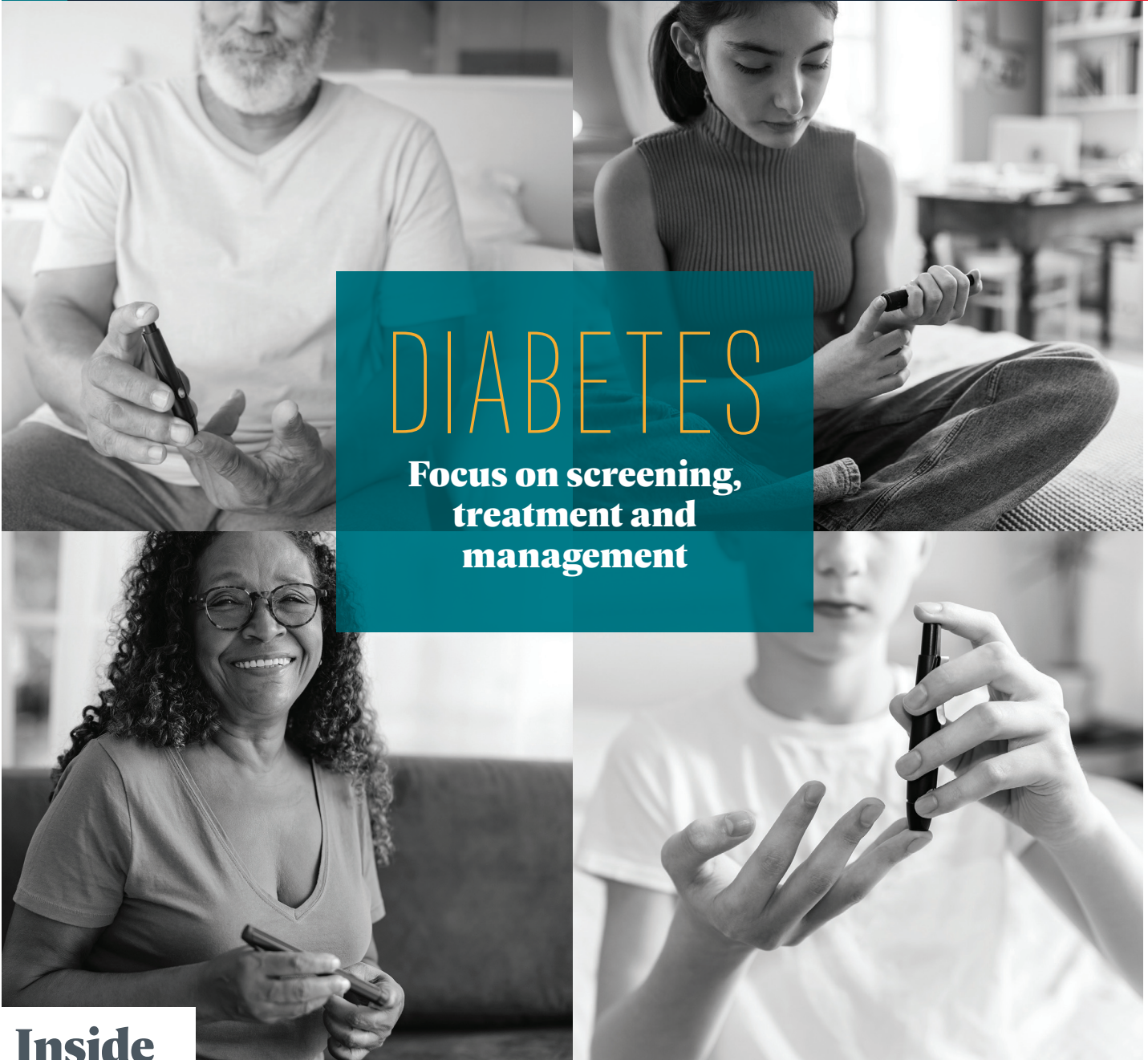


Patient Care[®]

PRESENTED BY

Medical Economics[®]



DIABETES

Focus on screening,
treatment and
management

Inside

Albany Med Health System Albany, NY

Empowering Early Intervention
Navigating Treatments
to Delay Type 1 Diabetes

AM Diabetes & Endocrinology Center Bartlett, TN

Empowering Early Intervention
Navigating Treatments
to Delay Type 1 Diabetes

Geriatric Diabetes Care

Optimizing
Type 2 Diabetes
Management

EMPOWERING EARLY INTERVENTION: **Navigating Treatments to Delay Type 1 Diabetes**

During a recent episode of *Patient Care Institutional Insights* titled “Empowering Early Intervention: Navigating Treatments for Delaying Type 1 Diabetes,” Jennifer D. Goldman, PharmD, RPh, CDCES, BC-ADM, led a trio of diabetes management experts from Albany Med Health System in Albany, New York, in a discussion of screening for type 1 diabetes and navigating the staged progression of the disease. They also discussed the landmark approval of teplizumab, the first drug indicated to slow the progression of stage 2 type 1 diabetes to stage 3, or frank diabetes, and the findings from the pivotal TrialNet 10 study (NCT01030861) that were the foundation for the FDA approval. The following transcript was edited for length and clarity.

MODERATOR

Jennifer D. Goldman, PharmD, RPh, CDCES, BC-ADM

Professor of Pharmacy Practice
Massachusetts College of Pharmacy and Health Sciences,
Boston, MA
Clinical Pharmacist and Director, Cardiometabolic Program
Well Life Medical, Peabody, MA

PANELISTS

Robert Busch, MD

Albany Med Health System
Community Endocrine Group: Albany Med Faculty Practice
Albany, NY

Nancy Jones, BSN, RN, CDCES

Department of Diabetes, Pediatric Endocrinology
Albany Medical Center
Albany, NY

Rebecca Ellwood, PA

Department of Medicine
Endocrinology, Diabetes and Metabolism, Insulin Pump Therapy
Albany Med Health System
Albany, NY

By Grace Halsey *Senior Editor*

Jennifer D. Goldman, PharmD, CDCES, BC-ADM: Let’s start with whom we should be screening for type 1 diabetes. Bob, would you go ahead?

Robert Busch, MD: We should be screening people who are at high risk, and that includes anyone with a family history of type 1 diabetes or other autoimmune conditions, such as Hashimoto disease or celiac disease or rheumatoid arthritis. When you take a family history of somebody with 1 of those conditions, you often find there’s type 1 in the family. So those are the key patients to look for. In the general population, the incidence of type 1 diabetes is about 3 in 1000. But for someone with a sibling or child or a parent with type 1, the chances are much higher, about 3 or 4 in 100. So somebody with a relative with type 1 diabetes is up to 15 times more likely to have the disease.

Rebecca Ellwood, PA: From a pediatric standpoint, we see siblings diagnosed when a brother or sister has it. But I’ve also had pediatric patients who present with type 1 at a young age, and we end up diagnosing one of their parents with type 1 diabetes when they’re in their 40s or 50s. When a parent has a child with type 1, they could have it themselves and were never tested. So I actually screen my parents who have children with type 1 diabetes.

Goldman: So, screening first-degree relatives is really essential. What about second generation or those who are not immediate family?

Ellwood: I think it’s our job to educate anyone about the risk and about screening. I typically will educate the patient with autoimmune disease and say, “Discuss this with all of your relatives, and for anyone who wants to be screened, here are the tests to order and here’s the diagnosis code to use.”

Goldman: So, wherever we can, we want to try to

delay the onset of type 1 diabetes. What's at stake? What are the consequences of delayed diagnosis?

Busch: Of course, the most dangerous consequence of delayed diagnosis is diabetic ketoacidosis, or DKA. Screening is critical so we can intervene at least with education and counseling for the parent of a young child or even a teenager. If the patient is in stage 2, now we can offer a treatment to put off the inevitable, and we need to educate on those benefits.

Goldman: Dr Busch just mentioned stage 2 type 1 diabetes. Rebecca, would you talk about the stages of type 1 diabetes and the risks at the different stages?

Ellwood: Sure. We used to think of diabetes as either you had it or you didn't have it. But in 2015, the American Diabetes Association [ADA] started to do more formal education around the staging of type 1 diabetes to help us understand that the onset of the disease is a process. So in stage 1, type 1 diabetes, there is a trigger—it could be genetic, could be environmental—that causes the immune system to start to produce antibodies to pancreatic β cells. Blood sugars are perfectly normal at this stage; no insulin is needed because the β cells still function at 95% to 99%.

But as the attack on the β cells continues, the disease progresses to stage 2, type 1 diabetes where we start to see dysglycemia, meaning that blood sugar levels are in the mildly elevated range, but typically not above 200 mg/dL. The person is usually still asymptomatic, and insulin still isn't indicated because the β cells are functioning at 50% or more. But as the antibodies continue to attack the pancreas, patients progress to type 1, stage 3, where β cells are damaged enough that they cannot make enough insulin to keep blood sugars normal. And that's when the patient formally develops hyperglycemia, and

again, a formal diagnosis of type 1. In this stage 3 of type 1 diabetes, we are trying to avoid DKA.

Goldman: Before we go on, the islet autoantibodies the ADA directs us to check for in high-risk individuals are IAA, GADA, IA-2A and ZnT8A [Figure 1]. What is the clinical relevance? And how often should we be checking once they are detected?

Busch: You order these like you order a lipid panel—as a group. It's very straightforward—a commercial lab or a hospital lab can do it. Some have a diabetes antibody panel and so you just order that. If the person is high risk but antibodies are negative, they should be rescreened every year until they're 18 years old. If there is a single antibody, we should rescreen to make sure there aren't others, then screen again annually. With 2 antibodies present, it's probably the earliest stage of type 1.

Ellwood: With a child of a patient with type 1, I screen them at the age of 2. If they're negative, I don't usually rescreen them again at age 3 unless there's another reason for bloodwork. I think age 2 and age 6 have been shown to be good times to screen your youngsters. But in my really high-risk patients, I might consider repeating things every 1 to 2 years.

Goldman: If they have more than 2 antibodies, what's the significance and what's the next step?

Nancy Jones, BSN, RN, CDES: Before teplizumab was approved, the next step was, "OK, let's wait and see. There's nothing we can do right now." So we're going to do finger pricks to watch and wait for that treatable 200 mg/dL blood sugar to come.

Busch: Right, with 2 or more antibodies, that's when you go to the next phase—checking for dysglycemia, and the gold standard is the oral glucose tolerance test. If the test comes back as frank

diabetes, then it's type 1 stage 3. If glucose is elevated or reads as dysglycemia, then it's type 1 stage 2, and that's the population we're targeting with teplizumab.

Goldman: That's the population because we can delay the progression to stage 3 now. How fast is that progression?

Ellwood: Progression from stage 1 to stage 3 is age dependent. Our younger population that has a more robust immune system progresses faster than our older [patients with] LADA [latent autoimmune diabetes of adults]. But the data say about 50% of patients will go from antibody-positive to full-blown diabetes; [in other words,] stage 1 to stage 3 in 5 years.

Busch: We know the person will progress to frank diabetes no matter what, but now finding it early on makes a difference. If you find 2 or more antibodies, you do want to have a conversation with the patient or the parent to explain the significance of the result and encourage them to schedule regular follow-up tests.

Goldman: That sounds like an important message when you're talking to parents about children at risk—how quickly the progression happens, and the benefits of delaying it.

Jones: An example of a benefit of delay is, say the patient is a teenager. The unfortunate thing with teenagers especially is they have no idea of what the consequences are. It's not real to them. So if we can delay an onset until they have a little bit more capacity to understand what the risks are, like for long-term irreversible complications, hopefully a lot of these risks could be prevented.

Ellwood: I love that. Delaying it until they're mature enough to really understand the repercussions. We have a lot of patients, unfortunately, in their 30s who have required dialysis or kidney

transplants. Same thing with neuropathy. Like Nancy was saying, pediatric patients don't often think about the consequences of their behaviors until it's too late. So those patients in their 20s and 30s who are having these comorbidities or complications...wish they had done something different or had more time to mature or to learn how to manage their disease before it became imperative.

Goldman: I called one of my patients who has type 1 diabetes as soon as teplizumab was approved because he has 3 children, and I told him, "Now we have a really good reason to screen them." He said, "Why would I do that? It's just going to delay the inevitable."

Ellwood: I have had that conversation with many patients, and I think initially that's their answer until they really start thinking about it. I have a family with 2 children with type 1, and the third is in stage 2 right now. And the mom was not going to go for the teplizumab treatment for the third child, until the 2 other brothers said, "Mom, I would love to not have diabetes for a couple of years. Can I have this?" Then she said, "You know what? I'm not thinking about it from my kid's perspective." So the third child is beginning infusions in a week.

Goldman: Let's talk more about the FDA approval of teplizumab, the first drug we have that can actually delay the progression from stage 2 type 1 to stage 3 type 1. Dr Busch, would you first talk about the mechanism of action? [Figure 2.]

Busch: Of course. Essentially, it slows the rate of loss of β -cell function in type 1 diabetes. As Becca

originally said, the immune system is triggered and produces antibodies to pancreatic β cells and then the antigen antibody reaction happens, and you get the killer lymphocytes. The CD3 antigen on the lymphocyte can be attacked with a monoclonal antibody specifically directed against it. And that inactivates the lymphocytes that would otherwise continue to destroy β cells. So by protecting the β cells, teplizumab creates a sort of pause in stage 2 type 1; it increases the time to the transition to full-blown type 1 diabetes. And right now, that delay is significant. As we will see, the delay can be for 2, 2.5, or 2.7 years, when you look at the TrialNet 10 findings.

Goldman: Rebecca, would you talk about the TrialNet 10 study data now?

Ellwood: In the initial trial analysis, in patients receiving teplizumab, we saw a 2-year delay in going on to develop type 1 stage 3 diabetes. [Figure 3]. Patients who did not get teplizumab progressed to type 1 stage 3 in about 2 years [median, 24.4 months] vs those who received teplizumab who progressed to stage 3 at an average of about 4 years—and the median was 48.4 months. The extended TrialNet 10 analysis data showed a delay of 2.7 years. At the conclusion, the percentage of diabetes-free patients in the teplizumab group was 57%, approximately double the proportion in the placebo group—28%.

Goldman: We mentioned the adverse effects of teplizumab earlier, and particularly lymphopenia. Nancy, what did you see?

Jones: We saw lymphopenia in the first 5 days and then it started to

resolve. I went to see the children every day when they were getting their infusion, and they had no complaints. They were premedicated with acetaminophen and Benadryl [diphenhydramine], and no one needed anything for nausea.

Goldman: What about other monitoring during the treatment period?

Ellwood: Well, as Nancy mentioned, none of her patients needed anti-nausea medications, but we have that as part of the plan if needed. And then we monitor complete blood cell count, with a baseline prior to the infusion. We also measure liver functions because we want to make sure that lymphocyte count doesn't go under $500/\text{mm}^3$ for more than a few days. We want to make sure liver enzymes or bilirubin don't peak above 3 times the upper limit of normal and stay there. So we monitor the labs periodically. I think as institutions get more comfortable with the teplizumab protocol, we might not even have to do that every day. Designs I've seen for infusion from other institutions are taking those measures at baseline, and then at day 3 and day 5, and then maybe once the next week just to make sure everything's fine. If the day 3 and day 5 results are OK, chances are the patient's going to be fine if they're feeling well.

Goldman: What about other options for infusion sites? Could those include a physician's office or even at home?

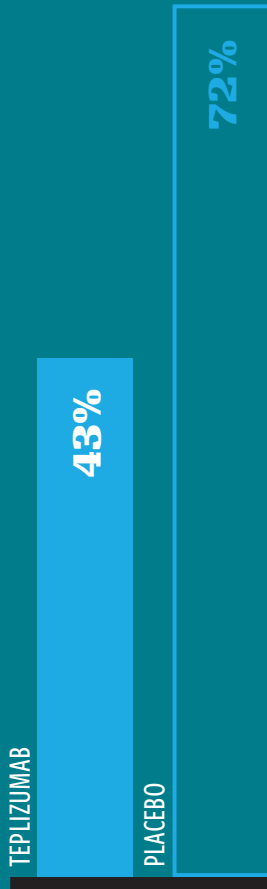
Ellwood: Our plan for the future is a hybrid model. The first dose of teplizumab is weight- or body surface area-based, and then it is doubled every day until day 5 and then remains consistent until day 14. We hope to have day 1 to 5 in the hospital because that's when any reactions are most likely, and as long as the lymphocyte count is over $500/\text{mm}^3$, treatment will continue, so why not continue at home if home care coverage is available. ■



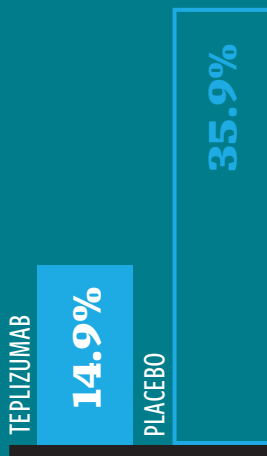
MORE ONLINE

To watch the entire discussion with Goldman, Busch, Jones, and Ellwood, visit:

<https://www.patientcareonline.com/institutional-insights/empowering-early-intervention-navigating-treatments-for-delaying-t1d-progression-insights-amc>



T1D was diagnosed in 19 (43%) of the participants who received teplizumab and in 23 (72%) of those who received placebo. (HR, 0.41; 95% CI, 22%-78%; $P = .006$)



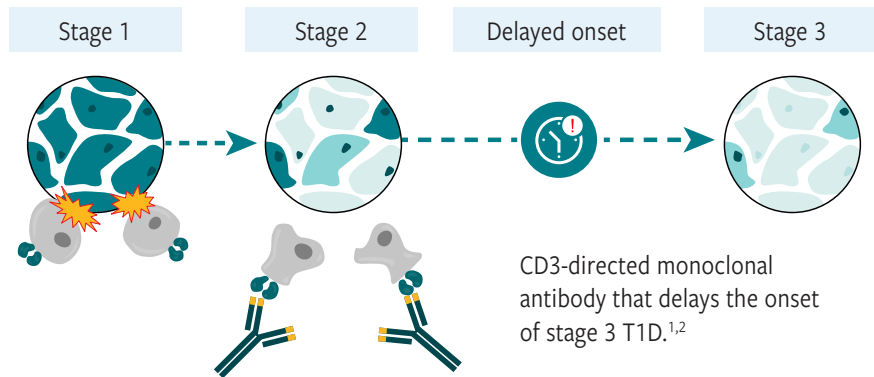
Annualized rates of diagnosis of diabetes were 14.9% (teplizumab) and 35.9% (placebo)

FIGURE 1. Autoantibodies Preceding Type 1 Diabetes

Antibody	Target
Insulin autoantibodies (IAA)	Insulin-producing β cells
Glutamic acid decarboxylase autoantibodies (GADA)	GAD enzyme in β cells
Insulinoma-associated-2 autoantibodies (IA-2A)	IA-2A protein in β cells
Zinc transporter 8 autoantibodies (ZnT8A)	ZnT8 transporter β cells

FIGURE 2. Teplizumab: Mechanism of Action

Teplizumab is thought to modify disease progression from stage 2 to 3 type 1 diabetes by preserving β -cell function.



¹FDA approves first drug that can delay onset of type 1 diabetes. FDA website. Accessed February 12, 2024. <https://www.fda.gov/media/164864/download>

²Thakkar S, Chopra A, Nagendra L, Kalra S, Bhattacharya S. Teplizumab in type 1 diabetes mellitus: an updated review. *touchREV Endocrinol.* 2023;19(2):22-30. doi:10.17925/EE.2023.19.2.7

FIGURE 3. Median Time to Onset of Stage 3 T1D 2 Times Longer in Teplizumab-Treated vs Placebo-Treated Patients¹

~2-YEAR DELAY

Teplizumab **significantly delayed** stage 3 T1D onset compared with placebo in stage 2 T1D (~4 vs ~2 years median time to progression, teplizumab vs placebo, respectively).¹

~2.7-YEAR DELAY

Extended analysis further demonstrated a median time to stage 3 T1D diagnosis of 59.6 vs 27.1 months for teplizumab vs placebo, respectively.¹

Clinical efficacy and safety end points were assessed in children and adolescents randomly assigned to either drug (n=44) or placebo (n=32) for a 14-day outpatient IV course.

Primary outcome: Change in β -cell function measured by stimulated C-peptide levels

1. Herold KC, Bundy BN, Long SA, et al; Type 1 Diabetes TrialNet Study Group. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. *N Engl J Med.* 2019;381(7):603-613. doi:10.1056/NEJMoa1902226

EMPOWERING EARLY INTERVENTION: **Navigating Treatments to Delay Type 1 Diabetes**

In this episode of *Patient Care Institutional Insights* titled “Empowering Early Intervention: Navigating Treatments for Delaying Type 1 Diabetes,” Jennifer D. Goldman, PharmD, RPh, CDCES, BC-ADM, led a trio of clinicians affiliated with the AM Diabetes & Endocrinology Center in Bartlett, Tennessee, in a discussion of advances in treating patients with type 1 diabetes. Topics included the importance of screening relatives of individuals with type 1 diabetes, the stages of type 1 diabetes and their significance to treatment, understanding antibody testing, and the new drug teplizumab, recently approved by the FDA to slow the progression of stage 2 type 1 diabetes to stage 3, or frank type 1 diabetes. The following transcript was edited for length and clarity.

MODERATOR

Jennifer D. Goldman, PharmD, RPh, CDCES, BC-ADM

Professor of Pharmacy Practice
Massachusetts College of Pharmacy and Health Sciences,
Boston, MA
Clinical Pharmacist and Director, Cardiometabolic Program
Well Life Medical, Peabody, MA

PANELISTS

Kashif Latif, MD

Founder, AM Diabetes & Endocrinology Center
Bartlett, TN

Kent Stoneking, PharmD, CDCES

Director, Diabetes Education & Patient Self-Management
Services
AM Diabetes Centers of America
Arlington, TN

Marianne Briggs, DNP, FNP-C

Consolidated Medical Practices of Memphis
Bartlett, TN

By Grace Halsey *Senior Editor*

Jennifer D. Goldman, PharmD, RPh, CDCES,

BC-ADM: Dr Latif, we all know the burden of diabetes in the US well, but would you give a brief overview?

Kashif Latif, MD: I think the number is quite large; about 1 in 10 people has diabetes in the US overall, but geographically, it varies. In the county where we practice, it’s about 1 in 13. In the adjacent county, in Mississippi, it’s about 1 in 15. It’s a huge burden, considering the cost of taking care of everybody with diabetes. We can’t overlook the fact, too, that for every person with type 2 diabetes, there are many people who have prediabetes that we have not identified. For type 1 diabetes, we have a similar issue where there may be relatives of people with type 1 diabetes who are not aware they are at risk. We can diagnose type 1 with the presence of 2 autoantibodies with a normal glycemic state.

Goldman: If somebody has a family history of type 1 diabetes, we know that first-degree relatives have a higher risk. Are you seeing that in your practice?

Kent Stoneking, PharmD, CDCES: Yes, we are seeing that. And the messaging to those first-degree family members is so important—about screening, about the presence of autoantibodies, about blood glucose that’s beginning to move off the mark of normal levels. We’ve always talked about prediabetes with our type 2 patients. In type 1, especially for first-degree family members, now we would look for dysglycemia when patients are positive for 2 antibodies, as Dr Kashif said. And the earlier we can identify those patients, the sooner we can intervene. And that’s the exciting part.

Goldman: Kent, would you talk a bit more about the messaging you mentioned and the emotional toll of a type 1 diabetes diagnosis?

Stoneking: I was diagnosed with type 1 diabetes when I was 11 years old. I had a great pediatric

endocrinologist who told, not me, but my parents (and I had the privilege of overhearing it), “Hey, it’s going to be OK. Let Kent play sports. Let Kent go to camp. Let him be a normal kid as he’s learning to navigate his diabetes because the more of a normal life he can lead, the more connected he’ll be to his peer group, which is positive from a psychosocial, emotional standpoint. But also, the better prepared he’ll be for the responsibilities of adulthood because he has taken on this other responsibility.” And really, the underlying message was to let me own it. And my parents did that. In fact, those first few years were difficult. They were very supportive. But they expected me to take my blood sugar reading; they weren’t taking it. I did what normal kids do just while taking insulin. But 10 years after my diagnosis, my youngest brother was diagnosed; he was 13 and I was 11.

And my parents thought, oh, we have another one. By then, though, they had acclimated to what needed to happen. And that positive messaging from the medical team right up front was so impactful.

I want our primary care colleagues here tonight to hear this. The messaging around first diagnosis is so vital — telling patients, telling families that by accessing the right resources, getting in with a good endocrinologist, and getting together with peers who have diabetes, you can manage much better.

Goldman: Marianne, if Kent is your patient and you now know that he and his brother have type 1 diabetes, who else gets screened?

Marianne Briggs, DNP,

FNP-C: His children. The risk in children and adolescents is quite significant when they have a first-degree relative with type 1; I believe they have an 8% to 15% risk of having it. I even had a patient today who is a type 1; her mother was a type 1 and both of

her children are type 1. One child has the positive antibodies, but his blood sugars are still fine so we started having the conversation today about whether we should intervene now before another child has to go through all of this and she has to readjust family life.

Goldman: How will you follow up with this family?

Briggs: This child would be considered in stage 1 type 1 diabetes because he has 4 positive antibodies. But even though we know his body is starting to attack his beta cells, his blood sugar levels are normal. With so many family members who have diabetes, they are all able to check his blood glucose level frequently; they’re looking for all the signs. ... He doesn’t need insulin, but he would have a diagnosis of type 1 diabetes otherwise. We usually do a glucose tolerance test every 6 months in a case like this. That’s just a really good way to get a full assessment of what’s going on.

Goldman: At what age is it appropriate to start checking children?

Briggs: I would like to check them when they’re born. But maybe starting at age 2 to see what’s going on and then again at 6 years is appropriate.

Goldman: I’ve read that the likelihood of the onset of type 1 diabetes by age 15, if a child has autoantibodies at ages 2 and 6, is about 79%. So your suggestion makes perfect sense.

Latif: We have data that show that the time from detection of antibodies to development of clinical type 3, stage 3 type 1 diabetes is close to a decade or more. We actually have a lot of time to intervene, and now we can offer an FDA-approved therapy. This is an ideal time for us to be alert to people in whose lives we can make a difference.

Goldman: We have been talking about autoantibodies, but let’s go

into some detail. The American Diabetes Association *Standards of Care* in Diabetes say to be on the alert for these 4 autoantibodies (see Figure). Dr Latif, would you review how the autoantibodies are used for T1D diagnosis and the progression of the T1D stages?

Latif: We now make a diagnosis of type 1 diabetes based on the presence of 2 autoantibodies. If there are 2 positive autoantibodies, by definition, you have type 1 diabetes, which is stage 1 with normal blood glucose levels. If the blood glucose starts to get erratic and it is in the prediabetes stage, then it’s referred to as dysglycemia, and that is stage 2 type 1 diabetes. And once you get to the stage where the blood glucose level is extremely high and you meet all the criteria for a diagnosis of diabetes, that is called stage 3—florid type 1 diabetes.

Goldman: How does the newly approved drug teplizumab work to slow down the progression from type 1 stage 2 to frank type 1 diabetes? [Figure 2]

Stoneking: Teplizumab, an anti-CD3 antibody, binds with CD3, and that shifts the proliferation of T cells toward the proliferation preferentially of T regulator cells. And it shifts that balance away from the proliferation of CD4 and CD8 T cells, the CD4 being the setup for the CD8, which directly impact the β cells in the pancreas and cause β cell destruction and the decline of insulin production. By shifting that balance toward T regulator cells and away from the CD4 and CD8s, we mitigate the risk of β cell destruction and preserve β cell function for a longer period of time.

Goldman: Marianne, would you give us a quick overview of the TrialNet 10 study [NCT01030861] data with teplizumab?

Briggs: The participants were relatives without diabetes of

persons with T1D and were at least 8 years old. They had 2 or more autoantibodies detected in 2 samples within 6 months. We found that teplizumab delayed progression from stage 2 to stage 3 type 1 diabetes compared with placebo by 2 years. That's 2 more years without needing full insulin. And even if it's just 2 years of life, that's 2 years that a child gets to be more of a child or that someone else can live without daily insulin. That's worth it to me. And it gives families some extra time to prepare for a really big change. In the TrialNet 10 extended analysis data, we saw an additional delay in time to progression to stage 3, so 2.7 years, and the analysis ran for about 79 months.

Goldman: When we look at the adverse reactions in the study, we see that 73% of participants experienced lymphopenia. Could you put it into perspective for us?

Briggs: I know, it sounds scary. We were all scared. I was very nervous in the beginning, but we didn't have to stop the infusion for any patient during the clinical trials or for the patient we had already treated. We are aware of it on the front end, so we know what to look for, and they do fine.

Latif: It is transient. You see that with dose escalation in days 1 to 3, and then after that it plateaus and it just stabilizes. So again, as Marianne said, there's no need for fear.

Goldman: Has your group treated any patients with teplizumab?

Briggs: Yes. We treated a 57-year-old woman — a good

reminder that it's not just children who can develop type 1 diabetes. And she is doing great now. She has a family history of type 1 diabetes, but she came in to see me for her thyroid. Nobody had even thought of type 1 diabetes; maybe prediabetes, but she is super thin, and it just didn't make sense. So that's something we need to look out for in primary care.

Goldman: Kent, would you talk about the 14-day dosing schedule for teplizumab?

Stoneking: We do start with a low dose and then we ramp up sequentially, essentially doubling the dose per day up until day 5. And we do that because of the risk of lymphopenia and the other adverse events that you mentioned, lymphopenia being the primary one. And quite frankly, if you see a reduction in lymphocytes, that's proof positive that your biologic therapy is working. After day 5, lymphocytes should begin to rebound. Our patient had a rash that developed around days 3 and 4. It was visible but not bothersome and resolved on its own after a few days.

Goldman: How should premedication be approached before the infusion?

Stoneking: Premedication is vitally important. The recommendation is to pretreat with acetaminophen. We gave our patient 500 mg of acetaminophen, 25 mg of diphenhydramine, and 4 mg of ondansetron ODT for nausea. By day 3, she asked us to stop the ondansetron and the diphenhydramine because she was too drowsy. "I can't function

the rest of my day," she said. So we bypassed that. And once we got past day 5, days 6 through 14 were very smooth.

Goldman: How are you monitoring for serious adverse effects? Are you checking complete blood counts, liver function tests, and anything else on a daily basis?

Stoneking: Absolutely. For this patient, we did a full lab panel including hepatic function and CBC baseline on day 1. And then we repeated that on days 4, 7, and 10, and then we did a closeout on day 14.

Goldman: What are the recommendations for follow-up after a patient completes 14 days of treatment?

Briggs: In our clinic, we're privileged to have access to putting a continuous glucose monitor on the patient. Our patient wore a sensor for 2 weeks, checking to see how her sugars were doing. And her blood sugars were doing great, so we felt comfortable pushing out the follow-up. We're waiting 3 months now to see her.

Stoneking: A quick note about monitoring and communication — we of course monitor during treatment, but also in between. We have ongoing conversations with the patient to make sure that he or she knows that they are at the center of this process.

Goldman: In your area, other than your clinic, are there other centers set up to do this?

Latif: I think in Tennessee we have 2 or 3. There are infusion centers that can do this, but you do need to have some kind of oversight. You need to have an endocrinologist or somebody partnering with the infusion center to make sure it's not going to stop or change infusion because of lymphopenia; they have to have someone to contact. Infusion is their specialty, not type 1 diabetes. ■



MORE ONLINE

To watch the entire discussion with Goldman, Latif, Stoneking, and Briggs, visit:

<https://www.patientcareonline.com/institutional-insights/empowering-early-intervention-navigating-treatments-for-delaying-t1d-progression-insights-from>

GERIATRIC DIABETES CARE:

Optimizing Type 2 Diabetes Management

In a recent *Patient Care*[®] ConsultantLive program titled “Geriatric Diabetes Care: Optimizing Type 2 Diabetes Management,” Medha Munshi, MD, director of the Joslin Diabetes Center Geriatric Diabetes Program and associate professor of medicine at Harvard Medical School in Boston, Massachusetts, and D. James Bailey III, MD, of Endocrinology Associates of Roanoke, in Virginia, discussed a range of challenges clinicians face when ensuring safe and effective care for older adults with type 2 diabetes. Topics included the physiologic changes associated with aging, medication choices, glucose level goals, and the unique impact of geriatric syndromes on older patients’ ability to care for themselves appropriately. The following transcript has been edited for length and clarity.

PARTICIPANTS

Medha Munshi, MD

Director
Geriatric Diabetes Program
Joslin Diabetes Center
Associate Professor of Medicine
Harvard Medical School
Boston, MA

D. James Bailey III, MD

Endocrinology Associates of Roanoke
Roanoke, VA

By Grace Halsey *Senior Editor*

Medha Munshi, MD: To start, we know that approximately 29% of Americans 65 years and older have diabetes—that’s 16.5 million seniors. Dr Bailey, what percentage of the patients in your practice are 65 years or older?

D. James Bailey III, MD: I’ve been in practice just over 30 years now. I’ve taken care of some folks here for decades now. And right now, about 40% of the patients I see are Medicare age. And obviously, they present some unique challenges in terms of type 2 diabetes management, and there are a lot of things to consider for this very special population.

Munshi: I am a geriatrician, so I see and work with the impact of geriatric syndromes on the health of my patients every day, health conditions that are specific to the older population that don’t fit into a distinct organ-based category—like physical decline and disability, cognitive dysfunction, frailty, and polypharmacy. For our older patients with type 2 diabetes, we have to understand how they are different from younger adults with diabetes because that affects our treatment goals and disease management decisions.

Dr Bailey, what would you say are some of the challenges in managing older vs younger adults with type 2 diabetes?

Bailey: Well, younger adults have a higher lifetime risk of complications, so we will be considering preventive strategies for weight management; preventing comorbidities like cardiovascular, renal, and liver disease; and thinking about reproductive health issues. The challenges in our older patients with type 2 diabetes are mostly different; now we will be dealing with the comorbidities we try to prevent when they are younger. We are going to be concerned about the risk of major adverse cardiovascular events but in the short term now, and so that becomes a priority. The focus will still be on glucose control, but we have to be very careful about causing hypoglycemia and also aware that older adults may have less awareness of both hypo- and hyperglycemia. As you said, cognitive decline is part of these unique challenges.

Also, a lot of the older patients are going to have more than 1 health care professional. As they start to develop more of these comorbidities, they’re seeing the nephrologist and the cardiologist. They are getting medications from a lot of different people, and somebody has to oversee that and try to decide what they need and what they don’t need. Polypharmacy makes it hard for them to follow these complex regimens. They have a lot of self-management impairments as well.

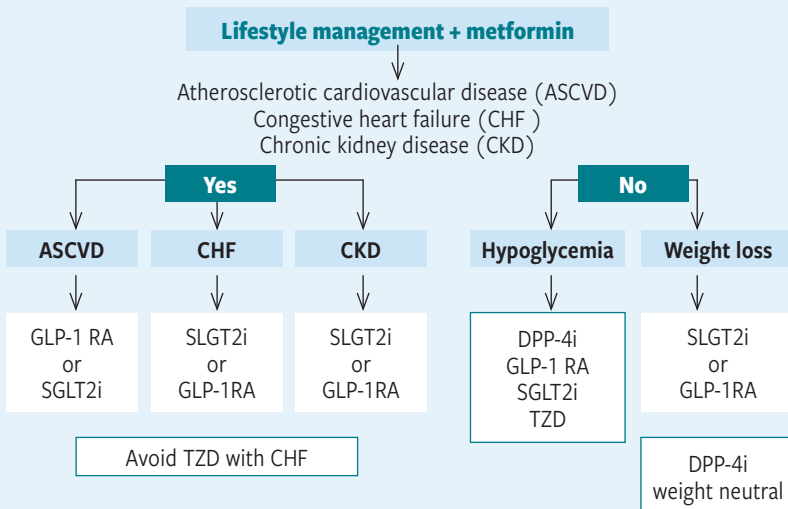
FIGURE 1. Older Adults: Standards of Care in Diabetes—2024: American Diabetes Association Recommendations

13.1 Consider the assessment of medical, psychological, functional (self-management abilities), and social domains in older adults to provide a framework to determine targets and therapeutic approaches for diabetes management.

13.2 Screen for geriatric syndromes (ie, polypharmacy, cognitive impairment, depression, urinary incontinence, falls, persistent pain, and frailty) in older adults, as they may affect diabetes self-management and diminish quality of life.

Adapted from ElSayed NA, et al.¹

FIGURE 2. Simplified Treatment Algorithm for Type 2 Diabetes



Adapted from ElSayed NA et al.¹
DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; SGLT2i, sodium-glucose cotransporter-2 inhibitor; TZD, thiazolidinedione.

FIGURE 3. Deprescribing Medication in Older Adults

Deprescribing is the planned and supervised process of reducing a dose or stopping medication that might be causing harm or no longer be of benefit. The goal is to reduce medication burden or harm while improving quality of life.

When older Adults Are Unable to Keep Up With Complex Regimens

Liberalize

Deintensify

Simplify

Adapted from Munshi and Neumiller.²

I encourage older patients to bring someone with them to an appointment, either a spouse or family member who's going to assist with their management or medications and their diabetes. And another set of ears is always very helpful.

Munshi: Let's step back a moment and ask the question: Who exactly is an older adult?

Bailey: Well it depends. How functional is the person? How youthful are they in their abilities to participate and to self-manage? And that's going to vary a great deal. The population is aging, and we have increasingly more people with type 2 diabetes in this country. You're going to see a broad spectrum of individuals, some of whom are very self-sufficient and independent and others who are going to need a lot of simplification of medication regimens and a lot of assistance from their team. It takes a village. Trying to get a good feel for where that patient stands with all of that is going to be critical to improving outcomes.

Munshi: Dr Bailey, if I asked you which of these is the most challenging aspect of managing type 2 diabetes in older adults, what would you say? Medication adherence, frailty, falls, mobility issues, cognitive impairment, increased risk of hypoglycemia?

Bailey: That would be a tough one for me to answer. All of these are important, of course. So I would say all the above. But with medication adherence we need to ask not only do they take their medication but can they administer it safely? That's the nice thing about having insulin pens vs vials. The chances for mistakes in terms of insulin dosing, for instance, are less. And a lot of times, it's just a matter of the patient's word. "Are you taking your medications?" "Yes." And then sometimes from across the room, you'll hear a family member say, "Not consistently." You don't always know what the truth is.

Munshi: So true; you have 1 head in the front saying yes and 2 heads in the back saying no.

The American Diabetes Association ADA publishes recommendations for management in older adults in the *Standards of Care in Diabetes* every year, and we have discussed a good deal of these topics today. [Figure 1]

We need to consider all these geriatric syndromes when we set targets for glycemic control for our older patients and of course when we choose medications to lower glucose levels.

Bailey: I think when the hemoglobin (Hb) A_{1C} goal of less than 7% came out we all became very A_{1C}-centric, and so laser focused on that. But that's not really the goal for everyone, necessarily. We should ask, how intensively do I need to manage this individual? You have to do an assessment in terms of their comorbidities, their life span, and then you

can make appropriate judgments in terms of what their HbA_{1C} goal is and what their treatment should include. Obviously the goal is always to try to minimize the risk of hypoglycemia because that's particularly problematic in this patient group.

Munshi: So which class of glucose-lowering medications should we be using as first-line treatment in older adults with type 2 diabetes? [Figure 2]

Bailey: You have to consider many things. What are the pros and cons of each with regard to availability, costs, and insurance? What comorbidities might push us toward one choice over another? Does the patient have chronic renal disease? Do they have chronic liver disease? Do they have some predisposition to hypoglycemia for one of those reasons? Obviously, there are limits in terms of what you can do with metformin, for example, as it relates to renal function. I am a fan of GLP-1 RAs

[glucagon-like peptide-1 receptor agonists], but does the older patient have any reason not to use them, like recurring pancreatitis and that sort of thing? I've seen a lot less use of sulfonylureas in almost all patients, including those older patients who are likely to have some renal disease that would increase the half-life of those drugs. And the major concern with that class would be the risk of hypoglycemia. So there are obviously a lot of considerations there.

Munshi: Now, we do recommend GLP-1 RAs as the first injectable but then, as you suggested, sometimes you do need to use the basal insulin. But we need to keep it simple too. So starting with once a day and then titrating. Once you have a baseline of better control you may need rapid-acting insulin before the largest meal and then add that on. Other thoughts, Dr Bailey?

Bailey: Well, I always said that when GLP-1s came along, for a lot of

FIGURE 4

Patient 1

- 89 years old with CAD, CHF, ESRF, and recent falls
- Lives alone
- Prescribed basal-bolus regimen due to contraindications to all other medications
- Finger stick glucose, 80-150 mg/dL; HbA_{1C}, 7.1%

Consider liberalization

- Raise HbA_{1C} or glucose goals for patients who will not benefit from tighter control and may be harmed.

For this patient: Liberalize the goal BG 100-200 mg/dL

CAD, coronary artery disease; CHF, congestive heart failure; ESRF, end-stage renal failure.

Patient 2

- 89 years old taking 3 antihypertensive and 2 lipid-lowering medications
- Diabetes medications: metformin BID, glipizide BID, GLP-1 RA QD
 - Forgets 2-3 doses of medications per week

Consider deintensification

- To decrease the burden of therapy
- To decrease polypharmacy, nonadherence, difficulty coping, adverse effects; consider end-of-life care
- Discontinue nonessential medications; use long-acting formulations

For this patient: add insulin, take away glipizide and add GLP-1 RA, use ER form

ER, extended release; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Patient 3

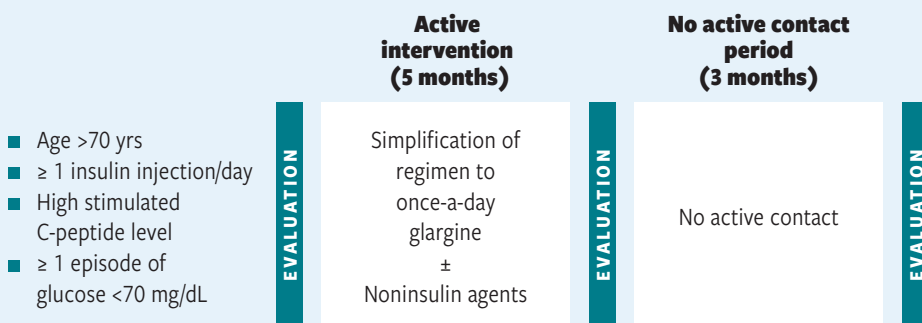
- 84 years old with type 2 diabetes on basal-bolus insulin for past 15 years
- Recently hospitalized for stroke, unable to self-monitor with finger sticks or manage multiple injections
- Lives with working husband who is unavailable all day to help manage medications

Consider liberalization

- Simplify strategy to match patient's coping ability
- Following medication regimens consistently is difficult when they are overly complex
- Change to strategy that is easier for patients or caregiver

For this patient: Basal insulin plus noninsulin agent

FIGURE 5. SIMPLE Study: Simplification of Insulin Regimen



Adapted from ElSayed NA et al.¹

of care. Participants were age 70 or older, on multiple daily insulin injections, and having hypoglycemia. We simplified the regimen by using once-a-day glargine plus noninsulin agents and observed whether they could maintain the simplified regimen and what the results would be. [Figure 5]

Most of the patients did better with glargine and a GLP-1 RA once a

my patients it eliminated their need for mealtime bolus insulin when coupled with basal insulin. So it was kind of a poor man's basal bolus and much simpler to do. The GLP-1 RAs helped to address a lot of that postprandial hyperglycemia that needed to be addressed to get more optimal control but without further challenging the patient or the caregiver.

Munshi: Let's talk more about simplifying treatment for the patients who are 65 and older with type 2 diabetes. Maybe they aren't doing so well now on a regimen they have been taking for many years.

So the next step should be deprescribing [Figure 3]. And that doesn't always mean stopping a drug but instead modifying the schedule or simplifying the regimen. But it won't be the same thing for all patients because when you are deprescribing you are targeting a problem that is specific to that patient, a problem that is affecting their care or quality of life.

Let's use some examples to help illustrate these concepts [Figure 4].

Patient 1 is 89 years old with multiple comorbidities. He lives alone, is on a basal-bolus regimen, and he falls. He says, "I'm fine," but the finger stick log readings are 80 to 150 mg/dL and his A_{1c} is 7.1%. Lots of red flags. He is living alone and has had recent falls. Was it hypoglycemia? Is he eating well? What is his cognitive function like? We can consider

deprescribing by changing the regimen 1 of 3 different ways: liberalize or de-intensify or simplify.

So patient 1 might do well with liberalization. In this case that could mean setting higher A_{1c} or glucose goals for someone who is not going to benefit from tighter control and could be harmed. Does he really need an A_{1c} level of 7.1% or a glucose level below 80 mg/dL?

And for patient 2, who says she is missing a few doses per week but could be forgetting even more,... it's probably a good idea to consider deintensifying her regimen. So I would add insulin and take away the glipizide and GLP-1 RA.

Patient 3 is really not suited to self-care at this point. She was doing fine on the basal-bolus insulin, but a new comorbidity is straining her ability to cope; the regimen is now just too much for her to follow consistently. A good strategy here would be to keep the basal insulin but add a noninsulin injectable, a GLP-1 RA.

We actually conducted a study where we developed the algorithm for simplification of an insulin regimen that is now part of the ADA standard

day. Simplifying the regimen actually decreased the duration of hypoglycemia without changing the HbA_{1c} level, so that showed us that HbA_{1c} levels may not predict hypoglycemia risk in the older population. That shouldn't be the only parameter used in goal setting.

Bailey: Exactly. And I love the combination of long-acting insulin, basal insulin, and GLP-1 RA; for me that'll solve a lot of people's problems. And it's very simple, once a day; you can get it in a premixed form so that patients can just do it all at one time. And assuming they have some reasonable sense of their diet, they'll do very well. ■

REFERENCES

1. ElSayed NA, Aleppo G, Bannuru R, et al; on behalf of the American Diabetes Association Professional Practice Committee. 13. Older adults: standards of care in diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S244-S257. doi:10.2337/dc24-S013
2. Munshi MN, Neumiller JJ. Liberalisation, deintensification, and simplification in diabetes management: words matter. *Lancet Diab Endocrinol*. 2020;8(2):95-97. doi:10.1016/S2213-8587(19)30379-1



MORE ONLINE

To watch the entire discussion with Munshi and Bailey, visit:

<https://www.patientcareonline.com/consultantlive/geriatric-diabetes-care-optimizing-type-2-diabetes-management>