preparations and their effects on glycemic variability and hypoglycemic risk	126	28.17% (38.06%)	69.44% (37.78%)	+146.50%*	92	40.22% (39.18%)	66.85% (39.89%)	+66.21%*

- ❖ Substantial and significant improvements were measured across all curriculum Learning Objectives, for both nurse practitioners and physicians

- ❖ Nurse practitioners achieved similar scores compared to physicians at Post-Test, from lower Pre-Test scores, on three of the four curriculum Learning Objectives

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Learning Domains by Professional Cohort

Learning Domain	Nurse Practitioners				Physicians			
	N	Pre-Test	Post-Test	% Change	N	Pre-Test	Post-Test	% Change
Knowledge	122	27.73% (29.77%)	71.99% (33.08%)	+159.61%*	93	28.14% (29.23%)	73.30% (31.03%)	+160.48%*
Competence	120	37.50% (37.22%)	56.25% (36.26%)	+50.00%*	90	51.67% (37.60%)	61.11% (37.84%)	+18.27%*

- ❖ Substantial and significant improvements were measured in both Knowledge and Competence by nurse practitioners and physicians
- ❖ Both nurse practitioners and physicians demonstrated low (56% and 61%) at Post-Test on Competence items asking learners to modify therapy for T2D patients having uncontrolled hypoglycemic episodes in spite of their current treatment

4-Week Retention Analysis
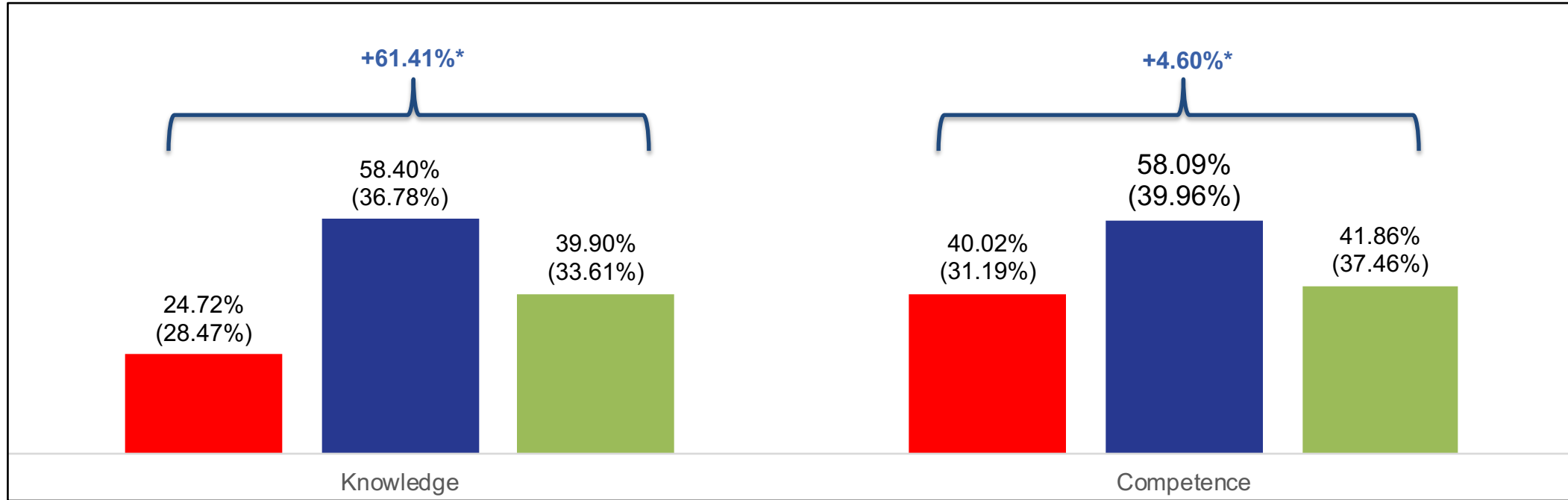
At follow-up:

❖ In addition to collecting Confidence and Practice data for the curriculum, the Post Curriculum Assessment (PCA) included questions from the Knowledge and Competence domains

❖ Statistically significant net gains were measured from Pre-Test to the Post Curriculum Assessment (PCA) in both Knowledge and Competence

❖ In both Knowledge and Competence, some decrease in score was measured between Post-Test and PCA

Please select the specific areas of skills, or practice behaviors, you have improved regarding the recognition and management of patients with diabetes since this CME activity. (Select all that apply.)
N=467

59%	58%	59%	48%
Patient education	Disease state awareness	Pharmacotherapy	Diagnostic evaluation

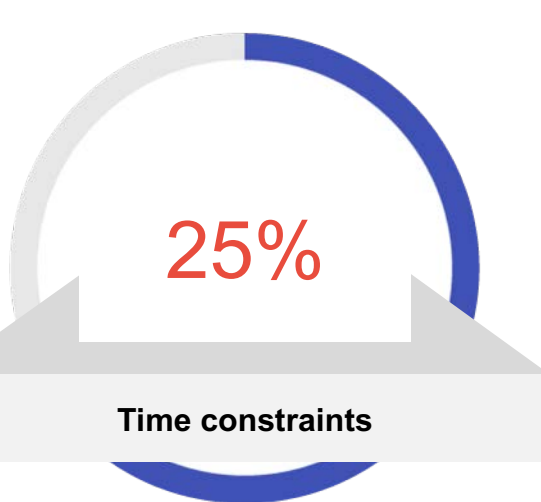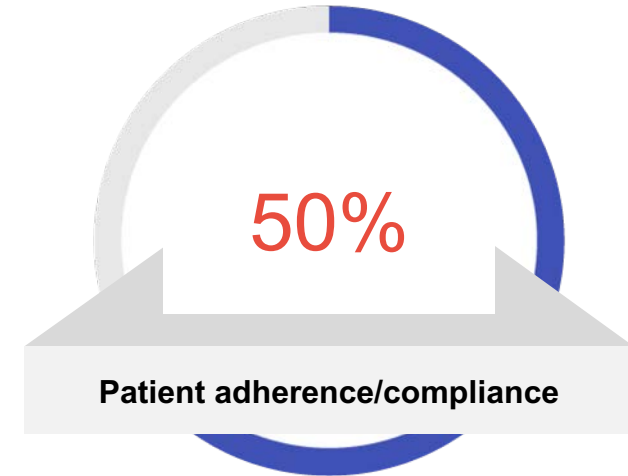| 46%	40%	40%	40%
Screening protocols	Timely referral	Non-pharmacotherapy	Patient education regarding treatment options

What specific barriers have you encountered that may have prevented you from successfully implementing strategies for patients with diabetes since this CME activity? (Select all that apply.) N=467

53%
Medication costs

47%
Insurance/financial issues

50%
Patient adherence/compliance

25%
Time constraints

30%
Lack of knowledge

29%
Formulary constrictions

22%
System constraints
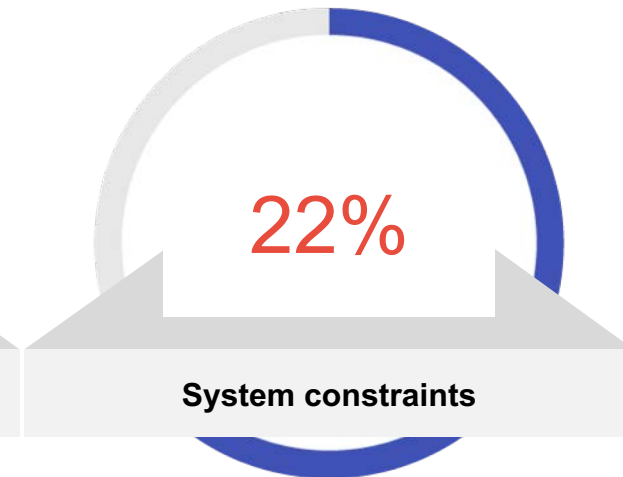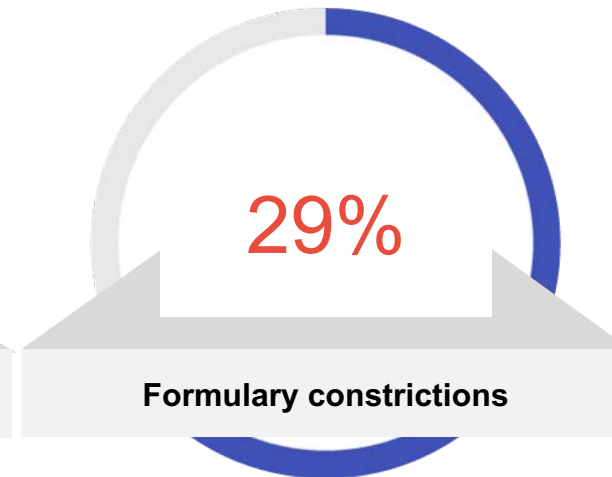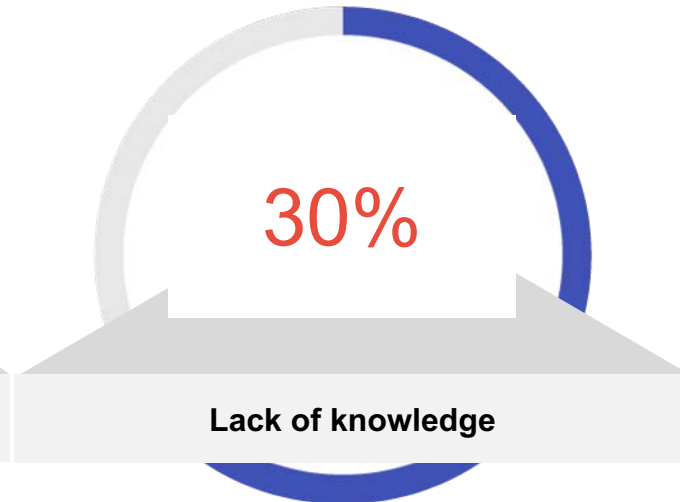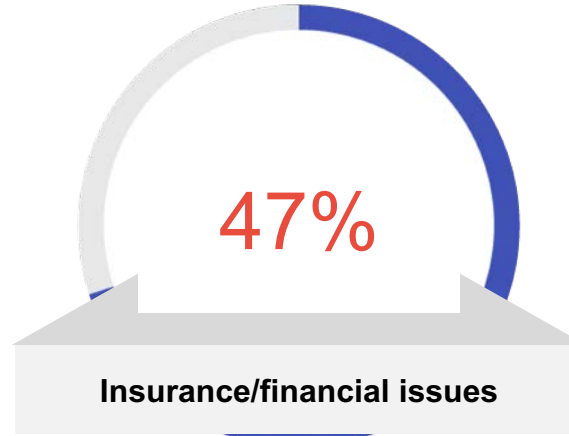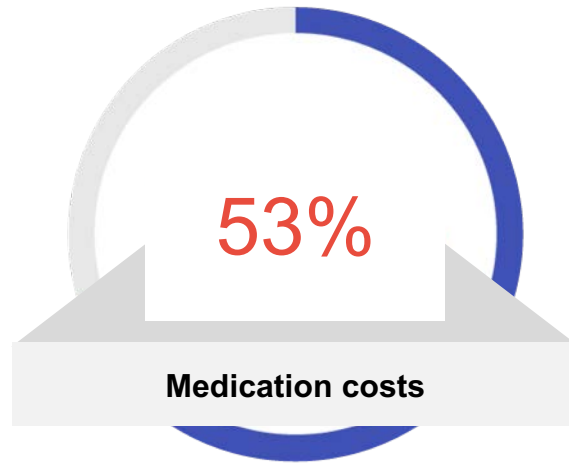
Identified Learning Gap, 1 of 3:
Appropriate context for use of continuous glucose monitoring

Despite improvements in score on a Competence item presenting the case of a patient with a 9-year history of type 2 diabetes and an A1C of 7.6%, learners struggled at Post-Test to identify continuous glucose monitoring as the most appropriate next step.

54 y/o man with 9-year history of T2D presents for checkup. His A1C is 7.6%. SMBG: AM 150-200 mg/dL; HS 120-150 mg/DL. Medications: metformin 1000 mg bid, canagliflozin 300 mg qd, and insulin glargine U100 48 units HS. Attempts to increase basal insulin dose in the past have led to daytime hypoglycemia. What might you do now?

Results:

- At Post-Test, only 57% of learners correctly answered: "Ask patient to use continuous glucose monitor or SMBG 4 times a day, for 4 days and adjust meds based on findings"

Add GLP-1 receptor agonist — 23.12% / 12.44%

Switch from basal insulin to premixed insulin — 3.76% / 1.44%

Switch from glargine u100 to glargine u300 and decrease dose by 10% — 20.43% / 29.19%

✓ Ask patient to use continuous glucose monitor or SMBG 4 times a day, for 4 days and adjust meds based on findings — 52.69% / 56.94%
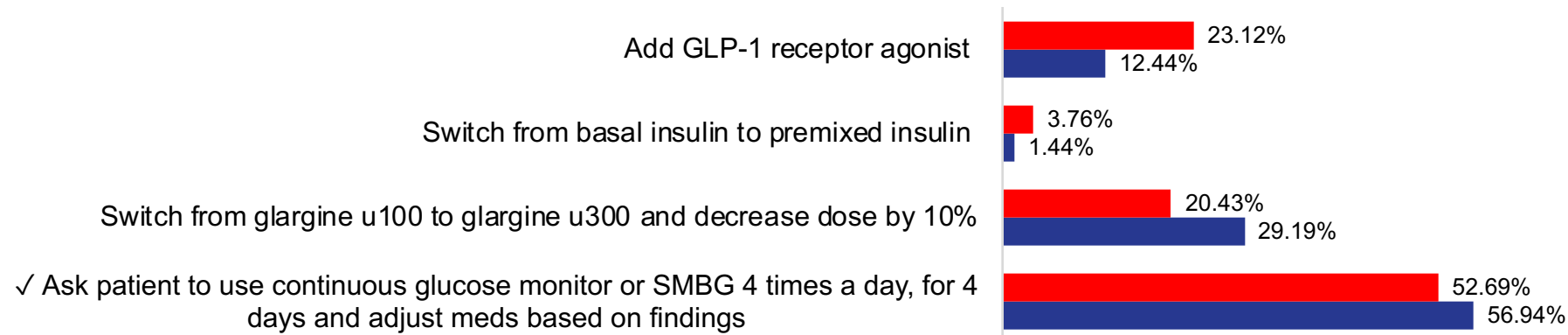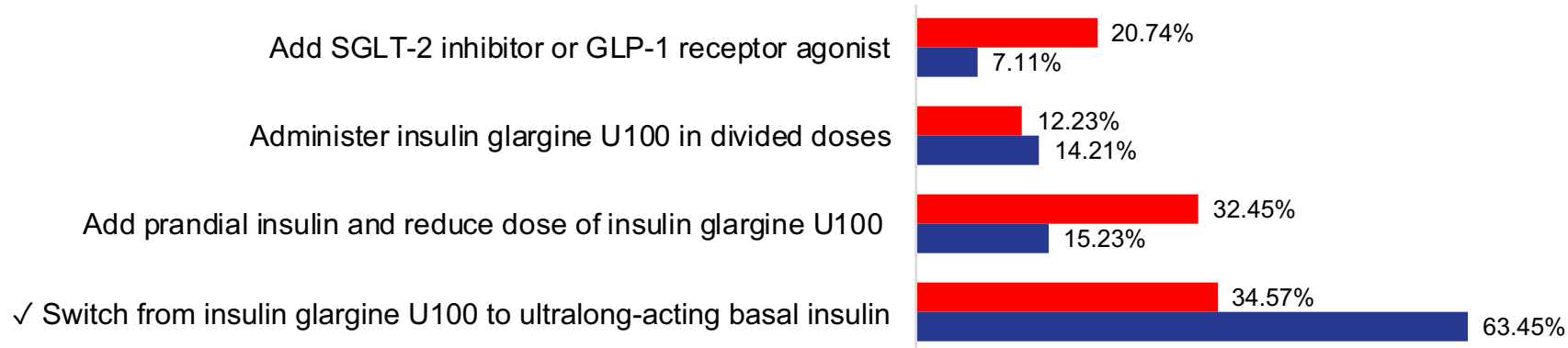
Identified Learning Gap, 2 of 3:
Adjustments to therapy for type 2 diabetic patients with uncontrolled episodes of hypoglycemia

On a Competence item presenting the case of a patient with a 10-year history of type 2 diabetes, currently on both metformin and insulin glargine but with an A1C of 7.6%, learners struggled to correctly identify the most appropriate adjustment in therapy.

44 y/o woman with a 10-year history of T2D presents with A1C 7.6%. Meds: metformin 1000 mg bid and insulin glargine U100 56 units qhs. Because of inconsistent fasting self-monitored blood glucose readings, her clinician recommended she use a continuous glucose monitor for several days which show a high degree of glycemic variability throughout the day, and occasional episodes of nocturnal hypoglycemia. What might you do now?

Results:

- At Post-Test, only 63% of learners correctly answered: "Switch from insulin glargine U100 to ultralong-acting basal insulin"

Add SGLT-2 inhibitor or GLP-1 receptor agonist	20.74% / 7.11%
Administer insulin glargine U100 in divided doses	12.23% / 14.21%
Add prandial insulin and reduce dose of insulin glargine U100	32.45% / 15.23%
✓ Switch from insulin glargine U100 to ultralong-acting basal insulin	34.57% / 63.45%

Identified Learning Gap, 3 of 3:
Prevalence of asymptomatic episodes of hypoglycemia in type 2 diabetic patients

Despite improvements in score from a very low (15%) average score at Pre-Test, Post-Test scores remained low on a Knowledge item about the prevalence of hypoglycemic episodes in patients with T2D.

In patients treated for T2D, approximately what proportion have asymptomatic hypoglycemic episodes?

Results:

- At Post-Test, only 60% of learners correctly answered: ">50%"

Overall Educational Impact

- **Significant improvements (ranging from 38% – 170%) were seen across all learning domains.**
    - Live onsite and live online learners experienced similarly strong increases across learning objectives, though online learners had lower scores at Pre- and Post-Test
    - At follow-up, learners most often selected "moderately confident" to describe their confidence in their ability to individualize diabetes therapy to minimize the risk for glycemic variability, indicating a need for additional reinforcement in this area
- Analysis of Knowledge and Competence items identified **three persistent learning gaps related to appropriate context for use of continuous glucose monitoring, adjustments to therapy for type 2 diabetic patients with uncontrolled episodes of hypoglycemia, and the prevalence of asymptomatic episodes of hypoglycemia in T2D patients**
    - Learners struggled to correctly identify continuous glucose monitoring as the most appropriate recommendation at Post-Test on a Competence question presenting the case a patient with poorly managed diabetes
    - On a Competence item which asked learners to modify therapy after being presented with the case of a patient under treatment for T2D but high glycemic variability, learners struggled to identify the best change
    - On a Knowledge item about the rate of occurrence of hypoglycemic episodes, learners continued to underestimate their frequency at Post-Test

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Appendix

Cohort Comparison by Profession: Learning Objectives

| Learning Domain	Live onsite learners				Live online learners			
	N	Pre-Test	Post-Test	% Change	*N*	Pre-Test	Post-Test	% Change
Recognize the risk for, and impact of hypoglycemia in patients with diabetes	189	26.98% (33.52%)	72.75% (36.53%)	+169.64%*	275	24.18% (36.27%)	54.18% (42.97%)	+124.07%*
Describe strategies for reducing the occurrence of glycemic variability	196	31.63% (39.38%)	69.13% (38.52%)	+118.56%*	297	30.98% (41.44%)	59.43% (44.52%)	+91.83%*
Understand effective SMBG vs. newer CGM in managing diabetes and reducing risk of dysglycemia / hypoglycemia	186	44.09% (39.72%)	61.02% (37.74%)	+38.40%*	192	39.58% (39.47%)	59.90% (39.28%)	+51.34%*
Differentiate between available insulin preparations and their effects on glycemic variability and hypoglycemic risk	196	31.63% (39.38%)	69.13% (38.52%)	+118.56%*	297	30.98% (41.44%)	59.43% (44.52%)	+91.83%*

❖ Live onsite and live online learners experienced similarly strong increases across learning objectives, though online learners had lower scores at Pre- and Post-Test

Knowledge Items

In patients treated for T2D, approximately what proportion have asymptomatic hypoglycemic episodes?

N = 195 – 199

<10%
- 20.51%
- 4.52%

~25%
- 42.56%
- 18.59%

~40%
- 21.54%
- 17.09%

✓ >50%
- 15.38%
- 59.80%

+288.69%
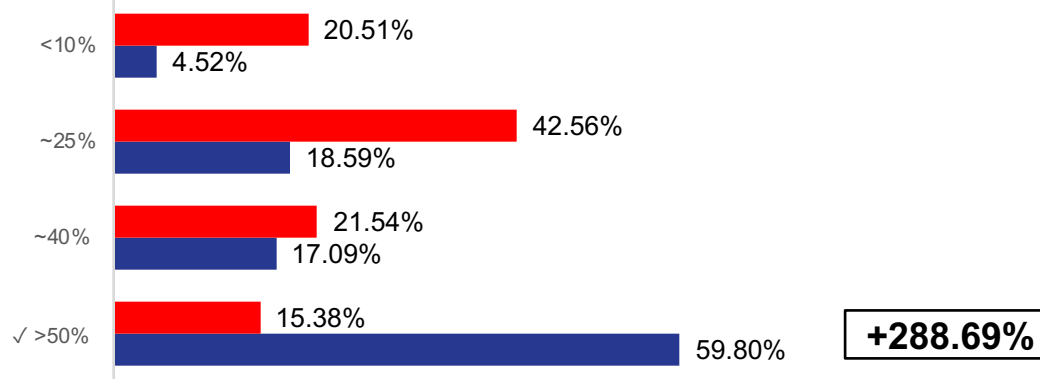
In clinical trials, which of the following insulin formulations has demonstrated the lowest glycemic variability?

N = 188 – 216

Glargine U-100
- 20.21%
- 4.17%

Insulin detemir
- 20.74%
- 3.24%

✓ Insulin degludec
- **+153.20%**
- 29.26%
- 74.07%

Insulin glargine U300
- 29.79%
- 18.52%
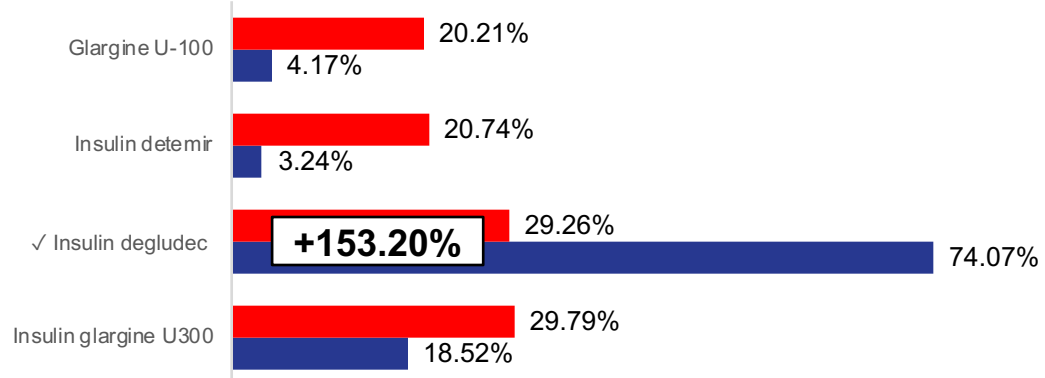
Knowledge Items

Severe hypoglycemia can result in all of the following sequelae except:

N = 186 – 206

QT prolongation and cardiac arrhythmias
22.58%
4.37%

Higher likelihood of cardiovascular death in older patients with coronary artery disease
9.14%
3.88%

✓ Increase in subsequent counter-regulatory hormone response
+113.92%
34.95%
74.76%

Decreased awareness of subsequent hypoglycemic events
33.33%
16.99%

RealCME

NACE

Competence Items

54 y/o man with 9-year history of T2D presents for checkup. His A1C is 7.6%. SMBG: AM 150-200 mg/dL; HS 120-150 mg/DL. Medications: metformin 1000 mg bid, ca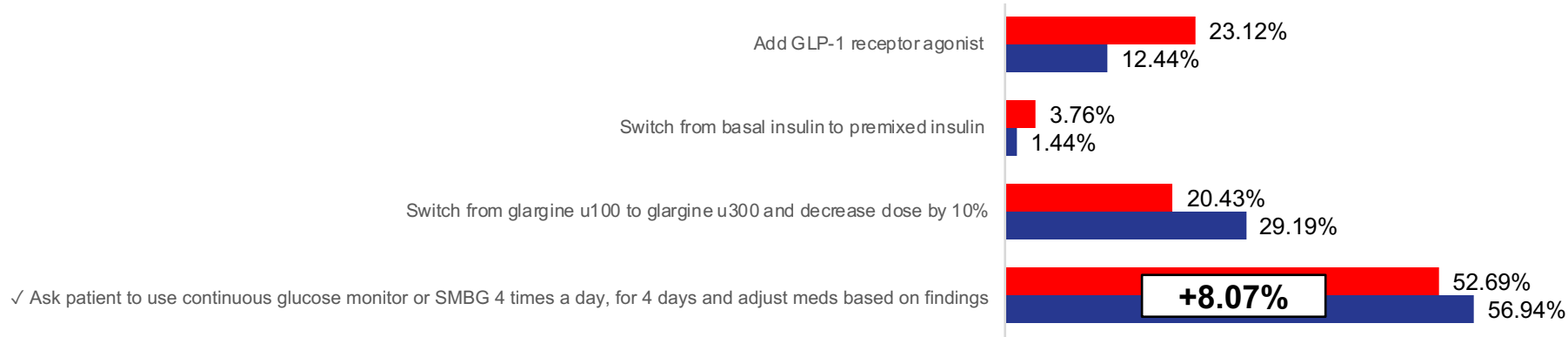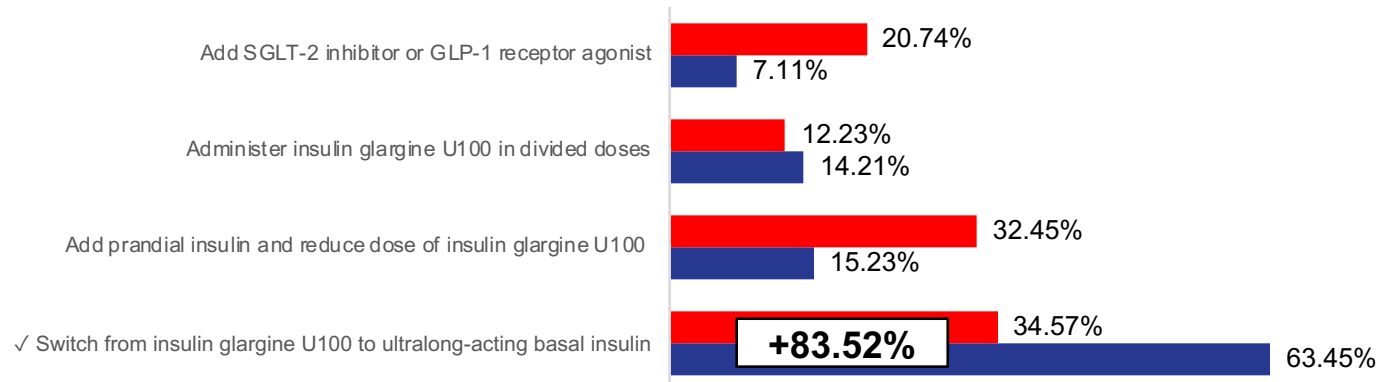nagliflozin 300 mg qd, and insulin glargine U100 48 units HS. Attempts to increase basal insulin dose in the past have led to daytime hypoglycemia. What might you do now?

N = 186 – 209

- Add GLP-1 receptor agonist — 23.12% (Pre-Test), 12.44% (Post-Test)
- Switch from basal insulin to premixed insulin — 3.76% (Pre-Test), 1.44% (Post-Test)
- Switch from glargine u100 to glargine u300 and decrease dose by 10% — 20.43% (Pre-Test), 29.19% (Post-Test)
- ✓ Ask patient to use continuous glucose monitor or SMBG 4 times a day, for 4 days and adjust meds based on findings — **+8.07%** — 52.69% (Pre-Test), 56.94% (Post-Test)

44 y/o woman with a 10-year history of T2D presents with A1C 7.6%. Meds: metformin 1000 mg bid and insulin glargine U100 56 units qhs. Because of inconsistent fasting self-monitored blood glucose readings, her clinician recommended she use a continuous glucose monitor for several days which show a high degree of glycemic variability throughout the day, and occasional episodes of nocturnal hypoglycemia. What might you do now?

N = 188 – 197

- Add SGLT-2 inhibitor or GLP-1 receptor agonist — 20.74% (Pre-Test), 7.11% (Post-Test)
- Administer insulin glargine U100 in divided doses — 12.23% (Pre-Test), 14.21% (Post-Test)
- Add prandial insulin and reduce dose of insulin glargine U100 — 32.45% (Pre-Test), 15.23% (Post-Test)
- ✓ Switch from insulin glargine U100 to ultralong-acting basal insulin — **+83.52%** — 34.57% (Pre-Test), 63.45% (Post-Test)
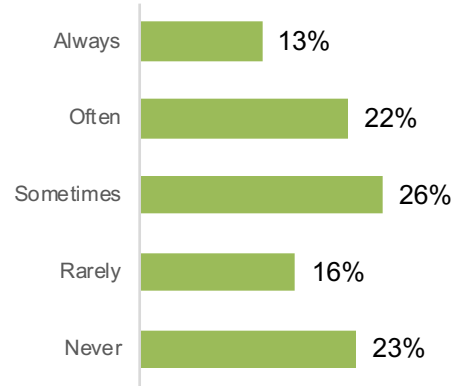
RealCME   NACE

Practice Strategy Items (given at 4 week follow-up)

After completing this CME activity, how often do you use continuous glucose monitoring in your practice?

N = 467

Always	13%
Often	22%
Sometimes	26%
Rarely	16%
Never	23%

After completing this CME activity, how often do you utilize concentrated insulin for patients that experience nocturnal hypoglycemia or require >60 units of basal insulin?

N = 467

Always	20.77%
Often	14.35%
Sometimes	28.91%
Rarely	25.91%
Never	10.06%
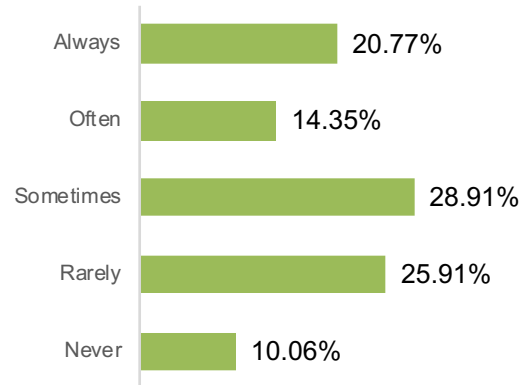
Confidence Item (given at 4 week follow-up)

After completing this CME activity, please rate your confidence in your ability to understand how to individualize diabetes therapy to minimize the risk for glycemic variability

N = 467

Category	Percentage
Very confident	10.28%
Pretty much confident	23.98%
Moderately confident	43.47%
Slightly confident	18.20%
Not at all confident	4.07%