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RICHARD BERGENSTAL: I'd like to thank you all for attending this virtual diabetes session. And today, it's a pleasure for me to have an opportunity to talk about using CGM data to optimize diabetes care. And I'm going to focus on moving from standardized metrics to personalized diabetes management. These are my disclosures.

And as you all know, CGM technology is growing worldwide as we are all in a connected world today. And CGM is perfectly suited, since it's cloud based, for remote diabetes monitoring and for helping us manage care remotely. More, now than ever, during this COVID 19 pandemic, optimal diabetes management is critical. So we'll see how CGM can help in that regard as well. Let's look at where we are and where we need to go. Right now, we're using CGM as part of connected care in so many instances. We finally have standardized CGM metrics and reporting, and now I really think it's time that we move on to personalized and optimized diabetes care. That's what using CGM, really, should be all about.

Over the last couple of years, 2019, 2020, there have been at least three key advances in standardizing CGM data. And I want to talk to you, just very briefly, about that. In June of 2019, there was, really, an important meeting the International Consensus Meeting on time and range led by Dr. Battelino. And then in 2020, the American Diabetes Association incorporated into their standards of care that many of us read and depend on, three key features about CGM that I want to highlight with you today.

They outlined 10 core CGM metrics, which include the time and ranges, they included the time and range targets that came from this International Consensus Meeting I just mentioned, and they also emphasized using a standardized report called the Ambulatory Glucose Profile just to help interpret data and guide decision making. So let me briefly go through a couple of these key elements that were in the ADA 2020 standards of care. First was this table on core metrics. I think you all know that when you have CGM and you're getting hundreds of glucose values a day, there's lots of metrics to look at.

But these are the 10 that the international community could agree on and say these are core for most clinicians and even for patients to begin to understand. And I'll go through them quickly. The first two are just, do you have adequate glucose data, the numbers of days worn. 10 to 14 days is optimal, and having at least 70% of data in those days gives you a solid report. Some people like to look at the mean glucose so that's included.

Then there was one called the Glucose Management Indicator. Everyone may not be familiar with that term but I think you know the concept. It's what we used to call the estimated A1C. And sometimes there's a mismatch between your lab A1C and your estimated A1C from the CGM, a term we now call Glucose Management Indicator. And this helps you really personalize your A1C, and I'll just show you the one paper that we published in 2018.

And the table on the left just highlights that only about 19, 20% of the time does the lab A1C and the CGM derived A1C or GMI exactly match, but 28% of the time, if you see right down here, there's more than a 0.5% difference. So that's important to know, and I'll give you one example because examples are always better than just lots of tables. The lab A1C comes back 7.4, the GMI is 6.7, which is the CGM derived A1C value. And you have to take that seriously. You're at 6.7 for this individual with their data and that's not uncommon. Look at that. 12% of people have that 0.7% difference. So be careful in this patient when you're intensifying therapy, smoothing it out, that you don't go too far because their estimated A1C or GMI is 6.7.

So let's look a little further. After the GMI you see the glucose variability, there's hundreds of ways to characterize this up and down and glucose variability. We've selected the coefficient of variation. We want to keep it under 36 if possible. And then the next five of the 10 are really the time in ranges. The middle one is the Time In Range, TIR. It's such a common term now that we're all starting to throw around that to use, which is good, and that's the target value. Can you keep the glucose between 70 to 180 and be in range?

And then there's two values above range, there's two time in ranges below range, and sometimes we give them names like a level two hypo, level two hypo. I like the term, very simple, just low and very low, or high and very high. So let's just explore those for a minute. Remember, I mentioned that time in range consensus meeting, which was an important one, because it took these time in ranges that we all agreed on and said, OK you've got a standard range, what should the value be for optimal, clinical care? What should the target be? And that's important.

So greater than 70% time in range, 70 to 180, or for those of you who use millimoles, 3.9 to 10. Now some people like it to be in minutes and not just 70% of all your values, but can you get up close to 17 hours a day being in that green target range. I want to keep the time below range of less than 70, or 3.9, under 4%, or about an hour. I want to keep the time very low, under 1%. Ideally, we'd like this to be 0, of course, but that's less than 54 milligrams per deciliter, or three millimoles, less than 15 minutes a day. And then we have targets for the high and for the very high as well. Minimize those, increase that time in range, if possible. So now we have got some targets.

Let's come back and look at this table from the standards of care and the last note that's highlighted in red down here below is, why not start with a standardized report so we're all on the same page. One page, a simple report, and the ADA said the Ambulatory Glucose Profile is a good way to start. I'll just show you the picture that was in that consensus meeting and the ADA standards of care. Here's a AGP report. Three panels, metrics and targets on the top, a 24 hour profile in the middle that goes from midnight to midnight that's made up of the 14 days that you're collected, and then the daily views shows every day.

And I'll go through these a little more in detail but that's the one page report, regardless of what device you're using, what CGM. Let's start with one page to start to understand the data. So if we explore it just a little bit more at the top there and we look at that time in range bar, some people call this a stacked bar, but it gives you the values that you've achieved over the period you're looking at, in this case was 14 days. I call these the personal glucose management time in ranges.

This is what you get from your data and we're looking at it together and saying, gosh I want to get that time in range a little higher, remember 70%. I want to get that low, get rid of as much of that red, or low, values as possible. Level one, level two hypo, level one, level two hyper, if you like those terms. The regulatory agencies kind of like these levels.

So on the other side of the equation, while these are the personal management goals over here on the left, on the right, I'm showing you what you'll see sometimes when you look at the journals and you see an article comparing, how did CGM work, how did advanced automated insulin delivery work, and you've got all the CGM data. When you see those articles, they often put it in your time in range, 70 to 180, then they'll say time in range below 70 or time in range above 180. Well, that's easy for the middle target range, 70 to 180, 47%. Personal to population health, it's the same.

When you go time below 70, it's really kind of a combination of level one and two. So just keep that in mind when you're reading the papers. Time below 70, they combine them and then time above 180, combine level one and level two. If you want to report out the 54 and the 250, and I recommend that you do because those are the extremes we really want to get rid of. Those will be added into your metrics as well. So that adds up to not always 100% because you're combining factors. So that's the stacked bar, the personal management time in ranges, what you might see in the journals, talking about time in range. But is this time in range really a valid outcome marker? Should we be spending so much time on it? It makes a lot of sense to see your personal time in range, but does it really work like A1C in terms of correlating with complications? We really have to have confidence in that.

And I'll show you one paper that I think leads us down that path of confidence in using time and range. And this was a study that Dr. Roy Beck and I and many other good colleagues published in 2013, where we took the DCCT data and we calculated the time in range that patients were spending and tried to see if that was a valid indicator, or correlation, at least, with complications. And there was a lot of data. You may not realize, but those 1,440 patients did seven point profiles four times a year for 10 years.

So that's thousands of glucose points that we can look at to see how much time they were spending in range from those seven point profiles. No, it wasn't CGM. It wasn't even around during DCCT, but it's a lot of glucose data to look at. Now, remember the DCCT, everyone knows this curve. As your mean A1C goes up, your risk of retinopathy, in this case, goes up. What would this look like if we did the time in range as opposed to the A1C? Well, here's what it looked like. The curve is very similar. In this case, on the bottom x-axis, you have over here on the left. But those patients from their seven point profile that were spending 70% time in range, had a 5% risk of developing retinopathy.

Whereas if you only had 10% time in range, you had a 58% chance of developing retinopathy. And the curve is very similar to the A1C. So as you have more time in range, you reduce your risk of retinopathy. So we feel like this study put a stake in the ground to say, yep, time in range is a pretty good correlation with long term complications just like A1C. Yes, we want more studies. Yes, we want more data. But it's giving us confidence.

Now, let's look at AGP now and help us guide personalized diabetes management. Here is the upper panel again. You see the key metrics I talked about. And then you see the targets in the middle here. So just if anybody has any question, what was that again? 70 to 180? Oh, yes. 70%, or close to 17 hours, is my goal.

So I like to look at this upper panel and just ask the question, do I have a problem? We're all busy today. We're all incredibly busy. You only have got a few minutes, let's use it wisely. So I like to scan this upper panel, but go like a laser right in here to this time in range bar, or stacked bar, and say, how does it look? Does it tell me I have a problem? And I go right to the green and the red. I want more green and less red. I'd love to see hardly any red at all.

So I use those terms, can I get more green with less red? And can I get that green close to 70% because remember, look right here, that's the target. Can I get this red less than four and even less than 1% for the very low values? So that's how I start. Is there a problem? What would you say for this patient? Yes, there's a problem. They're at 47%. I'd like to be at 70. We can get there. I'd like to get rid of this red first. There's 10% under 70 and we only want it to be 4.

So now I go straight down to the next panel, which is the middle panel called the AGP or Ambulatory Glucose Profile. It goes from midnight to midnight. There is a median line of all these thousands of values of glucose put together. There is the interquartile range, a measure of variability, the wider it is the more variability you're having at that time of day, and then the outlying 5% to 95% of the values. You're trying to keep this as clean as possible as a graph.

So you have the target range, you have the low, very low, the high, the very high, and you should focus in first on hypoxemia. Are there values that are below that 70 or even below the 54? And you can see at least 2 times in the day here, we have to be concerned. There's 5%, 10%, of the values under 70, under 54. So we want to focus in on those. Then you might come back later to these high values that look like it's after breakfast, after supper, we'll find out if that's what the timing really is in just a minute.

And then, before you make that change because of the hypoglycemia or the hyperglycemia, look at the daily views quickly. Just scan them and say, do they agree with your impression from that middle panel. And I just circled for you, here, the overnights and said yes, in a vast majority of this two week period, that patient was low overnight or was dropping, dropping, dropping, about to get low. So you can feel comfortable it wasn't just a weekend they were low, it was weekends, weekdays. So go ahead and make that change to minimize that hypoglycemia.

And then people say, well, OK, but what should my pattern really look like. And people use all kinds of ways to describe it. And I've thought that maybe the easiest way to describe it is sort of a funny term called FNIR and that stands for Flat and Narrow and In Range. And so look at this patient in the upper left hand corner. I don't think you'd call that flat. I don't think you'd call it narrow. There's pretty wide variability, and it's certainly not in this target range of 70 to 180. You go over here to the right, then, to this panel and you say, OK, a little better. Look at that median line, it's pretty flat, but still a lot of variability. It's not narrow. It's not in range. And now we're flat and we're narrow but we're not in range, we're still hovering always at 180 or 200.

So finally, on the lower right, we've got to where we really want to be. We're flat, we're narrow, we're in range. And it's a process. It's a process. Visit by visit, phone call by phone call, now, in this world that we're living in, remote visit by remote visit, we're using CGM to try to get the profiles flat, narrow, and in range.

So let's move on to see how you really do that. And I think there's two important elements. Sometimes we've got to step out of the diabetes world and take other people's advice. Here's Daniel Kahneman, a Nobel winning economist who actually talked about how we make decisions. And I think it's really apropos to CGM. He talked about thinking fast and in the CGM world that means using the data you've got right on your CGM, on your phone, or just on your swipe, and look at your reader. And take corrective action, if you need to, right then and there.

And then, thinking slow means take a breath, look at the patterns, look at what you're finding, and see what adjustments should be made. So let me just walk you through these very briefly because you really want to do both. This is an and, it's not which is better. With CGM, if you do both of these we have a really good chance of reaching that optimized control with minimizing hypo. So retrospectively, how do you just download a profile and look at it? A lot of these we're doing remotely now but we have a profile sitting in front of us. Well the IDC in Minneapolis developed this 9 step guide. And it doesn't mean you take every step, necessarily, point by point with every patient. But you get a feel for a quick systematic interpretation.

So instead of going through the guide, which you can find on our website or you can see in the various publications, let's look at a patient. So here's Jean. 72-year-old. Type 2. 12 years. BMI of 32. GFR is OK. A1C, 7.9. Has a history of heart disease, that's important to note. And we just look quickly and you sort of say, well, do I have enough data to really act on this report today? Yes, there's 14 days, we're in good shape.

Have I reviewed all these factors over here on the left about the patient? Really understand who this patient is. That's really critical for interpreting your AGP. And then I strongly advise you to just print this out and ask the patient what they see. It takes them just a minute to get oriented when you tell them midnight to midnight, but they'll quickly say, oh my gosh I see it going up overnight or I see it high after breakfast. Yeah I know why that might be.

Then you want to look for patterns together, but certainly yourself. You want to look for lows first, look for highs next, and then think about the variability that you see in the report. If you have a previous AGP, and I strongly recommend snipping these and putting it in your electronic medical records so you have the past one and you could say, look at your improvement. You really are doing a nice job even if we're not quite to target yet. And then always leave with a plan. Leave with a focused plan.

So what would the plan be for Jean? Well, before we delve into it. I like to calculate this GMI. It should be on the report. If it's not, there's little calculators out there. And here her GMI was 7.2 but her A1C in the lab was 7.9. Remember, I said there can be a difference. I'd really put a lot of stock in this GMI as her indicator. So what's our action plan for Jean? I'm really struck by this history of heart disease, and I don't see any diabetes medications specifically addressing the heart disease. And remember, GLP-1s or SGLT-2s, if you know the ADA EASD algorithms, they say if you've got known heart disease, known heart disease, you really should consider one of these two agents.

So in our case she has heart disease. Her time in range is 65%. She's got a little ways to go yet. Can we find something that's going to address her heart disease and maybe even help with her glucose? So in this case, we really targeted that heart disease. We gave her a long acting GLP-1 receptor agonist and not only did we address her heart disease, but look at the glucose profile now. We went from 65% up to 89% time in range.

And we actually got rid of the hypo. The reason we got rid of the hypo, and you might notice down on this little bar at the bottom, is we got rid of the sulfonylurea. We thought, this GLP-1's pretty potent and she's on metformin already. So those two together are giving us heart protection and a good time in range. The GMI calculated has gone down also to 6.5 now. Still that little gap between the laboratory and the GMI. That tends to be pretty consistent for most patients, whatever their gap is.

One more case, if I can. Type 2. 60 years old. 95 kilograms. A1C, 7.5. This person, again, on metformin. And sulfonylurea, so many patients are in primary care. And then, also glargine. Remember, we start glargine, usually, 10 units and we go to 15, 20, 25, 30. We keep moving it up, moving it up, moving it up, to try to get that morning glucose down and get that morning glucose in target. And sometimes we get up to pretty high doses. Here, 70 units at night.

And when we do this, we had what I described, this picture I'm showing you of the glucose profile. And this is the classic stair step. Breakfast, lunch, dinner. Maybe didn't step up but didn't come down. So a classic stair step picture. That often means you're over basalinzed. Too much basal insulin. You're pouring in the basal insulin to try to get the morning down but it's going back up every day.

So this patient really needs something at the meal time and remember, I didn't emphasize it, but over here he can't take a GLP-1. He just didn't tolerate it. He tried it. So I think we really got to use mealtime insulin. Now, you can start one bolus a day at one of the meals or you can put bolus insulin in at every meal. I would say, let's give some bolus insulin right here at breakfast and stop this stair step. If that was flat, the whole day might be better. So reduce the glargine, add in the bolus insulin, either one or all three meals. I, personally, would stop the sulfonylurea because now we're going to put mealtime insulin, background insulin. We have metformin. So that's how I would address this case and I think we're well on our way to smoothing out this curve.

Now, Daniel Kahneman says, OK, that's great about slow thinking but most of us spend a lot of time fast thinking. Corrective action. Let's do that with our CGM data. Let's look at the trend arrows and make adjustments in diet and exercise and medications based on where the sugars are headed. We have all that data in front of us. So look up these publications and you'll see some really nice tables, whether it's on the left using the Libre, on the right using a Dexcom. Both have really nice tables of saying, if you see rising glucoses rising relatively fast or very fast, increase the amount of insulin you're taking at that meal. If they're falling or falling quickly, reduce, reduce, reduce. And both of them have nice guides for each patient, depending on their characteristics of how to make that adjustment.

So I'm going to just give you one case very quickly because it's pretty striking. At least it has been to me. An insulin dose is usually made up of the insulin you need for the food, the insulin to carb ratio, how much correction you're making because of the level of glucose you are at the time of the meal with a correction factor. Now, we have a new, third factor. Not only what is that glucose at the meal, but what's the rate of rise? Is it rising quickly? Dropping quickly?

So here's an example. This patient must have been hyperglycemic. They are taking four units for insulin to carb ratio, but they had a correction factor of five units. And they looked at their arrow and it was going up fast. So not only was it high before the meal, it was rising quickly. So this patient's little table that you printed out for them to have says, with an up arrow, you need three and a half extra units. So this person would take 12.5 units before that meal. OK.

What if that trend arrow had been going down? They had the same meal, the same blood sugar before the meal, but they were dropping rapidly before the meal. They would have reduced by 3.5 units as you can see down here. That would have been 5.5 units. That's a big difference. So really valuable data if we just take the time to explain it to our patients. They can smooth out these curves a lot more effectively. Now, it's not all insulin. It's not all medications, medications, medications. Adjusting the food you're eating, looking at your values and seeing what foods affect the glucose excursions is really important too.

And one of our dietitians, Dr. Holly Willis, gave me this idea saying, you're trying to increase the time in range by at least 5% because that's clinically significant. That's about an hour, 1.2 hours a day. Or if you have three meals, only 24 minutes per meal. And so here was a nice study that made her point very well. 27 people with type 2 diabetes either eating a fairly high carb meal or a low carb meal in the lighter gray. And look at the time over 180 or 10 millimoles. At breakfast, it's several hours over, at lunch it's at least an hour or two, and at dinner, maybe an hour out of target. If we eat this lower carb meal, you've reduced your time and you've improved your time in range dramatically just from a food adjustment.

So I'll close, again, with some patients. We always learn the most from looking at profiles really on our patients and how we can adjust from there. Here's three patients. Three glucose profiles. Two week periods. A1Cs, 6.7, 6.7, 6.7. All would get a congratulatory pat on the back in most cases, but look at the difference from profile one to profile three. There's twice the glucose variability. I think you could spot that right off. Look at that variability. There's nine times the level of hypoglycemia in the bottom profile versus the top profile. And the time in range is considerably less as well.

When we look over on the right side here, you see that in order to get this nice, flat, narrow, and in range profile, they were using more advanced technology, hybrid closed loop therapy. Sometimes, you can do it with MDI or with a pump if you add in CGM to those, you really can start to flatten it. And then in some cases, it's just still not quite enough. You really got to go to hybrid closed loop therapy if you want to get the flat, narrow, and in range. At least in type 1 diabetes.

So I'm going to conclude and make a few summary remarks just to tell you that I really think that knowing these standardized metrics, knowing the time in range targets, can really help patients and clinicians work together to achieve these goals. And we can do it with virtual visits just about as well as face to face, as much as we like to make that personal contact with our patients.

So if you use the data, you use the story that's behind those profiles, we can begin to really personalize our management decisions. And I'm really pretty convinced now, more than ever, that CGM has the potential to transform the way we're caring for diabetes if we're willing to use that data in a real time mode, use it retrospectively. I think we're really, finally going to be able to individualize and personalize care. So I'd like to thank you very much for your attention, and I hope we can stay in contact. And I'm happy to take any questions that you have offline in the future. Thank you.