AMGA Member Best Practices

Time-in-Range: An Intuitive CGM Metric to Integrate in Your Clinical Practice
Continuous glucose monitoring (CGM) use has created new glucose metrics for people with diabetes and their healthcare providers. Standard A1C tests only measure an average blood glucose. CGM highlights glucose data on time in range (within, above, below). This valuable insight provides critical information for treatment decisions and opportunities for health behavior changes.

Dr. Karen Earle, the Chief of Endocrinology and Director of Diabetes Services at California Pacific Medical Center and Chief of Division of Medical and Surgical Specialties at Sutter West Bay Medical Group, shared consensus guidelines for time in range (TIR) measurement and goals, why TIR is an intuitive metric to guide treatment, and key principles when educating people with diabetes about TIR goals.

**Moving Toward Better Measurement**

Dr. Earle began with a discussion of the traditional treatment for people with diabetes. She stated, “For most of my 14 years in practice, patients would come see me every three months. They’d come into the office. We do a point of care, hemoglobin A1C, and then we’d make some management decisions based on that A1C. If I was lucky enough to get some fingerstick blood glucose data, we would certainly look at those data as well. But as you know, it’s difficult, one, to get patients to collect the data for you. And, too often they forget their meter or don’t write it down or it’s impossible to get data from the patients.” This model is not practical for managing diabetes.

Furthermore, A1C alone really does not help people understand their diabetes. It does not explain the impact of exercise or dietary behavior on glucose. If the A1C is high, it shows they are not meeting their healthy diabetes goals. However, it does not direct a path for improved care. Frankly, A1C, while a valuable measurement, does not provide all the information necessary for diabetes care. Dr. Earle identified several specific areas where A1C falls short.

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— Karen Earle, M.D., Chief of Endocrinology and Director of Diabetes Services, California Pacific Medical Center, and Chief of Division of Medical and Surgical Specialties, Sutter West Bay Medical Group
First, she reminded participants that A1C is an average, and the target goal of A1C less than 7% corresponds to a blood glucose level of 154 mg/dL, but in reality, it encompasses a range from 123 to 185 mg/dL. “So, you can actually under- or overestimate an individual’s average blood glucose level using an A1C.” Other limitations on A1C include:

- It does not indicate the extent or timing of hypoglycemia or hyperglycemia
- It does not reveal glycemic variability
- It has limited utility for insulin dosing decisions
- It is unreliable in patients with hemolytic anemia, hemoglobinopathies, or iron deficiency
- It underestimates in those with end stage kidney disease and in those who are pregnant
- Correlation with mean glucose can vary among races

Real-time continuous glucose monitoring (RT-CGM) addresses many of these issues. In particular, it provides real-time sensor glucose readings, not just averages. It highlights variability with directional arrows that indicate glucose rate of change; and it provides key information on the extent and timing of hypoglycemia or hyperglycemia. Guided by the International Consensus on TIR, the American Diabetes Association and American Association of Clinical Endocrinologists guidelines, (see Figure 1), CGM use can help clinicians and people with diabetes make more informed decisions about healthy eating, exercise, and medication dosing for diabetes.

The Dexcom G6 real-time CGM system, used by Dr. Earle in her practice, records up to 288 glucose readings throughout the day. It can be used with Android or Apple devices, as well as a separate receiver. Color-coded data are displayed in real-time in a manner that is easy to read and understand. No finger sticks are required, which is life-changing for people who used to check their blood glucose as frequently as 10 times a day. It provides options for customizable alerts and has a fixed “urgent low” alarm and a predictive “urgent low soon” alert, which is a very helpful feature to warn individuals of an impending low glucose, less than 55 mg/dL, within 20 minutes, so they can take action to avoid a low. The Dexcom CLARITY app allows patients to share these data with their healthcare providers and up to 10 “followers,” using the separate Follow App, which is especially useful for children and seniors who have multiple caregivers.

Figure 1: Core CGM Metrics and Goals for Time in Range (TIR)
**Time in Range (TIR)**

Dr. Earle identified key metrics provided by the CGM reports to help people increase TIR. First, she noted, the number of days the patient is actually using the CGM. Ideally, you want to be looking at about 10 days to two weeks worth of data. It is also important to know the percentage of time that the CGM is active, which ideally is at least 70% of the time. The mean glucose for the overall time period is another useful metric. Dr. Earle noted that it is very important to explain to patients that the glucose management indicator (GMI) is not the same as A1C. The GMI takes the mean glucose level and provides an approximate A1C based on the glucose levels during the time range.

Per the International Consensus Guidelines, the TIR goal is at least 70% of glucose values between 70-180 mg/dL. Because you want to minimize time outside of range, you are looking for time below range (< 70 mg/dL) of less than 4% and time above range (>180 mg/dL) of less than 25% of the day. Time significantly above range (>250 mg/dL) should be no more than 5% (see Figure 2).

Another key metric is the coefficient of variation (CV), which shows glucose variability. It is basically the amplitude, frequency and duration of glucose fluctuations. The goal is to keep variability under 36% for most patients. A high CV typically indicates a higher risk of hypoglycemia.

Dr. Earle noted that the goals cited are designed for most non-pregnant adults with type 1 and type 2 diabetes. They may need to be adjusted for high-risk or older patients. For example, for individuals you are really concerned about the risk of hypoglycemia and have less concern about hyperglycemia, you might increase the time above range to <50% and adjust the TIR goal to be >50%, and the goal for all lows may be less than 1%. You may also want to lower the CV goal to 33%.

**Why is TIR important?** Studies have shown than increasing TIR correlates with improved A1C. One study showed being within range (70-180 mg/dL) for 70% of the time correlates approximately with an A1C of 6.7%. In addition, every 10% increase in TIR correlated with a 0.8% A1C reduction. In another study, 70% TIR correlated with a 7.0% A1C, and every 10% increase in TIR was associated with a 0.5% A1C reduction.

![Figure 2: Time in Range Targets and Hours per Day](image)
Dr. Earle stated, “more time in range, lower A1C, and our standard of at least 70% TIR correlates with an A1C at goal.”

Also, a post hoc analysis of several studies highlighted an association between TIR and diabetes complications. The data demonstrated each 10% decrease in TIR was associated with a 64% increase in retinopathy progression and a 40% increase in microalbuminurea. However, a 10% increase in TIR was associated with a 19% reduction in urinary albumin excretion. TIR was significantly associated with a prevalence of all stages of retinopathy in type 2 diabetes, even after adjusting for clinical risk factors, including A1C. A 10% decrease in TIR was also associated with a 5% increase in cardiovascular-related mortality and an 8% increase in all-cause mortality. “I know these are not randomized clinical trials,” stated Dr. Earle, “but the data are certainly very promising that by achieving goal time in range—or even if you’re not at goal, but increasing that time in range—is going to help prevent complications for a patient. And that’s a really, really important concept.”

Improving Treatment

Dr. Earle shared CGM reports from two patients, both with A1C of 7% (see Figure 3). One patient (upper panel) experiences both hypoglycemia (pink zone) and hyperglycemia (yellow zone) with glucose levels above 180. Also, the patient is within TIR goal (between 70 and 180 mg/dL) only 40% of the time. This patient is spending most of the day either above or below their goal range. Compare that to the patient in the lower panel, who is spending 70% of the time within range. “I think all of us would agree,” noted Dr. Earle, “that we’d prefer to see that lower panel with our A1C of 7%. And the person living with diabetes will feel much better.”

“One thing that I think is important for patients to visualize or to be thinking about, as I’m talking about time in range is ‘what does that mean for me?’” Dr. Earle explained that a recommended TIR of >70%, correlates to over 16 hours per day. Each 15 minutes is about 1%. So, minimizing severe lows, for example, to less than 1% means less than 15 minutes throughout the day should be spent below 54 mg/dL. “We want to minimize time spend less than 54 mg/dL as much as possible.”
For time above 180 mg/dL, the goal is less than six hours total with less than one hour greater than 250 mg/dL.

“When I have a patient with diabetes who’s wearing a CGM, I really want to be looking at the data with the patient, talking with them about the data and making decisions.” Dr. Earle shared several other strategies for helping patients understand and respond to the CGM data to improve TIR:

- **Strive for FNIR:** Flat, Narrow, and In Range. Patients using CGM with their smartphone can see their glucose number in the middle, an arrow indicating whether it is going up, down, or staying steady. There is also a graph displaying levels for the past few hours. Dr. Earle suggested FNIR as an easy reminder to keep that visual a flat and narrow line that stays in the gray zone as much as possible (i.e., in the range of 70-180 mg/dL.)

- **Be curious.** Encourage patients to experiment. “One thing that I think is really amazing, is when patients start asking themselves questions like ‘what happens when I go on the treadmill for half an hour? What happens to my glucose if I, you know, eat, under 30 grams of carbs with each meal for a day?’ They do little experiments and figure out what the response is, which leads to discoveries about what works or doesn’t work in terms of managing glucose levels and what keeps them in-range.”

- **Ongoing learning.** At first, people using CGMs may feel a little overwhelmed by all the data, but over time they will start learning more and asking more sophisticated questions. Help them understand it is a continuous process.

- **Using patterns.** Looking for the patterns is part of what Dr. Earle does when she reviews CGM reports, but she also commented that it’s important that the person with diabetes try to look at their patterns, as well. Using the CLARITY app on their phone or computer, people with diabetes have access to the same reports as clinicians.

- **Use empowering language.** When talking with people about their CGM reports, be objective about data (no judgement) and empower action. Help the person to actively participate in developing the treatment plan. Ask them what choices they are able to make to help them be successful.

- **Celebrate:** “Having diabetes is really, really hard,” said Dr. Earle. It’s important to focus on the small wins rather than the negatives. For example, Dr. Earle has said, “Look this day was your best day! How did you manage to stay in range 90% of the time? What was happening on this day? Can you do more of what was working?” This positive approach encourages people and empowers them to engage in diabetes self-management.

Dr. Earle provided a case study to show how this approach can help improve outcomes. The patient, a 53-year-old man with longstanding diabetes, arrived at the clinic as a new patient. He did not check his blood glucose on a regular basis and did not bring in his blood glucose meter with him. He was on Metformin, 2000 mg a day, and Tresiba long-acting insulin, 10 units a day. His A1C was 13%. “So, I think he needs more insulin, but I’m not really sure. He hasn’t been checking. It’s unclear exactly how much insulin he’s been taking over the last couple of months. And so, whenever I don’t know what to do in clinic, my next step is to gather more information. And so, for this patient, I said, ‘I’m going to put a Dexcom G6 on today and I want to see you back in two weeks because I need to know what’s happening with your glucose levels before I make a decision to increase your insulin dose without all the facts.’”

The report two weeks later showed an average glucose of 243 mg/dL. He was not having any hypoglycemia, but TIR was only 15% and he was spending most of his time above range. One thing Dr. Earle noticed is
that the patient was fairly flat and in-range overnight, but spiked at breakfast, then more after lunch, and even more after dinner. She stated, “And so, he’s really having a postprandial hyperglycemic problem.” So, Dr. Earle added Humalog 10 units three times a day with meals, and the patient was advised if his glucose values were high, he could add a correction dose. After another month of using the Dexcom G6, he improved significantly (see Figure 4).

“I would love to take credit for all of this,” said Dr. Earle, “but a lot of this is the patient making changes. He understood. ‘Wow. When I eat this food, my glucose really, really spikes. And when I take the insulin, it really avoids some of those spikes.’ He’s still having some highs after lunch and probably needs a little bit more insulin with lunch or maybe needs to adjust the carbs he’s eating with lunch. But again, much improved with just six weeks on a Dexcom G6.” Indeed, Dr. Earle noted there are some data suggesting that people who are looking at the Dexcom CLARITY app weekly to learn from their glucose patterns and make decisions based on those levels have seen an improvement in their TIR, in some cases by as much as a 15%.

In closing, Dr. Earle encouraged participants to not be intimidated by CGM. “Patients aren't intimidated. They really embrace it. And honestly, now,” she said, “I can't imagine managing people with diabetes without CGM. I've just found CGM to be a game changer for people with diabetes. So, I really encourage everyone to give it a try and see if you can make a difference for some of these people living with diabetes.”

References