POCT

Diabetes Dilemmas: CGM, A1c Measurements, & New Management Strategies

POINT OF CARE TESTING UNIVERSITY

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Learning Objectives

1. Discuss roles of CGM and A1c glucose measurements
2. Evaluate discordance between CGM TIR and A1c values
3. Assess new strategies for improving accuracy of glucose measurements
4. Outline emerging trends in managing diabetes in disadvantaged populations
5. Address benefits of utilizing point-of care A1c testing
6. Discover how to assess bias between test and device type in diabetes management
7. Apply current quality control measures for improved glucose management

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Agenda

1. Continuous Glucose Monitoring and HbA1c in Clinical Practice
2. New Strategies and Emerging Trends in Diabetes Management
3. Point-of-Care HbA1c Testing and Quality Control Measures

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Continuous Glucose Monitoring and HbA1c in Clinical Practice

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Disclosures:

- Research funding and honoraria from Vertex Pharmaceuticals
- Investigator initiated research grant from Dexcom
- Scientific Advisory Board member for Anagram Therapeutics

Learning Objectives

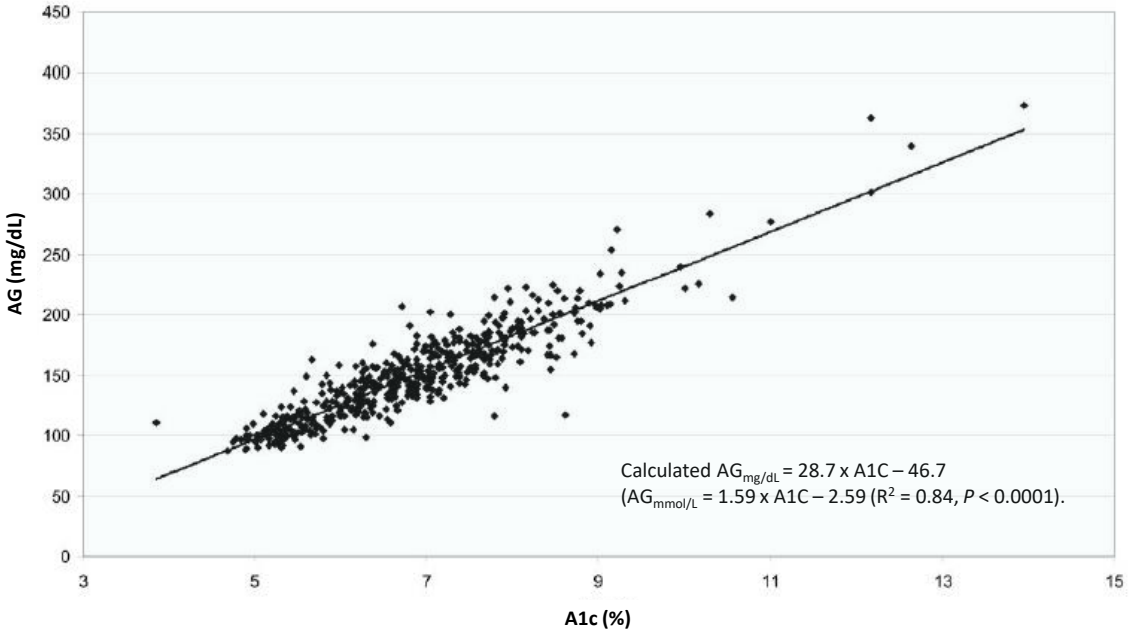
1. Review background of hemoglobin A1c (HbA1c) and continuous glucose monitoring (CGM)
2. Identify the benefits and shortcomings of CGM and HbA1c in the management of type 1 and type 2 diabetes
3. Discuss the complementary role of A1c and CGM in the assessment of glycemia, including when results are disparate

HbA1c Is the Gold Standard Measure of Chronic Glycemia

Measure of red blood cell exposure to glucose (nonenzymatic glycation) over the past 2-4 months

- Studies like ADAG established the equation correlating HbA1c with average glucose (using both fingerstick and CGM)
- Labs will typically report both A1c and calculated mean blood glucose (CMBG)

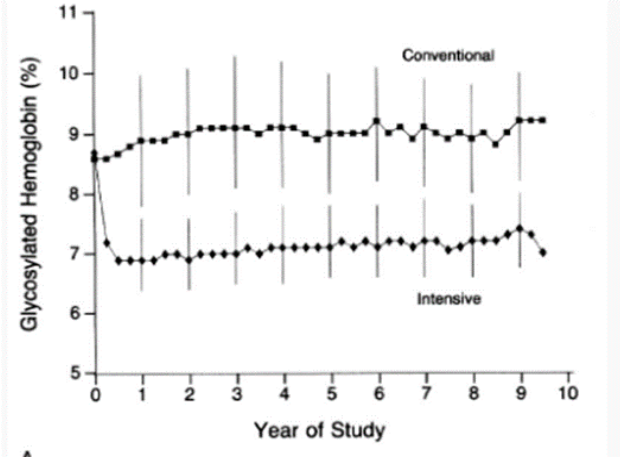
Linear regression of A1C at the end of month 3 and calculated AG during the preceding 3 months.

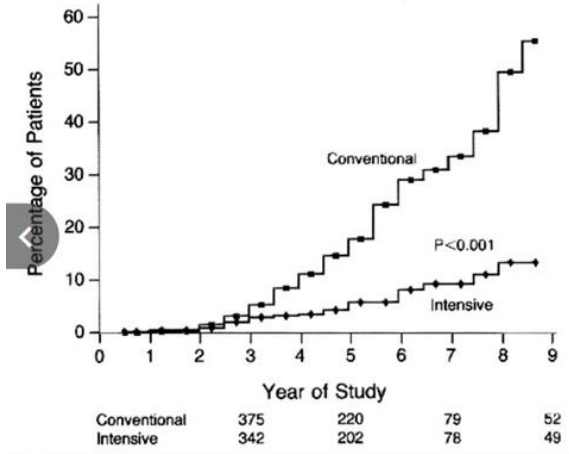


Nathan DM, et al. *Diabetes Care.* 2008;31:1473-1478.

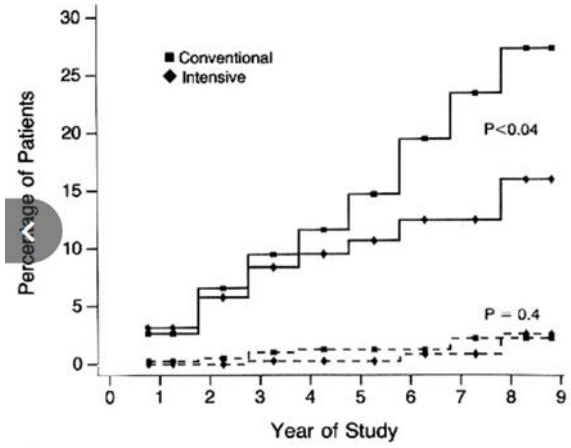
HbA1c Is the Gold Standard Measure of Chronic Glycemia

- DCCT/EDIC and UKPDS established A1c goal <7% to reduce microvascular complications
- National Glycohemoglobin Standardization Program (NGSP) standardized assays to ensure accuracy and precision





Retinopathy



Albuminuria

DCCT Research Group. *N Engl J Med*. 1993;329(14):977-986.

Conditions Affecting HbA1c Accuracy

Falsely elevated HbA1c

- Slower RBC turnover
  - Iron, B12, or folate deficiency

Falsely low HbA1c

- Faster RBC turnover
  - Hemolysis
  - Erythropoietin treatment
  - Pregnancy
  - Recently treated iron/B12/folate deficiency
- RBC transfusion
- CKD/ESRD (particularly hemodialysis and erythropoietin treatment)

Hemoglobin variants can increase or decrease HbA1c, but most assays are no longer affected by this.

Prescription-Only Continuous Glucose Monitoring (CGM) Systems

Currently available prescription CGM devices:

Dexcom G6 and G6Pro

Dexcom G7

Senseonics Eversense

Medtronic Guardian

Freestyle Libre 2

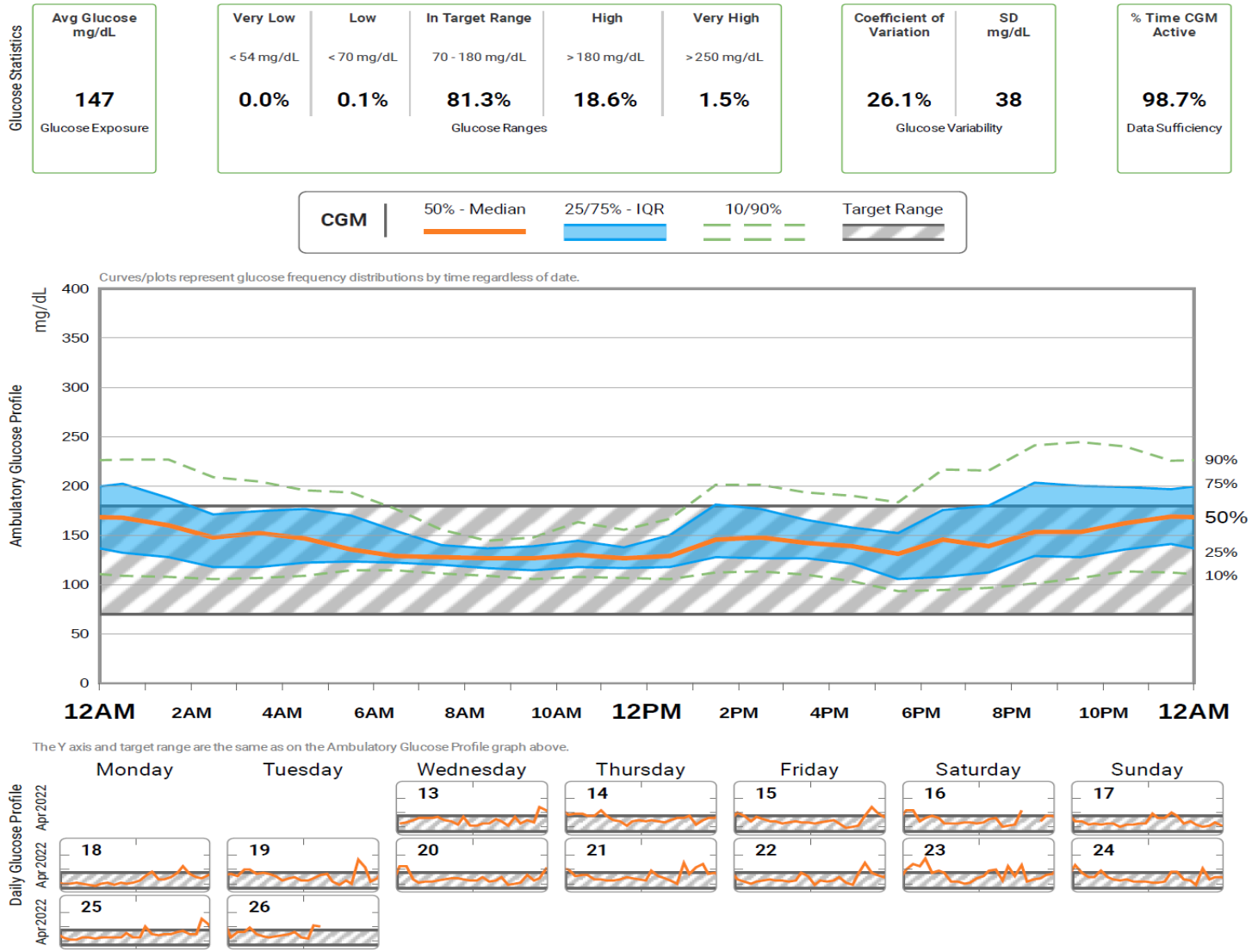
Libre 3

Available as of August, 2024.

Ambulatory Glucose Profile (AGP) Provides a Comprehensive Picture of Glycemia

CMG Outcomes

- Average glucose
- Time in Range (TIR) 70-180 mg/dL
- Time above range (TAR)
- Time Below Range (TBR)
- Glycemic variability (CV, SD)
- Glucose Management Indicator (GMI)
  - calculated from an equation that translate CGM average glucose into an estimation of A1c

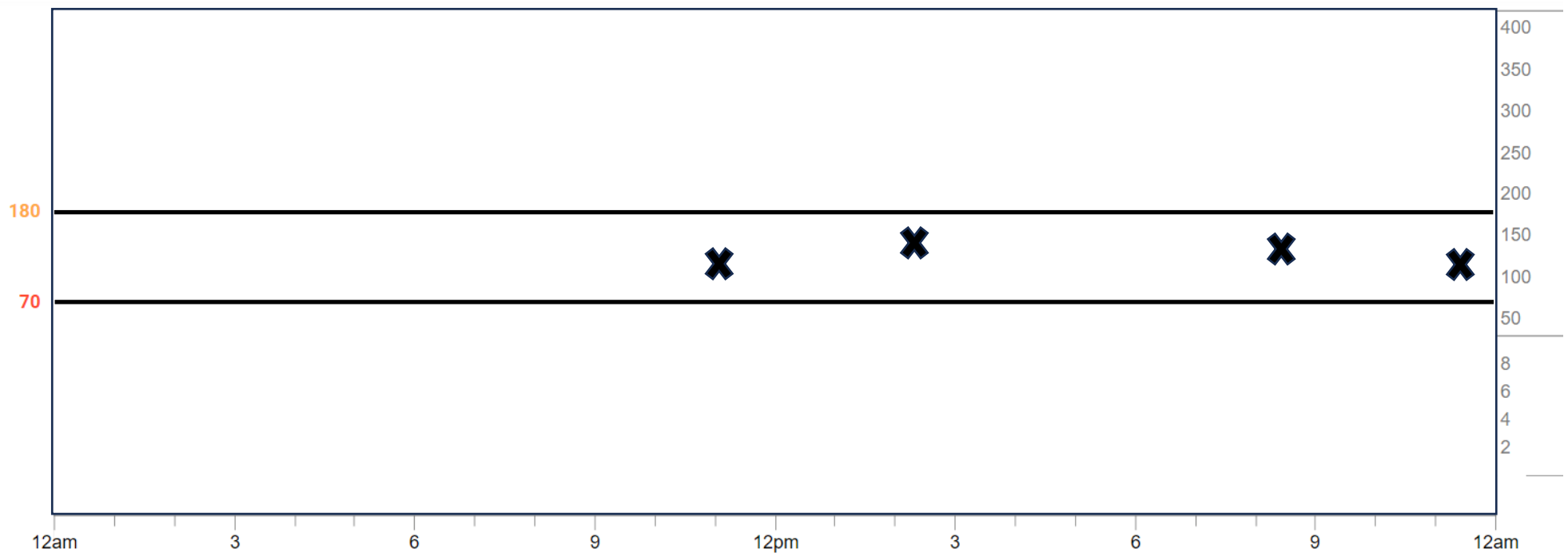


CGM Improves Glucose Levels and Reduces Hypoglycemia In People With Type 1 and 2 Diabetes

- Real time alerts and trend arrows
- Pattern identification (carbohydrate intake, exercise, etc.)
- Favorable patient reported outcomes (PROs)
- Can be used as an educational tool to see how different foods and activities impact glucose levels

Heinemann L, et al. *Lancet*. 2018;391:1367-1377.
Beck RW, et al. *J Am Med Assoc.* 2017;317:371-378.
Lind M, et al. *J Am Med Assoc.* 2017;317:379-387.
Martens T, et al. *J Am Med Assoc.* 2021;325:2262-2272.
Beck RW, et al. *Ann Intern Med.* 2017;167:365-374.
Jancev M, et al. *Diabetologia*. 2024;67:798-810.

Advantages of CGM Over Conventional Glucose Monitoring

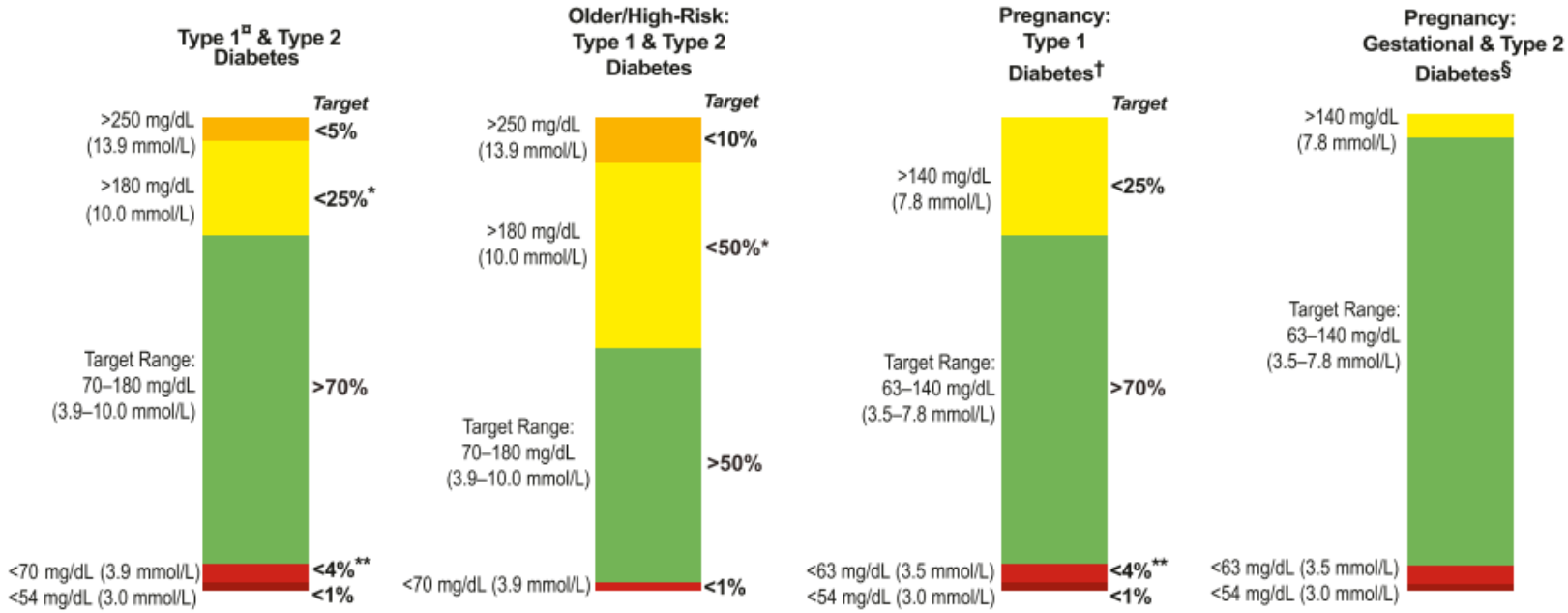


Consensus Recommendations for CGM Targets

Targets established based on correlations with A1c and with diabetes complications

- TIR 70% correlates with HbA1c 7.0%
- 10% increase in TIR correlates with clinically significant decrease in HbA1c of 0.6-0.8%

Minimum 2-weeks of data needed

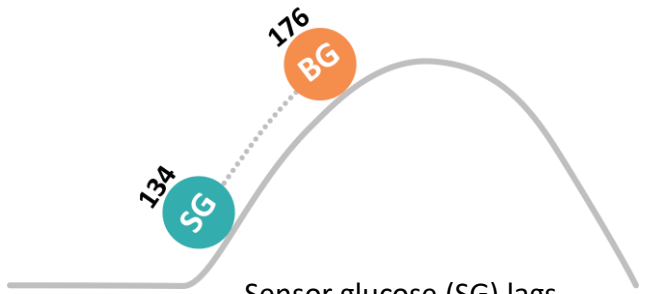


¤ For age <25 yr., if the A1C goal is 7.5%, then set TIR target to approximately 60%. (See *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management.)
† Percentages of time in ranges are based on limited evidence. More research is needed.
§ Percentages of time in ranges have not been included because there is very limited evidence in this area. More research is needed. Please see *Pregnancy* section in text for more considerations on targets for these groups.
* Includes percentage of values >250 mg/dL (13.9 mmol/L).
** Includes percentage of values <54 mg/dL (3.0 mmol/L).

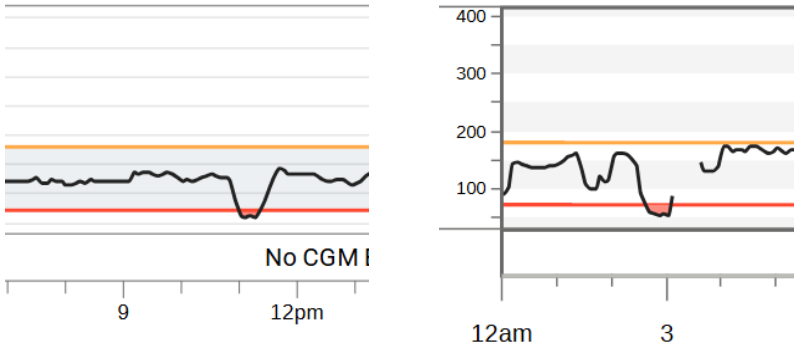
Battelino T, et al. *Diabetes Care.* 2019;42:1593-1603.

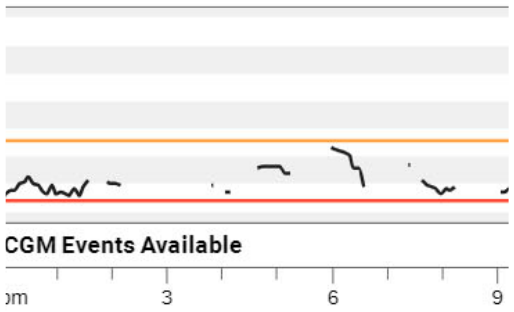
Disadvantages of CGM

- **Interstitial vs blood glucose**
  - Lag time
  - %20/20 expectation
    - CGM glucose should be within 20% of blood glucose >100mg/dL and within 20 mg/dL below 100 mg/dL
- **Artifact**
  - Compression lows
  - Sensor failure
- **Lower accuracy in lower glucose ranges**
- **Medications affecting accuracy**
  - Hydroxyurea and high doses of acetaminophen (Dexcom)
  - High dose vitamin C (Libre)



Sensor glucose (SG) lags behind blood glucose (BG)





CGM vs. HbA1c: Similar, But At the Same Time Different and Complementary

HbA1c

- Captures a measure of average glucose
- **More data** informing HbA1c targets

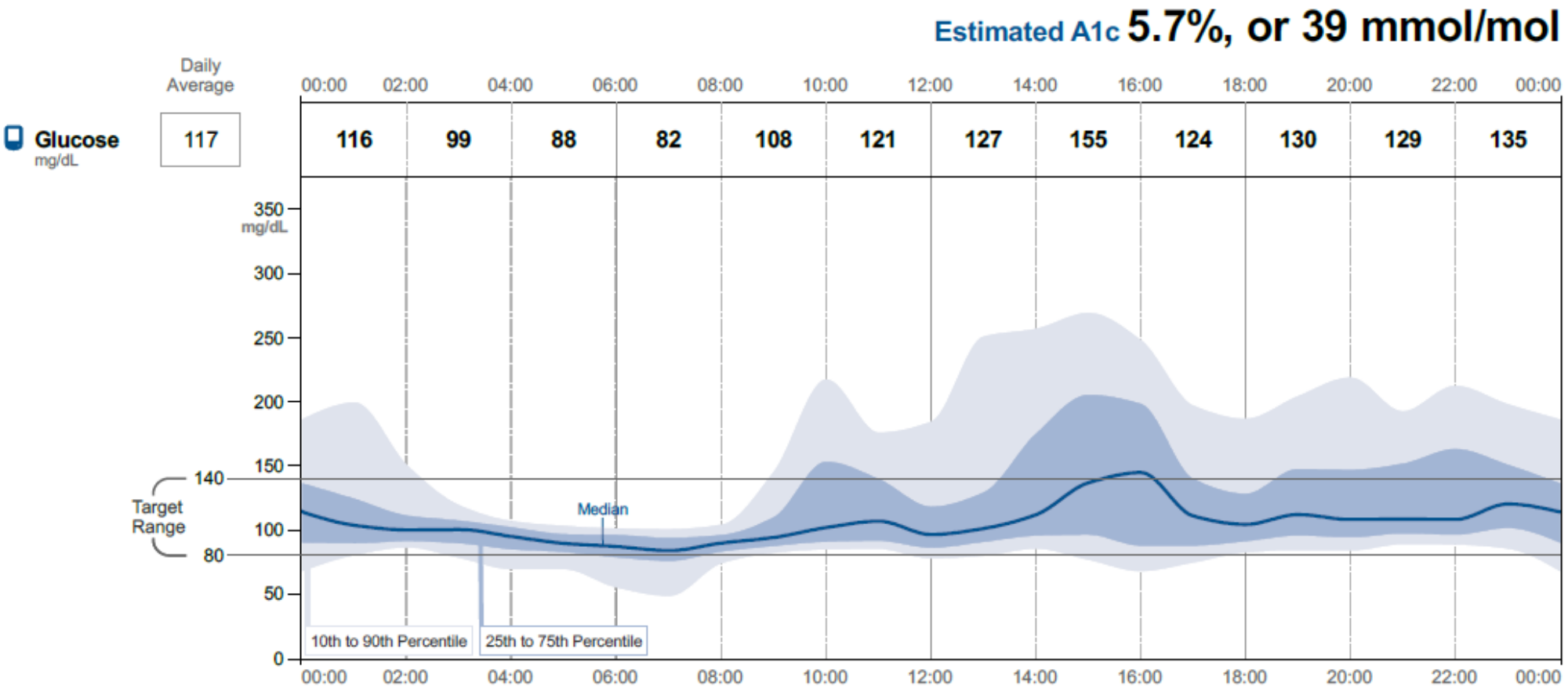
CGM

- Captures a measure of average glucose
- **Much less data** informing CGM targets compared to HbA1c
  - Minimal longitudinal data to link CGM goals with reduction in the development of diabetes complications

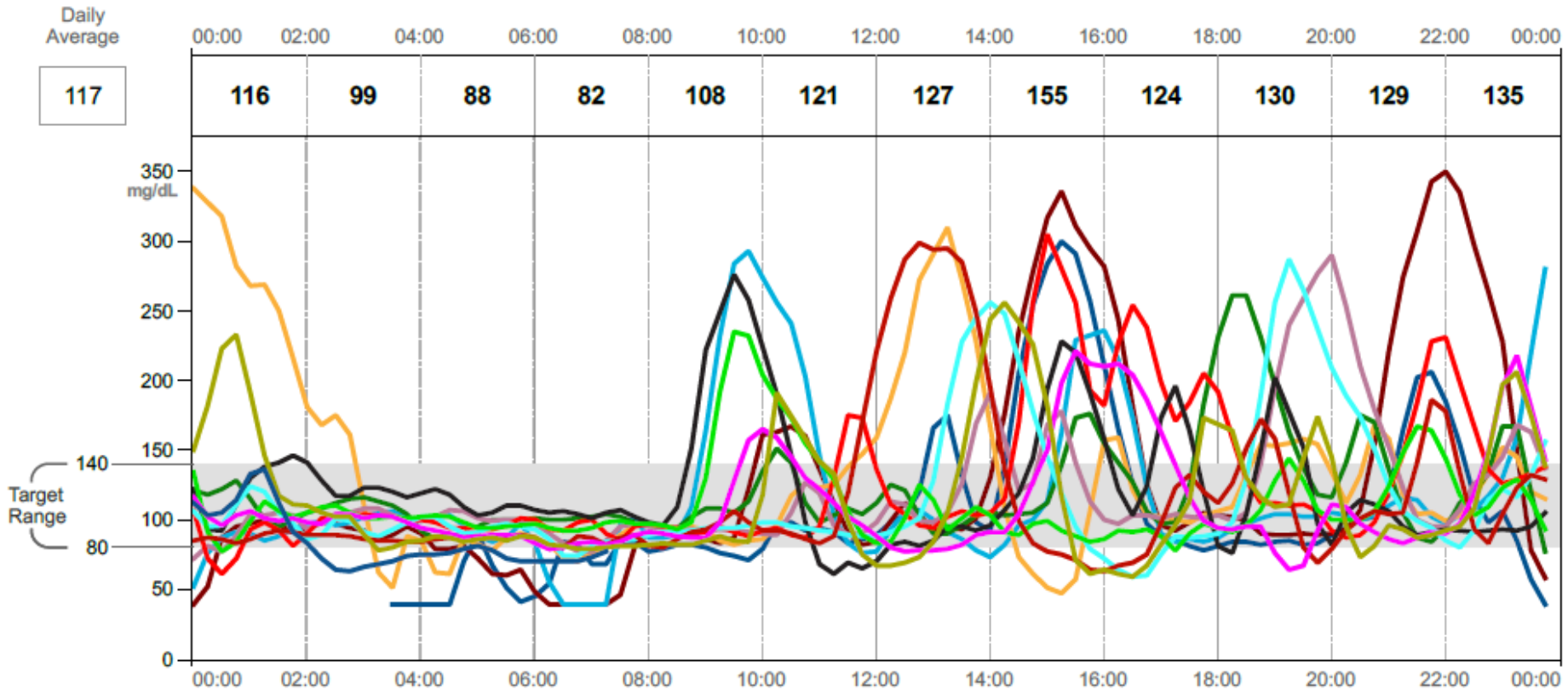
HbA1c **2-4 months duration of time**

CGM **2 weeks duration of time**

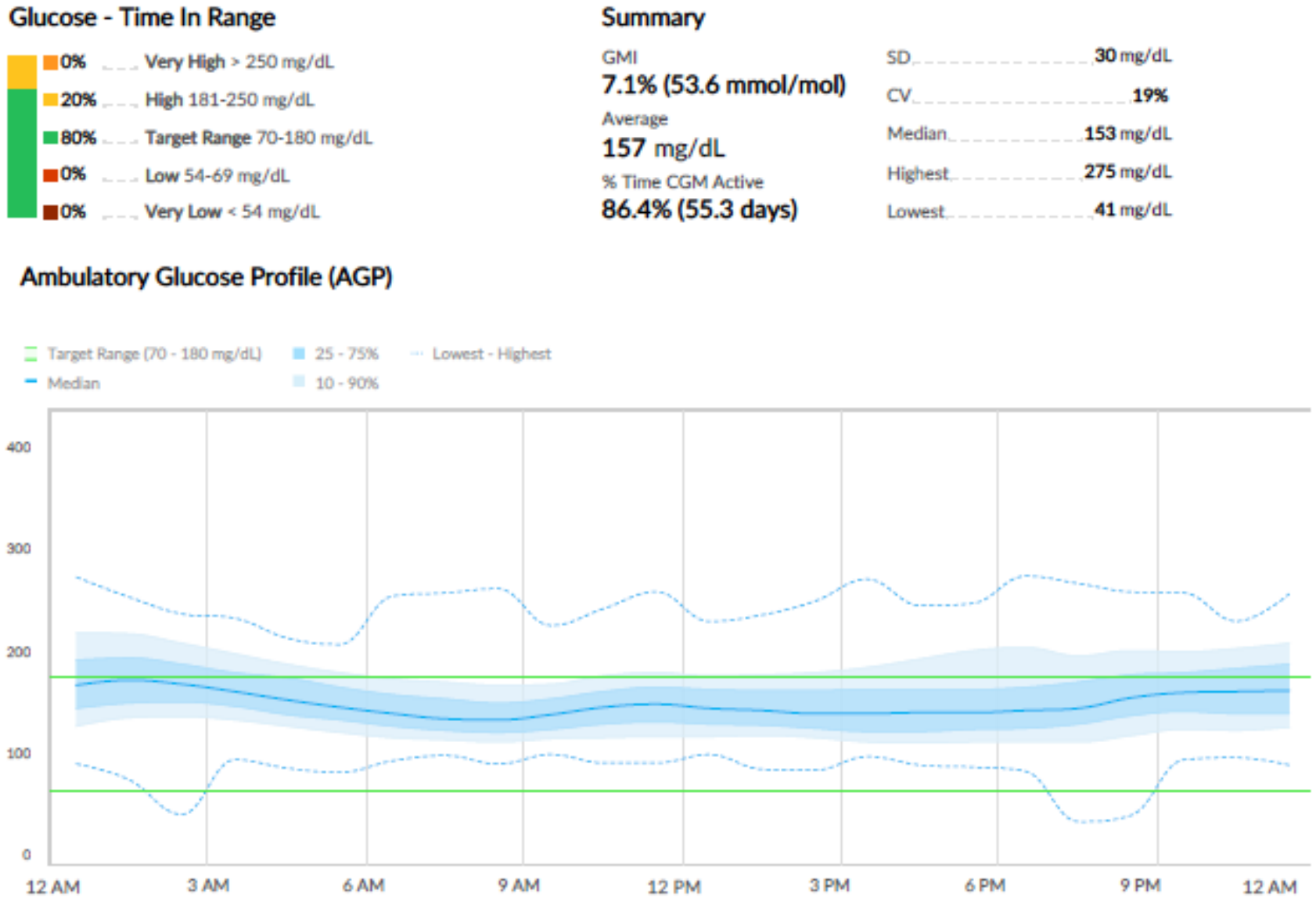
CGM Can Identify Glycemic Variability Missed By HbA1c



CGM Can Identify Glycemic Variability Missed By HbA1c



Time in Range May Miss An Average Glucose (and HbA1c) That Could Be Suboptimal



GMI Is Not the Same As HbA1c

Discordance more than 0.5% occurs in 26-68% of people, likely due to:

CGM issues

- Calibration
- Sensor brand discrepancies
  - Missing data with flash devices
- Artifact and other accuracy issues
- Drug interference

HbA1c issues

- Acute or recent change in glycemia not fully reflected in HbA1c
- Impacts from red cell turnover or other factors

Selvin E. *Diabetes Care.* 2024;47:906-914.

Complementary Tools to Optimize Diabetes Care

HbA1c

- Assess overall glycemia to gauge and inform risk of complications, tailored to the specific patient

CGM

- Real time data to improve glycemic control
- Capture glycemic variability
- Determine most recent glycemic trends
- Inform specific therapy adjustments

2023 ADA Guidelines for Providers

> Assess glycemic status (A1C or other glycemic measurement such as time in range or glucose management indicator) at least two times a year in patients who are meeting goals . . . and at least quarterly and as needed in patients whose therapy has recently changed and/or who are not meeting glycemic goals.

Take Home Points

1 **HbA1c is the gold standard measure of chronic glycemia**

2 Conditions affecting RBC turnover can impact HbA1c accuracy

3 CGM provides a real-time, comprehensive picture of glycemia and has been shown to improve glucose levels in people with diabetes treated with insulin

4 Disadvantages of CGM include lag time, artifact, and medication interference

5 Together HbA1c and CGM can provide important and complementary information to optimize diabetes care

POCT U

New Strategies and Emerging Trends in Diabetes Management

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Dr. Whitley has no disclosures for this program.

Learning Objectives

1. Assess new strategies for improving accuracy of glucose measurements
2. Outline emerging trends in managing diabetes in disadvantaged populations

Monitoring Diabetes Can Improve Outcomes

American Diabetes Association (ADA) recommended glycemic goal is **< 7.0% A1c** in individuals diagnosed with diabetes.

Glycemic assessment by A1c and/or appropriate continuous glucose monitoring (CGM) metrics **at least two times a year**.

- More frequently for individuals not meeting treatment goals, with frequent or severe hypoglycemia or hyperglycemia, changing health status, or growth and development in youth.
- At least quarterly in individuals whose therapy has recently changed and/or who are not meeting glycemic goals.

Only **1 in 4** achieve the ADA goal.

American Diabetes Association Professional Practice Committee; 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Supplement_1): S111–S125.

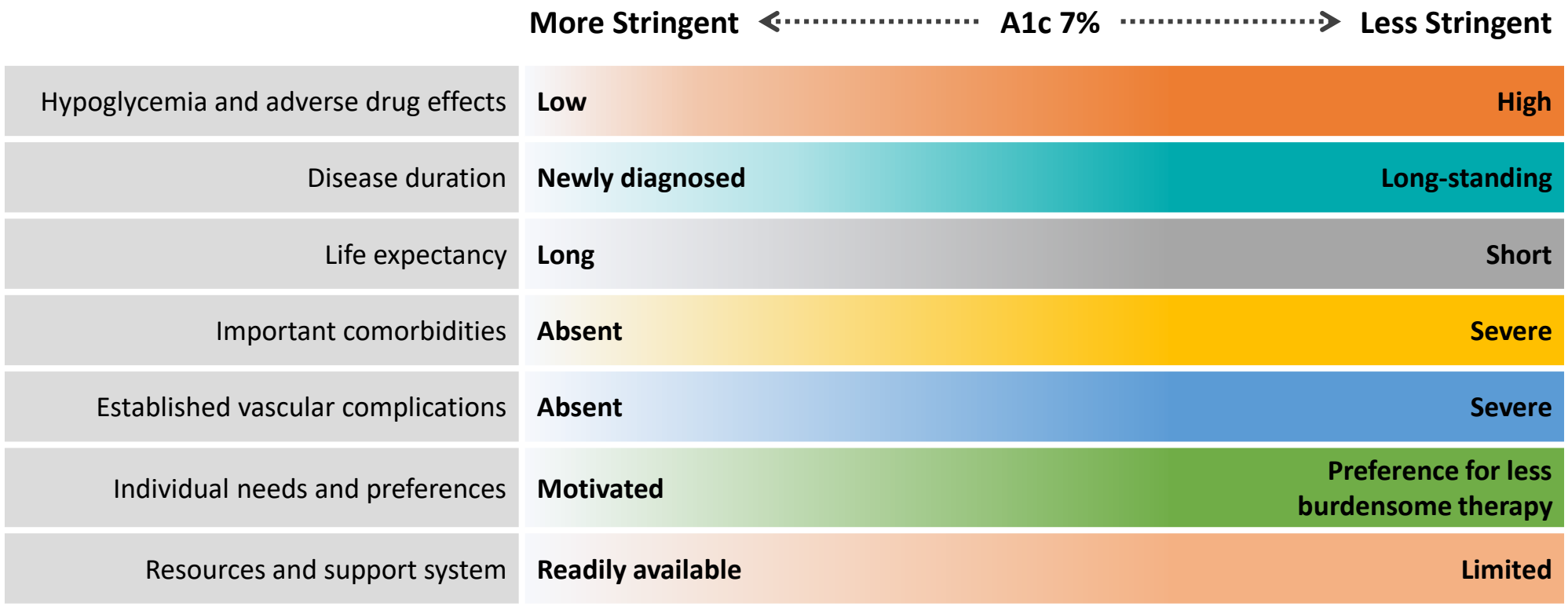
Glycemic Goals Should Be Based on Individual Patient Circumstances

ADA Recommended Glycemic Goals
A1c in non-pregnant adults of < 7%.
Achievement of lower A1c levels than the goal of 7% may be acceptable and even beneficial if it can be achieved safely and without significant hypoglycemia or other adverse treatment effects.
Less stringent glycemic goals may be appropriate for individuals with limited life expectancy or where harms of treatment are greater than benefits.
De-intensify medications for individuals who are at high risk for hypoglycemia or for whom the harms and/or burdens of treatment may be greater than the benefits, within individualized glycemic goals.
Reassess glycemic goals based on individualized criteria.
Setting a glycemic goal during consultation is likely to improve patient outcomes.

American Diabetes Association Professional Practice Committee; 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Supplement_1): S111–S125.

A1c Targets Can be Individualized In Multiple Areas

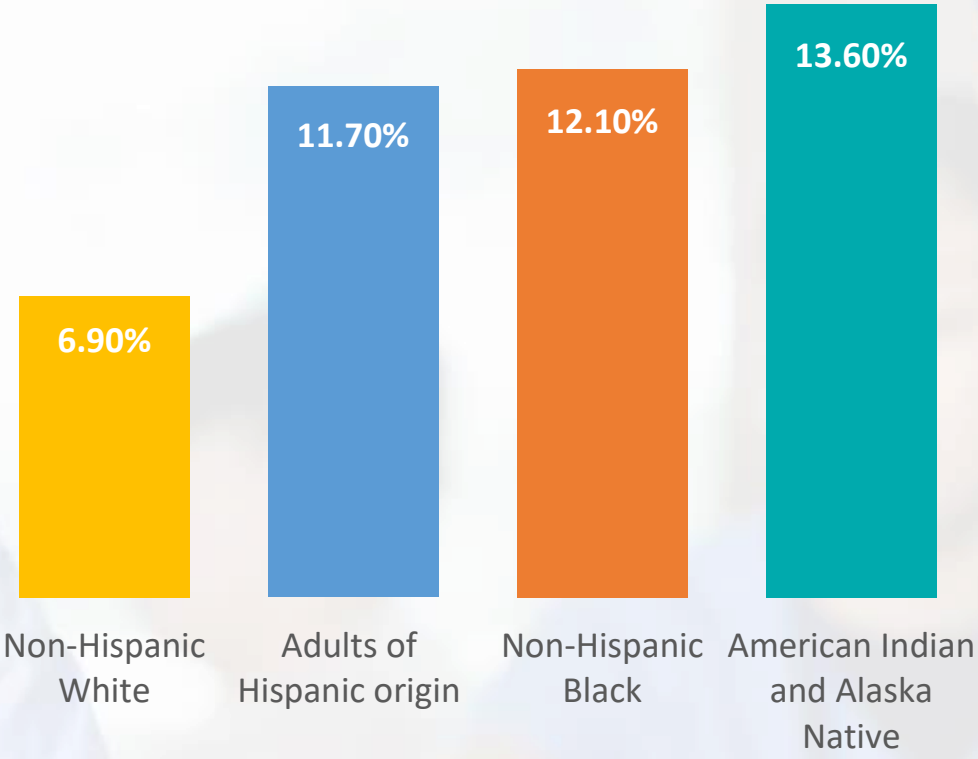
POCT A1c may provide an opportunity to develop individualized glycemic targets during patient visits, eliminating the need for follow-up.



American Diabetes Association Professional Practice Committee; 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Supplement_1): S111–S125.

Health Equity: Diabetes rates are higher in certain groups

- Racial and ethnic minorities carry a higher burden of undiagnosed and diagnosed diabetes in the U.S.
- Among U.S. adults, both men and women aged 18 years or older, age-adjusted data for 2019–2021 indicated the prevalence of diagnosed diabetes was highest among American Indian and Alaska Native Adults.



CDC. National Diabetes Statistics Report. https://www.cdc.gov/diabetes/php/data-research/. Accessed August 9, 2024.

Social determinants of health affect diabetes prevalence and outcomes

- Social determinants account for 50-60% of health outcomes
  - Conditions where people live, learn, work, play

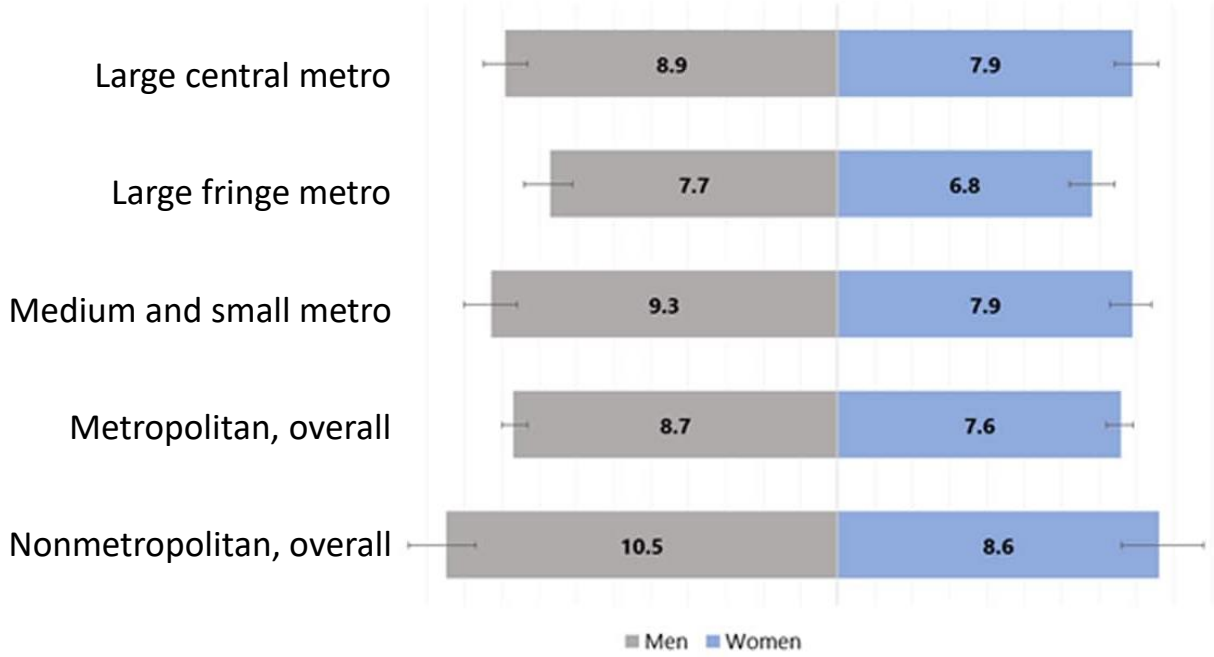
13.1% Adults with less than a high school education had diagnosed diabetes

9.1% Adults with a high school education had diagnosed diabetes

6.9% Adults with more than a high school education had diagnosed diabetes

- Adults with higher family income (above 500% of the federal poverty level) had the lowest prevalence for both men (6.3%) and women (3.9%)

For both men and women, diabetes was **higher among adults living in nonmetropolitan areas** compared to those in metropolitan areas



CDC. National Diabetes Statistics Report. https://www.cdc.gov/diabetes/php/data-research/. Accessed August 9, 2024.

Barriers to Diabetes Care and Management

Lack of:

- Linguistically or culturally tailored services, curricula, or staff
- Insurance or insurance with high costs or copayments
- Family support
- Transportation or childcare
- Patient preparation between appointments

Additional barriers:

- Competing demands for time and attention
- Length of time between appointments
- Communication between patient and provider
- Providers “talking down” to patients

https://www.healthwellfoundation.org/realworldhealthcare/life-with-diabetes-reducing-barriers-to-care/ Accessed July 28, 2024.
Kirk BO, et al. *PEC Innov*. 2023;3:100188.

Barriers to CGM Use

CGM use was associated with **improved** HbA_{1c} among those with type 2 diabetes (−1.2% [13.1 mmol/mol]; $P < 0.001$).

That was comparable between major racial/ethnic groups.

Those with **higher fill adherence achieved greater HbA_{1c} reduction** (−1.4% [15.3 mmol/mol]; $P < 0.001$) compared with those with lower adherence (−1.0% [10.9 mmol/mol]; $P < 0.001$).

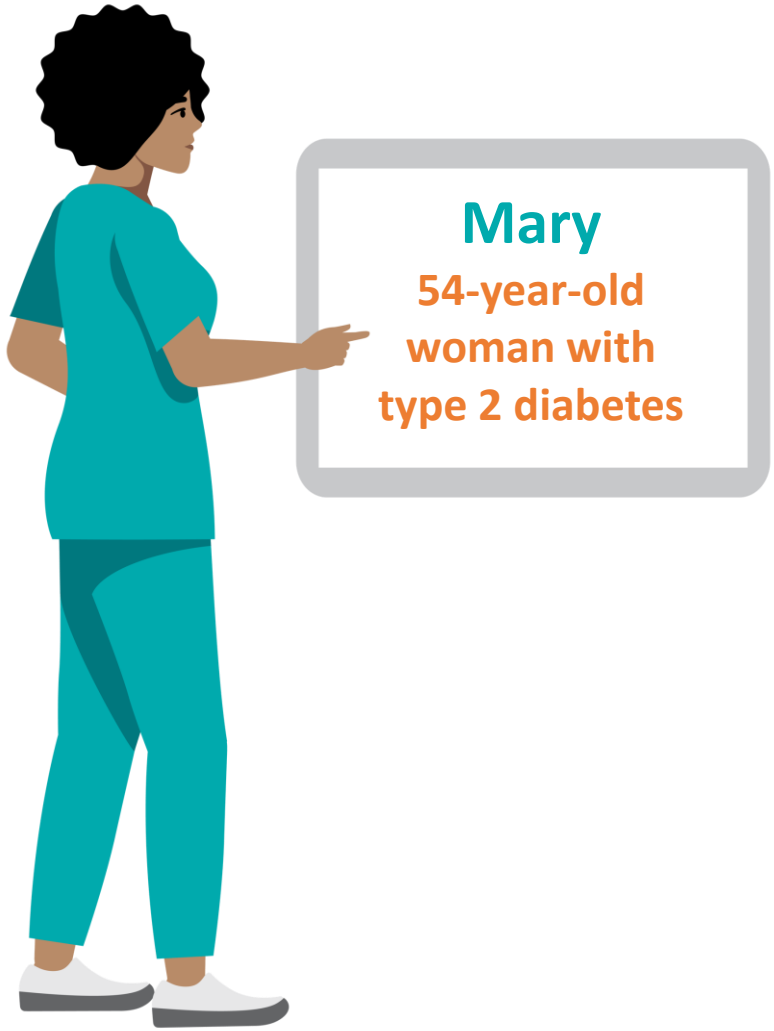
Adherence primarily related to device cost.

Insurance status, race and socioeconomic status remain as barriers to CGM use.

Education and training are vital for both health care providers and patients.

Ni K, et al. *Diabetes Care*. 2023;46(2):391–398.
https://www.healio.com/news/endocrinology/20230524/we-have-to-make-it-easy-barriers-hinder-cgm-access-for-some-people-with-diabetes. Accessed August 3, 2024.

Case 1: Mary



- Patient was prescribed a CGM by her primary care physician (PCP)
- At her latest appointment, her CGM data showed consistent elevated glucose levels over the last 14 days
- PCP referred her to diabetes clinic for follow-up and additional education

This patient has a CGM and should be able to see her blood sugar is high.

Is she non-adherent?

Case 1: Mary

At diabetes clinic point-of-care HbA1c:

12.2%

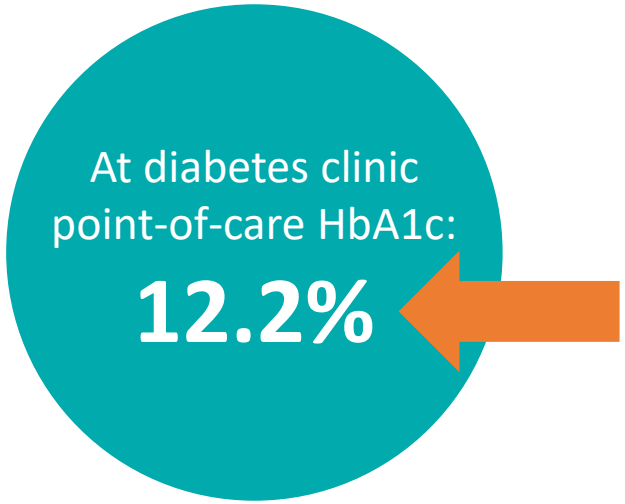
Patient is very frustrated

- Doesn't understand how CGM works and thinks it is not working
- Has difficulty with CGM instructions including downloading and using the phone app
- Had to call PCP office multiple times for assistance and is still struggling to understand how to read the data and what the data means

Upon taking a more thorough history, Certified Diabetes Educator (CDE) discovers:

1. Patient did not graduate high school and has a limited reading level.
2. She has an older model phone that does not get good service in the rural area where she lives and sometimes looses connectivity to the CGM.
3. She does not have the capability to go to frequent PCP or clinic visits due to issues with her car.

Case 1: Mary



Certified Diabetes Educator (CDE):

- Used the patient's HbA1c value to show the patient that her diabetes **wasn't** under control
- Educated her on the use of the CGM
- Encouraged patient to agree that a professional CGM twice a year along with HbA1c levels to monitor and inform dietary changes would be more beneficial than using a personal CGM that she has to monitor herself
- Reviewed with patient the food choices and snacking that were leading to her elevated glucose levels

Professional vs. Patient CGM

- Professional use CGM systems are clinic-owned devices that can be placed on patients for intermittent or short-term use as a diagnostic and clinical decision-making tool.
- Professional CGM has been shown to assist patients in lowering their A1C, as well as improving their physical activity and making other positive behavior changes.
- Beneficial for patients who aren't interested in personal CGM, don’t qualify for it, can’t afford it, or it may serve as a trial run for patients considering a personal CGM device.

Adkinson JD, et al. *Fam Pract Manag*. 2021;28(2):7-14.

Cost

- Most currently available CGMs require a prescription
- Costs vary depending on device
- Without insurance ~$164 - $540
  (28-30 day supply including sensors and readers)
- Three new over-the-counter CGMs are approved for individuals who are not on insulin.
  - No automatic hypoglycemia alarms
  - Pricing is expected to be similar to uninsured prices of prescription models and may be as low as $89 a month for subscription versions.

https://www.goodrx.com/conditions/diabetes-type-2/dexcom-vs-freestyle-libre. Accessed July 15, 2024.
https://www.medtechdive.com/news/abbott-dexcom-over-the-counter-cgm-launch/719928/. Accessed July 15, 2024.
https://www.cnbc.com/2024/08/26/dexcom-launches-stelo-its-first-over-the-counter-continuous-glucose-monitor.html. Accessed August 26, 2024.

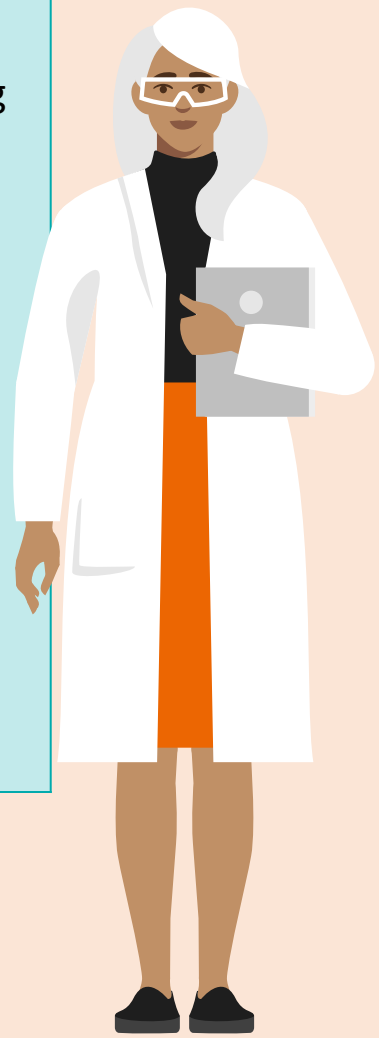
Continuous Glucose Monitoring Doesn't Eliminate the Need for A1c

- A1c reflects average glycemia over 3 months while CGM or other capillary monitoring provides data over a more recent time period.
- CGM or blood glucose monitoring (BGM) by capillary device may be useful for individuals who are insulin dependent or who have substantial glycemic variability.
- Individual discrepancies in CGM and A1c values can occur.
  - Non-glycemic factors (medications, interruptions in CGM data sets, short CGM time course, device bias)
  - Glycemic factors (RBC lifespan, hemoglobin variants, transfusions)

ADA Standards of Care

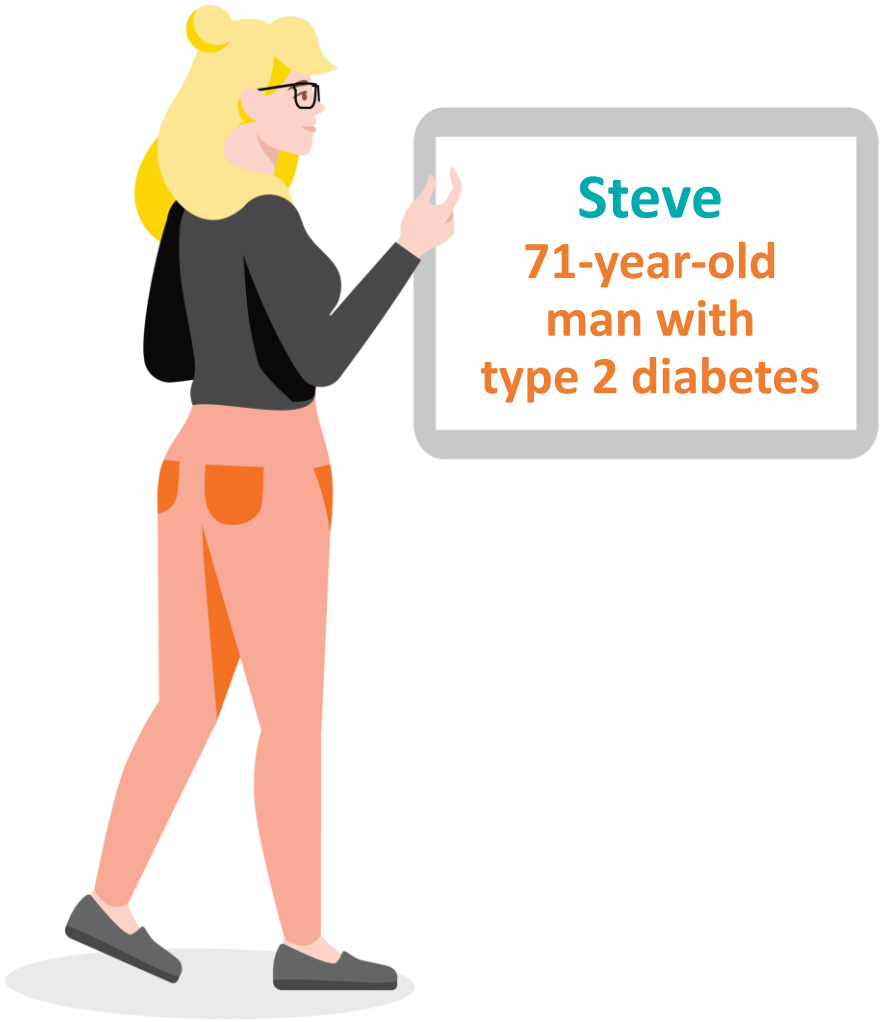
For many people with diabetes, glucose monitoring, either using BGM or CGM **in addition to regular A1C testing,** can help achieve glycemic goals.

For individuals prone to glycemic variability, especially people with type 1 diabetes or type 2 diabetes with severe insulin deficiency, glycemic status is best evaluated by the **combination** of results from BGM or CGM and A1C.



American Diabetes Association Professional Practice Committee; 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Supplement_1): S111–S125.
Tozzo V, et al. *Diabetes Care* 23 February 2024; 47 (3): 460–466.

Case 2: Steve



- Struggling to control elevated glucose levels with diet alone on metformin
- Prescribed insulin and CGM
- Patient cannot afford sensors every month so there are numerous data gaps
- At follow-up, PCP requests POC HbA1c 8.9%, reduced from previous 9.3%
- Upon further questioning, patient admits to following his diet more closely with the CGM but can't always afford to keep it

PCP uses opportunity to further discuss diet and exercise, as well as a referral to a diabetes clinic for financial and educational assistance.

Best practices to reach people with limited healthcare access

- Diabetes educators
- Pharmacists
- Community health workers
- Telehealth
- Community outreach
- Professional vs. personal CGM
- Point-of-care HbA1c

American Diabetes Association Professional Practice Committee; 1. Improving Care and Promoting Health in Populations: Standards of Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Supplement_1): S11–S19.
https://www.cdc.gov/diabetes/health-equity/improving-access-education.html. August 9, 2024.

POCT U

Point-of-Care HbA1c Testing and Quality Control Measures

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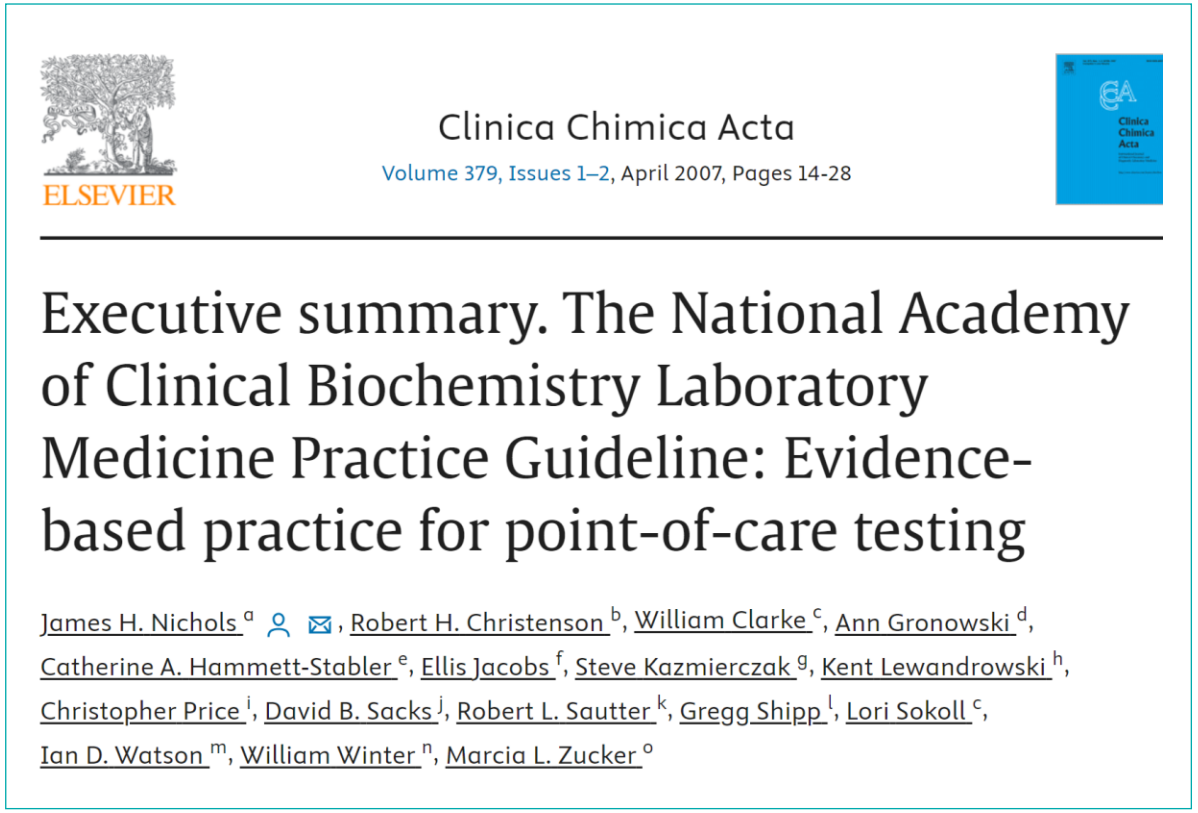
Dr. Nichols has no disclosures for this program.

Learning Objectives

1. Address benefits of utilizing point-of-care HbA1c testing
2. Discover how to assess bias between test and device type in diabetes management
3. Apply current quality control measures for improved glucose management

POCT Definition

- Clinical laboratory testing conducted close to the site of patient care, typically by clinical personnel whose primary training is not in the clinical laboratory sciences or by patients (self-testing).
- POCT refers to any testing performed outside of the traditional, core or central hospital laboratory.



ELSEVIER

Clinica Chimica Acta

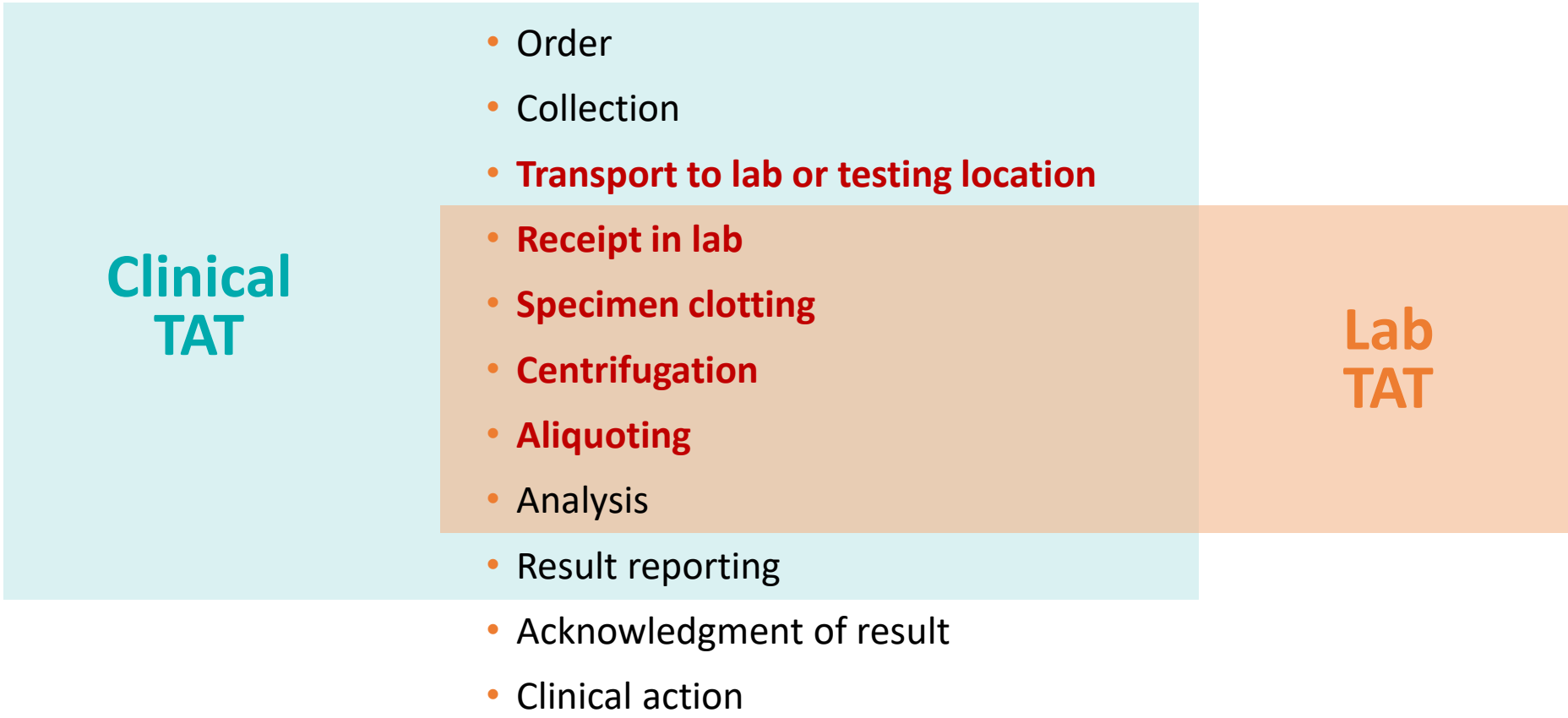
Volume 379, Issues 1–2, April 2007, Pages 14-28

Executive summary. The National Academy of Clinical Biochemistry Laboratory Medicine Practice Guideline: Evidence-based practice for point-of-care testing

James H. Nichols [a], Robert H. Christenson [b], William Clarke [c], Ann Gronowski [d], Catherine A. Hammett-Stabler [e], Ellis Jacobs [f], Steve Kazmierczak [g], Kent Lewandrowski [h], Christopher Price [i], David B. Sacks [j], Robert L. Sautter [k], Gregg Shipp [l], Lori Sokoll [c], Ian D. Watson [m], William Winter [n], Marcia L. Zucker [o]

Nichols JH (editor); National Academy of Clinical Biochemistry. Laboratory Medicine Practice Guidelines: Evidence Based Practice for Point of Care Testing. AACC Press: 2007.

Test Result Turnaround Times



Steps eliminated with POCT

Point-of-Care Testing

- Rapid test result turnaround times
- Onsite patient counseling, faster modification of diet and medications
- Reduced staff time, fewer phone calls, fewer patients lost to follow-up

- Convenience - capillary fingerstick vs. venous phlebotomy
- Native samples (unprocessed blood)

- Simple - can be performed by non-laboratory operators with minimal training and orientation
- Most POCT are CLIA-waived tests in the U.S.
- Minimal regulations

CLIA

- Clinical Laboratory Improvement Amendments of 1988
- CLIA describes good laboratory practices for U.S. tests
- Applies to all tests performed for clinical/patient care
- Enforced by CMS the CLIA regulations cover testing regardless of location
- CLIA waived testing has only 3 requirements
  - Pay biennial fee (every 2 years) for CLIA certificate renewal
  - Follow manufacturers instructions for use
  - Allow the site conducting testing to be inspected

Clinical Benefits of POCT HbA1c

Improved diabetes management/ treatment adaptation

- More appropriate in POCT group (79% vs. 71% $P = 0.003$
- > 1000 type 2 diabetics)

Improved glycemic control

- (-0.57 ± 1.44% $P < 0.01$) at 6 months in 100 insulin treated type 1 and type 2 diabetics where HbA1c available at visit vs. 101 controls lab HbA1c)

Higher patient satisfaction with sample collection process

- More confidence in process ($P < 0.001$)
- Enhanced relationship with physician ($P = 0.01$)
- Decreased patient revisits (up to 61% fewer after implementing POCT)

Emerging evidence supports POCT cost-effectiveness

- Total test number/per patient visit (-21% $P < 0.0001$)
- Telephone calls to patients (-89% $P < 0.0001$)
- Number of results letters mailed to patients (-85% $P < 0.0001$)
- Number of follow-up visits for abnormal lab result (-61% $P = 0.002$)

Schnell O, et al. *J Diabetes Sci Technol.* 2017;11:611-617.

HbA1c Accuracy

Room for improvement

While some POCT HbA1c systems have shown acceptable analytic performance, not all have.

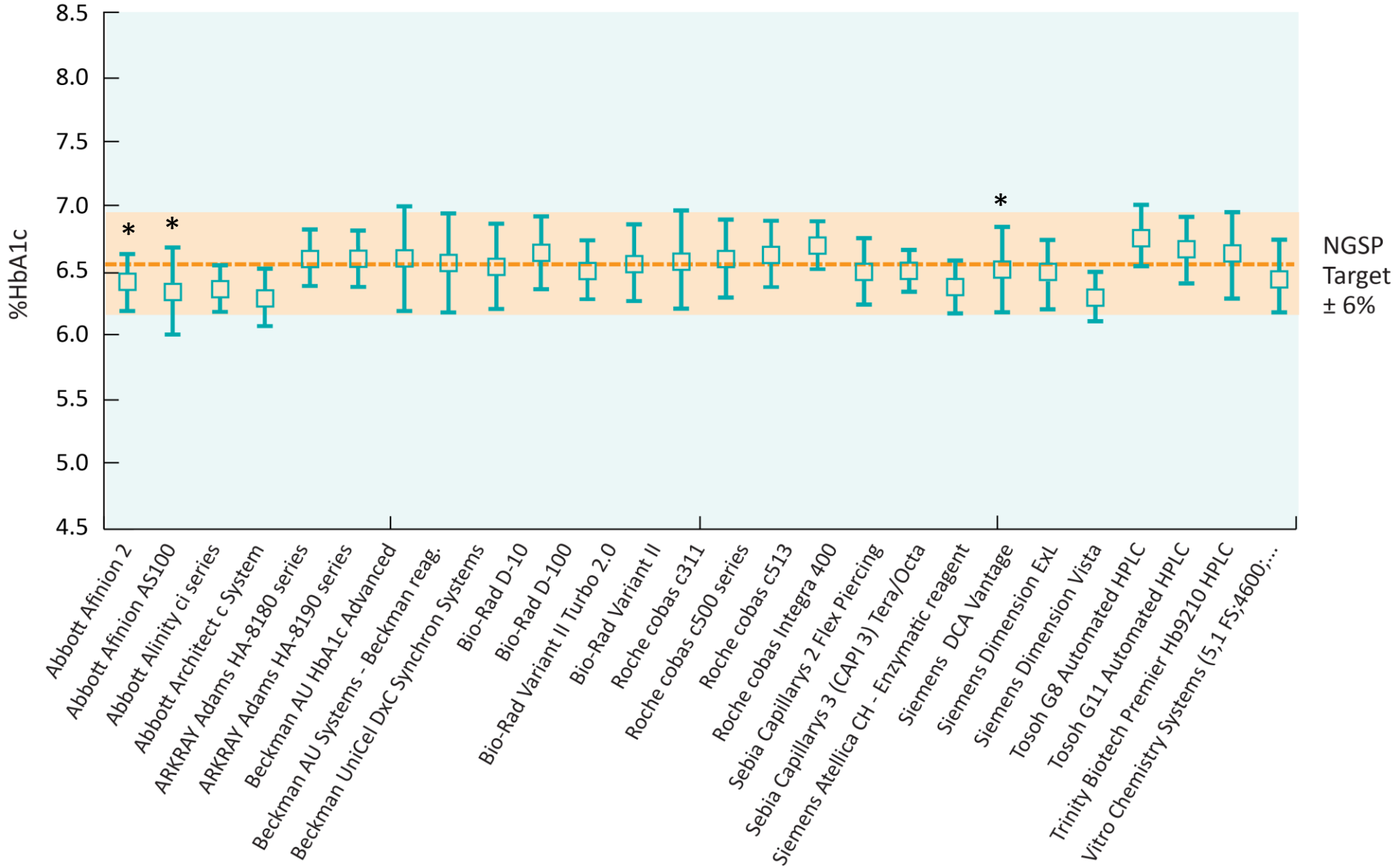
- Limits the use of POCT HbA1c for diagnosis of diabetes.

NGSP = National Glycohemoglobin Standardization Program

- NGSP's purpose is to standardize HbA1c test results to those of the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) — which established the direct relationships between HbA1c levels and outcome risks in patients with diabetes.
- U.S. reports HbA1c (% total Hb); Europe IFCC HbA1c (mmol/mol Hb)
- Bias for each methodology calculated from NGSP Target using fresh samples

Schnell O, et al. *J Diabetes Sci Technol.* 2017;11:611-617.
NGSP.org

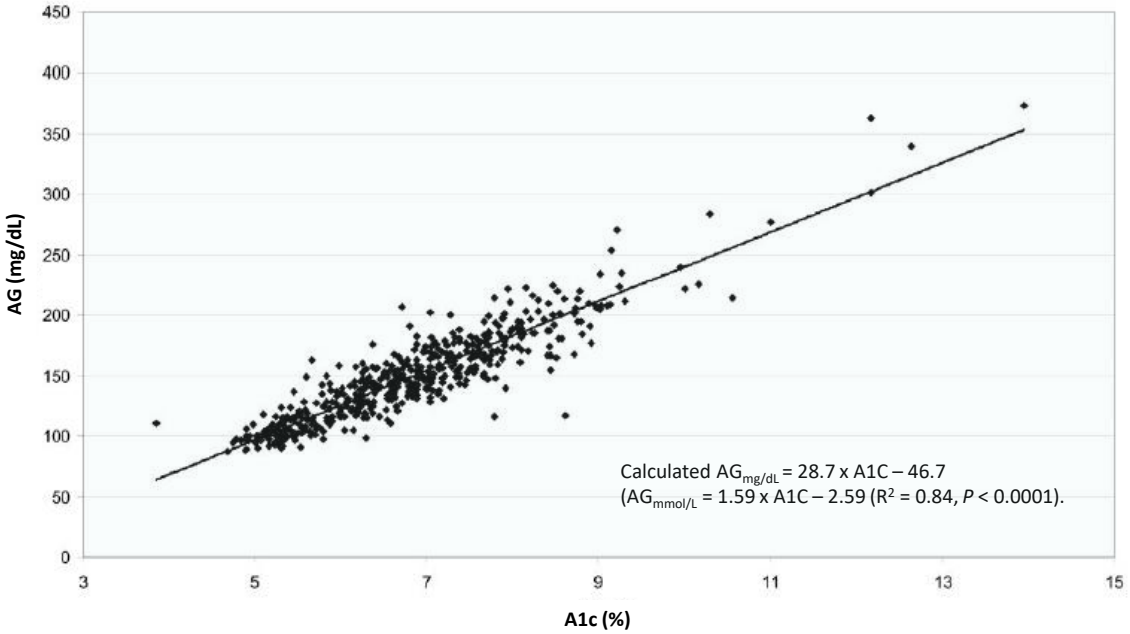
CAP
GH5B 2024
6.55% level
(mean ± 2SD)



* Point-of-care devices

Estimated Average Glucose

Linear regression of A1C at the end of month 3 and calculated AG during the preceding 3 months.



Estimated Average Glucose

A1C (%)	mg/dL*	mmol/L**
5	97 (76-120)	5.4 (4.2-6.7)
6	126 (100-152)	7.0 (5.5-8.5)
7	154 (123-185)	8.6 (6.8-10.3)
8	183 (147-217)	10.2 (8.1-12.1)
9	212 (170-249)	11.8 (9.4-13.9)
10	240 (193-282)	13.4 (10.7-15.7)
11	269 (217-314)	14.9 (12.0-17.5)
12	298 (240-347)	16.5 (13.3-19.3)

Data in parentheses are 95% CIs. *Linear regression eAG (mg/dL) = 28.7 x A1C – 46.7. **Linear regression eAG (mmol/L) = 1.59 x A1C – 2.59.

- Hemoglobin A1c reflects average hemoglobin glycosylation over span of red blood cell life (90 - 120 days)
- Converting HbA1c (%) to glucose (mg/dL) more familiar to insulin dosing for diabetic patients
- eAG mg/dL = 28.7 x HbA1c % - 46.7

Nathan DM, et al. *Diabetes Care.* 2008;31:1473-1478.

Ensuring Analytical Quality

Follow manufacturer recommendations
for quality control frequency

CLIA - minimum 2 levels of QC each day

Develop an Individualized Quality Control Plan

- Based on risk management to reduce frequency of QC
- Understand risks at each step of testing process

Implement total quality assurance

- Ensure operator training and competency
- Maintain the analyzer – Correlate POCT A1c with lab HbA1c
- Manage the environment, reagents, controls

Supplement QC with proficiency testing

Schnell O, et al. *J Diabetes Sci Technol.* 2017;11:611-617.

Verify Clinical Quality

- Does the HbA1c result match the clinical picture?
- eAG agrees with glucose levels prior 4 months?
- Consider conditions affecting Red Cell Turnover
  - Hemoglobin variants (HbS, HbC, HbD, methemoglobin, etc.)
  - Drugs (dapsone, antiretrovirals)
  - Chronic liver disease
- Recent red cell transfusion

Inappropriately Low HbA1c	Inappropriately High HbA1c	Variable Effect on HbA1c+
Hemolysis	Iron deficiency	Fetal hemoglobin
Certain hemoglobinopathies	Vitamin B12 deficiency	Methemoglobin
Recent blood transfusion	Alcoholism	Certain hemoglobinopathies
Acute blood loss	Uremia	
Hypertriglyceridemia	Hyperbilirubinemia	
Drugs	Drugs	
Chronic liver disease		

Postulated Mechanism	Falsely Low HbA1c
Increased erythrocyte destruction	Dapsone
	Ribavirin
	Antiretrovirals
	Trimethoprim-Sulfamethoxazole
Altered hemoglobin	Hydroxyurea
Altered glycation	Vitamin C
	Vitamin E
	Aspirin (small doses)

Unnikrishnan R, et al. *Indian J Endocrinol Metab.* 2012;16(4):528-531.

Fructosamine

- Consider fructosamine as HbA1c alternative
- eAG = (0.5157 x Fructosamine) - 20

Fructosamine levels and estimated mean glucose levels

Fructosamine level µmol/L	Estimated mean glucose level (mg/dL)*
205	85.7
215	90.8
225	96.0
235	101.1
245	106.3
255	111.5
265	116.6
275	121.8
285	126.9

*Average glucose levels = 0.5157 x fructosamine – 20.

Approximate comparison of glucose, fructosamine, and A1c

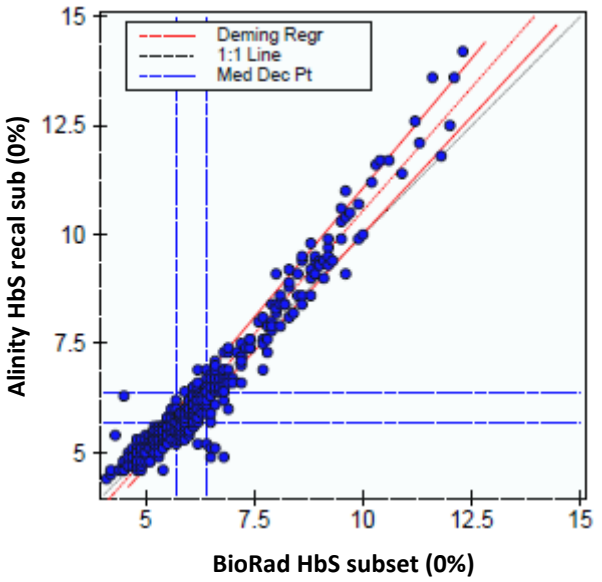
Glucose (mg/dL)	Fructosamine (µmol)	A1C (%)
90	212.5	5.0
120	250	6.0
150	287.5	7.0
180	325	8.0
210	362.5	9.0
240	400	10
270	437.5	11.0
300	475	12.0
330	512.5	13.0
360	550	14.0
390	587.5	15.0

de Andrade ML, et al. *Arch Endocrinol Metab.* 2023;67:262-5.

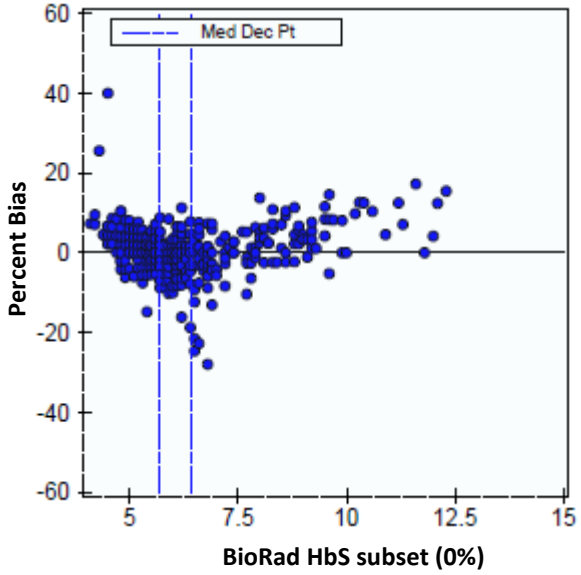
Hemoglobin Variants and HbA1c

- Without Hemoglobin A, cannot make HbA1c, S Disease (HbSS), C disease (HbCC), etc.
- We examined 700 samples analyzed by HPLC and automated Clinical Chemistry HbA1c tests
- Biases outside ± 5% noted with all hemoglobin trait conditions (the proposed NGSP target goal)
- Mean difference (640 samples) -0.05 to +0.13%
- 60 samples without paired result both methods
- 35/700 samples reported results on Clinical Chemistry analyzer when outside HPLC reporting range (low HbA < 40% or elevated Hb variant > 40%)
- Methods that report only an HbA1c result (including POCT analyzers) without separating Hb fractions may give misleading results

Scatter Plot



Percent Bias



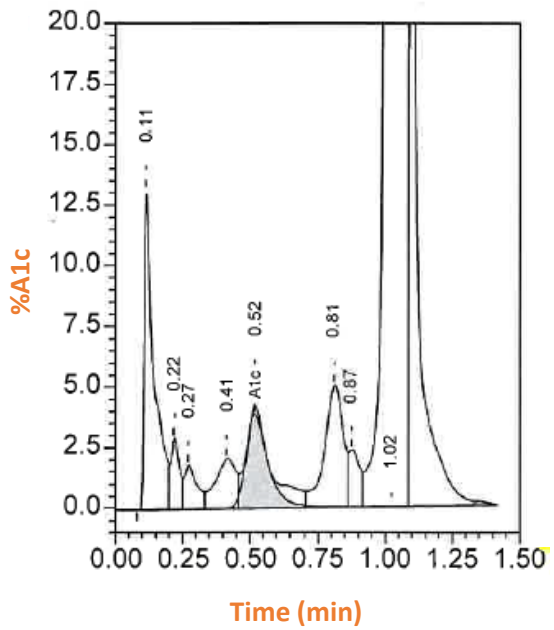
Nichols JH, et al. *J Appl Lab Med.* 2023;8:1127-1132.

Recent Blood Transfusion

- 48 y/o Female - cirrhosis
- HbA1c = 3.9%
- eAG = 65 mg/dL
- Glucose = 72 - 144 mg/dL
- Recently transfused 2 units packed RBC 10 days prior to sample collection

Peak Name	NGSP %	Area %	Retention Time (min)	Peak Area
Unknown	—	4.4	0.112	92901
A1b	—	0.8	0.217	17247
F	—	0.8	0.271	16455
LA1c	—	1.1	0.414	23722
A1c	3.9*	—	0.518	61991
P3	—	3.2	0.809	67283
P4	—	0.8	0.874	17929
Ao	—	86.0	1.023	1829488
*Values outside of expected ranges			Total area:	2,127,015

HbA1c (NGSP) = 3.9*%

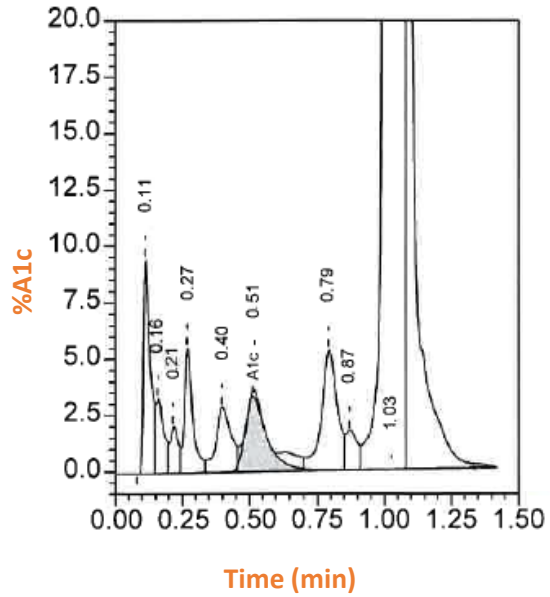


Nichols JH, Berman M, Carrillo A, Manning S. Comparison of HbA1c Quantification in the Presence of Hemoglobin Variants of an HPLC Assay with an Enzymatic Assay. *JALM* 2023; 8:1127-1132.

Cirrhosis

- 35 y/o Female - Cirrhosis
- HbA1c = 3.3%
- eAG = 48 mg/dL
- Glucose = 78 - 123 mg/dL

Peak Name	NGSP %	Area %	Retention Time (min)	Peak Area
Unknown	—	2.2	0.109	34428
A1a	—	0.8	0.156	13161
A1b	—	0.5	0.215	8068
F	—	1.5	0.268	23259
LA1c	—	1.4	0.398	22465
A1c	3.3*	—	0.513	36534
P3	—	2.7	0.790	43005
P4	—	0.6	0.867	10034
Ao	—	87.8	1.025	1372895
*Values outside of expected ranges			Total area:	1,563,849



HbA1c (NGSP) = 3.3*%

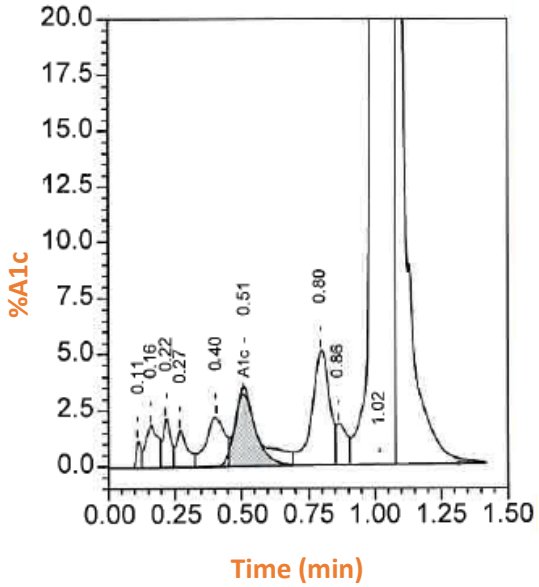
Nichols JH, Berman M, Carrillo A, Manning S. Comparison of HbA1c Quantification in the Presence of Hemoglobin Variants of an HPLC Assay with an Enzymatic Assay. *JALM* 2023; 8:1127-1132.

Lung Transplant on Dapsone

- 71 y/o Female - Lung Transplant on dapsone (an anti-infective drug)
- HbA1c = 3.2%
- eAG = 45 mg/dL
- Glucose = 83 - 107 mg/dL
- Fructosamine = 254 mmol/L
- eAG from fructosamine = 111 mg/dL

Peak Name	NGSP %	Area %	Retention Time (min)	Peak Area
Unknown	—	0.2	0.109	3827
A1a	—	0.8	0.156	15633
A1b	—	0.6	0.215	11106
F	—	0.6	0.268	12100
LA1c	—	1.1	0.401	22544
A1c	3.2*	—	0.508	46047
P3	—	3.0	0.795	60066
P4	—	0.6	0.862	12333
Ao	—	90.7	1.016	1787966
*Values outside of expected ranges			Total area:	1,971,623

HbA1c (NGSP) = 3.2*%

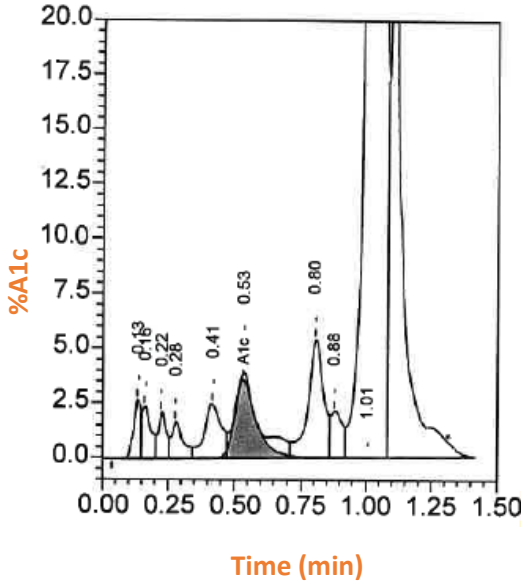


Antiretroviral Drugs

- 48 y/o Male - HIV+ on Biktarvy
- HbA1c = 3.6%
- eAG = 57 mg/dL
- Glucose = 87 - 113 mg/dL prior month
- Fructosamine = 209 mmol/L
- eAG fructosamine = 88 mg/dL

Peak Name	NGSP %	Area %	Retention Time (min)	Peak Area
Unknown	—	0.6	0.158	7740
A1a	—	0.7	0.132	7924
A1b	—	0.5	0.223	6481
F	—	0.6	0.278	7220
LA1c	—	1.2	0.414	15067
A1c	3.6*	—	0.532	30429
P3	—	2.8	0.804	33333
P4	—	0.8	0.879	9719
Ao	—	90.2	1.006	1087840
*Values outside of expected ranges			Total area:	1,205,752

HbA1c (NGSP) = 3.6*%



Summary

- POCT HbA1c can provide faster turnaround of test results by improving diabetes management adjustments made at time of clinic visit
- Efforts by NGSP to harmonize HbA1c methods and minimizing method biases, but POCT methods still have room for improvement
- Analytical assay quality can be achieved with good laboratory practice and regular QC, operator competency checks and management of analyzer and environment (reagent, QC and supplies)
- Differences between HbA1c result and patient condition may be due to alteration in red cell turnover, drugs, liver disease or recent transfusion
- Clinicians should “treat the patient not the number” and consider analysis by a different HbA1c method or fructosamine

POCT

Q&A

Current and Future Device Data & Approvals

Information presented on these slides is current as of August, 2024.

For updated information on CAP data and device approvals, please visit the following:

- CAP surveys: https://ngsp.org/CAPdata.asp
- CGM approvals: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm

To access the full ADA *Standards of Care in Diabetes*, please visit:

https://professional.diabetes.org/standards-of-care

POCT

Thank you.