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## DIABETES

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## EMPOWERING EARLY INTERVENTION

# Navigating Treatments to Delay Type 1 Diabetes

In the *Patient Care*® *Institutional Insights* episode titled “Empowering Early Intervention: Navigating Treatments for Delaying Type 1 Diabetes,” Jennifer D. Goldman, PharmD, RPh, CDCES, BC-ADM, engaged diabetes experts from Pediatric Endocrinology of North Texas in a discussion about advances in the management of individuals 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, and understanding autoantibody testing for early diagnosis. They also discussed teplizumab, (Tzield; Sanofi), which recently received an FDA indication for slowing the progression of stage II type 1 diabetes to stage III, or frank type 1 diabetes. The following transcript has been edited for length and clarity.

#### MODERATOR

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By **Grace Halsey**, Senior Editor

**Jennifer D. Goldman, PharmD, RPh, CDCES, BC-ADM:** Dr Burton, would you talk about the prevalence of type 1 diabetes and also about the myth around who is at risk for the disease?

**Amy Burton, MD:** What’s interesting is that we are definitely seeing increased rates of type 1 diabetes diagnoses. And there are a number of different causes, including COVID-19 and other viruses. But although most people tend to think of type 1 diabetes as a disease diagnosed in children, over the past few years we’ve seen that the majority of new cases are in adults older than 20 years. And that’s the myth, that it’s always kids and that’s what we need to watch. It’s so important that we also consider adults and young adults when we think about diabetes and screening.

**Goldman:** How does family history affect the risk of type 1 diabetes?

**Burton:** A family history of type 1 diabetes increases a first-degree relative’s risk for the condition by 15-fold, so this is something that we need to speak to our patients about. We don’t take care of all of the children in a family or the adults; we may treat 1 person in a family of 5. We need to make the person we treat or the caregiver aware of the family risk and that there is screening available.

**Goldman:** What about the socioeconomic and emotional burdens of type 1 diabetes?

**Deborah Shenkman, RDL, CDCES:** Both burdens are huge. Financially, there are the direct costs of insulin, continuous glucose monitoring (CGM) supplies, pump supplies, and doctor’s visits, including other specialists and therapists. There are potential hospitalizations. The emotional aspect is sometimes even bigger. For a kid, there are the social implications: You’re a little bit different than your peers, and things

might look a little bit different for you at school or parties or sports. You might have to pay attention to things that nobody else has to pay attention to, such as carbohydrate counting and blood sugar monitoring. And then the strain on families is pretty incredible.

We see a lot of difficulties in marriages. Maybe one parent assumes the role of caring for the affected child, and resentment builds. All around, the impact of type 1 diabetes on a family can be huge.

**Goldman:** Very well characterized; thank you, Dr Shenkman. Now I'd like to talk some more about the different stages of type 1 diabetes.

**Kathryn Springfield, PA-C:**

I can highlight that. In the first stage, there are 2 or more autoantibodies for type 1 diabetes present. The immune system has not started attacking the pancreatic  $\beta$  cells, and blood glucose is still normal. The person is asymptomatic, and the body is still producing normal levels of insulin. In stage II, there are still 2 or more antibodies present, but you begin to see dysglycemia, higher fasting and postprandial blood glucose levels. There are still  $\beta$  cells able to produce insulin, so exogenous insulin isn't indicated. Stage II is the point where there is now something we can offer our patients, and we'll discuss this more. Stage III type 1 diabetes is frank type 1 diabetes. Antibodies have essentially destroyed pancreatic  $\beta$  cells, and the person is hyperglycemic and requires insulin to be stable.

**Goldman:** Dr Burton, what are the consequences of not being able to delay progression of stage II to stage III type 1 diabetes?

**Burton:** The most serious risk of not finding it early—and it can progress quickly from stage II to stage III—is that the first presentation can be diabetic ketoacidosis (DKA). Patients come to the hospital with hyperglycemia, dehydration, and elevated ketones because the body

hasn't produced insulin in so long. DKA has a high mortality rate and is also associated with significant morbidity. In the end, there is a very high cost to the patient and family as well as to the health care system.

**Goldman:** Let's talk about screening, which can help avoid that crisis. Who is at high risk? How should we screen?

**Burton:** The first group to think about are those with a first-degree relative with type 1 diabetes. When you're taking a family history or seeing a new patient on follow-up, just ask, "Do you have any type 1 diabetes in your family?" Anyone who answers "yes" needs to be screened. We also need to screen anyone with a history of autoimmune disease such as Hashimoto thyroid disease, celiac disease. We need to remember, too, that it's not only children at risk. We know that 1 in 300 children will develop type 1 diabetes, but the incidence peaks between the ages of 10 and 14, and again in young adulthood, between the ages of 20 and 30. Overall, I would say if you see somebody in clinic with dysglycemia, or blood glucose in the prediabetes range, it does not hurt to check for type 1 diabetes antibodies.

**Goldman:** Staying on the topic of screening, what antibody tests specifically should we be ordering? If we're in primary care what should we be doing?

**Shenkman:** There are 4 autoantibodies to screen for (**Figure 1**). They are insulin autoantibodies, glutamic acid decarboxylase autoantibodies, insulinoma-associated-2 autoantibodies, and zinc transporter 8 autoantibodies. If a person screens positive for 2 or more antibodies, their risk of developing type 1 diabetes over 10 years is about 70%. Their lifetime risk is 100%. You always want to confirm with a repeat laboratory test for anyone who has positive antibodies. Even if there is only 1, we still want to monitor for progression. This is where our primary

care and pediatric colleagues can help by doing this type of screening. As we said, we don't see the whole family, the siblings of our patients who have type 1. If we can start screening more proactively, we'll be able to catch these patients sooner to delay progression to stage III.

**Goldman:** That brings us to how we can delay that progression. Let's talk about the importance of the FDA approval of teplizumab for individuals at risk of type 1 diabetes.

**Springfield:** This approval is incredibly significant. We have this critical window of opportunity that we've never had before to be proactive instead of reactive. We can say, "Hey, we're going to catch it at stage II and you don't ever have to end up in the hospital with DKA." That's huge. We've never been able to do that. We've always been managing and treating, but never preventing.

Teplizumab is indicated for people at high risk who are 8 years and older. That is also incredible—think of these pivotal developmental years for kids. Puberty, teenagers, kids going to college—if we could prevent the onset during those times, it could decrease stress, improve quality of life overall for these patients. This medication is a game changer. And that's why we need to start screening and seeing who we can catch at stage II. We can buy some time.

**Goldman:** How does this game changer work? What is the mechanism of action of teplizumab?

**Burton:** Teplizumab is a CD3-directed monoclonal antibody (**Figure 2**). It binds to the autoreactive T cells that are destroying the pancreatic  $\beta$  cells. By binding to the T-cell receptor, teplizumab inactivates them. So the attack on the  $\beta$  cells is slowed down. The drug also increases the regulation of the protective T cells. The protection of the  $\beta$  cells is 2-fold.

**Goldman:** Would you now walk us through the pivotal study of

teplizumab, the phase 3 TrialNet 10 (TN10) [NCT01030861] study?

**Burton:** The TN10 study enrolled first-degree relatives of patients with type 1 diabetes who did not themselves have type 1. They were 8 years or older and at high risk for type 1 diabetes, meaning that they had 2 or more auto-antibodies detected in 2 blood samples within 6 months. They also had to have evidence of dysglycemia based on an oral glucose tolerance test (OGTT) and to meet several other blood glucose criteria. The primary outcome was the change in cell function as measured by C-peptide levels. The secondary outcomes were insulin doses, hemoglobin A<sub>1C</sub> (HbA<sub>1C</sub>), hypoglycemic events, and time in target glucose range.

The initial analysis showed that teplizumab compared with placebo significantly delayed the onset of stage III type 1 diabetes by 2 years (**Figure 3**). In the extended analysis that ran for about 79 months, they saw an additional delay in the time to progression to stage III, of almost 3 years (2.7 years). That's almost 3 more years before a teenager, maybe a college student, would need to be on daily insulin. It only takes one time overdosing on insulin after a party.

**Goldman:** At Pediatric Endocrinology of North Texas, you have had experience with teplizumab infusions. What type of outcomes have you seen?

**Burton:** I have a patient who is a sibling of one of my other patients who has type 1 diabetes, and I was seeing her for Hashimoto disease. She started showing symptoms of dysglycemia when she was 17 years old. We did the teplizumab infusion

about 9 months ago, and she still does not require insulin. Her blood glucose levels are normal as of the laboratory testing we did a few weeks ago. She's starting college this fall and won't be starting with an insulin pump. This is just such a relief for these families to not have to worry about their children in a way that families with kids who have full stage III, insulin-dependent diabetes have to worry about them.

I follow her every 6 months and screen for fasting blood glucose level and HbA<sub>1C</sub>. At home, I have her check her 2-hour postprandial blood glucose once every few weeks.

**Goldman:** What about adverse events with teplizumab? The rate of lymphopenia in the TN10 trial was quite high.

**Burton:** Lymphopenia happens in almost everyone, and I tell families that means the teplizumab is working. But it resolves quickly. A pruritic allergic-looking rash is common but topical hydrocortisone cream takes care of it. Mild flulike symptoms, headache, and runny nose also are common but transient.

**Goldman:** In terms of where infusions are being done, where are you sending your patients?

**Shenkman:** Right now, we're using a couple of local infusion centers. We are also exploring other options, such as home health or partial home health, where the patient starts treatment in an infusion center for the first few days to be monitored, and then the remainder is done through home health. A lot depends on whether there is space available 14 days in a row. The teplizumab treatment is a 2-week process with a 30-minute infusion every day. The first dose

is a low one and then it is doubled each day until day 5 and that is the maximum dose and given from day 5 through 14. Any adverse effects typically appear within those first 5 days of dose escalation. We always check patients in the office after the infusion, and we have an after-hours phone line. We see them after each infusion, then again right after the 2-week treatment, and then I see them in a month after the last dose.

As far as blood tests, we do complete blood count and liver function tests (LFTs) during the infusion. We check them again during the office visit after the 2-week treatment to make sure things are resolving, and they do. As in the TN10, lymphopenia and elevated LFTs all resolved between 2 and 6 weeks after treatment.

**Goldman:** What has your experience been like with payers?

**Shenkman:** We are seeing that each insurance company has different criteria to gain approval. The treatment was approved pretty quickly when we started it in 2023. This year has been much more difficult. Earlier, they might have asked for 1 set of autoantibodies, and now they want repeat levels within 6 months of each other. They want OGTT results, B-peptide levels, and specific fasting glucose levels. It may require a little more for approvals. But we're prepared, we're appealing, and we're fighting it because when you see these kids that are 100% stage II and you want to slow down that progression to stage III, you just feel like you've got to do everything you can to get this approved. ■



#### MORE ONLINE

To watch the entire discussion with Goldman, Burton, Shenkman, and Springfield, visit,

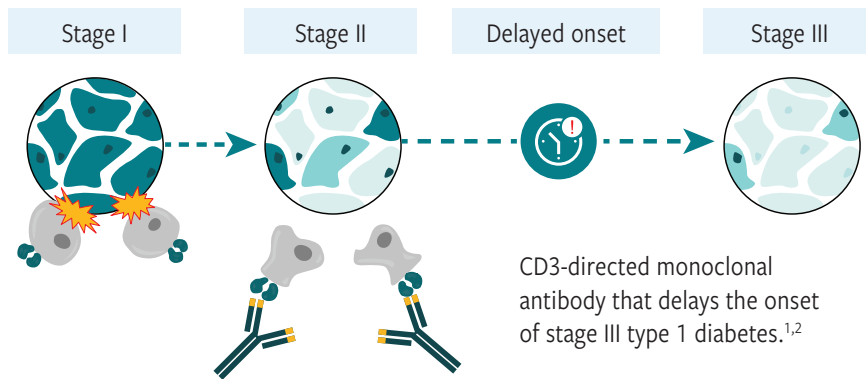
<https://www.patientcareonline.com/institutional-insights/empowering-early-intervention-navigating-treatments-for-delaying-t1d-progression-north-texas>

## FIGURE 1. Autoantibodies Preceding Type 1 Diabetes

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

## FIGURE 2. Teplizumab: Mechanism of Action

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



1. FDA approves first drug that can delay onset of type 1 diabetes. FDA. January 1, 2023. Accessed February 12, 2024.

<https://www.fda.gov/media/164864/download>

2. Thakkar 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 III T1D 2 Times Longer in Teplizumab-Treated vs Placebo-Treated Patients<sup>1</sup>

**~2-YEAR DELAY**

Teplizumab **significantly delayed** stage III T1D onset compared with placebo in stage II T1D (~4 vs ~2 years median time to progression, teplizumab vs placebo, respectively).<sup>1</sup>

**~2.7-YEAR DELAY**

Extended analysis further demonstrated a median time to stage III T1D diagnosis of 59.6 vs 27.1 months for teplizumab vs placebo, respectively.<sup>1</sup>

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  $\beta$ -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

IV, intravenous; T1D, type 1 diabetes.

## GERIATRIC DIABETES CARE

# Optimizing Type 2 Diabetes Management

In recent episodes of the *Patient Care ConsultantLive* program, Medha Munshi, MD, a geriatrician with expertise in type 2 diabetes (T2D), discussed the challenges of ensuring safe and effective care for older adults with 2 experts: John E. Anderson, MD, an internist focused on diabetes treatment in primary care, and Conan Tu, MD, MBA, DACD, BC-ADM, a diabetologist and primary care clinician. Transcripts from each discussion follow and have been edited for length and clarity.

## A Conversation With John E. Anderson, MD

By **Grace Halsey**, *Senior Editor*

**Medha Munshi, MD:** What percentage of your patient population with T2D is 65 years old or older?

**John Anderson, MD:** I think between 10% and 25% of the patients in my practice are in that age range. When you've been in practice for a while, your patients tend to grow older with you. And now, about 10,000 adults are turning 65 every day [in the US].

**Munshi:** Older and younger patients with T2D really are different and need a different focus. For example, we know that older adults have a higher likelihood of both hyper- and hypoglycemic episodes and that they may not be aware of these changes. They're at greater risk for adverse cardiovascular

events and complications, more likely to have polypharmacy, and increasingly less able to manage their disease on their own.

I want to talk about who is an *older adult* for a minute because not all 85-year-old individuals with T2D are going to be the same. Some may still be agile and independent, but others may be more frail. They will require different approaches to care and to setting appropriate glycemic goals. The message is that it's a very heterogeneous population, that the number doesn't tell us the whole story and neither does physical appearance. What we have to be aware of and always keep in mind is the patient's biological age because part of aging is the process of homeostenosis, a decline in the physiological reserve that allows us

to maintain homeostasis in the presence of any kind of stress. The stress could be environmental, physiological, or emotional; there is a physiological limit beyond which the body cannot bounce back. We might give a younger person with a urinary tract infection (UTI) an antibiotic and they would improve. An older person might end up admitted to the hospital for the same UTI.

**Anderson:** We have to be very careful not to just treat all of our patients with T2D the same and to pay particular attention to these older adults, regardless of how healthy they appear at the time of the presentation of the stressor. To your point about bouncing back, for an older patient with T2D, a hypoglycemic episode could have a long-term impact.

**Munshi:** As a geriatrician, there is another concept I want to discuss that has to be considered when caring for our older patients with T2D: the so-called geriatric syndrome. These are health

In this episode of *Patient Care ConsultantLive*, Medha Munshi, MD, and John Anderson, MD, discussed the challenges of ensuring safe and effective care for older adults with type 2 diabetes (T2D). Topics included the physiologic changes associated with aging, appropriate medication choices and glycemic goals, and the unique impact of geriatric syndromes on older patients' ability to tolerate treatment and care for themselves appropriately.

#### PARTICIPANTS

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conditions that are specific to the older population and don't impact a specific organ or system but can significantly impact our approach to care and the individual's ability to care for themselves. The most prominent elements of geriatric syndrome are things such as cognitive dysfunction, depression, physical disability, and effects of polypharmacy. In our day-to-day assessment of our patients, these things may not be top of mind, but we have to remember to factor them in. Other examples of geriatric syndrome conditions are urinary incontinence, pain, and frailty. Dr Anderson, does this topic resonate with you?

**Anderson:** Yes, it does. It is a matter of making sure you're taking a thorough history. If you're doing

an annual wellness visit, you ask about urinary symptoms, you ask about urinary incontinence, and then you break down whether there is urinary stress incontinence. Is this urge incontinence? You look for things such as neurogenic bladder. We always want to ask about neuropathy and pain, [do a] foot inspection, that type of thing.

Assessing cognitive impairment requires a delicate balance, I think. Often, we need family members in the room to be able to address that issue. If the patient is alone, it's "I am fine, Dr Anderson, I am great," until you realize that they're not great. A family member can help navigate that situation. I am going to say that one of the most challenging aspects of ensuring the best care for our older patients can be medication adherence, and I think that the issue of cognitive impairment, a part of the geriatric syndrome, is underlying that.

**Munshi:** Let's talk about how to set glycemic goals for an older adult because, as we have been saying, it's not about the number, how old they are; the goal needs to be based on a range of patient characteristics. The American Diabetes Association (ADA) Standards of Care in Diabetes for older adults suggests using 3 categories of health status when deciding how stringent the goals should be for hemoglobin A<sub>1C</sub> (HbA<sub>1C</sub>). First, is the patient *healthy*? That is, without many chronic comorbidities that would impact self-care and with cognitive function intact and good functional status. For that person, a reasonable HbA<sub>1C</sub> goal might be between 7% and 7.5%. Is the patient's health status considered *complex/intermediate*? That would mean they have several other chronic conditions, 2 or more impairments in instrumental activities of daily living (ADLs), or mild/moderate cognitive impairment. Then you'd want a more moderate glycemic goal of under 8%. The last

category is considered *very complex/poor health*, with a patient likely in long-term care, maybe with late- or end-stage chronic disease, and with moderate/severe cognitive impairment and significant impairment of ADLs. In these patients, we really do not want to rely on HbA<sub>1C</sub> as a reliable measure because of the other conditions that can impact HbA<sub>1C</sub> measurements. We will focus on avoiding hypoglycemia and symptomatic hyperglycemia.

Which of the 3 categories the older person with T2D fits into will also affect our choice of medication. We do have newer drug classes that pose less risk of hypoglycemia, and maybe we can be a little more aggressive with treatment in the healthy and intermediate groups, depending on age and life expectancy.

**Anderson:** If we look at the most common medication classes, those would be metformin, sulfonyleureas, thiazolidinediones, dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), sodium-glucose cotransporter-2 (SGLT2) inhibitors, and insulin. We have to consider the patient-related factors and match them with the characteristics of the medication class. For the medication classes, some of the most important characteristics we need to consider are whether the medications pose a risk of hypoglycemia, whether the class is known to promote weight loss or is associated with weight gain, the efficacy of the class in reducing hyperglycemia compared with other classes, and the cost of the drugs.

**Munshi:** Also, the newer classes of glucose-lowering drugs have multiple benefits so that you can approach your choice from the perspective of the patient's comorbidities and disease-specific effects of the medication in addition to being antihyperglycemic. (**Figure 1**). Does the person have

atherosclerotic cardiovascular disease (ASCVD)? Choose a GLP-1 RA over an SGLT2 inhibitor. If they have congestive heart failure or chronic kidney disease that is progressing rapidly, the SGLT2 inhibitors would be the better choice. The SGLT2 inhibitors have been shown highly effective in reducing hospitalization for heart failure and also mortality. The GLP-1 RAs, as we know, are also potent antiobesity medications, and one has recently received an indication for reduction of cardiovascular risk in adults with obesity with ASCVD.

I am going to change the subject to deciding which medications to stop or to replace: the concept of deprescribing. Dr Anderson, what are your thoughts about deprescribing?

**Anderson:** I have an example of when it is appropriate. I have a patient who was referred to me because her physician had left another practice. She is a frail 83-year-old, just got out of rehabilitation after a fall, has cognitive impairment, and was taking a glinide 3 times a day with meals. Her HbA<sub>1C</sub> was 5.8%. She was also on a DPP-4 inhibitor, so I left that on board and stopped the glinide. I am not going to worry if her HbA<sub>1C</sub> goes up to 7%. The risk of hypoglycemia was tremendous for this fragile person. Why would we risk that to keep her HbA<sub>1C</sub> below 6%? Once again, it is about individualizing the approach to care, talking to the patients and their families. The No. 1 priority for our older, frail patients is keeping them safe.

**Munshi:** Absolutely, and that is really the definition of deprescribing: identifying and discontinuing

medications that no longer provide benefits to the patients and could be causing harm, with the goal of minimizing the risk associated with unnecessary polypharmacy (**Figure 2**). It is not like the deprescribing concept for drugs such as antipsychotics or narcotics where you might completely discontinue a regimen or cut the dose in half. It's a whole different idea, and that has to be emphasized to our patients, their families, and sometimes, too, our colleagues. Keeping in mind the 3 main tenets of deprescribing—liberalize, deintensify, simplify—let's look at some cases.

For example, the first patient (**Figure 3a**) is an 89-year-old man with multiple comorbidities. He lives alone and was prescribed a basal-bolus insulin regimen because he can't really take anything else. He has been falling but insists that he is OK. But his fingerstick blood glucose readings are between 80 and 150 mg/dL. His HbA<sub>1C</sub> is 7.1%. So even though overall things look all right, HbA<sub>1C</sub> may not be an appropriate measure with which to judge control of his T2D because of his end-stage renal disease. I would consider liberalization of his goal, setting it higher for a person who will not benefit from tight control and in fact could be harmed. Instead of relying on HbA<sub>1C</sub>, I recommend keeping his blood glucose level between 100 and 200 mg/dL.

The second patient (**Figure 3b**) is an 89-year-old woman taking many medications for cardiovascular comorbidities plus metformin and glipizide twice daily and a GLP-1 RA once a day. She admits to forgetting 2 or 3 doses a week, and if she's forgetting 2 or 3 doses,

she likely doesn't remember how many she actually forgets. For her, I would consider deintensifying the regimen. I would consider starting basal insulin and discontinuing the glipizide; I would swap the daily GLP-1 RA for an injectable weekly formulation and possibly think about discontinuing the metformin.

The third patient (**Figure 3c**) is an 84-year-old woman with T2D on long-standing treatment with basal-bolus insulin, but a stroke has limited her ability to cope with the regimen and her husband can't step in to cover. In this case, we want to simplify the strategy to match a person's coping ability. A good strategy would be to keep the basal insulin but add a noninsulin injectable—a GLP-1 RA—that would provide the benefit of the prandial insulin.

We conducted a study where we developed the algorithm for simplification of an insulin regimen that is now part of the ADA standard of care. Participants were 70 years or older, received multiple daily insulin injections, and had 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. Most of the patients did better with glargine and a GLP-1 RA once a day. Simplifying the regimen actually decreased the duration of hypoglycemia without changing the HbA<sub>1C</sub> level, so that showed us that HbA<sub>1C</sub> levels may not predict hypoglycemia risk in the older population. That shouldn't be the only parameter used in goal setting. ■



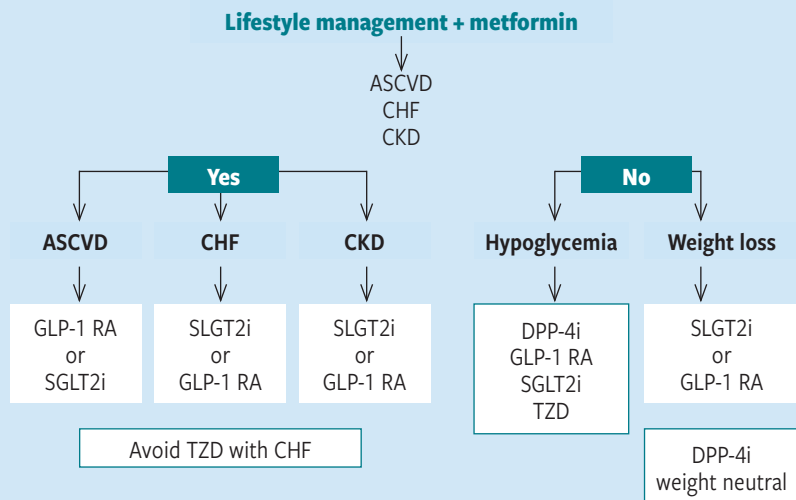
#### MORE ONLINE

To watch the entire discussion with John E. Anderson, MD, visit:

<https://www.patientcareonline.com/consultantlive/tailored-diabetes-care-customizing-management-strategies-across-life-stages>



**FIGURE 1. Simplified Treatment Algorithm for Type 2 Diabetes**

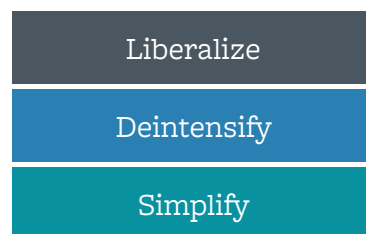


ASCVD, atherosclerotic cardiovascular disease (ASCVD); CHF, congestive heart failure; CKD, chronic kidney disease; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; SGLT2i, sodium-glucose cotransporter-2 inhibitor; TZD, thiazolidinedione. Adapted from American Diabetes Association Professional Practice Committee.

**FIGURE 2. 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:**



Adapted from Munshi and Neumiller.

**FIGURE 3A**

### 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<sub>1c</sub>, 7.1%

#### Consider liberalization

- Raise HbA<sub>1c</sub> or glucose goals for patients who will not benefit from tighter control and may be harmed.

**For this patient:** Liberalize the blood glucose goal to 100-200 mg/dL

CAD, coronary artery disease; CHF, congestive heart failure; ESRF, end-stage renal failure, HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>.

**FIGURE 3B**

### Patient 2

- 89 years old taking 3 antihypertensive and 2 lipid-lowering medications
- Diabetes medications: metformin twice a day, glipizide twice a day, GLP-1 RA daily
  - 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.

**FIGURE 3C**

### 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

# A Discussion With Conan Tu, MD

By **Grace Halsey**, *Senior Editor*

**Medha Munshi, MD:** According to the Centers for Disease Control and Prevention, the diabetes rate among US adults 65 years and older is about 30%. Dr Tu, do you see more older patients now with type 2 diabetes (T2D)?

**Conan Tu, MD, MBA, DACD, BC-ADM:** As a diabetologist, and also as a primary care physician, I feel that the population of older patients with T2D is significantly more, and then, of course, we're in this epidemic of obesity right now. And as people get older, they tend to gain weight, especially with the American diet and lifestyle, or lack thereof. And exercise is challenging. But as more medications have become available, patients are living longer. And with that, they're also living with more comorbidities as well.

**Munshi:** More comorbidities at older ages is one of the key challenges in managing the older population versus younger adults with T2D, isn't it? They are likely to be taking more medications, given their comorbidities, and polypharmacy is a risk factor for drug-drug interactions. Older patients are at greater risk for major adverse cardiovascular events; they also could be at greater risk for hypoglycemia and lower awareness of hypoglycemia and hyperglycemia events. Of course, there are the impairments to self-management in the older population that we don't typically see in the younger.

**Tu:** I think those issues between older and younger patients with T2D require us to individualize

our approach, depending on our patients specifically. Everybody is different. Some people like steak, and some people like fish; it's that you have to customize your approach, depending on the unique needs of each individual patient.

**Munshi:** Yes, there is heterogeneity among our patients with T2D and also within different age groups. We need to be aware of a particular sort of heterogeneity in older adults. You might have two 85-year-old patients in your waiting room, and one might still be active and full of vitality, and the other one might use a cane. They are going to have different goals, and our treatment approach is going to be different for each of them. But even though we'll see older adults who don't appear or behave their age, we still need to think about age in terms of the decades that have passed, because everybody is affected by homeostasis, a progressive constriction of homeostatic reserve. We all experience a decline in the ability of our bodies to maintain homeostasis in the presence of stress, whether that's environmental, physiological, or emotional. There is a physiological limit beyond which the body cannot bounce back, and this limit narrows with increasing age. So, if a younger person with T2D has a hypoglycemic episode and is admitted to the hospital, they'll be discharged in 2 days. An older person can be there longer, develop other complications; the outcomes will be much worse.

I am a geriatrician. I want to discuss another concept we all need to consider when caring for

In this episode of *Patient Care ConsultantLive*, Medha Munshi, MD, and Conan Tu, MD, MBA, DACD, BC-ADM, discussed the challenges of ensuring safe and effective care for older adults with type 2 diabetes (T2D). Topics included the physiologic changes associated with aging, appropriate medication choices, and glycemic goals, and the unique impact of geriatric syndromes on older patients' ability to tolerate treatment and care for themselves appropriately.

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our older patients with T2D: the so-called geriatric syndrome. This is a group of health conditions that are specific to the older population and don't impact a specific organ or system but can significantly impact our approach to care and the individual's ability to care for themselves. Some prominent elements of geriatric syndrome are cognitive dysfunction, depression, physical disability, and polypharmacy. I don't think we intuitively think about them when we are thinking about diabetes, and patients probably don't recognize the impact they can have on their T2D.

## What HbA<sub>1c</sub> Target Makes Sense?

**Munshi:** We have talked about the challenges of treating our older patients with T2D—more comorbidities, reduced cognitive ability, lower functional status, reduced independence. All of those elements are going to impact how we decide on a target glycemic goal for an individual. The American Diabetes Association (ADA) Standards of Care for older adults suggest using 3 categories of health status when deciding how stringent the goals should be for hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>).

First, is the patient *healthy*? That is, without many chronic comorbidities that would impact self-care and with cognitive function intact and good functional status? For that person, a reasonable HbA<sub>1c</sub> goal might be between 7% and 7.5%.

Is the patient's health status considered *complex/intermediate*? That would mean they have several other chronic conditions, 2 or more impairments in instrumental activities of daily living (ADL), or mild/moderate cognitive impairment. Then you'd want a more moderate glycemic goal of under 8%.

The last category is considered *very complex/poor health*, with a patient likely in long-term care, maybe with late- or end-stage chronic disease, and with moderate/severe cognitive impairment and significant impairment of ADLs. In these patients, we really do not want to rely on HbA<sub>1c</sub> as a reliable measure of glycemic control because of the other conditions that can impact HbA<sub>1c</sub> measurements. For patients in this category, the focus is on avoiding hypoglycemia and symptomatic hyperglycemia.

## Choosing Medication Class

**Munshi:** And since we are considering patient-specific factors for determining treatment goals, we can also talk about how some of those factors influence the medication

class we choose. For primary care, it can be confusing; the good news is that we have many choices, and that's also sort of the bad news. If we look at the most common medication classes, those would be metformin, sulfonylureas, thiazolidinediones (TZDs), dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), sodium-glucose cotransporter-2 (SGLT2) inhibitors, and insulin. There are the factors specific to the patient and those that are specific to the drug class that we have to balance when selecting. For patients who are prone to or have low awareness of hypoglycemia, you'd stay away from sulfonylureas or insulin. If weight loss is a concern with a patient, we wouldn't prescribe a GLP-1 RA and possibly wouldn't worry about choosing a sulfonylurea, a TZD, or even insulin. If overweight or obesity is a patient-specific factor, we know that the newer classes, the GLP-1 RAs and SGLT2 inhibitors, and particularly the former, are also indicated for their antiobesity effects. In terms of efficacy, the DPP-4 inhibitors and SGLT2 inhibitors are not as efficacious as other classes for lowering HbA<sub>1c</sub> and may need to be prescribed with another class. And cost, a medication-specific factor, will continue to be an issue with the new, nongeneric medications.

The newer classes of glucose-lowering medications have proven effective in other cardiometabolic diseases, and the ADA in its diabetes treatment guidelines recommends choosing second-line medication to treat T2D based on an individual's comorbidities or risk for those comorbidities (**Figure 1, page 9**). If the patient has atherosclerotic cardiovascular disease, a GLP-1 RA is recommended over an SGLT2 inhibitor. But for a patient with congestive heart failure (CHF) or at risk for progression of chronic kidney disease (CKD), the SGLT-2

inhibitors are known, in the case of CHF, to reduce the risk for hospitalization for HF and for HF-related mortality and, in CKD, to reduce the rate of disease progression.

## The Concept of Deprescribing

**Munshi:** Now we're going to talk about the patient-specific factors in our older adults with T2D and consider how we may need to change our treatment approach over time. We're going to talk about the concept of deprescribing. I think that term has a very different connotation for primary care physicians than endocrinologists. I think that primary care physicians feel very comfortable with the idea but endocrinologists feel as though we are taking something away that the patient needs.

Deprescribing involves identifying and discontinuing medications that either no longer provide benefits or could be causing harm, with the goal of minimizing the risk associated with unnecessary polypharmacy. This isn't a new concept, but there can be barriers and challenges associated with it, such as clinician awareness and education, possibly patient resistance or concerns, health system or practice barriers or limitations, and we really don't have clear guidelines or protocols for how best to do deprescribing. Anything you'd like to add to that, Dr Tu?

**Tu:** I vote for all of the above, and I would also throw in clinical inertia. I would throw in time constraints. All clinicians are under time pressure, and it takes time to do deprescribing appropriately.

**Munshi:** Absolutely true, those are both important barriers. Now I have 3 sample cases to share that highlight the main tenets of deprescribing to keep in mind when that older adult with T2D comes to clinic and has been following a complex medication regimen

for years but now you see some red flags that make you think this approach isn't working anymore. You can think about liberalizing goals or targets, deintensifying the therapy, or simplifying the regimen (**Figure 2**). There are multiple approaches. For example, you have an 89-year-old patient with multiple comorbidities (**Figure 3a**) who lives alone and has been falling. He tells you he's OK, but you have to wonder: Is he eating well, are the falls due to hypoglycemia? Then he brings his finger stick readings in, and his blood glucose levels are between 80 mg/dL and 150 mg/dL. His HbA<sub>1c</sub> is 7.1%, which is reasonable for his age. My approach here would be to think about liberalizing his goals. He is an example of a patient who could benefit from higher HbA<sub>1c</sub> or blood glucose goals because he is not benefiting from the tighter control. In this case, I would not focus on the HbA<sub>1c</sub> because the end-stage renal disease may affect that measure. I would liberalize the blood glucose goal, keep his finger stick reading at 100 mg/dL to 200 mg/dL. Any tighter control than that is really not going to benefit him.

**Tu:** Yes. In that patient population, your goal is not to prevent retinopathy or nephropathy in 15 years. The patient's already 89 years old. Do no harm, treat the patient. We're not worrying about reducing comorbidities in 20 years. It's a different focus.

**Munshi:** Avoid the harm today, don't try to avoid something in the limited future. The second example (**Figure 3b**) is a woman, also 89 years old, who is a very good example of polypharmacy. When

asked, she says she takes most of her medicines, maybe forgets 2 to 3 doses a week. That's a red flag. If she remembers that she forgets 2 to 3 doses, we don't know how many doses she does not remember that she forgot. I would deintensify her regimen to reduce the burden of her therapy because she has some cognitive decline and is dealing with polypharmacy. To deintensify, you could discontinue any nonessential medications or consider using long-acting formulations to limit dosing. My recommendation is to actually add basal insulin, discontinue glipizide, and replace the daily oral GLP-1 RA with an injectable formulation. Deprescribing in the context of diabetes is a change in strategy; it's focusing on the barriers to optimal care and looking at ways to improve patients' coping skills and get better control with less risk.

**Tu:** And those forgetful patients who are missing doses may also err on the other side; they think they might have missed a dose, and they will actually double dose and take it again because they don't remember. And that is so dangerous for somebody who takes 50 units of additional insulin.

**Munshi:** That is such a good reminder. Let's look at one more hypothetical case (**Figure 3c**). She is 84 years old with T2D and has been taking basal-bolus insulin for many years. She's had a stroke, and after discharge, she is not able to self-monitor her blood glucose or manage the multiple daily injections. She lives with her husband, but he can't help during the day. So, this is the patient where you want to

simplify the regimen to match the patient's coping ability and, in this case, the caregiver's, too. The recommendation for this patient is to keep once-a-day basal insulin, and then add a noninsulin agent to address the postprandial rise. Or you have the option of using a fixed dose insulin-GLP-1 RA combination formulation.

### Simplifying an Insulin Regimen

**Munshi:** As we have mentioned, there are algorithms and recommendations on adding medications to our patients' therapies, but not much guidance on taking medications away. My colleagues and I did a study on simplification of insulin regimen where we took people older than 70 years with T2D, all on multiple daily insulin injections, and all had 1 or more episodes of hypoglycemia (blood glucose of less than 70 mg/dL) as measured by continuous glucose monitoring. For 5 months of active intervention, we simplified the regimens with once-a-day insulin glargine plus noninsulin agents. We then didn't have contact for 3 months to see if they could maintain the simplified strategy. We found that simplification of strategy not only lowered the duration of hypoglycemia, but it did so without impacting HbA<sub>1c</sub> level. So the concern that a simpler regimen could mean losing control of HbA<sub>1c</sub> isn't supported. If you make the regimen easier to follow, glycemic control can improve. The results of the study are included in the ADA standards of medical care in diabetes, in the section on older adults. ■



#### MORE ONLINE

To watch the entire discussion with Munshi and Tu, including 2 patient cases from Tu's practice, visit:

<https://www.patientcareonline.com/consultantlive/geriatric-diabetes-care-optimizing-type-2-diabetes-management-insights-from-dr-conan-tu>