

Adult Diabetes

Clinician Guide

NOVEMBER 2017

Introduction This evidence-based guideline summary is based on the 2017 KP National Diabetes Guideline. It was developed to assist primary care physicians and other health care professionals in the treatment of diabetes in adults. In 2017, an additional set of recommendations was created for rescreening interval in people with prediabetes. The guideline is not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners.

Definitions

Fasting Plasma Glucose (FPG)	(100-125mg/dl) is impaired fasting glucose (IFG)
Oral Glucose Tolerance Test (OGTT)	(140-199 mg/dl) 2-h plasma glucose concentration after a 75-g glucose load with an FPG concentration < 126 mg/dl is impaired glucose tolerance (IGT)
Hemoglobin A1C (HbA1C)	(5.7-6.4%)

Prevention of Diabetes

- Interventions to Delay the Onset of Type 2 Diabetes**
 - ▶ In people with pre-diabetes, initiate lifestyle interventions (healthy eating, physical activity, and sustained weight loss of 5%-7%) to delay the onset of type 2 diabetes.
 - ▶ In people with pre-diabetes, consider metformin in addition to lifestyle interventions (healthy eating, physical activity, and sustained weight loss of 5%-7%) to delay the onset of type 2 diabetes.
- Postpartum Screening for Diabetes in Women with a History of Gestational Diabetes Mellitus (GDM)**
 - ▶ For women with gestational diabetes, consider offering screening for diabetes six weeks after delivery.
- Postpartum Follow-Up of GDM**
 - ▶ For women with gestational diabetes, consider offering information/education about the increased risk of developing type 2 diabetes following a diagnosis of gestational diabetes.
 - ▶ For women with recent gestational diabetes, consider offering long-term postpartum follow-up, including advice on diet, exercise, and behavior modification, to prevent future progression to type 2 diabetes.
- Rescreening Interval for**
 - ▶ For patients who receive an intensive lifestyle behavior change intervention, consider repeating lab testing within six months after completion of the core/intensive program intervention.

- Individuals with Prediabetes**
- ▶ Consider ongoing surveillance for diabetes risk in other patients with prediabetes every 1-3 years. A reasonable approach is:
 - Screen adults with a baseline A1C of 6.3-6.4% annually.
 - Screen other adults with a baseline A1C of 5.7-6.2% every 2-3 years, with the interval varying by baseline BMI (≥ 30 vs. < 30), recent weight gain, and patient preference.
 - Screen those taking chronic systemic glucocorticoids (equivalent of > 5 mg of prednisone per day for > 3 months) every 1-3 years, with the interval depending on baseline HbA1C, baseline BMI (≥ 30 vs. < 30), overall dosage and duration of glucocorticoids, and patient preference.

Screening for Type 2 Diabetes

- ▶ For all other adults with risk factors for diabetes, consider offering screening if:
 - Aged ≥ 45 years
 - Aged < 45 years and overweight (BMI ≥ 25 kg/m², may be lower in some ethnic groups) with ≥ 1 additional risk factor:
 - physical inactivity
 - first-degree relative with diabetes
 - members of a high-risk ethnic population (eg, Black/African American, Latino, Native American, Asian American, Pacific Islander)
 - for women, ≥ 1 of the following: delivery of a baby weighing > 9 lbs, a diagnosis of GDM or polycystic ovary syndrome (PCOS)
 - hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
 - High-density lipoprotein cholesterol (HDL-C) level < 35 mg/dl (0.90 mmol/l), triglyceride level > 250 mg/dl (2.82 mmol/l), or both
 - HbA1c $\geq 5.7\%$, IGT or IFG on previous testing
 - other clinical conditions associated with insulin resistance (eg, severe obesity [defined as BMI ≥ 40], acanthosis nigricans)
 - history of cardiovascular disease (CVD).

Pharmacological Management of Diabetes and Hypertension

- Blood Pressure Threshold to Initiate Drug Therapy and Blood Pressure Target in Patients with Diabetes and Hypertension**
- ▶ In the population aged ≥ 60 years with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥ 140 mmHg or DBP ≥ 90 mmHg and treat to a goal SBP < 140 mmHg and goal DBP < 90 mmHg.
- Initial Treatment of Diabetes and Hypertension in the Absence of Microalbuminuria**
- ▶ In the general non-African American population with diabetes, consider initiating antihypertensive treatment to include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACE-I), or angiotensin receptor blocker (ARB).

- ▶ In the general African American population with diabetes, consider initiating initial antihypertensive treatment to include a thiazide-type diuretic or CCB.
- ▶ Consider prescribing combination therapy with hydrochlorothiazide (HCTZ)/ACE-Is as first-line therapy because most individuals with HTN and diabetes will need more than one drug to control their HTN effectively.

Step Therapy in the Treatment of Diabetes and Hypertension in the Absence of Heart Failure or Known Coronary Heart Disease

- ▶ For two drugs: Consider prescribing an ACE-I plus a diuretic when two drugs are required for hypertension control.
- ▶ For three drugs: Consider prescribing a thiazide-type diuretic, an ACE-I, and a calcium channel blocker if blood pressure is not controlled on a thiazide-type diuretic plus ACE-I.

Drug Therapy for Patients with Diabetes, Hypertension, and Albuminuria or Diabetic Nephropathy

- ▶ For people with diabetes or hypertension, when accompanied by albuminuria, consider prescribing a medication regimen that includes an ACE-I. If intolerant to an ACE-I, in the absence of contraindications, consider substituting an ARB to prevent progression of renal disease.

Drug Therapy for Microalbuminuria in Normotensive Patients

- ▶ In normotensive adults aged < 55 years who have diabetes and microalbuminuria, consider prescribing an ACE-I to prevent progression to end-stage renal disease.
- ▶ In normotensive adults with diabetes, microalbuminuria (or albuminuria) and ACE-I allergy or intolerance, there is insufficient evidence to recommend for or against the use of angiotensin receptor blockers to prevent progression to end-stage renal disease (ESRD).

Hypertension Treatment for Women of Childbearing Potential

- ▶ Because half of all pregnancies are unplanned, unless there is a compelling indication, do not prescribe medications contraindicated in pregnancy, such as ACE-Is/ARBs, to women of childbearing potential.
- ▶ For women of childbearing potential taking medications contraindicated in pregnancy, such as ACE-Is/ARBs:
 - Discuss the potential risks to the fetus should they become pregnant.
 - Discuss practicing contraceptive measures with extremely low failure rates (sterilization, implant, or IUD).
- ▶ Advise women using ACE-Is/ARBs to stop these medications and contact their OB/GYN provider immediately if they become pregnant.

Lipid Management

LDL Goals

- ▶ There is no recommendation for or against specific low-density lipoprotein cholesterol (LDL-C) or non-high-density lipoprotein cholesterol (non-HDL-C) targets for the primary or secondary prevention of atherosclerotic cardiovascular disease (ASCVD).

Statin Therapy

- ▶ In adults aged 40-75 years with diabetes, LDL-C 70-189 mg/dl, and no ASCVD, initiate or continue moderate-intensity statin therapy.

- ▶ In adults aged 40-75 years with diabetes, LDL-C 70-189 mg/dl, no ASCVD, and an estimated 10-year ASCVD risk > 7.5%, consider prescribing high-intensity statin therapy unless contraindicated.
- ▶ In adults aged < 40 or > 75 years with diabetes, LDL-C 70-189 mg/dl, and no ASCVD, consider evaluating the potential for ASCVD benefits, adverse effects, and drug-drug interaction and consider patient preferences when deciding to initiate, continue, or intensify statin therapy.

ACE Inhibitor Therapy for Primary and Secondary Prevention of ASCVD in Diabetes

- ▶ For patients with diabetes aged ≥ 55 years with ≥ 1 cardiovascular risk factor (total cholesterol > 200 mg/dl, HDL-C ≤ 35 mg/dl, hypertension, microalbuminuria, or current smoking) or a history of CVD (coronary artery disease [CAD], stroke, or peripheral vascular disease), consider prescribing ACE-I therapy.

Aspirin Therapy in Diabetes for Prevention of ASCVD

- ▶ Refer to the KP National Aspirin Recommendations at:
https://clm.kp.org/pkc/national/cmi/programs/aspirin/aspirin_recommendations.html

Glucose Control

- ▶ In patients aged < 65 years with diabetes and no serious comorbidities, such as CAD, congestive heart failure (CHF), ESRD, blindness, amputation, stroke, and dementia, start treatment to achieve intensive glucose control.

Initial Drug Therapy for Glucose Lowering in Type 2 Diabetes

- ▶ In patients with type 2 diabetes, initiate first-line glucose-lowering drug with metformin.

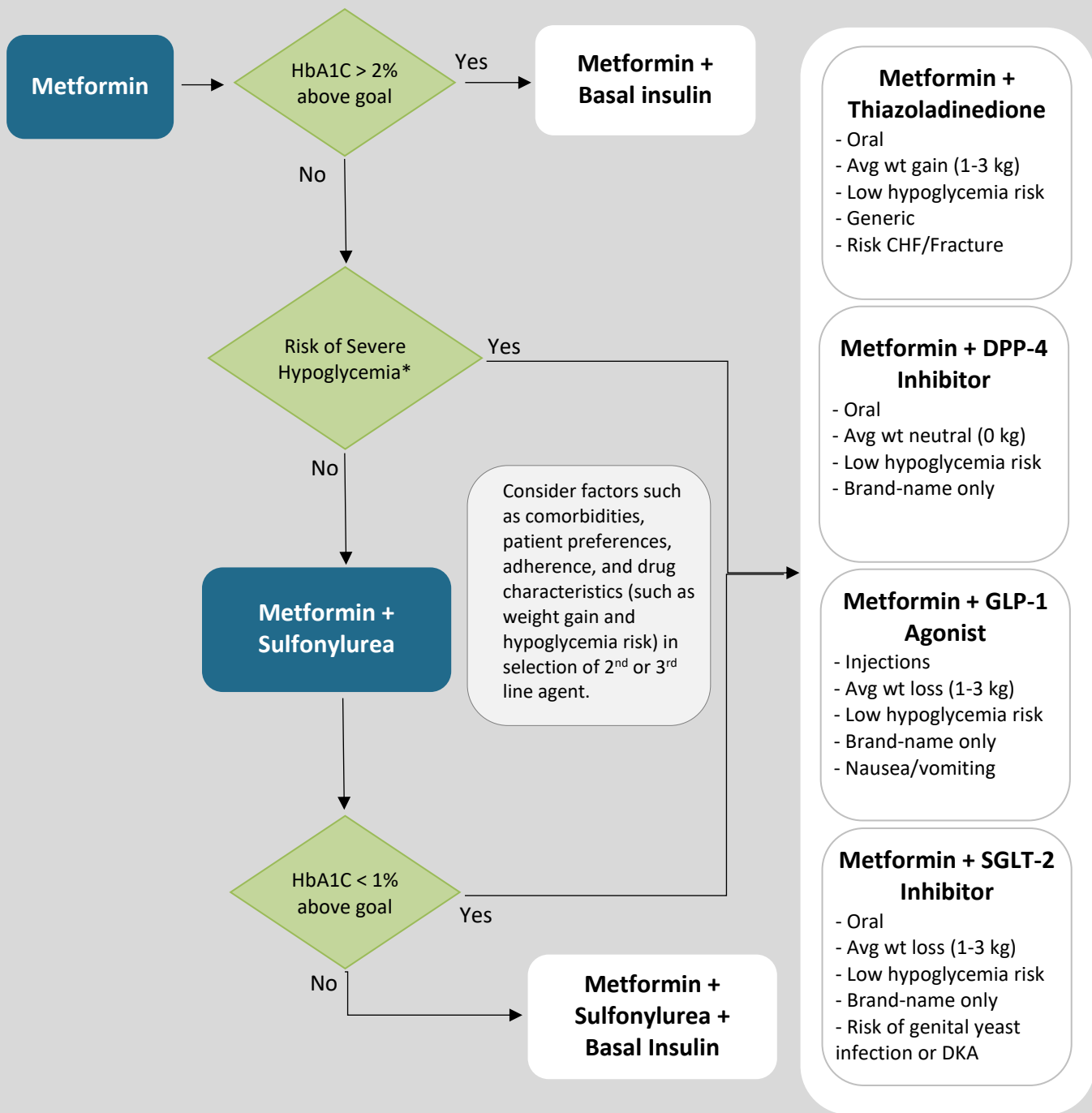
Step Therapy for Glucose Control

- ▶ In patients with type 2 diabetes not controlled on metformin monotherapy, initiate combination therapy using a second-line agent (sulfonylurea, thiazolidinediones [TZDs], DPP-4, basal insulin, SGLT-2 inhibitor, or GLP-1 receptor agonist).¹
- ▶ When selecting second- or third-line agents after metformin, consider factors such as comorbidities (eg, presence of clinical atherosclerotic cardiovascular disease [ASCVD]), patient preferences (eg, oral vs injectable route, side effect profile, cost to patient, etc.), adherence, and drug characteristics.

Highlighted factors in differentiating the second-line agents:

- Sulfonylureas and basal insulin are associated with higher incidence of hypoglycemia; with sulfonylureas, severe hypoglycemic episodes occurred in 1-3% of patients.
- Thiazolidinediones are associated with higher rates of CHF (< 0.2% in general studies and 2-5% in high-risk patients with CVD), resulting in a contraindication for patients with Class III or IV heart failure.
- Some add-on therapies are associated with weight gain (TZDs, sulfonylureas, and insulin); average weight gain is modest (generally < 5 kg). DPP-4 inhibitors are associated with weight maintenance, and SGLT-2 inhibitors and GLP-1 agonists are associated with modest weight loss.
- GLP-1 agonists are associated with an increased risk of gastrointestinal side effects.
- Some patients may prefer an oral add-on agent (sulfonylureas, TZD, DPP-4 inhibitor, SGLT-2 inhibitor) over an injectable agent (basal insulin, GLP-1 agonists). Cost differences between older and newer therapies are significant and may determine both individual patient decisions (depending on prescription coverage) and regional formulary decisions.
- In patients with clinical ASCVD (includes acute coronary syndromes, history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, carotid stenosis \geq 50%, or symptomatic peripheral arterial disease presumed to be of atherosclerotic origin), empagliflozin may reduce cardiovascular disease risk if used to achieve glucose control.
- Data on meglitinides and alpha-glucosidase inhibitors are limited and no recommendations for or against use of these medications are made.
- ▶ For patients not at glycemic control target on metformin plus a second-line agent, consider adding a third-line oral agent if HbA1c is within 1% of goal.
- ▶ For patients not at glycemic control target on metformin plus a second-line agent, consider adding basal insulin if the HbA1c is \geq 1% above goal.

FIGURE 1: Type 2 Diabetes Medication Treatment Algorithm



- ▶ If intolerant to immediate-release metformin, consider sustained-release metformin
- ▶ If HbA1c remains over goal after 3 months despite 2-3 non-insulin agents, consider discontinuing therapy and initiating insulin + metformin

- ▶ There is no evidence to support strong conclusions regarding cancer risk for pioglitazone or GLP-1 agonists.
- ▶ Data on meglitinides and alpha-glucosidase inhibitors are limited and no recommendation for or against use of these medication are made.

*Severe hypoglycemia is hypoglycemia resulting or likely to result in seizures, loss of consciousness, or requiring help from others, and not mild hypoglycemia resulting or likely to result from a change in meal pattern or activity.

Glycemic Control Target

- ▶ For adults with known diabetes,² consider an overall treatment goal of HbA1c < 7%.

Initiate an individualized HbA1c goal using shared decision-making:

- For patients aged > 65 years or with significant comorbidities,² initiate a less stringent treatment goal.³
- Conversely, in individual patients, consider a more stringent goal.

Microalbumin Assessments for Patients with Diabetes and Documented Microalbuminuria on ACE-Is or ARBs

- ▶ In patients with diabetes and established microalbuminuria who are taking an ACE-I or ARB, consider continued monitoring of microalbumin.

Retinal and Foot Screening

- Retinal Screening**
- ▶ In patients with diabetes and background retinopathy or more severe disease, consider monitoring at least annually; in those without retinopathy, consider screening every 1-2 years.

- Foot Screening**
- ▶ In all patients with diabetes, consider initiating foot screening that includes a monofilament test.
 - ▶ For patients with an abnormal monofilament test (ie, at high-risk for lower limb complications), consider referral to or management by a podiatry population-based foot care program or equivalent.

- Frequency of Foot Screening**
- ▶ For patients with diabetes, consider initiating annual foot screening examinations.

Self-Management

- Education**
- ▶ Initiate patient training in self-care behaviors to improve glucose control.

- Monitoring of Blood Glucose in Type 1 Diabetes**
- ▶ For individuals with type 1 diabetes, advise self-monitoring of blood glucose (SMBG).
 - ▶ Advise individuals with type 1 diabetes that the results of SMBG should lead to appropriate adjustment in therapy.

- Monitoring of Blood Glucose in Type 2 Diabetes**
- ▶ For individuals with type 2 diabetes, consider offering SMBG.
 - ▶ When SMBG is used for individuals with type 2 diabetes, consider advising appropriate adjustment in therapy with results.

- Titration of Insulin** ▶ For patients with type 2 diabetes taking bedtime long-acting insulin, consider advising self-titration to improve glucose control.

TERMINOLOGY		
Recommendation Language	Strength*	Action
Start, initiate, prescribe, treat, etc.	Strong affirmative	Provide the intervention. Most individuals should receive the intervention; only a small proportion will not want the intervention.
Consider starting, etc.	Conditional affirmative	Assist each patient in making a management decision consistent with personal values and preferences. The majority of individuals in this situation will want the intervention, but many will not. Different choices will be appropriate for different patients.
Consider stopping, etc.	Conditional negative	Assist each patient in making a management decision consistent with personal values and preferences. The majority of individuals in this situation will not want the intervention, but many will. Different choices will be appropriate for different patients.
Stop, do not start, etc.	Strong negative	Do not provide the intervention. Most individuals should not receive the intervention; only a small proportion will want the intervention.

*Refers to the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects.

DISCLAIMER

This guideline is informational only. It is not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners, considering each patient's needs on an individual basis. Guideline recommendations apply to populations of patients. Clinical judgment is necessary to design treatment plans for individual patients.

i

¹ DPP-4 = dipeptidyl-peptidase 4; GLP-1 = glucagon-like peptide-1; SGLT-2 = sodium-glucose co-transporter 2; SU = sulfonylurea; TZD = thiazolidinedione; HbA1c = hemoglobin A1c.

² HEDIS 2014 lists the following exclusions (comorbidities) for the HbA1c indicator < 7% goal; ≥ 65 years of age; and/or, coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) in the current and/or prior measurement year; ischemic vascular disease (IVD), thoracoabdominal or thoracic aortic aneurysm in the current and/or prior measurement year; or any of the following at any time through Dec. 31 of the measurement year: congestive heart failure (CHF) or cardiomyopathy; prior myocardial infarction (MI); stage 5 chronic kidney disease, end-stage renal disease (ESRD) or dialysis; chronic kidney disease (stage 4).

³ HEDIS 2014 offers HbA1c < 8% as a treatment goal for those not eligible for the treatment goal of < 7%. Eligibility is based on laboratory data to identify the most recent HbA1c test during the measurement year.