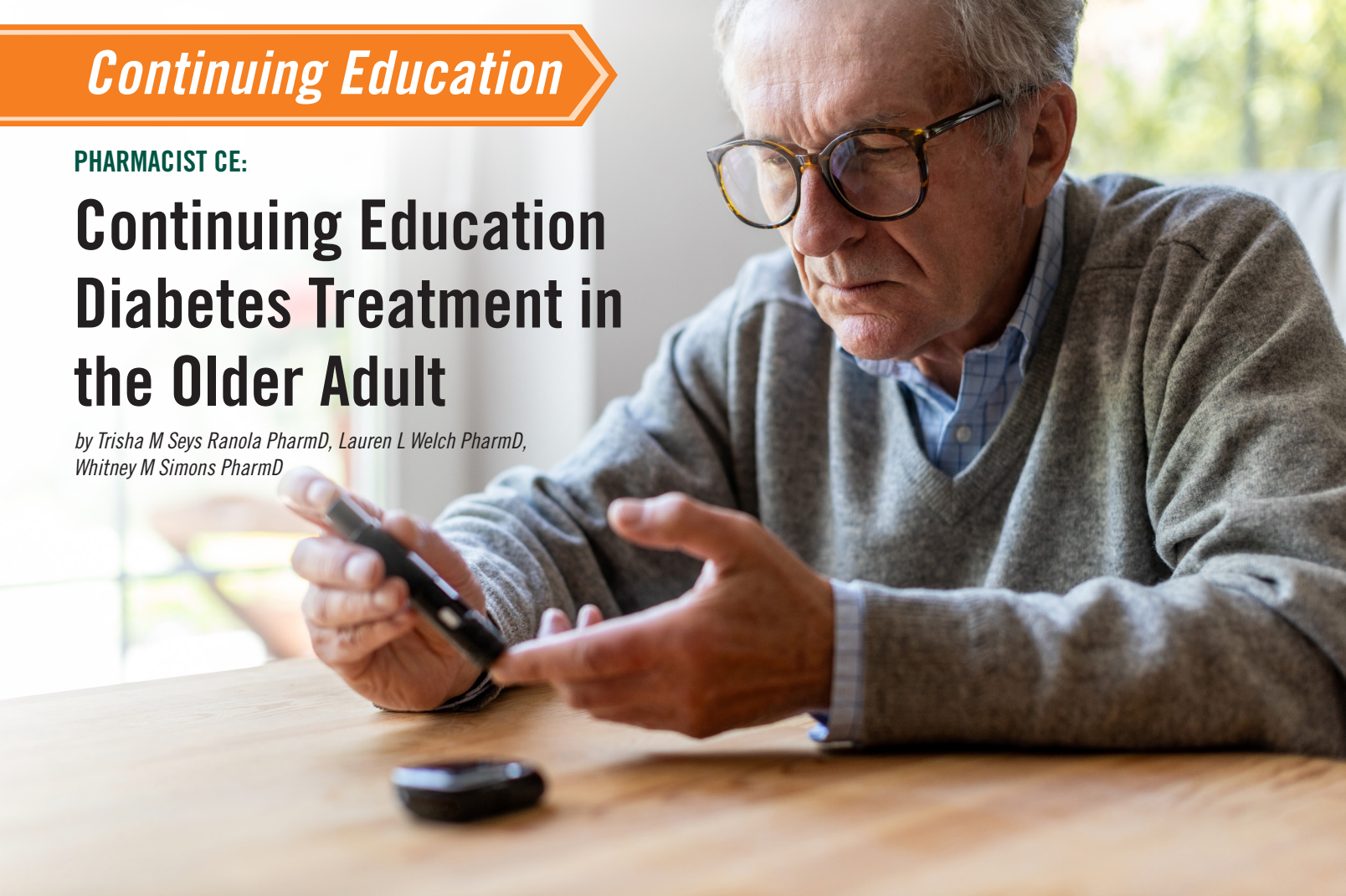


PHARMACIST CE:

Continuing Education Diabetes Treatment in the Older Adult

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Type 2 diabetes mellitus (T2DM) has been on the rise over the past several decades. With the advances in diabetes treatment, we are seeing a growth in the number of older adults living with the condition. As treatments for all chronic conditions have improved, there are now more older adults living with T2DM.¹ In 2018, there were 14.3 million adults over the age of 65 (26.8% of that age group) living with T2DM; this is predicted to increase to 26.7 million by the year 2050.¹ The rise in diabetes rates brings up substantial questions for the geriatric provider: What treatments can we use safely for our older adults? Which medications will cause the fewest side effects? What therapies have the potential to improve or worsen comorbidities that diabetic patients are living with? In this article, we will address these geriatric considerations and offer an overview of diabetes therapies as they apply to this unique patient population.

Geriatric providers know that older adults are not a homogeneous

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Learning Objectives

- Define the present and future epidemiology of diabetes in older adults
- Identify potential complications and considerations in older adults with diabetes
- Discover assessment tools including screening, diagnostic, and prevention strategies for diabetes in older adults
- Discuss individualization of care of diabetes in older adults
- Identify best practices to involve patients in decisions related to diabetes care in older adults

population. Many suffer from multiple morbidities, while others continue to lead active lives with few complications.² Despite this spectrum of differences, physiological changes do occur that impact recommended lifestyle modifications and diabetic medications.^{2,3} Among the most notable changes to physiology is a decrease in renal function, which can limit medication choices. Renal function decline also requires more self-monitoring for hypoglycemia, which in turn necessitates adequate dexterity and

often presents as a challenge for older adults. Likewise, vision might be impacted, making drawing up insulin or dialing a medication pen extremely challenging, and creating adherence and safety concerns. Neurohormone levels change, altering expression to the central nervous system. In turn, these changes can lead older adults to be less responsive to changes in position, thereby increasing the risk of falls.^{2,4} Digestive systems become sluggish, impacting the rate of food and medication absorption, and resulting in changes in

blood glucose. In older adults, the immune system response is not as robust, making infections more likely yet harder to diagnose and treat.² These considerations will be explored in more detail below.

In addition to physiological presentations/symptoms, older adults are often members of a vulnerable financial population. Older adults might be at increased risk for lack of financial independence, leading to food insecurity, unaffordable medications, and less overall access to healthcare.⁵ In 2017, an estimated 14.1% of adults over the age of 65 lived at or below the poverty threshold.⁵ Additionally, only 17% (55 million) of people age 65 and older are enrolled in Medicare. Of those enrolled, only 39 million are enrolled in Part D for prescription drug coverage.⁶ One in five uninsured adults in 2018 went without needed medical care due to cost.⁷ Together, these insecurities are part of a larger issue that comprises the social determinants of health (SDH). While SDH is a familiar term in population and public health, it is only recently being addressed by family medicine clinics.⁸ Additionally, the American Diabetes Association (ADA) states that the SDH, including socioeconomics; physical and neighborhood environment; food environment (food security); and health care and social support, have a significant impact on diabetes treatment and must be addressed to improve health outcomes.⁴ During clinical interactions with patients, pharmacists should routinely ask patients about aspects of SDH, including food security, feeling safe in their home, and what social supports they have available, among others.⁹ Often, the SDH are part of a lifelong risk and might be out of the control of the patient. Addressing limitations on finances, food insecurity, and social support might impact the lifestyle change recommendations and medication therapy selections given by healthcare professionals.

Due to the variance in older adult health, diabetes care for older adults requires shared decision making between the patient/caregiver and provider(s), and a shift in focus from targeting pre-determined glucose levels to improving overall quality of life for the patient.¹⁰

A team-based approach is considered best practice for older adults living with diabetes and should include discussions on what the patient values, the best methods to minimize side effects including hypoglycemia, the impact on mood, and cognitive decline. Additionally, attention should be placed on the patient's goals, including a discussion surrounding quality of life and function.¹⁰

Clinical Presentation

The majority of people with T2DM are diagnosed prior to the age of 65, after which the incidence and prevalence remain stable.¹¹ Hyperglycemia is a prominent feature of type 2 diabetes in older adults; national guidelines for diagnosing T2DM are based on hemoglobin A1c (A1c) and fasting blood glucose levels, leaving about one-third of older adults with diabetes undiagnosed due to a wide variety of factors that might include asymptomatic mild to moderate elevations in blood sugar, lack of follow-up or access to medical care.² Diagnosis after the age of 65 is more common in non-Hispanic whites and typically manifests with lower

A1c and decreased insulin requirements. Additionally, while retinopathy is more common with younger age of onset, there is no difference in cardiovascular disease or peripheral neuropathy compared with older cohorts.²

Symptoms of T2DM in the older adult population are not limited to the classic three polys (polyuria, polyphagia, and polydipsia), in part due to the physiologic changes seen with age. For example, consider an older adult male presenting to his provider with nocturia; this might be easily confused with prostate concerns.¹⁰ Typical symptoms might be vague, including feeling more confused, or feeling tired, or frequent urination. Often, these symptoms are simply attributed to "old age," when in fact they might be manifesting as a new condition, primarily related to hyperglycemia.¹⁰ Table 1 below provides a comparison of T2DM symptoms and co-conditions older adults could have that might lead to missed opportunities for screening of diabetes.²

TABLE 1. Symptoms of Type 2 Diabetes Mellitus and Other Conditions with Similar Symptoms in the Older Adult Population²

<i>Symptoms of Type 2 Diabetes Mellitus</i>	<i>Older Adult Co-conditions with Similar Symptoms</i>
Polyuria	Benign prostatic hyperplasia (BPH) Overactive bladder Stress incontinence
Polydipsia	Thyroid changes Or not present due to impaired thirst mechanism
Polyphagia	Thyroid changes
Confusion	Cognitive changes Dementia Infection
Fatigue	"Old age"
Poor wound healing	Peripheral vascular disease
Neuropathy	Peripheral vascular disease
Hyperglycemia	Medications Common to Older Adults: Thiazides Beta Blockers Statins Oral Steroids Antipsychotic Serotonin Inhibitors Others

TABLE 2. 2021 Standard of Medical Care in Diabetes

See [Table 12.1 in the 2021 Standard of Medical Care in Diabetes](#) for information on the treatment goals of glycemia, blood pressure and dyslipidemia in the older adult population.

Older Adults Considerations

Not only is it important to consider the physiological changes that might occur in later life, but other geriatric-related syndromes should also be considered when selecting the most appropriate diabetic medication choice for older adults. Some of these syndromes might be both physical and social in nature, and might include issues such as bladder control, sleep, weight gain or loss, balance, and dementia. The next section of the paper will explore several of these concerns and the impact they may have on therapy considerations.

Dexterity

Older adults are more susceptible to osteoarthritis (OA), which can greatly impact overall dexterity, especially in the hands. The prevalence of hand OA increases with age, and it is reported that 13% of men and 26% of women over the age of 70 suffer from OA.¹² Providers should ask whether patients have difficulty opening pill bottles with safety caps, especially if it appears that non-adherence may be impacting overall diabetes control. Limited dexterity can significantly impact a patient's ability to draw up and inject insulin or use glucagon-like peptide (GLP-1 RA) injectables. Insulin vial-and-syringe combinations are typically more cumbersome for these patients, and options using insulin pens/GLP-1 RA may be considered. Assessment of use of pens should still be undertaken, as dexterity may impact use of these devices as well. Dexterity can also impact the patient's ability to use a glucometer effectively to monitor blood glucose. Creative solutions might be needed to engage family members or caregivers to aid in either safe medication administration or effective blood glucose monitoring strategies for some of these patients.

Sensory Impairments

Vision impairments increase as patients age, impacting nearly one out of five older adults with diabetes.¹³ Cataracts are more commonly diagnosed in diabetic patients.¹³

Additional microvascular complications related to diabetic retinopathy can also impact overall vision quality for older adults. It is important to screen for vision impairments. Offering recommendations for corrective measures or appropriate vision aids can prevent medication-related errors and improve overall quality of life.¹³ Vascular disease and neuropathy have been linked to hearing impairments in older adults. Hearing impairments are twice as common in older adults with diabetes.² Both vision and hearing impairments should be factors to assess and consider when managing and educating patients on diabetic medication regimens and lifestyle modifications to reach specific patient diabetic goals. Large-print labels, medication bottles for the visually impaired, pocket talkers to assist with hearing, and talking blood glucose meters are all options during clinic appointments or when receiving counseling at the pharmacy that may promote independence and improved safety for patients with sensory impairments.

Polypharmacy

Given the increased complexity and additional comorbidities, polypharmacy is much more prevalent in this patient population. It is estimated that 40%-50% of people over the age of 65 have five or more medications, meeting the definition of polypharmacy agreed upon in the literature.^{14,15} The number of comorbidities typically results in an increase in prescribed medications.^{14,15} A direct correlation occurs between the number of medications and incidence of adverse drug events or drug-drug interactions (DDIs) resulting in increased incidence of adverse drug reactions. One study noted the prevalence of clinically relevant DDIs in older adults prescribed six or more medications was 26%; of these, 5% were classified as potentially serious DDIs.² Shared decision-making to address the patient's goals should be considered prior to adding additional medication therapy to treat a patient's

diabetes, due to the risks associated with polypharmacy in older adults.

Falls

It is estimated that one-third of community-dwelling adults aged 65 years or older fall at least once annually.² Falls can occur for a variety of reasons in older adults, but diabetes presents as an important risk factor. Microvascular complications related to diabetic neuropathy can contribute to decreased sensation in the feet, thereby increasing the risk of falls. Peripheral neuropathy is present in about 50%-70% of older adults with diabetes, increasing risks associated with postural instability and emphasizing more challenges associated with balance and muscle atrophy.² Overtreatment of diabetes can lead to unrecognized hypoglycemia, causing patients to feel more unsteady on their feet. Physical therapy in high fall-risk patients or patients who have recently experienced a fall can help minimize future falls. The longitudinal data from the Health, Aging and Body Composition study does imply that a heightened focus on diabetes-related complications, as noted above, has led to fall reduction.¹⁶

Mood

Mental health plays a role in every aspect of diabetes therapy, from self-care/effective lifestyle habits to taking medications correctly. It is estimated that about 14% of adults over the age of 55 have depression.¹⁷ People with diabetes typically have a higher prevalence of depression than non-diabetics, 32% vs. 16%.^{17,18} Given the higher incidence, the American Geriatric Society (AGS) recommends screening for depression within the first three months after initiation of diabetic treatment, utilizing tools such as the Geriatric Depression Scale.¹⁸ Many factors play a role in this increase in depression in older adults, but can also be mistaken for other geriatric conditions (e.g. fatigue, anemia) without a thoughtful assessment of mood symptoms. It is also thought that there is a bidirectional relationship between both major depressive disorder and diabetes.¹⁷ Poor mood or depressive symptoms can significantly impact other comorbidities, including

diabetes. Patients with poor mood may be apathetic in their approach to their health, and adherence to medications and healthy nutrition habits may decline. Studies have also found that improved blood sugars mitigate depressive symptoms and strengthen the desire for active self-care.¹⁹ Because of the impact that depression has on self-care, the ADA guidelines recommend providing psychosocial care to all people with diabetes and screening people 65 years and older for depression.⁴ Additionally, the American Geriatric Society (AGS) strongly recommends depression screening within the first three months after a new diabetes diagnosis, and treatment within two weeks of depression presentation. Re-evaluation should be completed every six weeks until depression is managed.²⁰

Cognitive Impairment

Cognitive impairment is a common syndrome in older adults for a variety of reasons. Medication-induced impairment, a dementia diagnosis, depression, vitamin deficiencies, and substance use can all be contributors to cognitive impairment. Mild cognitive impairment or mild dementia occurs in 10%-20% of older adults; 50% of these patients will progress into a diagnosis of dementia within five years, but it is estimated that 20%-30%

of these patients will return to normal cognitive functioning if risk factors are mitigated.²¹ It is also thought that patients with diabetes are twice as likely to develop cognitive impairment than non-diabetic patients.²² Unrecognized hypoglycemia can present as cognitive impairment; it is sometimes even misdiagnosed as delirium. Patients impacted by varying levels of cognitive impairment can present significant challenges for managing their diabetes. Safety with use of medications, especially insulin, should be a serious consideration in selection of agent and ongoing assessments for appropriateness of current treatments. Patients with cognitive impairment may forget to take their medications, accidentally take additional doses of medications, take different prescribed doses of medications/insulin, or refuse medications altogether. Medication simplification and eliciting assistance from caregivers/family members or visiting nurse services may become critical to successful outcomes for these patients. Safe use of insulin should be considered, especially with the shorter-acting varieties that are associated with higher rates of hypoglycemia events. Some patients with cognitive impairment forget to eat meals or do not take medications with meals, which can lead to a significant safety concern regarding hypoglycemia issues

as well. In these patients, avoiding agents such as bolus insulin and sulfonylureas is considered safe practice.¹

Hypoglycemia Unawareness

As we age, the counterregulatory responses to hypoglycemia, (e.g., sweating, palpitations, tremors) may decrease, impairing hypoglycemia symptoms.²³ Use of insulin continues to be a major contributor for hypoglycemia episodes in older adults, and other medications, such as beta-blockers, might mask some of the symptoms. The use of insulin is unavoidable for certain patients. In these situations, developing strategies to minimize risk, such as keeping the A1c above 6.5%, is recommended by the ADA.⁴ The newer treatment options, GLP-1 RA and sodium glucose co-transporter 2 (SGLT2i), have allowed for use of non-insulin therapies to treat diabetes with better efficacy and safety in the older adult population. Close monitoring of renal function is imperative, as several agents are renally cleared and will require dose adjustments based on renal function (e.g., sulfonylureas [SUs], SGLT2i, metformin). Severe hypoglycemia has been linked to an increased risk of dementia and, consequently, patients suffering with cognitive impairment experience hypoglycemia at a higher rate.²³

TABLE 3. Newer Treatment Considerations¹⁸

Medication Class	Pros	Cons
DPP-IVi	Used as monotherapy or combination therapy to lower A1c Minimal risk of hypoglycemia Weight Neutral	Avoid in heart failure Renal Adjustments
GLP-1 RA	ASCVD benefits >1% A1c lower potential Weight Loss Negligible risk of hypoglycemia Visiting nurse weekly administration possibility No renal dose adjustments Used as monotherapy or add on therapy	Weight loss Injectable High cost Gastrointestinal side effects Adherence may be impacted with once weekly formulation (pro/con)
SGLT2i	ASCVD benefits Renal benefits A1c lower potential Lower risk of hypoglycemia Weight loss	May worsen urinary incontinence leading to skin integrity issues and social isolation Increase risk of Urinary tract infections Renal dose adjustments Hypovolemia concerns Postural hypotension because of hypovolemia High Cost

ASCVD - Atherosclerotic Cardiovascular Disease; DPP-IVi - dipeptidyl peptidase; GLP-1 RA - glucagon-like peptide 1 receptor agonist ; SGLT2i - Sodium/glucose cotransporter-2 inhibitors

TABLE 4. Medication Dose Adjustments and Considerations⁴

Medication Name	Therapeutic Dose	Renal Dose Adjustments				Expected A1c Reduction	Effect on Blood Glucose	Caveats/Things to Consider
		Guideline	Do not initiate	Do not use	Max dose			
Metformin	2000 mg daily	AGS	Max dose of 1000 mg per day if eGFR is 30 - 60 mL/min/1.73m ²			1 - 2%	Fasting & Basal	<ul style="list-style-type: none"> Older adults may develop diarrhea, from metformin, even if they have tolerated it for years. Vitamin B12 deficiency secondary to metformin us, may lead to worsened neuropathy symptoms.
		AACE/ACE	eGFR < 45 mL/min/1.73m ²	eGFR < 30 mL/min/1.73m ²	500 mg BID if eGFR is between 30-45 mL/min/1.73m ²			
Sulfonylureas (SUs)								
Glipizide (IR and ER)	2.5 mg daily up to 20 mg daily	eGFR ≥ 50 mL/min/1.73m ²	eGFR ≥ 10 - 49 mL/min/1.73m ²	eGFR < 10 mL/min/1.73m ²	1 - 2%	Post prandial		Should be taken 15-30 minutes prior to eating a meal. This may be difficult for the older adult to accomplish, especially if they use a medication box.
		No dose adjustment warranted	Initial 2.5 mg daily. May increase to 20 mg daily, cautiously	Avoid if possible. If necessary, initial 2.5 mg daily and may cautiously increase to 20 mg daily				The 2019 Beer's Criteria by the AGS put forth a strong recommendation to avoid use in older adults.
Glyburide	Conventional Tablets: 2.5 mg up to 20 mg daily	No dose adjustments warranted. However, glyburide is typically avoided in chronic kidney disease. Glipizide is the preferred agent, if sulfonylurea therapy is necessary.			1 - 2%			The 2019 Beer's Criteria by the AGS put forth a strong recommendation to avoid use in older adults.
	Micronized Tablets: 1.5 mg up to 12 mg daily							
Glimepiride	1 mg daily up to 8 mg daily	Initial of 1 mg daily; dose titration and maintenance dosing should be conservative to avoid hypoglycemia. Alternate therapy should be considered if eGFR < 15 mL/min/1.73m ²			1 - 2%			
Thiazolidinedione (TZD)								
Pioglitazone	15 mg daily up to 45 mg daily	No dose adjustments warranted. May use in HD and PD without adjustment, as well.			0.5 - 1.4%	Fasting & Basal		<ul style="list-style-type: none"> Weight gain and peripheral edema typically occur with 30 mg doses or higher. It is not recommended to use more than 30 mg daily with insulin therapy.
Dipeptidyl Peptidase IV inhibitors (DPP-IVis)								
Alogliptin	25 mg daily	CrCL ≥ 60 mL/min	CrCL ≥ 30 - 59 mL/min	CrCL ≥ 15 - 30 mL/min	CrCL < 15 mL/min or HD	0.6%		
		No dose adjustment warranted	12.5 mg daily	6.25 mg daily	6.25 mg daily			
Linagliptin	5 mg daily	No dose adjustments warranted and can use in dialysis (HD & PD)				0.4%		
Saxagliptin	5 mg daily	eGFR ≥ 45 mL/min/1.73m ²	eGFR < 45 mL/min/1.73m ²	Dialysis		0.4 - 0.5%	Post Prandial	
		No dose adjustments warranted	2.5 mg daily	HD: use 2.5 mg daily and administer post-dialysis PD: not studied				
Sitagliptin	100 mg daily	eGFR ≥ 45 mL/min/1.73m ²	eGFR ≥ 30 - 44 mL/min/1.73m ²	eGFR < 30 mL/min/1.73m ²	Dialysis	0.5 - 0.8%		
		No dose adjustments warranted	50 mg daily	25 mg daily	HD: 25 mg daily PD: 25 mg daily			

TABLE 4. Medication Dose Adjustments and Considerations Cont.⁴

Medication Name	Therapeutic Dose	Renal Dose Adjustments			Expected A1c Reduction	Effect on Blood Glucose	Caveats/Things to Consider
Sodium Glucose co-Transporter 2 inhibitors (SGLT2is)							
Canagliflozin	100 mg daily up to 300 mg daily	eGFR ≥ 60 mL/min/1.73m ²	eGFR 45-59 mL/min/1.73m ²	eGFR 30-44 mL/min/1.73m ²	0.7 – 1%	Post Prandial	<ul style="list-style-type: none"> The black box warning regarding leg/foot amputation has been removed
		No dose adjustments warranted	100 mg daily	100 mg daily			
Dapagliflozin	5 mg daily up to 10 mg daily	eGFR ≥ 45 mL/min/1.73m ²		eGFR 30-44 mL/min/1.73m ²	0.7 – 1%		Post Prandial
		No dose adjustments warranted		Manufacturer recommends against use		Use is contraindicated	
Empagliflozin	10 mg daily up to 25 mg daily	eGFR ≥ 30 mL/min/1.73m ²		eGFR < 30 mL/min/1.73m ²	0.7 – 1%	Post Prandial	
		No dose adjustments warranted		Manufacturer recommends against use*			Dialysis Use is contraindicated in HD and PD
Glucagon Like Peptide-1 Receptor Agonists (GLP-1 RAs)							
Albiglutide	30 mg once weekly up to 50 mg once weekly	No dose adjustments warranted. No recommendations provided when eGFR < 15 mL/min/1.73m ² .			0.6 – 1.3%	Fasting & Post Prandial	<ul style="list-style-type: none"> The pen contains a diluent and a powder, which need to be mixed 15-30 minutes prior to injection of 30 mg and 50 mg doses, respectively
Dulaglutide	0.75 mg once weekly up to 4.5 mg once weekly	No dose adjustments warranted.			0.7 – 0.9%		<ul style="list-style-type: none"> The needle is housed within the pen device, lessening the number of steps required for the injection. The pen device only has 1 dose option thus limits concern about administering the incorrect dose. Good option for those with poor dexterity and low/poor vision.
Exenatide	IR: 5 mcg BID and may increase to 10 mcg BID ER: 2 mg once weekly	CrCL ≥ 30 mL/min	CrCL < 30 mL/min	ESRD	1 %	Fasting & Post Prandial	<ul style="list-style-type: none"> Daily injection Requires a titration schedule of 0.6 mg daily for 7 days then increase to 1.2 mg daily. May increase to max dose of 1.8 mg daily, if needed/tolerated
		No dose adjustments warranted. Use with caution when titrating dose if CrCL is between 30 – 59 mL/min		Use is not recommended.			
eGFR ≥ 45 mL/min/1.73m ²	eGFR < 45 mL/min/1.73m ²	ESRD					
No dose adjustments warranted.		Use is not recommended.	Use is not recommended.				
Liraglutide	1.2 mg daily up to 1.8 mg daily	No dose adjustments warranted. Use with caution in HD and PD.			1 %	Fasting & Post Prandial	<ul style="list-style-type: none"> Daily injection Requires a titration schedule of 0.6 mg daily for 7 days then increase to 1.2 mg daily. May increase to max dose of 1.8 mg daily, if needed/tolerated
Semaglutide	0.5 g once weekly up to 1 mg once weekly	No dose adjustments warranted.			1.3– 1.8%		<ul style="list-style-type: none"> Weekly injection Requires a titration schedule of 0.25 mg weekly for 4 weeks then increase to 0.5 mg weekly. May increase to 1 mg weekly after 4 weeks on 0.5 mg, if needed and tolerated Most potent in class

*In patients established on empagliflozin, some experts continue to use empagliflozin 10 mg daily in patients with eGFR < 30 mL/min/1.73m² off-label
 AACE/ACE - American Association of Clinical Endocrinologists/American College of Endocrinology; AGS - American Gem Society; BID - Twice a day; CrCl - Creatinine Clearance; eGFR - Estimated glomerular filtration rate; ER - Extended release; ESRD - End-Stage Renal Disease; HD - hemodialysis; HF - Heart failure; IR - Immediate release; PD - Peritoneal dialysis

Functional Impairments

Aspects of a patient's executive functioning may decline because of aging, cognitive changes, and change in social supports. This can greatly impact how patients are able to appropriately manage their medications (e.g., non-adherence or inappropriate dosing). Cooking and shopping for food may be limited based on food insecurities as previously discussed. Team-based approaches to care are key to addressing many of these functional or social issues that are common for older adults.²² Older adults are at higher risk for malnutrition due to factors such as anorexia, altered taste and smell, swallowing difficulties, and dental complications.¹³ Patients having difficulty in meal preparation may require assistance from a dietician, choosing pre-packaged meals that meet their functional abilities and nutritional and energy needs. Difficulty in meal preparation also leads to erratic meal schedules, which can lead to either hyperglycemia or hypoglycemia. Alternatively, patients may be unable to get to the store, or finances may be prohibitive, which limits food access altogether. As a result, unintentional weight loss due to not eating appropriately may lead to hypoglycemia, especially if unnecessary medications are continued after this weight loss occurs or if unintentional weight loss is not detected. Nutritional screening assessments exist to screen for food insecurities and can assist with determining when referral to a dietician is warranted.¹² Addressing functional impairments through additional assistance in the home (e.g. visiting nurse services, meals on wheels, senior centers, family and friends, etc.) can significantly improve outcomes for these diabetic patients.²³

Therapeutic Approach and Risk Reduction

Unfortunately, despite the high prevalence of diabetes in older adults, there is a limited presence of this patient population in clinical trials.²² In this article, we draw from four main clinical trials: the UK Prospective Diabetes Study (UKPDS); Action to Control Cardiovascular Risk in Diabetes (ACCORD); Action in Diabetes

and Vascular Disease: Preterax and Diabetes Controlled Evaluation (ADVANCE); and Veterans Affairs Diabetes Trial (VADT).²⁴⁻²⁷ These trials suggest that the legacy effect of tightly controlled blood glucose early in diagnosis prevents microvascular and macrovascular events from occurring. However, later in the disease process, tightly controlled blood sugars significantly increase the risk of severe hypoglycemia. These trials help direct therapy, but the lack of empirical evidence leaves much of the treatment guidance left to expert opinion for management.⁴ Treatment considerations should always include an assessment of the patient's comorbidities, functional status, atherosclerotic cardiovascular disease (ASCVD) risk, goals of care, and hypoglycemia risk. Using this information, goal setting should include establishing individualized A1c and blood glucose goals. Thoughtful consideration should be applied to insulin delivery devices, and how often patients should monitor blood glucose.

As described earlier, shared decision making about medication and life-style therapy is the gold standard in caring for older adults. This process also applies to setting patient-specific blood glucose goals. Given the homogeneity of the population, one level/goal does not apply to all patients. The 2021 American Diabetes Association (ADA) Standards of Care recommend less stringent goals for patients who have higher risk of hypoglycemia, shorter life expectancy, established vascular complications, patient preferences such as not using injections or preferring not to check blood sugars, and poor social support systems in place.⁴ Many older adults have one or more of these factors. The Standards of Care provide further clarification for older adults based on the number of comorbidities, categorizing patients into three groups: Healthy Adults, Complex/Intermediate, and Very Complex/Poor Health. Blood glucose and A1c goals become less stringent with advancement through the groups to help protect against hypoglycemia.⁴ All categories should maintain an A1c over 6.5% to decrease risk of hypoglycemia, potential negative cardiac outcomes, and falls.⁴ Healthy adults over the age of 65 with few comorbidities or functional limitations and no cognitive impairment should have tighter blood

glucose goals with an A1c goal of less than or equal to 7.5%. The Complex/Intermediate group is defined as having multiple comorbidities, 2+ activities of daily living (ADL) impairments, and mild to moderate dementia. This Intermediate group's A1c goal is less than or equal to 8%. The Very Complex/Poor Health group is defined as living in a long-term care facility, moderate to severe dementia, greater than 2 ADL impairments, and/or end-stage chronic illness. The A1c goal in this group is less than 8.5%. These goals can be found in table format, along with blood pressure, aspirin, and statin therapy goals outlined by the ADA in Table 2.⁴ All aspects of the treatment plan should be reviewed by the health care team with the patient and family, if indicated.

The 2021 ADA guidelines include specific recommendations for medication therapy following lifestyle modifications and metformin.⁴ The ADA recommends considering indicators of high risk or established ASCVD, chronic kidney disease (CKD) or heart failure (HF) and then utilizing GLP-1 RA if patients have predominating cardiovascular disease, and SGLT2i when heart failure or nephropathy predominates. If there are no indicators of high risk or established ASCVD, CKD, or heart failure, and a compelling indication to minimize hypoglycemia, consider alternative agents such as DPP-IVi or TZD. If there is a goal to minimize weight gain or promote weight loss, consider GLP-1 RA or SGLT2i agents. Finally, if cost is a major issue and there is no concern for hypoglycemia, consider using a preferred SU in older adults. If patients have significant renal disease or a history of pancreatitis, limit use of oral agents or GLP-1 RA and consider utilizing basal insulin. Special consideration to the newer agents as they pertain to older adults can be found in Table 3.

The patient's therapy goals, and treatment considerations, should be continually reassessed, yearly if stable, or every six months or as needed if therapy or condition changes occur.^{3,20} When choosing a medication to initiate or transition to or from, it is important in our older adult population to consider the agent's potential for hypoglycemia, especially as renal function declines. Generally, in the older

adult population, it is best to avoid the use of SUs due to their risk for hypoglycemia and appearance on the Beer's List.^{4,23} Additional hypoglycemia risk-reduction strategies include: avoiding sliding scale insulin due to risk for error; limiting prandial insulin use as much as possible to minimize risk for using incorrect amounts, or using the incorrect (longer-acting) insulin; reviewing other concurrent medications for possible additive effects; and ensuring adequate nutrition. Insulin degludec may be appropriate if nocturnal hypoglycemia is an issue and the therapy is acceptable and affordable to the patient.²⁹

Medication Therapy

Overview

Metformin

Metformin is the preferred first-line agent, along with lifestyle modifications, according to ADA and AGS.^{4,20} Additionally, it has established cardiovascular and mortality benefits important to many older adults. Studies have found that metformin can safely be used to an estimated Glomerular Filtration Rate (eGFR) of greater than or equal to 30. It should not be used with severe renal failure; caution should be used with hepatic impairment and heart failure, due to increased risk of lactic acidosis. Important side effects to consider in our older adult population are weight loss, anorexia, and diarrhea. Consideration to change metformin from the immediate release formulation to the sustained action formulation is a minor but impactful change, even if patients have tolerated the immediate release formulation previously; as the body changes and dietary intake diminishes, gastrointestinal (GI) upset and diarrhea can develop.⁴

Sodium Glucose co-Transporter 2 Inhibitors (SGLT2i)

According to the ADA, these are the preferred second-line agents for those with ASCVD risk factors ([ASCVD Risk Calculator](#)), established CKD, or HF, given the established cardiovascular and renal benefits.⁴ It should be noted that as eGFR declines, there is demonstrated lower glycemic benefit with use of these agents. Side effects may limit use in older adults

and include weight loss, genitourinary infections, polyuria, dehydration, urinary tract infections, and decreased blood pressure, which can increase the risk of falls.⁴ Of special note, while weight loss may be beneficial for some, it may not be in older adults. Special monitoring of fluid status and adjustment of other medications, such as diuretics and hypertension medications, should be considered. Cost may also be a prohibitive factor in initiation for these medications.⁴

Glucagon-like Peptide Receptor Agonists (GLP-1 RA)

Along with SGLT-2is, GLP-1 RA are considered second line for those with ASCVD risk factors, or established ASCVD. The GLP-1 RA have established cardiovascular event rate reduction and mortality in patients with established cardiovascular disease. No dose adjustments are warranted for the older adult population or for patients with renal impairment. Side effects to consider are weight loss, nausea, vomiting, diarrhea, and reduced appetite. Reduced appetite, in the setting of older adults, should be monitored closely to avoid other complications with excessive weight loss. As an example, poor oral intake can also lead to unintended dehydration leading to falls and potentially acute kidney injury.⁴

Dipeptidyl Peptidase IV inhibitors (DPP-IVi)

According to the ADA, DPP-IVi is a preferred second-line medication class if there is no established CKD or HF, and if there is compelling need to minimize hypoglycemia. Alogliptin, saxagliptin and sitagliptin are dosed based on renal function, while linagliptin does not require dose adjustments though should be used with caution when eGFR is less than 15 mL/min. Alogliptin and sitagliptin may be used when eGFR is less than 15 mL/min and/or in end stage renal disease requiring dialysis. Saxagliptin should be avoided when eGFR is less than 15 mL/min. These medications should be avoided in patients with a history of or recurrent pancreatitis and, in general, avoided in patients with HF.⁴ Side effects include nasopharyngitis and headache. These agents are beneficial for postprandial hyperglycemia control

with low risk for hypoglycemia. Until generics become available, cost may be a barrier for use.⁴

Thiazolidinediones (TZD)

According to the ADA, TZDs are a preferred second-line medication class if there is no established CKD or HF, if there is compelling need to minimize hypoglycemia, or if cost is a major issue. TZDs may be used with older adults but have significant considerations in this population, including risk of worsening HF, osteoporosis, falls or fracture, and macular edema.⁴ There are no dose modifications needed for renal impairment. TZDs should be avoided in patients with HF and with a history of bladder cancer. Side effects include peripheral edema, upper respiratory tract infections, headache, and weight gain. These agents may lower serum triglycerides and provide basal control with low risk for hypoglycemia.⁴

Sulfonylureas (SU)

The ADA notes that SUs may be used as a second-line medication class if cost is a major concern. Sulfonylureas, and other insulin secretagogues, are associated with hypoglycemia and should be avoided, if possible. Glyburide appears on the Beer's List due to its long half-life resulting in hypoglycemia risk.²⁸ However, should patients have difficulty paying for medications, SUs may be the best option due to the low cost. In these situations, shorter acting agents, such as glipizide, are preferred.⁴ Side effects include hypoglycemia, nausea, and weight gain.

Insulin

The ADA recommends deintensification of complex insulin regimens to prevent hypoglycemia and polypharmacy.⁴ The SIMPLE study shows that insulin regimen simplification can reduce risk of hypoglycemia without compromising glycemic control.³⁰ In the older adult population, consider reducing or discontinuing prandial insulin while continuing and titrating basal insulin as needed. If using a premixed insulin, consider using 70% of the total daily dose as a basal dose, administered in the morning, only to minimize risk of nocturnal hypoglycemia.³⁰ If possible, the

initiation of GLP-1 RA or SGLT2i could be considered in this patient population with the goal to de-escalate or discontinue insulin therapy.⁴ Use of premixed insulin may have a role in those patients who maintain predictable eating schedules.²² The use of U-200 and U-500 should be used cautiously in this vulnerable patient population due to the high concentration and higher risk of hypoglycemia with inappropriate use. Unfortunately, insulin resistance becomes more common in older adults and may require higher insulin doses. In these situations, the use of U-200 and U-500 insulins may be appropriate if the patient is cognitively intact and has appropriate social support systems to monitor their wellbeing. U-200 and U-500 insulin types do come in insulin pens that can further help reduce risk of dosing errors that can be seen with use of U-500 insulin vial and syringe dosing.³¹ However, the overarching goal with older adults is de-intensification of insulin whenever possible to avoid hypoglycemia.^{4,20} The 2021 ADA Standards of Care have provided strategies for clinicians to de-intensify insulin which can be found in Table 4.⁴

Summary

In conclusion, older adults with T2DM are a heterogeneous population with varied needs. Shared decision-making discussions among the patient, family/caregivers, and the healthcare team focusing on enhancing quality of life are essential and considered the gold standard. Older adult considerations should be considered when developing goals of care for these patients to ensure that the most effective and safest treatment course is selected. Metformin, plus lifestyle interventions, remains the first-line therapy due to its known effectiveness in controlling diabetes and carrying a very low risk of hypoglycemia. Newer agents, GLP-1 RA and SGLT2i, should be considered as second-line treatment options based on renal function, ASCVD risk, and demonstrated safety with a lower hypoglycemia risk profile. These newer agents should also be considered as replacements for insulin to further minimize risks associated with insulin use. Therapeutic decisions for older adults with T2DM include several important factors, highlighting the importance of

reviewing patients' social determinants of health, evidence-based medicine approaches, geriatric-related syndromes, and recent guidelines, with an emphasis on risk reduction, and patients' preferences. Treatment of older adults living with T2DM continues to be an evolving area with newer, safer therapies coming to the market over the last decade, patient goals of therapy changing over time, and a shared decision-making approach to care. Caring for these individuals requires a comprehensive approach to care, utilizing an interdisciplinary team approach that can be extremely rewarding for pharmacists in all types of care settings.

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Assessment Questions

1. It is estimated that 14.3 million adults over the age of 65 years old are living with T2DM. This is predicted to increase to 26.7 million by the year 2050. What issues does living longer with T2DM have for the patient and provider?
 - a. Medications may have more side effects due to changes in physiology
 - b. Blood glucose goals may need to be adjusted to decrease risk of hypoglycemia
 - c. Providers will need to include caregivers and family members in treatment plans.
 - d. All of the above
2. **True or False:** Social determinants of health should be reviewed in clinic and taken into consideration with treatment plans.
 - a. True
 - b. False
3. A provider sets a new A1c goal of <7% for a 90-year-old patient with advanced dementia, heart failure, and a history of falls. The patient currently lives in an assisted living facility. The current A1c is 8.3%. What might be your next step(s) as the pharmacist working on with this patient?
 - a. Discuss concerns over the potential for hypoglycemia with lower A1c goals with the health care team.
 - b. Review social determinants of health including, but not limited to, access to clinic appointments, living situation, social support, and functional abilities of the patient.
 - c. Increase the patient's medication doses and add medication as needed to achieve the A1c goal set by the provider.
 - d. All of the above
 - e. A and B
4. Symptoms of hyperglycemia in older adults can be overlooked due to the following potential co-conditions:
 - a. BPH
 - b. Peripheral vascular issues
 - c. Cognitive changes
 - d. All of the above
5. Multiple professional associations have published dosing guidance on metformin. According to the American Geriatrics Society (AGS) they recommend a maximum of ___ dose if the eGFR is between 30-60 mL/min/1.73m²:
 - a. 500 mg BID
 - b. 1500 mg daily
 - c. 500 mg daily
 - d. 1000 mg BID
6. There are many glucagon-like peptide 1 receptor agonist (GLP-1 RA) medications on the market with various delivery systems. Which GLP-1 RA agent may be the most user friendly, for an older adult with dexterity concerns?
 - a. Albiglutide
 - b. Dulaglutide
 - c. Liraglutide
 - d. Semaglutide
7. Mr. S is a 74-year-old gentleman with past medical history of T2DM, CHF, mild cognitive impairment and depression. His diabetes is complicated by albuminuria and peripheral neuropathy. Currently, Mr. S is on metformin 500 mg BID and alogliptin 25 mg daily. Unfortunately, Mr. S's A1c increased to 9.2%. After discussing Mr. S's goals of care, it was determined that he would like to achieve an A1c goal of < 8.5% and minimize his risk for hyper- or hypoglycemia symptoms. Which medication therapy would be the most appropriate next step for Mr. S?
 - a. No changes
 - b. Add glyburide
 - c. Add empagliflozin
 - d. Add insulin glargine

An 85yo male presents to your pharmacy and appears more confused and disoriented than normal baseline when picking up his monthly prescriptions for glipizide, lisinopril and amlodipine. His past medical history includes: DM2, CAD, HTN, CKD stage 3, BPH, and history of falls.
8. Based on his presentation what would be your next differential to consider for this patient:
 - a. Assess recent use of anticholinergics that may be impacting cognition.
 - b. Obtain consent from patient to contact PCP to provide suggestions to conduct a brief cognitive screen.
 - c. See if patient has a home blood glucometer to check blood glucose while in your pharmacy to assess potential for hypoglycemia.
 - d. Make sure patient uses his cane when coming into the pharmacy to minimize fall risk.

Further review of patient's record. Full list of medications include:
 Lisinopril 10mg daily
 Aspirin 81mg daily
 Glipizide 10mg BID
 Amlodipine 5mg daily
 Calcium/Vitamin D 1 tablet BID
 Tamsulosin 0.4mg daily

Labs:
 A1c: 8.2%
 SCr: 1.4mg/dL (EGFR: 32mL/min)
 Vit D: 38ng/mL
 BP: 138/69
9. Upon further discussion with patient, he reports that his wife has recently moved into a SNF and he isn't eating as well as he had before since she primarily cooked meals for him. He does tell you that

his daughter is able to check in on him weekly and assist in filling his med box that wife used to assist with. He has had some home blood sugars ranging from 60-80 recently and some elevated readings >200 post meals. Patient has insurance to cover medication costs. What might be a recommendation to make to the patient's PCP?

- Discontinue glipizide, initiate metformin 500mg daily and increase to 500mg BID after 7 days as tolerated
 - Discontinue glipizide, start semaglutide 0.25mg once weekly
 - Discontinue glipizide, start empagliflozin 12.5mg daily
 - Provide patient with contact for meals on wheels service in the community
10. Did the activity meet the stated learning objectives? (if you answer no, please

email sarahs@pswi.org to explain)

- Yes
 - No
- On a scale of 1 – 10 (1-no impact; 10-strong impact), please rate how this program will impact the medication therapy management outcomes or safety of your patients.
 - On a scale of 1 – 10 (1-did not enhance; 10-greatly enhanced), please rate how this program enhanced your competence in the clinical areas covered.
 - On a scale of 1 – 10 (1-did not help; 10-great help), please rate how this program helped to build your management and leadership skills.
 - How useful was the educational material?
 - Very useful
 - Somewhat useful
 - Not useful

- How effective were the learning methods used for this activity?
 - Very effective
 - Somewhat effective
 - Not effective
- Learning assessment questions were appropriate.
 - Yes
 - No
- Were the authors free from bias?
 - Yes
 - No
- If you answered “no” to question 18, please comment (email info@pswi.org).
- Please indicate the amount of time it took you to read the article and complete the assessment questions.

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Quiz Answer Form

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- | | |
|----------------------|---------------|
| 1) a b c d | 11) _____ |
| 2) a b | 12) _____ |
| 3) a b c d e | 13) _____ |
| 4) a b c d | 14) a b c |
| 5) a b c d | 15) a b c |
| 6) a b c d | 16) a b |
| 7) a b c d | 17) a b |
| 8) a b c d | 18) _____ |
| 9) a b c d | 19) _____ |
| 10) a b | |

May/June 2021

Continuing Education Diabetes Treatment
in the Older Adult

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