

# Adult Diabetes

## Clinician Guide

JANUARY 2016

**Introduction** This evidence-based guideline summary is based on the 2016 National Diabetes Guideline. It was developed to assist primary care physicians and other health care professionals in the treatment of diabetes in adults. In 2016, the clinical question pertaining to pharmacological therapy for type II diabetes was revised to align with the 2016 evidence review and synthesis performed by the Agency for Healthcare Research and Quality Evidence-based Practice Center (AHRQ-EPC). Additional guidance for shared-decision making and selection of second agent for combination therapy was derived from the 2015 American Diabetes Association (ADA) Standards for Medical Care and the 2013 Canadian Diabetes Association (CDA) Clinical Practice Guideline algorithms. In addition, the recommendation for initial pharmacological management was updated to align with the American College of Physicians (ACP) 2012 recommendations, with the 2016 and 2011 AHRQ-EPC evidence updates providing supporting justification. Finally, the remaining 2014 guideline recommendations were updated to include recommendation strength based on KP's revised National Guideline Program methodology.

### Definitions

**TABLE 1: ADA Definition of Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT)**

Impaired Fasting Glucose (IFG)	An elevated fasting plasma glucose (FPG) concentration ( $\geq 100$ and $< 126$ mg/dl)
Impaired Glucose Tolerance (IGT)	An elevated 2-h plasma glucose concentration ( $\geq 140$ and $< 200$ mg/dl) after a 75-g glucose load on the oral glucose tolerance test (OGTT) in the presence of an FPG concentration $< 126$ mg/dl

## 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. (Strong Recommendation)
  - ▶ 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. (Weak Recommendation)
- 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. (Weak Recommendation)

**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. (Weak Recommendation)
- ▶ 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. (Weak Recommendation)

## Screening for Type 2 Diabetes

- ▶ For all other adults with risk factors for diabetes, consider offering screening if:
  - Aged  $\geq 45$  years
  - Aged  $< 45$  and overweight (BMI  $\geq 25\text{kg/m}^2$ , may be lower in some ethnic groups) with  $\geq 1$  additional risk factor:
    - physical inactivity
    - first-degree relative with diabetes
    - members of a high-risk ethnic population (e.g., Black/African American, Latino, Native American, Asian American, Pacific Islander)
    - for women,  $\geq 1$  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) or 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 (e.g., severe obesity [defined as BMI  $\geq 40$ ], acanthosis nigricans)
    - history of cardiovascular disease (CVD).

(Weak Recommendation)

## 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  $\geq 60$  years with diabetes, initiate pharmacologic treatment to lower BP at SBP  $\geq 140\text{mmHg}$  or DBP  $\geq 90\text{mmHg}$  and treat to a goal SBP  $< 140\text{mmHg}$  and goal DBP  $< 90\text{mmHg}$ . (Strong Recommendation)

**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 (ACEI), or angiotensin receptor blocker (ARB). (Weak Recommendation)
- ▶ In the general African American population with diabetes, consider initiating initial antihypertensive treatment to include a thiazide-type diuretic or CCB. (Weak Recommendation)

- ▶ Consider prescribing combination therapy with HCTZ/ACE inhibitors as first-line therapy because most individuals with hypertension and diabetes will need more than one drug to effectively control their hypertension. (Weak Recommendation)

### 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 ACEI plus a diuretic when two drugs are required for hypertension control.
- ▶ For three drugs: Consider prescribing a thiazide-type diuretic, an ACEI, and a CCB if blood pressure is not controlled on a thiazide-type diuretic plus ACEI. (Weak Recommendation)

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

- ▶ For patients with diabetes or hypertension accompanied by albuminuria, consider prescribing a medication regimen that includes an ACEI. If intolerant to an ACEI and in the absence of contraindications, consider substituting an ARB to prevent progression of renal disease. (Weak Recommendation)

### Drug Therapy for Microalbuminuria in Normotensive Patients

- ▶ In normotensive adults aged < 55 years with diabetes and microalbuminuria, consider prescribing an ACEI to prevent progression to end-stage renal disease. (Weak Recommendation)
- ▶ In normotensive adults with diabetes, microalbuminuria or albuminuria, and ACEI allergy or intolerance, there is insufficient evidence to recommend for or against the use of ARBs to prevent progression to end-stage renal disease. (No recommendation for or against)

### Hypertension Treatment for Women of Childbearing Potential

- ▶ Because half of all pregnancies are unplanned, do not prescribe medications contraindicated in pregnancy, such as ACEIs/ARBs, to women of childbearing potential unless there is a compelling indication.
- ▶ For women of childbearing potential taking medications contraindicated in pregnancy, such as ACEIs/ARBs:
  - Discuss the potential risks to the fetus if they become pregnant.
  - Discuss practicing contraceptive measures with extremely low failure rates (sterilization, implant, or IUD).
- ▶ Advise women using ACEIs/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-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. (Strong Recommendation)
- ▶ 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. (Weak Recommendation)

- ▶ 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. (Weak Recommendation)

## ACE Inhibitor Therapy for Primary and Secondary Prevention of Atherosclerotic Cardiovascular Disease (ASCVD) in Diabetes

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

## 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](https://clm.kp.org/pkc/national/cmi/programs/aspirin/aspirin_recommendations.html)

## Glucose Control

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

## Initial Drug Therapy for Glucose Lowering in Type 2 Diabetes

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

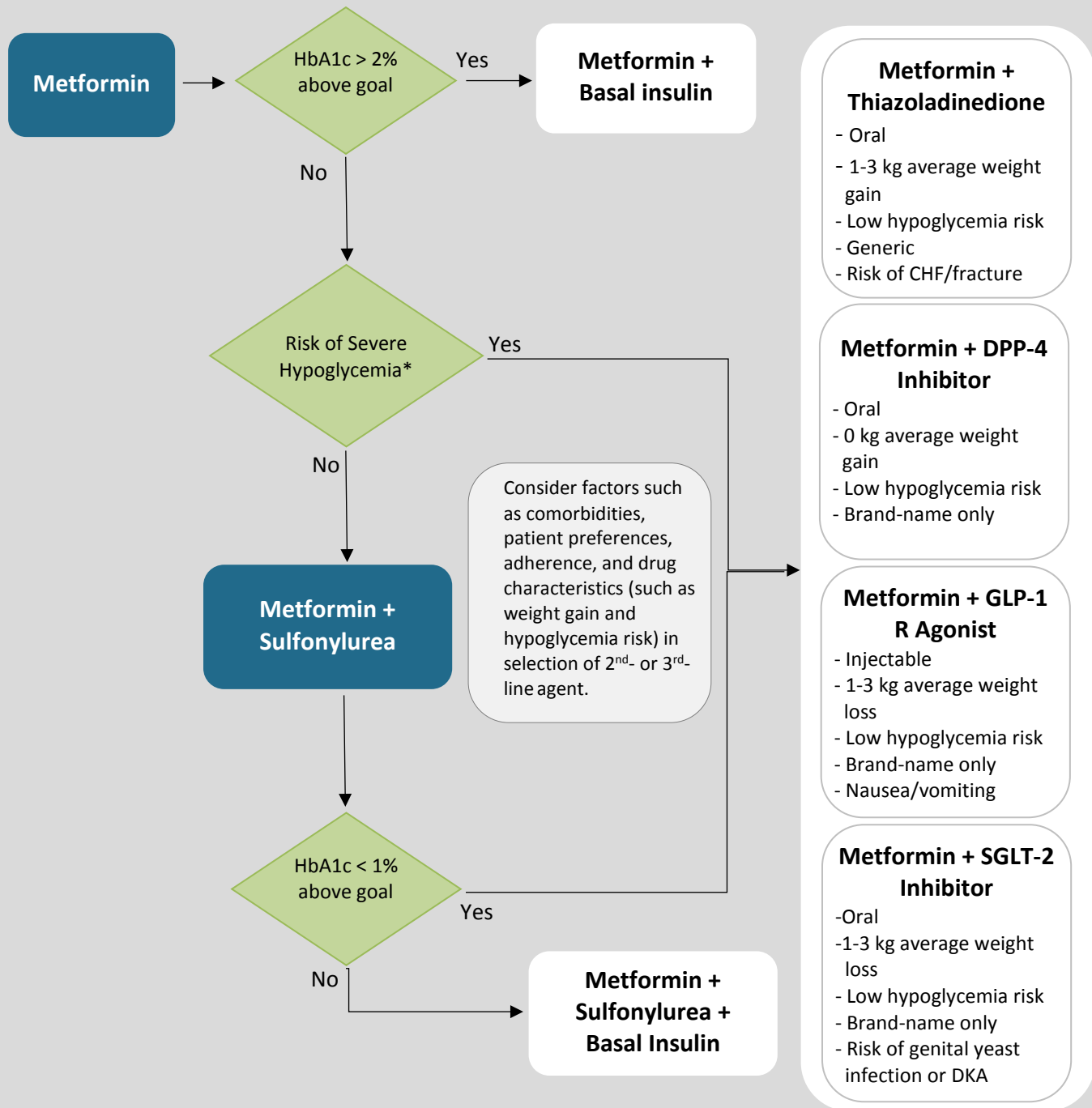
## Step Therapy for Glucose Control

- ▶ 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).<sup>1</sup> (Strong Recommendation)
- ▶ When selecting second- or third-line agents after metformin, consider factors such as comorbidities, patient preferences (e.g., oral vs injectable route, side effect profile, cost to patient, etc.), adherence, and drug characteristics. (Weak Recommendation)

**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.
  - 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. (Weak Recommendation)
  - ▶ 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. (Weak Recommendation)

FIGURE 1: Type 2 Diabetes Medication Treatment Algorithm



- ▶ If patient is 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; it is not mild hypoglycemia resulting or likely to result from a change in meal pattern or activity.

## Glycemic Control Target

- ▶ For adults with known diabetes,<sup>2</sup> consider an overall treatment goal of HbA1c < 7%. (Weak recommendation)

### **Initiate an individualized HbA1c goal using shared decision-making:**

- For patients aged > 65 years or with significant comorbidities,<sup>2</sup> initiate a less stringent treatment goal.<sup>3</sup>
- Conversely, in individual patients, consider a more stringent goal. (Weak Recommendation)

## Microalbumin Assessments for Patients with Diabetes and Documented Microalbuminuria on ACE Inhibitors or ARBs

- ▶ In patients with diabetes and established microalbuminuria who are taking an ACEI or ARB, consider continued monitoring of microalbumin. (Weak Recommendation)

## 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. (Weak Recommendation)

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

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

## Self-Management

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

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

- Monitoring of Blood Glucose in Type 2 Diabetes**
- ▶ For individuals with type 2 diabetes, consider offering SMBG. (Weak Recommendation)
  - ▶ When SMBG is used for individuals with type 2 diabetes, consider advising appropriate adjustment in therapy with results. (Weak Recommendation)
- Titration of Insulin**
- ▶ For patients with type 2 diabetes taking long-acting insulin at bedtime, consider advising self-titration to improve glucose control. (Weak Recommendation)

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.	Weak 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.	Weak 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.

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<sup>1</sup> 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.

<sup>2</sup> 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).

<sup>3</sup> 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.