

ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline

# Type 2 Diabetes

Approved June 27, 2024

Next review to begin December 2025

# **Type 2 Diabetes Executive Summary**

- **Prevention:** Weight loss, healthy eating, physical activity, and smoking cessation are essential in both prevention and treatment of diabetes.
- **Prevention:** Engage patients with overweight/ obesity and high risk of T2D in key prevention strategies, including referral to a Diabetes Prevention Program (DPP).
- **Screening**: Given the high risk nature of Eastern North Carolina (ENC) populations, screen adults annually starting at age 35. Patients who are high risk should be screened annually regardless of age.

#### **Principles of Care**:

- First line of treatment includes healthy lifestyle management and individualized pharmacotherapy based on comorbidities and goals.
- The choice of therapy depends on the patient's obesity, cardiac, cerebrovascular, and renal status. Combination therapy is usually required and should involve agents with complementary mechanisms of action.
- Comorbidities must be managed must be managed for comprehensive care, including management of lipid and BP abnormalities with appropriate therapies and treatment of other related conditions.
- The A1C target should be individualized based on numerous factors, such as age, life expectancy, comorbid
  conditions, duration of diabetes, and risk of hypoglycemia and adverse consequences of hypoglycemia, patient
  - motivation, and adherence. An A1C level of ≤6.5% is optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate and may change for a given individual over time. We endorse as a minimum standard an A1C of <9%. Minimizing the risk of both severe and non-severe hypoglycemia is a priority.
- Medication adjustments should be made at an interval where targets can be achieved as soon as possible. A person-centered shared decision making approach should guide choice of pharmacologic agents.
- Continuous Glucose Monitoring (CGM) is recommended whenever indicated to assist patients in reaching glycemic goals safely.
- Consider referral to Diabetes Self-Management Education and Support (DSMES) program, Certified Diabetes Care and Education Specialist (CDCES), Medical Nutrition Therapy (MNT), Dietitian, Behavioral Health Professional, and/or Lifestyle Medicine Clinic.
- Annually, perform a complete medical exam including history, physical exam, supporting labs, lifestyle factors, medications and vaccinations, behavioral and diabetes self-management skills, and technology use.
- Assess Social Determinants of Health (SDOH) needs and make referrals as needed.
- When experiencing uncontrolled glucose or unexpected complications, consider referral to appropriate specialists, including endocrinologist/diabetologist, ophthalmologist/ optometrist, nephrologist, podiatrist, dentists, audiologists, and others as needed.
- Utilize shared decision making throughout the trajectory of care to facilitate patient engagement in the process of their care.
- Address Potential Barriers to Effective DM Self-Care, including Social Determinants of Health (SDOH) needs, and implement interventions and make referrals as needed.
- Initiate goals of care and end of life discussions throughout care to empower the patient to make decisions.

We endorse as a <u>minimum standard an A1C level of <9%</u> consistent with the Coastal Plains Quality Metric, while adopting the AACE Principles of Management which state an A1C of  $\leq$ 6.5% is optimal, and <7% is often appropriate per the ADA standards .

#### **Recommended Follow-Up Intervals**

- For those with newly diagnosed T2D, follow up within one month of diagnosis.
- If hospitalized for diabetes, follow up within 7 days and monthly thereafter until stable.
- If A1C is >9%, follow up every 6 weeks 2 months.
- If A1C is 7-9%, follow up every 3 months.
- Once A1C is at goal and stable, we recommend a minimum 6month follow up for all patients for glycemic management.

The Type 2 Diabetes Care Pathway is sponsored by ECU Health in collaboration with partners from Access East, ECU Brody School of Medicine, ECU Physicians and The Outer Banks Medical Group.









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# **List of Abbreviations**

A1C Hemoglobin A1C

AACE American Association of Clinical Endocrinologists

ABCD Adiposity-based chronic disease

ACE American College of Endocrinology

ADA American Diabetes Association

ARB Angiotensin II receptor blockers

ASCVD Atherosclerotic cardiovascular disease

BGM Blood glucose monitoring

BMI Body mass index BP Blood pressure

CDCES Certified Diabetes Care and Education Specialist

CGM Continuous glucose monitoring

CrCl Creatinine clearance
CVD Cardiovascular disease
DKD Diabetic kidney disease

DPN Diabetic peripheral neuropathy
DPP Diabetes Prevention Program
DPP-4i Dipeptidyl peptidase-4 inhibitors

DSMES Diabetes Self-Management Education and Support

eGFR Estimated glomerular filtration rate

ENC Eastern North Carolina FPG Fasting plasma glucose

GDM Gestational diabetes mellitus

GIP Glucose-dependent insulinotropic polypeptide

GLP-1 RA Glucagon-like peptide 1 receptor agonist

HHS Hyperosmolar hyperglycemic state

IFG Impaired fasting glucose
IGT Impaired glucose tolerance
MNT Medical nutrition therapy
OGTT Oral glucose tolerance test
PAD Peripheral arterial disease
SDOH Social determinants of health

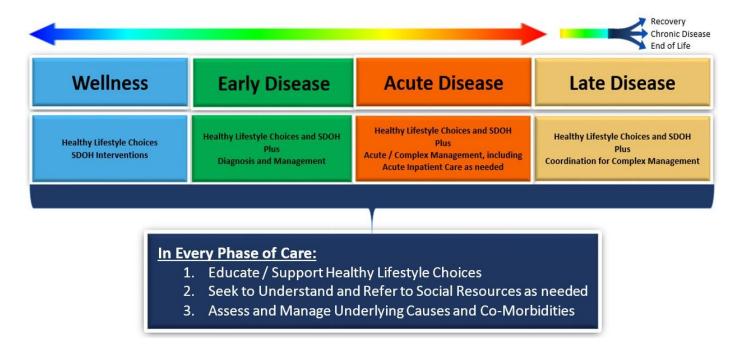
SGLT-2i Sodium-glucose cotransporter 2 inhibitor

SMBG Self-monitoring blood glucose

T2D Type 2 diabetes mellitus

UACR Urine albumin-to-creatinine ratio

# CARE PATHWAY MODEL The Full Continuum of Care



# **Call to Action**

- In North Carolina, 12.5% of the state's population (1.3 million) have been diagnosed with diabetes. The actual number of people in NC with diabetes is likely higher, since about 21% of the people with diabetes are undiagnosed. Diabetes rates differ across NC. The prevalence of diagnosed diabetes in ENC is 14.4% and is higher than the state average.
- Diabetes, particularly T2D, disproportionally affects all racial and ethnic minority groups in North Carolina. In 2018, the prevalence of diagnosed diabetes was about 31% higher for African Americans (15.9%) compared to non-Hispanic whites (12.2%).
- Complications of diabetes, particularly lower extremity amputation and end stage renal disease, are higher for African Americans and Native Americans.
- Diabetes was the primary cause for 23,713 hospitalizations at a cost of \$790 million in hospital charges in North Carolina in 2018, equaling over \$33,000 per hospitalized person with diabetes per year. If the state does not take steps to help bring the diabetes epidemic under control, annual healthcare costs are projected to surpass \$17 billion by 2025.

# **Care Pathway Purpose Statement**

The purpose of the Care Pathway project is to reduce morbidity and mortality associated with type 2 diabetes (T2D) in adults 18 years old and above through consistent application of evidenced based medicine. This pathway adopts the best practices described in the:

- American Diabetes Associations (ADA) Standards of Medical Care in Diabetes 2024
  - https://diabetesjournals.org/care/issue/47/Supplement 1
- Standards of Medical Care in Diabetes 2023 Abridged for Primary Care Providers
  - o <a href="https://diabetesjournals.org/clinical/article/41/1/4/148029/Standards-of-Care-in-Diabetes-2023-Abridged-for">https://diabetesjournals.org/clinical/article/41/1/4/148029/Standards-of-Care-in-Diabetes-2023-Abridged-for</a>
- The principles of management of Type 2 Diabetes in the Consensus Statement by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology on the Comprehensive Type 2 Management Algorithm – 2023 Update
  - o https://www.endocrinepractice.org/article/S1530-891X(23)00034-4/fulltext
- North Carolina's Guide to Diabetes Prevention and Management 2020.
  - o https://www.diabetesnc.com/
- "Treating Diabetic Peripheral Neuropathic Pain" by Tammy Lindsay MD et. al. Am Fam Physician. 2010 Jul 15;82(2):151-158.

The Type 2 Diabetes Care Pathway represents the best available information and will be updated periodically to reflect new findings. This Care Pathway is not intended to replace sound clinical judgement.

This Care Pathway should be used to facilitate conversations with the patient and family to make optimal care decisions with respect of available resources and with respect to special circumstances, preferences and needs of each individual patient. We adopt the 5 key recommendations from the ADA and the Association of Diabetes Care and Education Specialists consensus report "The Use of Language in Diabetes Care and Education" to guide the health care team on the use of language when speaking to patients with diabetes.

#### 5 key recommendations:

- Use language that is neutral, non-judgmental, and based on facts, actions, or physiology/biology.
- Use language free from stigma.
- Use language that is strength based, respectful, and inclusive and that imparts hope.
- Use language that fosters collaboration between patients and providers.
- Use language that is person-centered such as "person with diabetes" instead of "diabetic".

#### The goals of the Type 2 Diabetes Care Pathway are to:

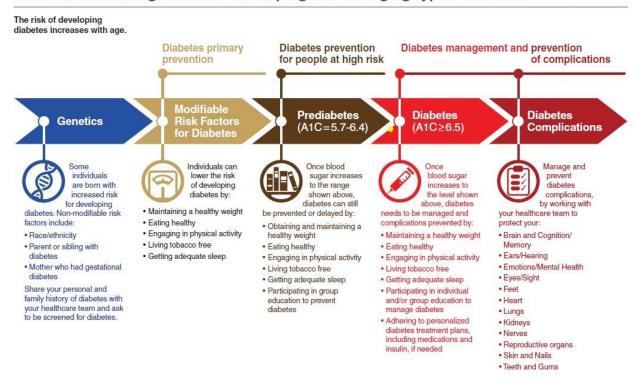
- Prevent T2D to the greatest degree possible
- Delay onset of T2D for as long as possible
- Provide a framework for T2D evidenced based care delivery in the most effective, efficient manner possible

#### **Type 2 Diabetes Evidence Overview**

Figures 1 and 2 outline our recommended patient centered approach for the prevention and treatment of T2D following the continuum of care.

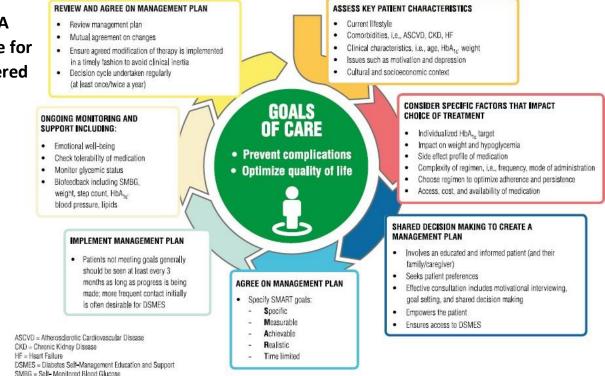
Figure 1 – Prevention and Management of T2D

Lifetime Risk Management for Developing and Managing Type 2 Diabetes



## DECISION CYCLE FOR PATIENT-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES

Figure 2 – ADA
Decision Cycle for
Patient-Centered
Glycemic
Management



## **WELLNESS**

**HEALTHY LIFESTYLE**: Adoption of a healthy lifestyle is critical for prevention and delay of T2D and is the first line in the treatment of T2D. Healthy lifestyle prevention strategies include:

#### **RECOMMENDATIONS:**

- Each patient should participate in the development of a lifestyle plan with the provider, a health coach, dietician, exercise specialist and/or the appropriate specialist.
- The plan should be documented and updated regularly during the first year of diagnosis and at least annually in future years.

Prevention Strategy	Recommendation
Maintain a healthy weight	Maintain normal body weight (body mass index of $18.5 - 24.9 \text{ kg/m}^2$ ) or if overweight/obese lose 5-7% of current weight.
Adopt healthy eating (examples of health eating patterns: Mediterranean style, DASH (Dietary Approaches to Stopping Hypertension), vegetarian, low fat, low carbohydrate, diabetes plate method)	Adopt diets rich in fresh fruits, non-starchy vegetables, whole grains and low-fat or fat-free dairy products.  Minimize saturated fats, sodium, added sugars and refined grains.  Avoid sugar-sweetened beverages and trans fats.  Drink alcohol in moderation if not contraindicated due to other medical conditions. Limit to one drink daily for women and two for men.
Be more physically active	Engage in 150 minutes or more of moderate to vigorous-intensity aerobic activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity. Include resistance training at least twice per week, with one or more sets of at least five different resistance-training exercises (unless not recommended).
Live tobacco free	Smoking is a proven risk factor for diabetes. People with diabetes that smoke are at heightened risk of premature death. Avoid using cigarettes, other tobacco products, and e-cigarettes.
Get adequate sleep	Adults need at least 7 hours of sleep per night to maintain good health.
Receive recommended vaccines	People with diabetes are at increased risk of severe illness from COVID-19, influenza, pneumococcal pneumonia, and respiratory syncytial virus. See Appendix (page X) for highly recommended immunizations for adults with diabetes.

#### Wellness Resources

Wellness activities can occur in a number of venues throughout the community, including clinics, health departments, and numerous medical and nonmedical resources. Some ENC resources that may be potential partners for T2D prevention are:

- Employer
- Non-Profit Organizations
- Commercial Programs

- Wellness Centers
- Hospital-Sponsored Programs
- Fire and Rescue Departments

- Faith-Based Programs State-Sponsored Programs
- Mental Health Programs

- Grants

- Insurance Carriers
- Corporate-Sponsored Programs (e.g., Roanoke Electric Membership Co-Op)

**SOCIAL DETERMINANTS OF HEALTH (SDOH):** It is estimated that 80% of a person's health is determined by social and environmental factors and the personal behaviors that emerge as a result. SDOH can support or adversely hinder a patient from adopting Healthy Lifestyle choices and from adhering to a medical regimen of

care.

The North Carolina Department of Health and Human Services and the Foundation for Health Care Leadership and Innovation launched a robust, web-based Resource Directory including local and state resources. The program, called NCCARE360 (<a href="https://nccare360.org/">https://nccare360.org/</a>), includes:

- Real Time Communication via a call center
- Capacity for Electronic Referrals
- Secure sharing of information [the patient must consent]
- Ability to track outcomes

See full SDOH Assessment example on page 33 in the Resources Section of this document.

#### **SDOH RECOMMENDATIONS:**

- Each patient should have a documented SDOH assessment.
- If needed, a consent should be obtained and SDOH referrals initiated.
- SDOH follow up should occur at minimum yearly with additional referrals as needed.
- Use the tools provided within the EHR to assess and track SDOH.
  - o Use the histories section of the chart.
  - SDOH Wheel is found in the Healthy Planet Longitudinal Plan of Care (HP LPOC) snapshot reports.
  - o All SDOH needs are found under Social

SCREENING: Screening is an effective way to detect T2D

at its earliest stages when lifestyle and medication options might be the most effective in preventing further progression or complications. Screening through an informal assessment of risk factors or with the ADA risk test (Figure 3, p. 13) is recommended to guide providers on whether performing a diagnostic test for prediabetes and previously undiagnosed T2D is appropriate.

Providers should begin testing at the age of 35 and should be repeated every three years for the adult who does not have risk factors or symptoms.

Providers should consider annual testing in overweight or obese individuals with a BMI ≥ 25 kg/m2, or 23 kg/m2 in Asian Americans, with one or more of the risk factors identified below:

- First degree relative (parent or sibling) with diabetes
- High risk race/ethnicity (African American, Hispanic/Latino, Native American, Asian American, or Pacific Islander)
- Hypertension (BP ≥ to 140/90 mm/Hg or on therapy for hypertension)
- HDL cholesterol ≤ 35 mg/dL (0.90 mmol/L) and/or triglycerides ≥ 250 mg/dL (2.82 mmol/L)
- Insulin-resistance-associated clinical conditions as noted above, acanthosis nigricans, pregnancy, or women who are overweight and currently planning pregnancy
- History of cardiovascular disease
- Women with Polycystic Ovarian Syndrome (PCOS)
- Physical inactivity

Annual testing is also recommended for patients with prediabetes.

#### **SCREENING RECOMMENDATIONS:**

- Test non-pregnant adults ≥ 35 y regardless of risk, repeat every three years if patient is risk and symptom free.
- Test non-pregnant adults who are high risk and patient with prediabetes yearly.
- Enroll patients with prediabetes to a DPP.
- Consider metformin therapy in those with prediabetes, with BMI > 35 kg/m2, those <60 years old, women with prior GDM.

#### **PREDIABETES**

- A1C 5.7 6.4%
- Impaired Glucose Tolerance (IGT) 140 – 199 mg/dL
- Impaired Fasting Glucose (IFG)
   100 125 mg/dL

Women who had gestational diabetes mellitus (GDM) should be tested 4-12 weeks postpartum and every 1-3 years for the remainder of their lives.

Figure 3 – Sample Screening Tool for Type 2 Diabetes in Asymptomatic Adults



# Are you at risk for type 2 diabetes?

Diabetes Risk	lest	WRITE YOUR SCORE IN THE BOX.	Height		Weight (lbs.)	.0
I. How old are you'	?		4'10"	119-142	143–190	191+
Less th	nan 40 years (O points)		4'11"	124-147	148-197	198+
40-	-49 years (1 point)		5'0	128-152	153-203	204+
50-	69 years (2 points)		5'1"	132-157	158-210	211+
60 yes	ars or older (3 points)		5.5	136-163	164-217	218+
Are you a man o	a woman?		100000	III CONTRACTOR AND CO	The State of the S	100 September 1981
Man (1 point)	Woman (0 points)	~ ()   f   3	5'3"	141-168	169-224	225+
man (1 point)	vvorial (o polita)		10000	145-173	174-231	232+
	an, have you ever been		5.5	150-179	180-239	240+
diagnosed with g	estational diabetes?		5'6"	155-185	186-246	247+
Yes (1 point)	No (0 points)		57	159-190	191-254	255+
Do you have a m	other, father, sister or brothe		5'8	164-196	197-261	262+
with diabetes?	outer, radier, sister of broater	1. AV	5.9.	169-202	203-269	270+
Yes (1 point)	No (O points)		5' 10"	174-208	209-277	278+
, too ( ) portag		< J >	5'11"	179-214	215-285	286+
	een diagnosed with high		6.0.	184-220	221-293	294+
blood pressure?	***************************************		6'1"	189-226	227-301	302+
Yes (1 point)	No (0 points)	,	6'2"	194-232	233-310	311+
. Are you physical	ly active?	. —	6.3.	200-239	240-318	319+
Yes (0 points)	No (1 point)		6'4"	205-245	246-327	328+
Veste du la contra				1 point	2 points	3 points
. What is your wei S	ght category?ee chart at right.	<			gh less than th dumn: 0 points	
f you scored 5	or higher:	ADD UP YOUR SCORE.		51:775-783, 200	ng et al., Arm Intern N 3 * Original algoriti al diabetes as part of	hm was validate
lowever, only your do	isk for having type 2 diabetes. octor can tell for sure if you do		1 Navebullion	er You	A CONTRACTOR	
which blood glucose out not yet high enoug	or prediabetes, a condition in levels are higher than normal h to be diagnosed as diabetes. ee if additional testing is needed.		risk for	type 2 diabe fference in f	ou can manag ites. Small step selping you live	os make
Type 2 diabetes is more common in African Americans, Hispanics/Latinos, Native Americans, Asian Americans, and Native Hawaiians and Pacific Islanders.			a big difference in helping you live a longer, healthier life.  If you are at high risk, your first step is to visit your doctor to see if additional testing is needed.  Visit diabetes.org or call 1-800-DIABETES (800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.			
ligher body weight inc Asian Americans are at	reases diabetes risk for everyone. increased diabetes risk at lower est of the general public (about 15		(800-34 getting	2-2383) for i started, and	r call 1-800-DI information, tip I ideas for sim to help lower	os on ple, small

## **EARLY DISEASE**

**MEDICAL EVALUATION**: A successful medical evaluation is dependent on meaningful interactions between the patient and the provider and care team.

ADA recommends a comprehensive diabetes medical evaluation at initial, follow-up, and annual visits that include:

- Past Medical and Family History
- Physical Examination
- Laboratory Evaluation
- Medications and Vaccinations
- Lifestyle Factors
- Behavioral and Diabetes Self-Management Skills
- Technology Use

Components of the Medical Evaluation and Frequency are referenced in the Appendix on pages 33-35.

<u>DIAGNOSIS</u>: Prediabetes requires 1 abnormal test result using one of the three testing methods in the chart below. T2D diagnosis requires two abnormal test results from the same sample or two separate test samples for FPG and A1C. Separate test samples must be without delay.

Testing Method	Range for Prediabetes	Range for T2D
	Diagnosis	Diagnosis
Fasting Plasma Glucose* (FPG)	100 mg/dL - 125 mg/dL	≥ 126 mg/dL
Oral Glucose Tolerance Test (OGTT) 2 hr. plasma glucose during 75 g of glucose	140 mg/dL - 199 mg/dL	≥ 200 mg/dL
Hemoglobin A1C	5.7% - 6.4%	≥ 6.5%
Random Plasma Glucose**	N/A	≥ 200 mg/dL

<sup>\*</sup>Fasting is defined as no caloric intake for at least 8 hours.

#### **RECOMMENDATIONS:**

- Use a patient-centered communication style that includes active listening and literacy and numeracy assessment.
- Identify and treat cardiovascular risk factors including hypertension, dyslipidemia, and smoking.
- Ensure patient has annual eye and foot exams.
- The plan should be documented and updated regularly during the first year of diagnosis and at least annually in future years.
- Follow ADA Diagnostic and Treatment Thresholds.
- Provide patient education on common terms and basic information about diabetes.
- Determine CGM possibility.
- Schedule follow up visits before the patient leaves the office.

<sup>\*\*</sup>Use in patients with classic symptoms of hyperglycemia or hyperglycemia crisis.

#### PRINCIPLES IN MANAGEMENT AND TREATMENT:

<u>Prediabetes</u>: Patients with prediabetes should be enrolled in a Diabetes Prevention Program (DPP) or a behavioral lifestyle intervention program. Technology-assisted or online diabetes prevention interventions may be helpful too. For patients who smoke, use e-cigarettes, or use tobacco; counsel patients on tobacco cessation.

#### Treatment and goals to prevent diabetes include:

Metformin therapy for prevention of T2D should be considered in those with prediabetes, especially for those with BMI  $\geq$ 35, age 25-59, A1C  $\geq$ 6.0%, fasting glucose  $\geq$ 110, and individuals with prior GDM. Initial treatment goals for patients with prediabetes include:

- Lose 7% of initial body weight and maintain this weight loss.
- Increase physical activity to at least 150 min/week of moderate intensity.
- Adopt a healthy eating plan.
- Stop using tobacco products.

<u>Type 2 Diabetes:</u> The first line of treatment for T2D is typically lifestyle modifications and metformin for weight loss. In people with T2D who have an A1C > 10.0% and have symptoms, insulin may be considered. **Treatment goals for patients with diabetes include:** 

- Diabetes Self-Management goals including:
  - Lose 7% of initial body weight and maintain this weight loss.
  - Increase physical activity to at least 150 min/week of moderate intensity.
  - o Adopt healthy eating plan.
  - Stop using tobacco products.
- Blood pressure control if hypertension is present (see Hypertension Care Pathway).
- A1C target as follows:
  - An A1C goal of <7% for many non-pregnant adults without significant hypoglycemia is appropriate per the ADA.
  - A1C target should be individualized based on factors including life expectancy, hypoglycemia history, T2D duration, comorbidities including CVD and renal disease, and cognitive and psychological status. This target should be reassessed and updated at each visit to improve patient outcomes.

We endorse as a minimum standard an A1C level of <9% consistent with the Coastal

consistent with the Coastal Plains Quality Metric, while adopting the AACE Principles of Management which state an A1C of ≤6.5% is optimal, and <7% is often appropriate per the ADA standards.

#### **RECOMMENDATIONS:**

- Consider enrolling patients with prediabetes to a DPP.
- Consider enrolling patients with T2D to a DSMES program. Critical times to evaluate the need for DSMES program:
  - At diagnosis.
  - When not meeting treatment goals.
  - When new complicating factors arise that influence self-management.
  - When transitions in life or care occur.

<u>Healthy Lifestyle</u>: Lifestyle modification should be used to prevent diabetes, and it should be used as the first line of treatment for diabetes and ongoing management. See prevention strategies on page 10.

**Referrals:** Consider referral to additional resources to address patient care needs and/or obtainment of goals.

<u>Pharmacologic Therapy:</u> A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include effect of cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, impact on weight, cost, risk for side effects, and patient preferences.

- Metformin is the preferred initial pharmacologic agent for the treatment of T2D. Once initiated, metformin should be continued as long as it is tolerated and not contraindicated. Other agents should be added to metformin as indicated.
- Early combination therapy can be considered in some patients at treatment initiation to extend the time to treatment failure.
- The early introduction of insulin should be considered if there is evidence of ongoing catabolism (weight loss), if symptoms of hyperglycemia are present, or when A1C levels (>10%) or blood glucose levels (>300 mg/dL) are very high.
- Among patients with T2D who have established atherosclerotic cardiovascular disease (ASCVD) or
  indicators of high risk, established kidney disease, or heart failure, a sodium—glucose co-transporter 2
  inhibitor (SGLT2i) or glucagon-like peptide 1 receptor agonist (GLP-1 RA) with demonstrated CVD benefit
  is recommended as part of the glucose-lowering regimen independent of A1C and in consideration of
  patient-specific factors.
- Metformin can be used in patients with stable eGFR >30 mL/min. However, it should not be started in patients with an eGFR <45 mL/min. Reduction in total daily dose is prudent in patients with eGFR between 30 and 45 mL/min.
- In patients with T2D, a GLP-1 RA, including a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA, is the preferred injectable to insulin when possible. GLP-1 RA or dual GIP and GLP-1 RA should be continued, if possible, after insulin is initiated.
- Recommendation for treatment intensification for patients not meeting treatment goals should not be delayed.
- The medication regimen and medication-taking behavior should be reevaluated at regular intervals (every 3-6 months) and adjusted as needed to incorporate specific factors that impact treatment choice.
- In up to 16% of users, metformin is responsible for vitamin B12 malabsorption and/or deficiency, a causal factor in the development of anemia and peripheral neuropathy. In patients taking metformin who develop neuropathy, B12 should be monitored periodically and supplements given to affected patients, especially in those with anemia and peripheral neuropathy.
- Determination of blood glucose control can be achieved using A1C, fasting and postprandial self-monitoring blood glucose (SMBG), or CGM. It is prudent to monitor for hypoglycemic events, other adverse events, (such as weight gain, fluid retention, hepatic or renal impairment, or cardiovascular disease) as well as development of comorbid conditions, addition of new medication therapies, or complications of diabetes.

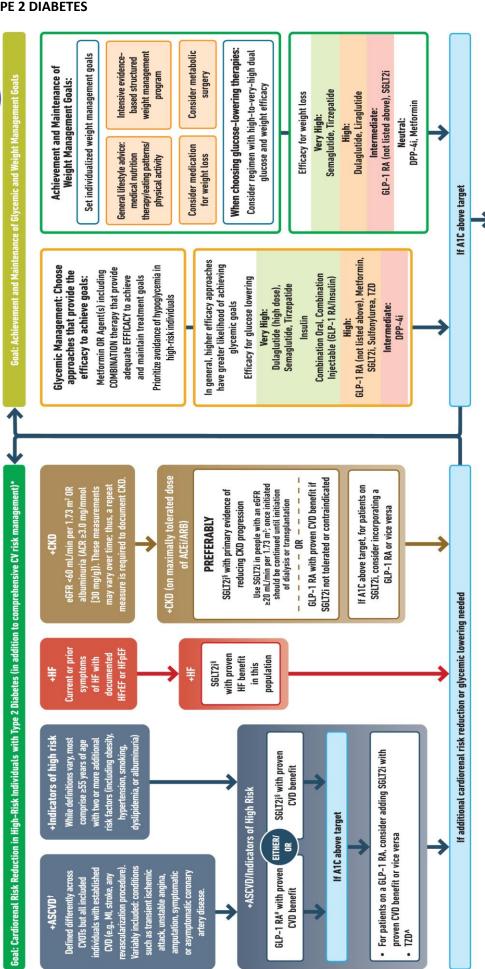
#### **FOLLOW UP INTERVALS:**

- For those with newly diagnosed T2D, follow up with care team within one month of diagnosis.
- If A1C is >9%, follow up with care team every 6 weeks 2 months.
- If A1C is between 7%-9%, follow up with care team every 3 months or 4 times per year.
- Once A1C is at goal and stable, follow up can usually occur at 3-6 month intervals. We recommend a minimum 6 month follow up of all patients for glycemic management.

Figure 9.3 from Standards of Care in Diabetes – 2024

# **USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES**

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

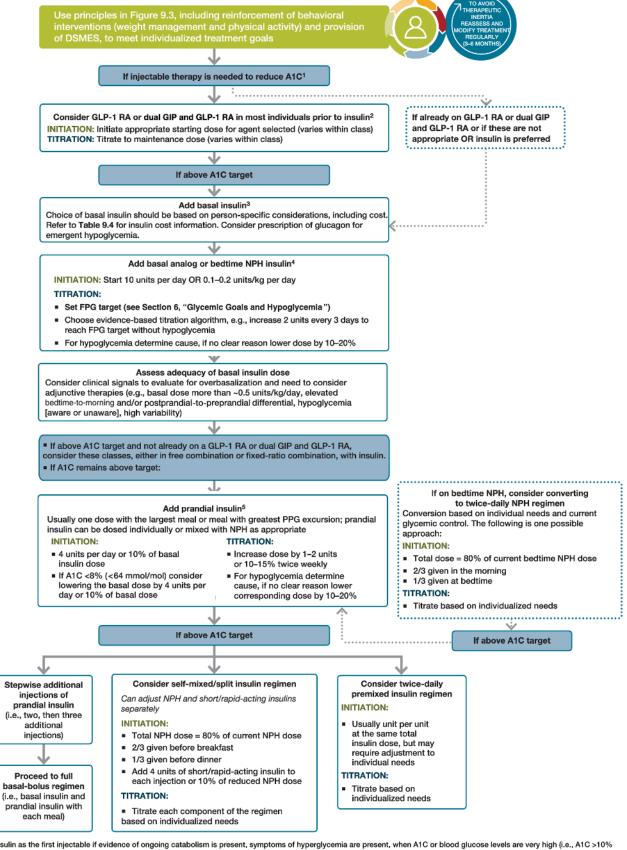


are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details. A Low-dose TZD may be better tolerated and similarly effective; § For SGLTZi, CVI recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, alt-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CV/D; In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of melformin; + A strong # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, alt-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVO.

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
   Consider technology (e.g., diagnostic C6M) to identify therapeutic gaps and tailor therapy Identify and address SD0H that impact achievement of goals

Figure 9.4: Intensifying to injectable therapies in T2DM, from Standards of Care in Diabetes – 2024



- 1. Consider insulin as the first injectable if evidence of ongoing catabolism is present, symptoms of hyperglycemia are present, when A1C or blood glucose levels are very high (i.e., A1C > 10%) [>86 mmol/mol] or blood glucose ≥300 mg/dL [≥16.7 mmol/L]), or when a diagnosis of type 1 diabetes is a possibility.
- 2. When selecting GLP-1 RAs, consider individual preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVO is present. consider GLP-1 RA with proven CVO benefit. Oral or injectable GLP-1 RAs are appropriate.
- 3. For people on GLP-1 RA and basal Insulin combination, consider use of a fixed-ratio combination product (IDeqLira 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 wtth 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 plan to decrease the number of injections required.

Table 9.2: Medications for lowering glucose, summary of characteristics, from Standards of Care in Diabetes – 2024

					Salar Sa	S. Carrier of the Control of the Con		and control of the co			
		Efficary1	Hypogly-	Weinht channe?	CV effects	ects		Renal effects	Oral/S0	Luct	Clinical considerations
		(apallia	cemia	of mengan	Effect on MACE	¥	Progression of DKD	Dosing/use considerations*		1000	כיווונים ריוויסותנו מוחוויס
Metformin		High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Neutral	• Contraindicated with eGFR <30 mL/min per 1.73 m²	Oral	Low	<ul> <li>GI side effects common; to mitigate GI side effects, consider slow dose titration, extended release formulations, and administration with food</li> <li>Potential for vitamin B12 deficiency; monitor at regular intervals</li> </ul>
SGLT2 inhibitors		to high	ON.	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	<ul> <li>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</li> <li>Increased risk of genital mycotic infections</li> <li>Necrotizing fascilis of the perineum (Fournier gangrene), rare reports: institute prompt treatment if suspected</li> <li>Attention to volume status, blood pressure; adjust other volume-contracting agents as applicable</li> </ul>
GLP-1 RAS		High to very high	No	Loss (intermediate to very high)	Benefit: dutaglutide, 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 amonitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse of reactions	SQ: oral (semaglutide)	High	<ul> <li>Risk of thyroid C-cell tumors in rodents; human relevance not determined (liraglutide, dulaglutide, exenatide extended release, semaglutide)</li> <li>Counsel patients on potential for GI side effects and their typically temporary nature; provide guidance on dietary modifications to mitigate Bi side effects freduction in meal size, mindful eating practices [ea., stop eating nonce full, decreasing intake of high-fat or spicy food);</li> <li>Connsel patients about potential for ileus (semaglutide SQ)</li> <li>Pancreatitis has been reported in clinical trials but causality has not been established.</li> <li>Discontinue if pancreatitis is suspected</li> <li>Evaluate for gallbladder disease if choletithiasis or cholecystitis is suspected</li> </ul>
Dual GIP and GLP-1 RA		Very high	No	Lass (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 61 reactions	os	High	<ul> <li>Risk of thyroid C-cell tumors in rodents; human relevance not determined</li> <li>Counset patients on potential for 6I side effects and their typically temporary nature; provide guidance on dietary modifications to mitigate 6I 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 6I challenges</li> <li>Not recommended for individuals with history of gastroparesis</li> <li>Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected</li> <li>Evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected</li> </ul>
DPP-4 inhibitors	itors	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	<b>O</b> ral	High	<ul> <li>Pancreatitis has been reported in clinical trials but causality has not been established.</li> <li>Discontinue if pancreatitis is suspected</li> <li>Joint pain</li> <li>Bullous pemphigoid (postmarketing): discontinue if suspected</li> </ul>
Thiazolidinediones	diones	High	<sup>Q</sup>	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	<ul> <li>Congestive HF (piogitiazone, rosigitiazone)</li> <li>Fluid retention (edema; heart failure)</li> <li>Benefit in NASH</li> <li>Risk of bone fractures</li> <li>Weight gain: consider lower doses to mitigate weight gain and edema</li> </ul>
Sulfonylureas (2nd generation)	as tion)	High	Yes	Gain	Neutral	Neutral	Neutral	Glyburide: generally not recommended in chronic kidney disease     Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	Oral	Low	<ul> <li>FDA Special Warning on increased risk of CV mortality based on studies of an older sulfonylurea (tolbutamide): glimeprinde shown to be CV safe (see text)</li> <li>Use with caution in persons at risk for hypoglycemia</li> </ul>
Insulin H	Human Analogs	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) High	<ul> <li>Injection site reactions</li> <li>Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs</li> </ul>

# **ACUTE DISEASE AND COMPLEX MANAGEMENT**

**GENERAL COMPLICATIONS:** This section addresses common complications including:

- Diabetic Peripheral Neuropathy, foot ulcers, and amputations
- Diabetic Retinopathy
- Diabetic Kidney Disease
- Atherosclerotic cardiovascular disease (ASCVD)

**Diabetic Peripheral Neuropathy (DPN), foot ulcers, and amputations** are known complications of diabetes involving the foot. Early recognition and treatment as well as providing good preventive foot care education can delay or prevent these adverse outcomes.

A comprehensive foot exam at least yearly should be performed. It is important to review past history with attention to risk factors or evidence of previous complications such as: ulceration, amputation, Charcot foot, previous vascular surgery, smoking history, retinopathy, renal disease, or current symptoms of neuropathy. Patients with a history of claudication or findings consistent with peripheral arterial disease (PAD) should be evaluated following guidelines in the PAD pathway. An exam should include inspection, notation of foot deformities, neurologic assessment (monofilament testing and vibratory testing at a minimum), and vascular assessment of pulses for both feet.

Specialized footwear is recommended in high risk patients who exhibit findings of severe neuropathy, foot deformities, ulcers, callous formation, reduced circulation, and history of prior amputation.

Diabetic peripheral neuropathy can occur in approximately 10-20% of those with diabetes and is characterized by burning, tingling, or aching discomfort that worsens at night. It is important to consider other causes of peripheral neuropathy when evaluating for this problem. Optimizing glucose control can slow the progression of the neuropathy. The goals of treatment are to slow progression, reduce pain, and improve the quality of life. The current drugs of choice for initial pharmacologic management are pregabalin, gabapentin or duloxetine when appropriate.

#### **Diabetic Peripheral Neuropathy**

A comprehensive foot exam at least yearly should be performed and the exam should include inspection, notation of foot deformities, neurologic assessment (monofilament testing and vibratory testing at a minimum) and vascular assessment of pulses for both feet.

Specialized footwear is recommended in high risk patients who exhibit findings of severe neuropathy, foot deformities, ulcers, callous formation, reduced circulation and history of prior amputation.

If the patient does not qualify for a diabetic shoe, encourage a cushioned stocking.

Refer people with diabetes who develop a foot ulcer or pre-ulcerative lesion to a podiatrist and encourage offloading.

In people with symptoms of DPN, consider pharmacologic therapy, including pregabalin, gabapentin, duloxetine, and topical lidocaine to treat symptoms and improve quality of life.

**Diabetic Retinopathy** is a major cause of morbidity in patients with diabetes. It is important to screen for retinopathy since the vast majority of patients do not develop symptoms until the late stages of retinopathy. Diabetic retinopathy can progress rapidly and early intervention with therapy can be beneficial to reduce symptoms and reduce the rate of progression. It is important to optimize glycemic

control, blood pressure and lipid management, as these efforts will reduce the risk and slow the progression of diabetic retinopathy.

#### **Diabetic Retinopathy**

All patients with T2D should have a comprehensive eye exam immediately after diagnosis. Preferably, this exam should be performed by an ophthalmologist/optometrist.

Screen for retinopathy yearly.

Patients with evidence of retinopathy should be followed at least yearly by ophthalmology/optometry.

To improve access for yearly screening, it is appropriate to use retinal photography in the primary care setting utilizing timely referral for a formal comprehensive exam when indicated.

**Diabetic Kidney Disease (DKD)** is a major cause of morbidity in patients with diabetes. Hypertension is a strong risk factor for the development and progression of DKD. It is important to screen for DKD in all patients with T2D regardless of treatment. The presence of DKD increases cardiovascular risk and health care costs. Optimization of glucose control and BP control are key to reducing the risk or slow the progression of DKD. Medication management of diabetes with select agents can result in cardiovascular risk reduction.

#### **Diabetic Kidney Disease**

To diagnose moderate or severe albuminuria, 2 of 3 specimens of urine albumin-to-creatinine ratio (UACR) collected within a 3-6 month period should be abnormal.

People with diabetes who have a UACR ≥30 mg/g and/or GFR <60 mL/min should be monitored twice annually.

People with diabetes and UACR ≥30 mg/g may benefit from an ACE inhibitor or an angiotensin II receptor blocker (ARB).

An ACE inhibitor or an ARB should be strongly recommended if UACR >300 mg/g.

If the patient is on an ACE inhibitor or ARB and still having albuminuria or proteinuria, an SGLT-2i may be considered if not already added and no contraindication.

ACE inhibitor and ARB should not be combined.

In people with diabetes and GFR <30 mL/min a referral to nephrology is recommended.

Metformin should be continued as long as GFR is >30 mL/min.

GLP-1RAs do not require renal dose adjustments except for exenatide.

SGLT-2i should typically be continued as long as GFR is >30 mL/min with albuminuria; varies based on agent.

Pioglitazone does not require renal dose adjustment and can be used as long as there are no fluid overload concerns.

Some DPP-4i require dose adjustments based on GFR or CrCl.

Sulfonylureas (if used) require caution due to risks of hypoglycemia and weight gain. Glipizide may be associated with lower incidence of hypoglycemia compared to other sulfonylureas in people with renal disease. Avoid extended release formulations.

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality for people with diabetes. ASCVD is defined as coronary heart disease, cerebrovascular disease, or PAD of atherosclerotic in origin. Heart failure is another major cause of morbidity and mortality from CVD. For prevention and management of dyslipidemia refer to the lifestyle management section and the dyslipidemia management chart in the appendix (pages 27-31 and 36).

#### **Atherosclerotic Cardiovascular Disease**

In people with diabetes, assess CVD risk factors annually. Consider using the Risk Estimator Plus tool from the American College of Cardiology & American Heart Association.

For prevention and management of Hypertension, PAD, and Heart Failure refer to the established care Care Pathways.

For prevention and management of dyslipidemia refer to the lifestyle management section and the dyslipidemia management chart.

In people with diabetes who are at an increased CV risk, aspirin therapy (75-162 mg/day) may be considered as a primary prevention strategy after a discussion with the patient on the benefits versus comparable increased risk of bleeding.

In people with diabetes and a history of ASCVD, use aspirin therapy (75-162 mg/day) or an alternative antiplatelet therapy as a secondary prevention strategy.

<u>EMERGENCIES</u>: Hyperosmolar hyperglycemic state (HHS) and hyperosmolar coma are life-threatening emergencies that most commonly affect adults with T2D. The hallmarks of HHS are dehydration, marked hyperglycemia, variable degrees of neurologic impairment, and mild or no ketosis. Any patient with T2D that presents with these findings should be emergently evaluated and treated in the appropriate inpatient setting. The mortality is estimated in the range of 10-50%. Treatment includes vigorous intravenous rehydration, electrolyte management, intravenous insulin, diagnosis, and management of precipitating problems.

# LATE DISEASE

#### **CARE COORDINATION:**

#### **Overall Care**

Perform hemoglobin A1C at least two times a year in people who are meeting treatment goals and who have stable glycemic control.

Monitor renal function at least once per year in people on metformin or SGLT-2i.

In people on metformin, monitoring vitamin B12 once yearly even without symptoms.

#### **Diabetes and Elderly**

In individuals with long history of diabetes, a less stringent goal may be considered (7.0-8.0% depending on comorbidities).

Screening for early detection of mild cognitive impairment or dementia should be performed for adults 65 years of age and older as appropriate.

In elderly people with diabetes, close glucose monitoring and avoiding hypoglycemia should be stressed.

Managing diabetes and health coaching are ongoing processes.

Unfortunately for many patients, late disease is often characterized by the presence of diabetes and multiple end-stage comorbidities. The Primary Care Provider is generally best positioned to be the central coordinator of care. This work is done in conjunction with Care Navigators, Case Managers, and

CDCES to coordinate complex care needs across numerous disciplines and specialties.

The goal is to maximize wellbeing and comfort to the greatest degree possible, while providing effective and efficient care.

#### **RECOMMENDATIONS:**

- Follow a standardized process for Care Coordination.
- Initiate end of life (EOL) discussions and participatory decision-making.

#### **END-OF-LIFE CARE:**

When palliative care is needed in older adults with diabetes, providers should initiate conversations regarding the goals and intensity of care. Strict glucose and blood pressure control may not be necessary and reduction of therapy may be appropriate. Similarly, the intensity of lipid management can be relaxed, and withdrawal of lipid lowering therapy may be appropriate.

Overall comfort, prevention of distressing symptoms, and preservation of quality of life and dignity are primary goals for diabetes management during end-of-life stages.

# **Appendix**

## **Patient-Centered Collaborative Care**

As identified in Figure 2, people with diabetes must assume an active role in their care to prevent or delay complications and optimize quality of life. This starts with the collaborative approach when creating the management plan. Open communication between the health care team and the patient is needed for patients to be successful. The use of empowering language can motivate, consider:

• Using language that is neutral, nonjudgmental, and based on facts, actions, or physiology/biology.

<b>Current Language Examples</b>	Preferred Language Examples
Bad/poor levels	Unsafe levels
Poor levels	Safe levels
Poor levels	Numbers/values
Adherent/nonadherent	Eats vegetables a few times a week.
Compliant/noncompliant	Takes medicine 60% of the time.
Compliant/noncompliant	Checks blood glucose level a few times a week.

- Using language free from stigma.
- Using language that is strength based, respectful, and inclusive and that imparts hope.
- Using language that fosters collaboration between patients and providers.
- Using language that is person centered (e.g., "person with diabetes" is preferred over "diabetic".

# **Principles of the AACE Comprehensive T2D Management Algorithm**

1.	Lifestyle modification underlies all therapy.
2.	Maintain or achieve optimal weight.
3.	Choice of antihyperglycemic therapy reflects glycemic targets, ASCVD, CHF, CKD, overweight/obesity, and NAFLD.
4.	Choice of therapy includes ease of use and access.
5.	Optimal A1C is ≤6.5% or as close to normal as is safe and achievable for most patients.
6.	Individualize all glycemic targets (A1C, GMI, TIR, FBG, PPG).
7.	Get to goal as soon as possible (adjust ≤3 months).
8.	Avoid hypoglycemia.
9.	CGM is highly recommended to assist patients in reaching goals safely.
10.	Comorbidities must be managed for comprehensive care.

For further detail see the full AACE Consensus Statement.

## **ADA Criteria for Diagnosis of Prediabetes and Diabetes**

<b>TABLE 2.2/2.5</b>	Criteria for the	Screening an	d Diagnosis of	Prediabetes and	Diabetes
IMDEL 6.6/6.0	Circeria for the	Screening an	u Diauliosis oi	r i eulabetes allu	Diabetes

	Prediabetes	Diabetes
A1C	5.7-6.4% (39-47 mmol/mol)*	≥6.5% (48 mmol/mol)†
Fasting plasma glucose	100-125 mg/dL (5.6-6.9 mmol/L)*	≥126 mg/dL (7.0 mmol/L)†
2-hour plasma glucose during 75-g OGTT	140-199 mg/dL (7.8-11.0 mmol/L)*	≥200 mg/dL (11.1 mmol/L)†
Random plasma glucose	-	≥200 mg/dL (11.1 mmol/L)‡

Adapted from Tables 2.2 and 2.5 in the complete 2022 Standards of Care. \*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range. †In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate samples ‡Only diagnostic in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.

# **ADA Criteria for Screening for Diabetes or Prediabetes in Asymptomatic Adults**

# Table 2.3—Criteria for screening for diabetes or prediabetes in asymptomatic adults

- Testing should be considered in adults with overweight or obesity (BMI ≥25 kg/m² or ≥23 kg/m² in Asian American individuals) who have one or more of the following risk factors:
  - · First-degree relative with diabetes
  - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
  - · History of CVD
  - Hypertension (≥130/80 mmHg or on therapy for hypertension)
  - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
  - · Individuals with polycystic ovary syndrome
  - · Physical inactivity
  - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- People with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
- 3. People who were diagnosed with GDM should have lifelong testing at least every 3 years.
- 4. For all other people, testing should begin at age 35 years.
- If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
- 6. People with HIV

CVD, cardiovascular disease; GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

# <u>Medication Tables: Relative Cost Comparison and Clinical Pearls</u> Noninsulin Glucose-Lowering Agents

| Cost Per Month | \$ | \$10 | \$ | \$10-50 | \$\$\$ | \$50-200 | \$\$\$\$ | >\$200 |

Many medications are available as combination drugs and may be more cost effective. Adapted from ADA 2024 table 9.3 showing National Average Drug Acquisition Cost

Medication	Medication Cost Clinical Pearls					
	_	Sulfonylureas				
Glimepiride	\$	·				
Glipizide	\$	- Risk of hypoglycemia				
Glipizide XL/ER	\$-\$\$	- Cheap				
Glyburide	\$	- Weight gain				
Glyburide (micronized)	\$\$					
		Biguanides				
		- Weight neutral				
Metformin	\$	<ul> <li>Nausea, vomiting, and diarrhea</li> </ul>				
Motformin ED	<b></b>	<ul> <li>No hypoglycemia when used alone</li> </ul>				
Metformin ER	\$-\$\$	- ER may be better tolerated than IR metformin				
Metformin ER (1000 mg)	\$\$\$\$					
		dase-4 inhibitors (DPP-4 inhibitors)				
Alogliptin (Nesina®)	\$\$\$\$					
Linagliptin (Tradjenta®)	\$\$\$\$	- Once daily				
Saxagliptin (Onglyza®)	\$\$\$\$	<ul> <li>No hypoglycemia when used alone</li> </ul>				
Sitagliptin (Januvia®, Zituvio®)	\$\$\$\$					
Dono dinido (Dron din ®)	<b>~</b> ~	Meglitinides				
Repaglinide (Prandin®)	\$\$ \$\$	- Take with each meal				
Nateglinide (Starlix®)		- Presumably less hypoglycemia				
		ansporter-2 inhibitors (SGLT2 inhibitors)				
Canagliflozin (Invokana®)	\$\$\$\$	Unaconital infections				
Dapagliflozin (Farxiga®)	\$\$\$\$	- Urogenital infections				
Empagliflozin (Jardiance®)	\$\$\$\$	- Weight loss				
Ertugliflozin (Steglatro®)	\$\$\$\$	izolidinediones (TZDs)				
Pioglitazono (Actos®)	\$	` ,				
Pioglitazone (Actos®)		- Once daily - Weight gain a glucosidase inhibitors				
	_	- Take with each meal				
Acarbose (Precose®)	\$\$	- No hypoglycemia				
Miglitol (Glyset®)	N/A					
Glucagon-like peptide 1 receptor agonists (GLP-1 agonists)						
Dulaglutide (Trulicity®) \$\$\$\$						
Exenatide (Byetta®)	\$\$\$\$					
Exenatide ER (Bydureon	\$\$\$\$	- Weight loss				
BCise®)		- N/V				
Liraglutide (Victoza)	\$\$\$\$	- All injectable except Rybelsus				
Semaglutide (Ozempic®)		- Tirzepatide is dual GIP/GLP-1 RA				
Oral semaglutide (Rybelsus®)	\$\$\$\$	, ,				
Tirzepatide (Mounjaro®)	\$\$\$\$					

# **Insulins and Insulin Combinations**

from ADA 2024 Table 9.4

	Key
	Cost Per Month
\$	<\$10
\$\$	\$10-50
\$\$\$	\$50-200

>\$200

\$\$\$\$

Madiantian	Cost		NI-1			
Medication	Cost		Notes			
Rapid-acting		Onset	Peak	Duration		
Lispro (Humalog®)	\$\$\$-\$\$\$\$					
Aspart (Novolog®, Fiasp®)	\$\$\$-\$\$\$\$	5-15 min	1 hr	4 hrs		
Glulisine (Apidra®)	\$\$\$\$					
Short-acting		Onset	Peak	Duration		
Regular	\$\$\$	1 hr	2-4 hrs	6-8 hrs		
Intermediate-acting		Onset	Peak	Duration		
NPH	\$\$\$-\$\$\$\$	1-2 hrs	4-6 hrs	18 hrs		
Long-acting		Onset	Peak	Duration		
Glargine (Lantus®, Basalgar®, Toujeo®)	\$\$\$-\$\$\$	1-2 hrs	Peakless	24 hrs		
Glargine biosimilar (Semglee®)	\$\$\$-\$\$\$\$	1-2 1115	Peakless	24 1113		
Detemir (Levemir®)	\$\$\$\$	1-2 hrs	6-8 hrs	12-24 hrs		
Degludec (Tresiba®)	\$\$\$-\$\$\$\$	30-90 min	Peakless	>24 hrs		
Premixed						
Humalog® 75/25	\$\$\$-\$\$\$\$	Mix of rapid-acting and long-acting insulin. Must be given immediately before a meal, usually twice daily.				
Humalog® 50/50	\$\$\$\$					
Novolog® 70/30	\$\$\$					
NPH/regular 70/30	\$\$\$-\$\$\$\$	Mix of short-acting and long-acting insulin. Given 30 minutes before a meal, usually twice daily.				
Injectable combinations						
Degludec/liraglutide (Xultophy®)	\$\$\$\$					
Glargine/lixisenatide (Soliqua®)	\$\$\$\$	]				

# **Online Resources**

- ECU Health Diabetes Blue Book
  - o https://myvidant.org/clinical/Diabetes/DiabetesBlueBook/Forms/ByCategory.aspx
- Prediabetes
  - o https://www.diabetesfreenc.com/
- Medication Discount Programs
  - o https://ecuphysicians.ecu.edu/pharmacy/savings-opportunities/
  - o https://ecuphysicians.ecu.edu/medication-assistance/
  - o https://medicaid.ncdhhs.gov/preferred-drug-list
- Tobacco Cessation
  - o https://www.quitlinenc.com
- Physical Activity Resources
  - o For patients:
    - Exercising with Type 2 Diabetes:
       <a href="https://www.exerciseismedicine.org/support">https://www.exerciseismedicine.org/support</a> page.php/type-2-diabetes1/
    - Living with Diabetes: Get Active:
      <a href="https://www.cdc.gov/diabetes/managing/active.html#:%7E:text=If%20you%20h">https://www.cdc.gov/diabetes/managing/active.html#:%7E:text=If%20you%20h</a>
      ave%20diabetes%2C%20being,heart%20disease%20and%20nerve%20damage
    - Diabetes and Exercise Video: <a href="https://healthlibrary.vidanthealth.com/MultimediaRoom/AnimationsPlus/#vm">https://healthlibrary.vidanthealth.com/MultimediaRoom/AnimationsPlus/#vm</a>
       <a href="https://healthlibrary.vidanthealth.com/MultimediaRoom/AnimationsPlus/#vm">https://healthlibrary.vidanthealth.com/MultimediaRoom/AnimationsPlus/#vm</a>
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       <a href="https://healthlibrary.vidanthealth.com/">https://healthlibrary.vidanthealth.com/</a>
       <a href="https://healthlibrary.vidanthealth.com/">https://healthlibrary.vidanthealth
  - For providers:
    - ADA Position Statement on Physical Activity/Exercise and Diabetes: https://care.diabetesjournals.org/content/39/11/2065
    - American College of Sports Medicine Frequency Intensity Time Type (FITT)
       Exercise Recommendation (see image 1, below)
- Nutrition Resources
  - o For patients:
    - Mediterranean Diet:
    - Diabetes Plate (see image 2 below, also in Epic Education References)
  - o For providers:
    - Tools for Diabetes Care and Education Specialists:
    - ADA Nutrition Therapy Recommendations (see image 3, below)

Image 1: American College of Sports Medicine Frequency Intensity Time Type (FITT) Exercise Recommendation

	Aerobic and/	or Resistance	Neuromotor**	Flexibility	The New ACSM FITT Exercise Recommendations
Frequency	≥2-3 sessions per week	≥2-3 sessions per week	≥2-3 session per week	≥2-3 sessions per week with daily being most effective	***On most, preferably all, days of the week
Intensity	*Moderate (i.e., 40% - 59% VO2R or HRR; RPE 12-13 on a 6–20 scale to Vigorous (i.e., 60% - 80% VO2R or HRR; RPE 14-16 on a 6–20 scale)	Moderate (i.e., 60% - 70% 1-RM; may progress to 80% 1-RM. For older adults and novice exercisers begin with 40-50% 1RM)	Low to Moderate	Stretch to the point of feeling tightness or slight discomfort	Low, Moderate, or Vigorous with an emphasis on Moderate
Time	≥20-30 min per session of continuous or accumulated exercise of any duration	2-4 sets of 8-12 repetitions of 8-10 resistance exercises of each of the major muscle groups per session to total ≥20 min per session with rest days interspersed depending on the muscle groups being exercised	≥20-30 min per session	Hold static stretch for 10-30 s with 2-4 repetitions of each exercise targeting the major muscle tendon units to total 60 s of total stretching time for each exercise; ≤10 min per session	≥20 to 30 min per day to total ≥90 to 150+ min per week of continuous or accumulated exercise of any duration
Type	Prolonged, rhythmic activities using large muscle groups (e.g., walking, cycling, swimming)	Resistance machines, free weights, resistance bands, and/ or functional body weight exercise	Exercise involving motor skills and/or functional body weight and flexibility exercise such as yoga, pilates, and tai chi	Static, dynamic, and/ or proprioceptive neuromuscular facilitation	An emphasis on aerobic or resistance exercise alone or combined in addition to neuromotor and flexibility depending on personal preference

VO,R=oxygen uptake reserve; HRR= heart rate reserve; RPE=rating of perceived exertion; 1-RM=one repetition maximum.



<sup>\*</sup> The magnitude of the BP reductions resulting from aerobic exercise are directly proportional to intensity such that the greatest BP reductions occur after vigorous intensity exercise if the patient/client is willing and able to perform vigorous intensity exercise (4).

<sup>\*\*</sup> Neuromotor functional body weight exercise can be substituted for resistance exercise, and depending on the amount of flexibility exercise integrated into a session, neuromotor flexibility exercise can be substituted for flexibility exercise depending on patient/client preference. The evidence is promising but limited for neuromotor exercise to be recommended alongside aerobic and resistance exercise as a primary exercise modality at this time (6).

<sup>\*\*\*</sup> The frequency recommendation is made due to the immediate blood pressure lowering effects of exercise, termed postexercise hypotension (4).

Image 2: Diabetes Plate (also in Epic Education References)

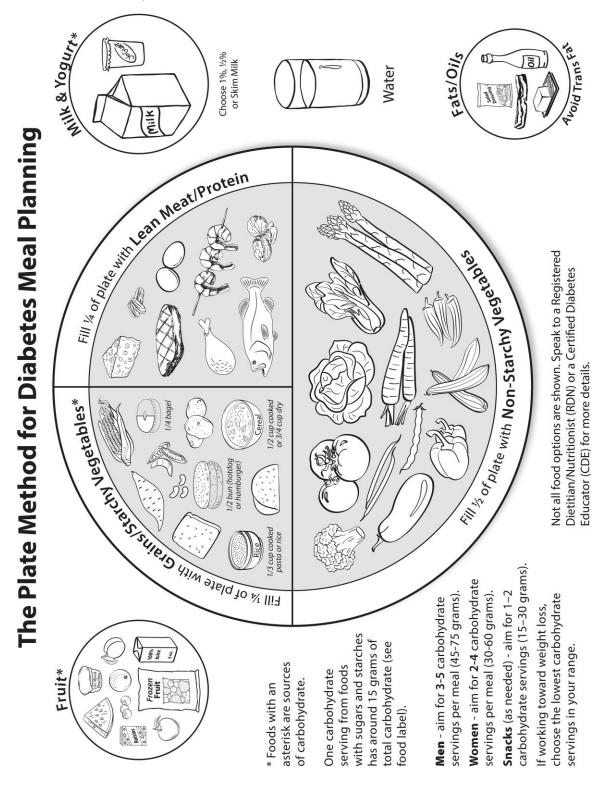


Image 3: ADA Nutrition Therapy Recommendations (Grading system on following page)

	Recommendations
Effectiveness of nutrition therapy	<ul> <li>5.10 An individualized medical nutrition therapy program as needed to achieve treatment goals, provided by a registered dietitian nutritionist, preferably one who has comprehensive knowledge and experience in diabetes care, is recommended for all people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus. A</li> <li>5.11 Because diabetes medical nutrition therapy can result in cost savings B and improve cardiometabolic outcomes A, medical nutrition therapy should be adequately reimburse</li> </ul>
	by insurance and other payers. E
Energy balance	5.12 For all people with overweight or obesity, behavioral modification to achieve and maintain a minimum weight loss of 5% is recommended. A
Eating patterns and macronutrient distribution	<ul> <li>5.13 There is no ideal macronutrient pattern for people with diabetes; meal plans should be individualized while keeping nutrient quality, total calorie, and metabolic goals in mind.</li> <li>5.14 A variety of eating patterns can be considered for the management of type 2 diabete and to prevent diabetes in individuals with prediabetes. B</li> <li>5.15 Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia and may be applied to a variety of eating patterns that meet individual needs and preferences. B</li> </ul>
Carbohydrates	<ul> <li>5.16 Carbohydrate intake should emphasize nutrient-dense carbohydrate sources that are high in fiber (at least 14 g fiber per 1,000 kcal) and minimally processed. Eating plar should emphasize nonstarchy vegetables, fruits, legumes, and whole grains, as well a dairy products, with minimal added sugars. B</li> <li>5.17 People with diabetes and those at risk are advised to replace sugar-sweetened beverage (including fruit juices) with water or low calorie, no calorie beverages as much as possible to manage glycemia and reduce risk for cardiometabolic disease B and minimiz consumption of foods with added sugar that have the capacity to displace healthier, more nutrient-dense food choices. A</li> <li>5.18 When using a flexible insulin therapy program, education on the glycemic impact of carbohydrate A, fat, and protein B should be tailored to an individual's needs and preferences and used to optimize mealtime insulin dosing.</li> <li>5.19 When using fixed insulin doses, individuals should be provided with education about consistent patterns of carbohydrate intake with respect to time and amount while considering the insulin action time, as it can result in improved glycemia and reduce the risk for hypoglycemia. B</li> </ul>
Protein	5.20 In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should be avoided when trying to treat or prevent hypoglycemia. B
Dietary fat	<ul> <li>5.21 An eating plan emphasizing elements of a Mediterranean eating pattern rich in monounsaturated and polyunsaturated fats may be considered to improve glucose metabolism and lower cardiovascular disease risk. B</li> <li>5.22 Eating foods rich in long-chain n-3 fatty acids, such as fatty fish (EPA and DHA) and nuts and seeds (ALA), is recommended to prevent or treat cardiovascular disease. B</li> </ul>
Micronutrients and herbal supplements	5.23 There is no clear evidence that dietary supplementation with vitamins, minerals (suc as chromium and vitamin D), herbs, or spices (such as cinnamon or aloe vera) can improve outcomes in people with diabetes who do not have underlying deficiencies, and they are not generally recommended for glycemic control. C There may be evidence of harm for certain individuals with β carotene supplementation. B
Alcohol	<ul> <li>5.24 Adults with diabetes who drink alcohol should do so in moderation (no more than one drink per day for adult women and no more than two drinks per day for adult men). C</li> <li>5.25 Educating people with diabetes about the signs, symptoms, and self-management of delayed hypoglycemia after drinking alcohol, especially when using insulin or insulin secretagogues, is recommended. The importance of glucose monitoring after drinking alcoholic beverages to reduce hypoglycemia risk should be emphasized. B</li> </ul>
Sodium	5.26 Sodium consumption should be limited to <2,300 mg/day. B
Nonnutritive sweeteners	5.27 The use of nonnutritive sweeteners as a replacement for sugar-sweetened products may reduce overall calorie and carbohydrate intake as long as there is not a compensatory increase in energy intake from other sources. There is evidence that low- and no-calorie sweetened beverages are a viable alternative to water. B

Table 1: ADA evidence-grading system for "Standards of Care in Diabetes" 2024

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including:  • Evidence from a well-conducted multicenter trial  • Evidence from a meta-analysis that incorporated quality ratings in the analysis Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:  • Evidence from a well-conducted trial at one or more institutions  • Evidence from a meta-analysis that incorporated quality ratings in the analysis
В	Supportive evidence from well-conducted cohort studies, including:  • Evidence from a well-conducted prospective cohort study or registry  • Evidence from a well-conducted meta-analysis of cohort studies  Supportive evidence from a well-conducted case-control study
С	Supportive evidence from poorly controlled or uncontrolled studies, including:  • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results  • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls)  • Evidence from case series or case reports  Conflicting evidence with the weight of evidence supporting the recommendation
Е	Expert consensus or clinical experience

# **Mobile Apps**

Mobile apps can help people working on preventing or people living with T2D. The North Carolina Guide to Diabetes Prevention and Management 2020 provides a list of apps that have proved successful for people with prediabetes and diabetes. These apps help with a variety of self-care behaviors and help the user to keep track of their goals, progress, and successes.

- Nutrition and Fitness
  - MyFitnessPal (Apple/Android); free with in-app purchases
  - Weight Watchers (Apple/Android); paid program; virtual DPP
  - Fooducate (Apple/Android); free with in-app purchases
  - Calorie Mama AI (Apple/Android); free with in-app purchases
  - o Calorieking (Apple and Android) free
  - Lose It! (Apple/Android); free with in-app purchases
  - Zombies, Run! (Apple); free with in-app purchases
  - o FitBit (Apple/Android); free with in-app purchases; requires wearable device
- Management, Monitoring, and Education
  - Tidepool (Apple/Android); free
  - MySugr (Apple/Android); free with in-app purchases
  - One Drop (Apple/Android); free with in-app purchases
  - Livongo (Apple/Android); through employers
  - Omada Health (Apple/Android); Virtual DPP and DSMES
  - WellDoc/BlueStar Diabetes (Apple/Android); Virtual
- Stress Management
  - Calm (Apple/Android); free with in-app purchases
  - Breathe2Relax (Apple/Android); free

# **SDOH Resources**

SDOH Resource: NC Care 360 (https://nccare360.org/)

Example of a SDOH Assessment (source-VH EPIC, 2019):

- Substance and Sex
  - o Tobacco assessment, type, amount and duration
  - Alcohol assessment, frequency, amount
  - Substance assessment, type, amount
  - o Sexual activity, birth control / method of protection, gender of partner
- Socioeconomic
  - Employment
  - o Demographics of household
  - Years of education
  - o Financial resource strain, food, housing, medical care and heat
  - Food Insecurity over last 12 months
  - o Transportation needs related to medical care and meeting daily living needs
- Lifestyle
  - o Physical activity assessment frequency and duration per week
  - Stress frequency
- Social Connections frequency with friends, family, religious or social organizations
- Intimate partner violence frequency and source
- Social Documentation free text box

# **Medical History Guide**

Past Medical and Family History	Initial Visit	All Follow- up Visits	Annual Visit
Diabetes History			
Characteristics at onset (age, symptoms)	Х		
Review previous treatment regimens and response	х		
Assess frequency, cause, and severity of past hospitalizations	Х		
Family History	·		
Family history of diabetes in a first-degree relative	х		
Family history of autoimmune disorder	х		
Personal history of complications and common	comorbiditi	es	
Macrovascular and microvascular	х		Х
Common comorbidities (e.g. obesity, obstructive sleep apnea)	х		Х
Hypoglycemia: awareness, frequency, causes, and timing of episodes	Х	х	Х
Presence of hemoglobinopathies or anemias	х		Х
High blood pressure or abnormal lipids	х		Х
Last dental visit	х		Х
Last dilated eye exam	х		Х
Visits to specialists	х		Х
Interval History			
Changes in medical/ family history since last visit		х	Х

Lifestyle Factors	Initial Visit	All Follow- up Visits	Annual Visit
Eating patterns and weight history	х	х	Х
Physical activity and sleep behaviors	х	Х	Х
Tobacco, alcohol, and substance use	х		Х

Medications and Vaccinations	Initial Visit	All Follow- up Visits	Annual Visit
Current medication regimen	Х	Х	Х
Medication-taking behavior	Х	Х	Х
Medication intolerance or side effects	х	Х	Х
Complementary and alternative medicine use	Х	Х	Х
Vaccination history and needs	х		х

Technology Use	Initial Visit	All Follow- up Visits	Annual Visit
Assess use of health apps, online education, patient portals (MyChart), etc.	х		х
Glucose monitoring (meter or CGM), results, and data use	х	Х	Х
Review insulin pump settings and use	х	х	х

Behavioral and Diabetes Self-Management Skills	Initial Visit	All Follow- up Visits	Annual Visit	
Psychosocial conditions				
Screen for depression, anxiety, and disordered eating, refer for further assessment or intervention if warranted	х		х	
Identify existing social supports	Х		х	
Consider assessment for cognitive impairment starting at age 65	Х		Х	
Diabetes self-management education and	l support			
History of dietitian, diabetes educator visits or classes	Х	х	Х	
Assess diabetes self-management skills and barriers	Х		х	
Pregnancy planning for those with childbearing capacity				
Review contraceptive needs and preconception planning	Х	х	х	

Physical Examination		Every Follow- up Visit	Annual Visit
Height, weight, and BMI	х	х	х
Blood pressure determination	х	х	Х
Orthostatic blood pressure measures (when indicated)	х		
Fundoscopic examination (refer to eye specialist)	х		х
Thyroid palpation	х		х
Skin examination (e.g. acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	x	x	х
Comprehensive foot examination			
Visual inspection (e.g. skin integrity, callous formation, foot deformity or ulcer, toenails)	х		х
Screen for PAD: pedal pulses (Refer for ankle-brachial index if diminished)	х		х
Determination of temperature, vibration, and pinprick sensation, and 10-g monofilament exam	x		х

Laboratory Evaluation (and Frequency)  To be done if results are not available within frequency period	Initial Visit	All Follow- up Visits	Annual Visit
A1C (3 months)	Х	х	Х
Lipid profile, including total, LDL, and HDL cholesterol and triglycerides (annually)	х	х	х
Liver function tests (annually)	Х		Х
Spot urinary albumin-to-creatinine ratio (annually)	Х		Х
Serum creatinine and estimated glomerular filtration rate (annually)	Х		Х
Vitamin B12 if on metformin (when indicated) (annually)	х		Х
Serum potassium levels on ACE inhibitors, ARBs, or diuretics (annually)	х		х

## **Lipid Management**

#### alternative statin with lower incidence of myopathy (pitavastatin, extended-release fluvastatin) or decrease dose/frequency, use non-statin Rx, check for Rx interactions, consider CoQ10. <sup>3</sup>lf TG > 200 management and fibrate/omega 3 therapy is needed. Suspect familial chylomicronemia syndrome or lipodystrophy, refer to lipid specialist. <sup>5</sup>For severe hypertriglyceridemia >1000 refractory LIFESTYLE INTERVENTION: increase ↑ dietary fiber | ↑ healthy fat | ↓ saturated fat | ↓ simple carbs | ↓ added sugars | ↑ physical activity | weight management and HDL <40, add fibrate/omega-2 to achieve apo B and non-HDL goals. <sup>4</sup>Elevated triglycerides Consider addition of icosapent ethyl to statin if DM and CVD or ≥2 risk factors TG >10004 >500 mg/dL to >1000 mg/dL can cause acute pancreatitis. Urgent intervention with dietary +Niacin5 Baseline LDL-C > 190 mg/dL, consider familial hypercholesterolemia. <sup>2</sup>Statin intolerance: Use to previous interventions, consider niacin to reduce the risk of pancreatitis. Niacin may HYPERTRIGLYCERIDEMIA MANAGEMENT: Major ASCVD Risk Factors: Age > 40 | HTN | CKD > 3a | Smoking | Family History of Premature ASCVD | Low HDL-C | High Non-HDL-C lower TG and Lp(a) but does not reduce ASCVD and can promote hyperglycemia. ntensify Lifestyle & Achieve Glycemic Targets PREDIABETES OR T2D + RISK FACTORS: USE ASCVD 10-YEAR RISK CALCULATOR Fibrate or/and Rx Grade Omega-3 TG >500 TG target achieved: Continue lifestyle therapy, maximally tolerated statin and achieve glucose targets DYSLIPIDEMIA ASSESS LIPID PANEL (LDL-C, HDL-C, Non-HDL-C, TG, Apo B)<sup>1</sup> TG 200-4993 COPYRIGHT © 2023 AACE. May not be reproduced in any form without express written permission from Elsevier on behalf of AACE. REDUCTION ALGORITHM: NITIATE STATIN THERAPY TG 135-199 Severe target organ damage: eGFR <45 mL/ min/1,73 m², UACR >300, ABI <0.9, LV systolic/ Monitor and titrate therapy every 3-6 months to achieve lipid targets according to risk $^{2}$ Consider additional therapy: bile acid sequestrant, bempedoic acid, PCSK9 inhibitor, inclisiran **EXTREME RISK >20%** diastolic dysfunction <150 9/2 88 \$5 72D & ASCVD Visit https://doi.org/10.1016/j.eprac.2023.02.001 to request copyright permission Intensify statin and lifestyle & optimize glycemic control High-intensity statin RISK VERY HIGH RISK 10%-20% No target organ damage >2 additional risk factors Add ezetimibe ASCVD 100 <150 89 8 ×100 <150 4130 8 Algorithm Figure 4-Dyslipidemia Moderate-intensity statin No target organ damage LDL-C (mg/dL) Apo B (mg/dL) T2D <10 years <2 other risk factors Non-HDL-C TG (mg/dl.) HIGH RISK <10% (mg/dL) O 0 4

<u>Highly recommended immunizations for adults with diabetes</u> - Advisory Committee on Immunization Practices and Centers for Disease Control and Prevention [Table 4.4 from *Standards of Care in Diabetes – 2024*]

Vaccine	Recommended ages	Schedule	GRADE evidence type
COVID-19	Recommended for all 6 months of age and older	Current initial vaccination and boosters	
Hepatitis B	Recommended for adults with diabetes aged <60 years; for adults aged ≥60 years, hepatitis B vaccine may be administered at the discretion of the treating clinician based on the person's likelihood of acquiring hepatitis B infection		
Influenza	All people with diabetes advised not to receive live attenuated influenza vaccine	Annual	
Pneumonia (PPSV23 [Pneumovax])	19–64 years of age, vaccinate with Pneumovax	One dose is recommended for those who previously received PCV13; if PCV15 was used, follow with PPSV23 ≥1 year later; PPSV23 is not indicated after PCV20; adults who received only PPSV23 may receive PCV15 or PCV20 ≥1 year after their last dose	2
	≥65 years of age	One dose is recommended for those who previously received PCV13; if PCV15 was used, follow with PPSV23 ≥1 year later; PPSV23 is not indicated after PCV20; adults who received only PPSV23 may receive PCV15 or PCV20 ≥1 year after their last dose	2
PCV20 or PCV15	Adults 19–64 years of age, with an immunocompromising condition (e.g., chronic renal failure), cochlear implant, or cerebrospinal fluid leak	One dose of PCV15 or PCV20 is recommended by the Centers for Disease Control and Prevention	3
	19–64 years of age, immunocompetent	For those who have never received any pneumococcal vaccine, the CDC recommends one dose of PCV15 or PCV20	
	≥65 years of age, immunocompetent, have shared decision-making discussion with health care professionals	One dose of PCV15 or PCV20; PCSV23 may be given ≥8 weeks after PCV15; PPSV23 is not indicated after PCV20	
RSV	Older adults ≥60 years of age with diabetes appear to be a risk group	Adults aged ≥60 years may receive a single dose of an RSV vaccine	
Tetanus, diphtheria, pertussis (Tdap)	All adults; pregnant individuals should have an extra dose	Booster every 10 years	2 for effectiveness, 3 for safety
Zoster	≥50 years of age	Two-dose Shingrix, even if previously vaccinated	1

References for this table can be found at: <a href="https://doi.org/10.2337/dc24-S004">https://doi.org/10.2337/dc24-S004</a>

For a comprehensive list of vaccines, refer to the Centers for Disease Control and Prevention website at cdc.gov/vaccines/. Advisory Committee on Immunization Practices recommendations can be found at cdc.gov/vaccines/acip/recommendations. GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PCV13, 13-valent pneumococcal conjugate vaccine; PCV15, 15-valent pneumococcal conjugate vaccine; PCV20,20-valent pneumococcal conjugate vaccine; PPSV23,23-valent pneumococcal polysaccharide vaccine. \*Evidence type: 1, randomized controlled trials (RCTs) or overwhelming evidence from observational studies; 2, RCTs with important limitations or exceptionally strong evidence from observational studies; 3, observational studies or RCTs with notable limitations; 4, clinical experience and observations, observational studies with important limitations, or RCTs with several major limitations