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CLINICAL GUIDELINE

Synopsis of the 2017 U.S. Department of Veterans Affairs/ U.S. Department of Defense Clinical Practice Guideline: Management of Type 2 Diabetes Mellitus

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Description: In April 2017, the U.S. Department of Veterans Affairs (VA) and the U.S. Department of Defense (DoD) approved a joint clinical practice guideline for the management of type 2 diabetes mellitus.

Methods: The VA/DoD Evidence-Based Practice Work Group convened a joint VA/DoD guideline development effort that included a multidisciplinary panel of practicing clinician stakeholders and conformed to the Institute of Medicine's tenets for trustworthy clinical practice guidelines. The guideline panel developed key questions in collaboration with the ECRI Institute, which systematically searched and evaluated the literature through June 2016, developed an algorithm, and rated recommendations by using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system.

Recommendations: This synopsis summarizes key features of the guideline in 7 areas: patient-centered care and shared decision making, glycemic biomarkers, hemoglobin A_{1c} target ranges, individualized treatment plans, outpatient pharmacologic treatment, glucose targets for critically ill patients, and treatment of hospitalized patients.

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Diabetes is the leading cause of major complications, such as end-stage renal disease and lower extremity amputations, and is a significant contributor to ischemic heart disease, stroke, peripheral vascular disease, and vision loss (1). There has been increasing acceptance of the importance of individualizing glycemic management and assessment of risk for adverse events, especially hypoglycemia (2–6). This is of great importance for all patients, especially older adults (aged ≥65 years) with comorbid conditions. In 2013, 12.0 million older adults in the United States had diabetes, comprising 40% of the 30.2 million persons with the disease (7). Older adults account for an estimated 60% to 70% of the U.S. Department of Veterans Affairs (VA) and U.S. Department of Defense (DoD) diabetic population (largely retirees) (VA/DoD. Unpublished data). These considerations make safe and effective diabetes management a policy priority for health care providers (physicians, nurses, dietitians, and pharmacists) and policymakers in both the VA and the DoD.

The 2017 VA/DoD Clinical Practice Guideline (CPG) for the Management of Type 2 Diabetes Mellitus in Primary Care offers health care providers an evidence-based framework to evaluate, treat, and manage persons with type 2 diabetes mellitus in the context of their individual needs and preferences (8). The current article is a summary of key CPG recommendations, which was developed with multiple stakeholders to ensure representation by a broad spectrum of clinicians. It provides practice recommendations for the care of patients with diabetes, with an emphasis on shared decision making.

Guideline Development and Review Process

These recommendations were developed using methods established by the VA/DoD Evidence-Based Practice Work Group (EBPWG) (9), which are aligned with standards for trustworthy guidelines (10). The EBPWG and the U.S. Army Medical Command selected guideline panel cochairs (1 each from the VA and the DoD). The cochairs then selected a multidisciplinary panel of practicing clinician stakeholders, including primary care physicians (family and internal medicine), endocrinologists, medical nutritionists, pharmacists, diabetes educators, and nurse practitioners. At the start of the CPG development process and at other key points throughout, all members were required to submit disclosure statements for potential conflicts of interest in the previous 24 months. Verbal affirmations of no conflicts were used during meetings throughout the development process. The project team was also subject to random Web-based surveillance (for example, ProPublica).

The VA/DoD contracted with The Lewin Group, a third party with expertise in clinical practice guideline development, to facilitate meetings. The guideline panel, in collaboration with the ECRI Institute, developed 9 key questions using the PICOTS (population, intervention, comparator, outcomes, timing of outcomes measurement, and setting) format. A systematic search of the peer-reviewed literature from January 2009 through March 2016 was conducted to find evidence relevant to the key questions that focused on randomized trials, systematic reviews, and meta-analyses of fair or better quality. One key question was

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Table. Summary of Recommendations From the 2017 VA/DoD CPG on the Management of Type 2 Diabetes Mellitus

General approach to type 2 diabetes care
Shared decision making to enhance patient knowledge and satisfaction is recommended.
All patients with diabetes should be offered ongoing, individualized diabetes self-management education via various methods tailored to their preferences, learning needs, and abilities and based on available resources.
Offer ≥1 type of bidirectional telehealth intervention (typically health communication via computer, telephone, or other electronic means) involving licensed independent practitioners to patients selected by their primary care provider as an adjunct to usual patient care.
Glycemic control targets and monitoring
Set an HbA_{1c} target range based on absolute reduction of risk for significant microvascular complications, life expectancy, patient preferences, and social determinants of health using shared decision making.
Develop an individualized glycemic management plan based on the provider's appraisal of the risk–benefit ratio and patient preferences.
Assess patient characteristics, such as race, ethnicity, chronic kidney disease, and nonglycemic factors (e.g., laboratory methods and assay variability), when interpreting results of HbA_{1c}, fructosamine, and other glycemic biomarker testing.
Individualize the target range for HbA_{1c}, taking into account individual preferences, presence or absence of microvascular complications, and presence or severity of comorbid conditions.
A target HbA_{1c} range of 6.0%–7.0% (if it can be safely achieved) is recommended for patients with a life expectancy greater than 10–15 y and no or mild microvascular complications.
In patients with type 2 diabetes, an HbA_{1c} target range of 7.0%–8.5% is appropriate (if it can be safely achieved) for most persons with established microvascular or macrovascular disease, comorbid conditions, or life expectancy of 5–10 y.
A target HbA_{1c} range of 8.0%–9.0% is recommended for patients with type 2 diabetes with a life expectancy <5 y; significant comorbid conditions; advanced complications; or difficulties with self-management attributable to mental status, disability, or other factors (such as food insecurity or insufficient social support).
Providers should be aware that HbA_{1c} variability is a risk factor for microvascular and macrovascular outcomes.
Nonpharmacologic treatments
Offer therapeutic lifestyle counseling that includes nutrition, physical activity, cessation of smoking and excessive use of alcohol, and weight control to patients with diabetes (see VA/DoD CPGs for obesity, substance use disorders, and tobacco use cessation).
A Mediterranean diet is recommended if it aligns with patients' values and preferences.
A nutrition intervention strategy to reduce the percentage of energy from carbohydrates to 14%–45% per day and/or foods with a lower glycemic index are recommended in patients with type 2 diabetes who do not choose a Mediterranean diet.
Inpatient care
Targeting blood glucose levels to <6.1 mmol/L (<110 mg/dL) for all hospitalized patients with type 2 diabetes receiving insulin is not recommended.
Adjust insulin to maintain a blood glucose level between 6.1 and 10.0 mmol/L (110 and 180 mg/dL) only for patients with type 2 diabetes who are critically ill or have acute myocardial infarction in ICU settings.
Use of a split-mixed insulin regimen for all hospitalized patients with type 2 diabetes is not recommended.
A regimen that includes basal insulin and short-acting mealtime or basal insulin and correction insulin is recommended for non–critically ill hospitalized patients with type 2 diabetes.
Provide medication education and diabetes survival skills to patients before hospital discharge.
Consideration for combination pharmacologic therapy
Metformin should be given as the first-line agent unless it is contraindicated.
When initial therapy no longer provides adequate glycemic control, addition of a second-line agent from another class rather than substitution (which should be reserved for intolerance of or adverse effects from a drug) is usually necessary.
When selecting an agent, consider efficacy, contraindications, drug interactions, comorbidities, and potential adverse effects. Discuss with patients the various treatment options, and arrive at a shared treatment plan.

CPG = clinical practice guideline; DoD = U.S. Department of Defense; HbA_{1c} = hemoglobin A_{1c}; ICU = intensive care unit; VA = U.S. Department of Veterans Affairs.

updated through 14 June 2016. The search methods and results are detailed in the full guideline (8). The guideline panel rated recommendations by using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) method (11).

The guideline panel focused on developing new and updated recommendations using the evidence review for the key questions. The panel also considered, without a complete review of the relevant evidence, the current applicability of recommendations that were included in the 2010 CPG.

As part of the development process, a patient focus group was also convened to better understand the perspectives of patients receiving diabetes treatment in the VA and the DoD. Five patients were included, consistent with the requirements of the federal Paperwork Reduction Act. All patients had type 2 diabetes and were veterans receiving care in the VA. The focus group explored knowledge of treatment options, views on the delivery of care, patients' needs and preferences, and the effect of diabetes on their lives. Important concepts that emerged from the focus group were shared with the panel and informed guideline development. It was acknowledged that this convenience sample may not be representative of all VA and DoD patients receiving treatment for type 2 diabetes.

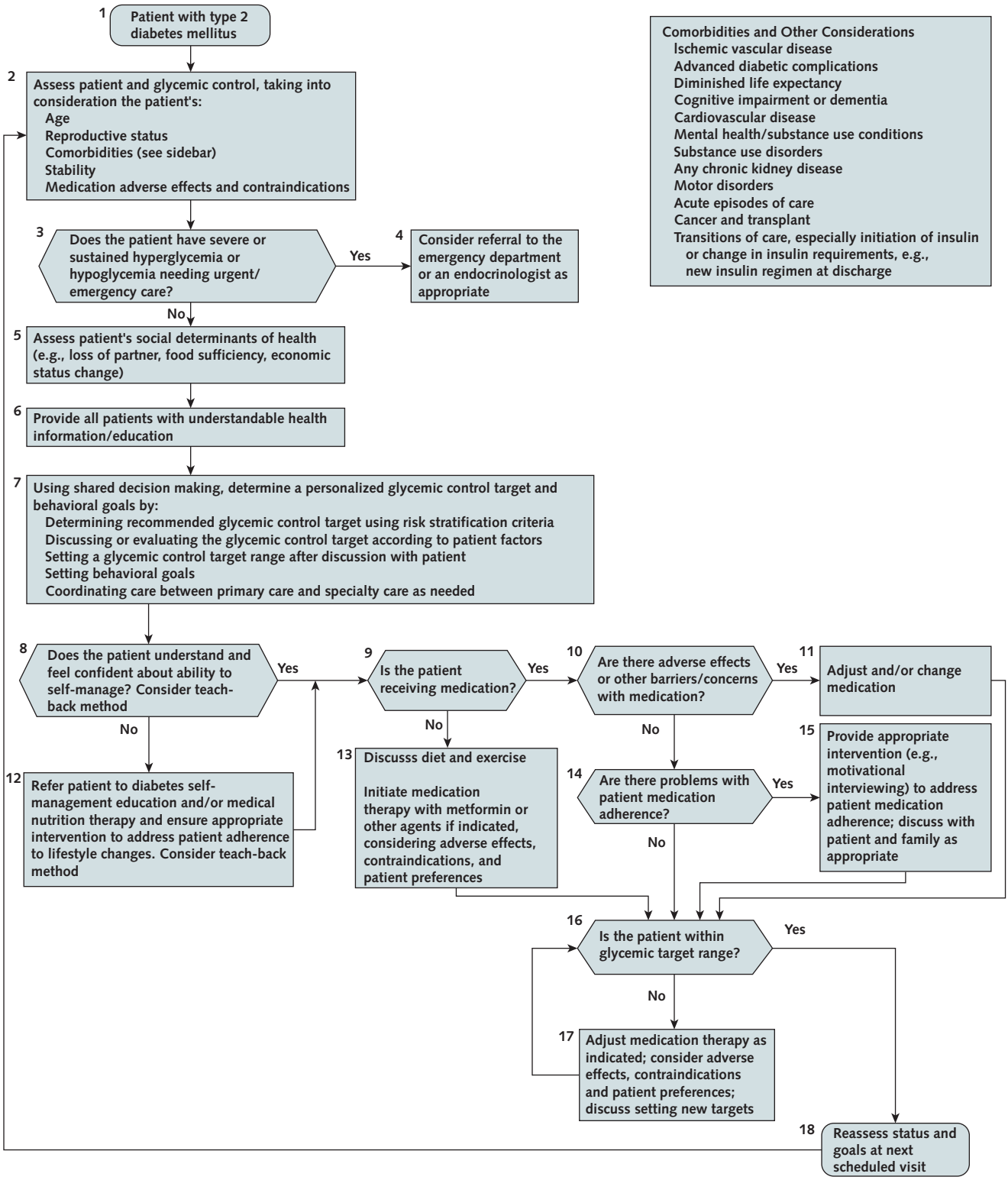
The draft guideline was sent to more than 15 expert reviewers inside and outside the federal sector. Comments were reviewed and, where appropriate, were incorporated into the final guideline based on panel consensus. The VA/DoD EBPWG approved the final document on 3 April 2017 and released it on 17 April 2017. Recommendations are presented in the **Table**, and an algorithm for establishing a personalized glycemic goal and treatment plan is presented in the **Figure**. Key recommendations are reviewed in this article.

RECOMMENDATIONS

Provide Patient-Centered Care and Incorporate Shared Decision Making

The CPG strongly encourages clinicians to incorporate shared decision making and partner with their patients. Shared decision making is the process by which the patient and family, in conjunction with the care provider, reach an agreement about a plan of care and

Figure. Algorithmic approach to evaluating glycemic control risk factors, setting a personalized glycemic control target range, providing self-management (including lifestyle and nutrition) education, and initiating or reevaluating medication therapy.



treatment. Key principles include readiness of the patient and family, tools with understandable information about the benefits and harms of all options, and strategies to identify and incorporate patient preferences. Patients cannot effectively participate in care and shared decision making unless they understand diabetes and how they can be involved in planning and carrying out the jointly developed care plan.

Shared decision making reinforces a trusted therapeutic relationship and increases patient satisfaction and treatment "buy-in" with regard to the methods used to reach a particular goal or treatment plan (12–14). It should be used not only for patients with stable glycemic control but also to assist those who are not able or willing to make lifestyle changes and decisions that affect their diabetes at any time during the course of treatment. At a minimum, shared decision making should be included at the time of diagnosis, during difficulties with management, and at times of transition or development of complications (14).

Benefits include greater knowledge of medications (13) and understanding of risks (14). In addition, patient-centered care and shared decision making together may decrease patient anxiety, increase trust in clinicians (15), and improve treatment adherence (16). Family involvement should be considered if appropriate, especially in older adults (17). Patient information should be culturally appropriate; understandable and actionable by people with limited literacy skills; and accessible to those with physical, sensory, or learning needs (18).

As part of the patient-centered care approach to diabetes management, clinicians should explore with the patient the outcomes of previous opportunities for shared decision making, their ability to self-manage, prior efforts to change health behaviors, past treatment experiences (including reasons for discontinuing treatment), and relevant clinical outcomes. In actively sharing decisions, they should involve the patient in prioritizing problems to be addressed and setting specific goals regardless of the setting or level of care.

Assess Patient Characteristics and Nonglycemic Factors When Interpreting Results of Hemoglobin A_{1c}, Fructosamine, and Other Glycemic Biomarker Testing

Many factors affect measurement of hemoglobin A_{1c} (HbA_{1c}) besides the level of glycemia (19). Because HbA_{1c} level depends on the duration of erythrocyte exposure to glucose, conditions that alter erythrocyte life span affect the measured level of HbA_{1c} (20, 21). Iron deficiency anemia, which prolongs erythrocyte life span and exposes the cell to glucose for a longer period, is associated with falsely elevated HbA_{1c} levels (22). In contrast, conditions that shorten erythrocyte life span (such as hemolytic anemia) may result in falsely low HbA_{1c} levels. Various other conditions, such as chronic kidney disease, may alter HbA_{1c} measurement. Hemoglobin variants can result in falsely elevated or falsely lowered HbA_{1c} levels, depending on the assay used (23–25). In addition, oral hypoglycemic agents (metformin or sulfonylureas) may alter the relationship between blood glucose and HbA_{1c} levels, although the clinical significance is unclear (26).

There are also racial/ethnic differences in HbA_{1c} levels for a given level of glycemia. A previous study found that African Americans with prediabetes (27) had HbA_{1c} values that were 0.4% higher than among white persons; those who were within 3 years of diagnosis (28) also had higher HbA_{1c} values than white persons for any measure of glycemia. This difference cannot be explained by measured differences in glycemia, clinical factors known to affect HbA_{1c} measurement, or sociodemographic factors (27, 28). Therefore, it is recommended that a new diagnosis of diabetes be based on a confirmatory fasting blood glucose level of at least 7.0 mmol/L (≥126 mg/dL) if the initial HbA_{1c} value is 6.5% to 6.9%.

How and where the HbA_{1c} level is measured can also affect results because of intralaboratory variation (variation in test accuracy and precision) and interlaboratory variation (variation related to use of different test methods). A single HbA_{1c} measurement, even from a high-quality laboratory, has a margin of error such that the true value is within a range defined by the coefficient of variation. Sequential HbA_{1c} values that are within 0.5% do not statistically differ from one another unless the assay coefficient of variation is less than 3%, and ideally less than 2% (29). Treatment decisions based solely on a single HbA_{1c} measurement without consideration of other clinical data, such as glucose monitoring results, may lead to unnecessary initiation or intensification of therapy. Comparing HbA_{1c} tests performed in different clinical laboratories introduces another source of error, as does use of point-of-care HbA_{1c} testing, which is not subject to systematic quality oversight. Assessing the effect of these patient characteristics and nonglycemic factors that affect HbA_{1c} levels allows for better individualization of management. For these reasons, the VA/DoD does not recommend the use of estimated average glucose level, which is derived from HbA_{1c} values using a formula.

Set HbA_{1c} Target Ranges Based on Absolute Reduction in Risk for Significant Microvascular Complications, Life Expectancy, and Patient Preferences

An individualized approach to treatment goals is recommended, based on the patient's absolute risk for microvascular complications balanced against comorbidities, estimated life expectancy, presence or absence of existing complications, the risk and inconvenience associated with polypharmacy, risk for hypoglycemia and other adverse events, effects on concomitant conditions (such as weight), and overall treatment burden.

The shared decision-making process might be affected by the framing of trial results. Clinicians should therefore consider a patient's values and preferences when discussing the magnitude of clinically important outcomes and harms from trials (11). The VA/DoD CPG recommends that clinicians discuss absolute risk reduc-

tion rather than relative risk reduction when conveying to patients their estimated likelihood of achieving a reduction in clinically significant complications or potential risks of therapy. The VA/DoD CPG summarizes the available evidence from major clinical trials as well as meta-analyses to inform strength of recommendations (30–44) that apply to patients with both recent-onset and longer-duration diabetes with established complications.

Develop Individualized Treatment Plans Based on Complications, Comorbidities, Life Expectancy, and Patient Preferences

The CPG proposes HbA_{1c} target ranges (rather than an all-or-nothing target value) based on the presence or absence of microvascular complications, comorbidities, and life expectancy. This is rooted in the substantial body of evidence showing a direct relationship between glucose control and microvascular complications (for example, retinopathy, neuropathy, and nephropathy). The overarching goal of these recommendations is to develop individualized treatment plans and HbA_{1c} target ranges that are tailored to a patient's unique characteristics and goals of care.

Higher HbA_{1c} levels carry greater risk for complications, and decreasing levels prospectively reduces risk (30, 31, 33, 34). The relationship between HbA_{1c} and risk for microvascular complications is continuous and accelerates when levels exceed 9% (35). There is no apparent HbA_{1c} threshold above which benefits are not accrued by decreasing levels, but the absolute risk reduction is less at lower levels (31). Thus, a decrease in HbA_{1c} level may have minimal clinical impact on complications in patients with limited life expectancy. Conversely, there are no data on the appropriate lower limit for achieved HbA_{1c} level, although strong data exist on the risks for hypoglycemia as HbA_{1c} is targeted to near-normal levels for patients receiving insulin (36). Lower levels of HbA_{1c} (closer to 6%) may be reasonable in younger patients treated with metformin alone.

Microvascular complications develop over an extended period. Thus, persons with long life expectancy and no or mild microvascular complications (such as early background retinopathy, microalbuminuria, or mild neuropathy) may benefit from a lower HbA_{1c} level (6.0% to 7.0%) (**Supplement**, available at Annals.org).

For patients with comorbidities or complications that shorten life expectancy (<10 years), higher HbA_{1c} target ranges are appropriate. Systematic reviews comparing intensive and conventional glucose control showed no statistically significant differences in all-cause mortality or death from cardiovascular disease but did show statistically significant risk reduction for microvascular complications, such as nephropathy, retinopathy, and lower extremity amputation (36–38). These trials provided no firm evidence that decreasing HbA_{1c} levels to less than 8.5% reduces risk for death from cardiovascular disease (39). Depending on the presence and degree of microvascular complications, HbA_{1c} target ranges of 7.0% to 8.0% or 7.5% to 8.5% are appropriate for most patients (**Supplement**).

The presence of major comorbidities that decrease life expectancy (<5 years) or advanced microvascular complications (such as severe nonproliferative or proliferative retinopathy, renal insufficiency [stage 3b or greater chronic kidney disease], insensate extremities, or autonomic neuropathy) may justify a higher HbA_{1c} target range. Such patients are less likely to benefit from intensive glucose control and more likely to have risks from treatment.

Intensive glucose control may cause frank harms, such as increased risk for death from cardiovascular events (40) and severe hypoglycemia (that is, hypoglycemia requiring help from another person). Risk factors for hypoglycemia include use of specific drugs (insulin and sulfonylureas), advanced age (>75 years), cognitive impairment, and chronic kidney disease (including causes unrelated to diabetic nephropathy) (41–43). Additional risk factors include lack of appropriate glucose monitoring, inadequate diabetes education, lack of family and social support systems, and food insufficiency. There are racial differences between estimated average glucose level and HbA_{1c} values in patients with established type 2 diabetes based on 7-point glucose testing (44). Thus, self-monitoring results and HbA_{1c} test results may be discordant. The presence of any of these factors should prompt a discussion about higher HbA_{1c} target ranges.

Assessing the effect of these patient characteristics and nonglycemic factors that affect HbA_{1c} levels allows for better individualization of management. Thus, we recommend that treatment goals involve target ranges for HbA_{1c} rather than levels above or below a specific value for most persons with diabetes. This approach is consistent with clinical and laboratory science and avoids unnecessary intensification of therapy due to fluctuations within the range. This recommendation allows for individualized treatment plans and is consistent with patient values.

Pharmaceutical Agents Should Be Selected on the Basis of Efficacy, Contraindications, Drug Interactions, Comorbidities, and Potential Adverse Effects and Patients Should Be Engaged With the Various Treatment Options and Should Arrive at a Shared Treatment Plan With Their Clinician

When individualized glycemic goals are not achieved with nonpharmacologic therapy, such as diet and increased physical activity, adjunctive therapy with medications is indicated. The magnitude of the reduction in HbA_{1c} level necessary to achieve goals should be considered when choosing medications, along with hypoglycemia risk, weight gain, administrative burden, and cost.

Although evidence for pharmacologic treatment options was not systematically reviewed as part of this guideline update, the VA/DoD CPG made the following recommendations based on a review of a recent systematic review conducted by the Agency for Healthcare Research and Quality (45). First, when selecting a medication, efficacy, contraindications, drug interactions,

comorbidities, and potential adverse effects must be considered. Clinicians should discuss the various treatment options with patients and arrive at a shared treatment plan. Second, metformin should be given as the first-line agent unless it is contraindicated. Third, when initial therapy no longer provides adequate glycemic control, addition of a second-line agent from another class rather than substitution is usually necessary. Substitution should be reserved for intolerance of or adverse effects from a drug. Finally, a combination of 2 antihyperglycemic drugs has the benefit of reducing hyperglycemia by working on different mechanisms that cause it. Combination therapy needs to be guided by clinical considerations in addition to antihyperglycemic efficacy.

Three medications (metformin, empagliflozin, and liraglutide) have shown a specific benefit for cardiovascular outcomes in patients with type 2 diabetes who are at high risk for cardiovascular events. However, although each of these medications decreases average blood glucose level, the mechanism for improved cardiovascular outcomes cannot be ascribed solely to intensive glycemic control.

A limitation of studies is that many patients seen in practice, especially older patients with significant risks for potential complications from newer therapies, are often excluded from clinical trials. Clinicians should therefore be aware of drug alerts from the U.S. Food and Drug Administration because harms of therapy will continue to evolve based on postmarketing surveillance. Both the VA (46) and the DoD (47) maintain criteria for use, which are updated frequently.

Aggressive Glucose Control Is Not Recommended in Hospitalized Patients

Hyperglycemia during hospitalization is associated with adverse outcomes, and glucose-lowering interventions reduce morbidity and mortality in critically ill patients. However, there is uncertainty about the appropriate glucose target for hospitalized patients and about which patients benefit from glucose-lowering interventions. Randomized trials examining inpatient glycemic control and/or insulin therapy are often limited to hospitalized patients with severe illness (for example, illness requiring admission to the intensive care unit, acute myocardial infarction, or acute stroke). A large multicenter trial among critically ill patients with diabetes showed that a blood glucose target less than 10.0 mmol/L (<180 mg/dL) resulted in lower mortality than a target of 4.4 to 6.1 mmol/L (80 to 110 mg/dL), and the lower range was associated with increased hypoglycemia (odds ratio, 14.7) (48). These data should not be extrapolated to inpatients who are not in the intensive care unit because the evidence on glycemic control targets in non–critically ill hospitalized patients is of low quality (49).

Achieving near-normal glucose levels in hospitalized patients without risk for hypoglycemia can be challenging. Hypoglycemic episodes are associated with increased risk for death in patients in the intensive care unit (50). Fingerstick blood glucose monitoring is often performed in hospitalized patients with diagnosed diabetes, hyperglycemia, or both to identify potentially harmful hyperglycemia and hypoglycemia. There is no evidence to support a given frequency of such monitoring. Therefore, the frequency of glucose monitoring should take into account the diabetes treatment method used (such as insulin or oral agents), the effect of hyperglycemia on the clinical condition requiring hospitalization, and the patient's overall stability.

Use Basal Insulin and Short-Acting Mealtime Insulin or Basal Insulin and Correction Insulin for Hospitalized Patients Who Are Not in the Intensive Care Unit

Although much attention has focused on the appropriate glucose target in hospitalized patients, the literature examining treatment methods for diabetes in hospitalized patients is growing (51–54). Key factors to consider in devising a glucose control strategy are prehospital diabetes treatment, in-hospital dietary intake, and factors that can either increase (for example, corticosteroids) or decrease (for example, renal or liver failure) insulin resistance. In patients with insulin deficiency (for example, type 1 diabetes or long-standing type 2 diabetes), providing basal insulin along with short-acting preprandial doses to cover food intake and correction doses for glucose elevations tends to work well. This is referred to as a basal–bolus-plus-correction regimen. Such treatment schemes are often underused in the hospital, possibly due to complexity, fear of hypoglycemia, and challenges in transferring home-based insulin regimens to the hospital setting. Many patients are instead prescribed correction insulin alone (for example, sliding-scale insulin), based on doses assigned to treat a prespecified glucose range on a scale or table. Sliding-scale insulin regimens are viewed as easy to implement but should be discouraged. Unlike regimens that use basal and preprandial insulin, sliding-scale insulin does not have favorable in-hospital outcomes. Basal insulin with preprandial correction doses used in general medical and surgical patients with type 2 diabetes produced similar glycemic control and rates of hypoglycemic events compared with a more complex regimen of basal–bolus and correction doses. Both regimens resulted in better glycemic control and fewer treatment failures than use of sliding-scale insulin alone (54). Use of basal–bolus insulin also reduced risk for postsurgical complications (51).

DISCUSSION OF DIFFERENCES BETWEEN GUIDELINES

There are similarities and differences between the recommendations from the VA/DoD CPG and those from the Standards of Medical Care in Diabetes, issued by the American Diabetes Association (ADA) (55–57); Diabetes in Older Adults: A Consensus Report, a joint report of the ADA and the American Geriatrics Society (ADA/AGS) (17); and the American Association of Clinical Endocrinologists (AACE) CPG (58).

Although the ADA notes that such factors as age, race/ethnicity, and certain clinical conditions may result in differences between HbA_{1c} level and measures of glycemic control, use of HbA_{1c} level alone for diagnosis of diabetes is acceptable (55). In contrast, the VA/DoD CPG concluded that evidence showing racial differences between HbA_{1c} level and glycemic control for diagnosis and treatment is strong (7). Therefore, the CPG recommends that to establish a new diabetes diagnosis, an HbA_{1c} value of 6.5% to 6.9% should be confirmed with an elevated fasting blood glucose level (>7.0 mmol/L [>126 mg/dL]). The guideline panel agreed that requiring a fasting blood glucose level in this setting did not pose an undue burden compared with the potential effect of an incorrect diagnosis of diabetes on life or disability insurance premiums or military career trajectory.

The VA/DoD (8), the ADA (56), and the ADA/AGS (17) recommend individualized approaches based on patient preferences. The VA/DoD CPG also recommends target ranges rather than thresholds. An emphasis on dichotomous HbA_{1c} thresholds may result in clinicians and patients viewing values marginally above the threshold as being clinically significant, which could result in inappropriate intensification of therapy without consideration for absolute benefits and risks. A range can accommodate known laboratory and clinical factors that affect interpretation of HbA_{1c} test results. In addition, the VA/DoD CPG is the only one to state that the evidence is strong that race affects the relationship between HbA_{1c} level and glycemic control. The ADA states that it is prudent to establish HbA_{1c} goals with consideration of both individualized self-monitoring blood glucose results and HbA_{1c} results in ethnic populations (56). In addition, the VA/DoD CPG recommends against the use of estimated average glucose level. Thus, the VA/DoD CPG was the most explicit in stating that a target glycemic range can best balance these competing priorities and avoid intensification of therapy to a marginally higher HbA_{1c} test result.

The VA/DoD CPG differs not only in the nature of the target but in what the target should be. For example, the ADA and the ADA/AGS recommend an HbA_{1c} level less than 8% for patients with advanced disease, limited life expectancy, or other mitigating factors but as high as 8.5% for frail adults. The AACE recommends that the goal of therapy should be an HbA_{1c} level of 6.5% or lower for most nonpregnant adults, if it can be achieved safely. A range of 7% to 8% is recommended in patients with a history of severe hypoglycemia, limited life expectancy, advanced renal disease, or macrovascular complications (58).

In contrast, the VA/DoD CPG concluded that, on average, the potential absolute benefit of decreasing HbA_{1c} level from 8.5% to 8.0% in high-risk patients was less than the potential risk for harms from increasing medication therapy. The VA/DoD CPG recommends a range of 7.5% to 8.5% for most patients with life expectancy less than 10 years and significant comorbid conditions and a range of 8% to 9% for those with limited life expectancy (<5 years).

Insulin management recommendations in the intensive care unit are similar between the VA/DoD and ADA guidelines. The ADA recommends that insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a glucose threshold of 10.0 mmol/L (180 mg/dL), with a target range of 7.8 to 10.0 mmol/L (140 to 180 mg/dL) for most critically ill patients. The VA/DoD CPG recommends that insulin doses be adjusted to maintain a blood glucose level of 6.1 to 10.0 mmol/L (110 to 180 mg/dL) for critically ill patients or those with acute myocardial infarction. These recommendations should not be extrapolated to other hospital settings in the absence of randomized controlled trials.

In summary, the VA/DoD CPG attempts to convey to clinicians, policymakers, and patients the rationale for personalizing treatment on the basis of results from major trials, limitations of the HbA_{1c} test, and evaluation of patient risk for adverse drug events. Conveying complex information in an understandable manner to individual patients and families through a formal process of shared decision making is thus foundational to setting and revising goals that are meaningful, safe, and achievable in everyday clinical practice (59).

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