

**RICHARD BERGENSTAL:** Hello, and welcome to today's discussion on sensor-based glucose monitoring. You're now in what we call the diabetes intelligence zone. We have a lot to discuss today on glucose sensing, and we're going to break this into three modules. I'm Dr. Richard Bergenstal, the executive director of the International Diabetes Center in Minneapolis, Minnesota. Let me outline the objectives of the three modules by showing you this graphic.

This is a graphic that shows our overall aim of these three modules, moving from A1c to the AGP and time and range. And over these three modules, module 1, we're going to learn how to analyze CGM data and the AGP. Module 2, we're going to personalize your treatment goals. And module 3, we're going to learn how to act on that AGP data to optimize diabetes management.

The three modules will be accordingly, analyzing glucose, ambulatory glucose profile. Module 2 will be personalizing the data management, and module 3 will be acting to improve care. Let's start with module 1, analyzing the ambulatory glucose profile. These are my conflicts.

And our goal today is really to optimize glucose management. That's what we're all doing as clinicians, as educators. We're going to be looking at the blood glucose monitoring and continuous glucose monitoring. The current standard is having an A1c and having a blood glucose test. The A1c is not particularly easy to describe, that glucose binding to the beta chain of the hemoglobin. Glucose monitoring can be complicated because there's a wide range of meters to choose from. And here's what you often see in the office, I'm sure.

You see a logbook, well, there's a lot of glucose in the morning, but not too much more data to guide you. So we want to move along and explain how in the middle panel here on the top, you see those three blood sugars a day. And they look pretty good. But when you look down below and you have continuous glucose monitoring with blood sugars every 5 minutes, 1 minute to 5 minutes, you have 288 values in a day, that makes a big difference.

All of a sudden, you start to see different patterns. And if we take all of those blood sugars in a day and put two weeks of them together, you get an ambulatory glucose profile report on the far right. One page, three components, and that's what we're going to walk through today in module 1, understanding the simplicity and yet the completeness of a one page report.

Well, what is this glucose monitoring that we're talking about? Very quickly, it's a sensor that's placed under the skin, a small filament that senses the interstitial glucose. And there's a little bit of lag time, maybe five to six minutes between that interstitial and the vascular space. But that hardly makes a difference when you're following the trends and multiple tests across the day.

We've moved a long ways in CGM technology to now, where we have factory calibrated sensors. We have non-injunctive use, which means you don't have to confirm it in most cases, with any blood glucose monitoring. And they're incredibly accurate today. There's a category called interoperable CGM, the highest level of accuracy.

We can use that real time and get a continuous reading, and with alerts and alarms. We can scan over the sensor intermittently and look at it whenever we want to get a reading. Or we can use a type of CGM that's called professional CGM, and that's where the clinic owns the system but gives it to a patient and they do a reading that can either be blinded or unblinded for a one time reading to look back at those 24-- at that 14 days of glucose patterns.

But you might ask, well, if we're going to move to a new technology, is it really better than the previous technology? So here is one of those meta-analysis I'll just show you quickly. But it basically looks at continuous glucose monitoring compared to finger stick blood glucose monitoring. And you see, if you just look at the bottom down to the right, that in almost every situation, this is showing in favor of the CGM, 0.25% to 0.3% of a A1c.

So sometimes, if you're sitting there at 7.8 and you'd like to be down to 7.5 or 7.4, the CGM really makes a difference compared to the SMBG. And then one more piece of data, just to get you comfortable that moving to the CGM is really a worthwhile endeavor. This is a meta-analysis done just in May of 2020. And it looked at type 1 and type 2 diabetes, and it looked at changes in A1c, but it also looked at changes in time and range.

And you can see in both of these graphics, A1c on the left, time and range on the right, that using the CGM was always, almost always more beneficial than using the control arm, which in most cases, was finger stick glucose. So we have good data. We have meta-analyses to say CGM can improve not only time and range, but time above range, time below range, glucose variability, type 1, and type 2 diabetes.

So there seems to be data. Here's the devices. We have four good systems in the United States. The DexCom, we're up to the G6 and the G6 Pro, which is the professional version. We have the Abbott FreeStyle and from Libre to Libre 2. And there's a Libra Pro that is a professional version. Medtronic has a Guardian, and there's even an implantable system three months in the US, six months overseas, hoping for even longer for an implanted sensor.

We've made advances in these standards over these last decade, but particularly, in the last two years. It's really been a turning point. We've determined what the standards should be for the metrics, which I'm going to go through. But in June of 2019, when an international group got together, they said let's refine those metrics and let's decide the targets. Where do we want to aim for with our continuous glucose monitoring? And that was a pivotal trial that was published in June of 2019.

Then, probably even more important, was the January 2020, the American Diabetes Association standards of care, which many of you know, comes out every January that says, this is our current state of knowledge. And in their technology chapters, in their diagnostic chapters, they included important elements of CGM. And there's three components we're going to go through in the next few minutes. There are 10 core CGM metrics. What are the CGM targets for time and range? And also, a systematic way to look at a single one page report called the ambulatory glucose profile-- all of those recommended in the ADA standards of care.

So here's the 10 core metrics. There are dozens, if not hundreds, of ways to look at all this incredible glucose data coming out of a sensor. But here's the 10 that this international group thought was really the core clinical metrics that every clinician, every educator, every pharmacist should know as they're working with patients. Do you have enough data, 10 to 14 days? Was the sensor worn at least 70%, 80% of the time? What's the mean glucose? What's the glucose management indicator? I'm going to come back to that in module 2. That's the old estimated A1c. What's the glycemic variability? How much do those sugars go up and down, up and down? And what should that value be? Less than 36 for the coefficient of variation.

But then you see on this 10 core metrics, 5 of them are different times and ranges. How much time are you spending in the target range, highlighted in the middle there, two levels of time above target range, and two levels of time below target range? And if you want, you can get familiar with those numbers on the right hand side, or those labels on the right hand side. Level 1 hypoglycemia, level 2 hypoglycemia, low, very low, high, very low, very high.

So those are the 10 core metrics. The more you understand them, the better we'll do. So here's the one page report. The consensus group said, it's really helpful to boil it down to a consistent look of the glucose data. And there's three panels on this report. The top panel is metrics and targets. The middle panel, we call the AGP profile, 14 days all put together from midnight to midnight. And the bottom are the daily views, the 10, 13, 14 days that get put together to make up that middle panel. One report, three panels.

Let's explore them just a little more so you can actually see them here and get to know these metrics. The AGP was picked in part because it did meet all the standards. All the 10 core metrics are right here for you in the top metrics panel. I'll label them out. These are the 10 that we said were important. All 10 are right there on the AGP CGM report. The first two again, are you getting adequate data?

Then you go to the average glucose. The glucose management indicators for the glucose variability is 5, and then the 5 times and ranges. And again, when we look at that time and target range of 47% on the right hand panel, some people like to know the percentage of values. That says, what percent of all your values over those two weeks were in the target range?

Other people say, well, I wish I knew how much time that was. I'm not really interested in percents. So we give you the time, 11 hours and 17 minutes. So if you like time, you've got time. If you want percentage of values, we've got percentages of values. And we can label them as in the target range, low, very low, high, or very high. So that gives you-- that gives you a sense of those metrics.

Now what's important is to have the targets. Because when I show you the 47% time and range, your first response might be, well, that's interesting. Is that good, or is that bad? Where should I be to minimize my risk of complications? Where would you like me to be? So we had to design the targets and come up with a consensus opinion. And you'll see over on the left hand side, well, no. 47% is not a target. The target is greater than 70%. Almost 17 hours a day, we'd like you to be in the target. And this patient was spending 11 hours, 17 minutes in the target.

And we'd like there to be less than 4% of values or less than an hour under 70. And we'd like there to be less than 1% of values or 15 minutes under 54. So that's the key. Those are the key metrics. Those are the targets. And you might say, well, where did you come up with those targets? You didn't just pull them out of a hat, I imagine.

No. We used the actual data that was available to us to say what's possible. And what can you strive for that's going to minimize your risk of complications? It turns out that if you have 70% time and range or greater, you're going to have an A1c of 7% or less. The correlation is pretty good. Again, that's an average correlation. Yours might vary a little bit on either side. 50% time and range gave you an A1c of 8%.

So if you do the math, it's about every 10% change in time and range, about a 0.5% change in the A1c. So you know the targets. We know what you're aiming for. You know the nomenclature. That's the top panel. Now you might say, OK, I'm ready. I understand it. What do I do when a patient walks in the / I'm just going to give you the very quick version here, and then the subsequent modules 2 and 3, we'll get more into the management.

But here's what I like to do. When a patient comes in, we've got all this incredible data available to us. Go straight to that time and range bar. Look at that time and range bar. It's really nice if you're looking at it together with a patient, or in this day and age, you're looking at it together remotely, virtually. But you're still looking at that bar. And just focus right down on the green and the red.

The goal is more green, less red. More time in range, less hypoglycemia. That's what we're aiming for. And you know the targets. The targets are right over there on the left hand side and they say, is the green at 70% or more? In this case, we tell the patient, no. We've got some work to do. We've got to get more green. We've got to get from 47. We've got to work towards that 70.

How about the red? We'd like it to be less than 4%. This patient has 10% under 74 and 6. We'd like the very low values. We'd love them to be 0, but at least under 1%. This person has 6%. So in our quest for more green and less red, this patient really has some work to do, particularly getting rid of that red, getting rid of those low blood sugars.

So that's the top panel. You've established with the patient that there's some work to do. But now you've got to go to the middle panel and say, well, where should we focus our attention? Where is there room for improvement in this profile? So again, this is the profile, midnight to midnight, all of the 14 days put into one picture, the black line being the median half of the values of all your glucoses are below that. Half are above it. The deeper shaded blue cloud I call it, or pattern there, is the interquartile range. 50% of all your values are within that darker blue, and 90% of all your values are in the lighter shaded blue or gray.

And you can see at a glance when you're low or very low, when you're high or very high. So we hope this will focus the attention. Where should we start? Start with the lows. Treat the hypoglycemia. Get rid of the hypoglycemia first, so just circle it right there. Point it out to the patient. I see that you're spending 5%, 10% of your time around 54, almost 25% of your time under 70 between 1:00 AM and 3:00 or 4:00 AM. Let's tackle that. Let's tackle the hypoglycemia in the afternoon. So address hypoglycemia first.

Remember that word first. It doesn't mean stop there. Let's start there. Then come back to the hyperglycemia, and that's just pretty clear here, something happening after breakfast each day. It probably has to do with that carbohydrate-rich breakfast, or maybe some needs in medication adjustments. But then, if you want to verify that, you're about to make a change. Look at the daily views and just confirm, were there really some lows overnight? Yes, there were.

Look at the red. Look at the red. Look at the red. Was there high in the afternoon? Look at the yellow. Was it weekdays and weekends? So this gives you a good picture of how to proceed and to be confident in your decision. And finally, patients ask me over and over again, OK. I'm beginning to understand the lingo. But what should that picture look like? What would an ideal picture really be that I can strive for over the next three months that we work together?

And I tell them, I'd really love that profile to look flat and narrow and in range. And they look a little funny and say, walk me through that again. So here you go. Patient number one, or let's call this the same patient. First visit, here's the profile. Up, down, it's not flat. That black line is not flat. It's not narrow. You've got quite a bit of variability and you're up above that shaded target range. Come back next time. Work on it.

OK, much better. You're flatter. You're not going up and down, but you still have a fair amount of variability around that median. And you're hovering always at the top of the target range. So you're flat, but you're not narrower in range. Back one more time. Ah, we're making progress. Much flatter, much narrower, but still a little high. You're still running on the top of the 180 mark all the time. Let's make one more adjustment. Keep working on it.

Now this is not easy, but this is our goal. Flat, narrow, and almost all in range. Congratulations, that's what we're aiming for. It's a process. Every 5% increase in that time and range has really helped you clinically. So that's our goal. Slow, steady, can we get there?

In summary then, at module 1, we've talked through this one page three panel ambulatory glucose profile report. On the top, we have the metrics and the targets. We're aiming for more green and less red. In the middle, we have the AGP profile where we're aiming for a flat, narrow, and in range profile. And finally, we have the daily views that show us the glucose patterns to help us optimize diabetes management.

So in module 1, how do you analyze the ambulatory glucose profile? Then in module 2, we're going to talk about personalizing diabetes management to optimize care. And then finally, in module 3, we're really going to learn how to act on all of that CGM data to get that flat, narrow, and end range profile. How do you make adjustments to medications and lifestyle to achieve those goals you're striving for?