MedStar Health

Management of Adult Diabetes Mellitus

Clinical Practice Guideline
MedStar Health

"*These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but should be used with the clear understanding that continued research may result in new knowledge and recommendations".*

This clinical practice guideline is based on *Standards of Care in Diabetes-2023* found in Diabetes Care Volume 46, Supplement 1, January 2023. MedStar Health Ambulatory Best Practices Committee endorses this guideline. https://professional.diabetes.org/content-page/practice-guidelines-resources

Introduction

The prevalence of diabetes in adults is estimated to be 14.7 percent of the United States adult population. Some estimates report that more health care resources are spent on diabetes than any other health condition. In addition to the economic impact, medical complications from diabetes impact quality of life**.**

General Principles

Hyperglycemia is the pathognomonic feature of all forms of diabetes. Treatment aimed at lowering blood glucose levels is mandated by the following proven benefits:

1. The danger of acute decompensation due to diabetic ketoacidosis or hyperosmolar hyperglycemic non-ketotic syndrome with their accompanying morbidity and mortality is markedly reduced.
2. The risk of blurred vision, polyuria, polydipsia, fatigue, weight loss with polyphagia, vaginitis or balanitis, days missed from work, emergency room visits, and hospital admissions may be reduced.
3. The risks of development or progression of diabetic retinopathy, nephropathy, and neuropathy are all greatly decreased. These complications may even be prevented by early normalization of metabolic status.
4. Targeted blood glucose control has been demonstrated to be associated with a less atherogenic lipid profile and fewer macrovascular events.

Strategies for Improving Care from the ADA Guideline

Recommendations

- A patient-centered communication style that incorporates individualized preferences, assesses literacy and numeracy, and addresses cultural barriers to care should be used.
- Referral to Diabetes self-management education and support (DSMES) and medical nutrition therapy (MNT) is recommended at four critical times: at the initial diagnosis of diabetes; annually and/or when the patient does not meet treatment targets; when factors that may affect self-management develop (such as pregnancy, ESRD, advancing age); and when transitions in life and care occur.

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date: May 2023**	**Next Scheduled Review Date:**
3/ 2011, 7/ 2013, 3/2014, 5/ 2015, 5/ 2016, 5/ 2017. 5/2018, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023	© Copyright MedStar Health, 2012	May 2024 Ambulatory Best Practice Condition: Diabetes Mellitus

- Treatment decisions should be founded on evidence-based guidelines that are tailored to individual patient preferences, prognoses, and comorbidities.
- Care should be aligned with components of the Chronic Care Model (CCM) to ensure productive interactions between a prepared proactive practice team and an informed patient. The CCM emphasizes patient-centered team care and ongoing collaborative communication and goal setting among all the team members.
- Care systems should support team-based care, community involvement, patient registries and decision support tools to meet patient needs.
- Treatment programs include the following: self-monitoring of blood glucose (SMBG) using a fingerstick blood glucose monitoring device or a continuous glucose monitor (CGM), meal planning, physical activity, when and how to take medication(s) and their benefits and potential side effects, information on the prevention and treatment of hypoglycemia as well as other acute and chronic complications, sick day protocol, and when to call their doctor or go to the emergency department
- Address psychosocial issues in all aspects of care including self-management, mental health, language barriers, complications, comorbidities, food insecurity, housing stability, financial barriers, and life-stage considerations

CRITERIA FOR SCREENING FOR DIABETES/PREDIABETES IN AYSMPTOMATIC ADULTS

The primary purpose of a screening program is to identify individuals without symptoms who are likely to meet the diagnostic criteria for diabetes or prediabetes.

The ADA recommends the following:

- Testing should be considered for all adults of any age who are overweight or obese (BMI $\geq$25 kg/m^{2,} BMI $\geq$ 23 kg/m$^{2\ for}$ Asian Americans) and have one or more additional risk factors listed below. *
    - First degree relative w/Diabetes Mellitus
    - African American, Native American, Latino, Asian American, Pacific Islander
    - Other clinical conditions associated with insulin resistance: severe obesity, acanthosis nigricans
    - History of cardiovascular disease
    - Polycystic Ovarian Disease
    - HDL cholesterol level<35 mg/dL (0.90mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
    - Hypertension $\geq$ 130/80 mmHg or on therapy for HTN
    - Physical inactivity

- Women who were diagnosed with gestational diabetes should have lifelong testing at least every three years.
- Patients with previous A1C $\geq$ 5.7%, Impaired Glucose Tolerance (IGT) or Impaired Fasting Glucose (IFG) (i.e., prediabetes) on previous testing should have yearly testing
- Screening for all other individuals should begin at age 35. *
- HIV patients should have screening with fasting serum glucose prior to initiating antiretroviral treatment and 3-6 months after starting or changing antiretrovirals. If initial screen is normal, fasting serum glucose should be done yearly.

* *If results are normal repeat testing should be performed at least every 3 years with consideration of more frequent testing depending on initial results and risk status.*

In addition to the above criteria, the ADA now states that clinicians may use an assessment tool, such as the ADA risk test (https://www.diabetes.org/risk-test) , to assist in determining if diagnostic testing for prediabetes/diabetes should be performed. The website is designed for non-medical persons to "Take the Risk Test" themselves. It asks age, sex, family history of diabetes, personal history of gestational diabetes, h/o HTN, physical activity, height, and weight. Based on these answers a score is given. A score of 5 or higher indicates the person is at increased risk for having type 2 diabetes.

The USPSTF recommends screening adults who are overweight or obese and who are between 35 and 70 years of age (https://uspreventiveservicestaskforce.org/uspstf/recommendation/screening-for-prediabetes-and-type-2-diabetes)

CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS AND PREDIABETES

Several ways to diagnose diabetes are possible.

	A1C[#]	Fasting Plasma Glucose (FPG)	Oral Glucose Tolerance Test (OGTT)[+]	Random Plasma Glucose (RPG)
Diabetes	A1C ≥6.5 %* *(NGSP certified lab)*	FPG ≥126 mg/dl (7.0 mmol/l)***** *(Fasting is defined as no caloric intake for at least 8 hrs.)*	Two-hour 75gm OGTT: plasma glucose (2hPG) ≥200 mg/dl* *(glucose load containing the equivalent of 75g anhydrous glucose dissolved in water)*	RPG: ≥ 200 mg/dl (11.1mmol/1) plus symptoms of hyperglycemia
Pre-diabetes**	A1C 5.7-6.4%	IFG=FPG 100 -≤125 mg/dl	IGT = 2hr PG on the 75gm OGTT: 140-199 mg/dl.	N/A
Normal	<5.6%	FPG <100 mg/dl	2h PG <140 mg/dl	N/A

***** In the absence of unequivocal hyperglycemia diagnosis of diabetes requires two abnormal test results from the same sample (i.e., Fasting plasma glucose and A1C from the same sample) or from two separate samples. If both an A1C and fasting PG are obtained and only one test result meets diagnostic cut point for pre-diabetes, repeat just the test that was abnormal for confirmation of diagnosis.

******Increased risk for diabetes: risk is continuous, extending below the lower limit of the tests range and becoming disproportionately greater at the higher ends of the range.

[#] Point of care A1c testing can be used for screening and diagnosis if restricted to FDA approved devices at labs by trained personnel

[+] There must be carbohydrate intake of at least 150g/day for 3 days prior to OGTT

For the diagnosis of type 2 diabetes A1C, FPG and OGTT are all equally appropriate. *In individuals with classic symptoms of hyperglycemia or hyperglycemic crisis a random plasma glucose ≥ 200mg/dL is sufficient to make the diagnosis of diabetes.*

If there are significant discrepancies between the A1C and plasma glucose, conditions that affect the A1C should be considered, these include conditions with increased red blood cell turnover (e.g., sickle cell disease, pregnancy ($2^{nd}/3^{rd}$ trimesters & post-partum period), HIV, G6PD deficiency, hemodialysis, recent blood loss or blood transfusion, erythropoietin use), in these situations only plasma glucose criteria can be used to diagnose diabetes.

PREDIABETES

Patients with a predisposition to diabetes (prediabetes) are individuals with impaired fasting glucose (IFG of 100/mg/dL (5.6mmol/L) to 125 mg/dL (6.9 mmol/L)), impaired glucose tolerance (IGT: 2-h PG in the 75-g OGTT 140 mg/dL (7.8mmol/L) to 199 mg/dL (11.0 mmol/L)) or an A1C of 5.7-6.4%.

- In systematic review of 44,203 individuals from 16 cohort studies with a follow-up interval averaging 5.6 years (range 2.8–12 years), those with A1C between 5.5% and 6.0% had a substantially increased risk of diabetes (5-year incidence from 9% to 25%). Those with an A1C range of 6.0–6.5% had a 5-year risk of developing diabetes between 25% and 50% and a relative risk 20 times higher compared with A1C of 5.0%.

Some pre-diabetes patients already have the characteristic microvascular changes associated with diabetes. Early identification of individuals with pre-diabetes will provide opportunities for lifestyle management and potentially prevent complications related to diabetes.

I. Screening:

Targeted screening for prediabetes is recommended for the populations at high risk for development of diabetes. (see "Criteria for Screening for Diabetes/Prediabetes in Asymptomatic Adults" section)

II. Treatment:

- Lifestyle modification is the fundamental treatment and should be reinforced at every visit
  ADA recommends referral to an intensive lifestyle intervention program modeled on the Diabetes Prevention Program
- Physical activity equivalent to at least 150 minutes (30 minutes on most days of the week) of moderate to vigorous intensityphysical activity per week such as walking. Resistance exercise consisting of 2-3 sessions per week on nonconsecutive days is also recommended. For older adults with diabetes flexibility and balance training 2-3 times per week is recommended. Breaking up sedentary time should also be encouraged as it is associated with moderately lower postprandial glucose levels.
- Weight loss equivalent to 7% of body weight, reducing caloric intake while maintaining a healthful eating pattern is recommended to promote and maintain weight loss.
- Limit or avoid intake of sugar-sweetened beverages (from any caloric sweetener including high-fructose corn syrup and sucrose) to reduce risk for weight gain and worsening of cardiometabolic risk profile. Individuals at high risk for type 2 diabetes should be encouraged to achieve the U.S. Department of Agriculture (USDA) recommendation for dietary fiber (14 g fiber/1,000 kcal) and foods containing whole grains (one-half of grain intake).
- According to the current *Standards of Care in Diabetes 2023,* Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially for those aged 25-59 years with BMI ≥35 kg/m2, higher fasting plasma glucose (e.g., ≥110mg/dL), higher A1C (e.g., ≥6.0%) and women with prior gestational diabetes. Long-term metformin use (more than 4 years) may be associated with vitamin B12 deficiency. Annual measurement of B12 levels is recommended.
  - Various other pharmacologic agents (e.g., α-glucosidase inhibitors, glucagon-like peptide 1 receptor agonists, thiazolidinediones, testosterone, insulin) have been evaluated for prevention of type 2 diabetes and have been shown to lower the incidence of diabetes in specific populations. No pharmacologic agent has been approved by the U.S. Food and Drug Administration for prevention of type 2 diabetes. The risk versus benefit of each medication must be weighed carefully, in addition to cost, side effects, and efficacy considerations. Metformin has the longest history of safety data as a pharmacologic therapy for prevention of diabetes.
- Monitoring for the development of diabetes in those with prediabetes should be performed every year.

- Screening and treatment of modifiable risk factors for CVD is suggested as prediabetes is associated with increased cardiovascular risk. Statins may increase the risk of developing type 2 diabetes, therefore if statins are used glucose should be regularly monitored. However, in people at high risk of developing type 2 diabetes it is not recommended that statins be discontinued.
- Tobacco cessation: evaluation for tobacco use and referral for tobacco cessation

Many hospitals and other community organizations offer diabetes prevention programs, education, and support groups. Medicare and Maryland Health Choice Medicaid plans cover diabetes prevention programs for individuals with prediabetics.

III. Goals of Management:
Individuals with prediabetes should have the same lipid and BP goals as those with diabetes. Pharmacotherapy may be considered for cardiovascular risk reduction, decreasing the progression of hyperglycemia and weight management in prediabetes. There is strong evidence that obesity management can delay the progression from prediabetes to type 2 diabetes.

Please see the MedStar Health Identification, Evaluation, and Treatment of Overweight and Obesity in Adults Clinical Practice Guideline

DIABETES

I. Classification (4 clinical classes classification criteria, 2022 American Diabetes Association)

- **Type 1 diabetes** (autoimmune *B*-cell destruction, usually leading to absolute insulin deficiency)
- **Type 2 diabetes** (results from a progressive insulin secretory defect on a background of insulin resistance)
- **Other specific types of diabetes** (due to other causes, e.g., genetic defects in *B*-cell function, genetic defects in insulin action, disease of the exocrine pancreas (pancreatitis, pancreatectomy, cystic fibrosis), drug or chemically induced (such as with glucocorticoid use in the treatment of HIV or after organ transplantation).
- **Gestational Diabetes Mellitus** (diagnosed during the second or third trimester of pregnancy that is not clearly overt diabetes prior to gestation)

II. Initial Comprehensive Diabetes Evaluation
Medical History and Physical Examination
See below table 4.1 copied from the 2023 Standards of Medical Care in Diabetes. Also, this section can be found at https://diabetesjournals.org/care/issue/46/Supplement_1

Laboratory/Other Evaluation

- A1C, if results not available within past 3 months
- If not performed/available within past year:
    - Fasting lipid profile, including total, LDL, HDL cholesterol and triglycerides
    - Liver function tests
    - Test for proteinuria with spot urine albumin-to-creatinine ratio
    - Serum creatinine and eGFR
    - TSH in type 1 diabetes, dyslipidemia, or women over age 50 years
- Consider serum testosterone in men with diabetes with signs/symptoms of hypogonadism

- Type 1 diabetes should be screened for celiac disease if they have gastrointestinal symptoms, signs, or other manifestations suggestive of celiac disease
- Vitamin B12 if on metformin
- Serum potassium if on ACE, ARB, diuretic
- Patients with type 2 diabetes or prediabetes withelevated LFTs or fatty liver on imaging should be evaluated for nonalcoholic steatohepatitis and liver fibrosis (see below in *V. Continuing Care* section for more information)

** Most payors provide coverage for Medical Nutritional Therapy (MNT) and/or Diabetes Self-Management Education and Support (DSMES) for diabetes patients with a provider referral/ prescription to a certified diabetes educator. Specify: type of diabetes;duration of education services and number of visits; MNT for nutrition/meal planning; DSMES for other services. See "Resources Available" section below for more information.*

III. Referrals

- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for Medical Nutrition Therapy (MNT)
- Diabetes Self-Management Education and Support (DSMES)
    - For Cerner users MNT and DSMES services may be requested by ordering a referral to "MedStar Diabetes Educator"
- Dentist for comprehensive periodontal examination
- Mental health professional, if needed
- Monitor for diabetes distress (Common; refers to emotional response to burdens and worries specific to an individual's experience in having to manage a severe, complicated, and demanding chronic condition such as diabetes. Routinely monitor people with diabetes for diabetes distress, particularly when treatment targets are not met and/or at the onset of diabetes complications.)
    - Refer to qualified mental health professional for further assessment and treatment if indicated. American Diabetes Association offers support and tools to help tackle the day-to-day challenges: **ADA Mental Health Toolkit.**
    - The ADA Mental Health Provider Referral Directory can help find mental health professionals with expertise in diabetes care: **ADA Mental Health Professional Directory**

- Social or Community Health worker and other community resources if needed
    - **Community Resources:** Meeting community needs around social determinants is essential to enhancing patient wellness and delivering quality, patient-centered care.
    - The MedStar Health Social Needs Tools within MedConnect enables care teams to efficiently screen patients and provide community referrals at the point of care.
    - **Social needs Screening:** Available in MedConnect in the Ambulatory setting visits under Scales and Assessments. Use the second tab for referral documentation.
    - **Social Needs Tool:** Located in MedConnect in the dark gray menu bar within a patient's chart. It helps care teams identify and address patients' social risk factors and needs and make referrals to appropriate programs and services for food, shelter, health care, work, financial assistance, and more. It provides instant access to comprehensive, localized listings with hundreds of programs in every zip code across the U.S.
    - For non-MedConnect users: Search and connect to support for financial assistance, food pantries, medical care, and other free or reduced cost help at: **Find Help**

- Referral to Podiatry is recommended in the following instances:
  - High risk patient (neuropathy, vascular disease, structural deformities, abnormal gait)
  - Hx. of previous ulcers or infections
  - Sensorimotor deficiencies for footwear modifications
  - Skin/nail deformities

- Referral to Endocrinology is recommended when:
  - The initial clinical and/or biochemical state is markedly abnormal
  - The response to standard therapy is unsatisfactory (i.e., A1c goal not attained in 6-12 months.
  - Metabolic complications.
  - Problems/challenges with continuous glucose monitor
  - Consideration of insulin pump therapy

- Referral to Cardiac or Vascular Specialist should be considered when:
  - EKG with left bundle branch block, myocardial infarction, or change from baseline at any time.
  - Decline in exercise capacity
  - Angina, atypical chest pain or claudication
  - Absent or diminished pedal pulses
  - Abdominal aortic aneurysm
  - Embarking on new exercise program if previously sedentary and/or over 40 years old, or longstanding DM

- Referral to Nephrology is recommended in the following situations:
  - if estimated GFR is <30mL/min/1.73m^2 or continued decrease in estimated GFR
  - continuously increasing urine albumin-to-creatinine ratio
  - there is uncertainty regarding the etiology of kidney disease
  - difficult management issues
  - rapidly progressing kidney disease.

- Referral to MedStar Diabetes Pathway "Boot Camp"
  - Available within MedStar Health for those with type 2 diabetes and an A1c of 8 or higher
  - This is an intensive virtual 12-week diabetes education and medication management program in which participants use a cellular-enabled blood glucose meter or a continuous blood glucose meter that sends their blood glucose readings to boot camp dashboards which are monitored in real-time by diabetes nurse practitioners and diabetes educators. Participants receive ongoing monitoring and support strategies to improve glycemic control.
  - In MedConnect select: **Referral to MedStar Diabetes Pathway/Boot Camp**
    - The referral order includes medication management, intense diabetes self-management education and medical nutrition therapy, as well as pre-(if not already available) and post-program A1Cs
  - **Patient information:** MedStar Health Diabetes Pathway Patient Information

- **Diabetes Self-Management: MedStar Health Diabetes Chatbot**

- MedStar now offers a *novel chat-based diabetes education program.* To successfully manage their diabetes, patients must learn and gain confidence in specific self-care routines. To expand the reach of diabetes education and support to more Persons with Diabetes and, in partnership with Conversa Health, researchers at MedStar Diabetes Institute have developed a digital chat algorithm, or "chatbot," to help participants manage type 2 diabetes. The system delivers education and support to participants on their schedules, without needing office visits or insurance forms.
- Early data from @MedStarResearch shows #DiabetesEducation via chatbot can help patients manage Type2 Diabetes and improve their health. Patients that are actively engaged in the chats experience about a 1-point drop in A1C, express high satisfaction with the chatbot and report that it helps them feel more connected with their MedStar Health providers. Discover more about this Digital Revolution in HealthCare: https://www.medstarhealth.org/blog/diabetes-chatbot
- **Eligibility:** Any person with type 2 diabetes, checking their blood sugars at home with a glucometer or a continuous glucose monitor.
- **Referral:** In MedConnect select: **Referral to MedStar Health Diabetes Chatbot**
- **Patient information:** MedStar Health Diabetes Chatbot Patient Information

Summary of the recommendations for the comprehensive diabetes medical evaluations.
Table copied from the 2023 Standards of Medical Care in Diabetes
(Section 4, pages S52 and S53 table 4.1).

Table 4.1 – Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history**			
	▪ Characteristics at onset (e.g., age, symptoms)	✓		
	▪ Review of previous treatment plans and response	✓		
	▪ Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	▪ Family history of diabetes in a first-degree relative	✓		
	▪ Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	▪ Common comorbidities (e.g., obesity, OSA, NAFLD)	✓		
	▪ High blood pressure or abnormal lipids	✓		✓
	▪ Macrovascular and microvascular complications	✓		✓
	▪ Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	▪ Presence of hemoglobinopathies or anemias	✓		✓
	▪ Last dental visit	✓		✓
	▪ Last dilated eye exam			✓
	▪ Visits to specialists			✓
	Interval history			
	▪ Changes in medical/family history since last visit		✓	✓
BEHAVIORAL FACTORS	▪ Eating patterns and weight history	✓	✓	✓
	▪ Assess familiarity with carbohydrate counting (e.g., type 1 diabetes, type 2 diabetes treated with MDI)	✓		✓
	▪ Physical activity and sleep behaviors	✓	✓	✓
	▪ Tobacco, alcohol, and substance use	✓		✓
MEDICATIONS AND VACCINATIONS	▪ Current medication plan	✓	✓	✓
	▪ Medication-taking behavior	✓	✓	✓
	▪ Medication intolerance or side effects	✓	✓	✓
	▪ Complementary and alternative medicine use	✓	✓	✓
	▪ Vaccination history and needs	✓		✓
TECHNOLOGY USE	▪ Assess use of health apps, online education, patient portals, etc.	✓		✓
	▪ Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	▪ Review insulin pump settings and use, connected pen and glucose data	✓	✓	✓
SOCIAL LIFE ASSESSMENT	**Social network**			
	▪ Identify existing social supports	✓		✓
	▪ Identify surrogate decision maker, advanced care plan	✓		✓
	▪ Identify social determinants of health (e.g., food security, housing stability & homelessness, transportation access, financial security, community safety)	✓		✓

Table 4.1 (cont.) - Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic examination (refer to eye specialist)	✓		✓
	▪ Thyroid palpation	✓		✓
	▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	▪ Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)**	✓		✓
	• Screen for PAD (pedal pulses—refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
	▪ Screen for depression, anxiety, and disordered eating	✓		✓
	▪ Consider assessment for cognitive performance*	✓		✓
	▪ Consider assessment for functional performance*	✓		✓
LABORATORY EVALUATION	▪ A1C, if the results are not available within the past 3 months	✓	✓	✓
	▪ If not performed/available within the past year	✓		✓
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#	✓		✓^
	• Liver function tests#	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate+	✓		✓
	• Thyroid-stimulating hormone in people with type 1 diabetes#	✓		✓
	• Vitamin B12 if on metformin	✓		✓
	• Serum potassium levels in people with diabetes on ACE inhibitors, ARBs, or diuretics+	✓		✓

ABI, ankle-brachial pressure index; ARBs, angiotensin receptor blockers; CGM, continuous glucose monitors; MDI, multiple daily injections; NAFLD, nonalcoholic fatty liver disease; OSA, obstructive sleep apnea; PAD, peripheral arterial disease.

*At 65 years of age or older.

+May be needed more frequently in people with diabetes with known chronic kidney disease or with changes in medications that affect kidney function and serum potassium (see **Table 11.1**).

#May also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes medications, blood pressure medications, cholesterol medications, or thyroid medications).

^In people without dyslipidemia and not on cholesterol-lowering therapy, testing may be less frequent.

**Should be performed at every visit in people with diabetes with sensory loss, previous foot ulcers, or amputations.

IV. Goals of Treatment for Diabetes

Management and goals should be guided by the assessment of overall health, cardiovascular risk, hypoglycemia risk, diabetes complications and shared decision making.

Some barriers to diabetes education and support may be overcome using telemedicine approaches.

Glycemic Goals in Adults

- Lowering A1C to below or around 7% has been shown to reduce microvascular complications of diabetes and if implemented soon after the diagnosis of diabetes is associated with long-term reduction in macrovascular disease. Therefore, a reasonable A1C goal for many nonpregnant adults is <7% if this can be achieved without significant hypoglycemia.

- Providers might reasonably suggest more stringent A1C goals (such as 6.5%) for selected individual patients if this can be achieved without significant hypoglycemia or other adverse effects of treatment. Appropriate patients might include those with short duration of diabetes, long life expectancy and no significant CVD.

- Less stringent A1C goals (such as 8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions and in those with longstanding diabetes in whom the general goal is difficult to attain despite DSMES, appropriate glucose monitoring, and effective doses of multiple glucose lowering agents including insulin.

- Postprandial glucose should be targeted if A1C goals are not met despite reaching pre-prandial glucose goals.

- Glycemic goals should be reassessed periodically.

- Continuous glucose monitoring or intermittently scanned continuous glucose monitoring should be offered to adult with diabetes on multiple daily insulin injections or continuous subcutaneous insulin infusion.
    - The Ambulatory Glucose Profile (AGP) obtained from continuous glucose monitoring (CGM) devices provides visual cues to assist with interpretation of data and treatment decisions.

    - Time in Range can be used to assess glycemic control; time above and below target glucose are also helpful in evaluating the need for adjustment to the treatment regimen.

    - Many insurances will cover CGM in patients with diabetes. If the practitioner believes that CGM will help the patient achieve better glucose control, it should be prescribed with the possibility that a prior authorization will be required. The Association of Diabetes Care and Education Specialists Danatech website is open access and has excellent info on all the available devices including payer coverage. For CGM Insurance Coverage: cgm-insurance-coverage-look-up

- Users should be educated on factors that may affect accuracy of their device (see below, Table 7.4, Continuous glucose monitoring devices interfering substances, copied from the 2023 Standards of Medical Care in Diabetes, Section 7, page S117)

Table 7.4—Continuous glucose monitoring devices interfering substances

Medication	Systems affected	Effect
Acetaminophen		
>4 g/day	Dexcom G6	Higher sensor readings than actual glucose
Any dose	Medtronic Guardian	Higher sensor readings than actual glucose
Alcohol	Medtronic Guardian	Sensor readings may be higher than actual glucose
Ascorbic acid (vitamin C), >500 mg/day	FreeStyle Libre	Higher sensor readings than actual glucose
Hydroxyurea	Dexcom G6, Medtronic Guardian	Higher sensor readings than actual glucose
Mannitol	Senseonics Eversense	Sensor bias within therapeutic concentration ranges
Tetracycline	Senseonics Eversense	Sensor bias within therapeutic concentration ranges

Hypoglycemia

- Classification of Hypoglycemia
  - Level 1 Glucose <70mg/dL and ≥54mg/dL
  - Level 2 Glucose <54mg/dL
  - Level 3 Any severe event with altered mental status and/or physical status requiring assistance for treatment of hypoglycemia
- Preferred Treatment
  - Glucose (15-20g) for conscious person with blood glucose <70mg/dL, however any form of carbohydrate that contains glucose can be used
  - Fifteen minutes after treatment, if blood glucose is still <70mg/dL treatment should be repeated
  - When blood glucose pattern begins to trend up, a meal or snack should be eaten
- All persons with diabetes at increased risk of level 2 or 3 hypoglycemia should be prescribed glucagon
- Risk and awareness (ability to feel signs and symptoms) of hypoglycemia should be reviewed at every encounter
- Any episodes of level 3 hypoglycemia should prompt adjustment of the treatment plan and hypoglycemia avoidance education
- Patients on insulin that have hypoglycemia unawareness, one level 3 hypoglycemic event, or an unexplained pattern of level 2 hypoglycemia should raise their glycemic target for at least several weeks. This assures safety and may allow return of insulin counterregulatory hormone responses to hypoglycemia and improved awareness or sensing of lows.

Glycemic Control	
Hemoglobin A1C*	▪ The A1C goal *for patients in general* is <7%. ▪ If using ambulatory glucose profile/glucose management indicator to assess glycemia, a parallel goal for many nonpregnant adults is time in range of >70% with time below range <4% and time <54 mg/dL <1% ▪ For patients at high risk of hypoglycemia a target of time in range >50% with time below range <1% is recommended ▪ The A1C goal *for the individual patient* is an A1C as close to normal as possible without significant hypoglycemia ▪ Less stringent A1C goals (such as <8%) may be appropriate for patients with a history of severe or recurrent problematic hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the general goal is difficult to attain despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple lowering agents including insulin.
Pre-prandial plasma glucose	80–130 mg/dl (4.4–7.2 mmol/l)
Postprandial plasma glucose	<180 mg/dl (<10.0 mmol/l) postprandial glucose measurements should be made 1-2hrs after beginning of meal
Other Goals	
Blood pressure	▪ Target blood pressure is SBP<130 and DBP<80 if these can be safely attained ▪ All diabetes patients with hypertension (HTN) should monitor their blood pressure at home
Lipids***	For adults not on lipid lowering therapy - screening lipid profile at diabetes diagnosis, at an initial medical evaluation and and every 5 years thereafter if under age 40 ; periodically thereafter. Treatment should be based on risk status. (See Table Below for additional information on age >40.)
LDL	Goals – see below table "Recommendations for statin treatment in people with diabetes"
Triglycerides	<150 mg/dl (<1.7 mmol/l)[ʂ]
HDL	>40 mg/dl (1.1 mmol/l) for males, and HDL goal > 50mg/dl (1.3mmol/l) in women

*****Referenced to a nondiabetic range of 4.0–6.0% using a DCCT-based assay; ADA Standards of Medical Care in Diabetes 2022

******Postprandial glucose measurements should be made 1 ½ to 2 hrs. after the beginning of the meal, generally peak levels in patients with diabetes.

******* Lipid treatment: Goals include diet and lifestyle modification with intense lifestyle therapy and optimizing glycemic control for patients with elevated triglyceride levels (≥150 mg/dL [1.7 mmol/L]) and/or low HDL cholesterol (<40 mg/dL [1.0 mmol/L] for men, <50 mg/dL [1.3 mmol/L] for women).

[ʂ]For patients with fasting triglyceride levels ≥500 mg/dL (5.7 mmol/L), evaluate for secondary causes and consider medical therapy to reduce the risk of pancreatitis.

In patients with ASCVD or other cardiovascular risk factors on a statin with controlled LDL cholesterol but elevated triglycerides (135–499 mg/dL), the addition of icosapent ethyl can be considered to reduce cardiovascular risk.

Recommendations for statin treatment in people with diabetes

Age	Risk factors	Recommended statin intensity*	Monitoring lipid panel
<40 years	None	None****	
	CVD risk factor(s)**	Moderate	
	10-year ASCVD risk of ≥20%	High (if LDL≥70mg/dL on maximally tolerated statin, consider adding ezetimibe or PCSK9 inhibitor)	Lipid profile at start of lipid lowering therapy, 4-12 wks after beginning or a dose change, annually thereafter/ as needed to monitor for adherence
	Overt CVD***	High; target LDL<55mg/dL	
	ASCVD and LDL > 55mg/dL on maximum tolerated statin dose	Consider adding additional LDL lowering agents (e.g., ezetimibe or PCSK9 inhibitor	
Age 40-75 years	None	Moderate	
	One or more CVD risk factors or 10-year ASCVD risk of ≥20%	High; target LDL <70mg/dL (if LDL≥70mg/dL on maximally tolerated statin, recommend adding ezetimibe or PCSK9 inhibitor)	Lipid profile at start of lipid lowering therapy, 4-12 wks after beginning or a dose change, annually thereafter/ as needed to monitor for adherence
	Overt CVD	High; target LDL<55mg/dL (if LDL>55mg/dL on maximally tolerated statin, recommend adding ezetimibe or PCSK9 inhibitor)	
	Patients with a history of ASCVD who cannot tolerate high-intensity statins	Consider adding additional LDL lowering agents (e.g., ezetimibe or PCSK9 inhibitor)	
>75 years	If already on statin therapy, it is reasonable to continue. If not on statin therapy, it may be reasonable to begin treatment after shared decision making	If treatment is started, a moderate intensity statin is recommended	

*In addition to lifestyle therapy.

**CVD risk factors include LDL cholesterol >100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, family history of premature ASCVD and overweight and obesity.
***Overt CVD includes those with previous cardiovascular events or acute coronary syndromes.
****Moderate-intensity statin may be considered based on risk-benefit profile and ASCVD risk factors

High-Intensity Statin Therapy*	**Moderate-Intensity Statin Therapy***
Lowers LDL-C ≥50%	*Lowers LDL-C 30-49%*
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg (FDA does not recommend use of simvastatin 80 mg due to increased risk of myopathy) Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Pitavastatin 2-4 mg

*Once daily dosing

Statin + ezetimibe: Adding ezetimibe to moderate-intensity statin therapy has been shown to provide CV benefit compared with moderate statin therapy alone. This combination is a consideration for individuals with recent ACS and LDL-C ≥50mg/dL or those who cannot tolerate a high-intensity statin.

Statin + fibrate: This combination has not been shown to improve ASCVD outcomes and as such, it is NOT recommended

Statin + niacin: This combination has not been shown to provide additional CV benefit above statin therapy alone and may increase the risk for stroke. Therefore, this combination is NOT recommended.

V. Continuing Care

Recommendations for continuing care:

Service	Recommendations
Frequency of return visits	At least quarterly * for type 1 patients. At least semi-annually * for type 2 patients if A1C at goal; quarterly if not at goal. **More frequently when indicated for follow up of DKA, hyperglycemia, hypoglycemia, hypertension, retinopathy, nephropathy, cardiovascular disease, neuropathy, or foot conditions.*
Review of Management Plan	During every regular follow up visit
Focused physical, including reflexes and monofilament exam	Annually
Hemoglobin A1C	Quarterly for type 1 diabetes or insulin using patients and not at A1C goal patients; Every 6 months for type 2 diabetes with A1C≤ 7.0%.
Fasting lipid profile	For adults not on lipid lowering therapy - screening lipid profile at diabetes diagnosis, at an initial medical evaluation and and every 5 years thereafter if under age 40 (note that for ages 40-75 statin therapy is recommended for all persons with diabetes; see "Recommendations for statin treatment in people with diabetes" above) For adults on lipid lowering therapy - 4-12 wks after beginning treatment or a dose change, annually thereafter/ as needed to monitor for adherence More frequent testing may be considered on an individual basis (e.g., to monitor for adherence and efficacy)

Vaccinations	Follow recommendations of CDC ACIP (Advisory Committee on Immunization Practices). This can be found at **www.cdc.gov/vaccines/**
Random urine microalbumin/creatinine	At least once a year, quantitatively assess urinary albumin (e.g., urine albumin-to-creatinine ratio [UACR]) and estimated glomerular filtration rate (eGFR) in patients with type 1 diabetes duration of ≥5 years and in all patients with type 2 diabetes. UACR ≥300 mg/g creatinine and/or eGFR 30–60 mL/min/1.73 m2 should be monitored 1-4 times per year depending on severity to guide therapy
Dilated eye exam (by Ophthalmology or Optometry)	Patients with type 1 diabetes should have an initial dilated and comprehensive eye examination within 5 years after the onset of diabetes. Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination shortly after the diagnosis of diabetes. Subsequent examinations should be repeated annually. Less frequent exams (i.e., every 2 years) may be considered with the advice of an eye care professional in the setting of a normal eye exam. Examinations will be required more frequently if retinopathy is progressing or patient planning to or becomes pregnant. Programs that use retinal photography can be appropriate for retinal screening provided pathways present for timely referral for a comprehensive eye examination when indicated
Foot Exam	Patients with type 1 diabetes should be assessed for diabetes-related peripheral neuropathy within 5 years of the diagnosis of diabetes and at least yearly thereafter. Patients with type 2 diabetes should be assessed for diabetes-related peripheral neuropathy at the time of diagnosis and at least yearly thereafter. Careful history & assessment of either temperature or pinprick sensation (small fiber function) and vibration sensation using a 128-Hz tuning fork (for large-fiber function). All patients should have annual 10-g monofilament testing to identify feet at risk for ulceration and amputation. Inability to feel a 10-g monofilament is consistent with an insensate foot. Examination should include skin and vascular assessment (pulses in legs/feet).
Diabetes education	Evaluate annually
Medical Nutrition Therapy	Evaluation at time of diagnosis and annually
Physical Activity Prescription	Adults with diabetes should be advised to perform at least 150 min/week of moderate-or vigorous-intensity aerobic physical activity (50–70% of maximum heart rate), spread over at least 3 days/week with no more than 2 consecutive days without exercise. Evidence supports that all individuals, including those with diabetes, should be encouraged to reduce sedentary time, particularly by breaking up extended amounts of time (>90 min) spent sitting. In the absence of contraindications, adults with type 2 diabetes should be encouraged to perform resistance training at least twice per week.

Smoking Cessation Counseling	Advise all patients not to smoke. Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care. e-cigarettes are not recommended as an alternative.
Dementia Screening	Screening for early detection of mild cognitive impairment or dementia should be done at least yearly on all persons with diabetes ≥65yoa
Ankle-Brachial Index (ABI)	Screening of ABI recommended for patients ▪ with symptoms/signs of peripheral vascular disease (PAD) ▪ >50 years of age ▪ and should be considered in patients <50 who have PAD risk factors
Nonalcoholic Fatty Liver Disease (NAFLD)/ Nonalcoholic steatohepatitis (NASH)	Type 2 diabetes and prediabetes patients with either elevated liver enzymes or fatty liver on imaging should be evaluated for nonalcoholic steatohepatitis and liver fibrosis ▪ Fibrosis-4 index (FIB-4) is the most cost effective strategy for the initial screening of people with prediabetes and cardiometabolic risk factors or type 2 diabetes. (mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis)If low risk score, repeat testing in 2-3 years; if intermediate/high FIB-4 additional risk stratification with transient elastography or if unavailable then do blood fibrosis biomarker ▪ There are no FDA approved medications for treatment of NASH ▪ Treatment is weight loss of at least 5%, preferably ≥10% as well as treating hyperglycemia
Other Treatment Modalities	
ASA	▪ Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes with a history of CVD (cardiovascular disease) ▪ Per ADA consider aspirin therapy (75–162 mg/ day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk >10%). This includes most men or women with diabetes aged ≥50yr with ≥1 additional major risk factor: family hx of premature ASCVD (atherosclerotic cardiovascular disease), hypertension, smoking, dyslipidemia, or albuminuria. (USPSTF no longer recommends using ASA for primary prevention). ▪ Do not use aspirin in pts. < 21 yr. of age because of the increase risk of Reyes syndrome ▪ Aspirin is not recommended for those at low CVD risk (women and men under age 50 years with no major CVD risk factors; 10-year CVD risk under 5%). Clinical judgment should be used for those in these age ranges with multiple risk factors. ▪ In patients with aspirin allergy and CVD, clopidogrel 75mg/day should be used. ▪ Presence of retinopathy is not a contraindication to aspirin therapy as it does not increase the risk of retinal hemorrhage
FDA Approved Weight Loss Medications	▪ Consider in select type 2 diabetes patients with BMI≥27kg/m^2 as an adjunct to diet, physical activity, and behavioral counseling ▪ If after 3 months response to weight loss medication is <5%, medication should be stopped, and alternative medications evaluated ▪ For additional information see guideline *Identification, Evaluation and Treatment of Overweight and Obesity in Adults*

Bariatric Surgery	▪ Should be recommended for BMI ≥40 kg/m2 (BMI ≥37.5 kg/m2 in Asian Americans) & BMI 35.0–39.9 kg/m2 (32.5–37.4 kg/m2 in Asian Americans) in adults who do not achieve durable weight loss and improvement in comorbidities & diabetes control with nonsurgical methods and may be considered for other T2 diabetics. ▪ People who undergo metabolic surgery should receive long-term medical and behavioral support and routine monitoring of micronutrient, nutritional, and metabolic status.
Diabetes-Related Neuropathic Pain	▪ Gabapentinoids, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, sodium channel blockers are recommended as initial pharmacologic treatment. Refer to pain specialist or neurologist when pain control is not achieved.
Service - Other Treatment Modalities	**Recommendations**
Hypertensive diabetics with coronary artery disease (CAD) or microalbuminuria ▪ initial agent of choice- ACE inhibitor or ARB	▪ Monitor serum potassium levels and renal function. ▪ Do not discontinue renin-angiotensin system blockade for minor increases in serum creatinine (≤30%) in the absence of volume depletion. ▪ ACEi/ARB are not recommended for the primary prevention of CKD in patients with diabetes who have normal BP, normal UACR (<30 mg/g creatinine), and normal eGFR. ▪ Type 2 diabetes patients with chronic kidney disease with albuminuria treated with max tolerated ARB or ACE inhibitor – addition of finerenone is recommended to reduce risk of kidney disease progression and to improve cardiovascular outcomes
Diabetes with CVD or kidney disease ▪ SGLT2 inhibitors or GLP-1 receptor agonist with known CVD benefit	▪ SGLT2inhibitors should only be used in patients with an eGFR≥20mL/min/1.73m^2 and urinary albumin ≥200mg/g creatinine ▪ SGLT2 inhibitor + GLP-1 receptor agonist may both be considered for additive reduction in risk of adverse cardiovascular and kidney events
Diabetes with heart failure (HF) ▪ SGLT2 inhibitor with proven HF benefit	
Diabetes with obesity ▪ GLP-1 receptor agonist	▪ Consider medications such as tirzepatide as a glucose lowering option with the potential for weight loss

Note: This guideline is for reference only and is not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by providers. This guideline is recommended for adults with either insulin dependent or non-insulin dependent diabetes mellitus. Patients younger than 18 years and pregnant females with diabetes are not included.

VI. Pharmacologic Treatment of Diabetes

- Type 1 diabetes should be treated with multiple daily injections of insulin (basal and prandial) or continuous subcutaneous insulin infusion.

- The ADA treatment recommendations for type 2 diabetes should take into consideration of the following:
    - patient comorbidities such as ASCVD, chronic renal disease and heart failure
    - risk of hypoglycemia
    - medication costs and side effects
    - effect on weight
    - patient preference

  (*See Table 9.2 and Figure 9.3 below)*

- The initial treatment of type 2 diabetes generally includes metformin. Metformin should be continued even after insulin therapy is initiated unless contraindicated or not tolerated.

- In type 2 diabetes with atherosclerotic cardiovascular disease (CVD) or at high risk for atherosclerotic CVD a sodium-glucose cotransporter 2 inhibitor (SGLT-2 inhibitor) and/or a glucagon-like peptide 1 receptor agonist (GLP-1 RA) with demonstrated cardiovascular disease disease benefit are appropriate for initial treatment as a part of glucose lowering regimen and comprehensive cardiovascular risk reduction independent of A1c.
- In type 2 diabetes with heart failure a SGLT-2i with proven heart failure benefit is recommended
- In type 2 diabetes with chronic kidney disease a SGLT-2i with primary evidence of decreasing chronic kidney disease progression is preferred; if SGLT-2i is not tolerated or is contraindicated then use GLP-1 RA with proven CVD benefit.

See Table 9.2 below for details

- GLP-1 agonist is preferred over insulin when feasible in type 2 diabetes. If insulin is used, it is recommended that it be in combination with a GLP-1 agonist.

- Consider early start of insulin if A1c>10% or blood glucose levels are very high (≥300mg/dL), if symptoms of hyperglycemia are present, or if there is ongoing catabolism (weight loss).

- Treatment intensification should not be delayed in patients not meeting goals
  (*See Figure 9.4 below)*

- In older adults glucose targets and pharmacologic treatments might need to be adjusted to minimize hypoglycemia
    - Simplification of complex treatment regiments, especially those using multiple daily insulin dosing, is recommended to decrease hypoglycemia risk (see *Figure 13.1* below for insulin simplification algorithm)
    - Avoid thiazolidinediones and longer-acting sulfonylureas

- Continuous glucose monitoring is recommended for older adults with type 1 diabetes to decrease hypoglycemia
  (*See Tables 13.1, 13.2 below)*

- Treatment regimens should be simplified in the presence of cognitive impairment to minimize the risk of hypoglycemia.

Below are tables/figures copied from the 2023 Standards of Medical Care in Diabetes (Section 9, page S148 Table 9.2, page S147 Figure 9.3, page S150 Figure 9.4; Section 13, Table 13.1-page S220, Table 13.2-page S223, Figure 13.1-page S222).

Table 9.2—Medications for lowering glucose, summary of characteristics

	Efficacy[1]	Hypoglycemia	Weight change[2]	CV effects		Renal effects		Oral/SQ	Cost	Clinical considerations
				Effect on MACE	HF	Progression of DKD	Dosing/use considerations*			
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Neutral	• Contraindicated with eGFR <30 mL/min per 1.73 m²	Oral	Low	• GI side effects common; to mitigate GI side effects, consider slow dose titration, extended release formulations, and administration with food • Potential for vitamin B12 deficiency; monitor at regular intervals
SGLT2 inhibitors	Intermediate to high	No	Loss (intermediate)	Benefit: canagliflozin, empagliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin	• See labels for renal dose considerations of individual agents • Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	Oral	High	• DKA risk, rare in T2DM: discontinue, evaluate, and treat promptly if suspected; be aware of predisposing risk factors and clinical presentation (including euglycemic DKA); discontinue before scheduled surgery (e.g., 3–4 days), during critical illness, or during prolonged fasting to mitigate potential risk • Increased risk of genital mycotic infections • Necrotizing fasciitis of the perineum (Fournier gangrene), rare reports: institute prompt treatment if suspected • Attention to volume status, blood pressure; adjust other volume-contracting agents as applicable
GLP-1 RAs	High to very high	No	Loss (intermediate to very high)	Benefit: dulaglutide, liraglutide, semaglutide (SQ) Neutral: exenatide once weekly, lixisenatide	Neutral	Benefit for renal endpoints in CVOTs, driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ)	• See labels for renal dose considerations of individual agents • No dose adjustment for dulaglutide, liraglutide, semaglutide • Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions	SQ; oral (semaglutide)	High	• Risk of thyroid C-cell tumors in rodents; human relevance not determined (liraglutide, dulaglutide, exenatide extended release, semaglutide) • Counsel patients on potential for GI side effects and their typically temporary nature; provide guidance on dietary modifications to mitigate GI side effects (reduction in meal size, mindful eating practices [e.g., stop eating once full], decreasing intake of high-fat or spicy food); consider slower dose titration for patients experiencing GI challenges • Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected • Evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected
GIP and GLP-1 RA	Very high	No	Loss (very high)	Under investigation	Under investigation	Under investigation	• See label for renal dose considerations • No dose adjustment • Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions	SQ	High	• Risk of thyroid C-cell tumors in rodents; human relevance not determined • Counsel patients on potential for GI side effects and their typically temporary nature; provide guidance on dietary modifications to mitigate GI side effects (reduction in meal size, mindful eating practices [e.g., stop eating once full], decreasing intake of high-fat or spicy food); consider slower dose titration for patients experiencing GI challenges • Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected • Evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Neutral (potential risk, saxagliptin)	Neutral	• Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment • No dose adjustment required for linagliptin	Oral	High	• Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected • Joint pain • Bullous pemphigoid (postmarketing): discontinue if suspected
Thiazolidinediones	High	No	Gain	Potential benefit: pioglitazone	Increased risk	Neutral	• No dose adjustment required • Generally not recommended in renal impairment due to potential for fluid retention	Oral	Low	• Congestive HF (pioglitazone, rosiglitazone) • Fluid retention (edema; heart failure) • Benefit in NASH • Risk of bone fractures • Weight gain: consider lower doses to mitigate weight gain and edema
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Neutral	• Glyburide: generally not recommended in chronic kidney disease • Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	Oral	Low	• FDA Special Warning on increased risk of CV mortality based on studies of an older sulfonylurea (tolbutamide); glimepiride shown to be CV safe (see text) • Use with caution in persons at risk for hypoglycemia
Insulin Human	High to very high	Yes	Gain	Neutral	Neutral	Neutral	• Lower insulin doses required with a decrease in eGFR; titrate per clinical response	SQ; inhaled	Low (SQ)	• Injection site reactions • Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
Insulin Analogs								SQ	High	

CV, cardiovascular; CVOT, cardiovascular outcomes trial; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; DPP-4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate; FDA, U.S. Food and Drug Administration; GI, gastrointestinal; GIP, gastric inhibitory polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; NASH, nonalcoholic steatohepatitis; MACE, major adverse cardiovascular events; SGLT2, sodium–glucose cotransporter 2; SQ, subcutaneous; T2DM, type 2 diabetes mellitus. *For agent-specific dosing recommendations, please refer to manufacturers' prescribing information. [1]Tsapas et al. (62). [2]Tsapas et al. (114). Reprinted from Davies et al. (45).

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date: May 2023**	**Next Scheduled Review Date:**
3/ 2011, 7/ 2013, 3/2014, 5/ 2015, 5/ 2016, 5/ 2017. 5/2018, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023		May 2024 Ambulatory Best Practice Condition: Diabetes Mellitus

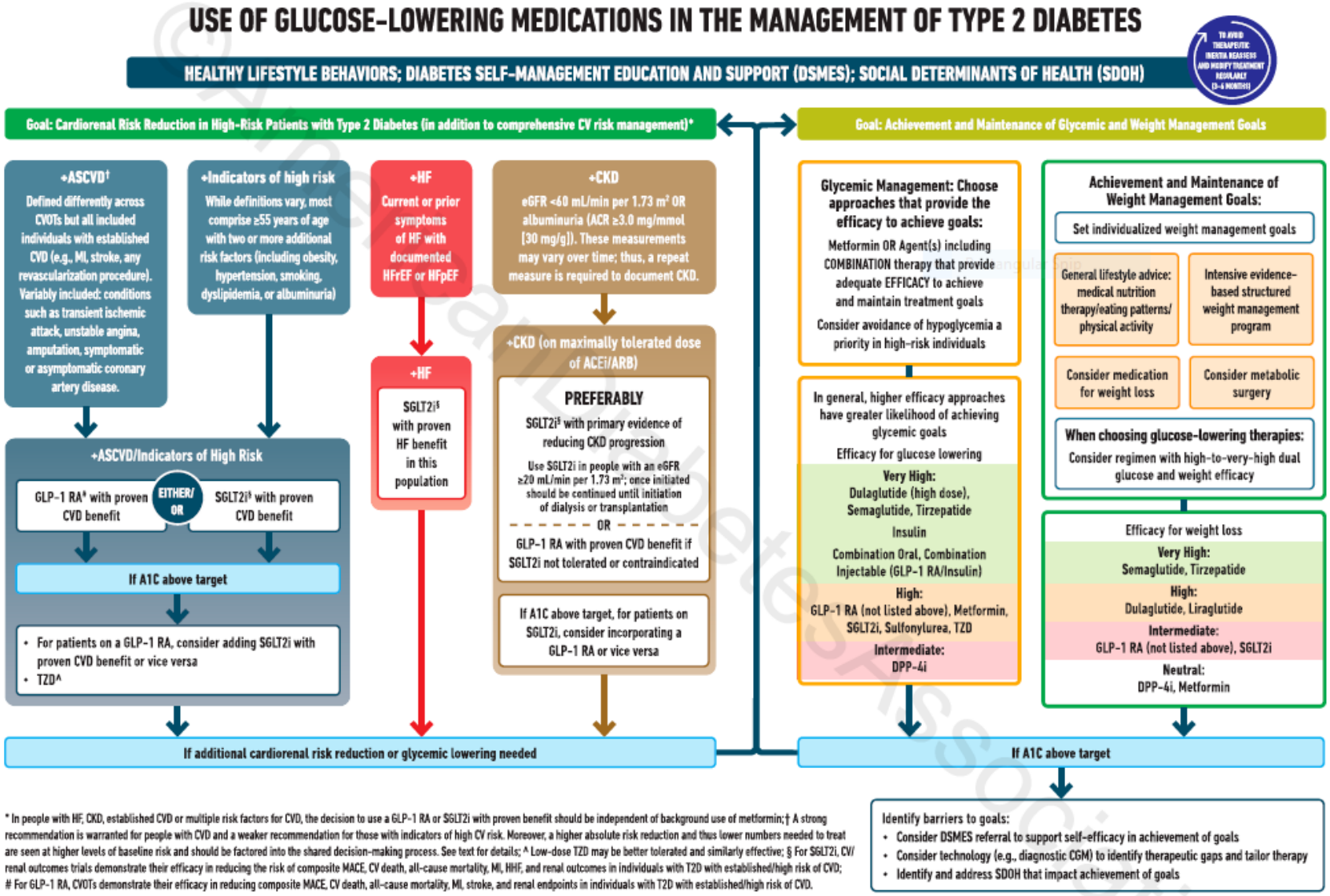
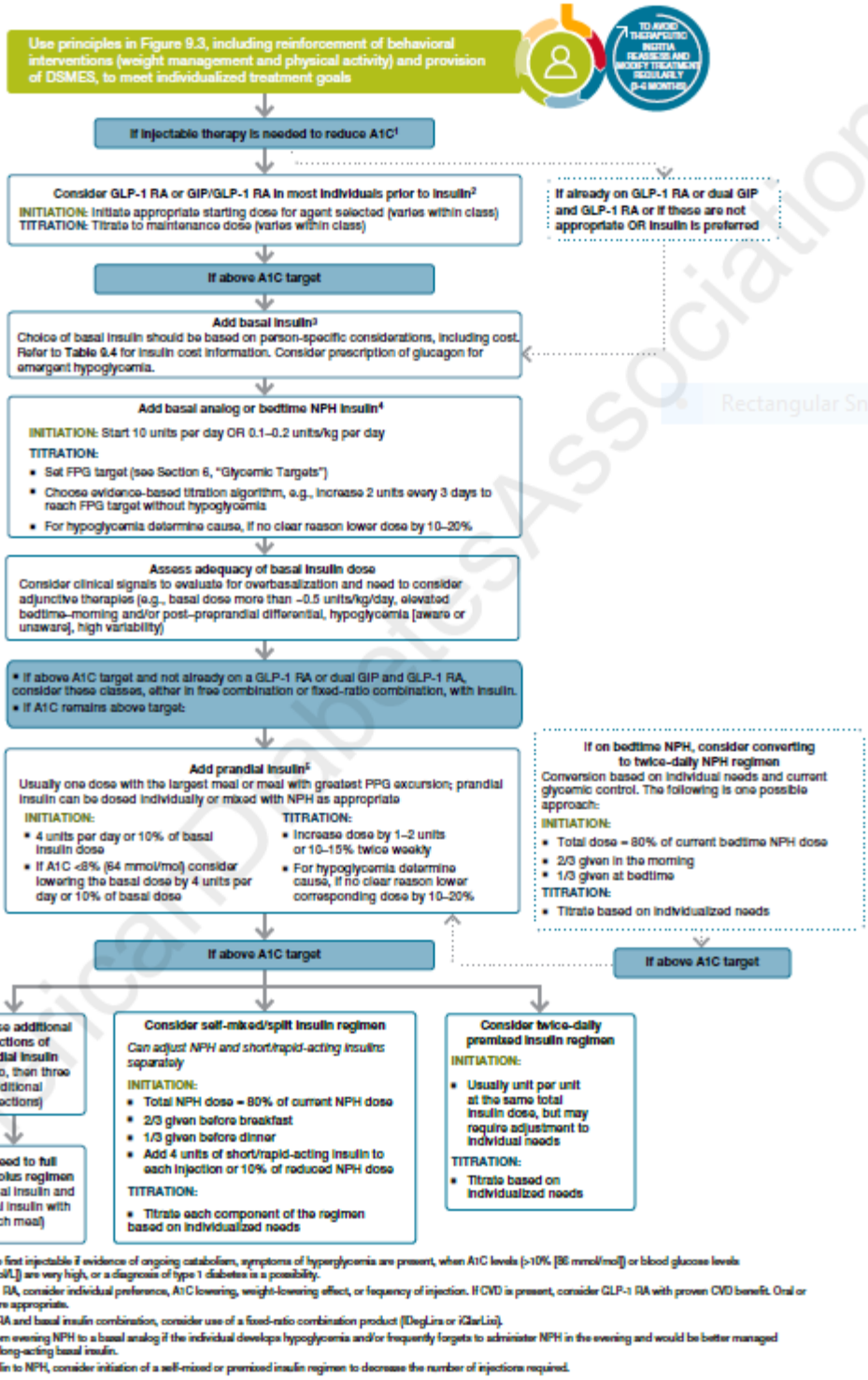


Figure 9.3—Use of glucose-lowering medications in the management of type 2 diabetes. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase 4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes; TZD, thiazolidinedione. Adapted from Davies et al. (45).

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date: May 2023**	**Next Scheduled Review Date:**
3/ 2011, 7/ 2013, 3/2014, 5/ 2015, 5/ 2016, 5/ 2017. 5/2018, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023		May 2024 Ambulatory Best Practice Condition: Diabetes Mellitus



1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (300 mg/dL [16.7 mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RA, consider individual preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD is present, consider GLP-1 RA with proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.
3. For people on GLP-1 RA and basal insulin combination, consider use of a fixed-ratio combination product (IDegLira or iGlarLixi).
4. Consider switching from evening NPH to a basal analog if the individual develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with an A.M. dose of a long-acting basal insulin.
5. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

Figure 9.4—Intensifying to injectable therapies in type 2 diabetes. DSMES, diabetes self-management education and support; FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide 1 receptor agonist; max, maximum; PPG, postprandial glucose. Adapted from Davies et al. (43).

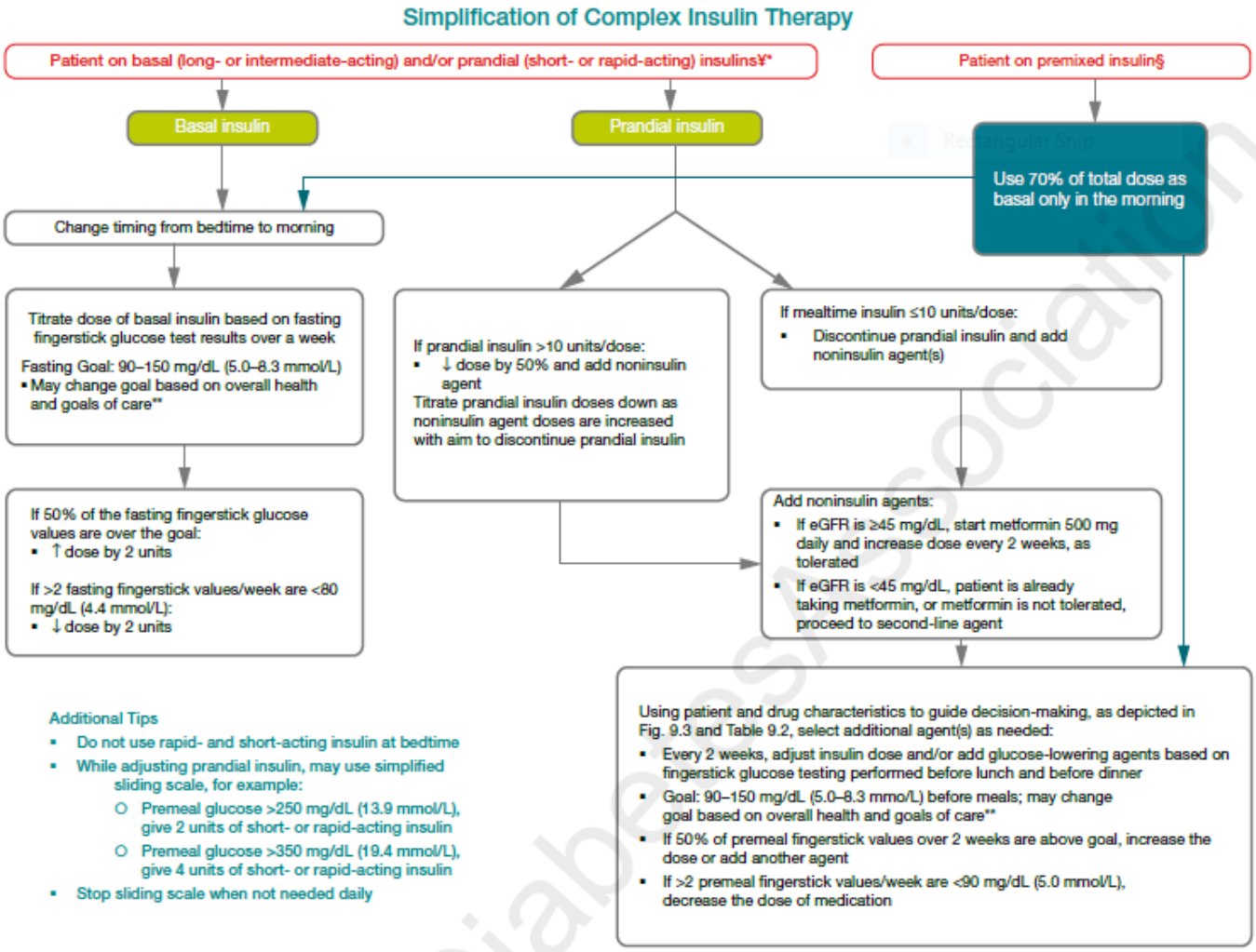


Figure 13.1—Algorithm to simplify insulin regimen for older adults with type 2 diabetes. eGFR, estimated glomerular filtration rate. *Basal insulins: glargine U-100 and U-300, detemir, degludec, and human NPH. **See **Table 13.1**. ¥Prandial insulins: short-acting (regular human insulin) or rapid-acting (lispro, aspart, and glulisine). §Premixed insulins: 70/30, 75/25, and 50/50 products. Adapted with permission from Munshi et al. (93).

Table 13.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (53–58 mmol/mol)	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or two or more instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit uncertain	Avoid reliance on A1C; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin

This table represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The patient characteristic categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualization. Additionally, a patient's health status and preferences may change over time. ADL, activities of daily living; LTC, long-term care. ‡A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden. *Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. "Multiple" means at least three, but many patients may have five or more (66). **The presence of a single end-stage chronic illness, such as stage 3–4 heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy. Adapted from Kirkman et al. (3).

Table 13.2—Considerations for treatment regimen simplification and deintensification/deprescribing in older adults with diabetes (93,128)

Patient characteristics/ health status	Reasonable A1C/ treatment goal	Rationale/considerations	When may regimen simplification be required?	When may treatment deintensification/ deprescribing be required?
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	<7.0–7.5% (53–58 mmol/mol)	• Patients can generally perform complex tasks to maintain good glycemic control when health is stable • During acute illness, patients may be more at risk for administration or dosing errors that can result in hypoglycemia, falls, fractures, etc.	• If severe or recurrent hypoglycemia occurs in patients on insulin therapy (regardless of A1C) • If wide glucose excursions are observed • If cognitive or functional decline occurs following acute illness	• If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (regardless of A1C) • If wide glucose excursions are observed • In the presence of polypharmacy
Complex/intermediate (multiple coexisting chronic illnesses or two or more instrumental ADL impairments or mild-to-moderate cognitive impairment)	<8.0% (64 mmol/mol)	• Comorbidities may affect self-management abilities and capacity to avoid hypoglycemia • Long-acting medication formulations may decrease pill burden and complexity of medication regimen	• If severe or recurrent hypoglycemia occurs in patients on insulin therapy (even if A1C is appropriate) • If unable to manage complexity of an insulin regimen • If there is a significant change in social circumstances, such as loss of caregiver, change in living situation, or financial difficulties	• If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (even if A1C is appropriate) • If wide glucose excursions are observed • In the presence of polypharmacy
Community-dwelling patients receiving care in a skilled nursing facility for short-term rehabilitation	Avoid reliance on A1C, glucose target 100–200 mg/dL (5.55–11.1 mmol/L)	• Glycemic control is important for recovery, wound healing, hydration, and avoidance of infections • Patients recovering from illness may not have returned to baseline cognitive function at the time of discharge • Consider the type of support the patient will receive at home	• If treatment regimen increased in complexity during hospitalization, it is reasonable, in many cases, to reinstate the prehospitalization medication regimen during the rehabilitation	• If the hospitalization for acute illness resulted in weight loss, anorexia, short-term cognitive decline, and/or loss of physical functioning
Very complex/poor health (LTC or end-stage chronic illnesses or moderate-to-severe cognitive impairment or two or more ADL impairments)	Avoid reliance on A1C and avoid hypoglycemia and symptomatic hyperglycemia	• No benefits of tight glycemic control in this population • Hypoglycemia should be avoided • Most important outcomes are maintenance of cognitive and functional status	• If on an insulin regimen and the patient would like to decrease the number of injections and fingerstick blood glucose monitoring events each day • If the patient has an inconsistent eating pattern	• If on noninsulin agents with a high hypoglycemia risk in the context of cognitive dysfunction, depression, anorexia, or inconsistent eating pattern • If taking any medications without clear benefits
At the end of life	Avoid hypoglycemia and symptomatic hyperglycemia	• Goal is to provide comfort and avoid tasks or interventions that cause pain or discomfort • Caregivers are important in providing medical care and maintaining quality of life	• If there is pain or discomfort caused by treatment (e.g., injections or finger sticks) • If there is excessive caregiver stress due to treatment complexity	• If taking any medications without clear benefits in improving symptoms and/or comfort

Treatment regimen simplification refers to changing strategy to decrease the complexity of a medication regimen (e.g., fewer administration times, fewer blood glucose checks) and decreasing the need for calculations (such as sliding-scale insulin calculations or insulin-carbohydrate ratio calculations). Deintensification/deprescribing refers to decreasing the dose or frequency of administration of a treatment or discontinuing a treatment altogether. ADL, activities of daily living; LTC, long-term care.

Resources Available

https://consumerguide.diabetes.org/
An ADA resource that can help practitioners and diabetics decide on the appropriate devices
Has information on the various CGMs, insulin pumps, meters, insulin, insulin pens, etc

https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases
An online resource with information about eye conditions and diseases. Includes large section on diabetic retinopathy

https://www.niddk.nih.gov/health-information/diabetes
Link goes directly to a page with links to multiple topics pertaining to diabetes. There is a section for health professionals and another for non-health professionals.

https://coveragetoolkit.org/medicare-advantage/mdpp-final-rule/
Above link is information for Medicare/Medicaid Diabetes Prevention Program (MDPP) —there is information regarding MDPP services, beneficiary eligibility criteria and referrals

https://innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program
Above link is a page on CMS.gov that has information on MDPP. For Medicare beneficiaries there is a 1-800 number and another website link for more information. There is also a "Frequently Asked Questions Page" and a place to subscribe to the MDPP listserv to receive updates on this program. Additionally, there is a link to find MDPP suppliers furnishing MDPP services.

https://www.findhelp.org/
Above link helps search for financial assistance, food pantries, medical care, and other free or decreased cost help

Centers for Disease Control and Prevention: Has online resources for professionals and laypersons
https://www.cdc.gov/diabetes/professional-info/index.html

List of the Centers for Disease Control and Prevention-recognized diabetes prevention lifestyle change programs can be found at this website: cdc.gov/diabetes/prevention/find-a-program.html

Diabetes Education: https://www.diabeteseducator.org

Diabetes Technologies: https://www.diabeteseducator.org/danatech/home

ADA Resources:
Diabetes.org:
http: www.diabetes.org

This site has a lot of information for patients ranging from how diabetes is diagnosed to details about insulin pumps.

Call 1-800-DIABETES (800-342-2383) Monday-Friday 9:00 a.m. to 7:00 p.m. ET

Facebook: American Diabetes Association
Twitter: @AmDiabetesAssn
Instagram: @AmDiabetesAssn

The American Diabetes Association maintains an online version of the Standards of Medical Care in Diabetes, titled Living Standards of Care. If updates to the Standards of Medical Care in Diabetes 2023 are needed they will be posted online as annotations. The website address is *professional.diabetes.org/content-page/living-standards*

Standards of Care App – free app available in App Store for iOS or Google Play for Android. This app has the most up-to-date Standards along with interactive tables and algorithms.

References

1. Standards of Care in Diabetes- 2023, American Diabetes Association. Diabetes Care volume 46, supplement 1, January 2023.

2. ACE/ACCE Consensus Statement: Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm-2020 Executive Summary
3. Centers for Disease Control and Prevention – National Diabetes Statistics Report

Attachments

- Treatment Algorithm for HTN in diabetes (Figure 10.2 copied from the 2023 Standards of Medical Care in Diabetes: Section 10, page S164)
- Oral Diabetes Agents
- Insulins and other injectables

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

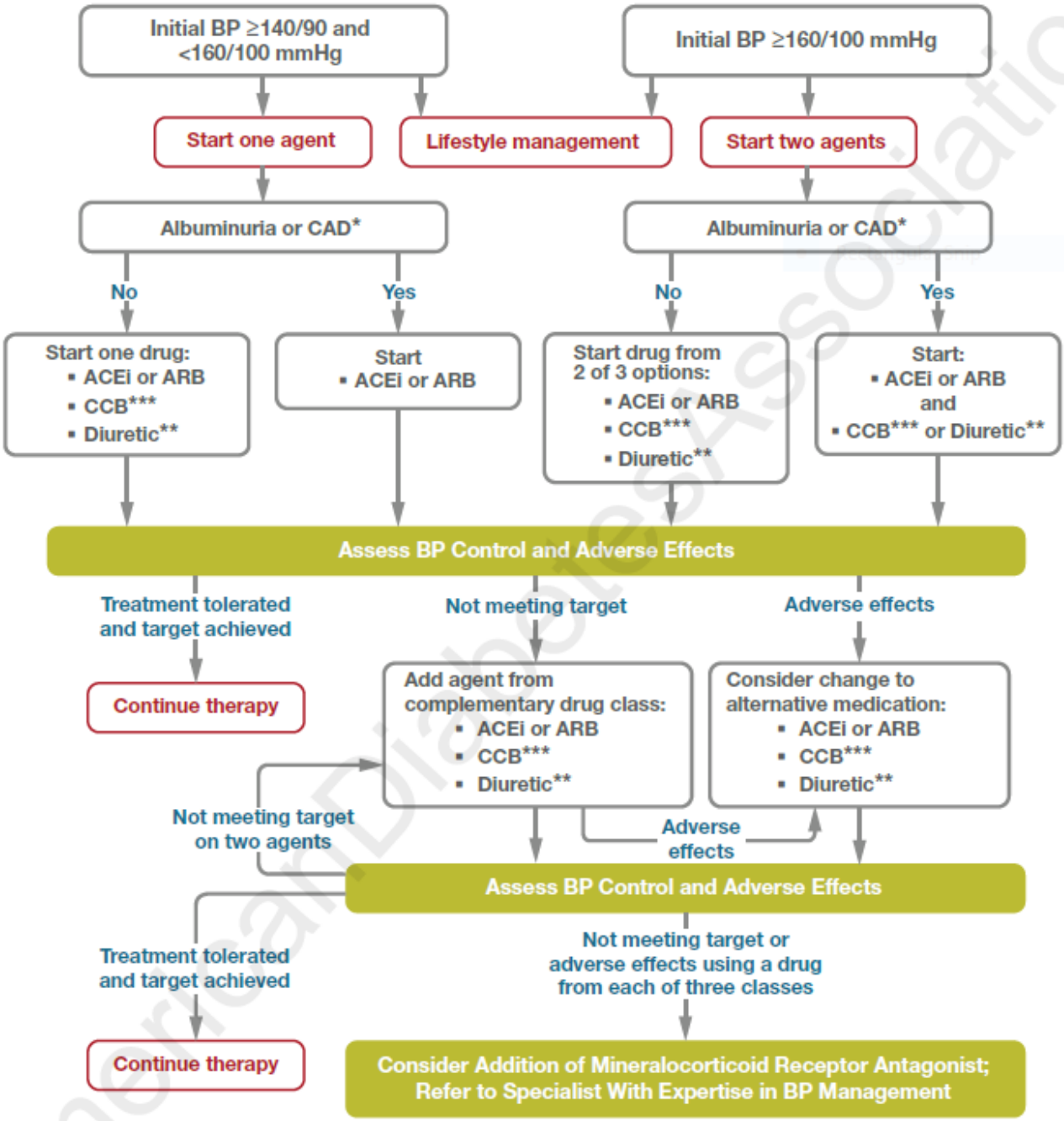


Figure 10.2—Recommendations for the treatment of confirmed hypertension in people with diabetes. *An ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) is suggested to treat hypertension for people with coronary artery disease (CAD) or urine albumin-to-creatinine ratio 30–299 mg/g creatinine and strongly recommended for individuals with urine albumin-to-creatinine ratio ≥300 mg/g creatinine. **Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine calcium channel blocker (CCB). BP, blood pressure. Adapted from de Boer et al. (20).

ORAL DIABETES MEDICATIONS

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
Sulfonylureas				
Glyburide (Glynase® [micronized], and generics) ($23)	Stimulates the release of insulin from the pancreas Glipizide immediate release is preferred in patients with moderate to severe renal function impairment	FPG: ⇩ 50-60mg/dl HbA1c: ⇩ 1.5-2%	Glynase (micronized)®: 0.75-12mg/day; max 12mg/day (divide doses >6mg) glyburide: 1.25-20mg/day; max 20mg/day (divide doses >10mg)	Common side effects: Hypoglycemia, weight gain, GI upset **Precautions** hepatic/renal impairment increased risk of hypoglycemia with Glucotrol® XL if the patient misses a meal glyburide implicated in negative outcomes post-MI empty Glucotrol® XL tablet shell may appear in stool Glyburide – increased risk of prolonged hypoglycemia in the elderly; micronized and conventional tablets are not bioequivalent Glimepiride – contraindicated if CrCl <15mL/min Glyburide and glipizide – preferred to not use in renal impairment, but dosing should be more conservative if use is needed
Glipizide (Glucotrol XL® and generics) ($20)			glipizide (immediate release): 2.5-20mg/day 30 min. prior to meals; max 40mg/day (divide doses >15mg) Glucotrol XL®: 2.5-10mg/day with breakfast; max 20mg/day	
Glimepiride (Amaryl® or generics) ($99)			1-4mg/day with breakfast; max 8mg/day	
Biguanides				
Metformin (Glumetza® and generics) ($144)	Decreases hepatic glucose production and	FPG: ⇩ 50-60mg/dl HbA1c: ⇩ 1.5-2%	500-2000mg/day with a meal increasing slowly by 500mg q1-2	Common side effects: Nausea, diarrhea

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3/ 2011, 7/2013, 3/2014, 3/ 2015, 5/2016, 5/2017, 5/2018, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023		May 2024 Ambulatory Best Practice Condition: Diabetes Mellitus

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
Available in Liquid form, Riomet®, at a concentration of 500mg/5mL. ($800)	improves insulin sensitivity	⇩ TG, LDL, Chol ⇧ HDL	weeks; max 2550mg/day (2-3 times a day dosing is more effective and better tolerated; divided doses >2000mg into 3x/day dosing) <u>Extended-release tablets:</u> 500mg-2000mg/day with evening meal increasing by 500mg weekly; 2000mg/day (if 2000mg/day ineffective, may try 1000mg twice a day or switch to regular release metformin on a mg-per-mg basis) Adjusting for reduced GFR: If eGFR ≥30 to <45 mL/minute/1.73 m^2: Do not initiate therapy. In patients currently receiving metformin, assess benefits and risks of continuing therapy; may continue at a reduced dose up to a maximum of 500mg 2x/day and advising patients to stop the drug for nausea, vomiting, or dehydration. If eGFR <30 mL/minute/1.73 m^2: Do not initiate therapy. If on metformin, discontinue use.	- often resolve after 2-3 weeks of use and minimized by taking with a meal or using XL formulation Vitamin B12 deficiency may occur with chronic use; periodic monitoring is recommended **Precautions** For patients who will receive intra-arterial contrast or patients with eGFR between 30 and 60 or patients with a history of liver disease or heart failure who will receive intravascular iodinated contrast media, do not administer metformin at the time of or for 48 hours after procedures and resume therapy only when normal renal function returns. Avoid in patients with frequent alcohol use, or liver or kidney disease due to increased risk of lactic acidosis. Avoid in patients with unstable heart failure. Obtain eGFR at least annually in all patients taking metformin. Assess more frequently in patients at increased risk of renal impairment such as the elderly.
Alpha-Glucosidase Inhibitors				
Acarbose (generics only) ($105)	Delays dietary absorption of complex carbohydrates thereby	FPG: little effect HbA1c: ⇩ 0.5-1% PPG: ⇩ 50mg/dl	25mg three times a day with the first bite of each main meal increasing to 50mg three times a day and then	Common side effects: abdominal pain, diarrhea, bloating.

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
	lowering postprandial glucose		100mg three times a day after 4-8 weeks; max 100mg three times a day if patient is >60kg and 50mg three times a day if ≤60kg	flatulence, ↑ LFTs (with acarbose only) **Precautions** Not recommended for patients with CrCL<25mL/min or SCr>2mg/dl. Asymptomatic / reversible increases in AST and/or ALT have occurred in up to 14% of acarbose-treated patients. Fulminant hepatitis- rare. Contraindicated in patients with inflammatory bowel disease, colonic ulceration, or intestinal obstruction. Use glucose to treat hypoglycemia – sucrose products are ineffective due to the medication's mechanism of action
Miglitol (generics only) ($347)			25mg three times a day with the first bite of each main meal increasing to 50mg three times a day after 4-8 weeks and may be increased to 100mg three times a day after 3 months; max 100mg three times a day	
Thiazolidinediones				
Pioglitazone (Actos® and generics) ($349)	Improves insulin sensitivity and increases peripheral glucose disposal	FPG: ⇩ 50-100mg/dl HbA1c: ⇩ 1-2% ⇧ LDL, Chol, HDL	15-30mg once daily (increase in15mg increments; max 45mg/day)	Common side effects: edema, weight gain, hypoglycemia, diarrhea, ↑ LFTs **Precautions** Not recommended for patients with NYHA class III or IV heart failure, CYP450 drug interactions, or with history of CAD. If patient is stable on medication continue at lower dosage and continue to monitor.

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Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
Meglitinides				
Repaglinide (generics only) ($330)	Stimulates glucose-dependent insulin secretion Short half-life (1 hr.) – quick onset (15-30 min)	FPG: 10-40mg/dl HbA1c: ⇩ 0.5-2% PPG: ⇩ 50mg/dl	0.5-2mg 15-30 minutes before each meal, depending on a1c; max 4mg/dose and 16mg/day At least 1 week should elapse between dose adjustments	Common side effects: hypoglycemia, weight gain **Precaution** hepatic and renal impairment, CYP450 drug interactions
Nateglinide (generics only) ($155)			60-120mg three times a day 30 minutes prior to each meal; max 120mg/dose and 360mg/day	
Dipeptidyl Peptidase IV Inhibitors				
Sitagliptin (brand only - Januvia®) ($657)	inhibits dipeptidyl peptidase IV (DPP-IV) enzymes resulting in prolonged active incretin levels.	HbA1c: ⇩ 0.5-0.6%	100 mg once daily	Adjust dose in renal dysfunction for sitagliptin, saxagliptin, and alogliptin No dosage adjustment required for mild-moderate hepatic impairment (sitagliptin, saxagliptin). Use 2.5mg saxagliptin daily for patients with CrCl ≤45 ml/min or if on a CYP3A4/5 inhibitor (ex: azole antifungal, protease inhibitor, clarithromycin). 2.5mg post dialysis for patients with ESRD requiring hemodialysis. Effectiveness of linagliptin is decreased when used in combination with CYP3A4 inducers (ex: rifampin) – use alternative therapy
Saxagliptin (brand only - Onglyza®) ($582)			2.5-5mg once daily	
Linagliptin (brand only - Tradjenta®) ($630)			5mg once daily	
Alogliptin (Nesina® and generics) ($234)			25mg once daily	

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Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
				No dosage adjustment for linagliptin needed for renal or hepatic impairment. Acute and chronic pancreatitis have been reported with DPP-IV inhibitor use; monitor for signs/ symptoms of pancreatitis Cases of fatal and nonfatal hepatic failure have been reported. Monitoring and appropriate therapy interruption is necessary
Sodium-Glucose-Cotransporter 2 Inhibitors				
Canagliflozin (brand only - Invokana®) ($718) FDA approved for cardiovascular disease benefit	Reduces reabsorption of filtered glucose from the tubular lumen and lowers renal threshold for glucose	HbA1C ↓0.77-1.03% FBG↓36-43 mg/dl	Initial 100 mg once daily prior to first meal of day; may increase to 300 mg once daily (only in patients with CrCL ≥60). Max dose 300 mg once daily. CrCL 30 to <60: Max dose 100 mg daily CrCL <30, ESRD, and hemodialysis: avoid use	SGLT2 inhibitor use may lead to ketoacidosis. Patients should seek medical attention if they experience any signs or symptoms they may be related to ketoacidosis. Side Effects: May increase risk of genital mycotic infections; may cause hypotension due to intravascular depletion in patients with renal impairment; may cause hyperkalemia, may cause dose-related LDL elevation
Dapagliflozin (brand only - Farxiga®) ($678) FDA approved for cardiovascular disease, heart failure, and chronic kidney disease benefit		HbA1C ↓0.8-0.9% FBG↓ 24-29 mg/dl	Initial 5 mg once daily in the morning with or without food; may increase to 10 mg once daily CrCL <45: use not recommended CrCL <25, ESRD, and hemodialysis: avoid use	
Empagliflozin (brand only - Jardiance®) ($712)		HbA1C ↓0.8% FBG↓ 19 -25 mg/dl	Initial: 10 mg once daily; may increase to 25 mg once daily	

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Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
FDA approved for cardiovascular disease and heart failure benefit			CrCL < 30, ESRD, and hemodialysis: avoid use	
Ertugliflozin (brand only - Steglatro®) ($409)		HbA1C ↓0.7-0.8% FBG↓ 31-36 mg/dl	Initial 5mg once daily; may increase to 15mg once daily CrCL <45 use not recommended ESRD, and hemodialysis: use contraindicated	
Glucagon-Like Peptide-1 Receptor Agonists				
Semaglutide (brand only - Rybelsus®) ($1123)	Glucose dependent insulin release, lowers glucagon during hyperglycemia, slows gastric emptying, reduces food intake through increase in satiety. Secondary effect of medication is weight loss or prevention of weight gain as glucose control improves	HbA1C ↓1.2-1.4%	3mg daily for 30 days then increase to 7mg daily; 3mg dose is not clinically effective Can increase to maximum dose of 14mg daily after 30 days of 7mg daily Give 30-60 minutes before all food, medications, or beverages in the morning Do not split, crush, or chew To convert from SC to PO: 0.5mg weekly dose is equivalent to 7mg or 14mg of PO dose starting within 7 days of last injection 1mg weekly dose is equivalent to 14mg PO dose starting within 7 days of last injection To convert from PO to SC: 7mg and 14mg daily dose should be changed to 0.5mg weekly dose starting	Boxed warning: contraindicated in patients with personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2 Side effects: nausea and abdominal pain (decreased by starting at 3mg dose) Monitor for symptoms of acute kidney injury, diabetic retinopathy, cholelithiasis, pancreatitis

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			at when next PO dose would be given with close glucose monitoring during transition	
Combination Medications				
Sulfonylurea + Biguanide				
metformin + glyburide (generics only)($64)	Stimulates the release of insulin from the pancreas; increases the sensitivity of peripheral tissues to insulin; and decreases hepatic glucose production	FPG: ⇩ 50mg/dl HbA1c: ⇩ 2%	initial treatment: 1.25mg/250mg once daily with meals (twice daily if a1c>9% or FPG >200mg/dL) and increase by 1.25mg/250mg every 2 weeks; max 10mg/2000mg/day previously treated patients: 2.5mg/500-5mg/500mg twice a day with meals and increase by 5mg/500mg; max 20mg/2000mg/day	Hypoglycemia, weight gain, diarrhea, GI upset **Precautions** See individual agents The starting dose of metformin +glipizide should not exceed the current dose of metformin or glipizide already being taken
metformin + glipizide (generics only) ($59)			initial treatment: 2.5mg/250mg daily or 2.5mg/500mg twice a day with meals if FPG 280-320mg/dL and increase by 1 tablet daily every 2 weeks; max 10mg/2000mg daily in divided doses previously treated patients: 2.5mg/500mg – 5mg/500mg twice a day with meals and increase in increments not to exceed 5mg/500mg; max 20mg/2000mg daily in divided doses	
Thiazolidinedione + Sulfonylurea				

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
Pioglitazone + Glimepiride (Duetact(R) and generics) ($489)	Improves insulin sensitivity and increases peripheral glucose disposal; Stimulates the release of insulin from the pancreas		Initial dose should be based on current dose of pioglitazone and/or sulfonylurea. Patients inadequately controlled on glimepiride alone: Initial dose: 30 mg/2 mg or 30 mg/4 mg once daily Patients inadequately controlled on pioglitazone alone: Initial dose: 30 mg/2 mg once daily Maximum dose: Pioglitazone 45 mg/glimepiride 8 mg daily	Edema, weight gain, hypoglycemia, diarrhea, ↑ LFTs. May cause or exacerbate heart failure. Not recommended in any patient with symptomatic heart failure; initiation contraindicated with NYHA class III or IV heart failure
Thiazolidinedione + Biguanide				
Pioglitazone + metformin (Actoplus Met® and generics) ($320)	Improves insulin sensitivity and decreases hepatic glucose production	FPG: 33-48mg/dl HbA1c: ⇩0.6-0.8%	Initial dose should be based on current dose of pioglitazone and/or metformin; daily dose should be divided and given with meals. If not switching from individual components, initial dose is 15mg/500mg twice daily or 15mg/850mg once daily Patients inadequately controlled on metformin alone: Initial dose: 15mg/500mg or 15mg/850mg twice daily depending on current dose of metformin. Patients inadequately controlled on pioglitazone alone: Initial dose: 15mg/500mg twice daily or 15mg/850mg once daily	Edema, weight gain, hypoglycemia, diarrhea, ↑ LFTs, nausea, diarrhea **Precautions** CYP450 drug interactions Temporarily discontinue 48 hours prior to procedures involving intravascular iodinated contrast media or surgery and resume therapy only when normal renal function returns. Avoid in patients with frequent alcohol use, or liver or kidney disease due to increased risk of lactic acidosis. Check LFTs at baseline and periodically thereafter. D/C if LFTs>3x upper limit of normal.

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Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			Dosing adjustment: Doses may be increased as increments of pioglitazone 15 mg and/or metformin 500-850 mg, up to the maximum dose; doses should be titrated gradually. Guidelines for frequency of adjustment (adapted from rosiglitazone/metformin combination labeling): ▪ After a change in the metformin dosage, titration can be done after 1-2 weeks ▪ After a change in the pioglitazone dosage, titration can be done after 8-12 weeks ▪ Maximum dose: Pioglitazone 45 mg/metformin 2550 mg daily. Metformin daily dose >2000mg better tolerated as 3x/day dosing.	Contraindicated in severe renal impairment (eGFR < 30 ml/min)
Dipeptidyl Peptidase IV Inhibitor + Biguanide				
Sitagliptin + metformin (brand only - Janumet®, Janumet XR®) ($656)	inhibits dipeptidyl peptidase IV (DPP-IV) enzymes resulting in prolonged active incretin levels and decreases hepatic glucose production and improves insulin sensitivity	FPG: ⇩ 50-60mg/dl HbA1c: ⇩ 1.5-2% ⇩ TG, LDL, Chol ⇧ HDL	Initial doses should be based on current dose of sitagliptin and metformin; daily doses should be divided and given twice daily with meals (immediate release) or once daily (extended release). Maximum: Sitagliptin 100 mg/metformin 2000 mg daily Patients inadequately controlled on metformin alone: Initial dose: Sitagliptin 100 mg/day plus current daily dose of metformin. Note: Per manufacturer labeling, patients currently receiving metformin 850 mg twice daily should receive an initial	Avoid metformin in severe renal impairment, an eGFR <30 ml/min Avoid with hepatic insufficiency or clinical or laboratory evidence of hepatic disease

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			dose of sitagliptin 50 mg and metformin 1000 mg twice daily Patients inadequately controlled on sitagliptin alone: Initial dose: Metformin 1000 mg/day plus sitagliptin 100 mg/day. Note: Patients currently receiving a renally adjusted dose of sitagliptin should not be switched to combination product. Dosing adjustment: Metformin component may be gradually increased up to the maximum dose. Maximum dose: Sitagliptin 100 mg/metformin 2000 mg daily	
Linagliptin plus metformin (brand only - Jentadueto®, Jentadueto XR®) ($630)			Initial doses should be based on current doses of the components. Should be given in 2 divided doses (immediate release) or once daily (extended release). Patients inadequately controlled on metformin alone: Initial dose: linagliptin 5mg/day plus current daily dose of metformin Patients inadequately controlled on linagliptin alone: initial dose: linagliptin 5mg and metformin 1000mg daily When converting from immediate to extended-release dose is 5mg	

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			linagliptin and current daily dose of metformin once daily. Dosing Adjustment: Metformin component may be gradually increased to the maximum dose. Maximum dose: Linagliptin 5 mg / metformin 2000 mg daily.	
Saxagliptin plus metformin (brand only - Kombiglyze ER®) ($582)			Initial doses should be based on current daily dose of the components. Should be administered once daily. Note: Patients requiring saxagliptin 2.5mg and metformin >1000mg/day should not be switched to combination product. Patients inadequately controlled on metformin alone: initial: saxagliptin 2.5-5mg once daily plus current daily dose of metformin. Patients inadequately controlled on saxagliptin alone: initial: 5mg/500mg once daily. Maximum dose: saxagliptin 5mg/metformin 2000mg once daily	
Alogliptin plus metformin (Kazano® and generics) ($234)			Initial doses should be based on current daily dose of the components.	

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			Usual dosing: 12.5mg/500-1000mg twice daily Maximum dose: 12.5mg/1000mg twice daily	
Alogliptin plus pioglitazone (Oseni® and generics) ($234)			Initial doses should be based on current daily dose of the components Patients inadequately controlled on pioglitazone alone: 25mg alogliptin plus current daily dose of pioglitazone once daily Patients inadequately controlled on alogliptin 25mg/15mg or 25mg/30mg once daily Maximum dose: 25mg/45mg daily	
Sodium-Glucose Contransporter-2 Inhibitor + Biguanide				
Canagliflozin plus metformin (brand only - Invokamet®, Invokamet XR®) ($718)	See individual agents		Initial dose: 50mg/500mg twice daily (IR) or 100mg/1000mg once daily (XR) Max daily dose: 300mg/2000mg Patients on metformin: Initial dose: canagliflozin 100 mg plus similar total dose of metformin daily. Note: patients taking metformin ER in the evening should skip the last dose before starting combination product the following morning. Patients on canagliflozin: Initial dose: Metformin 1000 mg daily plus similar total dose of canagliflozin daily.	See individual agents

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			Patients switching from immediate to extended release: use current total daily dose once daily Invokamet®: daily dose is 1 tab twice daily Patients on metformin: Initial dose: canagliflozin 50 mg plus similar total dose of metformin daily. Patients on canagliflozin: Initial dose: Metformin 500 mg daily plus similar total dose of canagliflozin daily. Patients switching from combination therapy of canagliflozin and metformin as separate tablets: Use current total dose.	
Dapagliflozin plus metformin (brand only - Xigduo XR®) ($678)			Xigduo XR®: Initial daily dose: 5mg/500mg once daily Note: patients taking metformin ER in the evening should skip the last dose before starting the combination product the next morning Max daily dose: 10mg/2000mg once daily.	
Empagliflozin plus metformin (brand only - Synjardy®, Synjardy XR®) ($712)			Immediate release: administered in 2 divided doses Extended release: administered once daily	

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Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
			Patients on metformin: empagliflozin 10mg/day plus similar total daily dose of metformin Patients on empagliflozin: metformin 1000mg/day plus similar total daily dose of empagliflozin Max daily dose: 25mg/2000mg	
Ertugliflozin plus metformin (brand only - Segluromet®) ($409)			Patients on metformin: ertugliflozin 5mg/day plus similar total daily dose of metformin in 2 divided doses Patients on ertugliflozin: metformin 1000mg/day plus similar total daily dose of ertugliflozin in 2 divided doses Max daily dose: 15mg/2000mg	
Sodium-Glucose Contransporter-2 Inhibitor + Dipeptidyl Peptidase IV Inhibitor				
empagliflozin plus linagliptin (brand only - Glyxambi®) ($712)	See individual agents		Initial: Empagliflozin 10 mg/linagliptin 5 mg once daily; may increase to empagliflozin 25 mg/linagliptin 5 mg once daily	See individual agents
Dapagliflozin plus saxagliptin (brand only - Qtern®) ($678)			5mg dapagliflozin/ 5mg saxagliptin daily Max daily dose: 10mg dapagliflozin/5mg saxagliptin	
Ertugliflozin plus sitagliptin (brand only - Steglujan®) ($660)			5mg ertugliflozin/100mg sitagliptin once daily Max daily dose: 15mg ertugliflozin/100mg sitagliptin	

Class/Agent	Mechanism of Action	Efficacy	Typical Dose	Relevant Clinical Information
Sodium-Glucose Contransporter-2 Inhibitor + Dipeptidyl Peptidase IV Inhibitor + Biguanide				
Empagliflozin plus metformin plus linagliptin (brand only – Trijardy XR®) ($712)			Patients not taking empagliflozin: empagliflozin 10mg/day, linagliptin 5mg/day, and similar total daily dose of metformin with morning meal Patients taking empagliflozin: linagliptin 5mg/day, same total daily dose of empagliflozin, and similar total daily dose of metformin with morning meal Max daily dose: 25mg/2000mg/5mg	

INSULINS

Type	Onset	Peak	Duration	Rx/ OTC	Cost
Rapid					
lispro (Humalog®, Admelog®)*	15-30 minutes	30-90 minutes	3-5 hours	Rx	Vial $30/300units (=$99/1000 units) Pen $38/300 units (=$127/1000 units)
Lispro (Lyumjev®)	15-20 minutes	2-3 hours	4-7 hours	Rx	Vial $99/300 units (=$327/1000 units) Pen $127/300 units (=$424/1000 units)
Insulin aspart (NovoLog®, Flasp®) †	10-20 minutes	40-50 minutes	5-8 hours	Rx	Vial $174/1000 units. Pen $134/300 units
Insulin glulisine (Apidra®)	12-30 minutes	30-90 minutes	3-4 hours	Rx	Vial $341/1000 units. Pen $132/300 units
Insulin Oral Inhalation - Rapid					
Afrezza® (contraindicated in patients with COPD or asthma)	15-30 minutes	53 minutes	2-3 hours	RX	$510/360 units (=$1417/1000 units)
Short					
Regular (Humulin R , Novolin R, ReliOn)	30-60 minutes	2-4 hours	6-8 hours	OTC/Rx	$165/1000 units
Intermediate					
NPH (Humulin N, Novolin N, Novolin N Relion N)	1-2 hours	4-12 hours	10-24 hrs.	OTC	$165/1000 units
Long					
Insulin glargine (Lantus® Toujeo®, Semglee®, Rezvoglar®) ‡	1-2 hours	(No pronounced peak)	>24 hours	Rx	Vial $118/1000 units Pen $35/300 units
Insulin glargine (Basaglar®)	1-2 hours	(No pronounced peak)	>24 hours	Rx	Pen $78/300 units
Insulin detemir (Levemir®)	3-4 hours	6-8 hours	6-23 hours	Rx	Vial $370/1000 units Pen $111/300 units
Insulin glargine 300u/ml (Toujeo®, Toujeo Max®)	Up to 6 hours	12-20 hours	Up to 36 hours	RX	Pen $163/450 units
Insulin degludec 100 or 200 units/mL (Tresiba®)	1 hour	(No pronounced peak)	>42 hours	Rx	Vial $142/1000 units Pen $244/600 units
Combination					
70/30 (Humulin 70/30, Novolin 70/30) (70% NPH/30% regular)	30-60 minutes	3-12 hours	12-20 hours	OTC	Vial $166/1000 units Pen $62/300 units
Humalog® Mix 75/25 (75% lispro protamine/25% lispro)*	15-30 minutes	1-3 hours	10-20 hours	RX	Vial $342/1000 units Pen $127/300 units
Humalog 50/50 (50% lispro protamine/50% lispro) *	15-30 minutes	1-3 hours	10-20 hours	RX	Vial $342/1000 units Pen $127/300 units
NovoLog® Mix 70/30 (70% insulin aspart protamine/30% insulin aspart) †	10-20 minutes	1-4 hours	12-24 hours	RX	Vial $180/1000 units Pen $134/300 units

*Lispro insulin (Humalog®), Humalog® Mix 75/25, and Humalog® 50/50 should be given 0-15 minutes before a meal or immediately after a meal

†Insulin aspart (NovoLog®) and NovoLog® Mix 70/30 should be given 0-10 minutes before a meal

‡Dosing recommendations for insulin glargine (Lantus®): Note: Insulin glargine should not be mixed with other types of insulin

Switching from once daily NPH to insulin glargine: no change in dosage.

Switching from twice a day NPH to insulin glargine: decrease insulin glargine dose by 20% and titrate to patient's response to reduce incidence of hypoglycemia

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date: May 2023**	**Next Scheduled Review Date:**
3/ 2011, 7/2013, 3/2014, 3/ 2015, 5/2016, 5/2017, 5/2018, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023		May 2024 Ambulatory Best Practice Condition: Diabetes Mellitus

NON-INSULIN INJECTABLE MEDICATIONS				
Class/Agent	**Mechanism of Action**	**Efficacy**	**Typical Dose**	**Relevant Clinical Information**
Amylinomimetic Agent				
Pramlintide (brand only - Symlin®)($603-$715/pen)	Slows the rate of postprandial glucose increase by slowing gastric emptying, suppressing glucagon secretion, and decreasing food intake through increase in satiety.	HbA1c: ⇩0.5- 1% Weight: ⇩1-2kg	Type 1 diabetes: initiate with 15 mcg SC immediately prior to each main meal and increase by 15 mcg increments every 3 days to 30-60 mcg Type 2 diabetes: initiate with 60 mcg SC immediately prior to each main meal and increase to 120 mcg when tolerated Increase dose only when no significant nausea has occurred for 3-7 days. If significant nausea, reduce to prior dose.	Common side effects: hypoglycemia, nausea, diarrhea, vomiting (usually mild) Contraindications: gastroparesis, hypoglycemia unawareness Do not mix with insulin Reduce pre-prandial insulin doses (rapid and short acting insulin and 70/30, 50/50, 75/25) by 50% Administer into abdomen or thigh only due to variable absorption through the arm
Glucagon-Like Peptide-1 Receptor Agonist				
Exenatide (brand only - Byetta®) ($412-$825/pen)	Glucose dependent insulin release, lowers glucagon during hyperglycemia, slows gastric emptying, reduces food intake through increase in satiety. Secondary effect of medication is weight loss or prevention of weight gain as glucose control improves	FPG: 15-25mg/dl HbA1c: ⇩ 1% Weight: ⇩2.5-4kg	5mcg SC up to 60 minutes prior to the morning and evening meals. After 1 month, can increase to 10mcg per dose Use not recommended in severe renal impairment (CrCl<30 mL/minute).	**Class Warning**: Risk of thyroid tumors Contraindicated in patients with a personal or family history of medullary thyroid cancer or Multiple Endocrine Neoplasia Syndrome type 2. Cases of acute pancreatitis have been reported **Class side effects**: Hypoglycemia Nausea, diarrhea, vomiting (usually mild) Exenatide, Dulaglutide, Albiglutide
Exenatide extended release (brand only – Bydureon BCise®) ($241/pen)			2 mg once weekly without regard to meals (may administer missed dose as soon as noticed as long as the next scheduled dose is at least 3 days away, then resume schedule of every 7 days) Converting from immediate release: start ER the day after stopping IR. This may cause high blood glucose for ~2 weeks.	

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NON-INSULIN INJECTABLE MEDICATIONS				
Class/Agent	**Mechanism of Action**	**Efficacy**	**Typical Dose**	**Relevant Clinical Information**
Liraglutide (brand only - Victoza®) ($447/pen) FDA approved for cardiovascular disease benefit			0.6mg SC daily x 1 week, then 1.2mg SC daily. 0.6mg dose is not therapeutic. May increase to 1.8mg SC daily. Allow at least 1 week in between dose increases. Given independent of meals.	Not recommended to be used in patients with gastroparesis or severe gastrointestinal disease. Liraglutide: Most common side effects are GI and may be dose related. Exenatide: Can be used in combination with metformin, a sulfonylurea, or both. May need to reduce sulfonylurea dose. Anti-exenatide antibodies: Use may be associated with the development of anti-exenatide antibodies. Semaglutide: Monitor for symptoms of: Acute kidney injury, diabetic retinopathy, cholelithiasis, pancreatitis Tirzepatide: monitor for symptoms of: acute kidney inury, diabetic retinopathy, gallbladder disease, medullary thyroid carcinoma, and pancreatitis
Dulaglutide (brand only - Trulicity®) ($279/pen) FDA approved for cardiovascular disease benefit			0.75 mg SubQ once weekly; may increase by 1.5mg increments after at least 4 weeks at previous dose if inadequate response up to a max dose of 4.5mg weekly	
Semaglutide (brand only – Ozempic®) ($1123/pen) FDA approved for cardiovascular disease benefit			0.25mg weekly for four weeks, then increased to 0.5mg weekly. Can increase to 1mg weekly in another 4 weeks if needed (0.25mg dose is not clinically effective) To convert from SC to PO: 0.5mg weekly dose is equivalent to 7mg or 14mg of PO dose starting within 7 days of last injection 1mg weekly dose is equivalent to 14mg PO dose starting within 7 days of last injection	
Tirzepatide (brand only – Mounjaro®) ($307/pen)			2.5 mg once weekly for four weeks, then increase to 5mg once weekly. Can continue to increase by 2.5mg weekly increments every 4 weeks if needed up to a maximum weekly dose of 15mg/week. (2.5mg dose is not clinically effective)	
Insulin + Glucagon-Like Peptide-1 Receptor Agonist				
Insulin degludec plus liraglutide (brand only - Xultophy®)	See individual components		In patients not taking basal insulin or GLP-1 agonist: Initial dose: 10 units/0.36mg once daily	See individual components

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NON-INSULIN INJECTABLE MEDICATIONS				
Class/Agent	**Mechanism of Action**	**Efficacy**	**Typical Dose**	**Relevant Clinical Information**
($297/pen)			In patients already using basal insulin or GLP-1 agonist: Initial dose: 16 units/0.58mg once daily Dose may be titrated up or down every 3-4 days in increments of 2 units/0.072mg Maximum daily dose: 50units/1.8mg	