Type 2 Diabetes Screening and Treatment Guideline

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Last guideline approval: June 2015

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.
Major Changes as of June 2015

<table>
<thead>
<tr>
<th>New</th>
<th>Previous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider screening patients <strong>every 3 years</strong> who have multiple risk factors for type 2 diabetes, including:</td>
<td>Age of 45 years or older was not included as one of the risk factors for type 2 diabetes, and no specific screening interval was recommended.</td>
</tr>
<tr>
<td>- <strong>Age of 45 years or older</strong></td>
<td></td>
</tr>
<tr>
<td>- Overweight or obesity (BMI ≥ 25)</td>
<td></td>
</tr>
<tr>
<td>- First-degree relative with diabetes</td>
<td></td>
</tr>
<tr>
<td>- Polycystic ovarian syndrome</td>
<td></td>
</tr>
<tr>
<td>- Certain racial/ethnic minorities; African Americans, American Indians/Alaska Natives, Asian Americans, Hispanics/Latinos, and Native Hawaiians/Pacific Islanders</td>
<td></td>
</tr>
<tr>
<td>Consider screening adults <strong>at high risk for ASCVD every 3 years</strong>.</td>
<td>The previous version recommended screening adults with hypertension every 2 years.</td>
</tr>
<tr>
<td>Recommend that type 2 diabetics follow a <strong>low-carbohydrate Mediterranean diet</strong>.</td>
<td>No specific diet was recommended; instead, the guideline only referred to the U.S. Department of Agriculture’s Choose My Plate website.</td>
</tr>
<tr>
<td><strong>Empagliflozin (Jardiance), other Novo insulins, and insulin glulisine (Apidra; PA for allergies to insulin)</strong> were added to the list of pharmacological options that are not recommended.</td>
<td>—</td>
</tr>
</tbody>
</table>

Prevention

Studies have shown that increasing physical activity and eating a healthy diet can significantly delay the onset of type 2 diabetes, including for patients diagnosed with impaired glucose tolerance. Studies have also shown the use of metformin can delay the diagnosis of diabetes for patients with impaired glucose tolerance, but there is no evidence that metformin leads to long-term better clinical outcomes prior to diagnosis of diabetes.

Screening and Tests

The draft U.S. Preventive Services Task Force (2014) recommends screening patients who are at **increased risk for diabetes**.

**Risk factors** for type 2 diabetes include:
- Age of 45 years or older
- Overweight or obesity (BMI ≥ 25)
- First-degree relative with diabetes
- Polycystic ovarian syndrome (in women)
- Certain racial/ethnic backgrounds, including African American, American Indians/Alaska Natives, Asian American, Hispanic/Latino, and Native Hawaiian/Pacific Islander

**It is reasonable to have a higher clinical index of suspicion in adults with multiple risk factors** and to use clinical judgment or shared decision making about whether to screen these individuals for type 2 diabetes.

If the decision is to screen, consider a frequency of every 3 years using either fasting plasma glucose or HbA1c.
Adults at high risk for cardiovascular disease (see the guidelines for primary and secondary prevention of ASCVD) should be considered for screening. While ASCVD itself is not a risk factor for type 2 diabetes, type 2 diabetes is a serious complicating comorbidity in patients with ASCVD. If they elect screening, these patients should be screened every 3 years using either fasting plasma glucose or HbA1c.

Annual screening is recommended for women with a history of gestational diabetes (using HbA1c) and for men and women with impaired fasting glucose (using either fasting plasma glucose or HbA1c).

**Diagnosis**

Diagnosis for an asymptomatic patient requires two abnormal test results, which can be from the same test on different days, or from different tests performed on either the same day or different days. If only one test comes back abnormal, repeat the abnormal test on a different day. An abnormal result on the repeated test is diagnostic for diabetes.

Diagnosis for a patient with classic symptoms of hyperglycemia (i.e., polyuria, polydipsia, weight loss) can be made with a single random plasma glucose result of 200 mg/dL or higher. A repeat measurement is not needed.

<table>
<thead>
<tr>
<th>Table 1. Diagnosing diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test</strong></td>
</tr>
<tr>
<td>HbA1c</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Random plasma glucose</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
</tr>
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<td></td>
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<tr>
<td></td>
</tr>
</tbody>
</table>

¹ Impaired glucose tolerance (IGT) is similar to impaired fasting glucose (IFG) but is diagnosed with a confirmed oral glucose tolerance test (OGTT). Both IGT and IFG are risk factors for future diabetes and for cardiovascular disease. They are sometimes jointly referred to as pre-diabetes. Group Health recommends avoiding the term pre-diabetes because not all patients with IGT and/or IFG will develop diabetes.

Patients with type 2 diabetes most commonly present as overweight and hyperglycemic, with gradual onset of symptoms such as fatigue, blurred vision, polydipsia, and polyuria.

Consider islet cell antibody (ICA) with reflex to glutamic acid decarboxylase antibody (GADA) testing for differential diagnosis in the following patient populations:

- Children and teenagers to distinguish early type 1 diabetes from type 2 diabetes.
- Adults who are not overweight who are not responding well to oral hypoglycemic and lifestyle (diet/exercise) modification.

The following laboratory tests are **not recommended**:

- Fasting C-peptide is not recommended because the test cannot distinguish well between people without diabetes and those with impaired endogenous insulin secretion. C-peptide is released from a person's pancreas in equimolar amounts to endogenous insulin. Because the amount of endogenous insulin secreted is dependent on a patient's blood glucose level, low or undetectable C-peptide levels may indicate either an inability to produce insulin or an absence of insulin secretion due to low blood sugar levels. In the latter case, a person without diabetes would not secrete much C-peptide and would have an abnormal test result.
- Plasma insulin is not recommended as it does not add any additional useful information.
Treatment

Primary Care clinicians manage diabetes care—including overall plans of care and annual reviews of care—for all patients with diabetes, with help as needed from diabetes experts in Consulting Internal Medicine or from David McCulloch, MD, diabetologist at Group Health.

Risk-reduction goals

Cardiac risk reduction is the most important management issue for patients with diabetes.

<table>
<thead>
<tr>
<th>Table 2. Selected cardiac risk factors and goals for risk reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factor</strong></td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Age 79 or younger</td>
</tr>
<tr>
<td>Age 80 or older</td>
</tr>
<tr>
<td>With microalbuminuria (at any age)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
</tr>
<tr>
<td>Hemoglobin A1c (HbA1c)</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
</tr>
</tbody>
</table>

\(^1\) Use clinical judgment to determine if a target lower than 7% is appropriate for an individual patient. It can be challenging to push a patient’s HbA1c levels from just above 7% to below 7%. There are potential benefits (decreased nonfatal myocardial infarction) and potential harms (hypoglycemia, weight gain, and possible increase in all-cause and cardiovascular-cause mortality) of intensive glucose therapy, especially in patients with known cardiovascular disease. For frail elderly patients, a target HbA1c of 7–9% is reasonable.

Lifestyle modifications and nonpharmacologic options

Diet and physical activity

There is some evidence that intensive programs of lifestyle interventions targeting patients with impaired fasting glucose reduce the incidence of type 2 diabetes. Lifestyle interventions include dietary and physical activity counseling.

All patients should strive to:

- Make smart choices from every food group to meet their caloric needs.
- Get the most and best nutrition from the calories consumed.
- Find a balance between food intake and physical activity.
- Get at least 30 minutes of moderate-intensity physical activity on most days.

For personalized eating plans and interactive tools to help patients plan and assess food choices, see the U.S. Department of Agriculture’s Choose My Plate website (http://www.choosemyplate.gov).

A low-carbohydrate Mediterranean diet rich in fruits, vegetables, nuts, whole grains, legumes, fish, and healthy fats from plant and fish sources is recommended. There is evidence to suggest that this type of diet improves diabetes-related health outcomes more than low-fat diets in patients with type 2 diabetes. Use the SmartPhrase .avsmediterraneandiet in Epic.

For patients who have been inactive, recommend slowly working up to at least 30 minutes of moderate physical activity per day. If they are unable to be active for 30 minutes at one time, suggest accumulating activity in 10- to 15-minute sessions throughout the day.

Weight management, including bariatric surgery

The risk of serious health conditions—such as high blood pressure, heart disease, arthritis, and stroke, as well as diabetes—increases with body mass index (BMI) of 25 or higher. (BMI = weight in kilograms divided by height in meters squared [kg/m\(^2\)].) Overweight is defined as a BMI of 25 to 29.9, obesity as a
BMI of 30 or higher. While most overweight or obese adults can lose weight by eating a healthy diet or increasing physical activity, doing both is most effective.

There is evidence that surgically induced weight loss results in better blood glucose control and less need for diabetic medications than conventional diabetes therapy focused on weight loss through lifestyle changes. Evidence from a large cohort study suggests that failure to sustain blood glucose control is an adverse predictor of diabetes relapse after surgery (Arterburn 2013). See Clinical Review Criteria: Bariatric Surgery.

See the Group Health Weight Management guidelines (for adults and for children and adolescents) for recommendations and further information.

**Foot care**

For patients at very high risk or increased risk of developing foot ulcers, recommend daily foot care.

Foot-ulcer risk definitions:

- **Patients at very high risk** are those with a previous foot ulcer, amputation, or major foot deformity (claw/hammer toes, bony prominence, or Charcot deformity).
- **Patients at increased risk** are those who are insensate to 5.07 monofilament at any site on either foot or who have bunions, excessive corns, or callus.
- **Patients at average risk** are those with none of the aforementioned complications.

Encourage patients to check their feet regularly. If the patient or a family member cannot perform the patient’s foot care, encourage the patient to find someone who can provide assistance.

**Sick-day management**

Patients experiencing acute illnesses need to be extra vigilant about blood glucose monitoring and control. The following information and help is available:

- The pamphlet “Living Well with Type 2 Diabetes: Taking Care of Yourself When You’re Sick” is available online and can be ordered (#338) from the Group Health Resource Line. Or use SmartPhrase .chronicdiseasedmtype2sickdayplan in Epic.
- Pharmacy staff can help with selecting sugar-free cold medicines and cough syrups.
Pharmacologic options for blood glucose control

**Recommended medications**
See also the prescribing notes that follow Table 3.

<table>
<thead>
<tr>
<th>Eligible population</th>
<th>Line</th>
<th>Medication</th>
<th>Initial dose</th>
<th>Therapeutic/goal dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c above goal</td>
<td>1st</td>
<td>Biguanide</td>
<td>Metformin 250 mg once daily</td>
<td>1,000 mg twice daily or 850 mg 3 times daily</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>HbA1c above goal</td>
<td>2nd</td>
<td>Add insulin¹</td>
<td>NPH 12 units at bedtime</td>
<td>Increase bedtime NPH by 4 units until fasting blood glucose is lower than 120 mg/dL or use treat-to-target strategy</td>
</tr>
<tr>
<td>on metformin</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>and/or</td>
<td>2nd</td>
<td>Add sulfonylurea</td>
<td>Glimepiride 1–2 mg once daily at breakfast or first main meal (1 mg daily for elderly patients)</td>
<td>1–8 mg once daily</td>
</tr>
<tr>
<td>HbA1c above goal</td>
<td>3rd</td>
<td>Add pre-meal rapid-acting insulin</td>
<td>Lispro (Humalog)</td>
<td>Consider consultation with CIM and/or diabetologist David McCulloch, MD</td>
</tr>
<tr>
<td>on metformin and</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>on insulin or</td>
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<tr>
<td>sulfonylurea</td>
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</tbody>
</table>

¹ Insulin glargine (Lantus) should be considered only for patients with type 2 diabetes who have progressed to the point of needing intensive insulin schedules. See additional information on glargine below, under "Insulin glargine."

**Prescribing notes—Table 3**

**Metformin**
Metformin should be titrated as tolerated. A reasonable initial titration schedule is:
- 500 mg ½ tab once daily X 7 days;
- 500 mg 1 tab once daily X 7 days;
- 500 mg 1 tab twice daily.

If a patient does not experience any GI side effects after 2–3 days, dose may be titrated to goal more quickly.

If a patient develops GI side effects, reduce dose and reassess. Consider a more conservative titration schedule starting with 500 mg ¼ tab (125 mg) orally once daily; alternatively, consider prescribing the XL formulation for patients who cannot tolerate the dose with regular release formulation.

Precautions with metformin prescribing:
- **Avoid use of metformin** in patients with known binge or excessive alcohol use. Instruct patients to avoid excessive acute or chronic alcohol use.
- **Suspend use of metformin** if a patient is to undergo a surgical procedure or be given iodinated contrast media for a radiological procedure. Restart metformin when normal renal function is verified. Metformin should be withheld in patients with dehydration and/or prerenal azotemia.
NPH insulin
Check fasting blood glucose (FBG) every day and get weekly average. Target is mean FBG of 120 mg/dL. For adults over age 65, a higher target (140 mg/dL) may be considered.

- Less than 200 lb, FBG lower than 200 – 12 U and up by 4 U/week.
- Less than 200 lb, FBG higher than 200 – 16 U and up by 8 U/week.
- More than 200 lb, FBG lower than 200 – 20 U and up by 4 U/week.
- More than 200 lb, FBG higher than 200 – 30 U and up by 10 U/week.

Treat-to-target strategy:
1. Initial dose of 10 units of background insulin at bedtime.
2. If FBG is higher than 130, increase bedtime insulin dose by 1 unit.
3. Continue increasing bedtime insulin dose by 1 unit at a time until FBG is in the target range.
4. If FBG is lower than 80 mg/dL, decrease bedtime insulin dose by 1 unit.
5. Continue decreasing bedtime insulin dose by 1 unit at a time until FBG is in the target range.

If HbA1c is higher than 7.0% and BG checks before lunch, dinner, and bedtime are indicating a steady rise in BG throughout the day, the patient very likely needs daytime insulin therapy.

Sulfonylurea
For preferred sulfonylurea (glimepiride), a reasonable titration schedule is:
- Increase to 2 mg once daily for 1–2 weeks;
- Increase by 2 mg once daily at 1- to 2-week intervals to maximum of 8 mg once daily.

For alternative sulfonylurea (glipizide), a reasonable titration schedule is:
- 5 mg ½ tab twice daily X 7 days;
- 5 mg 1 tab twice daily X 7 days;
- 5 mg 2 tab twice daily X 7 days.

Consider prescribing the XL formulation for patients who cannot tolerate regular release formulation.

Insulin glargine
Glargine (Lantus) offers no significant advantage over NPH insulin when given at bedtime to reduce fasting hyperglycemia and is considerably more expensive. For patients with type 2 diabetes who need intensive insulin schedules—which typically include both basal insulin and pre-meal boluses of fast-acting insulin—glargine can be considered, similar to the way we manage patients with type 1 diabetes (see “Intensive insulin schedules” in the Type 1 Diabetes Treatment Guideline). (Prior Authorization for glargine is required for patients with type 2 diabetes.)

U-500 insulin
Consider U-500 insulin for patients who are very insulin resistant and need more than 200 units of insulin per day. Consult with a diabetes expert before switching to U-500 insulin. Within Group Health, contact David McCulloch, MD, or Dan Kent, PharmD. See “Regular Insulin U-500: Considerations for Safe Use” on the Group Health staff intranet for more information.

Several other concentrated insulin formulations are becoming available (e.g. U-200, U-300).

Continuous subcutaneous insulin infusion (insulin pumps or infusion pods)
There is evidence to support the use of insulin pumps for a subset of patients with type 2 diabetes. Motivated patients with type 2 diabetes who are having difficulty controlling their blood glucose with conventional intensive insulin regimens may be considered for insulin pumps. To qualify for a pump, a patient with type 2 diabetes must have no detectable endogenous insulin production (undetectable C-peptide level—which is measured by taking a fasting C-peptide level at a time when the blood glucose is over 200mg/dL).
For more information, see Clinical Review Criteria: Insulin Pump. Patients with Medicare coverage must meet both Group Health’s clinical review criteria and Medicare requirements in order to acquire and maintain use of a pump.

Note that Endocrinology sees patients with diabetes who are using or considering insulin pumps. The Insulin Pump Program can provide device training and consultation, at which time a care plan can be established to assist Primary Care with ongoing management. Primary Care retains responsibility for those patients’ overall diabetes plans of care and annual reviews of care.

**Continuous glucose monitoring (CGM) systems**

CGM systems have not been shown to be of benefit in patients with type 2 diabetes.

**Pharmacologic options that are not recommended**

The following pharmacologic options are not recommended or not on the Group Health formulary; consider consultation with a diabetes expert:

- DPP-4 inhibitors—sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), alogliptin (Nesina)
- GLP-1 receptor agonists—exenatide (Byetta, Bydureon), liraglutide (Victoza)
- Alpha-glucosidase inhibitors—acarbose (Precose), miglitol (Glyset)
- Meglitinides—repaglinide (Prandin), nateglinide (Starlix)
- Thiazolidinediones—rosiglitazone (Avandia), pioglitazone (Actos)
- Sodium-glucose cotransporter 2 inhibitors—dapagliflozin, canagliflozin (Invokana), empagliflozin (Jardiance)
- Amylinomimetics—pramlintide (Symlin)
- Insulin analogs—insulin detemir (Levemir; PA for children), other Novo insulins, insulin glulisine (Apidra; PA for allergies to insulin)
- Dopamine agonists—bromocriptine (Cycloset)

There is no high-quality evidence to determine the effect on blood glucose control of any of the following:

- Chromium
- Cinnamon
- Vanadium
Follow-up and Monitoring

Self blood glucose monitoring

Table 4. Self blood glucose monitoring (SBGM)
Note that for patients with diabetes, SBGM is useful only if they are testing and using the result information to make changes to their diabetes self-management plans.

<table>
<thead>
<tr>
<th>Eligible population</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Patients on lifestyle changes and/or metformin only      | • These patients are at no risk for hypoglycemia. It is reasonable for them not to do SBGM.  
  • Changes to therapy can be made based on HbA1c values every 3 months. 
  • Some patients may find that SBGM helps them see the effect of particular food items or exercise on their blood glucose, thus helping them stay motivated with lifestyle changes. |
| Patients on sulfonylureas and/or insulin                  | • These patients may develop hypoglycemia. It is advisable that they do SBGM when they “feel funny” to confirm whether or not their symptoms are due to hypoglycemia.  
  • If patients are using treat-to-target approaches, especially if using insulin (for example, titrating their dose of bedtime NPH insulin until they reach a fasting blood glucose target of 120 mg/dL), then testing the fasting blood glucose once a day is advisable. 
  – Once patients achieve their fasting blood glucose target, there is no need to continue testing every morning if they feel well and their HbA1c stays below their target range.  
  – However, if such patients are at their target for fasting blood glucose but their HbA1c is still above target, then testing before and 2 hours after their main meal may give useful information about the need for additional daytime treatment (with sulfonylurea or insulin). |
| Patients on basal insulin and pre-meal fast-acting insulin| • These patients should do SBGM 3–4 times daily if they are using the information to adjust how much fast-acting insulin they take before the meal.  
  • They may also want to test 2 hours after their main meal or under other circumstances where they want to know the effect of food, exercise, or stress on their blood glucose levels.                                                   |

1 Several studies have shown that improvement in HbA1c is almost identical whether patients test their blood glucose or not (Poolsup 2009).
### Periodic monitoring of conditions and complications

<table>
<thead>
<tr>
<th>Condition/complication</th>
<th>Tests</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>BP taken with appropriate size cuff using optimal technique</td>
<td>Every visit</td>
</tr>
<tr>
<td>Blood glucose control</td>
<td>HbA1c</td>
<td>Every 3 months until the target level is reached; thereafter, patients should be monitored at least every 12 months</td>
</tr>
<tr>
<td>Foot ulcers</td>
<td>Physical exam focused on ankle reflexes, dorsalis pedis pulse, vibratory sensation, and 5.07 monofilament touch sensation performed by a provider qualified to determine the level of risk for foot ulcers</td>
<td>Patients at very high risk should be seen every 3 months by a wound care nurse. Patients at increased risk and average risk should be screened annually.</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>Microalbumin/creatinine ratio</td>
<td>Annually</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Fasting LDL</td>
<td>Annually</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>Dilated eye exam by a trained eye services professional or Nondilated digital photography followed by a comprehensive exam for those who test positive</td>
<td>Patients with evidence of retinopathy should be screened annually. Patients without evidence of retinopathy should be screened every 2 years.</td>
</tr>
<tr>
<td>Electrolyte and chemistry abnormalities</td>
<td>Serum creatinine and Serum potassium</td>
<td>At least annually</td>
</tr>
</tbody>
</table>

1. The microalbumin/creatinine ratio test can identify patients with microalbuminuria by giving a quantitative estimate of protein loss that correlates with 24-hour urinary protein measurements. Test results are expressed in micrograms of urinary albumin per milligram of urinary creatinine (or A:C ratio). A positive test is more than 30 mcg/mg. Two positive tests are diagnostic for microalbuminuria, ideally 3–6 months apart.

2. See “Foot care” in the “Lifestyle modifications and non-pharmacologic options” section for foot-ulcer risk definitions.

3. Annual screening is not recommended because the benefits of more frequent screening are marginal: For every 1,000 persons screened annually (instead of every second year), one additional case of proliferative diabetic retinopathy and one additional case of clinically significant macular edema will be detected.
Medication monitoring

### Table 6. Monitoring for medication side effects

<table>
<thead>
<tr>
<th>Eligible population</th>
<th>Test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who are being treated with metformin&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Serum creatinine</td>
<td>Annually if serum creatinine is 1.5 or lower or Twice a year if serum creatinine is higher than 1.5</td>
</tr>
</tbody>
</table>

<sup>1</sup> For patients on metformin, serum creatinine should be monitored because the medication is primarily excreted by the kidney. Metformin can be prescribed if the serum creatinine is lower than 2.5 and if the eGFR is higher than 30, provided this value is not 25% worse than the previous reading. Use of concomitant medications that may affect renal function (i.e., affect tubular secretion) may also affect metformin excretion. **Metformin should be withheld in patients with dehydration and/or prerenal azotemia**: also hold prior to radiologic procedures (i.e., studies requiring administration of IV contrast) and prior to surgery.

### Recommended immunizations

#### Table 7. Recommended immunizations for patients with diabetes<sup>1</sup>

<table>
<thead>
<tr>
<th>Immunization</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Annually, as early as possible when vaccine becomes available</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSv23)</td>
<td>• Once between ages 19 and 64 years</td>
</tr>
<tr>
<td></td>
<td>• Booster after age 65 years (at least 5 years after previous dose)</td>
</tr>
<tr>
<td>Hepatitis B&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Three-dose series for ages 19 to 59 years</td>
</tr>
<tr>
<td></td>
<td>• Ages 60 years and older, depending on risk</td>
</tr>
</tbody>
</table>

<sup>1</sup> See the CDC’s Recommended Adult Immunization Schedule (http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf) for more detailed information.

<sup>2</sup> Results from observational studies suggest that patients with diabetes are at higher risk for hepatitis B compared with patients without diabetes (CDC 2011).

## Comorbidities

### Depression screening

Screen for depression by using the Patient Health Questionnaire (PHQ-9). Evidence suggests that patients with depression are less likely to be adherent to recommended management plans and less likely to be effective at self-management of diabetes.

See the Group Health Depression Guideline for additional guidance. Patients with major depression can be treated in Primary Care or offered a referral to Behavioral Health Services for counseling and/or drug therapy.

### ASCVD prevention

Risk-reduction measures to consider include smoking cessation, blood pressure control, statin therapy, ACE inhibitor or angiotensin receptor blocker (ARB) therapy, and antiplatelet therapy. See the Group Health Cardiovascular Disease (ASCVD) Guidelines (Primary Prevention and Secondary Prevention) for details.

### Hypertension management

See the Group Health Hypertension Guideline.
Evidence Summary

Group Health developed the Type 2 Diabetes Screening and Treatment Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

Pharmacologic treatment to delay diabetes

Metformin

Results from a meta-analysis of 31 randomized controlled trials (RCTs) illustrated that treatment with metformin reduced the absolute risk of diabetes by 6% over a mean duration of 1.8 years. Subjects receiving metformin also experienced modest improvements in BMI, LDL cholesterol, and HDL cholesterol compared with subjects receiving either placebo or no intervention (Salpeter 2008). The study analyzed metabolic risk factors and not clinical outcomes, leaving unanswered the question of whether delaying diabetes improves clinical outcomes.

Use of HbA1c to diagnose diabetes

A cross-sectional study compared HbA1c of 6.5% or higher and fasting plasma glucose (FPG) of 126 mg/dL or higher for the identification of undiagnosed diabetes among National Health and Nutrition Examination Survey (NHANES) participants. When HbA1c of 6.5% or higher and FPG of 126 mg/dL or higher were used as the cut-points for diabetes, results showed that there was moderate agreement between the two tests for the diagnosis of diabetes. Diabetes classification was consistent for the majority of the subjects, with 95.9% being classified as positive by both tests and 1.8% being classified as negative by both tests. Only 0.5% of subjects were classified as positive by one test and negative by the other (Carson 2010).

Blood glucose control goal

Three meta-analyses compared the effects of tight blood glucose control versus standard therapy (Turnbull 2009, Kelly 2009, Ray 2009). Tight blood glucose control appeared to reduce the risk of nonfatal myocardial infarction; however, there was an increased risk of hypoglycemia and weight gain. Additionally, the ACCORD trial suggests that all-cause mortality is increased with intensive treatment compared to standard treatment (ACCORD 2008). Results from an exploratory post hoc analysis from the ACCORD trial suggest that this trend may be even more striking among patients with baseline HbA1c levels higher than 8.5% and those with neuropathy (Calles-Escandon 2010).

There is evidence from two major randomized controlled trials (RCTs), the Diabetes Control and Complications Trial (DCCT) for type 1 diabetes and the UK Prospective Diabetes Study for type 2 diabetes (UKPDS), that blood glucose control delays the onset and slows the progression of diabetic retinopathy (DCCT 1993, UKPDS Lancet 1998). Both studies randomized patients with diabetes to receive intensive blood glucose control or conventional treatment.

The DCCT found that among patients with no retinopathy at study entry, intensive blood glucose control therapy reduced the risk of progression of retinopathy—defined as a sustained change on retinal photography—by 3.5% per year (NNT = 29). However, the reduction in the risk of retinopathy progression associated with a lower HbA1c was accompanied by an increased risk of hypoglycemia. For patients with mild retinopathy at the beginning of the DCCT, intensive therapy reduced the risk of laser treatment of retinopathy by 1.4% per year (NNT = 71).

Target HbA1c

There were no RCTs that addressed the appropriate HbA1c levels for patients with type 2 diabetes. Evidence pertaining to target HbA1c levels comes from a retrospective cohort study that was designed to address the association between all-cause mortality and HbA1c levels. Results from this study showed that for those in cohort 1 (metformin plus sulfonfonylurea), subjects with HbA1c levels lower than 6.72% or higher than 9.85% were at increased risk for all-cause mortality. For those in cohort 2 (insulin regimen), subjects with HbA1c levels lower than 7.4% or higher than 9.12% were at increased risk for all-cause mortality (Currie 2010).
Diet
There is evidence from a small RCT indicating that low carbohydrate Mediterranean diets improve diabetes related health outcomes more than low-fat diets in patients with type 2 diabetes (Esposito 2014). The Mediterranean diet used in the study was rich in vegetables and whole grains and low in red meat, which was replaced with poultry and fish. Energy intake was restricted to 1,500 kcal/day for women and 1,800 kcal/day for men, with the goal of no more than 50% of calories from complex carbohydrates. The diet had no less than 30% calories from fat, with the main source of added fat being 30–50 g of olive oil.

Exercise
A meta-analysis of 14 RCTs on exercise in patients with type 2 diabetes showed an improvement in HbA1c of 0.6 points (95% CI, 0.3 to 0.9 points). The duration of exercise training ranged from 8 weeks to 12 months (Thomas 2006).

Bariatric surgery
There is evidence that surgically induced weight loss results in better blood glucose control and less need for diabetic medications than conventional diabetes therapy focused on weight loss through lifestyle changes (Schauer 2014). A multisite retrospective cohort study specifically examining the long-term rates and clinical predictors of diabetes remission and relapse post–gastric bypass suggests that, while gastric bypass is a valuable option for type 2 diabetics, failure to sustain blood glucose control post-surgery may cause relapse in a third of patients (Arterburn 2013).

Pharmacologic treatment for controlling blood glucose

Metformin
A study found that metformin improved blood glucose control and lipid concentrations in patients with type 2 whose diabetes was poorly controlled by diet and glyburide. The addition of up to 2,500 mg metformin per day resulted in a 20% absolute increase in the proportion of patients with fasting plasma glucose levels of lower than 140 mg/dL (DeFronzo 1995).

Sulfonylureas
A subgroup analysis of a prospective cohort study that included 459 patients assessed the impact of different classes of sulfonylureas on in-hospital mortality and rhythm or ischemic complications (a composite of reinfarction, arrhythmias, and stroke) in diabetic patients admitted for an acute myocardial infarction. Findings from this study suggest that when the newer sulfonylureas (glimepiride/gliclazide) were compared with glibenclamide, an older sulfonylurea, patients who were prescribed the newer agents had significantly lower mortality rates and rhythm or ischemic complications (Zeller 2010).

Rapidly acting insulin analogs versus regular insulin
A Cochrane Library meta-analysis of RCTs published through September 2005 found a statistically significant reduction of HbA1c with short-acting insulin analogs compared with regular human insulin for patients with type 1 diabetes. However, the difference in HbA1c was small and may not be clinically significant (weighted mean difference = 0.1% [-0.2% to 0.1%]). There were no statistically significant differences in HbA1c for patients with type 2 diabetes, or in hypoglycemic episodes for patients with type 1 or type 2 diabetes (Siebenhofer 2006). The meta-analysis was limited by the overall low quality and short duration of the RCTs.

Insulin detemir
A recent meta-analysis of RCTs compared insulin detemir with NPH insulin in people with type 2 diabetes. Results indicated that patients taking NPH insulin had lower HbA1c levels than those taking insulin detemir; however, patients taking detemir were less likely to experience nocturnal hypoglycemia. There was no data available regarding the long-term safety of insulin detemir (Singh 2009).

Continuous subcutaneous insulin infusion (CSII)
To assess the efficacy of CSII in type 2 diabetics, Reznik and colleagues carried out a multicenter RCT in which pump therapy was compared with multiple daily injections (MDI) in meeting glycemized hemoglobin targets. The results of the study indicate that patients with poorly controlled type 2 diabetes who received
pump therapy achieved significantly greater reductions in HbA1c levels than those in the MDI group (Reznik 2014).

Screening

Microalbuminuria
There is no direct evidence from randomized or nonrandomized controlled screening trials that microalbuminuria screening improves health outcomes. The recommendation for microalbuminuria screening is based on indirect evidence that the natural history of diabetic renal disease is well known, that screening can identify early disease, and that treatment of patients with microalbuminuria has been shown to improve health outcomes. According to data from the UK Prospective Diabetes Study (UKPDS), for patients newly diagnosed with type 2 diabetes, the annual rate of progression from no nephropathy to microalbuminuria is 2% and from microalbuminuria to macroalbuminuria is 2.8% (Adler 2003).

Neuropathy
There is fair evidence that diabetic foot screening prevents adverse outcomes. One RCT reported outcomes in patients with diabetes assigned to a foot screening and protection program versus outcomes in those receiving usual care. At the end of 2 years, there were significantly fewer amputations in the foot-screening group, but no significant difference in the incidence of ulcers. The number needed to screen (NNS) to prevent one amputation = 63 and to prevent one major amputation = 91 (McCabe 1998). No RCTs attempting to replicate these findings were identified.

Retinopathy
There is no direct evidence from randomized or nonrandomized controlled screening trials that retinal screening improves health outcomes. The recommendation for retinal screening is based on indirect evidence: namely, that the natural history of diabetic retinal disease is well known, that screening can identify early disease, and that treatments such as blood glucose control and laser therapy have been shown to improve health outcomes. Two cohort studies investigated the optimum screening interval by grade of retinopathy. Both studies found that for patients at low risk for retinopathy, a 2-year screening interval was not associated with increased risk (Younis 2003, Misra 2009).

Nonmydriatic digital stereoscopic retinal imaging
A recent meta-analysis that included 20 observational studies and 4,059 patients examined how mydriasis influenced the accuracy of screening for diabetic retinopathy. Findings from this analysis suggest that mydriatic status alone did not significantly influence the sensitivity or specificity to detect any diabetic retinopathy (Bragge 2011). Results from an observational study that examined the sensitivity and specificity of nonmydriatic digital stereoscopic retinal imaging (NMDSRI) compared with dilated retinal examination performed by an ophthalmologist or an optometrist found that NMDSRI had a sensitivity of 98% and a specificity of 100% for retinopathy within one grade of that indicated by dilated retinal exam (Ahmed 2006). These findings were supported by the results of several other observational studies (Aptel 2008, Boucher 2003, Lin 2002, Vujosevic 2009).

Self-monitoring of blood glucose (SMBG)
A meta-analysis indicated that for patients with established type 2 diabetes not using insulin, SMBG significantly reduced HbA1c levels compared with non-SMBG; however, this is only of modest clinical significance. In a subgroup analysis, SMBG—with its results used to modify treatment regimens—significantly decreased HbA1c compared with non-SMBG (Poolsup 2009). Only one RCT looked at the effect of SMBG in newly diagnosed type 2 diabetic patients. This study found that SMBG had no effect on blood glucose control but was associated with a 6% higher score on a depression index (O’Kane 2008).
References


Guideline Development Process and Team

Development process
Group Health developed the Type 2 Diabetes Screening and Treatment Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in June 2015.

Team
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Disclosure of conflict of interest
Group Health Cooperative requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care-related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Diabetes Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.