Adult Type 2 Diabetes Guidelines 2024

Background

More than 37.3 million American adults have diabetes, which is just increased to 11.3% of United States population.[1] Diabetes more than doubles the risk of heart disease and strokes and is the leading cause of adult-onset blindness, kidney disease and lower- limb amputations.[1] The prevalence of diabetes over the last 30 years has increased 4-fold.[1] Given the dramatic impact of diabetes on the lives of our patients and our entire health care system, it is critical that high-quality best-practice diabetes care be provided consistently by all members of the health care teams. This guideline is written to optimize that care.

Clinical Practice Guidelines Benefit

A clinical practice guideline can improve consistency of best practice care in a health care organization. It unites all members of a care team to screen, diagnosis, monitor, treat and educate patients using standard recommendations. It links outcome metrics to evidence-based patient care. It helps translate best practice care into electronic health record tools, patient education materials, and staff training resources. It provides a means to adjust care efficiently and consistently across the organization when new evidence emerges.

Sutter Health Type 2 Diabetes Adult Guideline

The following Sutter Health Type 2 Diabetes Adult Clinical Practice Guideline was written by a 28-person multi-disciplinary team. The team was carefully crafted to represent the wide spectrum of Sutter Health's clinical community: geography (both Bay and Valley geographic regions), level of care (acute and ambulatory care), types of providers (endocrinologists, family physicians, internists, advanced practice clinicians, registered nurses, registered dieticians, pharmacists, certified diabetes educators), type of practice (foundation and independent affiliates), type of department (local office and system office), and type of work (in-person patient care, case management, quality, and population health). A patient representative was included in the writing team.

Writing this guideline was a multi-step process. Major sources of standards for diabetes were identified which rely on clinical outcome trials and report the level of evidence for their recommendations – including the United States Preventive Service Task Force (USPSTF), the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists (AACE), and the American Heart Association (AHA). Other sources were identified for specific content – such as the Association of Diabetes Care and Education Specialists (ADCES), and Kidney Disease, Improving Global Outcomes (KDIGO) and the American Academy of Neurology (ANN). The key recommendations from each source were carefully reviewed by the committee, and those recommendations with the strongest evidence and those most consistent with best practice care for the Sutter Health population were included. When there was more than one approach for management or the evidence was less clear, the approach with the most evidence and agreement was stated first, and alternate options were also described. In addition, the level of evidence was stated in the guideline for all recommendations from USPSTF and ADA and other national guidelines when available (level of evidence is included in the superscript of the citations).

This guideline is intended for the care of adults with type 2 diabetes in an ambulatory setting. It is not intended for patients with Type 1 diabetes, patients with ketosis or acute insulin deficiency, pregnant patients, hospitalized patients, children or adolescents. It is intended to help clinicians, educators, care managers and patients make decisions according to standard clinical practice. It should not replace individual clinical judgment. All clinical decisions should be made within the context of the specific situation for each patient, including current health, medications, risk of hypoglycemia, quality of life, life expectancy, and patient preference.

The guideline is divided into the following major topics:
(click on the topic to jump to that section)

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report website. https://www.cdc.gov/diabetes/data/statistics-report/index.html Access 1/27/22

Rev. 04/2024
24-SHSO-003804

Adult Type 2 Diabetes Guidelines 2024

I. Screening and Prevention of Diabetes

Screen adults for diabetes risk using assessment of risk factors or validated risk screen tool[1(B)] such as

- https://diabetes.org/diabetes-risk-test
- https://www.cdc.gov/diabetes/prevention/pdf/Prediabetes-Risk-Test-Final.pdf

Screen for pre-diabetes and diabetes using any of the following tests[1(B)]

- Hemoglobin A1C (A1C)[1,2]
- Fasting glucose[1,2]
- 2-hour 75 gm Oral Glucose Tolerance Test (OGTT)[1,2]

In general, screenings should be done in a health care setting[1,2] but may be considered in a community setting if there is a referral system for positive tests.[1]

Screen for pre-diabetes and diabetes at following ages and intervals.[1,2]

Note: USPSTF and ADA are different, so use clinical consideration and shared decision-making with patients when considering the strategy for each patient.

- USPSTF

  USPSTF recommends:

  - Screen people aged 35-70 who are overweight/obese **(Grade B Recommendation).**[2]
  - Consider screening earlier in persons with one or more additional risk factors for diabetes.[2]
  - Consider rescreen every 3 years.[2]
- ADA

  The ADA recommends:

  - Screen people aged 18 and older who are overweight/obese (BMI ≥ 25 or ≥ 23 if Asian-American) and also have one or more additional risk factors (see table 1 below)[1(B)]
  - Screen all people aged 35 and older.[1(B)]
  - Rescreen at least every 3 years (more often if symptoms or change in risk)[1(C)]

  The ADA also recommends screening the following populations:

  - Women with risk factors who are considering pregnancy.[(1B)] Note: may consider screening all women considering pregnancy[1(E)]
  - People with HIV before starting antiretroviral therapy, when switching antiretroviral therapy, and 3-6 months after starting and then annually.[1(E)]
  - People starting 2nd generation antipsychotic medications at baseline and 3-4 months after starting medication.[1(B)]
  - After people have an organ transplantation (using the oral glucose tolerance test),[1(B)] or history of pancreatitis[1(E)]

Table 1: Risk factors for diabetes in addition to overweight/obesity[1]

A1C ≥ 5.7%, Fasting glucose 100-125, or 2 hour 75 gram OGTT 140-199 mg/DL on previous testing	First-degree relative with diabetes	High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)	Women who were diagnosed with Gestational Diabetes	History of cardiovascular disease (CVD)	Use of 2nd generation antipsychotic medications, steroids, thiazide diuretics, statins, HIV medications and checkpoint inhibitors (a treatment for cancer)	
HDL level <35 mg/dL and/or triglyceride level ≥250 mg/dL	Hypertension (≥130/80 or therapy for Hypertension)	Clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)	Polycystic ovary syndrome	Physical inactivity	Recent smoking cessation	HIV

Diagnosis of Pre-diabetes

Use any of the following laboratory tests to diagnose pre-diabetes[1(B)]

- A1C: 5.7-6.4%[1,2,3]
- Fasting glucose: 100-125 mg/dL (Impaired Fasting Glucose)[1,2,3]
- 2 hour 75-gram OGTT:* 140-199 mg/dL (Impaired Glucose Tolerance)[1,2,3]

Notes:

- Risk is continuous, starting below the lowest value and increasing disproportionately at the higher values in the range.[1]
- The tests do not necessarily pick up the same individuals.[1]

*Ensure adequate carbohydrate intake (at least 150 g/day) for the 3 days before the 2 hour 75-gram OGTT test.[1(A)]

Diagnosis of Diabetes

Use any of the following laboratory tests to diagnose diabetes.[1]

- A1C: ≥ 6.5%[1,2]
- Fasting glucose: ≥ 126 mg/dL (8 or more hour fast)[1,2]
- 2 hour 75-gram OGTT: ≥ 200 mg/dL[1,2]
- Random glucose ≥ 200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis[1]

Classify diabetes after diagnosis (i.e., type 1, type 2, gestational, or due to specific causes). This may aid in choosing personalized treatment - although some individuals cannot be clearly classified into one of these conventional categories.

Notes from the ADA:

- A1C, fasting glucose, and 2-hour 75-gram OGTT are equally appropriate for diagnostic testing.[1]
- Repeat test to confirm diagnosis, by obtaining a test on two different samples (do second test without delay) or 2 different tests on the same sample.[1,2] If feasible and in the absence of unequivocal hyperglycemia, two abnormal tests results are required for diagnosis.[1]

- If tests are discordant, repeat the test that is abnormal to confirm the diagnosis.[1,23]
- A significant discordance between the A1C and glucose results may suggest that the A1C results are not reliable, and the glucose values should be used instead of the A1C.[1(B)] If diagnosis remains equivocal, follow closely every 3-6 months.[1]
- The A1C test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay.[1(B)]
- Point-of-care A1C testing for diabetes screening and diagnosis should use FDA approved devices.[1(B)]
- Red blood cell turnover can impair the reliability of A1C. Glucose criteria (not A1C criteria) should be used to diagnose diabetes for people with high turnover of their red blood cells (such as sickle cell disease, anemia, glucose-6-phosphate dehydrogenase deficiency, HIV, recent blood loss/transfusion, 2nd and 3rd trimester pregnancy and post-partum period, dialysis, or erythropoietin therapy)[1(B)]

Table 2: Summary of diagnosis criteria for pre-diabetes and diabetes[1]

	Normal	Pre-Diabetes	Diabetes
A1C	< 5.7%	5.7%-6.4%	≥ 6.5%
Fasting Glucose	< 100	100-125	≥ 126
2-hour 75-gram OGTT	< 140	140-199	≥ 200
Random Glucose			≥ 200 (if classic symptoms)

Treatment of Pre-Diabetes

- Focus on individual risk-benefit assessment.[1(E)]
- Per the ADA, "In adults with overweight/obesity at high risk of type 2 diabetes, care goals should include weight loss or prevention of weight gain, minimizing the progression of hyperglycemia, and attention to cardiovascular risk and associated comorbidities."[1(B),3]
- Primary treatment goal is lifestyle and weight management.[1,2,3]
- Recommend post-partum breastfeeding, including to reduce the risk of maternal type 2 diabetes in people with a history of gestational diabetes.[1(B)]
- Consider pharmacotherapy for weight management, slowing progression of hyperglycemia, and cardiovascular risk reduction.[1(B),3]
- Provide more intensive care (and consider metformin) if particularly high risk of progression such as BMI ≥35, higher glucose levels (FPG 110–125 mg/dL, 2-h post-challenge glucose 173–199 mg/dL, A1C ≥6.0%), and/or a history of gestational diabetes.[1(A)]
- Refer patients with overweight/obesity to an intensive behavioral lifestyle intervention program **(USPSTF Grade B Recommendation)**[2] modeled on the Diabetes Prevention Program (DPP), to achieve and maintain a 7% of body weight loss, and to increase physical activity to at least 150 min/week of moderate activity.[1(A),3]

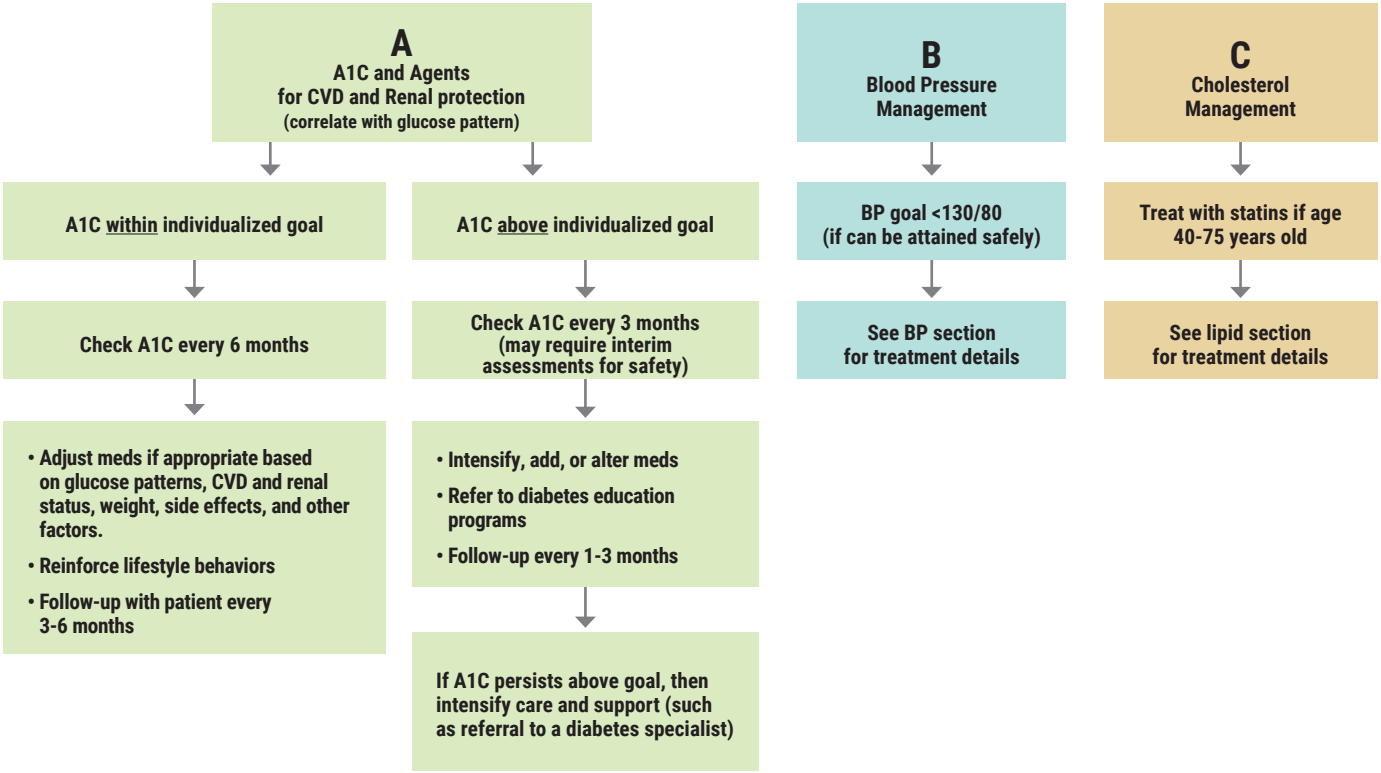
  - CDC-recognized DPP Programs can be in-person, technology-assisted, smartphone, web-based, or telehealth (all must use an approved curriculum, include interaction with a coach and attain the outcomes for recognition). Selection of an in-person or virtual program should be based on patient preference.[1(B)]
  - Patients can choose from a variety of eating patterns for diabetes prevention.[1(B)]
- See the Center for Disease Control and Prevention (CDC) National Diabetes Program Site for specific program details and resources: https://www.cdc.gov/diabetes-prevention/index.html[4] A variety of insurance plans include coverage of CDC-recognized DPP.
- Screen for and treat other modifiable CVD risk factors including hypertension and dyslipidemia.[1(B),3]
- Monitor glucose status regularly and provide diabetes prevention support if a person at high risk for diabetes is taking a statin (due to increased risk of diabetes). However, don't stop statins if diabetes develops.[1(B)]
- Re-test for diabetes annually, based on specific clinical situation.[1(E)]
- Consider use of technology-assisted tools including internet-based social networks, distance learning, and mobile applications.[1(B),3]

II. Overview of Diabetes Management

Following is a general overall algorithm recommended for evaluating and managing patients with diabetes using a coordinated multidisciplinary team. Note that Agents to lower CVD risk are now part of the ABCs.

Care systems should facilitate in-person and virtual team–based care, utilizing patient registries, decision support tools, and community involvement to meet patient needs.[1(B)]

Figure 1: The A, B, Cs of Diabetes Management added to lifestyle intervention.



III. Diabetes Testing Frequency

A1C Frequency (see management algorithm above)

- Every 6 months if at goal[1(E),3]
- Every 3 months if not at goal[1(E),3] or if therapy has changed[1(E)]

  Note: Point of care A1C testing provides opportunity for more timely treatment changes

A1C Goal (individualize according to patient characteristics in figure 2 and notes below)[1]

Goal < 7.0% is a reasonable goal for many adults if

- Can be achieved without significant hypoglycemia [1(A)]

Less stringent goals may be appropriate if

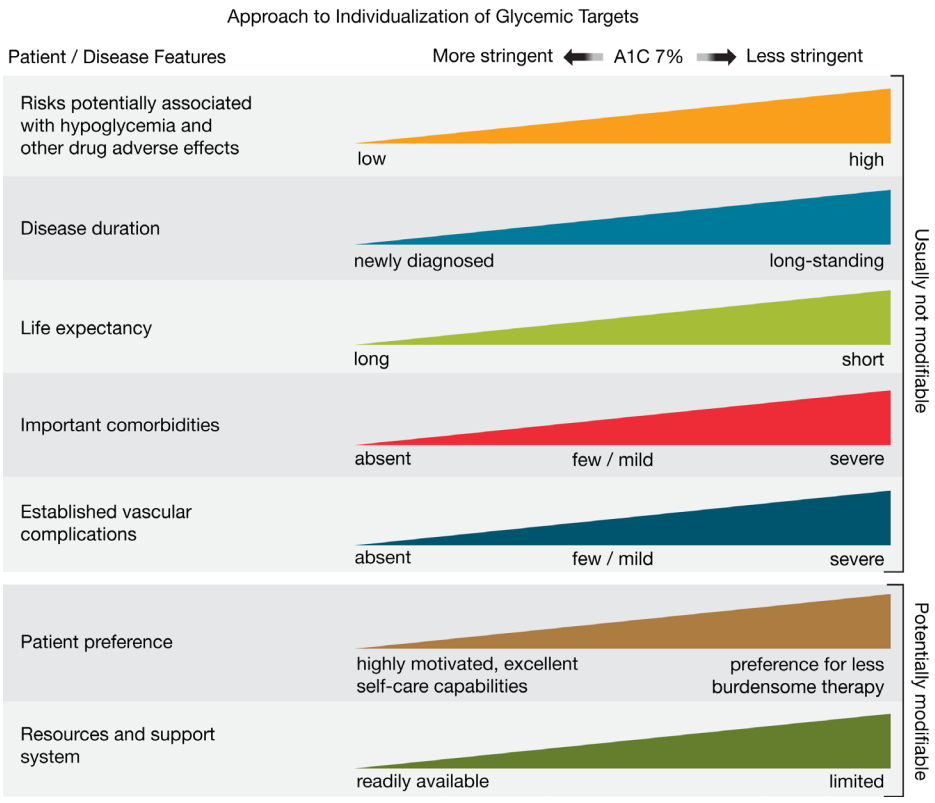
- Limited life expectancy[1(B)]
- Harms of treatment are greater than benefits[1(B)]
- Older adults with multiple coexisting chronic illnesses, cognitive impairment, or functional dependence

Goal lower than 7% may be acceptable/beneficial if

- Can be achieved safely without significant hypoglycemia or other adverse effects of treatment[1(B) 3]

See the American Diabetes Association Table of Mean Glucose Levels by A1C Levels in the appendix **(Table 12)**

Figure 2: Factors to help individualize patient glucose targets[1]



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Patient and disease factors used to determine optimal glycemic targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. A1C 7% = 53 mmol/mol. Adapted with permission from Inzucchi et al. (68).

Glucose Monitoring

- Individualize frequency of testing based on patient preference, how patient is adjusting medication or lifestyle behaviors based on results, A1C result, risk of hypo and hyperglycemia, types of medications, frequency of injections, type of activity (e.g. driving, exercise) and risk of complications.[1(B)]
- Consider checking glucose levels at a variety of times of day (such as pre and 1-2 hours post meal).[1]
- Ensure that patients and care givers receive ongoing instruction and regular evaluation of glucose self- monitoring technique, results, and the use of data to adjust therapy.[1(C)]

Glucose Monitoring Devices

Glucose Meters

- Provide patients a monitoring device most ideal for their individual circumstances, preferences, and treatment.[1(A)] Patients should always have access to their glucose monitor.[1(A)]
- Prescribe U.S. Food and Drug Administration–approved meters with proven accuracy and unexpired strips.[1]
- Note medications, high-dose vitamin C, hypoxemia and other factors that can interfere with monitors.[1(E)]
- Check on insurance coverage of glucose meter given to patient to ensure patient has the lowest co-pay available for strips. Help patient overcome barriers to cost of covering glucose monitoring supplies.

Continuous Glucose Monitors or Intermittent Scanned Glucose Monitors (CGMs)

- Consider offering to patients with evidence of insulin deficiency (or type 1 diabetes) at the time of diagnosis[1(A)]
- Recommend CGM for patients with high risk for hypoglycemia.[1(A)]
- Patients on basal insulin, multiple daily insulin injections or insulin pumps should use real-time CGMs as close to daily as possible for maximal benefit.[1(A, B, C),3] (Scan intermittent CGM devices at least every 8 hours).[1(A)]
- Consider CGM in patients for whom the A1C is inaccurate (such as advanced CKD or dialysis).[6]
- Provide uninterrupted access to CGM supplies[1(A)]
- Consider periodic or office-based professional CGM if not using continuous CGM.[1(C),3]
- Use standardized glucose reports such as the Ambulatory Glucose Profile (AGP) for CGM devices.[1(E)]
- Proactively prevent and treat skin reactions to enable success[1(E)]
- Educate CGM users on interfering substances and factors that affect accuracy. See the manufacturers' information for details.[1(C)]

Sensor-augmented Insulin Pumps

- Offer sensor-augmented automated insulin pumps to insulin-deficient diabetes patients who can use the device safely (either by themselves or with a caregiver).[1(A,E)]

Do-it-yourself closed-loop systems

- Assist patients with their do-it-yourself closed-loop systems not approved by the FDA if patients are using one, in order to ensure patient safety. [1(E)]

  Note: ensure patients/caregivers receive initial and ongoing education and training about their device[1(E)]

Glucose Monitoring Goals

General goal (per the ADA) – individualize per patient and adjust by A1C goal [1]

- Pre-meal 80-130 mg/dL[1]
- Peak post-meal (1-2 hours after beginning meals) <180 mg/dL [1]
- Time in range (70-180 mg/dL) > 70%, time below range <4%, and time <54 mg/dL <1%[3] [1(B)] See Figure 3.
- If frailty or at high risk of hypoglycemia, time in range >50% with <1% time below range [1(B)]
- Consider 14-day CGM history to make treatment decisions

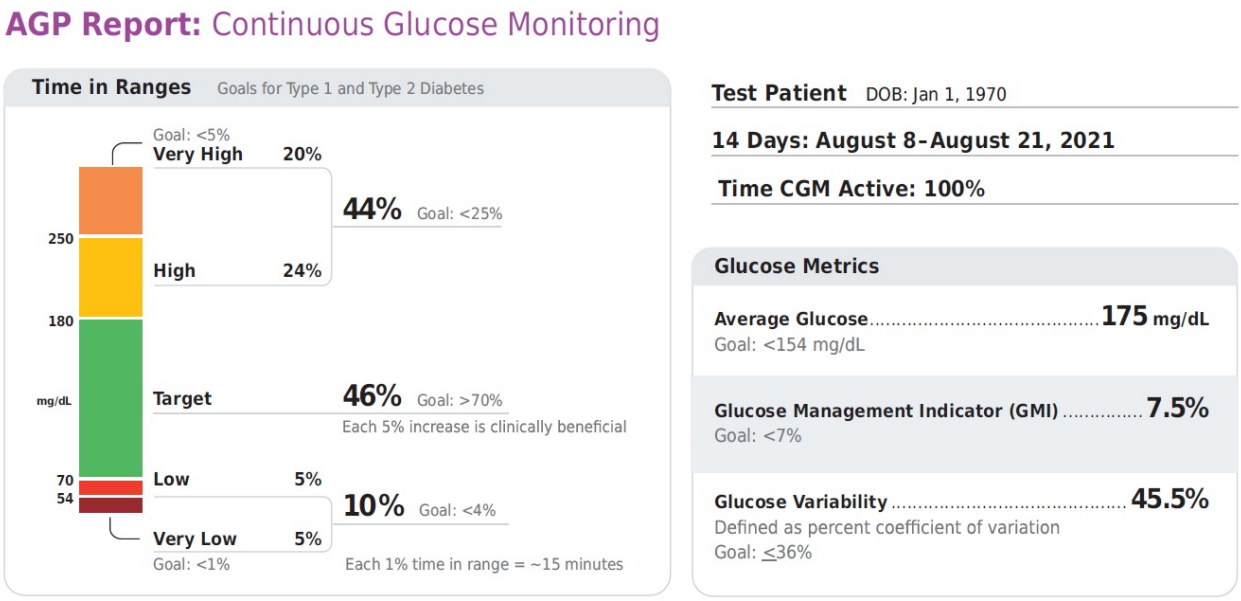

Figure 3: Ambulatory Glucose Profile

Standardized CGM metrics for clinical care (as stated by the ADA)[1]

Metric	Interpretation	Goals
1. Number of days CGM device is worn		14-day wear for pattern management
2. Percentage of time CGM device is active		70% of data from 14 days
3. Mean glucose	Simple average of glucose values	*
4. Glucose management indicator	Calculated value approximating A1C (not always equivalent)	*
5. Glycemic variability (%CV) target	Spread of glucose values	≤36%
6. TAR: % of readings and time >250 mg/dL	Level 2 hyperglycemia	<5% (most adults); <10% (older adults)

7. TAR: % of readings and time 181–250 mg/dL	Level 1 hyperglycemia	<25% (most adults); <50% (older adults)
8. TIR: % of readings and time 70–180 mg/dL	In range	>70% (most adults); >50% (older adults)
9. TBR: % of readings and time 54–69 mg/dL	Level 1 hypoglycemia	<4% (most adults); <1% (older adults)
10. TBR: % of readings and time <54 mg/dL	Level 2 hypoglycemia	<1%

*CGM, continuous glucose monitoring; CV, coefficient of variation; TAR, time above range; TBR, time below range; TIR, time in range. *Goals for these values are not standardized. Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas. Goals are for level 1 and level 2 hyperglycemia combined. Goals are for level 1 and level 2 hypoglycemia combined. Adapted from Battellino at al. [32].*

- For all patients, regardless of goals, strive to:
  - Avoid hypoglycemia[1,3]
  - Avoid high glucose levels that cause acute symptoms or increase risk for acute complications of hyperglycemia[1(C)]

The ADA notes: "Individualize based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations"[1] *see more detailed information about mean glucose levels and A1C in Table 12*[1]

A1C and Glucose Goals in Older Adults

Individualize glucose goals in older adults (such as age > 65) based on health and functional status.[1(C)] Reassess goals over time, as age and health status change.[1]

- Consider similar goals to younger adults in older adults who are cognitively and functionally intact and have significant life expectancy.[1(C)]
- Diabetes, hyperglycemia and hypoglycemia increase the risk of dementia. Dementia also increases the risk for hyperglycemia and hypoglycemia. Adjust glycemic targets and avoid medications that cause hypoglycemia to decrease the risk of cognitive decline and other major adverse outcomes.[1(B)]
- Avoid diabetes overtreatment in older adults.[1(B)]
- Adjust treatment if needed (and if possible, within A1C targets) such as
  - Adjust goals to reduce the risk of hypoglycemia ("Deintensification").[1(B)]
  - Simplify complex treatment plans to reduce risk of hypoglycemia, polypharmacy, and burden of the disease ("Simplification").[1(B)]
- High glucose levels (such as above 200s) should be avoided due to elevated risk of the acute symptoms of hyperglycemia: polyuria, dehydration, poor healing, etc.[1(C)]
- Modify screening for complications in older adults to focus most on those that affect function and quality of life.[1(C)]

Table 3: Framework for considering treatment goals for glycemia in older adults with diabetes[1]

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 to 7.5%	80-130 mg/dL	80-180 mg/dL	<130/80 mmHG	Statin, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Variable life expectancy. Individualized goals, considering: • Severity of comorbidities • Cognitive and functional limitations • Frailty • Risk-to-benefit ratio of diabetes medications • Individual preference	<8.0%	90-150 mg/dL	100-180 mg/dL	<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 2+ 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	110-200 mg/dL	<140/90 mmHG	Consider likelihood of benefit with statin

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This table represents a consensus framework for considering treatment goals for glycemia 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 (60).*

*** 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)*

Hypoglycemia

- Prioritize avoiding both severe and non-severe hypoglycemia.[3]
- Assess risk for and investigate hypoglycemia at every encounter, using validated tools.[1(C)]
- Assess for hypoglycemia in older adults and if the patient has low or declining cognitive function.[1(B, C)]
- In adults with type 2 diabetes at increased risk of hypoglycemia, prefer medication classes with low risk of hypoglycemia.[1(B) 3]
- If on insulin or at risk for hypoglycemia, provide education about hypoglycemia prevention and treatment.[1(A,C)]
- If any level 3 hypoglycemia (or pattern of level 2) then teach about hypoglycemia avoidance, re-evaluate and adjust current treatment regime, and consider raising glycemic targets if on insulin to avoid hypoglycemia for several weeks to reverse hypoglycemia unawareness.[1(A,E)]
- Consider CGM for older adults if on multiple daily doses of insulin[1(B)] or on daily insulin or on sulfonylureas.[1(E)]
- Prescribe glucagon if on insulin or high risk of level 2 or 3 hypoglycemia.[1(E)]

Table 4: Classification of hypoglycemia[1]

Classification	Characteristics
Level 1	Glucose 54 to 69 mg/dL
Level 2	Glucose <54 mg/dL
Level 3	severe event with altered mental and/or physical status requiring assistance for treatment

Risk Factors for Hypoglycemia[1]

The ADA notes the following factors that increase risk of treatment-associated hypoglycemia[1]

- Use of insulin or secretagogues (i.e., sulfonylureas, meglitinides)
- Impaired kidney or hepatic function
- Longer duration of diabetes
- Frailty and older age
- Cognitive impairment
- Impaired counter regulatory response, hypoglycemia unawareness
- Physical or intellectual disability that may impair behavioral response to hypoglycemia
- Alcohol or substance use disorder
- Polypharmacy (especially ACE inhibitors, ARBs, nonselective beta blockers)
- History of hypoglycemic
- Female
- High glucose variability
- CVD, neuropathy, retinopathy, major depression
- Food insecurity, low-income status, homelessness, fasting for cultural reasons, low health literacy.

Mild to Moderate hypoglycemia – Rule of 15

- If glucose level is low (usually below 70 mg/dL), eat or drink 15-20 grams of quickly digestible carbohydrates (such as 3-4 glucose tabs).
- **After 15 minutes,** recheck glucose.
- If glucose level is still low or symptoms persist, eat or drink 15 more grams of carbohydrates.
- Once glucose level is in goal range, eat a light snack or meal within an hour.

IV. Lifestyle and Weight Management

Patient Education

- Refer all patients with diabetes to comprehensive diabetes self-management and education[1(A)] that is conducted by trained diabetes educator(s).[1,6] Education can be individual or group-based,[1(A)] and can be in-person or virtual.[1(B)]
- Consider education programs that combine virtual glucose monitoring technology and online virtual coaching.[1(B)]
- Offer diabetes self-management education and support (DSMES) at five key times [1,6]
  1. At diagnosis of diabetes
  2. Annually
  3. When not meeting treatment targets
  4. When complicating factors develop (medical, physical, psychosocial)
  5. When transitions in life and care occur
- Set goals collaboratively with the patient to develop attitudes, beliefs, knowledge, and skills to self-manage diabetes.[1, 7]
  - Use behavioral strategies that support self-management.[1(A)]
- Assess patient numeracy, literacy, and barriers to care as part of care plan.[1(B)]
- Use patient-centered communication style that is person-first (e.g., use "person with diabetes" instead of "diabetic"), strength-based, respectful, inclusive, and imparts collaboration and hope.[1(B)]
- Include additional self-management support from lay health coaches, navigators, and/or community health workers when available.[1(A)]
- Include screening and management of social determinants of health (SDOH), with a goal of increasing health equity across populations.[1(C)]
- Assess and refer for help for food insecurity, hunger, and access to healthy food, housing insecurity/homelessness, financial barriers, and social and community support[1(C)]
- For older adults, also encourage optimal lifestyle[1(B)] and consider an intensive lifestyle intervention focused physical activity and modest weight loss.[1(A)]
- Use the *Sutter Health Diabetes Handbook Understanding Type 2 Diabetes Your Guide to Healthy Living* as a source for diabetes education and resource for the patient https://content.sutterhealth.org/ehr/documents/HospitalDiabetesTeachingGuide.pdf

IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIORS FOR TYPE 2 DIABETES

SITTING/BREAKING UP PROLONGED SITTING

Limit sitting. Breaking up prolonged sitting (every 30 min) with short regular bouts of slow walking/simple resistance exercises can improve glucose metabolism.

STEPPING

- An increase of only 500 steps/day is associated with 2–9% decreased risk of cardiovascular morbidity and all-cause mortality.
- A 5- to 6-min brisk-intensity walk per day equates to ~4 years' greater life expectancy.

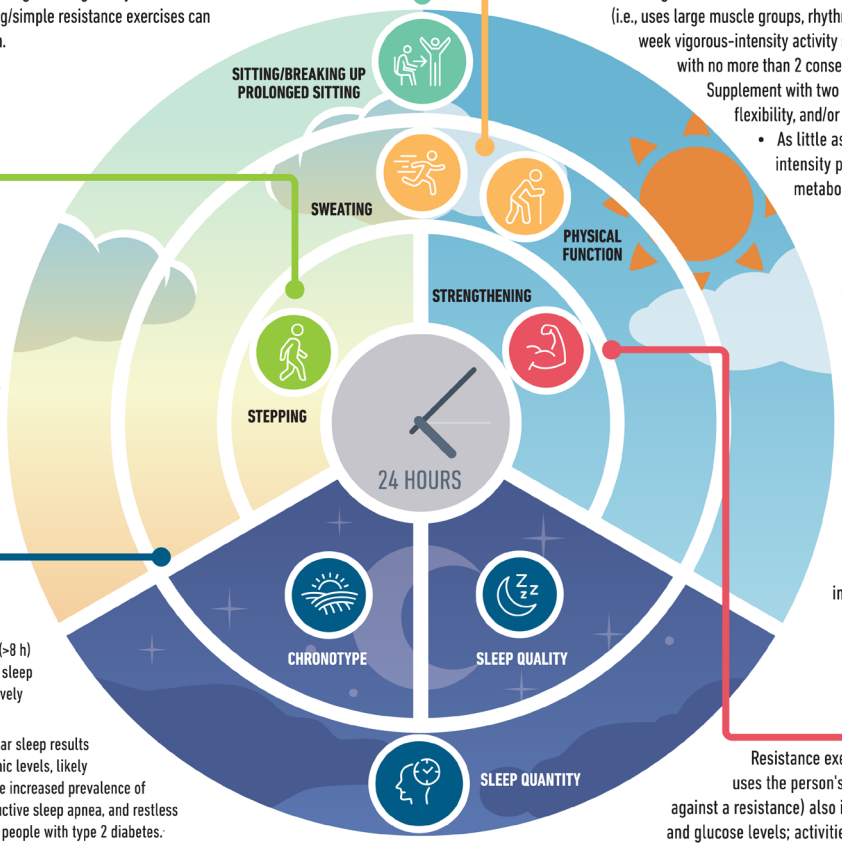
SLEEP

Aim for consistent, uninterrupted sleep, even on weekends.

Quantity – Long (>8 h) and short (<6 h) sleep durations negatively impact A1C.

Quality – Irregular sleep results in poorer glycemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnea, and restless leg syndrome in people with type 2 diabetes.

Chronotype – Evening chronotypes (i.e., night owl: go to bed late and get up late) may be more susceptible to inactivity and poorer glycemic levels vs. morning chronotypes (i.e., early bird: go to bed early and get up early).



SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)

- Encourage ≥150 min/week of moderate-intensity physical activity (i.e., uses large muscle groups, rhythmic in nature) OR ≥75 min/week vigorous-intensity activity spread over ≥3 days/week, with no more than 2 consecutive days of inactivity. Supplement with two to three resistance, flexibility, and/or balance sessions.
  - As little as 30 min/week of moderate-intensity physical activity improves metabolic profiles.

Physical function/frailty/sarcopenia

- The frailty phenotype in type 2 diabetes is unique, often encompassing obesity alongside physical frailty, at an earlier age. The ability of people with type 2 diabetes to undertake simple functional exercises in middle age is similar to that in those over a decade older.

STRENGTHENING

Resistance exercise (i.e., any activity that uses the person's own body weight or works against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.

	Glucose/insulin	Blood pressure	A1C	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

IMPACT OF PHYSICAL BEHAVIORS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

↑ **Higher levels/improvement** (physical function, quality of life); ↓ **Lower levels/improvement** (glucose/insulin, blood pressure, A1C, lipids, depression); ? no data available;
↑ **Green arrows = strong evidence;** ↑ **Yellow arrows = medium-strength evidence;** ↑ **Red arrows = limited evidence.**

Davies, Melanie & Aroda, Vanita & Gabbay, Robert & Green, Jennifer & Maruthur, Nisa & Rosas, Sylvia & Del Prato, Stefano & Mathieu, Chantal & Mingrone, Geltrude & Rossing, Peter & Tankova, Tsvetalina & Tsapas, Apostolos & Buse, John. (2022). Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 65. 1-42. 10.1007/s00125-022-05787-2.

Nutrition

- Refer all people with diabetes to a registered dietitian nutritionist or certified diabetes educator with specialized nutrition training for Medical Nutrition Therapy (MNT) to individualize diet based on patient preference, finances, medical conditions.[1(A),6]
- There is no one ideal diet for all patients with diabetes.[1(E)] Individualize eating plans to patient's needs.[1(A)] Ask about food availability and cultural factors affecting diet.[1(C)]
- Emphasis for nutrition therapy:
  - Whole foods in place of highly processed foods[1(B)]
  - Non-starchy vegetables[1(B)]
  - Carbohydrates:
    - Mostly from whole intact grains, vegetables, whole fruit, legumes, and dairy products.[1(B)]
    - High fiber[1(B), 7]
    - Minimize sugar, sweets, and sweetened beverages (including juice)[1(B,A), 7]
  - Notes:
    - Reducing overall carbohydrate intake improves glycemia and can be incorporated into all eating patterns to meet individual preferences.[1(B)]
    - Self-monitoring carbohydrate intake is a key strategy to achieve glycemic targets.[1]
    - Carbohydrate counting and understanding the effect of protein and fat on glucose levels can improve glycemic control, especially for those on a flexible insulin therapy program.[1(A,B),3] A consistent carbohydrate meal pattern can help manage glucose levels in patients on a fixed insulin schedule.[1(B)]
    - May consider a low or very low-carbohydrate eating plan for those who want to limit medications or who cannot achieve glycemic goals.[1, 3]
      - Use in caution if pregnant or lactating, at risk for disordered eating, renal disease, or on SGLT-2 inhibitors due to risk of ketoacidosis.[1]
      - Reassess regularly due to difficult with sustainability.[1]
  - Sodium:
    - Limit sodium to <2,300 mg/day[1(B)]
  - Fats:
    - Include fats that are high in polyunsaturated fatty acids and monounsaturated fatty acids and low in saturated fat and trans fatty acids.[1(B),]
    - Include long-chain n-3 fatty acids, such as fatty fish (eicosapentaenoic acid EPA and docosahexaenoic acid DHA) and nuts and seeds (alpha-linolenic ALA) to prevent or treat cardiovascular disease.[1(A)]
- Dietary styles: a variety of eating plans including DASH (Dietary Approaches to Stop Hypertension) diet, Mediterranean style diet, or plant-based diet, or low-carbohydrate can be successful.[1(A), 3] Plans should be individualized based on patient needs and preferences.[1]
- Consider simplified approaches such as the plate method (may be helpful for those with limited numeracy or literacy, the elderly, those not taking insulin, those not at risk for hypoglycemia and personal preference).[1(B)]

- Time-restricted feeding (daily caloric restriction based on limiting the window of time when one eats) may be a practical eating management tool, though it does not produce superior weight loss than continuous caloric restriction.[1]
- Alcohol: Limit to 1 drink per day in women or up to 2 per day for men (one drink equals 12 oz beer, 5 oz wine, 1.5 oz spirits).[1(C) 7]
  - Educate about the risks of delayed hypoglycemia if using insulin or secretagogues after drinking alcohol and emphasize the importance of glucose monitoring.[1(B)]
  - Minimize/limit alcohol on low calorie diet to help with weight loss.[1,7]
  - Avoid alcohol completely with high TG[1,7] or signs of liver inflammation.[7]
- Supplements:
  - The routine use of multivitamins, mineral supplements, and herbal supplements (such as chromium, cinnamon, curcumin, and aloe vera) for glycemic control is not supported by evidence.[1(C)]
  - A multivitamin may be needed for pregnant or lactating women, older adults, vegetarians, and people following very low-calorie or low-carbohydrate diets.[1]
- Assess vitamin B12 level intermittently, especially if the patient is on metformin for more than 4 years[5] or has neuropathy or anemia. May need supplementation if deficient.[1,5]
- Drink water as the primary beverage, in place of sugar-sweetened beverages.[1(B)]
- May consider use of non-nutritive sweeteners (calorie-free) as an acceptable substitute to sugar which can reduce overall calorie and carbohydrate intake when there is not a compensatory increase in food consumption.[1(B)]
- The International Diabetes Federation diabetes guideline include advice about prolonged fasting for Ramadan. They note that prolonged fasting is not recommended for high-risk groups such as below[7]
  - Persistent poor glycemic control
  - Severe or recurrent hypoglycemia, or hypoglycemic unawareness,
  - Hyperosmolar hyperglycemic nonketotic syndrome (HHNS) or diabetic ketoacidosis (DKA) in the 3 months before Ramadan
  - Acute illness
  - Pregnancy
  - Advanced macrovascular complications
  - Chronic Kidney Disease (CKD) stage 3 or higher
  - Factors that may affect or be affected by cognitive function (such as multiple daily dose or premix insulin therapy or elderly with ill health)

For those who choose to fast – adjust sulfonylurea or insulin dose and/or timing to reduce risk of hypoglycemia, perform self glucose monitoring, and interrupt fasting if glucose is < 70 mg/dL or the patient has symptoms of hypoglycemia.[7]

Physical Activity

- Type of Activity
  - Aerobic:
    - ≥150 minutes of moderate to vigorous intensity activity weekly[1, 3, 7]

      Note: According to the National Weight Control Registry people who lost weight and kept it off exercised on average about an hour a day.[8]
    - ≥ 3 days per week[1, 3]
    - Avoid missing ≥ 2 consecutive days.[1,7]
    - May break up time into segments (minimum of 10 minutes).[1]
    - Consider building up time and intensity gradually in sedentary or deconditioned individuals.
  - Resistance training: 2-3 x per week on non-consecutive days[1(B), 3]
  - Flexibility and balance training for older adults or those with neuropathy: 2-3 x per week[1(C)]
- Increase non-sedentary activities such as walking, yoga, housework, gardening, swimming, and dancing.[1(B)]
- Decrease time spent in sedentary activity[1(B)]
  - Break up prolonged sitting every 30 minutes for blood glucose benefits[1(C)]
- Evaluate patients for cardiovascular risk factors, safety concerns and limitations before starting a new exercise program if previously sedentary.[1]

Weight Management

- Obesity is a progressive chronic disease with genetic, environmental, and behavioral determinants.
- Weight management should be a primary treatment target for people with diabetes.[1(A)]
- Incorporate evidence-based approaches to treatment that include lifestyle, medical and surgical options, and balancing risk/benefits.
- Consider patient preferences, motivation, and clinical conditions when discussing weight management options.[1(C)]
- Also consider social issues that may impact options such as food insecurity, access to healthy food choices, and other social determinants of health.[1(C)]
- Use a patient-centered communication style that is person-first (e.g., use "person with obesity" instead of "obese person") collaborative, respectful, non-judgmental.[1(E)]
- Measure weight, height, and BMI (and other measures of body fat distribution such as waist circumference, wait-to-hip ratio and/or waist-to-height ratio) annually[1(E), 3] (or more frequently if indicated).[1(B)] Provide privacy during weighing. Consider weight trajectory when discussing options.[1(B)]
- Consider inpatient evaluation if rapid change of weight association with clinical deterioration.[1(E)]
- Help prevent weight gain in normal weight patients.[3]
- Any amount of weight loss provides benefit.[1(B)]
  - Smaller amounts of weight loss (3-7%) improves glycemia and cardiovascular risk factors[1(A), 3]

- Larger, sustained amounts weight loss (>10%) provides more benefits, including disease-modifying effects, possible diabetes remission, and possible improved CVD outcomes and mortality. [1(B), 3]

Lifestyle Management

- Tailor specific dietary advice and eating plans to the patient's preferences and nutritional needs.
- Reduce overall calories by 500 or more per day.[1(A), 3,7] Strive to achieve and maintain ≥ 5% weight loss or by setting individualized calorie reduction goals (such as by a registered dietician).
- Refer to high intensity weight loss program (≥16 sessions in 6 months) that focus on diet, physical activity, and behavioral strategies.[1(A),3]

  Note: USPSTF recommends referring obese patients to intensive multicomponent behavior intervention **(USPSTF Recommendation Level B).**[24]
- May consider a structured medically supervised very low-calorie diet plan (800–1,000 kcal/day) with close monitoring. Integrate long-term strategies and counseling into the plan to sustain weight loss.[1(B), 3]
- Once weight loss goal is achieved, encourage regular weight monitoring (weekly or more often), self-monitoring strategies, regular physical activity (200-300 min/week) and referral to long-term weight maintenance programs (> 1 year) if available.[1(A)]

Medications

- Prioritize the use of medications that are associated with weight loss (GLP1 agonists, dual GIP and GLP1 agonists, SGLT2 inhibitors, metformin, and amylin mimetics).[1(A) 3]
- Minimize the use of medications for diabetes that cause weight gain (sulfonylureas, meglitinides, thiazolidinediones, and insulin).[1(E), 3]
- Anticipate diabetes medication dosage reductions and counsel patient about recognizing and treating hypoglycemia when actively losing weight (if taking insulin or sulfonylureas).
- Note dietary supplements lack evidence that they are effective for weight loss.[1(A)]
- Consider weight loss medications in addition to diet, physical activity and behavioral counseling for patients with BMI ≥ 27 kg/m^2 after reviewing potential risks and benefits.[1(A) 3]
- Of currently approved available agents, semaglutide and terzepatide have the most pronounced weight loss efficacy.[1(A)]
- If medication is effective (such as ≥ 5% weight loss after 3 months), it is likely to continue to be so with ongoing use.[1(A)]
- If patient is not reaching goals, avoid clinical inertia and intensify treatment (e.g., metabolic surgery, additional medication or lifestyle intervention).[1(A)]

Metabolic Surgery (multidisciplinary bariatric team with long term follow-up) per ADA[1,3]

- Consider if
  - BMI ≥ 30 (≥ 27.5 Asian) and the patient is a good surgical candidate.
- Metabolic surgery should be performed in high-volume centers with multidisciplinary teams with long term follow-up, monitoring and support.[1(E)]
- Routinely monitor micronutrient, nutritional, and metabolic status after surgery.[1(B)]
- Evaluate patient in advance for psychosocial issues that could affect the surgery and offer psychological support after surgery if needed to help with adjustment to changes.[1(B)]

- Monitor weight post-metabolic surgery at least every 6-12 months and consider further evaluation and treatment if insufficient weight loss.[1(C)]
- Evaluate and manage post-metabolic surgery hypoglycemia when needed:
  - Exclude other potential causes of hypoglycemia[1(A)]
  - Provide education and MNT by a dietician skilled in bariatric nutrition[1(A)]
  - Treat with medication as needed[1(A)]
  - Use a CGM if severe hypoglycemia or hypoglycemia unawareness.[1(E)]

Smoking

USPSTF Recommendation Level A:

- Ask all patients about tobacco use.[1(A),9]
- Advise all patients not to use cigarettes or other tobacco products, or e-cigarettes.[1(A), 5, 7]
- Assist patients by including smoking cessation counseling and pharmacologic treatment as part of diabetes care.[1(A),9]
- Note: there is an increased risk of prediabetes and diabetes after smoking cessation so monitor and support prevention of diabetes and weight gain.[1]

In California, a patient can contact the California Smoker's Hotline 1-800-NO-BUTTS or 1-800-662-8887.

V. Psychosocial Care

- The ADA states, "Psychosocial care should be provided to all persons with diabetes … and integrated with routine medical care and delivered by trained health care professionals using a collaborative, person-centered culturally informed approach."[1(A)] "Providers should consider assessment for diabetes distress, depression, anxiety, disordered eating, and cognitive capacities"[1(B)] as well as special needs (financial, social, emotional).[1(E)]
- Referral for treatment of mental health disorders should be to providers who use evidence-based treatment approaches and collaborate with the patient's clinical care team.[1(A)]
- Depression
  - Screen all patients with diabetes for depression with a validated screening tool (such as Patient Health Questionnaire PHQ-2, PHQ-4 and/or PHQ-9),[1(B) 3]
    - Annually[1(B)]
    - When there are changes in status[1(B)]
    - When the patient develops complications[1(B)]
  - Offer further evaluation and treatment by mental health providers who use evidence-based approaches evaluation for those who screen positive and collaborate with the diabetes treatment team.[1(A),3]

    Note: USPSTF recommends screening for depression **(Recommendation Level B).** People who screen positive for depression should be evaluated and provided evidence-based care.[10]
- Anxiety
  - Screen for anxiety especially in patients with significant worries about diabetes complications, treatment and injection effects, hypoglycemia, etc.[1(B)] Offer further evaluation and treatment for those whose anxiety affects quality of life or diabetes management.[1(B)]

Note: USPSTF recommends screening adults for anxiety. **(Recommendation Level B)**. People who screen positive for anxiety should be evaluated and provided evidence-based care.[11]

- Screen for and treat hypoglycemia unawareness (such as with glucose awareness training) which may co-exist with patients who have significant anxiety about hyperglycemia.[1(A)]

- Diabetes Distress
  - Screen for diabetes distress, especially in patients who don't meet treatment targets and/or at onset of complications and address distress.[1(B)] Refer to a mental health specialist familiar with diabetes management if symptoms persist.[1]
- Disordered or Disrupted Eating
  - Screen for disordered or disrupted eating using validated screening measures when hyperglycemia and weight loss are unexplained. Offer further evaluation for those who screen positive.[1(B)]
  - Evaluate diabetes treatment plan for patients with disordered or disrupted eating and identify effects of treatment/medications on hunger and caloric intake.[1(B)]
- Serious Mental Illness
  - Screen patients on 2nd generation antipsychotics for prediabetes or diabetes before starting, 3-4 months after starting the medication and then at least every year.[1(B)]
  - Enhance support, assistance and monitoring for patients with diabetes and serious mental illness.[1(B)]
  - Monitor patients using atypical antipsychotics for changes in weight, glycemic control, and lipid levels. Adjust diabetes treatment as needed.[1(C)]
- Cognitive impairment
  - Screen adults ≥ 65 years old for cognitive impairment[1(B)] and cognitive capacity (the ability to make decisions) annually.
  - Monitor cognitive capacity (the ability to make decisions) in all patients especially in the elderly, very young children, people with cognitive disabilities, and people with severe hypoglycemia.[1(B)] Consider formal evaluation if suspect impairment.[1(E)]
  - To help prevent cognitive decline and other major adverse outcomes, avoid hypoglycemia in older adults by adjusting treatment targets and types of medications.[1(B)]

VI. Diabetes Medications

General Medication Recommendations

- Use a patient-centered approach and shared decision making to choose diabetes medications.[1(E) 3]
- Consider comorbidities (ASCVD, heart failure and CKD), patient preference, patient goals, efficacy, proven outcome benefits, cardiorenal risk, risk of side effects and hypoglycemia, effect on weight, age, cost, and SDOH in decisions.[1(A,E), 3]
- Routinely identify and address barriers to medication adherence.[1(A)]
- Follow-up and monitor A1C every 3-6 months. Evaluate medication regimen and medication-taking behavior. Intensify medications promptly when patients are not reaching their goals (overcome clinical inertia) [1(A) 3]

Specific Medication Recommendations

- Patients with multiple CVD risk factors or established ASCVD, regardless of A1C.
  - Use SGLT-2 inhibitors[1(A), 3] or GLP-1 RAs[1(A), 3]
- Patients with heart failure, use regardless of reduced or preserved EF and regardless of A1C.
  - Use SGLT-2 inhibitors[1(A), 3]

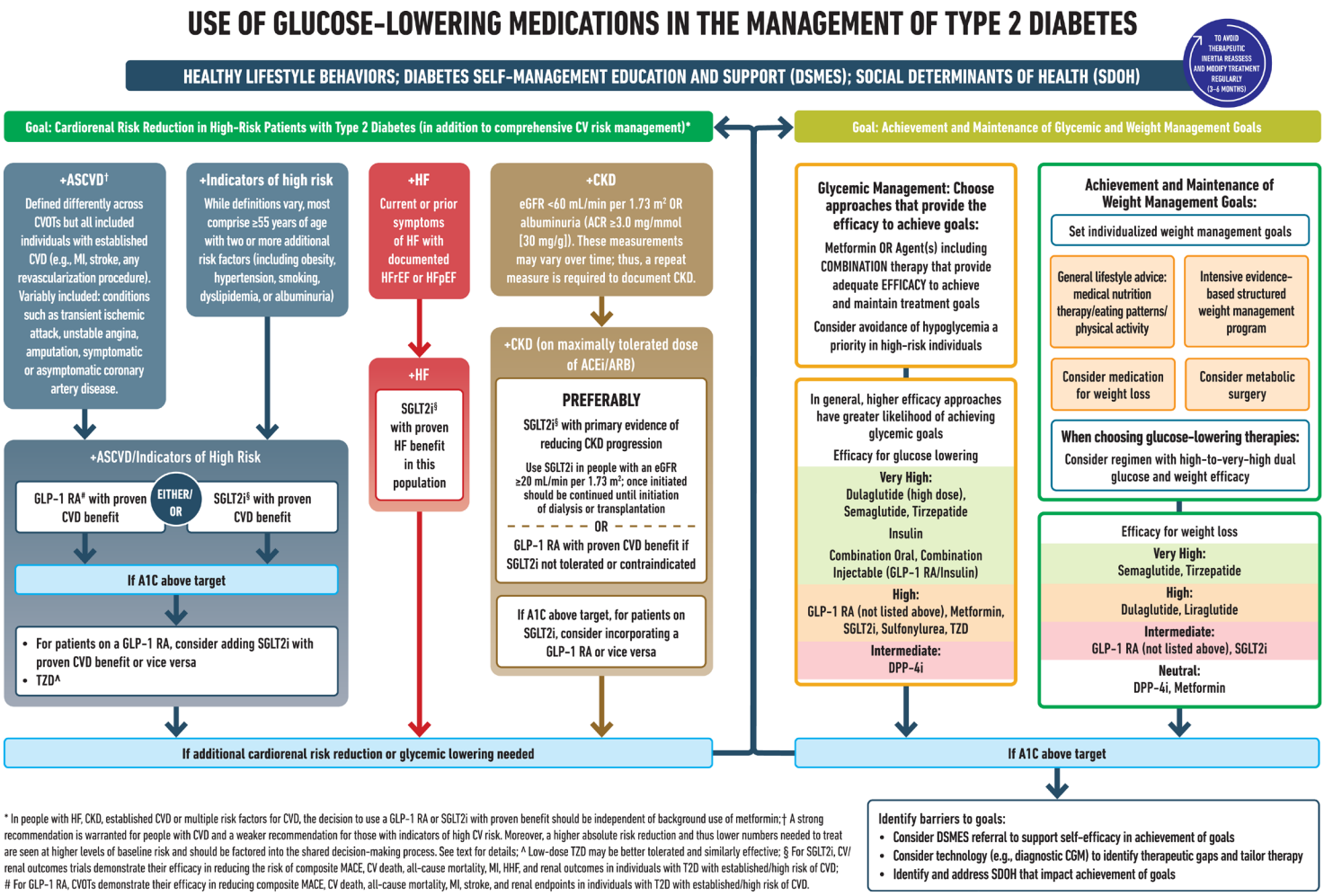
    Note: SGLT-2 inhibitors lead to ⊠ hospitalizations, ↓ mortality, ↓ worsening HF, ↓ symptoms, ↓ physical limitations and ↑ quality of life.[1(A)]
- Patients with chronic kidney disease (eGFR 20-60 or albuminuria), regardless of A1C.
  - Use SGLT-2 inhibitors[1(A), 3]
- Patients with advanced CKD (eGFR < 30)
  - GLP-1 RA is preferred for glycemic management due to its CVD risk reduction and lower risk of hypoglycemia. SGLT2 inhibitors have diminished glucose-lowering effect when eGFR < 45.[(B)]
- Patients who have not reached weight-loss goals.
  - Use GLP-1 RA or GLP-1/GIP [1(A)]
- Very high glucose levels (such as > 300 mg/dL) or A1C level (such as > 10.0%) or evidence of insulin deficiency (such as weight loss).
  - Use early introduction of insulin[1(E), 3]
- Need insulin in type 2 diabetes
  - If able, continue other diabetes medications (including GLP-1 RAs, GLP-1 RA/GIP, and SGLT2s) that improve glucose control, weight management and CKD risk when starting insulin.[1(A) 3]
  - Consider adjust dose or stop sulfonylureas and meglitinides, if needed to lower risk of hypoglycemia risk when starting insulin[1(A)]
- Metformin
  - Continue metformin when adding other diabetes medications or insulin (if able).[1(A)]
  - Can be used in HF if eGFR remains >30 mL/min but avoid if unstable or hospitalized patients with HF[1(B)]
  - For the goal of shortening time to meeting treatment targets, consider early combination therapy[1(A), 3]

Use the 2023 ADA Diabetes Medication Algorithm (Figure 4) and **Medication Summary Table 5** below to help inform medication choices and decisions.[1]

Use the Diabetes Medication Table (Table 13) in the appendix at the end of the guideline with detailed information about common oral and non-insulin injectable medications for type 2 diabetes.

The Mayo Diabetes Medication tool is published by the Mayo Clinic Shared Decision-Making National Resource: https://diabetesdecisionaid.mayoclinic.org/index

Figure 4: Type 2 Diabetes Medication Algorithm[1]



Davies, Melanie & Aroda, Vanita & Gabbay, Robert & Green, Jennifer & Maruthur, Nisa & Rosas, Sylvia & Del Prato, Stefano & Mathieu, Chantal & Mingrone, Geltrude & Rossing, Peter & Tankova, Tsvetalina & Tsapas, Apostolos & Buse, John. (2022). Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 65. 1-42. 10.1007/s00125-022-05787-2.

Table 5: Medication Summary[1]

Medication Class	Efficacy	Hypo-glycemia	Weight Change	Cardiovascular Effect		Cost	Oral or SQ	Renal Effect		Additional Considerations
				Atherosclerotic Cardiovascular Diseae (ACSVD)	Heart Failure			Progression of Chronic Kidney Disease (CKD)	Renal Dosing Use Considerations*	
Metformin	High	No	Neutral (or loss)	Potential benefit	Neutral	Low	Oral	Neutral	Contraindicated with eGFR < 30	• 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
SGLT-2 Inhibitors: Empagliflozin (Jardiance®) Canagliflozine (Ivokana®) Dapagliflozein (Farxiga®) Ertugliflozin (Steglatro) Bexagliflozin (Brenzavvy®)	Intermediate to high	No	Loss (intermediate)	**Benefit:** *Canagliflozin* *Empagliflozin*	**Benefit:** *Canagliflozin* *Dapagliflozim* *Empagliflozin* *Ertugliflozin*	High	Oral	**Benefit:** *Canagliflozin* *Dapagliflozim* *Empagliflozin*	• See labels for renal dose considerations of individual agents. • Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	• 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: Dulaglutide (Trulicity®) Liraglutide (Victoza®) Semaglutide (Ozempic Rybelsus®) Exenatide ER (Bydureon®) Lixisenatide (Adlyxin®)	High to very high	No	Loss (intermediate to very high)	**Benefit:** *Dulaglutide* *Liraglutide* *Semaglutide(SQ)* --- Neutral *Exenatide ER* *Lixisenatide*	Neutral	High	SQ Oral	Benefit on renal end-points 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	• 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. Counsel patients about potential for ileus (semaglutide SQ) • 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

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-I 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. ITsapas et al. (62). 2 Tsapas et al. (114). Reprinted from Davies et al. (45).

Medication Summary, *cont*

Medication Class	Efficacy	Hypo-glycemia	Weight Change	Cardiovascular Effect		Cost	Oral or SQ	Renal Effect		Additional Considerations
				Atherosclerotic Cardiovascular Diseae (ACSVD)	Heart Failure			Progression of Chronic Kidney Disease (CKD)	Renal Dosing Use Considerations*	
GIP and GLP-RAs: Tirzepatide (Mounjaro®)	Very high	No	Loss (very high)	Under Investigation	Under Investigation	High	SQ	Under Investigation	See label for dose considerations. No dose adjustment Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions	• 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 • Not recommended for individuals with history of gastroparesis • 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: Sitagliptin (Januvia®) Saxagliptin (Onglyza®) Linagliptin (Tradjenta®) Alogliptin (Nesina®)	Intermediate	No	Neutral	Neutral	Neutral **(Potential risk:** *Saxagliptin)*	High	Oral	Neutral	• Renal dose adjustment required (*Sitagliptin, Saxagliptin, Alogliptin); can be used in renal impairment.* • No dose adjustment required for Linagliptin	• 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
TZDs: Pioglitazone (Actos®)	High	No	Gain	**Potential benefit:** *Pioglitazone*	Increased risk	Low	Oral	Neutral	• No dose adjustment required • Generally not recommended in renal impairment due to potential for fluid retention	• 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 Glipizide (Glucotrol®) Glyburide (Diabeta®) Glimepiride (Amaryl®)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	• *Glyburide:* generally not recommended in CKD • *Glipizide* and *glimepiride:* initiate conservatively to avoid hypoglycemia	• FDA Special Warning 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	High to Very High	Yes	Gain	Neutral	Neutral	High	SQ	Neutral	• Lower insulin doses required with a decrease in eGFR • Titrate per clinical response	• Injection site reactions • Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs

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-I 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. ITsapas et al. (62). 2 Tsapas et al. (114). Reprinted from Davies et al. (45).

Pre-operative Medication Guidelines

See the Pre-operative medication guidelines https://www.content.sutterhealth.org/ehr/documents/DiabetesBeforeSurgeryHandout.pdf

GI Procedures

See the Bowel Prep Instructions within the Sutter Health Before GI Procedure Instructions

VII. Immunizations

- Provide routine vaccinations for children and adults with diabetes as for the general population including below.[1(A), 3]
- Influenza vaccine annually to all people with diabetes ≥ 6 months of age[1(C)] (Note: generally, do not use the live attenuated for people with diabetes.)[1(C),3]
- Pneumococcal vaccine for Adults[1]
  - Sutter Health recommends adult patients with diabetes receive PCV20. See this CDC summary and this CDC guideline for specific recommendations.
- Hepatitis B vaccination to all adult unvaccinated diabetes patients 19-59 years old (and consider Hepatitis B vaccine for patients ≥ 60 years old).[1(C), 3]
- COVID vaccine according to the most recent CDC guidelines.[3]
- HPV (≤26 years of age; 27–45 years of age may also be vaccinated against HPV after a discussion with health care professionals)
- TDaP (every 10 years; extra dose with pregnancy)[3]
- Zoster (≥ 50 years old or ≥ 19 years old with another specific immunocompromising condition such as malignancy, transplant, or HIV)[1,3]
- RSV (consider if ≥ 60 years old)[1]

VIII. Cardiovascular Risk Reduction

Blood Pressure

Screening and Monitoring

- Measure blood pressure (BP) at every routine office visit.[1(A), 12, 13 (B)]

  USPSTF recommends BP screening for all adults **(USPSTF Recommendation Level A)**[14]
- Measurement Technique:
  - Measure in the seated position, with feet on the floor and back supported, after 5 minutes of rest, over bare arm. Support arm at heart level, cuff size should be appropriate for the upper arm circumference.[3,12,13]
  - Avoid alcohol, cigarettes, and caffeine for 30 minutes before measurement. Ensure bladder is empty. Avoid patient or staff talking during rest or measurement. Take BP twice and use the average of ≥ 2 measurements.[3, 12]
- Inform all patients with diabetes and hypertension to monitor their BPs at home.[1(A), 14, 13(B),15]
- Train patients on accurate technique using upper arm cuff. Avoid wrist or finger cuffs since they are less accurate.[15]

Definition

- SBP ≥130 mmHg or a DBP ≥80 mmHg based on an average of ≥2 measurements obtained on ≥2 occasions.[1(A)]
- BP ≥180/110 mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit.[1(E)]

Goal

- Individualize BP goals with shared decision-making based on CV risk, potential treatment side effects and risks, and patient preferences.[1(B),3,12]
- Consider the following goals:
  - BP goal **< 130/80 mmHg** if it can be safely attained[1(A),3]

Treatment

- Lifestyle changes
  - Recommend lifestyle changes (and increase monitoring) if BP ≥ 120/80.[1(A) 3, 13(B)]
  - Lose weight if overweight or obese, reduce sodium intake, follow DASH diet (increase fruits, vegetables, and low-fat dairy products), limit alcohol, and increase physical activity levels.[1(A), 3, 12, 13,(B), 15]
- Medication
  - Start medication if BP is > 130/80 [1(A)]
  - Start two medications simultaneously if the BP is ≥ 150/90 (or a single pill combination of two medications). [1(A), 3, 13(A),15]
  - Note: taking ≥ 2 medications is often necessary to reach target.[1(A), 3, 12, 13(A),15]
- Type of Medication
  - In general, treat hypertension with the drug classes demonstrated to reduce CVD events in patients with diabetes. [1(A),3, 12, 13(A), 15]
    - > Angiotensin Converting Enzyme inhibitors (ACE inhibitors) or ARBs*

      *For example, if a patient cannot tolerate an ACE inhibitor due to the side effect of a cough, consider an ARB [3,13(B)]
    - > Thiazide-like diuretics
    - > Dihydropyridine calcium channel blockers (CCBs)
  - If CAD, then treat with an ACE inhibitor or ARB [1(A)]
  - If albuminuria (UACR ≥ 30) then treat with an ACE inhibitor or ARB.[1(A,B), 12, 13(A,B) 15]
  - Do not use ACE inhibitors and ARBs in combination [1(A),3,12,13(A,B) 15]
  - Check creatinine, estimated Glomerular Filtration Rate (eGFR) and potassium at initiation and 1-2 weeks after starting ACE inhibitor, ARB or diuretic and annually [12, 13(B),15]
  - If elevated BP despite use of maximum (max) tolerated doses of all three medications, then consider mineralocorticoid receptor antagonist therapy[1, 3,13(B), 15] and/or refer to expert in BP management. [12,13(E),15]

See the Sutter Health Hypertension Guideline 2018 for more detailed information: https://sutterhealth.sharepoint.com/sites/MySutter/ResourcesSHSSDeptsCLTQCEClinicalGuidelines/Sutter%20Health%20Adult%20Hypertension%20Guideline%20Final%2010.1.18.pdf?cid=89ba3ff4-06d7-433e-8370-6c87d9515f76

See patient handout about how to measure home blood pressures https://sutterhealth.sharepoint.com/sites/MySutter/ResourcesSHSSDeptsCLTQCEClinicalHandouts/Measuring%20Your%20Blood%20Pressure%20At%20Home.pdf

See the Sutter Health poster to place near blood pressure measurement sites https://sutterhealth.sharepoint.com/sites/MySutter/ResourcesSHSSDeptsCLTQCEClinicalHandouts/Hypertension%20Measurement%20CorrectTechnique%20Poster_11x16.pdf

Lipid Screening and Monitoring

- Check lipids at diagnosis (initial evaluation) and when starting medications.[1(E), 3]
- Patients **< 40-year-old**
  - **Not on statin** (and/or other lipid treatment): repeat lipids at least every 5 years (or individualize as indicated).[1(E)]
  - **On statin** (and/or other lipid treatment): repeat lipids every 1 year (to monitor adherence/treatment response) and 1-3 months after medication or dose change.[1(A),3]
- **Patients ≥ 40-year-old** (note all diabetes patients ≥ 40 years old should be on a statin)
  - Repeat lipids every 1 year and 1-3 months after medication or dose change.[1(A)]

  Note: USPSTF recommends lipid panel screening for all adults age 40-75 **(USPSTF Recommendation Level B).**[16]

Treatment

- **Lifestyle recommendations** 1) lose weight (if overweight), 2) reduce saturated fat, cholesterol, and trans-fat, 3) increase omega-3 fatty acids (such as fish two days per week),[1] viscous fiber (such as in oats, legumes, citrus), plant stanols/ sterols, 4) consider a Mediterranean or DASH eating pattern, 5) increase physical activity, and 6) eliminate smoking.[1(A),3,17]
- **Statin recommendations** by age group and risk status are summarized in the table below. Decisions should be made with patient using shared decision-making strategies.[1,16]

Table 6: Recommended Statin Intensity by Age and ASCVD Risk Factors[1]

Age	Established ASCVD	Statin recommendation and dose intensity*
<40 yrs old	No	None (or consider moderate intensity statin if ASCVD *RFs)**[1(C)]
	Yes	High intensity statin****[1(A)]
≥ 40 years old	No	Moderate intensity statin (or high intensity statin if ASCVD RFs)***[1(A,B)]
	Yes	High intensity statin****[1(A)]

** If the patient cannot tolerate the recommended statin intensity, then use the max tolerated statin dose[1(E), 3]*

*** Consider moderate intensity statin for diabetes patients < 40 years old if the patient has additional ASCVD risk factors (such as LDL ≥ 100 mg/dL, HTN, smoking, CKD, albuminuria, and family history of premature ASCVD)*

**** If ≥ 1 ASCVD risk factor, goal to reduce LDL ≥ 50% and < 70 mg/dL.[1(A)]*

***** If established ASCVD, then goal to reduce LDL ≥ 50% and < 55 mg/dL[1(B), 3]*

Add ezetimibe or PCSK9 inhibitor with proven benefit if don't reach goal despite maximally tolerated statin dose[1(A,B),3] See details below.

Treat with bempedoic acid[1(A)] if statin intolerant [1(A)]

If >75 years old, it is reasonable to continue statin[1(C)] or start moderate intensity statin[1(C)]

USPSTF concurs with recommendation to use statin for diabetes patients 40-75 years old.[16]

Table 7: Names and Doses of Statins by Intensity[1, 3]

High Intensity Statins	Moderate Intensity Statins
Atorvastatin 40-80 mg	Atorvastatin 10-20 mg
Rosuvastatin 20-40 mg	Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Pitavastatin 1-4 mg

- Non-Statin Medication
  - Ezetimibe[1,3]
    - Consider adding to statin therapy if

      LDL cholesterol persists < 50% reduced or >55 mg/dL in patient with established ASCVD on maximally tolerated statin dose.[1(B)]

      LDL cholesterol persists < 50% reduced or >70 mg/dL in patient with multiple CVD risk factors on maximally tolerated statin dose.[1(B,C)]
  - PCSK9 Inhibitors (Proprotein convertase subtilisin/kexin type 9 inhibitors)[1,3]
    - Consider adding to statin therapy if

      LDL cholesterol persists < 50% reduced or >55 mg/dL in patient with established ASCVD on maximally tolerated statin dose.[1(B)] If intolerant to statin, use PCSK9 inhibitor with monoclonal antibody[1(A)] or with the siRNA inclisiran (Leqvio).[1(E)]

      LDL cholesterol persists >70 mg/dL in patient with multiple CVD risk factors on maximally tolerated statin dose.[1(B)]
  - Fibrates are generally not recommended for cardiovascular risk reduction (except to treat very high TG to avoid pancreatitis).[1(A)]
  - Niacin generally not recommended for cardiovascular risk reduction (and may increase risk of stroke).[1(A)]
- Moderate elevation of TG (175-499 mg/dL)
  - Optimize lifestyle therapy and optimize diabetes management, treat other secondary factors and identify medications that raise TG.[1(C) 3,18]
  - Consider adding icosapent ethyl to reduce CVD risk if ASCVD and other CVD risk factors and on a statin with controlled LDL but elevated TG (135-499).[1(A),1,3]
- Very High TG (TG ≥ 500 to 1000 mg/dL)
  - Refer to a registered dietitian to optimize lifestyle therapy (including weight loss and abstinence from alcohol)
  - Optimize diabetes management
  - Consider doing a workup for secondary causes[1(C), 17,18]
  - Consider medications to reduce risk of pancreatitis[1(C), 3,17,18]
- Risk of Diabetes
  - Studies have reported increased risk of diabetes from statin use, which appears specific to those with diabetes risk factors.[1, 17, 16]
  - The ADA states, "the cardiovascular event rate reduction with statins outweighs the risk of incident diabetes even for patients at highest risk for diabetes."[1,17,18]

Antiplatelet Agents

Primary Prevention (no known ASCVD)

- Discuss low-dose aspirin with patient if increased CVD risk[1] **USPSTF Recommendation Grade C**[19]
- Don't start aspirin for primary prevention if 60 years or older. **USPSTF Recommendation Grade D**[19]
- Note: retinal disease is not a contraindication to aspirin[1(A)]

Secondary Prevention (history of or known ASCVD)

- Use low dose aspirin (75-162 mg/day) for secondary prevention in patients with history of or established ASCVD.[1(A)]
- Use clopidogrel (75 mg/day) for secondary prevention if history of known ASCVD and documented aspirin allergy.[1(B)]
- Use dual antiplatelet therapy (low-dose aspirin and a P2Y12 inhibitor) after acute coronary or ischemic cerebral vascular event as per relevant specialists.
- Consider aspirin plus low-dose rivaroxaban if stable coronary disease and/or PAD and if low bleeding risk to prevent major adverse limb and cardiovascular events.[1(A)]

Heart Disease Evaluation and Treatment

Screening

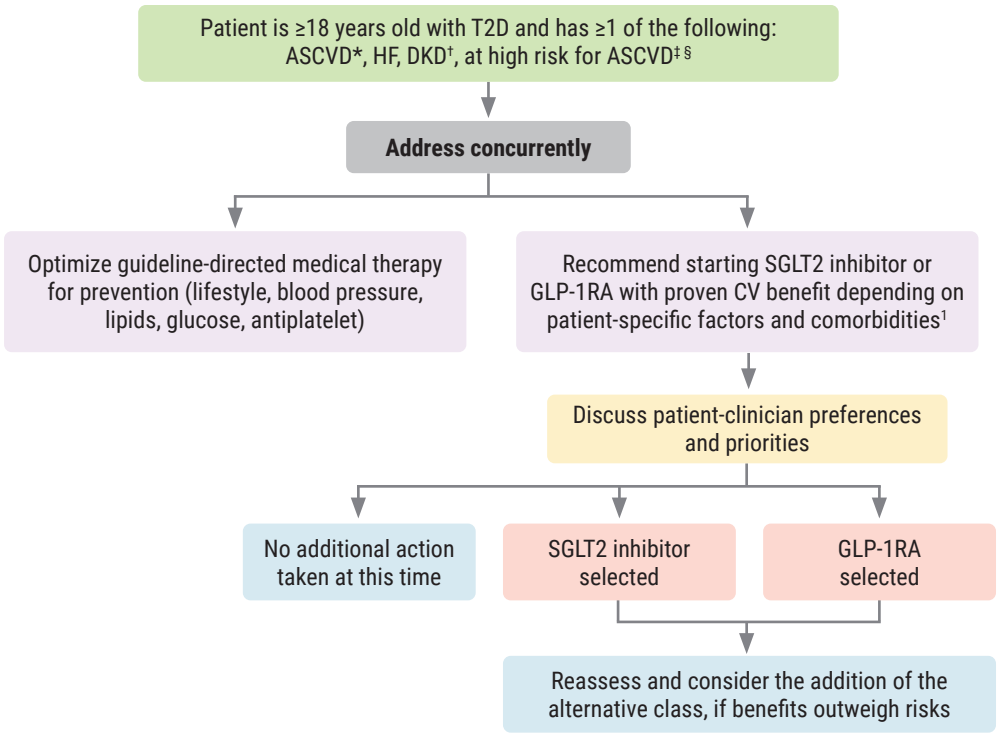
- Evaluate patients for ASCVD risk factors annually.[1]
- Don't order cardiac tests to screen patients for ASCVD (there is no evidence of benefit if risk factors are treated)[1(A)] – unless the patient has typical or atypical signs or symptoms of ASCVD or other indication for testing.[1(E)]
- Consider screening adults with diabetes with a BNP or NT-proBNP to identify HF.[1(B)] If BNP or NT-proBNP is elevated, do an echocardiogram to evaluate for the presence of HF [1(B)]

Treatment

- If established ASCVD treat with
  1) Aspirin[1(A)]
  2) Statin[1(A)]
  3) ACE inhibitor or ARB[1(A)]
  4) SGLT2 inhibitors or GLP-1 RAs with demonstrated CV benefit [1(A)] Note: may consider the use of both an SGLT2 inhibitors and GLP-1 RAs.[1(A)]
  5) Beta blockers for ≥ 3 years after event if history of MI.[1(B)]
- If multiple ASCVD risk factors (without established ASCVD) treat with
  1) Statin[1(A)]
  2) ACE inhibitor or ARB if ≥ 55 yo[1(A)]
  3) SGLT2 inhibitors or GLP-1 RAs with demonstrated CV benefit[1(A)] Note: may consider the use of both an SGLT2 inhibitors and GLP-1 RAs.[1(A)]

- If heart failure treat with (and see the Sutter-Health-Ambulatory-Heart-Failure-Guideline_Dec-2023.pdf)
  1) Care by cardiac specialist.[1(A)]
  2) ACE inhibitor or ARB or ARNi[1(A)]
  3) Beta blockers that are identified for use in heart failure (metoprolol XR, carvedilol or bisoprolol)[1(A)]
  4) Aldosterone Receptor Antagonist
  5) SGLT2 inhibitor (or SGLT1/2 inhibitor) with demonstrated CV benefit if either reduced or preserved ejection fraction (HFrEF or HFpEF)[1(A)]
  6) OK to use metformin if eGFR > 30 (but stop if unstable or hospitalized)[1(B)]

Figure 5: Risk Reduction with SGLT2 Inhibitors and GLP-1 RAs[1]



**ASCVD is defined as a history of an acute coronary syndrome or MI, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.*

† DKD is a clinical diagnosis marked by reduced eGFR, the presence of albuminuria, or both.

‡ Consider an SGLT2 inhibitor when your patient has established ASCVD, HF, DKD or is a high risk for ASCVD. Consider a GLP-1RA when your patient has established ASCVD or is at high risk for ASCVD.

§ Patients at high risk for ASCVD include those with end organ damage such as left ventricular hypertrophy or retinopathy or with multiple CV risk factors (e.g., age, hypertension, smoking, dyslipidemia, obesity).

[1] Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; MI = myocardial infarction; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes

IX. Kidney Disease

General recommendation:

- The ADA states: Optimize glucose and BP control and decrease BP variability to reduce the risk or slow the progression of diabetic kidney disease and CVD [1(A)]

Screening

- Check eGFR and albumin to creatinine ratio (UACR) annually [1(B)]
- If eGFR or UACR are abnormal and/or the patient has established diabetic kidney disease, then monitor labs 1-4 times per year and refer to a nephrologist as per the table below[1, 5]

  Note: Discontinue practice of adjusted GFR for African Americans[20]

Table 8: Definition and stages kidney disease and frequency of monitoring (noted as number in box)[1]

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer* 3	Treat and refer* 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)
High risk
Moderately increased risk
Very high risk

Risk of CKD progression, frequency of visits, and referral to nephrology according to GFR and albuminuria. The numbers in the boxes are a guide to the frequency of screening or monitoring (number of times per year). Green reflects no evidence of CKD by estimated GFR or albuminuria, with screening indicated once per year. For monitoring of prevalent CKD, suggested monitoring varies from once per year (yellow) to four times or more per year (i.e., every 1–3 months, [deep red]) according to risks of CKD progression and CKD complications (e.g., cardiovascular disease, anemia, hyperparathyroidism). These are general parameters based only on expert opinion and underlying comorbid conditions, and disease state must be taken into account, as well as the likelihood of impacting a change in management for any individual. CKD, chronic kidney disease; GFR, glomerular filtration rate. Reprinted and adapted from de Boer et al. (1).

Treatment Goals

- Optimize glucose management to reduce the risk of chronic kidney disease.[1(A)]
- Optimize BP management and reduce BP variability to slow the progression of chronic kidney disease.[1(A)]
- Goal to reduce albuminuria by 30% (if UACR ≥ 300).[1(C)]

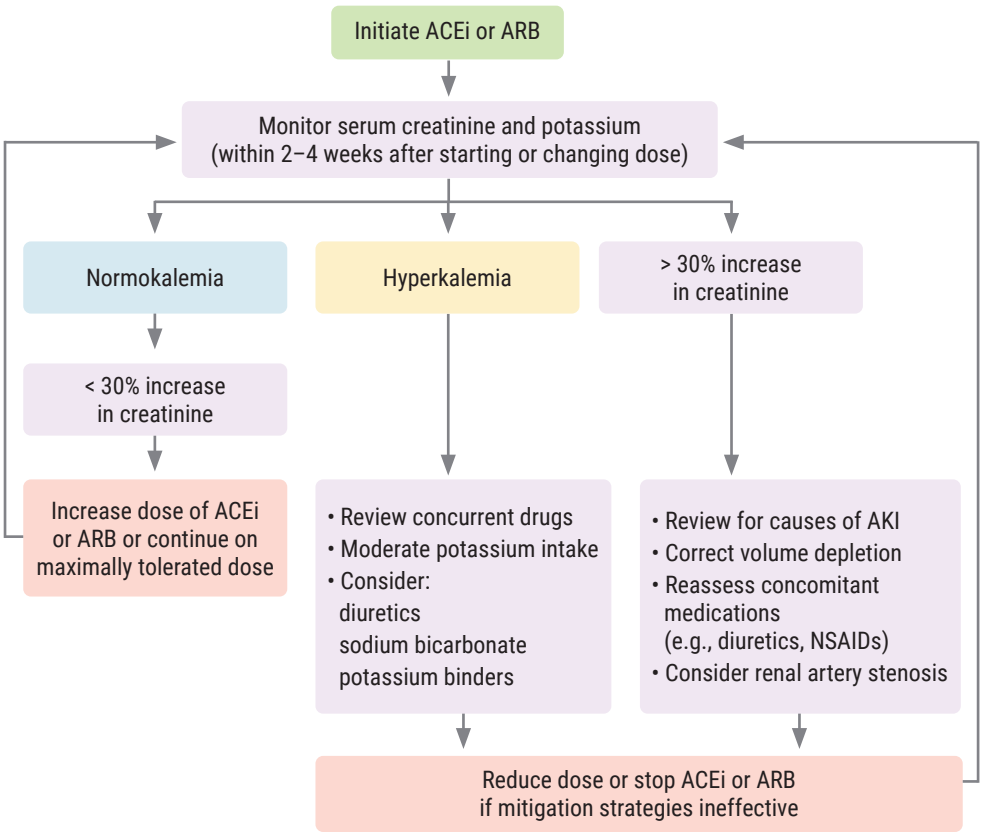
Key Medication Recommendations for patients with kidney disease:

1. Treat with an **ACE inhibitor or ARB** if the patient has hypertension and either the UACR ≥ 30[1 (A,B), 5 (1B)] or the eGFR <60 [1 (A,B)] Titrate to the highest approved dose that is tolerated[5 (1B)]
   See algorithm below for key details

Notes:

- Do not use ACE inhibitor/ARB together.[1,3,5]
- Do not use ACE inhibitor/ ARB If normal UACR (<30 mg/g), normal eGFR and normal BP.[1(A)]
- Monitor Cr, eGFR and K.[1(B)5] Do not stop for Cr increase ≤30% unless due to volume depletion.[1(A),5]

Figure 6: Algorithm for the use of ACE inhibitor or ARB therapy in Kidney Disease[5]



Monitoring of serum creatinine and potassium during ACEi or ARB treatment – dose adjustment and monitoring effects. ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; GI gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug.

Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102(5S):S21

2. Treat with a **SGLT2 inhibitor**[5(1A)] **(and/or GLP-1 RA)** if the patient has kidney disease, in order to decrease progression of CKD and CVD risk[1(A,B) 5 21]

- Use SGLT2[1(A,B) 5(1A)] if the patient has albuminuria (UACR ≥ 30[1(B)] and esp. if ≥ 200[1(A)])
  - Only initiate if eGFR ≥ 20[5(1A)] May consider continuing even after eGFR drops below 20 [5] (stop once on kidney replacement therapy [5]).
  - May need to lower sulfonylureas or insulin to prevent hypoglycemia.[5]
  - May need to lower diuretic dose initially to prevent low BP.[5]
  - There may be an initial drop in eGFR which is not an indication to stop the medication.[5]
  - Consider hold SGLT2 inhibitor during prolonged fast or incurrent illness.[5]
- Use either SGLT2 or GLP-1 RA[1(A)] if the patient does not have albuminuria (UACR < 30).

3. Treat with **metformin.**[5 (1B)]

- If GFR < 45, reduce metformin dose by 50%.[5]
- If GFR < 30 or on dialysis, stop metformin. [1, 5]

4. Treat with a **nonsteroidal mineralocorticoid receptor antagonist** (i.e., finerenone) if patient has CKD and persistent albuminuria on max tolerated dose ACE/ARB [1(A), 3, 5(2A)]. and if eGFR > 25 and K normal at baseline.[5] Monitor K closely.[1(A) 5]

Referral

- Refer to specialist in kidney disease if eGFR < 30, continuously increasing albumin level or continuously decreasing creatine,[1(A)] uncertainty about diagnosis, or difficulties with management.[1(B)]

Nutrition

- If kidney disease not on dialysis – eat the recommended protein daily allowance of 0.8 g/kg/day (based on ideal body weight).[1(A),5,(2C)] If on dialysis, eat higher protein amount (1.0-1.2 g/kg/day).[1(B),5]
- Eat < 2 gram of salt per day if diabetes and kidney disease[5, 2(C)]

X. Microvascular Complications

Neuropathy and Foot Care

General recommendation

- Optimize glucose, blood pressure and lipid control to slow the progression of neuropathy.[1(A,B,C)]

Screening

- Screen for diabetic peripheral neuropathy (DPN) at diagnosis in type 2 diabetes and 5 years after diagnosis in type 1 diabetes, and then annually.[1(B)] Assess its effect on function and quality of life.[22(B)]
- In addition, screen for autonomic neuropathy in patients annually (and with microvascular complications, CKD or DPN) by assessing:[1(E)]
  - Orthostatic dizziness/hypotension, or dizziness/syncope, or resting tachycardia. [1(E)]
  - Dry cracked skin in the extremities.[1(E)]
  - Sexual dysfunction (erectile dysfunction and retrograde ejaculation in men and decreased sexual desire and arousal and pain and inadequate lubrication during intercourse in women).

- Bladder dysfunction (incontinence, nocturia, urinary stream issues, and urinary tract infections).
- Gastroparesis, constipation, diarrhea, fecal incontinence.
- Sudomotor dysfunction (increased or decreased sweating).

Treatment of Painful Diabetic Neuropathy

- Treat patients with neuropathy to reduce symptoms[1(B)] and to improve quality of life.[1(E)]
  - Screen and treat patients for comorbid mood and sleep disorders.[16(B)]
  - Counsel patients of goal of pain reduction (not necessarily elimination) for painful neuropathy.[22(B)]
  - Treat painful neuropathy with gabapentenoids (pregabalin, gabapentin), SNRIs (duloxetine), tricyclic antidepressants and sodium channel blockers.[1(A)22(B)]
  - May consider use of other treatment options including topical agents (such as capsaicin), exercise, cognitive behavior counseling (CBT), Tai Chi, and mindfulness [22(C)]
  - Refer to neurologist or pain specialist if pain is not controlled[1(E)]
  - Avoid use of opioids or opioid/SNRIs combinations for painful neuropathy [22(B/C)]

Foot Care

Screening

- Do foot exam annually to assess for loss of protective sensation and risk for ulcers and amputation including below:[1(A)]
  - Ask about history of ulceration, amputation, Charcot joint, angioplasty, surgery, smoking, retinopathy, kidney disease, and symptoms of neuropathy and vascular disease.[1(B)]
  - Inspect skin and assess for foot deformities (at each visit if history of neuropathy).[1(B)]
  - Neurological assessment
    - 10-g monofilament testing[1(B)] and
    - Pinprick or temperature (small fiber function)[1(B)] or
    - Vibration with a 128-Hz tuning fork (large-fiber function)[1(B)]
- Screen for Peripheral Arterial Disease (PAD)
  - Ask about history of decreased walking speed, leg fatigue, claudication
  - Assess pulses in legs/feet and capillary and venous refill time.[1(B)]
  - Assess for dependent rubor/pallor on elevation[1(B)]
  - Perform noninvasive arterial studies (doppler ultrasound with pulse volume recordings) if signs or symptoms of PAD (including decreased or absent pulses).[1(B)] Ankle Brachial Index (ABI) will be calculated but may be inaccurate in patients with diabetes.
  - Toe systolic blood pressure < 30 mmHg is suggestive of PAD.
  - Consider screening with noninvasive arterial studies for people ≥ 50 yo and any other diabetes complication.[1(A)] Repeat every 5 years if normal.
  - Consider screening people with diabetes for ≥ 10 years for PAD.[1(B)]

Treatment and Referral

- Provide foot education to all patients[1(B)] about
  - foot monitoring daily.
  - care of the foot, including nail and skin care.
- Prescribe specialized therapeutic footwear if
  - History of amputation[1(B)]
  - Loss of protective sensation[1(B)]
  - Foot deformity[1(B)]
  - Ulcers[1(B)]
  - Callous formation[1(B)]
  - Poor peripheral circulation[1(B)]
- Provide specialized and/or multidisciplinary foot care if
  - Prior foot ulcers/amputations[(B)]
  - Loss of protective sensation and structural abnormalities[1(B)]
  - Tobacco smokers[1(C)]
  - Prior lower extremity complications[1(C)]
  - Peripheral arterial disease[1(B)]
  - Charcot joint[1(B)]
  - On dialysis[1(B)]
- Additional treatment of non-healing ulcer may include evidence-based therapies such as below[1(A)]
  - Negative pressure wound therapy
  - Placental membranes
  - Bioengineered skin substitutes
  - Several acellular matrices
  - Autologous fibrin
  - Leukocyte platelet patches
  - Topical oxygen therapy

Retinopathy

General recommendation

- The ADA states, "Optimize glycemic, BP, and lipid control to reduce the risk or slow the progression of retinopathy."[1(A)]

Treatment

- Screening dilated and comprehensive eye examination by ophthalmologist or optometrist at the time of diagnosis[1(B)] and then
  - may consider screening every 1-2 years if no evidence of retinopathy or abnormality and blood glucose levels at goal.[1(B)]
  - screen every 1 year (or more often) if any evidence of retinopathy or abnormality.[1(B)]
  - Inform women who are considering pregnancy about the increased risk of development and progression of diabetic retinopathy during and after pregnancy and need for increased screening during that time.[1(B)]
  - May consider retinal photography as a screening tool for retinopathy if can ensure full exam when needed.[1(B)]

Referral

- Refer patients with macular edema and moderate to severe non-proliferative diabetic retinopathy or proliferative retinopathy to an ophthalmologist specialized in the management of diabetic retinopathy.[1(A)]
- Refer patients with vision loss to vision rehab, educational support and self-management support.[1(E)]

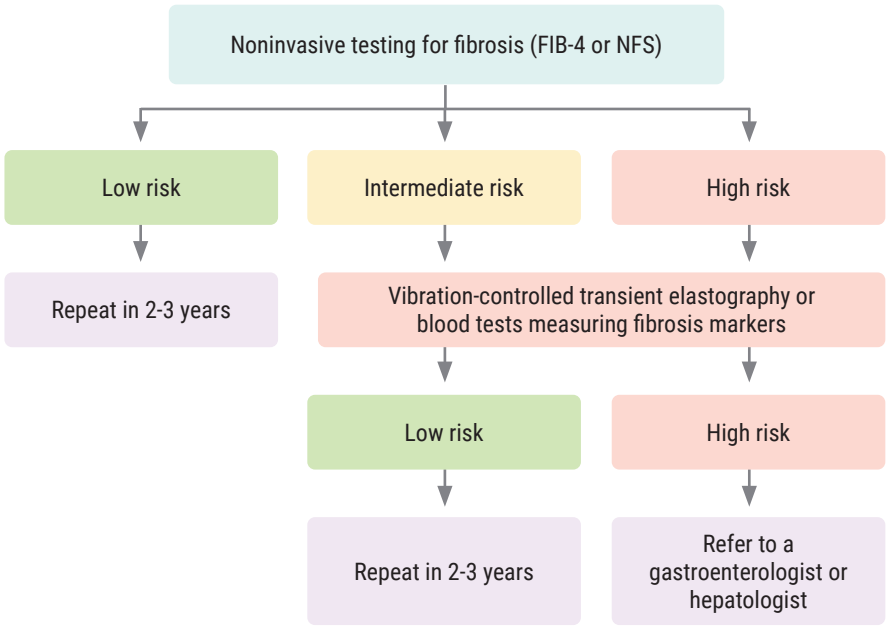
XI. Other Comorbidities

The ADA recommends taking the following common diabetes-associated conditions into consideration when assessing and treating patient[1]

- Nonalcoholic Fatty Liver Disease (NAFLD)
  - Screen patients with diabetes or prediabetes – especially if they have obesity, CVD risk factors and/or established CVD disease – with a calculated fibrosis-4 index (which is based on AST, ALT and platelet count). Do so even if the patients' AST/ALT are within normal limits.[1(B)]
  - If the fibrosis-4 index is low and the AST/ALT is persistently elevated for 6 months or more, then evaluate the patient for an alternate underlying etiology.[1(B)]
  - If the fibrosis-4 index is indeterminant or high, then evaluate the patient for liver stiffness with

    (1) a liver stiffness measurement (LSM) by transient elastography[1(B)] (fibroscan) or

    (2) the blood test ELF "Enhanced Liver Fibrosis" (if the LSM is unavailable).[1(B)]
  - If one of the two tests above are indeterminate or high-risk, then refer to gastroenterologist for evaluation and management.[1(B)]
  - Consider treating patients with NAFLD with lifestyle therapy, GLP-1 RAs, pioglitazone, statins.[1(A,B)]
  - Treat with insulin in decompensated cirrhosis.[1(C)]
  - Consider statins to reduce CV risk (but use with caution and monitor if decompensated cirrhosis).[1(B)]
  - Consider metabolic surgery (depending on the status of the liver function). Use caution if compensated cirrhosis and avoid if decompensated cirrhosis.[1(B)]



- Low testosterone in men
  - Consider checking a morning serum testosterone level in men with diabetes who have erectile dysfunction or decreased sexual desire/activity.[1(B)]
- Periodontal disease[1]
- Hearing impairment[1]
  - Hearing impairment is more frequent in people with diabetes, (esp. in younger patients).[1]
- Hepatitis C Infection[1]
- Pancreatitis[1]
- Cancer[1]
- Bone Health
  - Assess for fracture risk [1(A)]
  - Use DEXA scan to screen high risk people > 65 (and younger if multiple risk factors every 2-3 years) [1(A)]
  - Consider avoiding diabetes medications associated with increased fractures (thiazolidinediones, insulin, and sulfonylureas) in patients with high fracture risk[1(A)]
  - Try to avoid hypoglycemia for patients with high fracture risk [1(E)]
  - Optimize calcium and vitamin D as recommended if fracture risk.[1(B)]
  - Consider treatment for osteoporosis if T-score ≤ -2.0 or history of fragility fractures. Note: T-scores may underestimate fracture risk in patients with diabetes.[1(B)]
- Cognitive impairment and dementia
  - Poor glycemic control and longer duration of diabetes are associated with cognitive decline.
  - Screen for cognitive impairment and dementia annually in people ≥ age 65.[1(B)]
- Sleep pattern and duration
  - Screen for sleep disorders, disruptions to sleep, worries about sleep or symptoms of sleep apnea (e.g., excessive daytime sleepiness, snoring, witnessed apnea).[1(B)3]
  - Recommend healthy sleep hygiene.[1(A)]
  - Refer for sleep study if indicated.[1(B)] Treat sleep apnea if diagnosed.[1(B)]
  - Refer to sleep medicine or behavioral health professional as needed.[1(B)]
- COVID
  - Prioritize COVID vaccination for patients with diabetes.[1(B)]
  - If a patient develops new-onset diabetes during a COVID diagnosis, monitor the patient to see if the diabetes is transient.[1(B)]
  - Monitor for psychosocial wellbeing in patients with diabetes and COVID.[1(E)]
  - Address the impact of COVID on high-risk groups of people with diabetes.[1(B)]
  - Assess for evidence of long-COVID in people with diabetes.[1(E)]
  - Monitor people with diabetes and COVID for DKA.[1(C)]
  - Encourage patients to reach glucose targets to mitigate risks of COVID.[1(B)]
- Human immunodeficiency virus (HIV)
- Geriatric syndromes (i.e., polypharmacy, cognitive impairment, depression, urinary incontinence, falls, persistent pain, and frailty)[1(B)]

XII. Transitions of Care from Acute Care Settings

- Create a structured, individualized discharge plan for each patient.[1(B),23]
- Check A1C if there is no recent result available (within the last 1-3 months)[1]
- Include the following in the discharge process[1]
  - Medication reconciliation and double-checking pre-hospital medication list to confirm that no needed medications are inadvertently stopped and to ensure the safety of new and changed medications.[1,23]
  - Fill new and changed medications and supplies before discharge.[1]
  - Review all new and changed medications with the patient and their care giver before discharge.[1]
  - Reinforce new or changed medications at follow-up ambulatory visits.[1]
- Include the following in the discharge summary[1,23]
  - Medication changes[1]
  - Tests and studies still pending[1]
  - Follow-up needs[1,23]
- Send the discharge summary to primary care physician and diabetes management providers (such as endocrinologists or diabetes specialists) immediately after discharge.[1]

Patient education and follow-up

- Identify who will provide diabetes care after discharge.[1,23]
- Schedule the post-discharge follow-up visit for diabetes before discharge (ensure visit is soon after discharge with frequent contact if medications have been changed or glucose levels are not at goal).[1]
- Use teach back method and health literate tools and education materials.[23]
- Include the following topics for education[1,23]
  - Diabetes diagnosis[1]
  - Signs and symptoms related to diabetes[1]
  - Sick-day management.[1]
  - Blood glucose self-monitoring and goals[1]
  - When to call the provider [1] (use the Sutter diabetes teach back tools)
  - Identification, prevention, and treatment of hyperglycemia and hypoglycemia
  - Adjustment of medications when appropriate (sulfonylureas and insulin are particularly high risk for emergency room visits) [1]
  - Nutrition and lifestyle recommendations[1]
  - Use and disposal of diabetes supplies[1]

Ask about concerns and barriers before being discharged and connect to community resources when appropriate.[23]

XIII. Abbreviations:

A1C	Hemoglobin A1C
AACE	American Association of Clinical Endocrinologists
AAN	American Academy of Neurology
ACE inhibitor	Angiotensin Converting Enzyme Inhibitor
ADA	American Diabetes Association
ADCES	The Association of Diabetes Care and Education Specialists
ADL	Activities of daily living
AGP	Ambulatory Glucose Profile
AHA	American Heart Association
ALT	alanine transaminase
AST	aspartate aminotransferase
ARB	Angiotensin Receptor Blocker
ARNi	Angiotensin Receptor-Neprilysin Inhibitor
ASCVD	Atherosclerotic cardiovascular disease
BID	twice daily
BMI	Body Mass Index
BP	blood pressure
CCB	Calcium Channel Blocker
CDC	Center for Disease Control and Prevention
CGM	Continuous Glucose Monitors
CKD	Chronic Kidney Disease
CrCl	Creatinine Clearance
CVD	Cardiovascular disease
DASH diet	Dietary Approaches to Stop Hypertension diet
DBP	Diastolic blood pressure
DKA	Diabetic ketoacidosis
DPN	Diabetic peripheral neuropathy
DPP	Diabetes Prevention Program
DPP-4 inhibitors	Dipeptidyl Peptidase-4 Inhibitors
DSMES	Diabetes self-management education and support
eGFR	estimated Glomerular Filtration Rate
ESRD	End Stage Renal Disease
ER	Extended Release
FDA	United States Food and Drug Administration
GI	Gastrointestinal
GLP-1 RAs	Glucagon-like peptide-1 receptor agonists
HIV	human immunodeficiency virus
HDL	High-density lipoprotein cholesterol
INR	international normalized ratio
KDIGO	Kidney Disease, Improving Global Outcomes
LFTs	Liver Function Tests
LDL	Low Density Lipoprotein Cholesterol
MACE	major adverse cardiac events
Max	maximum
MNT	Medical nutrition therapy
OGTT	Oral Glucose Tolerance Test
PCV13	Pneumococcal Conjugate Vaccine
PPSV23	Pneumococcal Polysaccharide Vaccine 23
QID	four times daily
SBP	systolic blood pressure
SC	subcutaneous
SGLT-2 inhibitors	Sodium-glucose co-transporter 2 inhibitors
TG	Triglycerides
TID	three times daily
TZD	Thiazolidinedione
UACR	urine albumin-to-creatinine ratio
USPSTF	United States Preventative Service Task Force
UTI	urinary tract infection

XIV. References:

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XV. Evidence Tables

Table 9: ADA Evidence Table

ADA 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 Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford 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
B	Supportive evidence from well-conducted cohort studies • 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
C	Supportive evidence from poorly controlled or uncontrolled studies • 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
E	Expert consensus or clinical experience

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Table 10: USPSTF Evidence Table

Grade	Description	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Table 11: KDIGO Evidence Table [5]

Grade	Implications		
	Patients	Clinicians	Policy
Level 1, strong "We recommend"	Most people in your situation would want the recommended course of action, and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2, weak "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect is close to the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of effect is very uncertain, and often it will be far from the true effect.

XVI. A1C and Mean Glucose Levels

Table 12: Mean glucose levels for specified A1C levels

A1C (%)	mg/dL*	mmol/L
5	97 (76-120)	5.4 (4.2-6.7)
6	126 (100-152)	7 (5.5-8.5)
7	154 (123-185)	8.6 (6.8-10.3)
8	183 (147-217)	10.2 (8.1-12.1)
9	212 (170-249)	11.8 (9.4-13.9)
10	240 (193-282)	13.4 (10.7-15.7)
11	269 (217-314)	14.9 (12.0-17.5)
12	298 (240-347)	16.5 (13.3-19.3)

Data in parentheses are 95% CI. A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG.

•These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes. The correlation between A1C and average glucose was 0.92 (12,13). Adapted from Nathan et al. (12).

XVII. Table 13: Type 2 Diabetes Non-Insulin Medication Table

- This table is a summary of the most common classes and brands of oral and non-insulin injected type 2 diabetes medications including key considerations in terms of dose, generic status, titration, effectiveness, monitoring, management considerations, warnings, side effects, dose adjustments, and contraindications.
- This table is not meant to be a comprehensive inclusion of all information about each medication. In particular drug-drug interactions are not included in this table. Please refer to the references below, each medication's package insert, and electronic health record prescribing details and alerts for full information.
- The United States Food and Drug Administration (FDA) has started considering cardiovascular outcome by the standard of "major adverse cardiac events" (MACE) outcome trials including cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke for diabetes drug approval. MACE outcome results are included in the table below when available.
- Note about generic status and cost:
  - Note that Lexicomp includes details about medication prices: https://online.lexi.com
  - Generic status and cost is one of the considerations when prescribing medications.
  - There can be substantial difference between the average price of medications and the actual cost of medications to a patient, which is affected by insurance and formulary status, financial assistance programs, pharmacy type, discount programs, effectiveness of medication, dose of medication, side effects/risks/benefits of medications, and the amount and cost of monitoring required by the medication.
  - Patients should be offered resources to overcome barriers related to costs of medications.

- Notes about combination medications (combination options are not included in the table below):
  - Combination medications can be an excellent option for some patients and situations as there is potential for improved adherence and cost savings (especially in regard to co-pays). Combination medications are best for patients on stable doses of multiple medications.
  - Considerations in regard to combination medications
    - Does not allow for flexibility of titrating dose of individual agents
    - Baseline and ongoing monitoring parameters should be consistent with individual products
    - Monitoring and contraindication information for individual products should be reviewed

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Pharmacist's Letter. Drugs for Type 2 Diabetes. Therapeutic Research Center

Biguanides

Generic Name (Brand Name)	Generic Available	Initial Dose	Titration/Adjustment
Metformin (Glucophage®)	Y	500 mg daily or BID *take with food*	Increase by 500 mg weekly; Max dose: 2550 mg daily
Metformin ER (Glucophage XR®) Long acting	Y	500 mg or 750 mg	Increase by 500 mg or 750 mg weekly to max dose of 2000 mg daily
Fortamet® Long acting	N	1000 mg PM	Increase by 500 mg weekly; Max dose of 2500 mg qPM
Glumetza® Long acting	N	1000 mg qPM	Increase by 500 mg weekly; Max dose 2000 mg qPM
Meformin Solution 500 mg/5mL (Riomet®)	N		

Management Considerations

Effectiveness

- May Lower A1C% 1% to 1.5% – Max effect at 3-4 weeks

Monitoring:

- Monitor renal function at baseline and at least annually
- Monitor more frequently (every 3 to 6 months) if susceptible to renal injury
- Assess vitamin B12 level intermittently, especially if the patient is on metformin for more than 4 years[5] or has neuropathy or anemia. May need supplementation if deficient.[1,8]

Management Consideration

- May cause gastrointestinal (GI) Intolerance – less with long acting formulations – which may improve over time
- Start at a low dose and gradually increase dose to minimize GI symptoms – if GI side effects occur as dose is advanced, decrease to previous lower dose and try to advance at a later time.
- Low risk of hypoglycemia
- May help prevent weight gain
- May experience a metallic taste

Black Box Warning:

- **Lactic Acidosis is rare but serious – the risk of accumulation increases with the degree of renal impairment – suspect if acidosis without ketoacidosis**

Warnings/Side Effects:

- Elderly
  - Caution in patients > 80 years old unless normal renal function established
  - Avoid max dose in elderly patients
- Use with caution in patients with
  - congestive heart failure requiring pharmacologic management, particularly in patients with unstable or acute heart failure
  - alcoholism; avoid excessive acute or chronic ethanol use
  - hepatic impairment; caution due to potential for lactic acidosis

Dose Adjustment:

- Renal function
  - eGFR >60: No dosage adjustment necessary. Monitor renal function at least annually.
  - eGFR 45-60: No dosage adjustment necessary. Consider monitor renal function every 3 to 6 months.
  - eGFR 30-45: Do not initiate therapy; if eGFR falls to <45 during therapy, consider discontinue therapy (based on risks/benefits) or reduce dose (eg, 50% reduction or 50% of max dose). Monitor renal function every 3 months.
  - eGFR <30: Contraindicated.
- If patient using metformin despite eGFR < 60 consider hold the metformin when the patient is at risk for dehydration (such as illness with nausea/vomiting, etc.)
- Stop metformin at the time of, or prior to, an iodinated contrast imaging procedure in patients
  - with an eGFR 30-60 mL/min/1.73 m^2
  - with a history of hepatic impairment, alcoholism or heart failure
  - who will be administered intra-arterial iodinated contrast
  - who are at increased risk for lactic acidosis

  In the patients above, re-evaluate eGFR 48 hours after the imaging procedure, and restart metformin if renal function is stable.

Contraindications:

- Acute or chronic metabolic acidosis
- eGFR < 30

SGLT2 inhibitors

Generic Name (Brand Name)	Generic Available	Dose	Titration/Adjustment
Canagliflozin (Invokana®)	N	100 mg once daily prior to first meal of the day	Titrate to max dose 300 mg once daily only for patient with normal renal function ***Renal Dosing:*** • eGFR 45-60 max dose: 100 mg once daily. • eGFR < 45: Use not recommended.
Dapagliflozin (Farxiga®)	N	5 mg daily in the morning, with or without food	Titrate up to 10 mg once daily. ***Renal Dosing:*** • GFR > 60mL/min: No dosage adjustment • eGFR < 60 mL/min: Not recommended.
Empagliflozin (Jardiance®)	N	10 mg daily	Titrate to 25mg once daily ***Renal Dosing:*** • eGFR ≥ 45 mL/min No dosage adjustment necessary • eGFR < 45 mL/min: not recommended
Ertugliflozin (Steglatro™)	N	5 mg daily	Titrate to 15 mg daily (max dose) ***Renal Dosing:*** • eGFR > 60mL/min: No dosage adjustment • eGFR < 60 mL/min: Not recommended
Bexagliflozin (Brenzavvy®)	N	20 mg daily	***Renal Dosing:*** • eGFR ≥ 30 mL/min: No dosage adjustment • eGFR < 30 mL/min: Not recommended. Not recommended with severe hepatic impairment.

Management Considerations

Effectiveness

- May lower A1C 0.5-1.0%

Monitor

- Monitor potassium in those who are predisposed to potassium abnormalities
- Monitor renal function baseline and annually. An initial reversible decrease in eGFR may occur and is not indication for stopping the medication. Do not stop SGLT2 inhibitors if eGFR increase is less than 30%[5]
- Monitor and treat LDL abnormalities
- Monitor patients for signs and symptoms of ketoacidosis (eg, difficulty breathing, nausea, vomiting, abdominal pain, confusion, unusual fatigue or sleepiness)
- For type 1 diabetes and type 2 diabetes who are ketosis prone or on ketogenic diets, educate about ketoacidosis and provide ketone measuring tools [1(E)]
- Monitor patients receiving Canagliflozin for risk factors of amputation (new pain or tenderness, sores or ulcers or infections in their legs or feet.

Management Considerations

- Many potential side-effects
- Promotes weight loss
- Low risk of hypoglycemia
- Correct volume depletion prior to initiation

Black Box Warning:

- **2-fold increase risk of lower limb amputation with additive risk factors such as history of amputation, peripheral vascular disease, neuropathy and diabetic foot ulcer for Canagliflozin.**

Warnings/Side Effects:

- Ketoacidosis including in situations where the glucose was normal or only minimally elevated. Consider holding SGLT2 inhibitors at least 24 hours before situations at increased risk of ketoacidosis (such as prolonged fasting, surgery or critical illness).[8, 5]
- Lower limb amputations (Canagiflozin). Patients at high risk for CVD had 2-fold increase risk of amputations from Canagliflozin compared to placebo.[15] Consider risk factors for amputation before prescribing Canagliflozin (history of prior amputation, PVD, neuropathy, diabetic foot ulcers).
- Bone fractures and bone mineral loss. Patients at high risk for CVD had increase risk of fractures from Canagliflozin compared to placebo.[15] Patients with renal failure were at higher risk for fractures from dapagliflozin. No effect on bone fracture was found with empagliflozin. Consider avoiding SGLT-2 inhibitors in patients at high risk of bone fracture.

SGLT-2 inhibitors *continued. . .*

- Hypotension due to intravascular volume depletion especially in patients with renal impairment (i.e., eGFR <60), elderly, patients or those on anti-hypertensives (e.g. diuretics, ACE inhibitors, or ARBs) (symptoms include: hypotension, orthostatic hypotension, dizziness, syncope, and dehydration)
- Hyperkalemia: esp in patients predisposed to hyperkalemia (including patients with renal impairment or taking potassium-sparing diuretics, ACE inhibitors, and ARBs)
- Renal impairment esp in elderly patients and those with preexisting renal abnormalities
- Female and male genital fungal infections, urinary tract infection, and increased urination
- Thirst, constipation and nausea
- Lipid abnormality: May cause dose-related LDL elevation. Monitor LDL and treat as needed.
- Bladder cancer: Newly diagnosed bladder cancer occurred more frequently in dapagliflozin patients

Dose Adjustment

- Adjust for renal function

Contraindications:

- Severe renal impairment and ESRD
- Severe hepatic impairment
- Diabetic ketoacidosis

GLP-1 Receptor Agonists

Generic Name (Brand Name)	Generic Available	Dose	Titration/Adjustment
Human GLP1 Analogues			
Dulaglutide (Trulicity®)	N	0.75mg SC once weekly	May increase to max 1.5 mg once weekly
Liraglutide (Victoza®) May be used as combination with insulin degludec (Xultophy®)	N	0.6 mg subcutaneous (SC) daily	After 1 week, increase the to 1.2 mg SC daily. May be increased to 1.8 mg SC daily max dose. No dosage adjustment necessary for renal although caution advised.
Semaglutide (Ozempic®)	N	0.25mg SQ once weekly	If after 4 weeks, additional glycemic control is needed, increase to 0.5mg once weekly. Continue for at least 4 weeks then maximum 1mg if further control is necessary. No renal dosage adjustment needed.
Exendin-based GLP1 Analogues			
Exenatide (Byetta®)	N	5 mcg SC BID within 1 hour before morning and evening meals, approximately 8 hours apart	Increase to 10 mcg BID after one month if patient not at goal and tolerating GI effects ***Renal Dosing:*** • CrCl 30-50 mL/min: Use caution • CrCl <30 mL/min: Not recommended
Exenatide extended release (Bydureon®)	N	2mg SC weekly with or without meals	No titration. Max is 2mg SC weekly. ***Renal Dosing:*** • CrCl 30-50mL/min: Use caution • CrCl <30mL/min: Not recommended
Lixisenatide and insulin glargine (Soliqua®)	N	Only available mixed with insulin glargine. See Lexicomp and medication packaging information for prescribing details.	

Management Considerations

Effectiveness

- May lower A1C 1.0-1.5%

Monitor

- Monitor renal function at baseline and annually
- Monitor international normalized ratio (INR) if concurrent warfarin use

Management Considerations

- Low risk for hypoglycemia
- Promotes decrease appetite, decrease food intake, and weight loss
- Take oral medications with narrow therapeutic window or that require rapid absorption at least 1 hr before injection, (e.g. contraceptives, antibiotics)
- Missed dose for weekly GLP-1 RAs – if more than 3 days have passed since the dose was missed, omit the missed dose and resume administration at the next regularly scheduled weekly dose, otherwise administer as soon as possible
- Pen should be discarded 30 days after initial use

Major Adverse Cardiovascular Events (MACE) Trial Results

- Diabetes patients at high risk for CVD events on Liraglutide had a lower risk of death from cardiovascular causes, nonfatal myocardial infarction, and nonfatal stroke compared to placebo in the clinical trial LEADER, **(Note the FDA indicates liraglutide to reduce the risk of major adverse CV events in adults with type 2 diabetes and established CV disease)**

Black Box Warning:

- **Dose- and duration- dependent thyroid C-cell tumors have developed in animal studies with GLP-1 RAs therapy; relevance in humans unknown**

Warnings/Side Effects:

- May cause nausea/vomiting (improve over time)
- Cases of acute pancreatitis have been reported in patients on GLP-1 RAs. Monitor patients for signs and symptoms of pancreatitis and if suspected, discontinue use. It is unknown if GLP-1 RAs increase the risk of pancreatitis. (Note in the recent clinical trial LEADER, patients on liraglutide did not have an increased risk of pancreatitis compared to placebo[15])
- May increase INR, increase monitoring when initiating in patients on warfarin
- Cardiovascular effects: Tachycardia or conduction abnormalities (liraglutide or dulaglutide)
- Hypersensitivity reactions

Dose Adjustment

- Use with caution in patients with renal impairment (as acute renal failure/chronic renal failure exacerbations have been reported)
- Consider reducing dose of insulin for patients with A1C < 8.0%
- Consider reducing dose of sulfonylurea due to increased risk of hypoglycemia when used in combination

Contraindications:

- Preexisting severe gastrointestinal disease
- Acute or chronic pancreatitis
- History of or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia syndrome type 2 (MEN2)
- ESRD or CrCl <30 mL/min (Liraglutide, Exenatide, Dulaglutide, Lixisenatide)

GIP and GLP-1 Receptor Agonists

Generic Name (Brand Name)	Generic Available	Initial Dose	Titration/Adjustment
Tirzepatide (Mounjaro®)	N	Initial dose 2.5mg weekly for 4 weeks, then titrate up the dose.	Initial dose: 2.5 mg subcutaneously once weekly for 4 weeks May increase to 5 mg once weekly at 2.5mg/week increments every 4 weeks to achieve glycemic goal with the max weekly dose of 15mg/week. No dose adjustment recommended for renal or hepatic impairment

Management Considerations

Effectiveness

- May lower A1C 1 – 2%

Monitoring

- Monitor INR if concurrent warfarin use
- Renal function at baseline and following dose increases (patients with renal impairment may report severe GI symptoms)
- Signs/symptoms of pancreatitis, gallbladder disease and worsening of diabetic retinopathy

Management Consideration

- Promotes weight loss. The effect of delaying gastric emptying may have significant impact of other oral medication absorption and GI side effects
- Consider reducing the dose of concomitantly administered insulin or insulin secretagoues to reduce the risk of hypoglycemia
- Females using oral hormonal contraceptives should be encouraged to switch to nonoral contraceptive method(s) or to add a barrier method of contraception for 4 weeks after initiation of tirzepatide therapy and for 4 weeks after each dose escalation

Effects on Lipids:

- At week 40, all doses of tirzepatide produced improvements from baseline in total cholesterol, low-density lipoprotein cholesterol, very low–density lipoprotein cholesterol, and triglycerides compared to placebo (SURPASS-5). Mean change from baseline in lipid levels at 40 weeks: Greater improvements were observed in patients receiving tirzepatide than semaglutide for triglycerides, very low–density lipoprotein, and high-density lipoprotein levels. Total cholesterol and low-density lipoprotein levels were not significantly different between groups. (SURPASS-2 trial)

Major Adverse Cardiovascular Events (MACE) Trial Results

- The cardiovascular outcomes trial (SURPASS-CVOT) is still ongoing. Hazard ratio of 0.81 is resulted from pooled SURPASS data regarding four-component major adverse cardiac event (MACE-4) events (cardiovascular death, myocardial infarction, stroke and hospitalized unstable angina). Most MACE-4 events that were recognized were seen in SURPASS-4, suggesting a hazard ratio of 0.74 (95% CI, 0.51–1.08) (p=0.123).

Black Box Warning

- Tirzepatide caused thyroid C-cell tumors in rats; it is unknown whether tirzepatide causes thyroid C-cell tumors, including MTC, in humans.

Warnings/Side Effects

- Warnings include risk of thyroid C-cell tumors, pancreatitis, hypoglycemia with concomitant use of insulin or insulin secretagogues, CKD, Sever GI disease, and worsening of diabetic retinopathy
- Hypersensitivity reactions including anaphylaxis and angioedema may occur
- Adverse reactions reported in 5% or more of patients treated with tirzepatide included nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain

Dose Adjustment

- none

Contraindications

- Tirzepatide is contraindicated in patients with a personal or family history of MTC or patients with MEN2, and in patients with prior serious hypersensitivity to the drug or any of its excipients (sodium chloride and sodium phosphate dibasic heptahydrate; hydrochloric acid solution and/or sodium hydroxide solution may also be added to adjust pH)

Sulfonylureas

Generic Name (Brand Name)	Generic Available	Initial Dose	Titration/Adjustment
Glipizide (Glucotrol®)	Y	2.5-5 mg daily with breakfast	Titrate 2.5-5 mg to BID with breakfast and dinner. Max dose: 10 mg BID or 15 mg daily
Glipizide XL (Glucotrol XL®)	Y	2.5-5 mg daily with breakfast	Titrate 2.5-5 mg daily or BID with breakfast and dinner. Max dose: 20 mg daily
Glyburide (Diabeta®)	Y	2.5 mg/day daily with breakfast (consider 1.25 mg if high risk for hypoglcyemia)	Titrate 2.5-5 mg daily or BID with breakfast and dinner. Max dose: 20 mg daily
Micronized Glyburide (Glynase®)	Y	1.5-3 mg/day with breakfast (consider 0.75 mg if high risk for hypoglcyemia)	Titrate 2.5 mg daily or BID with breakfast and dinner. Max dose: 12 mg daily
Glimepiride (Amaryl®)	Y	1 mg daily with breakfast	Titrate to 2 mg daily then increase by 2 mg. Max Dose: 8 mg once daily

Management Considerations

Effectiveness

- May lower A1C 0.5% to 1% - Max effect at 5-7 days

Monitoring

- Monitor renal function baseline and annually

Management Consideration

- Glipizide preferred choice due to lower risk of hypoglycemia (especially in patients with renal compromise and the elderly)
- Avoid glyburide and long acting sulfonyureas in the elderly due to potential for severe hypoglycemia
- In general, titrate up each dose weekly until glucose levels at goal
- In general, take regular release 30 minutes prior to meals and extended release tablets with meal
- Weight gain (~2kg) may occur following initiation of treatment
- Monitor for hypoglycemia (particularly in elderly and in those with renal impairment)
- Micronized glyburide shows no advantage over non-micronized glyburide

Dose Adjustment:

- For elderly, use 50% of dose
- For those with mild to moderate renal dysfunction, use 50% of dose
- Not recommended for renal function below
  - Glyburide not recommended if creatinine clearance (CrCl) < 50mL/min/1.73m^2
  - Glipizide not recommended if CrCl < 10 mL/min/1.73m^2
  - Glimepiride not recommended if eGFR < 15 mL/min/1.73m^2

Warnings

- Monitor for hypoglycemia, especially when
  - decreased calorie intake, prolonged exercise, alcohol, or if used with other glucose-lowering drugs (e.g. insulin)
  - used with beta blockers that can mask hypoglycemia
- May cause hypersensitivity
- Do not use concurrently with meglitines (repaglinide/nateglinide) due to similar effect
- Sulfonamide allergy: potential for cross-reaction
- Consider alternative therapy in patients with known G6PD enzyme deficiency
- Use caution with hepatic impairment

Thiazolidinedione (TZD)

Generic Name (Brand Name)	Generic Available	Initial Dose	Titration/Adjustment
Pioglitazone (Actos®)	Y	15 mg daily	Increase by 15 mg every 4 weeks until max of 45 mg daily

Management Considerations

Effectiveness

- May lower 1.0-1.5% A1C. Max effect at 6-12 weeks. Glycemic benefit gradual onset and diminishes slowly after stopping.

Monitor

- Monitor ALT at baseline and at least annually thereafter
- Obtain routine ophthalmic exams
- Monitor cardiac status if clinical symptoms of HF

Management Considerations

- Generally used less often than other diabetes medications because of side effects
- May take with or without food
- Low risk of hypoglycemia
- Favorable lipid effects

Black Box Warning:

- **TZDs can cause or exacerbate congestive heart failure in some patients. Not recommended for use with heart failure symptoms. After initiation and dose increases monitor patients for signs and symptoms of heart failure (including dyspnea, edema, and excessive, rapid weight gain)**

Warnings/Side Effects:

- May cause significant peripheral edema. More prevalent when utilized with insulin.
- May exacerbate heart failure.
- May cause weight gain (which is dose-related)
- May increase risk of fractures of long bones, especially in women
- May cause macular edema
- May increase aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (assess liver function if patient complains of nausea, vomiting, abdominal pain, and dark urine)
- May decrease hemoglobin and hematocrit (use caution in patients with anemia)
- May be associated with an increased risk of bladder cancer if used for > 1 year
- Check for drug interactions prior to initiating treatment

Contraindications:

- Initiation of treatment for heart failure Class III or IV
- ALT > 2.5 x the upper limit of normal

Dipeptidyl peptidase-4 inhibitors (DPP4 Inhibitors)

Generic Name (Brand Name)	Generic Available	Dose	Titration/Adjustment
Sitagliptin (Januvia®)	N	100 mg daily	No titration ***Renal Dosing:*** • CrCl 30-50 mL/min: 50 mg daily • CrCl < 30mL/min or End Stage Renal Disease (ESRD): 25 mg daily
Saxagliptin (Onglyza®)	N	2.5-5 mg daily Reduce dose if given with strong CYP3A4/5 inhibitors	No titration ***Renal Dosing:*** • CrCl < 50 mL/min: 2.5 mg daily • ESRD: 2.5 mg administer post-hemodialysis
Linagliptin (Tradjenta®)	N	5 mg daily	No renal dose adjustments
Alogliptin (Nesina®)	Y	25 mg daily	No titration ***Renal Dosing:*** • CrCl 30-60 mL/min: 12.5 mg daily • CrCl 15-30 mL/min: 6.25mg daily • CrCl < 15mL/min or hemodialysis: 6.25 mg day

Management Considerations

Effectiveness

- May lower A1C 0.5%-1.0%. Max effect at 1-2 weeks

Monitor

- Monitor renal function baseline and annually

Management Considerations

- Often used in place of sulfonylurea for patients who are at high risk for hypoglycemia
- Low risk of hypoglycemia
- No weight gain
- May be taken with or without food

Warnings/Side Effects:

- May cause headache, runny nose, diarrhea, upper respiratory infection, urinary tract infection (UTI) (UTI-*saxagliptin only*)
- May increase joint pain
- Cases of acute pancreatitis have been reported with use. Monitor for signs and symptoms (persistent, severe abdominal pain, anorexia, nausea and vomiting). Discontinue use immediately if suspected.
- Advise patient to report development of blisters or erosion post start of therapy (due to association with bullous pemphigoid).
- Heart failure that may require hospitalization has been reported in trials in patients with type 2 diabetes with a history of, or at risk for, cardiovascular events; esp increased in patients with preexisting heart failure or renal impairment and during the first 12 months of therapy. Monitor for signs and symptoms of heart failure during therapy and consider discontinuation if condition develops. *(saxagliptin, alogliptin, sitagliptin)*

Dose Adjustment

- Adjust for renal function as noted in the column to the left
- Dose reduction may be needed if patient is on insulin
- Check for drug interactions prior to initiating treatment

Contraindications:

- Avoid in patients with a history of pancreatitis.
- Do not use GLP-1 RAs and DPP4-inhibitors together.

Meglitinides

Generic Name (Brand Name)	Generic Available	Dose	Titration/Adjustment
Nateglinide (Starlix®)	Y	120 mg three times daily (TID) prior to meals 60 mg TID If A1C close to goal	Titrate to 120 mg TID Max dose of 360 mg/day
Repaglinide (Prandin®)	Y	0.5 mg TID if A1C< 8% or untreated 1 mg–2 mg TID if previously treated or A1C > 8%	Can double pre-prandial dose every week until glucose goals reached or max of 4 mg 4 times daily (QID) Max Dose: 16 mg/day

Management Considerations

Effectiveness

- May lower A1C 0.5-1%

Monitor

- Monitor creatinine and ALT at baseline and annually

Management Considerations

- Take 15-30 minutes before meals. Skip dose if meal not eaten
- Use instead of sulfonylurea in patients with irregular meal schedules or who develop late postprandial hypoglycemia

Warnings/Side Effects:

- May cause hypoglycemia
- May cause weight gain
- Use caution with renal impairment due to risk of prolonged hypoglycemia
- Use caution with hepatic impairment due to risk of hypoglycemia

Dose Adjustment

- No dose adjustment for renal or hepatic disease

Contraindications:

- Do not use with sulfonylureas (same effect)

Alpha Glucosidase Inhibitors

Generic Name (Brand Name)	Generic Available	Dose	Titration/Adjustment
Acarbose (Precose®)	Y	25 mg TID with first bite of each main meal	Titrate by 25 mg per dose every 4-8 week intervals until 1 hour post-prandial at goal Max dose: 100 mg TID (if > 60kg) or 50 mg TID (if < 60kg)
Miglitol (Glyset®)	Y	25 mg TID with first bite of each main meal	Titrate by 25 mg per dose every 4-8 week intervals until 1 hour post-prandial at goal maximum of 100 mg TID Max dose: 100 mg TID

Management Considerations

Effectiveness

- May lower A1C 0.5-1%

Monitor

- Monitor renal function at baseline and annually
- Monitor ALT/AST every 3 months in the first year; and periodically thereafter (acarbose only)

Management Considerations

- Should be given with first bite of each meal; skip dose if with missed meal
- Start with a low dose and increase slowly to minimize GI intolerance
- Oral dextrose should be used in the treatment of mild to moderate hypoglycemia

Warnings/Side Effects:

- GI side effects; flatulence, diarrhea, and abdominal discomfort, generally diminish over time
- May cause dose-related, transient increase in AST/ALT

Contraindications:

- Significant renal impairment (creatinine > 2 mg/dL or CrCl < 25mL/minute/1.73^2)
- Bowel disease
- GI disease
- Cirrhosis (Acarbose only)