Clinical Protocol for the Prevention and Treatment of Diabetes in Adults

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Introduction

Currently, an estimated 30.3 million Americans continue to live with diabetes and more than 84 million live with prediabetes. In 2015, diabetes was the seventh leading cause of death in the United States and the leading cause for kidney failure, lower-limb amputations, and adult-onset blindness.[1] Heart disease and stroke are two to four times more likely for individuals with diabetes. With diabetes being a public health priority, the Centers for Disease Control and Prevention (CDC), public health professionals, state health departments and communities are working collaboratively to achieve optimal health outcomes for patients with diabetes. This will require an organized, systematic approach to providing high-quality, patient-centered care.

Purpose

To present practice guidelines and recommendations for primary health care providers serving adults diagnosed with diabetes or are at-risk of developing diabetes. This document provides population management tools and approaches to proactively monitor and manage diabetes, which includes evidence-based treatment protocols and approaches using clinical practice data to drive improvement.

[1] Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2017. Atlanta, GA: U.S. Department of Health and Human Services; 2017.

Classification of Diabetes

Diabetes is a disease that affects how the body produces or uses insulin. As a result, patients with diabetes are unable to process energy from food properly which leads to elevated levels of glucose. Prediabetes is asymptomatic and occurs when blood glucose levels are higher than normal but not high enough to be diagnosed as diabetes.[2,3] Among the population diagnosed with diabetes, there are three types of diabetes (Table 1).[4]

TABLE 1. Classification of Diabetes

Type	Classification
Type 1 Diabetes	Due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency
Type 2 Diabetes	Due to a progressive loss of β-cell insulin secretion frequently associated with insulin resistance
Gestational Diabetes Mellitus (GDM)	Diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation

Classification is important for determining therapy; however, it may be difficult at the time of diagnosis to determine an individual's type of diabetes. Contrary to traditional paradigms, both diseases occur in all age groups. As shown in Table 2, the common symptoms for type 1 and type 2 diabetes are similar, but may vary greatly between individuals. In some cases, individuals may not have any symptoms or symptoms may be so mild that they go unnoticed.

TABLE 2. Common Symptoms of Diabetes

Prediabetes
No symptoms

[2] Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997; 20:1183–1197

[3] Genuth S, Alberti KG, Bennett P, et al.; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26: 3160–3167

[4] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37(Suppl. 1):S81–S90

Diagnostic Criteria

Diabetes and prediabetes may be diagnosed using the plasma glucose criteria which includes fasting plasma glucose (FPG), 2-h plasma glucose (2-h PG) during a 75-g oral glucose tolerance test (OGTT), random plasma glucose (RPG), or glycosylated hemoglobin (A1C) screening test (Table 3).[5]

TABLE 3. Criteria for Diagnosis of Diabetes and Prediabetes

	Prediabetes	Diabetes
FPG Blood sample taken after overnight fasting	140–199 mg/dL (7.8–11.0 mmol/L)	≥200 mg/dL (11.1 mmol/L)
2-h PG Blood samples taken periodically for two hours after overnight fasting and drinking a glucose-containing liquid	100–125 mg/dL (5.6–6.9 mmol/L)	≥126 mg/dL (7.0 mmol/L)
A1C Measures average blood glucose control for the past 2 to 3 months. This test is more convenient because no fasting is required	5.7–6.4% (39 mmol/mol - <48 mmol/mol)	≥6.5% (48 mmol/mol)
RPG Blood sample taken at a random time, regardless of when last meal was eaten	----	≥200 mg/dL (11.1 mmol/L)

Unless there is a clear clinical diagnosis, a second test is necessary for confirmation. It is recommended that the same test be repeated or a different test be performed immediately using a separate blood sample. If test results are near the margins of the diagnostic threshold, the patient should continue to be monitored and a test should be repeated in 3–6 months.[6]

Criteria for Screening for Diabetes and Prediabetes

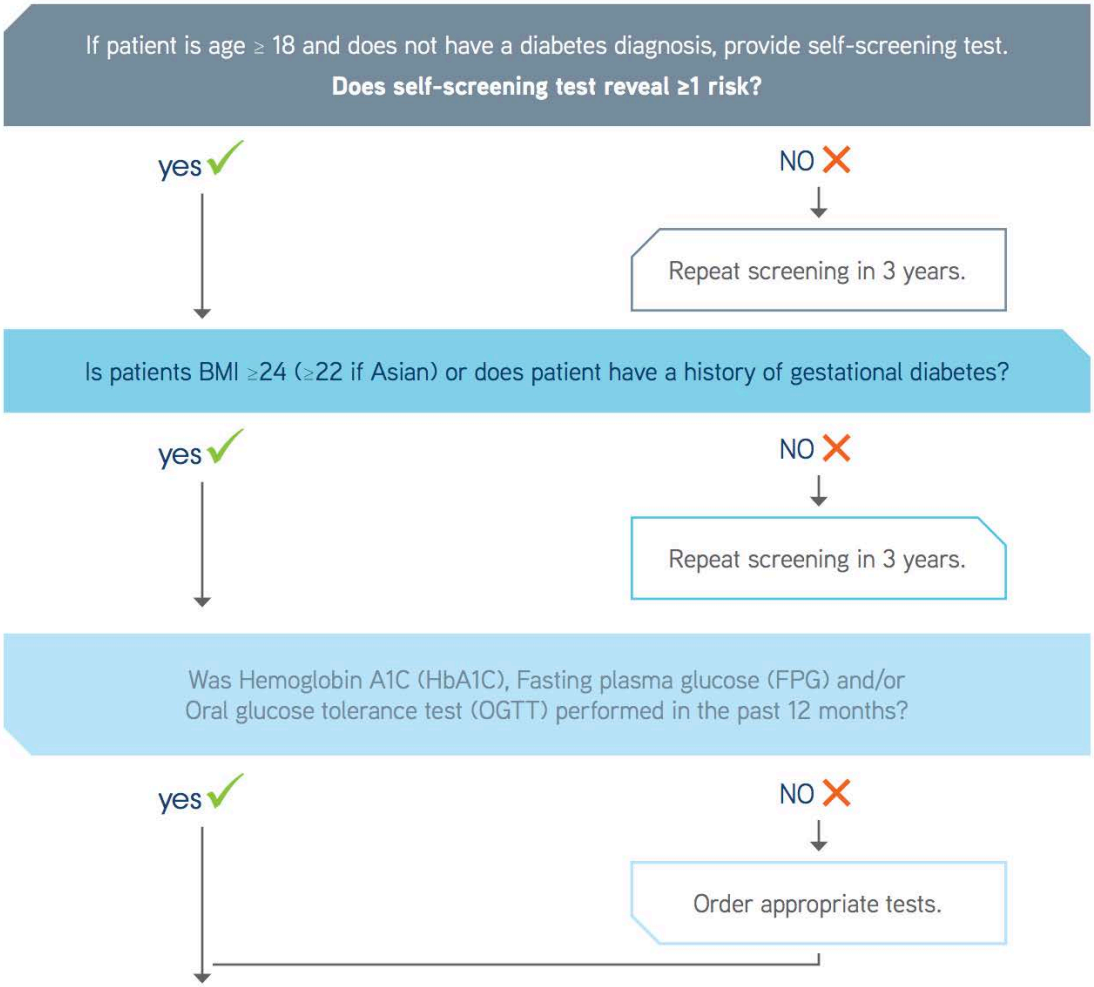
According to CDC and the American Diabetes Association (ADA) guidelines, patients should be screened for the following criteria:

- Physical inactivity
- First-degree relative with diabetes (sibling or parent)
- High-risk race/ethnicity
- Women who delivered a baby >9 lb or were diagnosed with gestational diabetes mellitus (GDM)
- HDL cholesterol (HDL-C) 250 mg/dL
- Hypertension (≥140/90 mm Hg or on therapy)
- A1C ≥ 5.7%, impaired glucose tolerance (IGT), or impaired fasting glucose (IFG) on previous testing
- Conditions associated with insulin resistance: severe obesity, Acanthosis Nigricans, Polycystic Ovarian Syndrome (PCOS)
- History of cardiovascular disease (CVD)

[5] International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009;32:1327–1334

[6] American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes 2018. Diabetes Care 2018;41(Suppl. 1):S13–S27

FIGURE 1. Point-of-Care Possible Prediabetes and Diabetes Identification



Diagnostic Test	Normal	Pre-Diabetes	Diabetes
HbA1C (%)	< 5.7	5.7–6.4	≥ 6.5
Fasting plasma glucose (mg/dL)	< 100	100–125	≥ 126
Oral glucose tolerance test (mg/dL)	< 140	140–199	≥ 200

Encourage patient to maintain a healthy lifestyle. Continue with exam/consult. Retest within three years of last negative test.

Refer patient to lifestyle change programs. Retest annually to check for diabetes onset.

Confirm diagnosis; retest if necessary. Counsel patient regarding diagnosis. Initiate therapy.

Screening should be performed on adults of any age who are overweight or obese, and who have one or more of the above diabetes risk factors. Assessing an individual's history of CVD is particularly important, as it is the major cause of morbidity and mortality for individuals with diabetes. Common conditions that coexist with type 2 diabetes (e.g., hypertension and dyslipidemia) are clear risk factors for CVD. Numerous studies have shown the efficacy of controlling individual CVD risk factors in

preventing or slowing CVD in people with diabetes. Large benefits are seen when multiple risk factors are addressed simultaneously.[7,8]

If a screening test is normal, it should be repeated at least every three years. The flow chart above outlines a sample workflow to assist providers in identifying patients for possible prediabetes (Figure 1).[9]

Data Extraction from Electronic Health Records (EHRs) to Identify Patients with Prediabetes

While a singular national standard algorithm for extracting data to identify patients with prediabetes using EHRs does not exist, there are several algorithms available as references. The key to a successful initiative is to begin small and to scale the program as resources allow. Extracting data from the EHR may result in an overwhelming amount of information; prioritizing and narrowing the scope of the extraction and/or subsequent outreach efforts can help mitigate the impact on the organization. The first and simplest dataset to examine may be patients with a prediabetes or diabetes diagnosis who have not received appropriate treatment or follow-up testing. Table 4 includes data specifications that can be used to identify at-risk patients.

TABLE 4. Specifications for Generating Prediabetes Reports from Electronic Health Records

Goal: Identify patients between 18-85 with no previous diagnosis of DM or insulin use, but who have A1C or plasma glucose levels within the prediabetes range noted in Figure 1 with a BMI >25 (or 22 if Asian).
1. Query all patients ≥ 18 and < 85 years old during the last 12 months (from date of query being run, back 1 year) where the patient has had an HbA1C result between 5.7–6.4% AND/OR a fasting plasma glucose level between 100–125 mg/dL, AND/OR an Oral glucose tolerance test between 140–199 mg/dL. 2. Exclude Patients that have had previous DM diagnosis or Insulin use at any point in time. 3. Exclude patients with a BMI <25 (or <22 if Asian).
Report Viewing Fields - Gender - Ethnicity and Race - Age - ZIP Code - Referred to National Diabetes Prevention Program, NDPP (where available) - Completed NDPP (where available) - Dropped out of NDPP and reason why (where available)

[7] Buse JB, Ginsberg HN, Bakris GL, et al.; American Heart Association; American Diabetes Association. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Diabetes Care 2007;30:162–172

[8] Gaede P, Lund-Andersen H, Parving H-H, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med 2008;358:580–591

[9] http://www.cdc.gov/diabetes/prevention/pdf/point-of-care-prediabetes-identification-algorithm_tag508.pdf

Outreach/Pre-Visit Planning/Panel Management (Recall)

Today, greater ease of communication between patients and their primary care providers has helped bridge the communication gap between clinical visits. Electronic systems may be used by clinicians to create reports on patients with varying risks of disease or with specific disease management needs, providing them with greater sophistication in developing plans to target outreach to patients.

Pre-Visit Planning and Panel Management are two tools that enable organizations to ensure:

- Patients receive appropriate confirming diagnostic tests;
- Proper diagnoses are entered into medical record accurately;
- Patients engage in developing an updated care plan and/or receive a referral to community resources to prevent further exacerbation, and proper management, of chronic diseases.

Pre-Visit Planning

Pre-Visit Planning offers opportunities to improve patient care and to identify gaps in care for patients with upcoming visits. Common pre-visit planning steps include:

- Gathering the necessary information for upcoming visits;
- Planning the current patient visit and preparing for the next;
- Pre-populating the next day's visit notes with diabetes risks (e.g., abnormal blood sugar, lifestyle risks, high blood pressure, etc.);
- Arranging for pre-visit lab testing.

The American Medical Association provides an interactive tool to assist practices in implementing Pre-Visit Planning, available at: https://www.stepsforward.org/modules/pre-visit-planning

Panel Management

In Panel Management (also known as "Recall") patients are systematically identified for gaps in care, preventive services, and/or chronic condition management. Panel Management allows organizations to proactively identify and contact patients who are currently accessing the health care system but may be unaware of risk factors or uncontrolled medical conditions. This approach allows clinical staff to improve care for patients who are not necessarily in the office for a visit.

Lifestyle Management

Lifestyle management (LM) is essential in diabetes care and includes diabetes self-management education and support (DSMES), medical nutrition therapy (MNT), physical activity, smoking cessation counseling, and psychosocial care. DSMES should be assessed at diagnosis, annually, when complicating factors arise, and when transitions in care occur.[10]

[10] Powers MA, Bardsley J, Cypress M, et al. Diabetes self-management education and support in type 2 diabetes: a joint position statement of the American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics. Diabetes Care 2015;38:1372–1382

Nutritional Therapy

MNT has an integral role in the overall management of diabetes and requires individualized eating plans (Appendix II). Each patient should be actively engaged in education, self-management, and treatment planning with his or her care team.[11,12]

Weight Management

Weight management is important for overweight and obese people with prediabetes, type 1 and type 2 diabetes. Care teams should work closely with patients to set and achieve weight reduction goals and improve clinical indicators. Modest, persistent weight loss can delay the progression from prediabetes to type 2 diabetes.[13,14,15]

Physical Activity and Exercise

Physical activity and exercise have been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve overall well-being. Adults with type 1 and type 2 diabetes should engage in 150 minutes or more of moderate-to-vigorous intensity aerobic activity per week with no more than two consecutive days without activity. Shorter durations (minimum 75 minutes per week) of vigorous-intensity or interval training may be sufficient for younger and more physically fit individuals. Amount of time spent in daily sedentary behavior should be decreased, particularly in adults with type 2 diabetes. Flexibility training and balance training are recommended 2–3 times per week for older adults (60 years or older) with diabetes.[16,17]

Tobacco and Smoking Cessation

Individuals with diabetes who smoke, are exposed to secondhand smoke, or use tobacco have a heightened risk of CVD, premature death, and microvascular complications. Smoking may have a role in the development of Type 2 diabetes. All patients are advised not to use cigarettes and other tobacco products or e-cigarettes. Therefore, it is important to include smoking cessation counseling and other

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[11] Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2015;38:140–149

[12] Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care 2014;37(Suppl. 1):S120–S143.

[13] MacLeod J, Franz MJ, Handu D, et al. Academy of Nutrition and Dietetics Nutrition practice guideline for type 1 and type 2 diabetes in adults: nutrition intervention evidence reviews and recommendations. J Acad Nutr Diet 2017;117:1637–1658.

[14] Mudaliar U, Zabetian A, Goodman M, et al. Cardiometabolic risk factor changes observed in diabetes prevention programs in US settings: a systematic review and meta-analysis. PLoS Med 2016;13:e1002095.

[15] Balk EM, Earley A, Raman G, Avendano EA, Pittas AG, Remington PL. Combined diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk: a systematic review for the Community Preventive Services Task Force. Ann Intern Med 2015;163:437–451.

[16] Boulé NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA 2001;286:1218–1227.

[17] Jankowich M, Choudhary G, Taveira TH, Wu W-C. Age-, race-, and gender-specific prevalence of diabetes among smokers. Diabetes Res Clin Pract 2011;93:e101–e105

forms of treatment as a routine component of diabetes care.[18]

Assessing Glycemic Control

Patient self-monitoring of blood glucose (SMBG) and A1C, and continuous glucose monitoring (CGM), are two methods that are often used to assess the effectiveness and safety of a diabetes management plan.[19]

The advantages of SMBG include accuracy and relatively low costs in the measurement of capillary glucose concentrations. Glucose meters can offer features including memory, downloading software, small blood sample requirements, and the option of no coding strips. Disadvantages include the impact of user error on test accuracy, the need for multiple finger-stick blood samples each day, and limitations of what clinicians can learn from a few daily snapshots of glucose concentrations.[20, 23]

The main advantage of CGM is continuously capturing interstitial glucose concentration, which can help identify trends and patterns in glucose control.[24,25] In addition, some monitors can be programmed to alarm for high or low glucose values, reducing fear related to the ability to detect hypo- or hyperglycemia.[26] Disadvantages include the cost of CGM, and lack of universal insurance coverage for this technology.

A1C reflects average glycemic level over approximately three months and has strong predictive value for diabetes complications. The A1C test should be performed at least twice per year in patients who are meeting treatment goals, and quarterly in patients whose therapy has changed or who are not meeting glycemic goals.[27] The ADA and the American Association for Clinical Chemistry (AACC) have determined that the correlation between the A1C and the estimated average glucose results is strong enough that

[18] Akter S, Goto A, Mizoue T. Smoking and the risk of type 2 diabetes in Japan: a systematic review and meta-analysis. J Epidemiol 2017;27:553–561

[19] Aleppo G, Ruedy KJ, Riddlesworth TD, et al.; REPLACE-BG Study Group. REPLACE-BG: a randomized trial comparing continuous glucose monitoring with and without routine blood glucose monitoring in adults with well-controlled type 1 diabetes. Diabetes Care 2017;40:538–545.

[20] Benjamin E. Self-Monitoring of Blood Glucose: The Basics. Clin Diabetes. 2002;20:45–47.

[21] 2008 resource guide. Blood glucose monitoring and data management systems. Before you buy a blood glucose monitor (also known as a blood glucose meter), check with your doctor and diabetes educator. Make sure the one you choose is well suited to your particular needs. Diabetes Forecast. 2008;61:RG31–RG32. RG34–RG48.

[22] Bode BW. The Accuracy and Interferences in Self-monitoring of Blood Glucose. US Endocrine Disease. 2007:46–48.

[23] Le Floch JP, Bauduceau B, Levy M, Mosnier-Pudar H, Sachon C, Kakou B. Self-monitoring of blood glucose, cutaneous finger injury, and sensory loss in diabetic patients. Diabetes Care. 2008;31:e73.

[24] Wadwa RP, Fiallo-Scharer R, Vanderwel B, Messer LH, Cobry E, Chase HP. Continuous glucose monitoring in youth with type 1 diabetes. Diabetes Technol Ther. 2009;11(Suppl 1):S83–S91.

[25] Nardacci EA, Bode BW, Hirsch IB. Individualizing care for the many: the evolving role of professional continuous glucose monitoring systems in clinical practice. Diabetes Educ. 2010;36(Suppl 1):4S–19S. quiz 20S–21S.

[26] Hirsch IB, Abelseth J, Bode BW, Fischer JS, Kaufman FR, Mastrototaro J, Parkin CG, Wolpert HA, Buckingham BA. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. Diabetes Technol Ther. 2008;10:377–383

[27] Jovanovič L, Savas H, Mehta M, Trujillo A, Pettitt DJ. Frequent monitoring of A1C during pregnancy as a treatment tool to guide therapy. Diabetes Care 2011;34:53–54

both measurements should be considered as part of the planning for glycemic management.[28] A summary of glycemic recommendations for adults with diabetes is shown in Table 5.

[28] Beck RW, Connor CG, Mullen DM, Wesley DM, Bergenstal RM. The fallacy of average: how using HbA1c alone to assess glycemic control can be misleading. Diabetes Care 2017;40:994–999.

TABLE 5. Recommended Glycemic Targets in Adults with Diabetes

Indicator	Targets
A1C	<7.0% (53 mmol/mol)
Preprandial capillary plasma glucose	80–130 mg/dL (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose	<180 mg/dL* (10.0 mmol/L)

Managing Hypoglycemia

Educating patients with diabetes to balance insulin use, carbohydrate intake and exercise is essential, especially for patients on insulin and/or insulin secretgogues. Hypoglycemia is a true medical emergency which requires prompt recognition and treatment to prevent organ and brain damage.[29] Patients should be educated on the symptoms (e.g. shakiness, irritability, confusion, tachycardia, hunger) and situations that increase their risk of hypoglycemia, such as fasting for tests or procedures, delayed meals, during or after intense exercise, and during sleep. SMBG and, for some patients, CGM are important tools to assess therapy and detect incipient hypoglycemia. The classification of hypoglycemia is shown in Table 6.

Table 6. Classification of Hypoglycemia

Level	Glycemic Criteria	Description
Level 1: Glucose alert value	≤70 mg/dL (3.9 mmol/L)	Sufficiently low for treatment with fast-acting carbohydrate and dose adjustment of glucose-lowering therapy
Level 2: Clinically significant hypoglycemia	<54 mg/dL (3.0 mmol/L	Sufficiently low to indicate serious, clinically important hypoglycemia
Level 3: Severe hypoglycemia	No specific glucose threshold	Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

Pharmacological Therapy for Patients with Type 1 Diabetes

Most individuals with type 1 diabetes are treated with multiple daily injections of prandial insulin and basal insulin or continuous subcutaneous insulin infusion (CSII). Rapid-acting insulin analogs should be used to reduce hypoglycemia risk. Education on matching prandial insulin doses to carbohydrate intake, pre-meal blood glucose levels, and anticipated physical activity is necessary. Generally, the starting insulin dose is based on weight, with doses ranging from 0.4 to 1.0 units/kg/day of total insulin.[30] The various types of insulin available are listed in Table 7. Concurrent reduction of prandial insulin is required to reduce the risk of severe hypoglycemia. Adding metformin to insulin therapy may also reduce insulin requirements.[31]

[29] Shafiee et al. Journal of Diabetes & Metabolic Disorders 2012, 11:17

[30] Peters AL, Laffel L, Eds. American Diabetes Association/JDRF Type 1 Diabetes Sourcebook. Alexandria, VA, American Diabetes Association, 2013

[31] Vella S, Buetow L, Royle P, Livingstone S, Colhoun HM, Petrie JR. The use of metformin in type 1 diabetes: a systematic review of efficacy. Diabetologia 2010;53:809–820

Table 7. Types of Insulin Available for the Treatment of Diabetes

Insulin Type and Name	Onset	Peak	Duration
Rapid-acting • Insulin aspart (NovoLog) • Insulin glulisine (Apidra) • Insulin lispro (Humalog)	5-15 min.	45-75 min.	3-4 hours
Short-acting • Insulin regular (Humulin R, Novolin R)	30-45 min.	2-4 hours	6-8 hours
Intermediate-acting • Insulin NPH (Humulin N, Novolin N)	2 hours	4-12 hours	16-24 hours
Long-acting • Insulin glargine (Lantus/ Toujeo) • Insulin detemir (Levemir)	2 hours	No clear peak	14-24 hours

Pharmacological Therapy for Patients with Type 2 Diabetes

A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include efficacy, hypoglycemia risk, history of atherosclerotic cardiovascular disease (ASCVD), impact on weight, potential side effects, renal effects, delivery method (oral versus subcutaneous), cost, and patient preferences. The ADA provided general guidance in the *Standards of Medical Care in Diabetes for 2018* Report on the treatment of patients with type 2 diabetes (Appendix III, IV). Table 8 lists the drug-specific and patient factors needed to be considered as part of the continuous reevaluation of the medication regimen.

Conclusion

Without major interventions, as many as one in three Americans could have diabetes by 2050. To help reverse that trend, the CDC, public health professionals, state health departments, and communities are committed to identifying and connecting with people who have diabetes or are at-risk for having diabetes. Efforts must continue to focus on educating people with diabetes to manage their conditions over the lifespan, promoting proven methods for reducing the risk of diabetes, tracking key risk factors and behaviors to guide public health policy, partnering with organizations to create and expand health promotion programs, and to increase the reach of these programs in communities.

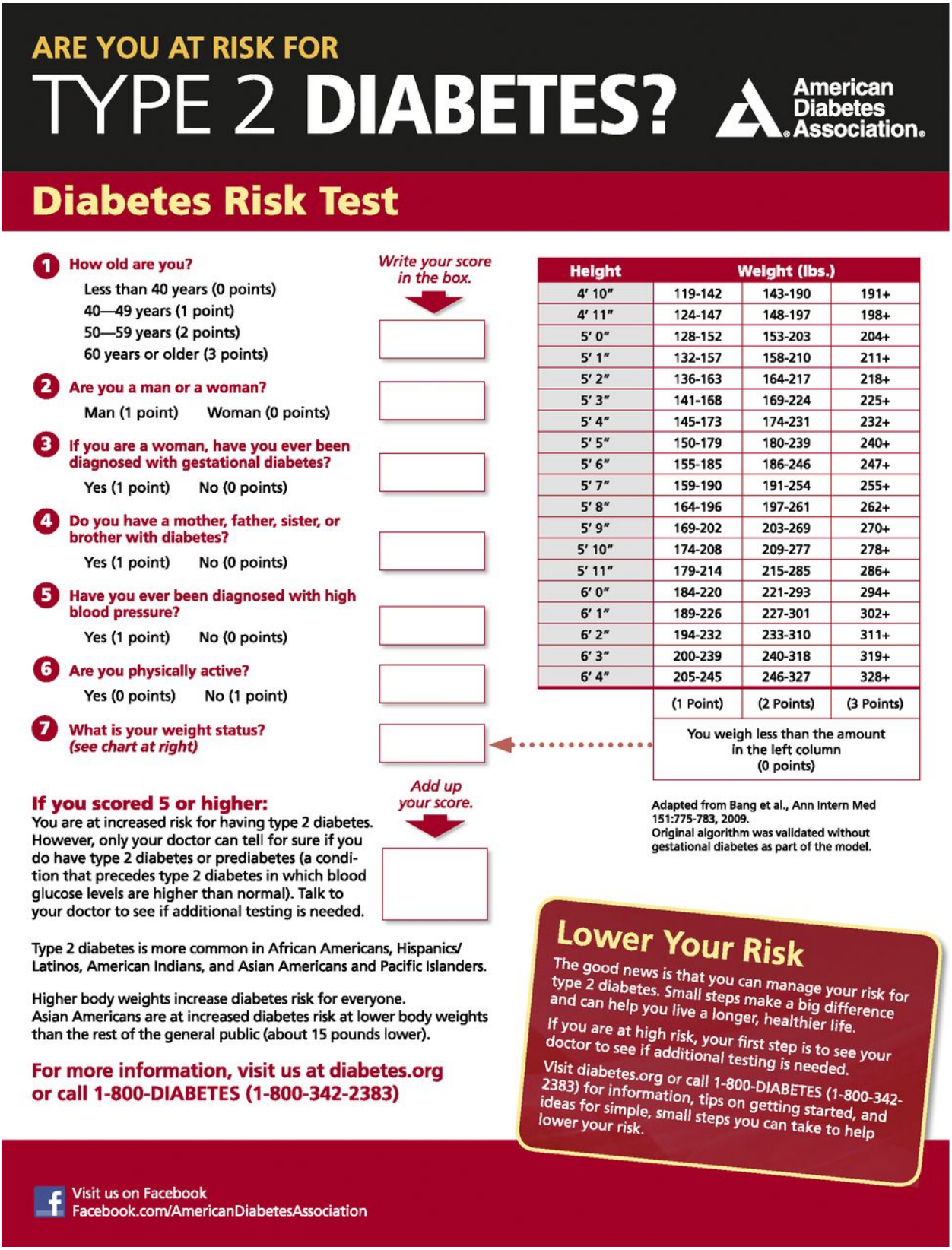
Table 8. Drug-Specific and Patient Factors to Consider When Selecting Antihyperglycemic Therapies [32]

	Efficacy	Hypoglycemia	Weight Change	CV Effects		Cost	Oral/ SQ	Renal Effects		Additional Considerations
				ASCVD	CHF			Progression of DKD	Dosing/Use considerations	
Metformin	High	No	Neutral (Potential for Modest Loss)	Potential Benefit	Neutral	Low	Oral	Neutral	• Contraindicated with (eGFR) <30	• Gastrointestinal side effects common (diarrhea, nausea) • Potential for B12 deficiency
SGLT-2 Inhibitors	Inter-mediate	No	Loss	Benefit: canagliflozin, empagliflozin	Benefit: canagliflozin, empagliflozin	High	Oral	Benefit: canagliflozin, empagliflozin	• Canagliflozin: not recommended with eGFR <45 • Dapagliflozin: not recommended with eGFR <60; contraindicated with eGFR <30 • Empagliflozin: contra-indicated with eGFR <30	• **FDA Black Box:** Risk of amputation (**canagliflozin**) • Risk of bone fractures (canagliflozin) • DKA risk (all agents, rare in T2DM) • Genitourinary infections • Risk of volume depletion, hypotension • ↑ LDL cholesterol
GLP-1 RAs	High	No	Loss	Neutral: lixisenatide, exenatide extended release Benefit: liraglutide	Neutral	High	SQ	Benefit: liraglutide	• Exenatide: not indicated with eGFR <30 • Lixisenatide: caution with eGFR <30 • Increased risk of side effects in patients with renal impairment	• **FDA Black Box:** Risk of thyroid C-cell tumors (**liraglutide**, **albiglutide**, **dulaglutide**, **exenatide extended release**) • Gastrointestinal side effects common (nausea, comiting, diarrhea) • Injection side reactions • Acute pancreatitis risk
DPP-4 Inhibitors	Inter-mediate	No	Neutral	Neutral	Potential Risk: saxagliptin, alogliptin	High	Oral	Neutral	• Renal dose adjustment required; can be sued in renal impairment	• Potential risk of acute pancreatitis • Joint pain
Thiazolidinedi-ones	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	• **FDA Black Box:** Congestive heart failure (**pioglitazone**, **rosiglitazone**) • Fluid retention (edema, heart failure) • Benefit in NASH • Risk of bone fractures • Bladder cancer (pioglitazone) • ↑ LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd Generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	• Glyburide: not recommended • Glipizide & glimepiride: Initiate conservatively to avoid hypoglycemia	• FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin **Human Insulin**	Highest	Yes	Gain	Neutral	Neutral	Low	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
Analogs						Low	SQ			

Diabetes Kidney Disease = DKD; Glumerular Filtration Rate = eGFR; T2DM = Type 2 Diabetes Management; Nonalcoholic Steatohepatitis = NASH

[32] Adapted from American Diabetes Association. *Diabetes Care 2018* Jan; 41(Supplement 1): S73-S85. https://doi.org/10.2337/dc18-S008

Appendix I: Diabetes Risk Test



ARE YOU AT RISK FOR

TYPE 2 DIABETES?

American Diabetes Association.

Diabetes Risk Test

1 How old are you?

Less than 40 years (0 points)
40—49 years (1 point)
50—59 years (2 points)
60 years or older (3 points)

Write your score in the box.

2 Are you a man or a woman?

Man (1 point) Woman (0 points)

3 If you are a woman, have you ever been diagnosed with gestational diabetes?

Yes (1 point) No (0 points)

4 Do you have a mother, father, sister, or brother with diabetes?

Yes (1 point) No (0 points)

5 Have you ever been diagnosed with high blood pressure?

Yes (1 point) No (0 points)

6 Are you physically active?

Yes (0 points) No (1 point)

7 What is your weight status? *(see chart at right)*

Height	Weight (lbs.)		
4′ 10″	119-142	143-190	191+
4′ 11″	124-147	148-197	198+
5′ 0″	128-152	153-203	204+
5′ 1″	132-157	158-210	211+
5′ 2″	136-163	164-217	218+
5′ 3″	141-168	169-224	225+
5′ 4″	145-173	174-231	232+
5′ 5″	150-179	180-239	240+
5′ 6″	155-185	186-246	247+
5′ 7″	159-190	191-254	255+
5′ 8″	164-196	197-261	262+
5′ 9″	169-202	203-269	270+
5′ 10″	174-208	209-277	278+
5′ 11″	179-214	215-285	286+
6′ 0″	184-220	221-293	294+
6′ 1″	189-226	227-301	302+
6′ 2″	194-232	233-310	311+
6′ 3″	200-239	240-318	319+
6′ 4″	205-245	246-327	328+
	(1 Point)	(2 Points)	(3 Points)

You weigh less than the amount in the left column (0 points)

Add up your score.

If you scored 5 or higher:
You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Adapted from Bang et al., Ann Intern Med 151:775-783, 2009.
Original algorithm was validated without gestational diabetes as part of the model.

Type 2 diabetes is more common in African Americans, Hispanics/Latinos, American Indians, and Asian Americans and Pacific Islanders.

Higher body weights increase diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weights than the rest of the general public (about 15 pounds lower).

For more information, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383)

Lower Your Risk

The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference and can help you live a longer, healthier life.

If you are at high risk, your first step is to see your doctor to see if additional testing is needed.

Visit diabetes.org or call 1-800-DIABETES (1-800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.

Visit us on Facebook
Facebook.com/AmericanDiabetesAssociation

Appendix II: Medical Nutrition Therapy (MNT) Recommendations[33]

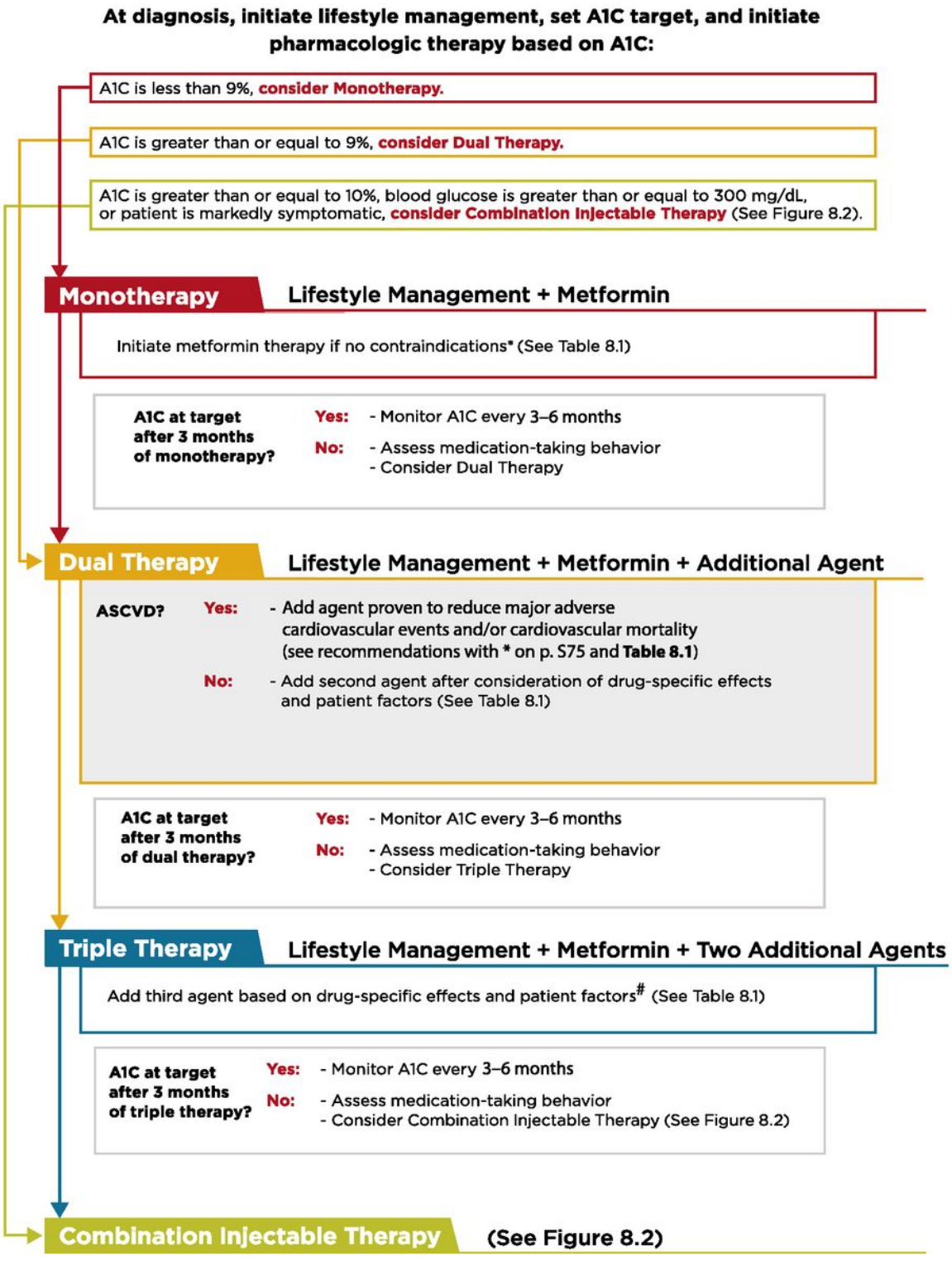
Topic	Recommendations
Effectiveness of Nutrition Therapy	An individualized MNT program, preferably provided by a registered dietitian, is recommended for all people with type 1 or type 2 diabetes, or gestational diabetes mellitus. A simple and effective approach to glycemia and weight management emphasizing portion control and healthy food choices may be considered for those with type 2 diabetes who are not taking insulin, who have limited health literacy or numeracy, or who are older and prone to hypoglycemia. Because diabetes nutrition therapy can result in cost savings and improved outcomes (e.g., A1C reduction), MNT is typically reimbursed by insurance and other payers.
Energy Balance	Weight loss (5 percent) achievable by the combination of reduction of calorie intake and lifestyle modification benefits overweight or obese adults with type 2 diabetes and those with prediabetes. Intervention programs to facilitate weight loss are recommended.
Eating Patterns and Macronutrient Distribution	There is no single ideal dietary distribution of calories among carbohydrates, fats, and proteins for people with diabetes; therefore, macronutrient distribution should be individualized while keeping total calorie and metabolic goals in mind. A variety of eating patterns are acceptable for the management of type 2 diabetes and prediabetes.
Carbohydrates	Carbohydrate intake from vegetables, fruits, legumes, whole grains, and dairy products, with an emphasis on foods higher in fiber and lower in glycemic load, is preferred over other sources, especially those containing added sugars.

[33] Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care 2014;37(Suppl. 1):S120–S143.

Topic	Recommendations
	For people with type 1 diabetes and those with type 2 diabetes who are prescribed a flexible insulin therapy program, education on how to use carbohydrate counting, and in some cases fat and protein gram estimation, to determine mealtime insulin dosing is recommended to improve glycemic control. For individuals whose daily insulin dosing is fixed, a consistent pattern of carbohydrate intake with respect to time and amount may be recommended to improve glycemic control and reduce the risk of hypoglycemia. People with diabetes and those at risk should avoid sugar-sweetened beverages in order to control weight and reduce their risk for CVD and fatty liver, and should minimize the consumption of foods with added sugar that have the capacity to displace healthier, more nutrient-dense food choices.
Protein	In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should be avoided when trying to treat or prevent hypoglycemia.
Dietary Fat	Data on the ideal total dietary fat content for people with diabetes are inconclusive, so an eating plan emphasizing elements of a Mediterranean-style diet rich in monounsaturated and polyunsaturated fats may be considered to improve glucose metabolism and lower CVD risk and can be an effective alternative to a diet low in total fat but relatively high in carbohydrates. Eating foods rich in long-chain n-3 fatty acids, such as fatty fish, nuts and seeds, is recommended to prevent or treat CVD; however, evidence does not support a beneficial role for the routine use of n-3 dietary supplements.
Micronutrients and Herbal Supplements	There is no clear evidence that dietary supplementation with vitamins, minerals, herbs, or spices can improve outcomes in people with

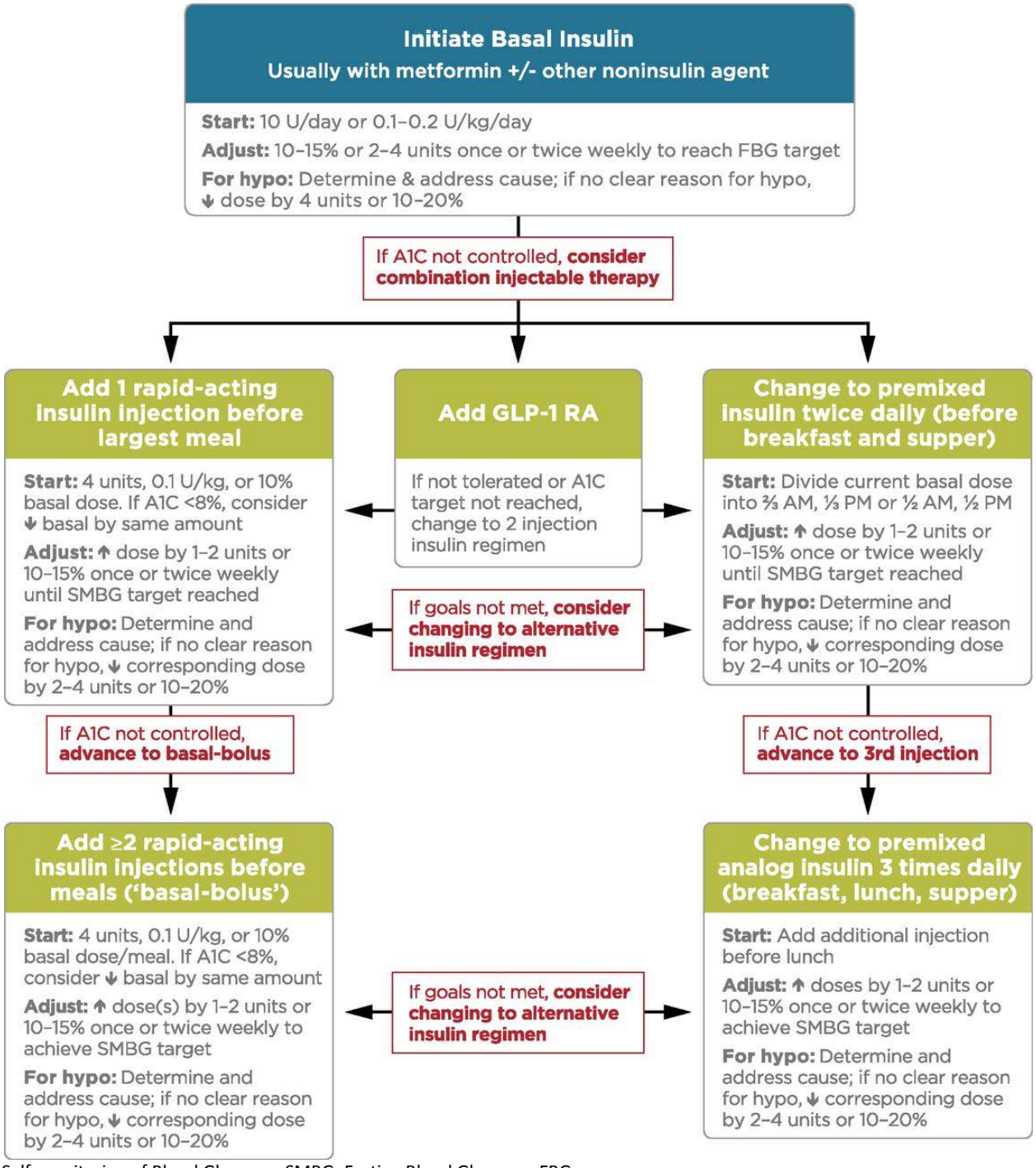
Topic	Recommendations
	diabetes who do not have underlying deficiencies, and they are not generally recommended. In addition, there may be safety concerns regarding the long-term use of antioxidant supplements such as vitamins E and C and carotene.
Alcohol	Adults with diabetes who drink alcohol should do so in moderation (no more than one drink per day for adult women and no more than two drinks per day for adult men). Alcohol consumption may place people with diabetes at increased risk for hypoglycemia, especially if taking insulin or insulin secretagogues. Education and awareness regarding the recognition and management of delayed hypoglycemia are warranted.
Sodium	As for the general population, people with diabetes should limit sodium consumption to 2,300 mg/day, although further restriction may be indicated for those with both diabetes and hypertension.
Nonnutritive Sweeteners	The use of nonnutritive sweeteners may have the potential to reduce overall calorie and carbohydrate intake if substituted for caloric (sugar) sweeteners and without compensation by intake of additional calories from other food sources. Nonnutritive sweeteners are generally safe to use within the defined acceptable daily intake levels.

Appendix III: ADA Antihyperglycemic Therapy Recommendations for Adults with Type 2 Diabetes[34]



[34] American Diabetes Association. *Diabetes Care 2018* Jan; 41(Supplement 1): S73-S85. https://doi.org/10.2337/dc18-S008

Appendix IV: ADA Combination Injectable Therapy Recommendations for Patients with Type 2 Diabetes[35]



Self-monitoring of Blood Glucose = SMBG; Fasting Blood Glucose = FBG

[35] American Diabetes Association Diabetes Care 2018 Jan; 41(Supplement 1): S73-85. https://doi.org/10.2337/dc18-S008