Health Monitor®

# Clinician Update

## Type 2 Diabetes Management

Scan here for a behind-the-scenes look at the case study on p. 20



Content reviewed by:

AACE®

# Overcoming clinical inertia: **The key to better outcomes**

Intensifying therapy to reach targets sooner can help stave off complications and improve quality of life. Here, experts offer strategies for proactively managing diabetes.

**Clinical inertia**—the failure to initiate or intensify treatment despite evidence of a need for a change in therapy—contributes to inadequate chronic disease care in patients with diabetes. Even more concerning is evidence that clinical inertia related to the management of diabetes, hypertension and lipid disorders may result in up to 80% of heart attacks and strokes.[1]

Jay Shubrook, DO, Professor in the Primary Care Department at Touro University in California and coauthor of a recent review on clinical inertia in *Diabetology*, says that despite the evolution in treatment options and improved understanding of pathophysiology, the treatment of type 2 diabetes remains unsatisfactory.[2] The study concluded that "intensive lifestyle modification, pharmacologic approaches and metabolic surgeries are each viable options for improving outcomes when implemented early in the disease course." When put into practice promptly, these treatment options can help patients reach their target goals and achieve optimal control. It's important to note, however, that healthcare providers must work closely with their patients and apply strategies for overcoming inertia to achieve treatment goals.

"Many people think diabetes progresses inevitably to complications," says Dr. Shubrook. "But if patients are willing to get screened, find the condition early and 'go big' in terms of treatment, their diabetes can be well controlled, significantly reducing the risk of complications. He stresses that treating diabetes is most effective in the first 2 years of the disease.

*Continued on p. 4* ►

Illustration by Ken Orvidas

When treating diabetes, targeting blood pressure and LDL cholesterol is as crucial as controlling blood glucose. Evidence-based therapies to manage cardiometabolic risk factors include:

- Two classes of antihyperglycemics: GLP-1 receptor agonists (GLP-1 RAs) and SGLT2 inhibitors, which help reduce the risk of cardiovascular disease independent of their ability to lower glucose. SGLT2 inhibitors are also indicated for treating chronic kidney disease and heart failure
- ACE inhibitors and angiotensin receptor blockers (ARBs) for hypertension
- Statins to reduce LDL cholesterol

## More options for tailored treatment

Betul Hatipoglu, MD, Director of the Diabetes and Metabolic Care Center at UH Cleveland Medical Center, recommends individualization of medication and treatment for patients. Prescribing metformin, although still a mainstay of treatment, is usually not enough by itself to maintain long-term control.[3] "Metformin has been around for a long time, and it's a safe medication," Dr. Hatipoglu says. "But we now have more tools in our toolbox, and we can do more specialized and individualized therapy for our patients."

GLP-1 RAs and SGLT2 inhibitors target not only blood sugar but also diabetes-related complications. Medications like these have allowed the treatment of type 2 diabetes to shift from a focus solely on lowering AIC to prioritizing agents with proven cardiovascular and renal benefits. According to a recent real-world study, combination therapy with SGLT2 inhibitors and GLP-1 RAs resulted in a 34% decreased risk of myocardial infarction, ischemic stroke and cardiovascular mortality.[4]

Statins and ACE inhibitors also allow for more specialized and individualized therapy. The AACE diabetes guidelines emphasize that any patient with diabetes who has cardiovascular disease, or is at high risk of it, should be receiving treatment to lower their LDL cholesterol and blood pressure.[5] "The best thing we can do for our patients is remind them that front-loading their regimen by getting control of glucose, blood pressure and lipids immediately upon diagnosis will have lasting effects," Dr. Shubrook advises. "The earlier we control this disease by considering all options, the easier it is to tame it, and the greater the potential for subtracting treatments down the road."

Dr. Shubrook also notes that in addition to antidiabetes medication, bariatric surgery may be an option for certain patients. In one study of insulin-treated patients with type 2 diabetes, gastric bypass surgery resulted in an improvement in AIC from 11.8% to 7.9%.[6] Of course, any surgery comes with risks, and patients with blood clots, liver disease and kidney stones may experience a worsening of these conditions post-surgery.

## Strategies for proactive management.

To help your patients achieve treatment targets and, ultimately, optimal outcomes, experts recommend the following:


Illustration by Ken Orvidas

### 1. Follow up often.

Regular monitoring of treatment goals and providing feedback to patients can help identify situations where intervention is needed. This can be achieved through regular follow-ups and by answering questions. In addition, Dr. Shubrook suggests that clinicians also try to put themselves in their patients' shoes. "If you are teaching me something new, like learning how to drive, you can't just give me a manual and say come back in 3 months," he says. "I wouldn't know where to begin." He recommends a minimum of 4 follow-up visits per year.

### 2. Incorporate team-based care.

"The touchpoints we have for our patients don't always have to be physicians," notes Dr. Shubrook. "We can utilize healthcare educators, community health workers, nutritionists and mental health professionals." Each team member can contribute their expertise and perspectives to help patients navigate their disease and ensure comprehensive and timely treatment changes between office visits.

### 3. Empower patients to be an equal partner in care.

In many cases, patients can be overwhelmed by the amount of treatment being recommended. "You have to be careful about how you approach your patients and how you recommend treatments to them," Dr. Hatipoglu advises. "As their clinician, you must help them understand the importance of getting treatment and managing their diabetes." Involving patients in shared decision-making and setting realistic goals together can empower patients to take control and be proactive in diabetes self-management. Also, when several recommendations are presented at once, it can be overwhelming. If patients implement one option at a time and build on it promptly, it can be more manageable.

### 4. Address adherence issues up front.

Many patients have no idea that they even have diabetes because it's a "silent" condition. "Patients often feel okay before they come to see me, and treatment may make them feel worse because they are 'detoxing,' " Dr. Hatipoglu says. "When start-

**"We now have more tools in our toolbox, and we can do more specialized and individualized therapy."**
***—BETUL HATIPOGLU, MD***

ing diabetes medications and working to lower blood sugar, patients may experience side effects such as dizziness, sweating and confusion. This can cause patients to become nonadherent to their treatment regimen. It's important to help them understand that they'll ultimately feel better as their body adjusts." In addition, Dr. Shubrook says clinicians must investigate the reason for nonadherence. "Adherence for many patients boils down to engagement," he says. "If a patient is struggling to keep up with their medication regimen, you should know why. Is it because they can't afford the medication? Is it because of intolerable side effects?"

## 5.
### Help them overcome financial barriers.

"We must remember to meet patients where they are, and that some treatment is better than no treatment if they can't afford what I recommend." Fortunately, insurance coverage for newer diabetes medications, statins and ACE inhibitors is becoming more commonplace.[7] It's important to become familiar with available resources for your patients, such as pharmaceutical patient assistance programs and co-pay cards as well as other options, such as *insulinhelp.org*. A pharmacist or social worker can also help patients find assistance programs they may be eligible for.

## 6.
### Stress the importance of lifestyle modification.

Lifestyle changes are key in the management of type 2 diabetes, particularly for patients with overweight/obesity who start a weight-loss plan. However, set realistic expectations for your patients. "People often think that 3 months of lifestyle modifications, which is a lot of work for most people, is going to change things immediately and when it doesn't, they end up believing it doesn't work." Encouraging your patients to continue with healthy habits, such as controlling portion sizes and being physically active for at least 30 minutes a day, can result in a loss of about 10 to 20 lbs. over time.[8]

For patients who smoke, quitting will vastly improve their health. In patients who have diabetes, smoking increases the risk of nerve damage, kidney disease and premature death from cardiovascular disease.[8] Advocate for your patients and give them resources to help them kick the habit, such as 1-800-QUIT-NOW or *smokefree.gov*.

Ultimately, a better understanding of clinical inertia and specific interventions to address it can help reduce diabetes-related morbidity and mortality. "Diabetes is a complex disease and healthcare providers are not set up to combat it alone," Dr. Shubrook says. "Decide who is going to be on the diabetes team. Whether it's nutritionists, PCPs or diabetes educators, utilize everyone as a resource and take the time to understand your patient and what works for them." ●

*—by Rikki Eccles*

## References


1. **O'Connor PJ, et al. Clinical inertia and outpatient medical errors. In: Henriksen K, et al, editors. *Advances in Patient Safety: From Research to Implementation*. Agency for Healthcare Research and Quality, Feb 2005.**
2. **Suits A, Gudoor R, Shubrook JH. Achieving remission in the era of clinical inertia: what is preventing us from treating type 2 diabetes? *Diabetology.* 2023;4(1):93-107.**
3. **Brown E, et al. SGLT2 inhibitors and GLP-1 receptor agonists: established and emerging indications. *Lancet.* 2021;398(10296):262-276.**
4. **Azoulay N, et al. The combined use of SGLT2 inhibitors and GLP-1 receptor agonists on the risk of cardiovascular events among patients with type 2 diabetes. *Diabetes.* June 2023;72(suppl 1).**
5. **Blonde L, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Plan—2022 Update. *Endocrine Practice.* 2022;28(10):923-1049.**
6. **Affinati AH, et al. Bariatric surgery in the treatment of type 2 diabetes. *Curr Diab Rep.* 2019;19(12):156.**
7. **Thomassian B. Diabetes meds on a budget. Diabetes Education Services. Available at *diabetesed.net.***
8. **American Diabetes Association. *Living Healthy with Diabetes.* Nov 1, 2023). Available at *diabetes.org.***

# Managing heart failure in patients with type 2 diabetes

**The challenges of managing heart failure (HF) and type 2 diabetes are intensified** when both diseases coexist—as they often do. As many as 47% of patients with HF also have diabetes, and that percentage is higher among hospitalized HF patients.[1] HF and diabetes have an interrelated pathophysiology and shared risk factors that converge to worsen outcomes for either condition.[2,3] In fact, emergency room visits, hospitalizations and deaths due to HF with preserved or reduced ejection fraction (HFpEF/HFrEF) are more common among HF patients with diabetes versus those with HF alone.[3] Fortunately, newer treatment options can help manage both conditions concurrently and improve patients' overall health. Yet many are missing out on the benefits of these breakthroughs. "The vast majority of patients are not receiving the combination of medications and dosing that will allow an optimal clinical outcome," says Gregg C. Fonarow, MD, Interim Chief of UCLA's Division of Cardiology, Director of the Ahmanson-UCLA Cardiomyopathy Center and Co-director of UCLA's Preventative Cardiology Program.

In addition, managing HF and diabetes concurrently presents unique challenges compared with treating either disease alone, including:

- ***Difficulty controlling blood pressure.*** Diabetes-associated cardiovascular autonomic neuropathy damages the autonomic nerve fibers that regulate vascular dynamics based on the patient's position, making treatment for hypertension more difficult. "Control of hypertension is essential for anybody living with heart failure," says cardiologist Raul J. Flores, MD, a heart failure specialist in Morristown and Summit, NJ. "But concurrent illness to the autonomic nervous system from diabetes can cause these patients' blood pressure to drop precipitously when they change positions, making it challenging to use traditional heart failure therapies." In fact, some patients need medications to raise symptomatically low blood pressure, he says.
- ***Treatment fatigue.*** Patients with diabetes take multiple medications to manage their blood glucose and complications such as dyslipidemia. "When you add heart failure to the mix, that's another four pills that I expect people to include on top of what they are already taking," Dr. Flores says. "The burden of care on these patients is quite heavy." Yet using these "four pills" is crucial for managing HF, Drs. Flores and Fonarow say.

## HF with reduced EF: optimizing the regimen

Clinical trial data [4,5] as well as HF guidelines from the American Heart Association/American College of Cardiology and European Society of Cardiology support initiating four agents concurrently or in rapid sequence in any order for HFrEF in patients with or without type 2 diabetes:

1. **A beta blocker** to counteract activation of the sympathetic nervous system and prevent ventricular remodeling.
2. **An angiotensin receptor/neprilysin inhibitor** (ARNI) to inhibit or augment various neurohormonal pathways and prevent ventricular remodeling.
3. **A mineralocorticoid receptor antagonist** (MRA) to regulate the renin-angiotensin-aldosterone system and prevent ventricular remodeling.

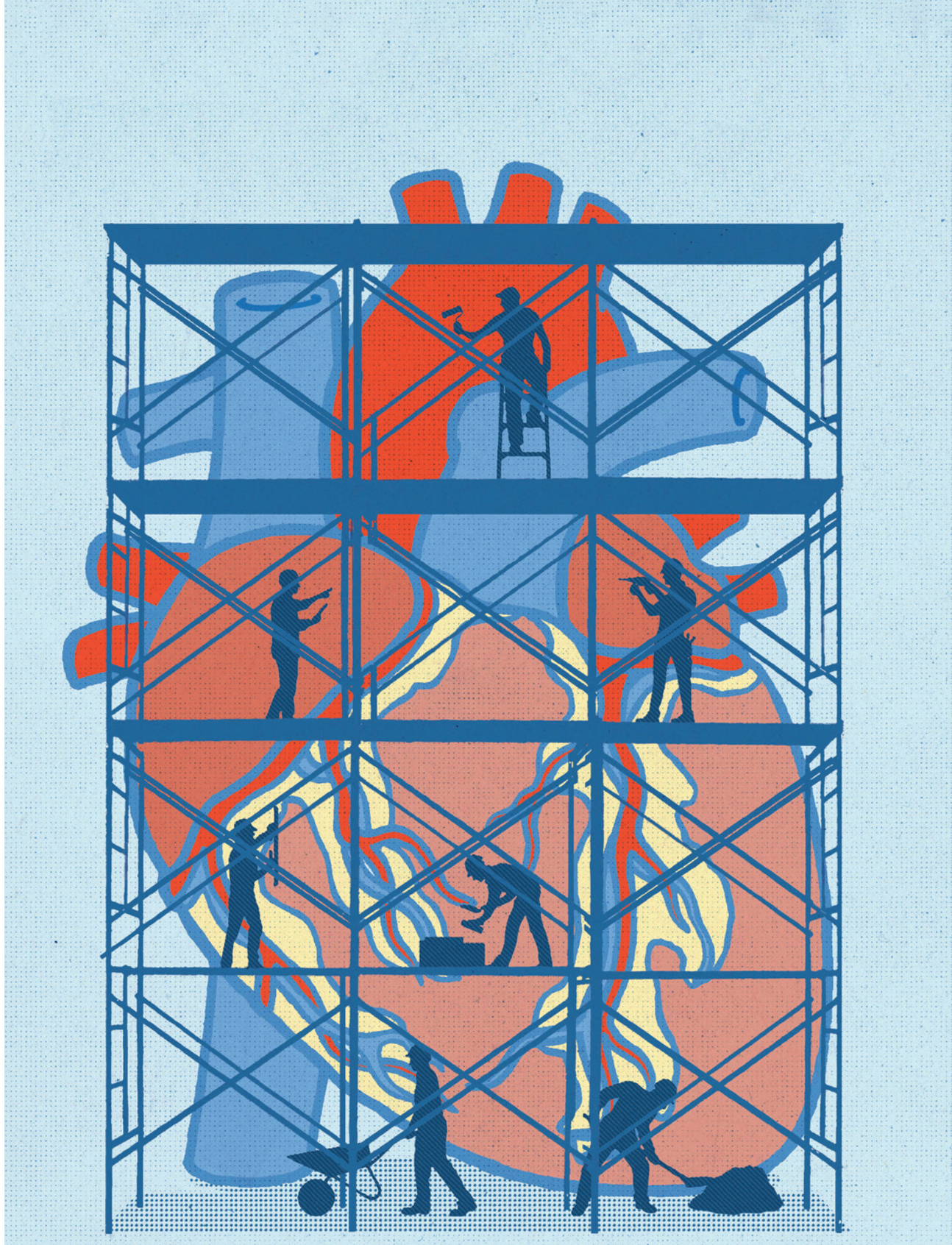

Illustration by Dan Page

## A key part of treatment:
# LIFESTYLE INTERVENTIONS

As with all cardiometabolic diseases, medications are only part of the management plan. Evidence shows that lifestyle interventions can help treat heart failure as well as vascular and metabolic complications of diabetes.[13,14] However, an unhealthy diet and physical inactivity—independent risk factors for heart failure and diabetes—are common among patients with both diseases, says Gregg C. Fonarow, MD, of UCLA's Division of Cardiology and Preventative Cardiology Program. But getting patients to change is a "monumental task," and physical inactivity among patients with heart failure and diabetes is a "vicious cycle," says heart failure specialist Raul J. Flores, MD, of Summit and Morristown, NJ. The patient's long-standing inactivity contributes to both diagnoses, but the shortness of breath that comes with heart failure prevents the patient from walking. "It's hard to say if people are having a sedentary lifestyle because of their heart failure, or they're having heart failure because of a lifetime of poor diet and lack of activity," he says. To help patients make lifestyle changes doable, Drs. Fonarow and Flores suggest the following:

**Set simple dietary goals.** Ask patients to think about their daily routines and what they could do differently to incorporate healthier habits. Also, suggest that patients make a checklist each morning and list intended changes, such as replacing one unhealthy food item for a nutritious one or making a healthy meal at home instead of going to a restaurant where the options are limited.

**Advise easy, gentle exercise.** Patients may want to consider low-impact, semi-static exercises, such as chair yoga or stretching. Another option is an at-home walking program where they walk at a moderate pace around the house or yard for 10 minutes and then gradually increase their time. "It can be intimidating to a patient who has been inactive, is fatigued, and may be dealing with neuropathy, osteoarthritis or other issues to get up and go out for a jog," Dr. Flores says.

**Use technology.** There are numerous smartphone apps that can encourage patients to track their daily steps and dietary habits. One to consider: The American Heart Association's HF Helper app, which gives patients an easy way to log not only their daily exercise and calorie intake but also HF symptoms, medications and more, Dr. Fonarow notes (available for download at *heart.org*).

**Help them connect with resources.** Referral to a cardiac rehab program can motivate patients toward positive change, Dr. Fonarow says. Also, consider referring patients to a dietitian for help with establishing healthy eating habits, Dr. Flores suggests. In addition, many towns have senior citizens centers where older patients can participate in activities and meet peers. "Often, my patients become socially isolated," notes Dr. Flores. "Encouraging them to meet other people and having a sense of community can help them feel more motivated."





4. **An SGLT2 inhibitor,** which is thought to offer cardiovascular (CV) benefit by reducing cardiac inflammation, among many other potential mechanisms.[4-6] CV outcomes trials showed that SGLT2 inhibitors improved HF outcomes and reduced the risk of HF-related hospitalizations in patients with or without type 2 diabetes, and certain SGLT2 inhibitors are approved for this indication.[5,8,9]

However, fewer than 1 in 10 eligible patients receive all four recommended HF agents,[10] with SGLT2 inhibitors and ARNIs often getting skipped, Dr. Fonarow says. Possible reasons: concern about side effects, changes in vital signs and lab results, insurance issues and an overall lack of knowledge on how these newer medications work. In some cases, Dr. Fonarow says, a patient shows improvement after taking just two of the recommended medications—a beta blocker and MRA—and then the other two agents are not prescribed.

### Individualizing treatment for HF

The importance of managing all cardiometabolic complications in HF patients with diabetes cannot be overemphasized. The following strategies can help ensure your patients get the most benefit from their regimen:

- Drs. Flores and Fonarow recommend immediately starting all four medications in patients with diabetes who are ***newly diagnosed with HFrEF*** to reduce the risk of CV death or hospitalization.
- For patients with diabetes who have ***comorbid HFpEF,*** start with an SGLT2 inhibitor and possibly a mineralocorticoid receptor antagonist (MRA) such as finerenone or either eplerenone or an aldosterone inhibitor, such as spironolactone, to manage hypertension, Dr. Flores recommends.
- For patients with ***comorbid chronic kidney disease (CKD),*** prescribing an SGLT2 inhibitor is especially crucial, as certain agents in this class are indicated not only for HF but also for slowing progression of CKD in patients with or without type 2 diabetes. ***One caveat:*** The most common side effects of SGLT2 inhibitors include genital mycotic infections and urinary tract infections, which can be problematic in certain older patients with HF. Before prescribing an SGLT2 inhibitor, Dr. Flores suggests making sure the patient can practice sound genital hygiene. If they have problems with self-care—for example, older patients with mobility issues or those who are in a nursing home—he recommends considering another type of agent. He also suggests avoiding SGLT2 inhibitors in patients with a history of recurrent urinary tract infections.
- In addition, for patients with ***comorbid obesity,*** a GLP-1 receptor agonist (GLP-1 RA) can be considered as an adjunct, say Drs. Flores and Fonarow. Robust data confirm the efficacy of GLP-1 RAs for aiding weight loss.[11] In turn, weight loss can help reduce HF exacerbations, notes Dr. Flores. "HF can be multifactorial," he says. "Often, it's much more complicated than putting them on the standard four medications and calling it a day. If we're seeing someone with obesity with a sedentary lifestyle that has a myriad factors contributing to fluid retention, it's important to be holistic." In addition, new research has definitively linked one GLP-1 RA with improved HF symptoms, although benefits on hard outcomes such as hospitalizations have not yet been established.[12] Still, extensive data show these agents reduce the risk of CV events and CV-related death, and certain GLP-1 RAs are approved for this indication.

### Incorporating newer diabetes agents to improve outcomes

Having SGLT2 inhibitors and GLP-1 RAs in the HF regimen helps cardiology specialists treat not only HF and type 2 diabetes but also CKD and overweight/obesity—and these agents' effectiveness in managing cardiorenal and metabolic conditions can help prevent complications that would be expensive to treat later on, Drs. Flores and Fonarow point out. Furthermore, these diabetes classes do not interact negatively with other medications used to treat HF. In fact, adds Dr. Fonarow, "SGLT2 inhibitors enhance tolerability of MRAs by reducing the risk of hyperkalemia, and they are compatible with ARNI and beta-blocker treatment."

*—by Pete Kelly*

## References


1. **Dunlay SM, et al. Type 2 diabetes and heart failure: a scientific statement from the American Heart Association and the Heart Failure Society of America. *Circulation*. 2019;140(7):e294-e324.**
2. **American Heart Association. Diabetes and heart failure are linked; treatment should be too. Published June 6, 2019. Available at *heart.org.***
3. **Kenny HC, Abel ED. Heart failure in type 2 diabetes mellitus. *Circ Res*. 2019;124(1):121-141.**
4. **McMurray JJV, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med.* 2019;381(21):1995-2008.**
5. **Packer M, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med*. 2020;383(15):1413-1424.**
6. **Bauersachs J. Heart failure drug treatment: the fantastic four. *Eur Heart J.* 2021;42(6):681-683.**
7. **Nelson AJ, et al. Use of lipid-, blood pressure-, and glucose-lowering pharmacotherapy in patients with type 2 diabetes and atherosclerotic cardiovascular disease. *JAMA Netw Open.* 2022;5(2):e2148030.**
8. **Packer M, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med.* 2020;383(15):1413-1424.**
9. **American College of Cardiology. Focus on heart failure—SGLT2 inhibitors in heart failure: the EMPEROR DELIVERS his SOLO. Published June 29, 2023. Available at *acc.org.***
10. **Pierce JB, et al. Contemporary use of sodium-glucose cotransporter-2 inhibitor therapy among patients hospitalized for heart failure with reduced ejection fraction in the US. *JAMA Cardiol.* 2023;8(7):652-661.**
11. **Wang J-Y, et al. GLP-1 receptor agonists for the treatment of obesity: role as a promising approach. *Front Endocrinol (Lausanne).* 2023;14:1085799.**
12. **Kosiborod MN, et al. Semaglutide in patients with heart failure with preserved ejection fraction and obesity. *N Engl J Medicine.* 2023;389:1069-1084.**
13. **Aggarwal M, et al. Lifestyle modifications for preventing and treating heart failure. *J Am College Cardiol.* 2018;72(19):2391-2405.**
14. **Geng T, et al. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: a cohort study. *PLoS Med.* 2023;20(1):e1004135.**

PAID ADVERTISEMENT

For adult patients with T2D, treated with diet and exercise to improve glycemic control

For adults with T2D and established CVD, to reduce risk of MACE[1,a]

## Start early. Choose Ozempic®

## TRI-ZONE

with the **power of 3**

**PROVEN CV RISK REDUCTION**[1,a]
In adults with T2D and atherosclerotic cardiovascular disease

**POWERFUL GLYCEMIC CONTROL**[1,2]

**COMPELLING WEIGHT LOSS**[1,2]
Ozempic® is not indicated for weight loss

**#1 PRESCRIBED GLP-1 RA WORLDWIDE IN PATIENTS WITH T2D**[3,b]

### PROVEN CV RISK REDUCTION[1,4,a]

**In adults with T2D and ASCVD**

Primary endpoint: 3-part composite MACE: CV death, nonfatal MI, nonfatal stroke

**In SUSTAIN 6**[1,4]

In a 2-year CVOT in 3297 adult patients with T2D and established CVD

Time to first confirmed MACE: 8.9% for placebo + SOC (n=146 of 1649) vs 6.6% for Ozempic® 0.5 mg and 1 mg + SOC (n=108 of 1648) at 109 weeks

HR, 0.74 (95% CI; 0.58-0.95); *P*<0.001 for noninferiority vs placebo plus SOC
*P*=0.02 for superiority, not prespecified

WHEN ADDED TO STANDARD OF CARE

**26% RRR OF MACE (2.3% ARR AT 109 WEEKS)**[1,c]

### POWERFUL GLYCEMIC CONTROL[1,2,5]

Primary endpoint: Mean change in A1C from baseline at Week 40

**In SUSTAIN 7**[2]

**–1.4% with Ozempic® 0.5 mg** (baseline: 8.3%) vs –1.1% with Trulicity® 0.75 mg (baseline: 8.2%); *P*=0.002

**–1.6% with Ozempic® 1 mg** (baseline: 8.2%) vs –1.3% with Trulicity® 1.5 mg (baseline: 8.2%); *P*=0.0004

**In SUSTAIN FORTE**[1]

**–1.9% with Ozempic® 1 mg** (baseline: 8.8%) vs **–2.1% with Ozempic® 2 mg** (baseline: 8.9%); *P*<0.01

**THE POWER TO DROP A1C BY MORE THAN 2% WITH Ozempic® 2 mg**[1,5]

### COMPELLING WEIGHT LOSS[1,2]

**Ozempic® is not indicated for weight loss.**

Secondary endpoint: Mean change in body weight from baseline at Week 40

**In SUSTAIN 7**[2]

**–9.3 lb with Ozempic® 0.5 mg** (baseline: 213 lb) vs –4.6 lb with Trulicity® 0.75 mg (baseline: 211 lb); ETD=–4.7 lb (95% CI; –6.5, –2.9)

**–12.8 lb with Ozempic® 1 mg** (baseline: 211 lb) vs –6.2 lb with Trulicity® 1.5 mg (baseline: 206 lb); ETD=–6.7 lb (95% CI; –8.5, –5.0)

**In SUSTAIN FORTE**[1]

**–12.5 lb with Ozempic® 1 mg** (baseline: 217 lb) vs **–14.1 lb with Ozempic® 2 mg** (baseline: 220 lb); ETD=–1.7 lb (*P*=NS)

**AVERAGE WEIGHT LOSS OF –9.3 LB TO –14.1 LB**[1-3,5]

[a]Composite MACE endpoint in SUSTAIN 6 included: CV death, nonfatal MI, or nonfatal stroke.[1]

[b]Based on internal analysis by Novo Nordisk using data from the following source: IQVIA MIDAS® monthly volume sales data, ATC3 A10S, for the rolling 3-month time period ending 11.2023 (41 countries) reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.[3]

[c]Results apply to Ozempic® 0.5 mg and 1 mg plus standard of care vs placebo plus standard of care.

## Indications and Limitations of Use

Ozempic® (semaglutide) injection 0.5 mg, 1 mg, or 2 mg is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus and to reduce the risk of major adverse cardiovascular (CV) events (CV death, nonfatal myocardial infarction, or nonfatal stroke) in adults with type 2 diabetes mellitus and established CV disease.

- Ozempic® has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Ozempic® is not indicated for use in patients with type 1 diabetes mellitus.

## Important Safety Information

**WARNING: RISK OF THYROID C-CELL TUMORS**

- **In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether Ozempic® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.**
- **Ozempic® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of Ozempic® and inform them of symptoms of thyroid tumors (eg, a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Ozempic®.**

### Contraindications

- Ozempic® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with a hypersensitivity reaction to semaglutide or to any of the excipients in Ozempic®. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with Ozempic®.

### Warnings and Precautions

- **Risk of Thyroid C-Cell Tumors:** Patients should be referred to an endocrinologist for further evaluation if serum calcitonin is measured and found to be elevated or thyroid nodules are noted on physical examination or neck imaging.
- **Pancreatitis:** Acute and chronic pancreatitis have been reported in clinical studies. Observe patients carefully for signs and symptoms of pancreatitis (persistent severe abdominal pain, sometimes radiating to the back with or without vomiting). If pancreatitis is suspected, discontinue Ozempic® promptly, and if pancreatitis is confirmed, do not restart.
- **Diabetic Retinopathy Complications:** In a 2-year trial involving patients with type 2 diabetes and high cardiovascular risk, more events of diabetic retinopathy complications occurred in patients treated with Ozempic® (3.0%) compared with placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline than among patients without a known history of diabetic retinopathy.

  Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.
- **Never Share an Ozempic® Pen Between Patients:** Ozempic® pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens.
- **Hypoglycemia:** Patients receiving Ozempic® in combination with an insulin secretagogue (eg, sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.



### Study Designs

**SUSTAIN 6: Cardiovascular outcomes**[4] **Study design:** 2-year, randomized, multicenter, multinational, placebo-controlled, double-blind cardiovascular outcomes trial designed to assess noninferiority of Ozempic® vs placebo, both in addition to standard of care, for time to first MACE using a risk margin of 1.3. **Patients:** A total of 3297 adult patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to once-weekly Ozempic® 0.5 mg (n=826), Ozempic® 1 mg (n=822), or placebo (n=1649), all in addition to standard of care treatments for diabetes and CVD such as oral antidiabetic treatments, insulin, antihypertensives, diuretics, lipid-lowering therapies, and antithrombotic medications at investigator discretion. **Primary composite endpoint:** Time from randomization to first occurrence of a 3-part composite MACE, defined as CV death, nonfatal myocardial infarction, or nonfatal stroke. **Secondary endpoints:** Time from randomization to event onset for each of the following components of the 3-part composite MACE: CV death, nonfatal myocardial infarction, and nonfatal stroke.

**SUSTAIN 7: Head-to-head vs Trulicity® (dulaglutide)**[2] **Study design:** 40-week, multinational, multicenter, randomized, open-label, four-armed, pairwise, active-controlled, parallel-group trial to evaluate the efficacy and safety of Ozempic® vs dulaglutide. **Patients:** A total of 1201 adult patients with type 2 diabetes inadequately controlled on metformin were randomized to receive Ozempic® 0.5 mg (n=301), Ozempic® 1 mg (n=300), dulaglutide 0.75 mg (n=299), or dulaglutide 1.5 mg (n=299) once weekly. **Primary endpoint:** Mean change in A1C from baseline at Week 40. **Secondary endpoints:** Mean change in body weight from baseline at Week 40; proportion of patients achieving A1C <7% at Week 40.

**SUSTAIN FORTE: Ozempic® 1 mg vs 2 mg**[5] **Study design:** 40-week, active-controlled, parallel-group, double-blind, phase 3B efficacy and safety trial of Ozempic® 2 mg vs Ozempic® 1 mg in patients with type 2 diabetes in need of treatment intensification. **Patients:** A total of 961 adult patients with inadequately controlled type 2 diabetes (A1C 8.0%-10.0%) on metformin with or without a sulfonylurea were randomized 1:1 to 2 mg (n=480) or 1 mg (n=481) of once-weekly Ozempic®. **Primary composite endpoint:** Mean change in A1C from baseline at Week 40. **Secondary endpoints:** Mean change in body weight from baseline at Week 40; proportion of patients achieving A1C <7% at Week 40.

T2D=type 2 diabetes; CVD=cardiovascular disease; MACE=major adverse cardiovascular event; CV=cardiovascular; MI=myocardial infarction; ASCVD=atherosclerotic cardiovascular disease; CVOT=cardiovascular outcomes trial; SOC=standard of care; HR=hazard ratio; CI=confidence interval; RRR=relative risk reduction; ARR=absolute risk reduction; ETD=estimated treatment difference; NS=not significant.

## Important Safety Information

### Warnings and Precautions (cont.)

- **Acute Kidney Injury:** There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of Ozempic® in patients reporting severe adverse gastrointestinal reactions.
- **Hypersensitivity:** Serious hypersensitivity reactions (eg, anaphylaxis, angioedema) have been reported in patients treated with Ozempic®. If hypersensitivity reactions occur, discontinue use of Ozempic®; treat promptly per standard of care, and monitor until signs and symptoms resolve. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist.
- **Acute Gallbladder Disease:** Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing. In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients treated with Ozempic® 0.5 mg and 1 mg, respectively, and not reported in placebo-treated patients. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

### Adverse Reactions

- The most common adverse reactions, reported in ≥5% of patients treated with Ozempic® are nausea, vomiting, diarrhea, abdominal pain, and constipation.

### Drug Interactions

- When initiating Ozempic®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia.
- Ozempic® causes a delay of gastric emptying and has the potential to impact the absorption of concomitantly administered oral medications, so caution should be exercised.

### Use in Specific Populations

- There are limited data with semaglutide use in pregnant women to inform a drug-associated risk for adverse developmental outcomes. Discontinue Ozempic® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide.

**Please see Brief Summary of Prescribing Information on following page.**

**References: 1.** Ozempic. Prescribing information. Novo Nordisk Inc. **2.** Pratley RE, Aroda VR, Lingvay I, et al; SUSTAIN 7 Investigators. Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial. *Lancet Diabetes Endocrinol*. 2018;6(4):275-286. doi:10.1016/S2213-8587(18)30024-X **3.** Data on file. Novo Nordisk Inc; Plainsboro, NJ. **4.** Marso SP, Bain SC, Consoli A, et al; SUSTAIN-6 Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2016;375(19):1834-1844. doi:10.1056/NEJMoa1607141 **5.** Frías JP, Auerbach P, Bajaj HS, et al. Efficacy and safety of once-weekly semaglutide 2.0 mg versus 1.0 mg in patients with type 2 diabetes (SUSTAIN FORTE): a double-blind, randomised, phase 3B trial. *Lancet Diabetes Endocrinol*. 2021;9(9):563-574. doi:10.1016/S2213-8587(21)00174-1

For additional information, please visit our HCP site at **OzempicPro.com**.

ONCE-WEEKLY OZEMPIC® semaglutide injection 0.5 mg, 1 mg, 2 mg

**OZEMPIC® (semaglutide) injection**

**Rx Only**

**BRIEF SUMMARY: Please consult package insert for full prescribing information.**

**WARNING: RISK OF THYROID C-CELL TUMORS: In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether OZEMPIC® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined *[see Warnings and Precautions]*. OZEMPIC® is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Contraindications]*. Counsel patients regarding the potential risk for MTC with the use of OZEMPIC® and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC® *[see Contraindications and Warnings and Precautions]*.**

**INDICATIONS AND USAGE:** OZEMPIC® is indicated: as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus; to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Limitations of Use: OZEMPIC® has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis *[see Warnings and Precautions]*. OZEMPIC® is not indicated for use in patients with type 1 diabetes mellitus.

**CONTRAINDICATIONS:** OZEMPIC® is contraindicated in patients with: A personal or family history of MTC or in patients with MEN 2 *[see Warnings and Precautions]*; A serious hypersensitivity reaction to semaglutide or to any of the excipients in OZEMPIC®. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with OZEMPIC® *[see Warnings and Precautions]*.

**WARNINGS AND PRECAUTIONS: Risk of Thyroid C-Cell Tumors:** In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures. It is unknown whether OZEMPIC® causes thyroid C-cell tumors, including MTC, in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans. OZEMPIC® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of OZEMPIC® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC®. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated. **Pancreatitis:** In glycemic control trials, acute pancreatitis was confirmed by adjudication in 7 OZEMPIC®-treated patients (0.3 cases per 100 patient years) versus 3 in comparator-treated patients (0.2 cases per 100 patient years). One case of chronic pancreatitis was confirmed in an OZEMPIC®-treated patient. In a 2-year trial, acute pancreatitis was confirmed by adjudication in 8 OZEMPIC®-treated patients (0.27 cases per 100 patient years) and 10 placebo-treated patients (0.33 cases per 100 patient years), both on a background of standard of care. After initiation of OZEMPIC®, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, OZEMPIC® should be discontinued and appropriate management initiated; if confirmed, OZEMPIC® should not be restarted. **Diabetic Retinopathy Complications:** In a 2-year trial involving patients with type 2 diabetes and high cardiovascular risk, more events of diabetic retinopathy complications occurred in patients treated with OZEMPIC® (3.0%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (OZEMPIC® 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (OZEMPIC® 0.7%, placebo 0.4%). Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy. **Never Share an OZEMPIC® Pen Between Patients:** OZEMPIC® pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens. **Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin:** Patients receiving OZEMPIC® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia *[see Adverse Reactions and Drug Interactions]*. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogue) or insulin. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. **Acute Kidney Injury:** There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of OZEMPIC® in patients reporting severe adverse gastrointestinal reactions. **Hypersensitivity:** Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported in patients treated with OZEMPIC®. If hypersensitivity reactions occur, discontinue use of OZEMPIC®; treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to OZEMPIC® *[see Contraindications and Adverse Reactions]*. Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to anaphylaxis with OZEMPIC®. **Acute Gallbladder Disease:** Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing. In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients-treated with OZEMPIC® 0.5 mg and 1 mg, respectively. Cholelithiasis was not reported in placebo-treated patients. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

**ADVERSE REACTIONS:** The following serious adverse reactions are described below or elsewhere in the prescribing information: Risk of Thyroid C-cell Tumors *[see Warnings and Precautions]*; Pancreatitis *[see Warnings and Precautions]*; Diabetic Retinopathy Complications *[see Warnings and Precautions]*; Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin *[see Warnings and Precautions]*; Acute Kidney Injury *[see Warnings and Precautions]*; Hypersensitivity *[see Warnings and Precautions]*; Acute Gallbladder Disease *[see Warnings and Precautions]*. **Clinical Trials Experience:** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Pool of Placebo-Controlled Trials: The data in Table 1 are derived from 2 placebo-controlled trials (1 monotherapy trial and 1 trial in combination with basal insulin) in patients with type 2 diabetes. These data reflect exposure of 521 patients to OZEMPIC® and a mean duration of exposure to OZEMPIC® of 32.9 weeks. Across the treatment arms, the mean age of patients was 56 years, 3.4% were 75 years or older and 55% were male. In these trials 71% were White, 7% were Black or African American, and 19% were Asian; 21% identified as Hispanic or Latino ethnicity. At baseline, patients had type 2 diabetes for an average of 8.8 years and had a mean $HbA_{1c}$ of 8.2%. At baseline, 8.9% of the population reported retinopathy. Baseline estimated renal function was normal (eGFR ≥90 mL/min/1.73m²) in 57.2%, mildly impaired (eGFR 60 to 90 mL/min/1.73m²) in 35.9% and moderately impaired (eGFR 30 to 60 mL/min/1.73m²) in 6.9% of patients. Pool of Placebo- and Active-Controlled Trials: The occurrence of adverse reactions was also evaluated in a larger pool of patients with type 2 diabetes participating in 7 placebo- and active-controlled glycemic control trials including two trials in Japanese patients evaluating the use of OZEMPIC® as monotherapy and add-on therapy to oral medications or insulin. In this pool, a total of 3150 patients with type 2 diabetes were treated with OZEMPIC® for a mean duration of 44.9 weeks. Across the treatment arms, the mean age of patients was 57 years, 3.2% were 75 years or older and 57% were male. In these trials, 60% were White, 6% were Black or African American, and 31% were Asian; 16% identified as Hispanic or Latino ethnicity. At baseline, patients had type 2 diabetes for an average of 8.2 years and had a mean $HbA_{1c}$ of 8.2%. At baseline, 7.8% of the population reported retinopathy. Baseline estimated renal function was normal (eGFR ≥90 mL/min/1.73m²) in 63.1%, mildly impaired (eGFR 60 to 90 mL/min/1.73m²) in 34.3%, and moderately impaired (eGFR 30 to 60 mL/min/1.73m²) in 2.5% of the patients. Common Adverse Reactions: Table 1 shows common adverse reactions, excluding hypoglycemia, associated with the use of OZEMPIC® in the pool of placebo-controlled trials. These adverse reactions occurred more commonly on OZEMPIC® than on placebo and occurred in at least 5% of patients treated with OZEMPIC®.

**Table 1. Adverse Reactions in Placebo-Controlled Trials Reported in ≥5% of OZEMPIC®-Treated Patients with Type 2 Diabetes Mellitus**

| Adverse Reaction | Placebo (N=262) % | OZEMPIC® 0.5 mg (N=260) % | OZEMPIC® 1 mg (N=261) % |
|---|---|---|---|
| Nausea | 6.1 | 15.8 | 20.3 |
| Vomiting | 2.3 | 5.0 | 9.2 |
| Diarrhea | 1.9 | 8.5 | 8.8 |
| Abdominal pain | 4.6 | 7.3 | 5.7 |
| Constipation | 1.5 | 5.0 | 3.1 |

In the pool of placebo- and active-controlled trials and in the 2-year cardiovascular outcomes trial, the types and frequency of common adverse reactions, excluding hypoglycemia, were similar to those listed in Table 1. In a clinical trial with 959 patients treated with OZEMPIC® 1 mg or OZEMPIC® 2 mg once weekly as add-on to metformin with or without sulfonylurea treatment for 40 weeks, no new safety signals were identified. *Gastrointestinal Adverse Reactions:* In the pool of placebo-controlled trials, gastrointestinal adverse reactions occurred more frequently among patients receiving OZEMPIC® than placebo (placebo 15.3%, OZEMPIC® 0.5 mg 32.7%, OZEMPIC® 1 mg 36.4%). The majority of reports of nausea, vomiting, and/or diarrhea occurred during dose escalation. More patients receiving OZEMPIC® 0.5 mg (3.1%) and OZEMPIC® 1 mg (3.8%) discontinued treatment due to gastrointestinal adverse reactions than patients receiving placebo (0.4%). In the trial with OZEMPIC® 1 mg and 2 mg, gastrointestinal adverse reactions occurred more frequently among patients receiving OZEMPIC® 2 mg (34.0%) vs OZEMPIC® 1 mg (30.8%). In addition to the reactions in Table 1, the following gastrointestinal adverse reactions with a frequency of <5% were associated with OZEMPIC® (frequencies listed, respectively, as: placebo; 0.5 mg; 1 mg): dyspepsia (1.9%, 3.5%, 2.7%), eructation (0%, 2.7%, 1.1%), flatulence (0.8%, 0.4%, 1.5%), gastroesophageal reflux disease (0%, 1.9%, 1.5%), and gastritis (0.8%, 0.8%, 0.4%). Other Adverse Reactions: *Hypoglycemia:* Table 2 summarizes the incidence of events related to hypoglycemia by various definitions in the placebo-controlled trials.

**Table 2. Hypoglycemia Adverse Reactions in Placebo-Controlled Trials in Patients with Type 2 Diabetes Mellitus**

| | Placebo | OZEMPIC® 0.5 mg | OZEMPIC® 1 mg |
|---|---|---|---|
| **Monotherapy** | | | |
| **(30 weeks)** | **N=129** | **N=127** | **N=130** |
| Severe† | 0% | 0% | 0% |
| Documented symptomatic (≤70 mg/dL glucose threshold) | 0% | 1.6% | 3.8% |
| Severe† or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold) | 1.6% | 0% | 0% |
| **Add-on to Basal Insulin with or without Metformin** | | | |
| **(30 weeks)** | **N=132** | **N=132** | **N=131** |
| Severe† | 0% | 0% | 1.5% |
| Documented symptomatic (≤70 mg/dL glucose threshold) | 15.2% | 16.7% | 29.8% |
| Severe† or Blood Glucose Confirmed Symptomatic (≤56 mg/dL glucose threshold) | 5.3% | 8.3% | 10.7% |

†"Severe" hypoglycemia adverse reactions are episodes requiring the assistance of another person.

Hypoglycemia was more frequent when OZEMPIC® was used in combination with a sulfonylurea *[see Warnings and Precautions]*. Severe hypoglycemia occurred in 0.8% and 1.2% of patients when OZEMPIC® 0.5 mg and 1 mg, respectively, was co-administered with a sulfonylurea. Documented symptomatic hypoglycemia occurred in 17.3% and 24.4% of patients when OZEMPIC® 0.5 mg and 1 mg, respectively, was co-administered with a sulfonylurea. Severe or blood glucose confirmed symptomatic hypoglycemia occurred in 6.5% and 10.4% of patients when OZEMPIC® 0.5 mg and 1 mg, respectively, was co-administered with a sulfonylurea. Injection Site Reactions: In placebo-controlled trials, injection site reactions (e.g., injection-site discomfort, erythema) were reported in 0.2% of OZEMPIC®-treated patients. Increases in Amylase and Lipase: In placebo-controlled trials, patients exposed to OZEMPIC® had a mean increase from baseline in amylase of 13% and lipase of 22%. These changes were not observed in placebo-treated patients. Cholelithiasis: In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients-treated with OZEMPIC® 0.5 mg and 1 mg, respectively. Cholelithiasis was not reported in placebo-treated patients. Increases in Heart Rate: In placebo-controlled trials, OZEMPIC® 0.5 mg and 1 mg resulted in a mean increase in heart rate of 2 to 3 beats per minute. There was a mean decrease in heart rate of 0.3 beats per minute in placebo-treated patients. Fatigue, Dysgeusia and Dizziness: Other adverse reactions with a frequency of >0.4% were associated with OZEMPIC® include fatigue, dysgeusia and dizziness. **Immunogenicity:** Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with OZEMPIC® may develop anti-semaglutide antibodies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, the incidence of antibodies to semaglutide in the studies described below cannot be directly compared with the incidence of antibodies in other studies or to other products. Across the placebo- and active-controlled glycemic control trials, 32 (1.0%) OZEMPIC®-treated patients developed anti-drug antibodies (ADAs) to the active ingredient in OZEMPIC® (i.e., semaglutide). Of the 32 semaglutide-treated patients that developed semaglutide ADAs, 19 patients (0.6% of the overall population) developed antibodies cross-reacting with native GLP-1. The *in vitro* neutralizing activity of the antibodies is uncertain at this time. **Postmarketing Experience:** The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of OZEMPIC®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. *Gastrointestinal Disorders:* Ileus; *Hypersensitivity:* anaphylaxis, angioedema, rash, urticaria; *Hepatobiliary:* cholecystitis, cholecystectomy.

**DRUG INTERACTIONS: Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin:** OZEMPIC® stimulates insulin release in the presence of elevated blood glucose concentrations. Patients receiving OZEMPIC® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating OZEMPIC®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia *[see Warnings and Precautions and Adverse Reactions]*. **Oral Medications:** OZEMPIC® causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials, semaglutide did not affect the absorption of orally administered medications to any clinically relevant degree. Nonetheless, caution should be exercised when oral medications are concomitantly administered with OZEMPIC®.

**USE IN SPECIFIC POPULATIONS: Pregnancy:** Risk Summary: There are limited data with semaglutide use in pregnant women to inform a drug-associated risk for adverse developmental outcomes. There are clinical considerations regarding the risks of poorly controlled diabetes in pregnancy *(see Clinical Considerations)*. Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. OZEMPIC® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In pregnant rats administered semaglutide during organogenesis, embryofetal mortality, structural abnormalities and alterations to growth occurred at maternal clinical exposure based on AUC. In rabbits and cynomolgus monkeys administered semaglutide during organogenesis, early pregnancy losses or structural abnormalities were observed at clinical exposure (rabbit) and ≥2-fold the MRHD (monkey). These findings coincided with a marked maternal body weight loss in both animal species *(see Data)*. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively. The estimated background risk of major birth defects is 6 to 10% in women with pre-gestational diabetes with a peri-conceptional $HbA_{1c}$ >7 and has been reported to be as high as 20 to 25% in women with a peri-conceptional $HbA_{1c}$ >10. The estimated background risk of miscarriage for the indicated population is unknown. Clinical Considerations: *Disease-Associated Maternal and/or Embryo/fetal Risk:* Hypoglycemia and hyperglycemia occur more frequently during pregnancy in patients with pre-gestational diabetes. Poorly controlled diabetes during pregnancy increases the maternal risk for diabetic ketoacidosis, pre- eclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity. Data: *Animal Data:* In a combined fertility and embryofetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.06-, 0.2-, and 0.6-fold the MRHD) were administered to males for 4 weeks prior to and throughout mating and to females for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental animals, pharmacologically mediated reductions in body weight gain and food consumption were observed at all dose levels. In the offspring, reduced growth and fetuses with visceral (heart blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities were observed at the human exposure. In an embryofetal development study in pregnant rabbits, subcutaneous doses of 0.0010, 0.0025 or 0.0075 mg/kg/day (0.02-, 0.2-, and 1.2-fold the MRHD) were administered throughout organogenesis from Gestation Day 6 to 19. Pharmacologically mediated reductions in maternal body weight gain and food consumption were observed at all dose levels. Early pregnancy losses and increased incidences of minor visceral (kidney, liver) and skeletal (sternebra) fetal abnormalities were observed at ≥0.0025 mg/kg/day, at clinically relevant exposures. In an embryofetal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.5-, 3-, and 8-fold the MRHD) were administered throughout organogenesis, from Gestation Day 16 to 50. Pharmacologically mediated, marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternebra, ribs) at ≥0.075 mg/kg twice weekly (≥3X human exposure). In a pre- and postnatal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.3-, 2-, and 4-fold the MRHD) were administered from Gestation Day 16 to 140. Pharmacologically mediated marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with an increase in early pregnancy losses and led to delivery of slightly smaller offspring at ≥0.075 mg/kg twice weekly (≥2X human exposure). **Lactation:** Risk Summary: There are no data on the presence of semaglutide in human milk, the effects on the breastfed infant, or the effects on milk production. Semaglutide was present in the milk of lactating rats, however, due to species-specific differences in lactation physiology, the clinical relevance of these data are not clear *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OZEMPIC® and any potential adverse effects on the breastfed infant from OZEMPIC® or from the underlying maternal condition. Data: In lactating rats, semaglutide was detected in milk at levels 3-12 fold lower than in maternal plasma. **Females and Males of Reproductive Potential:** Discontinue OZEMPIC® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide *[see Use in Specific Populations]*. **Pediatric Use:** Safety and efficacy of OZEMPIC® have not been established in pediatric patients (younger than 18 years). **Geriatric Use:** In the pool of placebo- and active-controlled glycemic control trials, 744 (23.6%) OZEMPIC®-treated patients were 65 years of age and over and 102 OZEMPIC®-treated patients (3.2%) patients were 75 years of age and over. In SUSTAIN 6, the cardiovascular outcome trial, 788 (48.0%) OZEMPIC®-treated patients were 65 years of age and over and 157 OZEMPIC®-treated patients (9.6%) patients were 75 years of age and over. No overall differences in safety or efficacy were detected between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. **Renal Impairment:** No dose adjustment of OZEMPIC® is recommended for patients with renal impairment. In subjects with renal impairment including end-stage renal disease (ESRD), no clinically relevant change in semaglutide pharmacokinetics (PK) was observed. **Hepatic Impairment:** No dose adjustment of OZEMPIC® is recommended for patients with hepatic impairment. In a study in subjects with different degrees of hepatic impairment, no clinically relevant change in semaglutide pharmacokinetics (PK) was observed.

**OVERDOSAGE:** In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdosage management recommendations. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of OZEMPIC® of approximately 1 week.

**More detailed information is available upon request.**

For information about OZEMPIC® contact: Novo Nordisk Inc.,
800 Scudders Mill Road, Plainsboro, NJ 08536, 1-888-693-6742
Date of Issue: 9/2023
Version: 9
Manufactured by: Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark



**PATENT INFORMATION:**
http://www.novonordisk-us.com/products/product-patents.html

 US23OZM00616 10/2023

novo nordisk®

PATIENT ENGAGEMENT

# Improving continuity of care with **telemedicine**

For many patients, keeping appointments can be challenging, especially for those who live in rural areas or have mobility issues. Enter telemedicine—since becoming popularized and refined during the pandemic, it's become a key means to ensure continuity of care.

**After being hospitalized for a diabetic foot ulcer,** Jack, a 77-year-old veteran, used a knee scooter to avoid putting weight on the wound. With driving out of the question and car services beyond his budget, he worried about how could he could see his endocrinologist Rashmi S. Mullur, MD. The solution: telehealth visits from Jack's home. "I was able to view his wound virtually to ensure proper healing, assess medication changes, discuss his diet and watch how well he was using the scooter at home," says Dr. Mullur, chief of telehealth at the VA Medical Center in Los Angeles and director of integrative medicine education at UCLA's David Geffen School of Medicine. Without telehealth visits to help Jack maintain blood sugar control, he likely faced foot amputation, Dr. Mullur says.

After the boon of telemedicine during the pandemic, many endocrinologists continued to offer virtual visits to their patients with diabetes. "Endocrinology is an ideal specialty for telemedicine since it's largely data-driven rather than procedure-based," says Gregory Dodell, MD, FACE, of Central Park Endocrinology in NYC. "I want my patients to come see me at least once a year, but monitoring blood glucose levels can easily be done virtually." During a virtual exam, Dr. Mullur says clinicians also can view wounds on the patient's feet, skin rashes, insulin injection sites, insulin pump and continuous glucose monitoring sites and if the patient has edema. "For chronic diseases like diabetes, telemedicine is a way to support patients between in-person visits."

## Better access to care

When Ricardo Correa, MD, EdD, was at the Phoenix VA Medical Center, veterans living in rural areas of the state often drove hours for a 30-minute appointment with him. Many were no-shows, leading to poor outcomes, especially for those with complicated or uncontrolled diabetes. When the Phoenix VA launched a telediabetes program in 2019, at least 40% of Dr. Correa's patients saw him virtually. "Patients in their 60s and 70s were motivated to learn how to use telemedicine," says Dr. Correa. "They not only showed up to every virtual appointment, but they were also more compliant with their diabetes treatment and their A1C and quality of life improved. Some patients told me telemedicine changed their lives."

Now with the Cleveland Clinic, Dr. Correa devotes 25% of his practice to telemedicine. While virtual visits can improve patients' access to care, telemedicine hasn't reduced the wait to see him. "Whether it's virtual or in-person, the number of patients I see each day is the same," says Dr. Correa. Still, virtual appointments can improve access to nurse practitioners and physician assistants who can help with the management of care. "Telemedicine can overcome the inertia of changing medication, so blood sugars are controlled faster," notes Dr. Correa. Patients also are more likely to see a nutritionist, a diabetes educator and an exercise physiologist remotely instead of traveling to the clinic on multiple days.

Telemedicine can also lead to greater continuity of care. "No-show rates are minimal compared with in-person visits," says Dr. Correa. If patients for-

Illustration by Jesse Zhang / Ikon Images

get about a virtual appointment, a phone call is often all it takes for them to log on. A patient who misses an in-person visit, however, might have to wait months to reschedule. Clinicians also can provide diabetes education and lifestyle management to multiple patients simultaneously. Dr. Mullur says she uses Zoom to teach patients how to improve glucose control through yoga. "A virtual group visit is ideal to teach mind-body approaches to manage diabetes," she says. "They learn from each other, and I can check in with patients individually during the session."

## Equal or better outcomes

Researchers who have studied the impact of virtual medicine on diabetes treatment have discovered equal or improved outcomes. One UCLA study evaluated quality-of-care outcomes among patients with type 2 diabetes who used telemedicine during the first 9 months of the pandemic compared with patients who received in-person care exclusively.[1] Investigators found that patients who opted for some virtual care during the pandemic performed just as well on measures of diabetes quality care as they did in the 18 months prior to the pandemic. (The quality measures included systolic/diastolic blood pressure less than 140/90 mmHg, AIC less than 8.0%, prescription for statins and/or aspirin, and no tobacco use.) Patients who eschewed telemedicine visits, on the other hand, had worse performance on the diabetes quality measures. "This discrepancy was likely related to patients following stay-at-home orders instead of coming into the clinic," says Dr. Mullur.

A 2021 meta-analysis of 43 randomized controlled trials found that telediabetes interventions significantly lowered AIC (-0.486%), diastolic blood pressure, postprandial glucose, fasting plasma glucose, weight, BMI, and improved mental and physical quality of life compared with control groups.[2]

Going forward, it will be important to see results from head-to-head trials of diabetes outcomes comparing virtual care with in-person care, according to Dr. Dodell. "If we find that telemedicine is equally effective or more so in patient compliance and decreases medication inertia, there should be a bigger push for specialists to offer virtual care," he says.

## Virtual visits not right for everyone

"If the patient doesn't speak English, has a visual, hearing, cognitive impairment or low digital literacy, telemedicine will be extremely difficult," says Dr. Mullur. "We may need to provide baseline education on how to access virtual visits and alert team members if caregivers need to join the call." And telemedicine visits, like any online meeting, can have glitches. "We need to allow for transmission delays and ensure that our patients fully hear our questions," she says. "It's important that patients understand that virtual visits add value to the care they receive," she says.

## The future of telemedicine: government action

According to Kyle Zebley, Senior Vice President of Public Policy at the American Telemedicine Association, reimbursable telemedicine services that made virtual care a viable option for clinicians and patients during the pandemic are set to expire at the end of this year. "This is the most important year since the beginning of the pandemic in terms of how our federal policymakers and regulatory agencies shape telehealth," Zebley says. Congress, he says, will likely either extend the current provisions or make them permanent. "Preserving telehealth will require a combination of regulatory and legislative actions and we shouldn't take for granted that all the flexibilities and advancements of telehealth that occurred during the pandemic will persist," he says. He urges clinicians to call their state's representatives. "Tell them what will make your jobs easier in delivering virtual care, and what they can do to improve telehealth to increase access to care for underserved patients." ●

*–by Anita Slomski*

**"Telemedicine can overcome the inertia of changing medication, so blood sugars are controlled faster."**
***—RICARDO CORREA, MD, EdD***

Illustration by Jesse Zhang / Ikon Images

## References


1. **Quinton JK, et al. The impact of telemedicine on quality of care for patients with diabetes after March 2020. *J Gen Intern Med.* 2022;37(5):1198-1203.**
2. **De Groot J, et al. Efficacy of telemedicine on glycemic control in patients with type 2 diabetes: A meta-analysis. *World J Diabetes.* 2021;12(2):170-197.**


## Keys to optimizing virtual visits: PATIENT PREPARATION AND CLINICAL OBSERVATION

For an optimal virtual exam, experts say patients should share their weight and vital signs using a home scale, blood pressure cuff and glucometer. "It may take more effort from the patient to be ready for a productive virtual visit," notes Gregory Dodell, MD, FACE, of Central Park Endocrinology in NYC. "Otherwise, the clinician has to send a message on the portal or call the patient to get the necessary data to make a clinical decision."

On the other hand, telemedicine provides clinicians with a unique opportunity to evaluate the patient's home environment and any concerns with medication use. "Looking inside my patients' pantries I can see what foods they are eating, and they can show me the bottles of medications and supplements they may be taking," says Rashmi S. Mullur, MD, chief of telehealth at the VA Medical Center in Los Angeles. "I can also get a sense of how well my disabled and elderly patients are managing their diabetes by having them demonstrate how they measure their blood sugar or administer their insulin. I can also assess the safety of my patient's home environment concerning falls."

It's also important that patients visit with their endocrinologist if they are new. Then again annually for a complete foot examination, retinal screening and to check for diabetes complications, according to Ricardo Correa, MD, EdD, of the Phoenix VA Medical Center. "The initial visit with a patient should be in person so you can build trust and establish a relationship," says Dr. Correa.

**PATIENT:** ROGER, 71, HAD POORLY CONTROLLED TYPE 2 DIABETES AND A FAMILY HISTORY OF DIABETES

# "He was concerned about medication that would cause hypoglycemia"

PHYSICIAN:

**Leslie S. Eldeiry, MD, FACE**

*Clinical Assistant Professor, Department of Endocrinology, Harvard Vanguard Medical Associates/ Atrius Health, Boston, MA; Board Member, AACE*

**History:**
Roger came to me with type 2 diabetes, which was diagnosed when he was 67. His diabetes was complicated by mild non-proliferative diabetic retinopathy and peripheral neuropathy. Roger had a history of obesity (peak weight, 220 lbs.) hyperlipidemia and hypertension. Both his parents and brother also had diabetes. At the initial exam, his weight was 209 lbs., BMI 29.8 and AIC 10.7%, with reduced vibratory sensation in his feet. He was treated with metformin for 2 years after the initial diagnosis, which he tolerated well.

Roger worked as a hospital technologist. He had no structured exercise routine. Breakfast consisted of a yogurt and banana or a glazed donut; he skipped lunch most days. Dinner was a large meal—around 2,500 calories. He drank diet soda and fruit juice daily. Roger did not use a glucometer to test his sugars, but he reported feeling fatigued and weak.

**Initiating treatment:**
We discussed reducing portions and carbohydrate intake, especially simple sugars, cutting down on juice and eating a midday meal or snack. He was unable to monitor his blood sugars while at work. We agreed to work on lifestyle modifications and re-evaluate his treatment plan. At the 3-month follow-up, Roger's AIC was 9.5%—still well above goal. We agreed to start him on an injectable GLP-1 receptor agonist (GLP-1 RA) because he was able to schedule weekly injections, and this medication would be expected to improve blood glucose levels, promote weight loss and not cause hypoglycemia. We discussed possible GI upset side effects and that symptoms typically resolve with time. We agreed to gradually increase the dosage to improve his glucose levels (and potentially achieve more weight loss). I told him it was important that he continue to follow a reduced-calorie and carbohydrate-controlled diet.

Roger began taking the lowest dose of the injectable GLP-1 RA. When he returned 3 months later, his AIC had markedly improved to 7.4%. The medication was increased to the next dosage, and his A1C at his next 3-month follow-up had reached our goal of 6.5%. He was able to reduce his weight to 197 lbs. Roger maintained this improvement for 2 years and subsequently retired from his job.

When I saw him again about a year later in 2020, his A1C was 9.2% and he had regained weight, which he attributed to decreased physical activity and dietary indiscretion. He recommitted himself to lifestyle changes and started continuous glucose monitoring. Roger improved in the spring of 2021, but his A1C climbed to 7.5%, so we increased his GLP-1 RA dose again. At his most recent visit in 2023, with new dietary efforts and the increased medication dose, Roger's weight was back down to 194 lbs. with an AIC of 7.3%.

**Considerations:**
GLP-1 RAs are widely used for the treatment of type 2 diabetes and can be considered first-line agents or add-on therapy for patients who are unable to get to goal with lifestyle efforts or who may have already been treated with metformin. Patients who are especially good candidates include those who have overweight/obesity, those with a history of atherosclerotic cardiovascular disease or stroke, and those for whom avoiding hypoglycemia is important; they can also be used in combination with basal insulin. ●

**NEW!**
**KOL ON DEMAND VIDEO**
Scan here for more insight on Roger's case.



**PATIENT:** WILLIAM, 61, HAD A HIGH A1C, RENAL INSUFFICIENCY AND CORONARY ARTERY DISEASE.

# "His A1C and kidney function were getting worse"

**History:**
William was hospitalized after complaining of shortness of breath. Upon admission, a chest X-ray showed a right lower lobe infiltrate with brain natriuretic peptide (BNP) of 1,200 pg/mL, and ECG showed 40% ejection fraction—all suggestive of heart failure. Atherosclerosis was seen in several blood vessels, but overall it didn't exceed 40% stenosis.

Before hospitalization, William was taking metformin 1,000 mg/day and linagliptin 5 mg/day to manage his diabetes, plus a statin and aspirin for hypertension and coronary artery disease (CAD). In the last 2 years, his AIC has increased from 6.6% to 7.4%, and his eGFR has decreased from 64 to 50 mL/min/1.73m$^2$. The latter finding, together with the BNP level, suggests worsening chronic kidney disease (CKD).

**Initiating treatment:**
William's rising AIC necessitated intensification, but we also needed to consider his established CAD and heart failure. Preserving kidney function was another necessity.

SGLT2 inhibitors are an add-on option recommended by the American Association of Clinical Endocrinology and American Diabetes Association for patients with type 2 diabetes and CKD to reduce risk of CKD progression, cardiovascular disease, or both. In renal outcomes trials, certain SGLT2 inhibitors reduced the risk of progression to serious or end-stage renal disease (ESRD) or death from cardiovascular or kidney disease by 30% among patients with type 2 diabetes and established renal insufficiency compared with placebo. Also, in previous trials, SGLT2 inhibitors reduced serious cardiovascular events and hospitalization for heart failure in patients with type 2 diabetes. Given these findings, we added an SGLT2 inhibitor to William's antihyperglycemic regimen. At discharge, he also received medication for community-acquired pneumonia and a beta-blocker and ARB to manage his heart failure. Six months later, William's AIC was down to our target of 7.1%, and his eGFR was stable in the low-50s.

"We needed to consider William's established CAD and heart failure."

**Considerations:**
Heart failure is typical for patients with multivessel CAD and demand ischemia. In addition, both William's glycemic control and kidney function had worsened. Data show that SGLT2 inhibitors are a safe glucose-control option for patients with type 2 diabetes and comorbid CKD and cardiovascular disease. However, SGLT2 inhibitors are contraindicated in patients with severe renal impairment (eGFR <30), ESRD or dialysis-dependent patients. William's case also underscores the need to individualize therapy. Whereas an AIC target of 7% or less is optimal for most patients, liberalizing that target may be advisable based on age, comorbidities and life expectancy. Keeping William's AIC at 7.1% in the presence of compromised medication clearance due to CKD decreases his risk of hypoglycemia. ●

PHYSICIAN:

**Javier Morales, MD**

*Associate Clinical Professor of Medicine, Hofstra/ Northwell; VP and clinical trial investigator, Advanced Internal Medicine Group, East Hills, NY*

Illustrations by Juhee Kim

# Q&A

*Expert insight on managing type 2 diabetes*


Illustration by Donna Grethen / Ikon Images

## Patient-centered care

**Q: How do you individualize a patient's treatment plan, and what variables do you consider?**

**A:** I start with a thorough evaluation of the patient. This evaluation must include medical, social and other factors that may impact our shared decision-making process to reach a mutually agreed upon treatment plan. Once a treatment plan is in place, the guidelines from the American Association of Clinical Endocrinology and the American Diabetes Association provide clear recommendations based on the patient's current health status and risks. The multiple factors that can help healthcare professionals individualize a patient's treatment plan include health issues and risks such as heart disease, kidney disease, obesity, age and high-risk status for hypoglycemia. If a patient has obesity and heart disease, the best therapeutic fit would be a GLP-1 receptor agonist, as this class promotes weight loss and reduces the risk of cardiovascular events as long as there are no complications.

*—**Nuha Ali El Sayed, MD, MMSc,** Joslin Diabetes Center; Instructor in Medicine, Harvard Medical School*

## Encouraging healthy eating habits

**Q: What are your strategies for encouraging patients to avoid "dieting," and make healthy dietary choices instead?**

**A:** I like to educate my patients that the best "diet" is the one that they can stick with and incorporate into their lives as a long-term plan. I frequently counsel patients to adopt a Mediterranean diet and explain that it is a heart-healthy eating plan that includes vegetables, fruits, whole grains, olive oil, nuts and seeds, and plant-based fats. There is weekly consumption of fish, poultry and eggs and limits on red meat. I try to share examples of what a meal would include on this type of food plan based on their personal preferences. Another key dietary change is limiting beverages with calories, including juices, and choosing healthy replacements such as calorie-free flavored seltzers instead. The goal is to find a plan that is calorie-reduced and portion-size-reduced, but also feasible for long-term adherence.

*—**Rachel Pessah-Pollack, MD, FACE,** Clinical Associate Professor of Endocrinology, Diabetes and Metabolism, NYU Langone Health*

## Cholesterol management

**Q: How do you optimize LDL-lowering therapy, and what do you say if patients are worried about statin side effects?**

**A:** People with type 2 diabetes are a high-risk population. Many have overt CVD, but diabetes makes them very high risk even if there is no overt CVD. We have clinician-patient risk discussions about it, highlighting the fact that diabetes is a cardiovascular disease, and that they need comprehensive CVD risk reduction. Many patients are surprised to learn that about 80% of diabetes patients die of a vascular or cardiovascular event. We frequently talk about the role of LDL-lowering therapy, the first of which is statins. We consider high-intensity statins to lower LDL as much as possible for people with diabetes-enhancing risk factors. We make the point that these drugs not only help lower cholesterol, but they also are proven and effective in lowering CV risk, including heart attack, stroke, and the need for stents, as well as bypass surgery.

A clinician-patient risk discussion is also important for patients who are worried about statin side effects. Side effects are real in some patients, but we see them in only about 5% to 10% of patients at most. The side effects in most patients are minor, most commonly SAMS—statin-associated muscle symptoms. We emphasize the benefits of statins and that most people will be able to be treated with one of several different statins without side effects. It's often about finding the right statin for the right patient, so you don't want to abandon this class of medications after one try. Again, it relates to partnered care and working with a team to find the right medications for the patient.

*—**Laurence Sperling, MD,** Founder, Preventive Cardiology at the Emory Clinic; Katz Professor in Preventive Cardiology, the Emory University School of Medicine and the Rollins School of Public Health in Global Health*

## Bariatric surgery

**Q: When would you consider bariatric surgery for a patient who has diabetes?**

**A:** The American Society of Metabolic and Bariatric Surgery and the International Federation for the Surgery of Obesity and Metabolic Disorders published updated indications for bariatric surgery, which include adults who have a BMI ≥35 kg/m$^2$ regardless of other medical issues. It's based on data that show bariatric surgery is superior to diet, exercise and other lifestyle interventions in attaining prolonged weight loss. Another consideration is patients with a BMI of 30 to 34.9 and type 2 diabetes who are unable to get to a sustainable weight with nonsurgical methods. Patients in this BMI range who have bariatric surgery can also show significant improvement in their diabetes control. Other conditions that can be improved with weight loss include sleep apnea, high blood pressure, high cholesterol and nonalcoholic fatty liver disease. There are also different BMIs considered normal based on race. For example, diabetes and heart disease can be found at a lower BMI in Asian persons, so the BMI cutoff is lower in this population. Patients are required to participate in a series of lifestyle modifications, including dietary changes and physical activity, to show their dedication to the overall bariatric surgery program. If there are underlying mood issues such as untreated major depression and/or untreated eating disorders, these would be contraindications and should be treated before moving forward with bariatric surgery. It's important to verify if the patient has been treated with a GLP-1 agonist, as many patients can have a robust weight loss response when treated with this class of medication prior to bariatric surgery.

*—**Rachel Pessah-Pollack, MD, FACE***

**Special thanks to our medical reviewer:**
**Alaleh Mazhari DO, FACE,** Professor Division of Endocrinology and Metabolism Loyola University Medical Center, Maywood, IL



Health Monitor

**Maria Lissandrello,** Senior Vice President, Editor-In-Chief; **Lori Murray,** Associate Vice President, Executive Editor; **Lindsay Bosslett,** Associate Vice President, Managing Editor; **Jodie Gould,** Senior Editor; **Joana Mangune,** Senior Editor; **Marissa Purdy,** Associate Editor; **Jennifer Webber,** Associate Vice President, Associate Creative Director; **Ashley Pinck,** Art Director; **Stefanie Fischer,** Senior Graphic Designer; **Sarah Hartstein,** Graphic Designer; **Kimberly H. Vivas,** Senior Vice President, Production and Project Management; **Jennie Macko,** Associate Director, Print Production; **Gianna Caradonna,** Print Production Coordinator

**Dawn Vezirian,** Senior Vice President, Financial Planning and Analysis; **Tricia Tuozzo,** Senior Sales Development Manager; **Augie Caruso,** Executive Vice President, Sales and Key Accounts; **Keith Sedlak,** Executive Vice President, Chief Commercial Officer; **Howard Halligan,** President, Chief Operating Officer; **David M. Paragamian,** Chief Executive Officer

Health Monitor Network is the leading clinical and patient education publisher in endocrinology and PCP offices, providing specialty patient guides, discussion tools and digital wallboards.

Health Monitor Network, 11 Philips Parkway, Montvale, NJ 07645; 201-391-1911; customerservice@healthmonitor.com. ©2024 Data Centrum Communications, Inc.

Cover illustration by Donna Grethen / Ikon Images

RAM24

Health Monitor

# Clinician Update

EXAM TOOL

## Assessing sleep hygiene

Diabetes and sleep are intricately connected, and many people with type 2 diabetes experience poor sleep quality or insomnia. The good news is that careful attention to diet, exercise and blood sugar levels can improve sleep quality and, in turn, overall health. AACE guidelines also recommend assessing patients for symptoms and signs of obstructive sleep apnea, an independent risk factor for cardiac, neurologic and perioperative morbidities, especially in the presence of obesity. To uncover barriers to restorative sleep and potential sleep disorders, consider the criteria below.

**Ask patients to choose the answer that best describes their sleep patterns:**

1. I typically sleep less than 7 hours per night.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
2. I have trouble falling asleep or staying asleep.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
3. I wake up frequently during the night.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
4. My sleep partner complains that I snore loudly.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
5. I feel sleepy during the day, even after a full night's sleep.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
6. I awaken suddenly during the night, gasping for breath, or with a choking sensation.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
7. I have an urge to move my legs when I lie down to sleep.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often
8. I use sleep aids or medications.
   - ☐ Rarely
   - ☐ Sometimes
   - ☐ Often

Source: Surani S, et al. *World J Diabetes*. 2015;6(6):868-873.