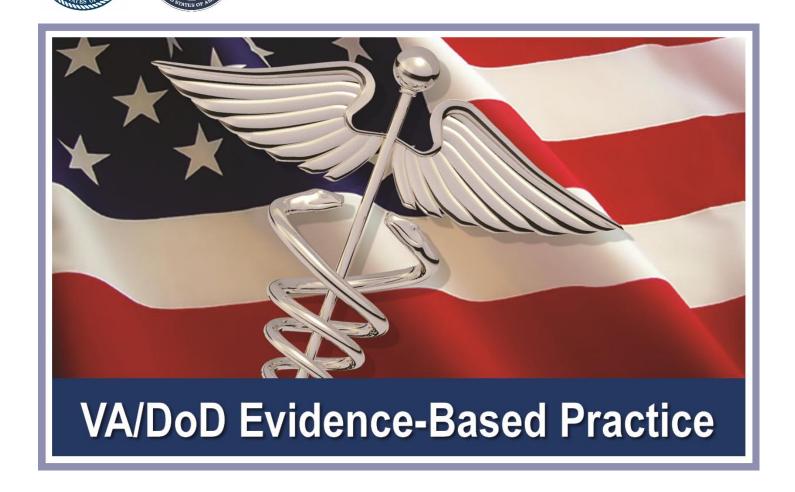
VA/DoD Clinical Practice Guidelines

VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus



Provider Summary

Version 6.0 | 2023





VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF TYPE 2 DIABETES MELLITUS

Department of Veterans Affairs

Department of Defense

Provider Summary

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and the Department of Defense (DoD) guidelines are based upon the best information available at the time of publication. The guidelines are designed to provide information and assist decision-making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This clinical practice guideline (CPG) is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DoD policies. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care.

Version 6.0 - 2023

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Introduction

The VA and DoD Evidence -Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the VA/DoD Health Executive Committee "... on the use of clinical and epidemiological evidence to improve the health of the population ..." across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.(1) Development and update of VA/DoD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and well-being.

In April 2017, the VA and DoD published a CPG for the Management of Type 2 Diabetes Mellitus (2017 VA/DoD DM CPG), which was based on evidence reviewed through March 2016. Since the release of that CPG, the evidence base on type 2 diabetes mellitus (T2DM) has expanded. Consequently, the EBPWG initiated the update of the 2017 VA/DoD DM CPG in 2021. This updated CPG's use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach reflects a more rigorous application of the methodology than previous iterations.(2) Therefore, the strength of some recommendations may have been modified due to the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

This CPG provides an evidence-based framework for managing care for individuals with T2DM with the aim of improving clinical outcomes. Successful implementation of this CPG will:

- Assess the patient's condition and collaborate with the patient, family and caregivers to determine optimal management of patient care
- Emphasize the use of patient-centered care and shared decision making
- Minimize preventable complications and morbidity
- Optimize individual health outcomes and quality of life

Background

A. Description of Type 2 Diabetes Mellitus

Diabetes mellitus (DM) is a disease caused by an absolute or relative insulin deficiency resulting in hyperglycemia. Type 1 DM (T1DM) is due to deficient insulin production and secretion and can present across the lifespan, with older patients often having a more indolent presentation that has been referred to as latent autoimmune diabetes of adults (LADA). In contrast, Type 2 DM (T2DM) is due to progressive insulin deficiency on a background of insulin resistance. The underlying insulin resistance seen in T2DM is thought to be due to genetic factors and obesity, especially increased visceral adiposity, which is frequently accompanied by ectopic fat accumulation within organs such as the

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liver, pancreas, and skeletal muscle. Prediabetes refers to the development of dysglycemia that does not reach the threshold for a diagnosis of diabetes. Gestational diabetes mellitus (GDM) is diabetes that is diagnosed in the second or third trimester of pregnancy that is typically not clinically overt. There are a variety of other causes of diabetes that include diabetes due to monogenetic defects including maturity-onset diabetes of the young (MODY); diabetes due to pancreatic diseases such as chronic pancreatitis or cystic fibrosis; diabetes due to other endocrinopathies including acromegaly or Cushing's syndrome; diabetes due to auto immune conditions and diabetes due to medications.(3) This guideline is focused on T2DM and prediabetes.

Several criteria have been developed to diagnose T2DM and prediabetes. The criteria used by this Work Group are summarized in Table 1. Prediabetes is usually seen on the continuum in the progression from normoglycemia to eventual T2DM.(3) Hyperglycemia not sufficient to meet the diagnostic criteria for DM has historically been categorized as either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), depending on the methodology through which it is identified. Both IFG and IGT are forms of prediabetes. The use of hemoglobin A1c (HbA1c) in the diagnosis of diabetes is derived from a study of the linear relationship between HbA1c values and microvascular complications, specifically retinopathy, with the diagnostic level occurring at the inflection point of a rise in the incidence of retinopathy. However, differences exist among laboratories in the acceptable variability of HbA1c test values (i.e., accuracy and precision). Additionally, there is evidence suggesting that there may be racial or ethnic differences such that HbA1c test results are not always congruent with fasting blood glucose concentrations. (3, 4) Racial differences were reported among participants in the Diabetes Prevention Program; despite having comparable measures of glycemia, African Americans had significantly higher HbA1c levels (6.2%) than Whites (5.8%).(4) Therefore, these differences should be considered when a diagnosis of diabetes is suggested by HbA1c values between 6.5-7.0% or when making treatment decisions based on small changes in HbA1c. Racial differences may impact the relationship between HbA1c and glycemia.(2)

One may consider screening for diabetes or prediabetes in adults who are overweight or obese (body mass index [BMI] \geq 25 kg/m² or \geq 23 kg/m² in Asian Americans) and have additional risk factors, including:

- First-degree relative with DM(2)
- Member of a high-prevalence population (e.g., African American, Hispanic American, Native American, Asian American, Pacific Islander)(2)
- Hypertension (blood pressure ≥ 140/90 mmHg or on therapy for hypertension)(2)
- High-density lipoprotein cholesterol (HDL-C) level < 35 mg/dL (0.90 mmol/L) and/ or a triglyceride (TG) level > 250 mg/dL (2.82 mmol/L)(2)
- History of cardiovascular disease (CVD)(2)
- Women with polycystic ovary syndrome (PCOS)(2)

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- History of GDM(2) or history of delivering babies weighing > 9 pounds (about 4 kg)
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)(2)
- Physical inactivity/sedentary lifestyle(2)
- Patients with human immunodeficiency virus (HIV)
- All adults over age 45

Consider, as well, screening in patients on medications increasing risk of T2DM, including antipsychotics, glucocorticoids, or statins.

The United States Preventive Service Task Force (USPSTF)(5) and American Diabetes Association (ADA) also suggest screening in all adults starting at age 35.(3)

Table 1 summarizes the diagnosis criteria used by this Work Group.

Table 1: Criteria for the diagnosis of diabetes mellitus and prediabetes(6)

Status	Fasting Plasma Glucose ^{a,b} or HbA1c ^{c,d}
Diabetes Mellitus	FPG ≥126 mg/dL (7.0 mmol/L) on two occasions OR HbA1c ≥6.5% with a confirmatory FPG ≥126 mg/dL (7.0 mmol/L) OR HbA1c ≥7.0% OR
	Two-hour plasma glucose on 75g OGTT of >200 mg/dl
Prediabetes	FPG ≥100 mg/dL and <126 mg/dL on two occasions OR HbA1c ≥5.7%–6.4% and FPG ≥100 mg/dL (5.5 mmol/L) and <126 mg/dL (7.0 mmol/L) OR Two-hour plasma glucose on 75g OGTT of 140–199 mg/dL (7.8–11.0 mmol/L) (IGT)
Normal	FPG <100 mg/dL (<5.5 mmol/L) HbA1c <5.7%

Abbreviations: dL: deciliter; FPG: fasting plasma glucose; HbA1c: hemoglobin A1c; hr: hour; IGT: impaired glucose tolerance; L: liter; mg: milligram; mmol: millimole

- ^a Fasting is defined as no caloric intake for at least eight hours.
- ^b FPG is the preferred diagnostic test, but either of the two listed is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these tests should be done on different days.
- ^c Using a clinical laboratory (not a point-of-care) methodology standardized to the National Glycohemoglobin Standardization Program (NGSP)
- d The VA/DoD DM CPG recommends that when HbA1c values between 6.5%-7.0% suggest diagnosis of diabetes mellitus, this observation should be confirmed with fasting plasma glucose levels to improve diagnostic specificity because HbA1c can vary among racial groups with comparable measures of glycemia.

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An oral glucose tolerance test (OGTT) is not commonly used to diagnose DM. Although both the ADA and the American Association of Clinical Endocrinology guidelines include the OGTT as a diagnostic criterion for T2DM, it is cumbersome and needs better reproducibility, making it less useful for routine diagnosis than fasting plasma glucose (FPG) or A1C.

B. Epidemiology and Impact on the General Population

Both globally and within the United States (U.S.), T2DM is a highly prevalent disease, including within military and Veteran populations. Globally, a marked increase has occurred in T2DM prevalence from approximately 151 million in 2000 to 537 million individuals in 2021 affected worldwide.(7) The number of Americans with diagnosed DM in 2022 has followed a similar trend, with approximately 29 million diagnosed and approximately 8.5 million undiagnosed individuals, impacting 11.3% of the U.S. population and about 13% of adults. The vast majority (~95%) of Americans with diabetes have T2DM.(8) Overall, approximately one in eight American adults has diabetes, and about one in three has prediabetes,(9) many of whom are unaware of their diagnosis.

In the MHS, the prevalence of diagnosed DM ranged from 7.3–11.2% in 2006 and from 8.3–13.6% in 2010.(10) Although the prevalence among active duty Service members remained stable, a significant increase was observed over time among non-active Service members.(10) In 2010, the prevalence among non-active duty military men and women was 15.0% and 13.3%, respectively, for those age 45–64 years, 32.9% and 26.9%, respectively, for those age 65–74 years, and 31.5% and 25.7%, respectively, for those age 75 years and older.(10) According to the VHA, nearly one in four Veterans (1.6 million individuals) currently receiving VA care has DM. Veterans 65 years and older comprise 70% of those with diabetes, reflecting the older age distribution of this population.(11)

Often, T2DM is preceded by prolonged asymptomatic hyperglycemic period where microvascular and macrovascular damage occurs. T2DM occurs with other comorbid conditions that influence the disease's pathogenesis, course, complications, and treatment. Insulin resistance, which often develops in the context of obesity, is a cardinal feature of T2DM. The increased prevalence of T2DM is closely associated with the increased prevalence of obesity in the U.S. Currently, ~42% of Americans are considered obese; diabetes is present in 6.6% of normal weight, 10.3% of overweight, and 23.3% of obese individuals. Briefly, when white adipose tissue lipid storage capacity is exceeded, lipids accumulate in ectopic sites (e.g., liver, skeletal muscle) and activate cellular pathways that impair insulin signaling.(12) Diets, therapies, and activities that promote weight loss often decrease ectopic lipid accumulation and increase insulin sensitivity. T2DM often develops as one of many obesity-related conditions, including non-alcoholic fatty liver disease (NAFLD), and obstructive sleep apnea. In addition, chronic hyperglycemia increases the risk of developing

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microvascular complications, such as retinopathy, nephropathy, and neuropathy. Additionally, the confluence of hyperglycemia and insulin resistance with other features of metabolic syndrome, including hyperlipidemia and hypertension, significantly increases the risk for macrovascular complications, including CVDs, such as ischemic heart disease, stroke, and peripheral vascular disease.(13) Other co-occurring conditions, such as chronic obstructive pulmonary disease (COPD), substance use disorder (SUD), and depression, can affect the management of T2DM. For guidance on addressing these comorbidities, see the respective VA/DoD CPGs for managing COPD, SUD, Overweight and Obesity (OBE), and Major Depressive Disorder.^{1, 2, 3, 4} Finally, T2DM and poor glycemic control might increase the risk of mortality from COVID-19 infection, and COVID-19 infection might itself increase the risk for development of T2DM in male veterans.(14, 15)

T2DM is a major contributor to morbidity and mortality in the U.S. It is associated with a two-fold to four-fold increased risk for atherosclerotic CVD, resulting in substantial morbidity and mortality from coronary events. For managing CVD risk factors and co-occurring conditions or comorbidities, refer to the VA/DoD CPGs for the Management of Hypertension, Chronic Kidney Disease (CKD), Dyslipidemia, and OBE.^{5, 6, 7, 8} The total costs of diagnosed DM in the U.S. were \$327 billion in 2017, including \$237 billion for direct medical costs and \$90 billion in reduced productivity.(16) Direct costs in the VHA and MHS are not known.

Scope of this Guideline

This CPG is based on published clinical evidence, and related information available through 2022. It is intended to provide general guidance on best evidence-based practices. Although the CPG is intended to improve quality of care and clinical outcomes (see Introduction), it is not intended to define a standard of care (i.e., mandated or strictly required care).

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See the VA/DoD Clinical Practice Guideline for the Management of Chronic Obstructive Pulmonary Disease (COPD), available at http://www.healthquality.va.gov/guidelines/CD/copd/.

See the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders (SUD), available at http://www.healthquality.va.gov/guidelines/MH/sud/.

³ See the VA/DoD Clinical Practice Guideline for the Management of Adult Overweight and Obesity (OBE), available at https://www.healthquality.va.gov/guidelines/CD/obesity/.

⁴ See the VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder (MDD), available at http://www.healthquality.va.gov/guidelines/MH/mdd/.

⁵ See the VA/DoD Clinical Practice Guideline for the Management of Hypertension (HTN), available at https://www.healthquality.va.gov/guidelines/cd/htn/index.asp.

See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease (CKD), available at Management of Chronic Kidney Disease (CKD) (2019) - VA/DoD Clinical Practice Guidelines.

See the VA/DoD Clinical Practice Guideline for the Management of Dyslipidemia for Cardiovascular Risk Reduction, available at http://www.healthquality.va.gov/guidelines/CD/lipids/.

See the VA/DoD Clinical Practice Guideline for the Management of Adult Overweight and Obesity (OBE), available at https://www.healthquality.va.gov/guidelines/CD/obesity/.

Patient-centered Care

Intended to consider patient needs and preferences, guideline recommendations represent a whole/holistic health approach to care that is patient centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities. VA/DoD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs, characteristics, and preferences). This approach aims to treat the particular condition while also optimizing the individual's overall health and wellbeing.

Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence. (17, 18) A whole/holistic health approach (https://www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and wellbeing goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to gender, culture, ethnicity, and other differences.

Shared Decision Making

This CPG encourages providers to practice shared decision making, a process in which providers, patients, and patient care partners (e.g., family, friends, caregivers) consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(19) Shared decision making is emphasized in *Crossing the Quality Chasm,* an Institute of Medicine, now NAM, report in 2001(20) and is inherent within the whole/holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels or settings of care or both, especially where patient heterogeneity in weighing risks and benefits might exist. Veterans Health Administration and MHS have embraced shared decision making. Providers are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

Patients with Co-occurring Conditions

Co-occurring conditions can modify the degree of risk, impact diagnosis, influence patient and provider treatment priorities and clinical decisions, and affect the overall approach to managing T2DM. Many Veterans, active duty Service members, and their families have one or more co-occurring conditions. Because T2DM is sometimes accompanied by co-occurring conditions, managing T2DM collaboratively with other care providers is often best. Some co-occurring conditions might require early specialist consultation to determine necessary changes in treatment or to establish a common understanding of how care will be coordinated. This approach might entail reference to

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other VA/DoD CPGs (e.g., for <u>Chronic Kidney Disease</u>, <u>Overweight and Obesity</u>, <u>Hypertension</u>, <u>Dyslipidemia</u>, and <u>Pregnancy</u>).⁹

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⁹ The VA/DoD Clinical Practice Guidelines are available at: https://www.healthquality.va.gov/

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Algorithm

This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in managing patients with T2DM. This algorithm format represents a simplified flow of the management of patients with T2DM and helps foster efficient decision making by providers. It includes

- Steps of care in an ordered sequence,
- Decisions to be considered,
- Decision criteria recommended, and
- Actions to be taken.

The algorithm is a step-by-step decision tree. Standardized symbols display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(21) Sidebars 1–8 provide more detailed information to assist in defining and interpreting elements in the boxes.

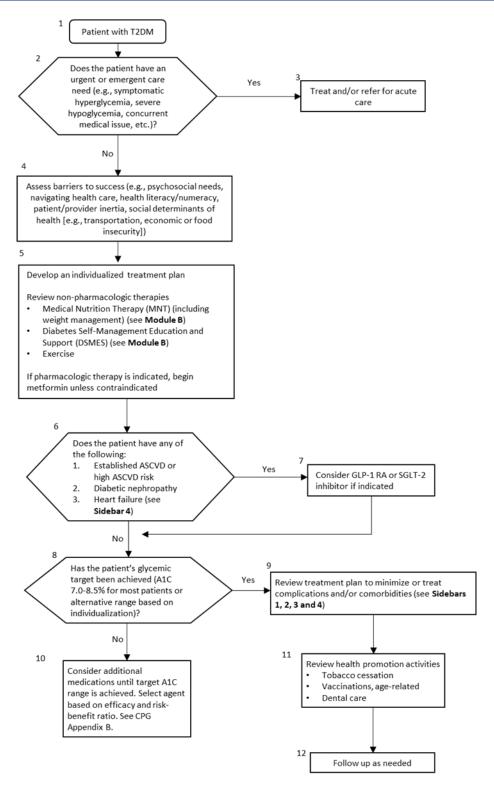
Shape	Description
	Rounded rectangles represent a clinical state or condition
	Hexagons represent a decision point in the process of care, formulated as a question that can be answered "Yes" or "No"
	Rectangles represent an action in the process of care
	Ovals represent a link to another section within the algorithm

The algorithm sidebars can be found in the full CPG at https://www.healthquality.va.gov/.

Appendix I (in the full CPG) contains the alternative text descriptions of the algorithm.

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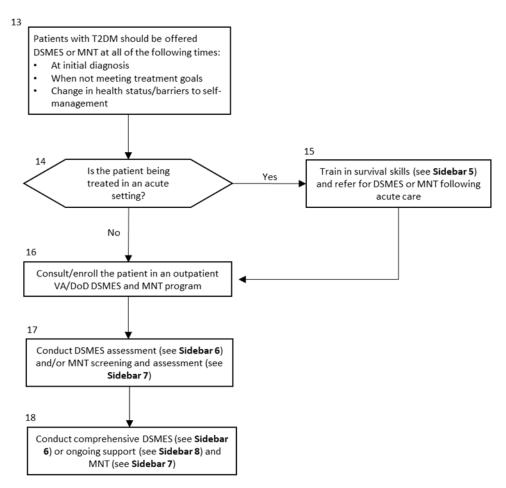
Module A: T2DM Management



Abbreviations: ASCVD: atherosclerotic cardiovascular disease; GLP-1 RA: glucagon-like peptide 1 receptor agonist; SGLT-2 inhibitor: sodium-glucose transporter 2 inhibitor; MNT: Medical Nutrition Therapy; T2DM: type 2 diabetes mellitus

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Module B: Self-Management Education and Support



Abbreviations: DoD: Department of Defense; DSMES: diabetes self-management education and support; MNT: Medical Nutrition Therapy; T2DM: type 2 diabetes mellitus; VA: Department of Veterans Affairs

Sidebar 1: Neuropathy and Foot Care

- Perform a comprehensive lower extremity risk assessment (including monofilament) annually and as needed.
- Refer patients with limb-threatening conditions.
- Provide pain management as needed.

Sidebar 2: Retinopathy and Eye Care

- · Provide BP, glycemic, and lipid management.
- Provide a dilated fundus examination by an eye care professional or retinal imaging with interpretation by a qualified, experienced reader to detect retinopathy.
- Obtain a retinal examination within 6 months of a new T2DM diagnosis and biennial screening for retinopathy for patients with no history of retinopathy on all prior examinations.

For some, more frequent retinal examinations might be indicated (e.g., patients with additional risk factors, existing retinopathy, risk factors for progression of retinopathy).

Abbreviations: BP: blood pressure, T2DM: Type 2 diabetes mellitus

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Sidebar 3: Nephropathy and Kidney Care

- Consider guideline-directed treatments and targets (see VA/DoD CPG for CKD).
- Monitor urine microalbumin/creatinine ratio at least annually.
- Consider ACEi/ARB use in patients with HTN, moderately increased albuminuria (i.e., microalbuminuria), or CKD.
- Consider SGLT-2 inhibitor or GLP-1 RA use in patients with diabetic nephropathy.
- Avoid nephrotoxic medications (e.g., NSAIDs).

Abbreviations: ACEi: ACE inhibitor; ARB: angiotensin receptor blocker; CKD: chronic kidney disease; CPG: clinical practice guideline; GLP-1 RA: glucagon-like peptide-1 receptor agonist; NSAID: non-steroidal anti-inflammatory drug; SGLT-2 inhibitor: sodium-glucose cotransporter 2 inhibitor

Sidebar 4: Comorbidities

- Consider guideline-directed treatments and targets (see VA/DoD CPGs for hypertension, dyslipidemia, obesity, CKD).
- Consider VA/DoD DM guideline-directed therapy for ASCVD and heart failure.

Abbreviations: ASCVD: atherosclerotic cardiovascular disease; CKD: chronic kidney disease; CPG: clinical practice guideline

Sidebar 5: Basic Education/Survival Skills as Needed

- Healthy eating
- · Use of prescribed medication
- · Ways to recognize and treat hypoglycemia and hyperglycemia
- Use of a glucose meter
- Management of glucose on sick days and knowing when to call the provider

Sidebar 6: Comprehensive DSMES

- · Assessment, including food insecurity and diabetes distress
- T2DM disease overview
- Monitoring (e.g., home glucose, HbA1c, BP, lipids, eGFR, moderately increased albuminuria [i.e., microalbuminuria])
- Nutrition and healthy eating
- · Comprehensive assessment and education on 8 topics
 - 1. Diabetes physiology
 - 2. Monitoring
 - 3. Healthy coping
 - 4. Taking medications
 - 5. Healthy eating
 - Being active
 - 7. Reducing risk
 - 8. Problem solving
- Individualized approach based on shared decision making

Abbreviation: BP: blood pressure; DSMES: diabetes self-management education and support; eGFR: estimated glomerular filtration rate; HbA1c: hemoglobin A1c; T2DM: type 2 diabetes mellitus

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Sidebar 7: Medical Nutrition Therapy

- Assessment (including food insecurity)
- Nutrition diagnosis and intervention
- Monitoring and re-evaluation

Sidebar 8: DSMES Ongoing Support

- Reassess and reeducate patient and family, support person, or both, as necessary.
 - Change of treatment regimen or care team
 - Change in health/cognitive/emotional/social status
- Maintain self-management gains by leveraging patient's community and primary care to reinforce education.

Recommendations

The following recommendations were made using a systematic approach considering four domains as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach as detailed in the section on Methods and Appendix A in the full text DM CPG. These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications, as appropriate (e.g., resource use, equity, acceptability).

Topic	Sub- topic	#	Recommendation	Strength ^a	Category ^b
se	Exercise/ Nutrition	1.	In adults with prediabetes, we suggest aerobic exercise (such as walking 8–9 miles a week) and healthy eating (with a goal weight loss >3%) to achieve a reduction in body fat mass, weight loss, and improvement in fasting blood glucose.	Weak for	Reviewed, New-added
Prediabetes	Pharmacotherapy	2.	In adults with prediabetes who have participated in healthy lifestyle modification and remain at high risk for progression to type 2 diabetes mellitus, we suggest evaluating patient characteristics (e.g., age, life expectancy, co-occurring conditions, BMI, other risk factors) and offering metformin or other select medications to reduce the risk of progression from prediabetes to type 2 diabetes mellitus.	Weak for	Reviewed, New-added
Telehealth		3.	In adults with type 2 diabetes mellitus, we suggest offering health care delivered through telehealth interventions to improve outcomes.	Weak for	Not Reviewed, Amended

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Topic	Sub- topic	#	Recommendation	Strength ^a	Category ^b
)r iS	4.	There is insufficient evidence to recommend for or against routine screening or using a specific tool to screen for or diagnose diabetes distress.	Neither for nor against	Reviewed, New-added
	Screening for Comorbidities	5.	In adults with type 2 diabetes mellitus and co-occurring non-alcoholic fatty liver disease, we suggest clinicians should assess for fibrosis using a non-invasive tool (e.g., Fibrosis-4).	Weak for	Reviewed, New-added
	S	6.	In adults with type 2 diabetes mellitus, there is insufficient evidence to recommend for or against routine screening for fall risk and cognitive impairment to improve outcomes.	Neither for nor against	Reviewed, New-added
agement of Type 2 Dia		7.	In adults with type 2 diabetes mellitus, we recommend diabetes self-management education and support.	Strong for	Not Reviewed, Amended
		8.	For adults with type 2 diabetes mellitus, we suggest using high glycemic variability over time (e.g., fluctuation in HbA1c or fasting blood glucose) as a prognostic indicator for risk of hypoglycemia, morbidity, and mortality.	Weak for	Reviewed, New- replaced
Managemer	nic Management	9.	We suggest setting an individualized HbA1c target range based on the clinician's appraisal of the risk benefit ratio, patient characteristics, presence or absence of type 2 diabetes mellitus complications, comorbidities, and life expectancy.	Weak for	Not reviewed, Amended
Glycemic		10.	We suggest an HbA1c range of 7.0–8.5% for most patients, if it can be safely achieved.	Weak for	Not reviewed, Amended
	9	11.	In insulin-treated adults with type 2 diabetes mellitus who are not achieving glycemic goals, we suggest real-time continuous glucose monitoring to decrease hypoglycemia and improve HbA1c.	Weak for	Reviewed, New-added

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Topic	Sub- topic	#	Recommendation	Strength ^a	Category ^b
	erapy	12.	For adults with type 2 diabetes mellitus, we suggest a Mediterranean style diet to improve glycemic control, body weight, and hypertension.	Weak for	Reviewed, New- replaced
	Medical Nutrition Therapy	13.	For adults with type 2 diabetes mellitus, we suggest a nutrition intervention strategy providing 13–50% of their total daily caloric intake from carbohydrates for diabetes management.	Weak for	Reviewed, New- replaced
nerapy	dical Nu	14.	For adults with type 2 diabetes mellitus, we suggest a vegetarian dietary pattern for glycemic control and weight loss.	Weak for	Reviewed, New-added
nacoth	ə <i>W</i>	15.	For adults with type 2 diabetes mellitus, we suggest against intermittent fasting.	Weak against	Reviewed, New-added
Non-Pharmacotherapy	Exercise	16.	In adults with type 2 diabetes mellitus, we suggest regular physical activity to improve glycemic control, including but not limited to aerobic exercise, resistance training, or tai chi.	Weak for	Reviewed, New-added
_	S	17.	In adults with stress related to type 2 diabetes mellitus, we suggest offering a mindfulness-based stress reduction program for short-term improvement.	Weak for	Reviewed, New-added
	Stress	18.	For adults with type 2 diabetes and diabetes distress, there is insufficient evidence to recommend for or against the use of acupuncture, biofeedback, hypnosis, guided imagery, massage therapy, yoga, or tai-chi to improve outcomes.	Neither for nor against	Reviewed, New-added
	19.		For adults with type 2 diabetes mellitus with atherosclerotic cardiovascular disease, we recommend glucagon-like peptide-1 receptor agonists or sodium-glucose cotransporter-2 inhibitors with proven cardiovascular benefits to decrease the risk of major adverse cardiovascular events.	Strong for	Reviewed, New-added
Pharmacotherapy		20.	For adults with type 2 diabetes mellitus at high risk of atherosclerotic cardiovascular disease (i.e., chronic kidney disease, left ventricular hypertrophy, heart failure), we suggest glucagon-like peptide-1 receptor agonists or sodium-glucose cotransporter-2 inhibitors with proven cardiovascular benefits to decrease the risk of major adverse cardiovascular events.	Weak for	Reviewed, New-added
P.		21.	For adults with type 2 diabetes mellitus and heart failure, we recommend a sodium-glucose cotransporter-2 inhibitor to prevent hospital admissions for heart failure.	Strong for	Reviewed, New-added
		22.	For adults with type 2 diabetes mellitus and chronic kidney disease, we recommend sodium-glucose cotransporter-2 inhibitors with proven renal protection to improve renal outcomes.	Strong for	Reviewed, New-added

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Topic	Sub- topic	#	Recommendation	Strength ^a	Category ^b
		23.	For adults with type 2 diabetes mellitus and chronic kidney disease who are not good candidates for a sodium-glucose cotransporter-2 inhibitor, we recommend a glucagon-like peptide-1 receptor agonist with proven renal protection to improve macroalbuminuria.	Strong for	Reviewed, New-added
Pharmacotherapy (cont.)		24.	In adults with type 2 diabetes mellitus who have cardiovascular disease or renal disease, we suggest that the addition of a sodium-glucose cotransporter-2 inhibitor or glucagon-like peptide-1 receptor agonist be considered, even if the patient has already achieved their individualized target range for glycemic control.	Weak for	Reviewed, New-added
Pharmacoth		25.	In adults with type 2 diabetes mellitus, especially those 65 years and older, we suggest prioritizing drug classes other than insulin, sulfonylureas, or meglitinides to minimize the risk of hypoglycemia, if glycemic control can be achieved with other treatments.	Weak for	Reviewed, New-added
		26.	In adults with type 2 diabetes mellitus who have co- occurring cognitive impairment or risk of falls, there is insufficient evidence to recommend for or against specific treatment strategies for glucose lowering to reduce the risk of harms.	Neither for nor against	Reviewed, New-added

^a Additional information is available in the full CPG: see Determining Recommendation Strength and Direction.

Glycemic Control Targets and Monitoring

Setting an HbA1c target range is an important treatment strategy in the management of Type 2 Diabetes Mellitus. <u>Table 2</u> provides general guidance for setting HbA1c target ranges based on patients' comorbidities, life expectancy, and extent of microvascular complications. Other factors might also be considered, and these are addressed in several footnotes. Setting target ranges with upper and lower bounds highlights the importance of considering the risks associated with both hyper- and hypoglycemia. These guiding principles are intended to complement Recommendations 9 and 10 and to help in creating individualized treatment strategies using shared-decision making.

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^b Additional information is available in the full CPG: see Recommendation Categorization.

Table 2: Determination of HbA1c target ranges a, b, c, d, e, f

Major Comorbidity ^g or	Microvascular Complications					
Physiologic Age	Absent or Mild ^h Moderate ⁱ		Advanced ^j			
Absent ^k >10–15 years of life expectancy	6.0–7.0% ¹	7.0–8.0%	7.5–8.5% ^m			
Present ⁿ 5–10 years of life expectancy	7.0–8.0%	7.5–8.5%	7.5–8.5% ^m			
Marked° <5 years of life expectancy	8.0–9.0% ^m	8.0–9.0% ^m	8.0–9.0% ^m			

HbA1c Laboratory Considerations

- ^a HbA1c assays should be based on the NGSP reference standard. Clinicians should obtain information regarding the coefficient of variation (CV) from the methodology used at their site. As an example, an HbA1c of 8.0% from a laboratory with a CV of 3% would be measured in a 7.8–8.2% range 13 out of 20 times (1 standard deviation) and would be between a 7.58.5% range 19 out of 20 times (2 standard deviations).
- ^b The HbA1c range reflects an "HbA1c average goal" over time. Intensification or relaxation of therapy should be undertaken based on individual clinical circumstances and treatment options.
- ^c We discourage medication changes in response to a single HbA1c test that falls slightly outside target ranges, especially if it is discordant with self-monitoring of blood glucose (SMBG) results.
- d African Americans, on average, have HbA1c levels about 0.4% higher than Whites and this difference cannot be explained by measured differences in glycemia. Caution is recommended when changing medications based on HbA1c results that slightly exceed target ranges, especially for patients on insulin therapy, without considering SMBG results.
- ^e The VA/DoD DM CPG does not recommend the use of estimated average glucose derived from HbA1c levels.

Social Determinant Considerations

Social determinants of health and factors such as social support, ability to self-monitor glucose, food insecurity, and cognitive impairment should be considered. Additionally, side effects of medications and patient preferences must be considered in a process of shared decision making.

Comorbid Illness Considerations

- ⁹ Major comorbidity includes, but is not limited to, any or several of the following conditions: significant CVD, severe CKD, severe COPD, severe chronic liver disease, recent cerebrovascular disease, and life-threatening malignancy.
- Mild microvascular disease is defined by early background retinopathy, moderately increased albuminuria, mild neuropathy, or any combination of the foregoing.
- Moderate microvascular disease is defined by pre-proliferative (without severe hemorrhage, intraretinal microvascular anomalies [IRMA], or venous bleeding) retinopathy severely increased albuminuria, demonstrable peripheral neuropathy (sensory loss), or any combination of the foregoing.
- Advanced microvascular disease is defined by severe non-proliferative (with severe hemorrhage, IRMA, or venous bleeding) or proliferative retinopathy, renal insufficiency (serum creatinine level >2.0 mg/dL), insensate extremities, autonomic neuropathy (e.g., gastroparesis, impaired sweating, orthostatic hypotension), or any combination of the foregoing.
- Progression to major complications of type 2 diabetes mellitus is likely to occur in individuals with longer than 10–15 years of life expectancy. Therefore, lower ranges might be beneficial in younger individuals or older adults with a longer life expectancy.
- ¹ Consider higher target ranges if significant treatment-related side effects occur, including but not limited to hypoglycemia.
- ^m Lower target ranges might be appropriate in some patients based on other factors, balancing safety and tolerability of therapy.
- ⁿ Major comorbidity is present, but is not end-stage, and management is achievable.
- Major comorbidity is present and is either end-stage or management is significantly challenging, including mental health conditions and substance/opioid use.

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Pharmacotherapy

Table 3: Pharmacotherapy for Type 2 Diabetes Mellitus

Drug Clas	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change		Adverse Effects	Dosing and Administration
Biguanide (Metformin	1–1.5%	No	Potential ASCVD benefit	Neutral	Neutral/ mild loss	Contraindicated eGFR <30; may continue at reduced dose, but do not initiate if eGFR <45 Increased risk of lactic acidosis (especially in setting of acute HF, dehydration, excessive alcohol intake, renal impairment, sepsis)	GI (diarrhea, nausea) Vitamin B12 deficiency; rarely associated with anemia	Slow titration, taking with food, and using SA formulation improve GI tolerability. Hold temporarily for radiologic studies with contrast and other procedures.

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Drug Class	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change	Contraindications or Precautions	Adverse Effects	Dosing and Administration
SGLT-2 inhibitor	0.5–1%	No	ASCVD benefit (empagliflozin, canagliflozin)	Benefit (empagliflozin, canagliflozin, dapagliflozin)	Moderate loss	 eGFR <20–30 (see labeling) Increased risk for DKA Increased risk for frequent or serious genitourinary infections Pregnancy/ breastfeeding 	 Genitourinary infections DKA (might be euglycemic) Volume depletion/ hypotension Initial reversible increase in serum creatinine; long-term improvement Bone fractures (canagliflozin) Lower limb amputations were increased with canagliflozin versus placebo in one trial (CANVAS). 	 Taken orally without regard to food Hold at least 3 days before surgery. Cardiorenal benefits are realized at initial doses. Glucose-lowering efficacy is reduced at lower eGFR, but other benefits are retained.

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Drug Class	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change	Contraindications or Precautions	Adverse Effects	Dosing and Administration
GLP-1 receptor agonist	1–2%	No	ASCVD benefit (liraglutide, dulaglutide, semaglutide injectable)	Benefit (primarily reduced albuminuria; liraglutide, dulaglutide semaglutide injectable)	Moderate - very high loss (Efficacy depends on agent and dose.)	 Personal or family history of medullary thyroid carcinoma Multiple endocrine neoplasia syndrome 2 Gastroparesis At high risk of pancreatitis Current gallbladder disease CrCl <15 (lixisenatide) <30 (exenatide) Pregnancy Proliferative Diabetic Retinopathy (semaglutide): This risk must be balanced against the risk of progressive retinopathy in the setting of persistent poor glycemic control. 	 GI (nausea, vomiting, diarrhea, constipation) Injection site reactions Possible renal impairment if dehydration from GI side effects occurs Increased risk of diabetic retinopathy complications in labeling for semaglutide and dulaglutide (significantly increased with semaglutide versus placebo in SUSTAIN-6) Post-marketing reports of pancreatitis (causality not established) 	 All are injected subcutaneously, except oral formulation of semaglutide. Administer via pens 1–2 times daily or weekly (depending on agent). Avoid concurrent use with DPP4 inhibitor or GIP/GLP-1 agonist.

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Drug Class	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change	Contraindications or Precautions	Adverse Effects	Dosing and Administration
GIP/GLP-1 agonist (Tirzepatide)	2–2.5%	No	Neutral based on available evidence Prospective studies to evaluate ASCVD and HF outcomes are ongoing.	Neutral based on available evidence	Very high loss	 Personal or family history of medullary thyroid carcinoma Multiple endocrine neoplasia syndrome Gastroparesis At high risk of pancreatitis Current gallbladder disease Pregnancy 	 GI (nausea, vomiting, diarrhea, constipation) Injection site reactions Possible renal impairment if dehydration from GI side effects occurs 	 Injected subcutaneously once weekly without regard to meals Supplied as single-dose pens Might decrease efficacy of OCP, especially 4 weeks after initiation and dose increases (alternative method recommended)
DPP4i	0.5–1%	No	Neutral for ASCVD risk, potential increased risk of HF (saxagliptin)	Neutral	Neutral	 At high risk of pancreatitis Pregnancy 	 Hypersensitivity reactions, including rare anaphylaxis and severe dermatologic reactions (bullous pemphigoid) Arthralgia Post-marketing reports of pancreatitis (causality not established) Incidence of HF hospitalization was increased with saxagliptin versus placebo in the SAVOR TIMI 53 trial 	 Taken orally without regard to food Renally dose adjusted (except linagliptin) Avoid concurrent use with GLP-1 and GIP/GLP-1 agonists.

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Drug Class	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change	Contraindications or Precautions	Adverse Effects	Dosing and Administration
SU	1–1.5%	Yes	Neutral	Neutral	Mild- moderate gain	 Possible cross-sensitivity in patients with sulfonamide allergies Increased risk for hypoglycemia (elderly, renal or hepatic impairment, poor intake and certain antimicrobials, such as fluoroquinolones, sulfamethoxazole-trimethoprim and others) 	 Hypoglycemia Weight gain Nausea Skin reactions Photosensitivity 	 Taken orally with or before a meal, depending on formulation Do not combine with meglitinide or prandial insulin.

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Drug Clas	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change	Contraindications or Precautions	Adverse Effects	Dosing and Administration
TZD	1–1.5%	No	Potential ASCVD benefit (pioglitazone), increased risk of HF	Neutral	Moderate gain	HF or evidence of fluid overload History or high risk of fracture Active liver disease (liver transaminases >2.5 times above the upper reference limit), unless NASH is known to be the underlying cause of the elevation Active or history of bladder cancer Pregnancy Macular edema	 Weight gain Fluid retention HF Macular edema Bone fractures Might increase risk of bladder cancer (pioglitazone) 	 Taken orally without regard to meals Full glycemic effect takes several weeks. HF risk is increased with concurrent insulin.
Meglitinid	0.5–1% e	Yes (less than SU)	Neutral	Neutral	Mild- moderate gain	Increased risk for hypoglycemia (elderly, renal or hepatic impairment, poor intake)	Upper respiratory infectionFlu-like symptoms	 Taken orally three times daily with meals (skip dose if skipped meal) Do not combine with SU or prandial insulin.

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Drug Class	Average A1c Reduction	Hypo- glycemia (as mono- therapy)	Cardio- vascular Effects	Renal Effects	Weight Change	Contraindications or Precautions	Adverse Effects	Dosing and Administration
Insulin	Variable (no limit)	Yes	Neutral	Neutral	Moderate gain	Hypokalemia Caution with dosing in hepatic and renal disease	 Hypoglycemia Weight gain Injection site reaction Hypersensitivity reactions 	 Available as subcutaneous injections or inhaled (rapid-acting only) Available in a variety of formulations to allow for flexibility for patient-specific treatment Rapid-acting and regular insulin should be taken before meals. Preferred in pregnancy

Abbreviations: ASCVD: atherosclerotic cardiovascular disease; CrCl: creatinine clearance; DKA: diabetic ketoacidosis; DPP4: dipeptidyl peptidase-4; eGFR: estimated glomerular filtration rate; GIP: gastric inhibitory polypeptide; GI: gastrointestinal; GLP-1: glucagon-like peptide-1; HbA1c: hemoglobin A1C; HF: heart failure; NASH: non-alcoholic steatohepatitis; OCP: oral contraceptive pills; SA: sustained action; SGLT2: sodium-glucose cotransporter-2; SU: sulfonylurea; TZD: thiazolidinedione

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Table 4: Pharmacotherapy Supplementary Evidence Table

	CVD-Related (Outcomes (Selected)	CKD Composite Outcome
Comparison Study, Follow-up	CVD Composite Outcome Effect, HR; 95% CI SOE	Hospitalizations for Heart Failure Effect, HR; 95% CI SOE	Effect, HR; 95% CI SOE
SGLT-2 inhibitors (combined effect) versus placebo CVD composite: 6 RCTs in 1 SR,(22) n=39,949; follow-up: 3.0 years median HF hospitalizations: 7 RCTs in 1 SR,(23) n=49,108, follow-up: 2.8 years median CKD composite: 7 RCTs in 1 SR,(23) n=44,993, follow-up: 2.5 years median	0.90; 0.85 to 0.95, (I ² =23%), SOE: High for benefit of SGLT-2 inhibitors ^a	0.70; 0.63 to 0.77, (I ² =0%), SOE: High for benefit of SGLT-2 inhibitors ^a	0.64; 0.57 to 0.72, (I ² =24%), SOE: High for benefit of SGLT-2 inhibitors ^a
Canagliflozin versus placebo 3 RCTs (CANVAS, CANVAS R, CREDENCE in 1 SR,(24) n=14,543, follow-up: 2.5 years	0.84; 0.76 to 0.93, (I ² =0%), SOE: High for benefit of canagliflozin ^a	0.64; 0.53 to 0.77, (l²=0%), SOE: High for benefit of canagliflozin ^a	0.64; 0.45 to 0.75, (I ² =0%), SOE: High for benefit of canagliflozin ^a
Dapagliflozin versus placebo CVD composite: 1 RCT (DECLARE— TIMI 58) in 1 SR,(22) n=17,160, follow- up: 4.2 years HF hospitalizations: 2 RCTs in 1 SR,(23) n=19,281, follow-up: 4.2 and 1.5 years CKD composite: 3 RCTs in 1 SR,(23) n=22,204, follow-up: 4.2, 1.5, and 2.4 years	1 RCT (DECLARE-TIMI 58) in 1 SR,(22) n=17,160, follow-up: 4.2 years 0.93; 0.84 to 1.03, ARD 95% CI: -1.4% to 0.3%, SOE: High for no difference	0.73; 0.61 to 0.88 (1 RCT: DECLARE–TIMI 58, n=17,160), favors dapagliflozin 0.76; 0.61 to 0.95 (1 RCT: DAPA-HF, n=2,121), favors dapagliflozin Overall effect: SOE: High for benefit of dapagliflozin ^a	0.53; 0.43 to 0.66 (1 RCT: DECLARE–TIMI 58, n=17,160), favors dapagliflozin 0.72; 0.39 to 1.34 (1 RCT: DAPA-HF, n=2,139), no difference 0.64; 0.52 to 0.79 (1 RCT: DAPA-CKD, n=2,905), favors dapagliflozin Overall effect: SOE: High for benefit of dapagliflozin ^a
Empagliflozin versus placebo CVD composite: 1 RCT (EMPA-REG OUTCOME) in 1 SR,(22) n=7,020, follow-up: 3.1 years HF hospitalizations and CKD composite: 1 RCT (EMPA-REG OUTCOME) in 1 SR,(23) n=7,020, follow-up: 3.1 years	0.86; 0.74 to 0.99, ARD 95% CI: -3.22% to - 0.05%, SOE: High for benefit of empagliflozin ^a	0.65; 0.50 to 0.85, ARD 95% CI: -2.3 to -0.5%, SOE: High for benefit of empagliflozin ^a	0.54; 0.40 to 0.75, ARD 95% CI: -2.1% to -0.5%, SOE: High for benefit of empagliflozin ^a

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	CVD-Related (CKD Composite Outcome	
Comparison Study, Follow-up	CVD Composite Outcome Effect, HR; 95% CI SOE	Hospitalizations for Heart Failure Effect, HR; 95% CI SOE	Effect, HR; 95% CI SOE
Ertugliflozin versus placebo CVD composite: 1 RCT (VERTIS CV) in 1 SR,(22) n=8,246, follow-up: 3.0 years HF hospitalizations and CKD composite: 1 RCT (VERTIS CV) in 1 SR,(23) n=8,246, follow-up: 3.0 years	0.99; 0.88 to 1.12, ARD 95% CI: -1.6% to 1.5%, SOE: Moderate for no difference	0.70; 0.54 to 0.90, ARD 95% Cl: -1.9% to -0.3%, SOE: High for benefit of ertugliflozin ^a	0.81; 0.63 to 1.04, ARD 95% CI: -1.6% to 0.1%, SOE: Moderate for no difference

^a Green shading indicates evidence of benefit.

Abbreviations: ARD: absolute risk difference; CKD: chronic kidney disease; CVD: cardiovascular disease; HF: heart failure; RCT: randomized controlled trial; SGLT-2: sodium-glucose cotransporter-2; SOE: strength of evidence; SR: systematic review

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Methods

A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence-based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see Determining Recommendation Strength and Direction in the full CPG):(25)

- 1. Confidence in the quality of the evidence
- 2. Balance of desirable and undesirable outcomes
- 3. Patient values and preferences
- 4. Other considerations, as appropriate (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong* or *Weak*). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(26) A *Strong* recommendation generally indicates *High* or *Moderate* confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The manner in which this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice although it is unsupported by clinical evidence and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text as shown in <u>Table 5</u>.

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B. Categorization of 2017 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(27) For example, the USPSTF has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every 5 years for either an update or reaffirmation.(28)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(29, 30) Table 5 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in Recommendation Categorization (in the full CPG). The 2023 CPG recommendation categories can be found in Recommendations (in the full CPG). Appendix F (in the full CPG) outlines the 2017 VA/DoD DM CPG's recommendation categories.

Evidence Reviewed	Recommendation Category	Definition			
	New-added	New recommendation			
	New-replaced	Recommendation from previous CPG was carried forward an revised			
Reviewed ^b	Not changed	Recommendation from previous CPG was carried forward but not changed			
	Amended	Recommendation from previous CPG was carried forward with a nominal change			
	Deleted	Recommendation from previous CPG was deleted			
	Not changed	Recommendation from previous CPG was carried forward but not changed			
Not reviewed ^c	Amended	Recommendation from previous CPG was carried forward with a nominal change			
	Deleted	Recommendation from previous CPG was deleted			

Abbreviation: CPG: clinical practice guideline

- ^a Adapted from the NICE guideline manual (2012) (29) and Garcia et al. (2014) (30)
- ^b The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.
- c The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.

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