

The prevalence of type 2 diabetes and obesity is increasing. Research has demonstrated the use of GLP-1 RA and SGLT-2i medications to be safe and effective for the long-term management of T2DM and obesity. As continued research supports the use of GLP-1 RA and SGLT-2i medications for additional indications, home care clinicians will increasingly care for patients on these medications. It is imperative that home care clinicians are aware of patient indications, adverse effects, and potential safety considerations related to these drugs to ensure patient goals are met.

In-Home Management of Diabetes and Obesity

Type 2 Diabetes Mellitus (T2DM) and obesity have significantly risen in prevalence over the last 2 decades. According to the Centers for Disease Control and Prevention (CDC), in 2019, 11.3% of the U.S. population had diabetes compared to 10.3% in 2004 (2022a). Since 2000, the prevalence of adult obesity (BMI of greater than or equal to 30 kg/m²) has risen from 30.5% to 41.9%, whereas severe obesity (BMI of greater than or equal to 40 kg/m²) nearly doubled (CDC, 2022b). Obesity continues to be a major driver of T2DM with approximately 30% to 55% of T2DM cases in the United States being attributed to obesity (Cameron et al., 2021). The increasing coexistence of T2DM and high-risk obesity presents complex treatment challenges and has been linked to cardiovascular morbidity and mortality (Piché et al., 2020). T2DM and obesity are also linked to the pathophysiological mechanisms underlying renal damage and disease (Prasad et al., 2022). As a result of the rising rates and severe risks associated with T2DM and obesity, new pharmacotherapeutics and guidelines have emerged for the dual treatment of these conditions.

Previous Recommendations

Previous recommendations for the management of coexisting T2DM and obesity often focused on lifestyle modification and separated the two conditions once pharmacologic therapy became necessary. The key elements for the management of

obesity included comprehensive lifestyle interventions: patient-centered behavioral guidance; dietary interventions to reduce caloric intake; and physical activity to create a negative energy balance (Department of Veterans Affairs, Department of Defense [VA/DOD], 2020). If lifestyle interventions alone were insufficient, a pharmacological treatment, such as liraglutide, naltrexone/bupropion, orlistat, or phentermine, could be added for patients with a BMI of 30 kg/m² or more or a BMI of 27 kg/m² or more with an obesity-related condition (VA/DOD, 2020). Bariatric surgery was an additional option for patients with a BMI of 40 kg/m² or more or a BMI of 35 kg/m² or more with an obesity-related condition (VA/DOD, 2020). Lifestyle modification therapy for obesity often failed to achieve sustainable weight loss and metabolic recovery, and pharmacological treatment was also of limited efficacy (Piché et al., 2020). According to the American Diabetes Association (ADA), previous T2DM guidelines included nutritional therapy, physical activity, and weight management to slow progression from prediabetes to T2DM. The initial oral medication recommended was metformin, which was continued when other medications, including insulin, were added in a stepwise progression (ADA, 2019).

Updated Recommendations

Recent research data have supported that the goals of weight loss and T2DM prevention and

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management are correlated (Cameron et al., 2021; ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Cusi, et al., 2023; Piché et al., 2020). Weight loss of 10% or more is correlated with improvement in long-term diabetes outcomes, and obesity management has been found to delay T2DM disease progression (ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023). Glucose-lowering management of T2DM “should consider approaches that support weight management goals” (ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023, pp. S142–S143).

In response to new pharmacological measures to support weight loss, the American Gastroenterological Association (AGA) has updated recommendations to consider glucagon-like peptide-1 receptor agonist (GLP-1 RA, e.g., Trulicity®, Byetta®, Ozempic®) medications for long-term management of obesity. Research has shown patients regain a significant amount of weight within a year of stopping the medication; therefore, the medication should be considered a chronic condition therapy. The guidelines additionally recommend considering co-indications in drug selection, such as T2DM, migraine, smoking cessation, and de-

pression. The GLP-1 RA semaglutide (Ozempic®) is the priority medication for weight loss. Additionally, the AGA recommends against the use of orlistat for weight loss because adverse gastrointestinal effects overshadow the small weight loss benefits (Grunvald et al., 2022).

In addition to lifestyle interventions, pharmacotherapy should be initiated in patients without contraindications at the time of the T2DM diagnosis (ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023). Although metformin remains the first-line medication option for the management of T2DM and is known to contribute to some weight loss, significant weight loss success and blood glucose reductions are supported with the use of the GLP-1 RA and sodium-glucose cotransporter 2 inhibitors (SGLT-2i; e.g., Invokana®, Jardiance®, Steglatro®) and use of these medication classes should be prioritized over metformin in patients with obesity (ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023). Initial combination therapy has been found to be more effective in meeting glycemic goals in patients with significant elevations in blood glucose than sequential medication additions to metformin alone, with GLP-1

RAs and metformin together leading to the greatest blood glucose reductions. Also, the concurrent use of a GLP-1 RA with basal insulin reduces the impacts of weight gain and hypoglycemia that are associated with insulin once it is added (Apovian et al., 2016; ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023). Updated T2DM recommendations also include prompt treatment intensification for patients who don't meet glycemic treatment goals, shared decision-making with the patient, considerations of co-morbidities in drug selection, as well as adverse effects, patient tolerance, and drug cost (ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023). The use of GLP-1 RA and/or SGLT-2i medications has been found to be beneficial for diabetic patients with cardiovascular disease and chronic kidney disease. The addition of SGLT-2i medications has been found to be beneficial for patients with heart failure, with or without diabetes (Patnaik, 2023).

Pharmacotherapeutics

GLP-1 RA medications work by mimicking the hormone GLP-1, which increases insulin production, slows gastric emptying, and suppresses appetite (Suran, 2023). The differences between the medications are in the indication, dosages, route, and frequency (Table 1). Although GLP-1 RA medications have been utilized for diabetes management for years, semaglutide and liraglutide have been recently approved by the Food and Drug Adminis-

tration (FDA) for weight loss (FDA, 2020, 2021). Tirzepatide is a dual GLP-1 RA and glucose-dependent insulinotropic polypeptide, which increases glucagon production and impacts blood lipids resulting in improved beta cell function and insulin sensitivity (Baker et al., 2023). Two GLP-1 RA medications are available at the time of this writing that are combined with a fixed dose of a basal insulin with once-daily dosing: insulin glargine with lixisenatide (Soliqua®); insulin degludec with liraglutide (Xultophy®) (ElSayed, Aleppo, Aroda, Bannuru, Brown, Bruemmer, Collins, Hilliard, et al., 2023).

GLP-1 RA medications are contraindicated in patients with hypersensitivity reactions; personal or family history of multiple endocrine neoplasia or medullary thyroid cancer; and caution should be used in patients with a history of pancreatitis, gastroparesis, or inflammatory bowel disease (Collins & Costello, 2023). GLP-1 RA medications are not recommended in pregnancy, and it is advised that patients using hormonal contraceptives use alternative contraception for 4 weeks after drug initiation and dosage increases (Baker et al., 2023).

The most common adverse effects of GLP-1 RA medications are gastrointestinal upset, including nausea, vomiting, and diarrhea, which could lead to acute kidney injury from fluid depletion. Pancreatitis and retinopathy have been reported. Hypoglycemia may occur when the medications are used in combination with other diabetes agents

Table 1. GLP-1 RA Drugs

GLP-1 RA Generic Name	Trade Name	Frequency	FDA-Approved Indication	Dose/Route
Dulaglutide	Trulicity	Weekly	Diabetes	0.75 mg–3 mg/Injection
Exenatide ER	Bydureon	Weekly	Diabetes	2 mg/Injection
Exenatide	Byetta	Twice daily in 60 minutes before meals at least 6 hours apart	Diabetes	5 mcg–10 mcg/Injection
Semaglutide	Ozempic	Weekly	Diabetes	0.5 mg–2 mg/Injection
Semaglutide	Wegovy	Weekly	Weight loss	0.25 mg–2.4 mg/Injection
Semaglutide	Rybelsus	Daily 30 minutes before first meal of the day	Diabetes ^a	7 mg, 14 mg oral
Liraglutide	Victoza	Daily	Diabetes	0.6 mg–1.8 mg/Injection
Liraglutide	Saxenda	Daily	Weight loss	0.6 mg–3 mg/Injection
Tirzepatide (GLP-1RA combined with GIP)	Mounjaro	Weekly	Diabetes ^a	2.5 mg–15 mg/Injection

^aAnticipated future FDA approval for weight loss

that cause hypoglycemia such as sulfonylureas or insulin. Injection site reactions are common (Filipatos et al., 2015). There have been recent media reports of “Ozempic Face” that attributes facial aging to use of the medication, but the loss of facial fat can occur with any weight loss method (Suran, 2023). There have been case reports of medication-induced gastroparesis that, while initially thought to be diabetic gastroparesis, resolved when the medication was discontinued (Kalas et al., 2021). There have been additional case reports in the perioperative setting of an increased risk of aspiration of stomach contents during anesthesia due to the delayed gastric emptying with the use of GLP-1 RA medications (Kalas et al., 2021).

SGLT-2i medications work by blocking glucose and sodium reabsorption in the kidneys and increasing glucose excretion in the urine (Simes & MacGregor, 2019). The differences between the medications are indications, dosages, and timing with food (Table 2). Although SGLT-2i medications have been used for years for the management of diabetes, dapagliflozin and empagliflozin have recently been FDA approved for the treatment of heart failure, with or without diabetes, due to improved cardiovascular patient outcomes (Talha et al., 2023). Sotagliflozin is a dual SGLT-2i and SGLT-1 inhibitor. SGLT-1 inhibitors block glucose reabsorption in the intestines (Inserro, 2023). SGLT-2i medications are available in fixed-dose combinations with metformin and dipeptidyl peptidase-4 (DPP-4) inhibitors (Table 2). Triple fixed-dose combinations with an SGLT-2i, DPP-4 inhibitor, and metformin may simplify medication regimens for patients and have been found to be safe and effective for the management of T2DM (Li et al., 2023).

SGLT-2i medications are contraindicated in patients with impaired renal function and estimated glomerular filtration rate (eGFR) of less than 30. Patients who have an eGFR less than 60 for ertugliflozin and less than 45 for the other SGLT-2i medications should not have the SGLT-2i started and if already taking an SGLT-2i, it should be discontinued with the lower eGFR (Simes & MacGregor, 2019). Adverse effects of SGLT-2i medications include increased risk for genital tract infections in patients with diabetes, euglycemic diabetic ketoacidosis (DKA), and increased risk of amputations with canagliflozin (Simes & MacGregor, 2019). In T2DM patients with euglycemic DKA, a history of DKA is not always present and



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most commonly is precipitated by infections and poor oral intake. Symptoms of euglycemic DKA included nausea, vomiting, and abdominal pain (Stamatiades et al., 2023). Hypoglycemia may occur when the medications are used in combination with other diabetic agents that cause hypoglycemia such as sulfonylureas or insulin.

Considerations for Home Care Practice

Due to the increased prevalence of patients with obesity and T2DM and the increased use of GLP-1 RA and SGLT2i medications, clinicians must be aware of drug contraindications, adverse effects, and patient monitoring considerations. Home care clinicians are responsible for assessing both the immediate and long-term effects of these medications. Patients who are prescribed GLP-1 RA and SGLT-2i medications should be evaluated for contraindications before beginning the medications.

Clinicians should also be aware of the risk of hypoglycemia when GLP-1 RA or SGLT-2i medications are used in conjunction with insulin, sulfonylureas, or glinides (American College of Cardiology, 2020). Patients should be educated on the need to closely monitor blood glucose at home for the first 4 weeks of therapy and monitor for signs and symptoms of hypoglycemia, such as headache, weakness, dizziness, confusion, and/or sweating (American College of Cardiology, 2020). If hypoglycemia persists, sulfonylureas or glinides may need to be discontinued, whereas insulin dosages may need to be reduced (American College of Cardiology, 2020).

In addition to the monitoring of blood glucose levels during the use of GLP-1 RA and SGLT-2i medications, clinicians should ensure kidney function is also routinely monitored. Patients with chronic kidney disease who have an eGFR less than 60 mL/min/1.73 m² and are on SGLT-2i medications should be frequently monitored for changing and/or worsening kidney function. Although SGLT-2i medications can offer renal protection and prevent decline in renal function in T2DM patients, dosages may need to be modified or the medication needs to be discontinued by the provider if worsening kidney function occurs (Simes & MacGregor, 2019). Kidney function (serum creatinine) should also be monitored in patients on GLP-1 RA medications within 4 weeks of initiating therapy and 2 to 3 months after an increase in dosage (Dungan & Desantis, 2023). Patients should be

educated on signs and symptoms of worsening kidney function, such as infrequent urination and dark-colored urine, dry mucous membranes, dizziness, and fatigue. Bladder infections are also an associated adverse effect of SGLT-2i medications, so patients should be taught to report signs and symptoms such as painful, frequent urination, foul odor or discolored urine, and fever.

The most common adverse effects of GLP-1 RA medications are nausea, vomiting, and diarrhea especially when first beginning the medication. Clinician should educate patients on these expected effects and encourage smaller, more frequent meals and avoiding foods that may contribute to gastrointestinal distress, such as high-fat or spicy foods. Patients may also experience some relief from these adverse effects if the medication is started at a lower dose with gradual dose increases and the medication is taken before bedtime. It is essential to educate the patient on staying hydrated as gastrointestinal distress can lead to fluid volume depletion and acute kidney injury. If severe gastrointestinal distress and subsequent dehydration occurs, it is important to contact the prescribing provider for any necessary supportive therapies as well as management of the GLP-1 RA medication and other medications that may be affected by the patient's gastrointestinal distress. Acute pancreatitis has also been associated with the use of GLP-1 RA medications and should be immediately considered if the patient reports severe abdominal or back pain, with or without

Table 2. SGLT-2i Drugs

SGLT-2i	Trade Name	Frequency	FDA-Approved Indication	Dose/Route
Canagliflozin	Invokana (combination with metformin is Invokamet XR)	Once a day before first meal of the day	Diabetes, chronic kidney disease	100 mg–300 mg/oral
Ertugliflozin	Steglatro (combination with metformin is Segluromet; with sitagliptin is Steglujan)	Once a day in the morning with or without food	Diabetes	5 mg–15 mg/oral
Dapagliflozin	Farxiga (combination with metformin is Xigduo; with saxagliptin is Qtern)	Once a day in the morning with or without food	Diabetes, heart failure, chronic kidney disease	5 mg–10 mg/oral
Empagliflozin	Jardiance (combination with metformin is Synjardy; with linagliptin is Glyxambi)	Once a day in the morning with or without food	Diabetes, heart failure, chronic kidney disease	10 mg or 25 mg/oral
Sotagliflozin (SGLT-1 and SGLT-2 inhibitor)	Inpefa	Once daily before first meal of the day	Diabetes, cardiovascular risk reduction, heart failure, chronic kidney disease	200 mg–400 mg/oral

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nausea (Dungan & Desantis, 2023). If acute pancreatitis is suspected, the provider should be notified and the medication should be held until further diagnostic tests are completed.

Due to delayed gastric emptying and the associated side effects, clinicians should be aware of any upcoming procedures and/or surgeries and instruct the patient to discuss the use of GLP-1 RA medication with the anesthesia team to reduce the risk of aspiration. Expert opinion advises consulting an endocrinologist, holding the medication and increasing fasting time prior to surgical procedures. Additional recommendations include pre-operative gastric ultrasound and transparent discussions of options with the patient (Jones et al., 2023). Diabetic retinopathy complications have also been reported in patients on the GLP-1 RA semaglutide (Dungan & Desantis, 2023). Prior to beginning the medication, patients should undergo an eye examination if not recently done and continue with routine retinal screening within 6 months to detect progression of retinopathy (American College of Cardiology, 2020; Dungan & Desantis, 2023). It is also important to ensure that patients are educated about the proper storage of GLP-1RA medications in the drug's original packaging in the refrigerator.

In the use of SGLT-2i medications, patients should be educated on signs and symptoms of DKA, such as nausea, vomiting, abdominal pain, and weakness in the presence of normal blood sugars especially if the patient has recently had an infection or reduced oral intake. SGLT-2i medications should also be discontinued at least 3 days before a planned surgery to prevent postoperative ketoacidosis (American College of Cardiology, 2020). Clinicians should also closely monitor the skin of patients on SGLT-2i medications and discuss the importance of proactive genital hygiene and foot care in addition to signs and symptoms of wounds and/or infections in these areas.

Research studies related to combination therapies are on-going, and though simplification of medication regimes with fixed-dose combinations are beneficial, it is also noted that cost is an important factor and medications with higher out-of-pocket costs for patients are much less likely to be utilized (Luo et al., 2023). Clinicians should be aware of cost considerations of GLP-1 RA and SGLT-2i medications and discuss their use as part of the patient-centered care plan in meeting mutual goals for glycemic control.

Conclusion

T2DM and obesity rates are increasing. Research has demonstrated the use of GLP-1 RA and SGLT-2i medications to be beneficial and they are becoming a standard of care for the long-term management of T2DM and obesity. As continued research supports the safety and efficacy of GLP-1 RA and SGLT-2i medications for additional indications, their use will continue to increase and be utilized in the home care environment. It is imperative that home care clinicians are aware of indications, adverse effects, and potential safety considerations related to these drugs to ensure outcomes are met. ■

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The authors declare no conflicts of interest.

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DOI:10.1097/NHH.0000000000001223

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