Type 2 Diabetes Screening and Treatment Guideline

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Last guideline approval: April 2019

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 April 2019

<table>
<thead>
<tr>
<th>New</th>
<th>Previous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring for lipohypertrophy and lipodystrophy is now recommended.</td>
<td></td>
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<tr>
<td>Because glimepiride has been added to the Beers list of drugs to avoid in the elderly, sulfonylurea recommendations are now as follows:</td>
<td>Glimepiride was not on the Beers list and was the preferred sulfonylurea regardless of patient age.</td>
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<tr>
<td>• Glimepiride continues to be recommended for patients aged &lt; 65 years with no CKD or renal dysfunction trend (for a favorable cardiovascular profile).</td>
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<tr>
<td>• Glipizide is now recommended for patients aged 65 years and older (for kidney disease toxicity avoidance to avoid excessive prolonged hypoglycemia).</td>
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<tr>
<td>The type 2 diabetes treatment workflow has been updated to reflect these changes.</td>
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<tr>
<td>The coverage criteria for the formulary (prior authorization) SGLT-2 empagliflozin were updated to add a third qualifying subgroup of type 2 diabetes patients: those with HbA1c ≤ 9% and either clinically significant weight gain or BMI ≥ 35 prior to insulin therapy.</td>
<td>Coverage criteria for empagliflozin did not take HbA1c level or BMI into consideration.</td>
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<tr>
<td>The KPWA coverage criteria for the non-formulary GLP-1 receptor agonists exenatide XR (Bydureon) and liraglutide (Victoza) were updated to require a minimum 3-month trial of empagliflozin before starting.</td>
<td>A 3-month trial of empagliflozin was not required prior to starting exenatide XR or liraglutide.</td>
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</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 that the use of metformin can delay the diagnosis of diabetes for patients with impaired glucose tolerance, but there is no evidence that metformin or any other medication leads to long-term better clinical outcomes prior to diagnosis of diabetes.

Screening and Tests

The U.S. Preventive Services Task Force (Siu 2015) 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 Indian/Alaska Native, 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 atherosclerotic cardiovascular disease** (see the KPWA 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 blood 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 performed 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>
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<tbody>
<tr>
<td><strong>Test</strong></td>
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<tr>
<td>HbA1c</td>
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<tr>
<td>Random plasma glucose</td>
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<tr>
<td>Fasting plasma glucose</td>
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</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**. This guideline 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 and 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 the 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 the Diabetes Team (use REF DIABETES).

**Risk-reduction goals**

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

<table>
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<th>Table 2. Selected cardiac risk factors and goals for risk reduction for patients with diabetes</th>
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<td><strong>Risk factor</strong></td>
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<tr>
<td>Blood pressure</td>
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<tr>
<td>LDL cholesterol</td>
</tr>
<tr>
<td>HbA1c</td>
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<tr>
<td>Fasting blood glucose</td>
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</table>

¹ Use clinical judgment to determine if a target lower than 7.0% is appropriate for an individual patient. It can be challenging to push a patient’s HbA1c levels from just above 7.0% to below 7.0%. 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 7.0–9.0% is reasonable.

**Lifestyle modifications and non-pharmacologic options**

For information on nursing management of patients with type 2 diabetes, see Nursing Protocol 132 on the KPWA staff intranet.

**Diet and physical activity**

There is some evidence that intensive programs of lifestyle interventions targeting patients with impaired fasting blood 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.

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.
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.

**Living Well Workshops**

Six-week workshops offered both in-person and online include Living Well with Chronic Conditions, Living Well with Diabetes, and Living Well with Pain. Participants support each other and work together to solve their problems. There is no charge for the workshops. Patients can register for the in-person workshops by calling the Resource Line at 1-800-2279 or for the web-based version at Better Choices, Better Health®. See the KPWA public website for more information.

**Foot care**

For patients at very high risk or increased risk of developing foot ulcers, recommend daily foot care. The pamphlet "Living Well with Diabetes: Foot care for people with diabetes" is available online and can be ordered from the Resource Line (#63).

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 Resource Line. Or use SmartPhrase .chronicdiseasedmtype2sickadayplan.
- Pharmacy staff can help with selecting sugar-free cold medicines and cough syrups.

**Weight management**

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/m²].) 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. See the Weight Management Guideline for recommendations and further information.

**Contraception and preconception counseling**

Preconception counseling should be provided to all female diabetic patients of childbearing age, as the risk of maternal-fetal complications is higher in the setting of uncontrolled blood glucose. Patients desiring conception should achieve an HbA1c < 6.5% prior to pregnancy. If a patient does not wish to conceive or is not at HbA1c target, contraception should be discussed. For more information, refer to the CDC U.S. Medical Eligibility Criteria for Contraceptive Use, 2016.
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. 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.

Pharmacologic options for glucose control

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.

This initial titration schedule is now the default in KP HealthConnect. It provides 39 tablets, which equates to a true 30-day supply.

If a patient does not experience any GI side effects after 2–3 days, the dose may be titrated to goal of 1000 mg twice daily more quickly. (The maximum dose is 2000 mg/day).

If a patient develops GI side effects, reduce the 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:
- **Monitor serum creatinine levels** because the medication is primarily excreted by the kidneys (see Table 6).
- **Reduce metformin dose** to a maximum of 500 mg twice daily in patients with eGFR 30–45.
- **Discontinue metformin dose** in patients with eGFR < 30, or whose eGFR has worsened by 25% or more since the previous reading.
- **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.

Sulfonylureas
- **Glimepiride** remains the preferred sulfonylurea for those aged < 65 years; however, it has been added to the Beers list for drugs to avoid in the elderly. Glimepiride is primarily metabolized by the liver, with renal excretion of active metabolites.

A reasonable titration schedule for glimepiride 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.

- **Glipizide** is the preferred sulfonylurea for those aged ≥ 65 years (for kidney toxicity avoidance to avoid excessive prolonged hypoglycemia). Glipizide is metabolized by the liver and primarily excreted in the urine as inactive metabolites, although one of its metabolites may have weak hypoglycemic activity.

A reasonable titration schedule for glipizide is:
- Adults < 65 years: Starting dose 5 mg daily prior to morning meal. May move to twice-daily dosing and increase based on before-meal response to maximum dose of 40 mg daily.
- Elderly ≥ 65 years: Starting dose 2.5 mg daily prior to morning meal. May move to twice-daily dosing and increase based on before-meal response to maximum dose of 20 mg daily. (If CrCl < 50, reduce dose by 50%.)
Consider prescribing the extended-release formulation of glipizide for patients who cannot tolerate the regular-release formulation. The most common side effect of sulfonylureas is hypoglycemia. Initiate and titrate with caution in those with chronic kidney disease.

Titration schedule for extended-release products:
- Adults < 65 years: Start 5–10 mg daily. Maximum dose is 20 mg daily.
- Elderly ≥ 65 years: 2.5–5 mg daily. Maximum dose is 10 mg daily.

**NPH insulin**

Check fasting blood glucose (FBG) every day and get weekly average. The target is mean FBG of 80–130 mg/dL. For adults over age 65, a higher target (140 mg/dL) may be considered.
- Less than 200 lb, FBG lower than 200 mg/dL: 12 U and up by 4 U/week.
- Less than 200 lb, FBG higher than 200 mg/dL: 16 U and up by 8 U/week.
- More than 200 lb, FBG lower than 200 mg/dL: 20 U and up by 4 U/week.
- More than 200 lb, FBG higher than 200 mg/dL: 30 U and up by 10 U/week.
- Alternatively, consider a weight-based dosing strategy (see Treatment Workflow, p. 9).

**Treat-to-target strategy:**
- Initial dose of 10 units basal insulin at bedtime.
- If FBG is higher than 130 mg/dL, increase bedtime insulin dose by 1 unit.
- Continue increasing bedtime insulin dose by 1 unit at a time until FBG is in the target range.
- If FBG is lower than 80 mg/dL, decrease bedtime insulin dose by 1 unit.
- 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 blood glucose checks before lunch, dinner, and bedtime are indicating a steady rise in blood glucose throughout the day, the patient very likely needs daytime insulin therapy.

**Sodium-glucose cotransporter-2 (SGLT-2) inhibitors**

Empagliflozin (Jardiance) is F-PA. It is recommended for a subset of patients with type 2 diabetes who meet the following Pharmacy criteria:

<table>
<thead>
<tr>
<th>Empagliflozin (Jardiance) Pharmacy criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients with type 2 diabetes:</td>
</tr>
<tr>
<td>• Currently on maximum tolerated dose of metformin with a history of clinical atherosclerotic cardiovascular disease (ASCVD), or</td>
</tr>
<tr>
<td>• Contraindication or intolerance to metformin therapy with a history of ASCVD, or</td>
</tr>
<tr>
<td>• Failure, contraindication, or intolerance of maximum tolerated dose of metformin, a sulfonylurea, and rapid plus basal insulin combination*, or</td>
</tr>
<tr>
<td>• With hemoglobin A1c (HbA1c) ≤ 9% or within 1% of goal and all of the following:</td>
</tr>
<tr>
<td>o Clinically significant weight gain while on insulin therapy or BMI ≥ 35 prior to insulin therapy</td>
</tr>
<tr>
<td>o Failure or intolerance to maximum tolerated dose of metformin</td>
</tr>
<tr>
<td>o Initial authorization: 6 months</td>
</tr>
<tr>
<td>o Reauthorization criteria: 1% reduction in HbA1c after 6 months or member is at HbA1c goal</td>
</tr>
</tbody>
</table>

*Note: Previously documented severe hypoglycemia would be considered an intolerance or contraindication to sulfonylureas or insulin therapy. Severe hypoglycemia includes hypoglycemia resulting in seizures, loss of consciousness, or needing help from others.

Source: [http://incontext.ghc.org/rx/ref/palist.html#empagliflozin](http://incontext.ghc.org/rx/ref/palist.html#empagliflozin) (staff internal website)

Dapagliflozin and canagliflozin are **not** recommended and remain non-formulary.
Non-formulary oral options that are non-preferred but can be considered in patients at high hypoglycemia risk where cost is an issue

- **Acarbose**: alpha-glucosidase inhibitor
  May have some cardiovascular benefit in those with impaired glucose tolerance. Generic, low risk of hypoglycemia.
  - Start 25 mg t.i.d. with first bite of food, can increase up to 100 mg t.i.d.
  - Predominant side effects include flatulence and diarrhea, which lead to low adherence in most patients.

- **Pioglitazone**: thiazoladinedione
  Generic, non-formulary agent, low risk of hypoglycemia.
  - Start with 15 mg daily, increase up to 30 mg daily.
  - Significant side effects include weight gain, edema, increased risk of congestive heart failure. Contraindicated in patients with active liver disease.
  - Other concerns include increased risk of bone loss and osteoporotic fracture in women, and a potential increase in the risk of bladder cancer.

**U-500 Regular insulin**
Consider U-500 Regular insulin for patients who are very insulin resistant and need more than 200 units of insulin per day. Consultation with the Diabetes Team is not required before switching to U-500 insulin. 
**Note**: Several other concentrated insulin formulations exist (e.g., U-200, U-300), but these are non-formulary.
Type 2 diabetes treatment workflow for Primary Care

HbA1c above target
Initiate medication therapy in type 2 diabetes.

Start metformin and titrate to max tolerated dose – up to 2000 mg. Switch to metformin XR if indicated.

A1C goal met?

YES → Continue regimen and monitor HbA1c.

NO → Add empagliflozin (Jardiance) 12.5 mg per day.

SmartPhrases: DMJARDIANCEPATIENTINFO
For After Visit Summary
DMORALMEDS DMJARDIANCE
Prescribing progress note/checklist

A1C goal met?

YES → Continue regimen and monitor HbA1c.

NO → Add glibenclamide (Amaryl) 1-2 mg or glipizide 5 mg (2.5 mg in elderly) daily.

-or-

Add bedtime Humulin N (NPH) insulin.

Start bedtime NPH insulin at 0.1-0.2 units/kg. RN may adjust insulin 1-10 units per week to target FBG 80-130 mg/dL.

-or-

Bedtime NPH Standing Order - For patient or RN Titration (initial dose 10 units, adjust by 1 unit/day to target FBG 80-130 mg/dL).

Consider referral to clinical pharmacist for oral titration to goal.

SmartPhrases: DMORALMEDS DMHSSINSULINNPH
Provider chooses initiation protocol with weight-based dosing or standing order.

A1C goal met?

YES → Continue regimen and monitor HbA1c.

NO → Add Humalog or Humulin R U-100 with meal(s) or AM NPH.

-or-

Add sulfonylurea.

SmartPhrases: DMDAYTIMEINSULIN
Initiation and titration orders DMORALMEDS

A1C goal met?

YES → Continue regimen and monitor HbA1c.

NO → Virtual consult to Diabetes Team.

Recommend metformin XR once daily with evening meal (can be taken all at once). If once daily XR not tolerated, can be split BID.

Glimepiride is recommended for ages < 65 and glipizide for ages ≥ 65 (based on liver and renal function)

If HbA1c above 10%, monotherapy will not likely be enough to bring patient into safe HbA1c range.

If FBG significantly above target, consider HS insulin over sulfonylurea.

Example: Patient weighs 112 kg → starting dose is 11-22 units (consider larger amount for higher BMI).

If patient is taking more than 1 unit/kg of basal insulin, consider adding mealtime insulin with largest meal of the day.

If hypoglycemia on BID NPH, consider glargine.

Testing before and 2 hours after the main meal may give useful info about need for additional daytime insulin or sulfonylurea.

Humulin R U-100 may be more affordable for some insurance plans.

If taking ≥ 200 units insulin daily, consider U-500 (see following page).
Type 2 diabetes treatment: when to consider glargine or U-500 insulin

**Glargine**

Does patient have symptomatic hypoglycemia or use 3+ injections a day?

- **YES**
  - Consider switch to **glargine** (*Lantus*). Decrease total daily dose (TDD) and titrate by 2-10 units/week to FBG target of 80-130 mg/dL.
  - **SmartPhrase:** DMLANTUSTITRATION
    - Initiation and titration orders
  - **A1C** goal met?
    - **YES**
      - Continue current regimen and monitor per guidelines.
    - **NO**
      - Add **Humalog** (*lispro*) or **Humulin** R U-100 with meal(s).
        - or-
        - Add **AM Humulin** N (NPH).
        - or-
        - Add **glimepiride** (see previous page).
  - **SmartPhrase:** DMDAYTIMEINSULIN
    - Initiation and titration orders

- **NO**
  - Continue to titrate **Humulin N (NPH)** insulin to target BG values (see previous page).

**U-500**

Is patient insulin resistant requiring ≥200 units total daily dose (TDD) of insulin?

- **YES**
  - Start **Humulin R U-500** insulin. BID dosing: BG checks before breakfast and dinner. TID dosing: BG checks before meals (TID dosing may be recommended if taking >300 units/daily).
  - **SmartPhrase:** DMU500TITRATION
    - Prescriber parameters for RN to convert patient to U-500 insulin
  - **A1C** goal met?
    - **YES**
      - Continue current regimen and monitor per guidelines.
    - **NO**
      - Virtual consult to Diabetes Team.

- **NO**
  - Continue to titrate standard insulin doses until HbA1c in target or patient is taking ≥200 units TDD.

**Medicare** patients will likely pay significantly more during the donut hole and should be advised or have a plan for management during that time frame.

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Additional pharmacologic options to consider in consultation with the Diabetes Team

**Insulin glargine (F-PA)**

Glargine (Lantus) insulin 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 rapid-acting insulin) or who experience unresolved patterns of hypoglycemia with NPH, glargine can be considered, similar to the way we manage patients with type 1 diabetes (see “Recommended physiologic insulin replacement schedule” in the Type 1 Diabetes Treatment Guideline). (Prior authorization of glargine is required for patients with type 2 diabetes.)

**Glucagon-like peptide-1 (GLP-1) receptor agonists**

**Exenatide XR (Bydureon)** and **liraglutide (Victoza)**, which are non-formulary, are used as adjuncts to diet and exercise to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes and established ASCVD. E Consult with the Diabetes Team is suggested. **Exenatide XR is to be tried first.**

**Pharmacy criteria for exenatide XR**

For patients with type 2 diabetes:
- Contraindication, intolerance, or failure of maximum tolerated doses of metformin, a sulfonylurea, rapid plus basal insulin combination*, and empagliflozin or
- With hemoglobin A1c (HbA1c) ≤ 9% or within 1% of A1c goal and all of the following:
  - Clinically significant weight gain while on insulin therapy or BMI ≥ 35 prior to insulin therapy
  - Failure or intolerance to maximum tolerated dose of metformin
  - Contraindication, intolerance, or failure to achieve A1c goal with empagliflozin 12.5 mg daily after trial of at least 3 months duration
  - Initial authorization: 6 months
  - Reauthorization criteria:
    - 1% reduction in HbA1c after 6 months or member is at HbA1c goal
    - No significant weight gain (defined as ≥ 3% over 6 months)

* Note: Previously documented severe hypoglycemia would be considered an intolerance or contraindication to sulfonyureas or insulin therapy. Severe hypoglycemia includes hypoglycemia resulting in seizures, loss of consciousness, or needing help from others.

Source: [http://incontext.ghc.org/rx/ref/palist.html#Exenatide](http://incontext.ghc.org/rx/ref/palist.html#Exenatide) (staff internal website)

If a patient meeting the criteria for exenatide XR is intolerant of or has a failure of exenatide XR, liraglutide is an alternative GLP-1 receptor option.

**Pharmacy criteria for liraglutide**

For patients with type 2 diabetes:
- Contraindication, intolerance, or failure of maximum tolerated doses of metformin, a sulfonylurea, rapid plus basal insulin combination*, exenatide, and empagliflozin or
- Diagnosis of type 2 diabetes with hemoglobin A1c (HbA1c) ≤ 9% or within 1% of A1c goal and all of the following:
  - Clinically significant weight gain while on insulin therapy or BMI ≥ 35 prior to insulin therapy
  - Contraindication, intolerance, or failure to achieve A1c goal with empagliflozin 12.5 mg daily after trial of at least 3 months duration
  - Failure or intolerance to maximum tolerated dose of metformin and exenatide (Bydureon/Byetta)
  - Initial authorization: 6 months
  - Reauthorization criteria:
- 1% reduction in HbA1c after 6 months or member is at HbA1c goal
- No significant weight gain (defined as ≥ 3% over 6 months)

*Note: Previously documented severe hypoglycemia would be considered an intolerance or contraindication to sulfonylureas or insulin therapy. Severe hypoglycemia includes hypoglycemia resulting in seizures, loss of consciousness, or needing help from others.

Source: http://incontext.ghc.org/rx/ref/palist.html#Liraglutide (staff internal website)

No other GLP-1 receptor agonists are covered due to the availability of preferred treatment alternatives.

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. For more information, see Clinical Review Criteria: Insulin Pump. Patients with Medicare coverage must meet both the clinical review criteria and Medicare requirements to acquire and maintain use of a pump.

Note that the Diabetes Team 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
Although several FDA-approved CGM systems are available, evidence from randomized controlled trials has not shown significant benefit except in specific situations, such as patients who have well documented frequent and/or severe hypoglycemia despite best-practice management. For more information, see Clinical Review Criteria: Continuous Glucose Monitor.

Pharmacologic options that are not recommended
The following pharmacologic options are not recommended or not on the formulary; consider consultation with the Diabetes Team:
- DPP-4 inhibitors—sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), alogliptin (Nesina)
- Meglitinides—repaglinide (Prandin), nateglinide (Starlix)
- Amylinomimetics—pramlintide (Symlin)
- Insulin analogs—insulin detemir (Levemir; PA for children), Fiasp aspart insulin, other Novo insulins, insulin glulisine (Apidra; PA for allergies to insulin), inhaled insulin
- Dopamine agonists—bromocriptine (Cycloset)
- Bile acid sequestrant—colesevelam

There is no high-quality evidence to determine the effect on blood glucose control of any of the following:
- Chromium
- Cinnamon
- Vanadium
Referral to Nursing or Clinical Pharmacy

Chronic disease management (CDM) is a population health improvement program offered to KPWA members by nursing and pharmacy services. The program’s goal is to promote evidence-based practice and improve health care outcomes. Patients work with a registered nurse (RN) or clinical pharmacist (CP) for an average of 3–6 months to gain better control of their chronic disease.

<table>
<thead>
<tr>
<th>Table 3. Referral to Nursing or Clinical Pharmacy for chronic disease management</th>
</tr>
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<tbody>
<tr>
<td><strong>Patient characteristics</strong></td>
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<tr>
<td>• Type 1 or type 2 diabetes not at goal</td>
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<tr>
<td><strong>Frequency of MD contact</strong></td>
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<tr>
<td><strong>Medication titration</strong></td>
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<tr>
<td><strong>Nutrition counseling</strong></td>
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<tr>
<td><strong>Glucose monitoring education</strong></td>
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<tr>
<td><strong>Referral name</strong></td>
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<tr>
<td><strong>Additional resources</strong></td>
</tr>
</tbody>
</table>

1 Newly diagnosed patients already at goal may be offered a visit with RN (CDM referral not required).
2 Patients referred with HbA1c below 8.0% will be evaluated by the RN and CP to determine if there is a legitimate need for case management services versus a brief consult or single contact. CDM referral is not appropriate for self-management and/or nutrition education when HbA1c is at goal. Please use the Living Well with Diabetes Program (1-800-992-2279 or .smlivingwell) or Wellness Coaching by phone (866-862-4295 or .avswellnesscoaching).
Follow-up and Monitoring

Self blood glucose monitoring

<table>
<thead>
<tr>
<th>Eligible population</th>
<th>Recommendations</th>
</tr>
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</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 (FBG) once a day is advisable.  
  o Once patients achieve their FBG target, there is no need to continue testing every morning if they feel well and their HbA1c stays below their target range.  
  o However, if such patients are at their FBG target 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 rapid-acting insulin | • These patients should do SBGM 3–4 times daily if they are using the information to adjust how much rapid-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>Elevated blood pressure</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 <strong>very high risk</strong> (^2) should be seen every 3 months by a wound care nurse. Patients at <strong>increased risk</strong> (^2) and <strong>average risk</strong> (^2) should be screened annually.</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>Microalbumin/creatinine ratio (^1)</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 <strong>with</strong> evidence of retinopathy should be screened annually. Patients <strong>without</strong> evidence of retinopathy should be screened every 2 years. (^3)</td>
</tr>
<tr>
<td>Electrolyte and chemistry abnormalities</td>
<td>Serum creatinine and Serum potassium</td>
<td>At least annually</td>
</tr>
<tr>
<td>Lipohypertrophy and lipodystrophy (^4)</td>
<td>Examine insulin injection sites or infusion set insertion sites.</td>
<td>At initial visit and 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, ideally 3–6 months apart, are diagnostic for microalbuminuria.

\(^2\) 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.

\(^4\) Lipohypertrophy and lipodystrophy can interfere with efficient insulin absorption.

### Medication monitoring

<table>
<thead>
<tr>
<th>Eligible population</th>
<th>Test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients being treated with metformin</td>
<td>Serum creatinine/eGFR</td>
<td>Annually if eGFR is 60 or lower or Twice a year if eGFR is 45 or lower</td>
</tr>
<tr>
<td>Patients being treated with sulfonylurea</td>
<td>HbA1c</td>
<td>Every 3 months until the target is reached; thereafter every 6 months</td>
</tr>
</tbody>
</table>
### Recommended immunizations

<table>
<thead>
<tr>
<th>Immunization</th>
<th>Frequency</th>
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</table>
| Influenza                            | • Annually by the end of October  
|                                      |   • Injectable vaccine recommended. Avoid LAIV (FluMist).                 |
| Pneumococcal polysaccharide          | • One dose of PPSV-23 between ages 19 and 64 years                        |
|                                      |   • Age 65 years and older, one dose of PCV-13, plus another dose of PPSV-23 at appropriate intervals |
| Hepatitis B ²                        | • Three-dose series for ages 19–59 years                                  |
|                                      |   • Age 60 years and older, depending on risk                            |

1. CDC Recommended Adult Immunization Schedule by Medical Condition and Other Indications (2019)  
   https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html

### Comorbidities

#### Depression screening

Screen for depression using the [Annual Mental Health Questionnaire](https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html). 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 [Depression Guideline](https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html) for additional guidance. Patients with major depression can be treated in Primary Care or offered a referral to Mental 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.

ACE inhibitor or ARB therapy should be included for:
- Patients with type 1 or type 2 diabetes who have hypertension (BP > 140/90 mm Hg).
- Patients with type 2 diabetes aged 55 or older who have elevated microalbumin to creatinine ratio and additional cardiovascular risk factors.

See the [ASCVD primary prevention](https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html) and [secondary prevention](https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html) guidelines for details.

#### Blood pressure management

- The target is to treat all adults—including those with diabetes—to a blood pressure of below 140/90 mm Hg. How far below 140/90 mm Hg depends on the patient's clinical circumstances and overall ASCVD risk.
- **The target for adults with diabetes has changed from below 130/80 mm Hg to below 140/90 mm Hg.** Diabetes alone does not qualify a patient for a systolic blood pressure goal of less than 130 mm Hg.
- A systolic blood pressure goal of 130 mm Hg or lower is recommended for adults who:
  - Have 10-year ASCVD risk of 10% or higher
  - Have chronic kidney disease
  - Are age 75 or older
Evidence Summary

To develop the Type 2 Diabetes Screening and Treatment Guideline, the KPWA guideline team:

- Adapted recommendations from externally developed evidence-based guidelines
- Reviewed additional literature using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis

Externally developed guidelines adapted


KPWA evidence review

The guideline team reviewed additional evidence in the following areas:

- Cardiovascular outcomes and safety
- Insulin pump therapy
- Biosimilar insulins with basal insulins
- U-500 or U-300 and U-100 insulin
- Insulin degludec versus U-100 insulin
- Bariatric surgery and type 2 diabetes with obesity

Cardiovascular outcomes and safety

Glucagon-like peptide-1 (GLP-1) receptor agonists

One high-quality meta-analysis (Palmer 2016) of 301 trials involving 120,000 adults found no difference in all-cause mortality, myocardial infarction, and stroke between GLP-1 receptor agonists and other medications. Likewise, no significant difference was found in the risk of mortality due to cardiovascular events between any single or metformin-based combination therapies in the short term (6 months). In addition, no significant differences were reported for metformin-based combination therapies in terms of all-cause mortality, serious adverse events, MI, and stroke.

Low- to moderate-quality evidence (RCTs and meta-analyses) showed inconsistencies: Four studies (Ding 2016, Ferdinand 2016, Howse 2016, and Wang 2016) found no significant difference in major cardiovascular adverse events (cardiovascular mortality, non-fatal MI, non-fatal stroke) between GLP-1 receptor agonists and placebo or active comparators (RR: 0.99; 95% CI, 0.88–1.12; p=0.872 [Ding 2016]); (HR 0.57; adj. 98.02% CI, 0.30–1.10 [Ferdinand 2016]).

Two RCTs reported a statistically significant reduction in the risk of major cardiovascular adverse events between semaglutide and placebo (HR: 0.74; 95% CI, 0.58–0.95; p < 0.001 [Marso, Bain, et al 2016]) and between liraglutide and placebo (HR: 0.87 [0.78–0.97]; p < 0.001 [Marso, Daniels, et al 2016]).

DPP-4 inhibitors (DPP-4-i)

A systematic review (Mannucci 2017) on the cardiovascular safety of DPP4-inhibitors reported that DPP4-inhibitors were not associated with increased cardiovascular risk. However, a number of meta-analyses from this review suggested that results were inconsistent for the drugs as a class, as at least four meta-analyses showed that DPP-4-inhibitors were significantly associated with a reduction in cardiovascular risk and at least four other studies reported no difference.

For individual drugs, the results were conflicting for saxagliptin and sitagliptin; vildagliptin significantly lowered major adverse cardiac event (MACE) risk; linagliptin significantly lowered the risk of stroke; alogliptin showed no difference in MACE risk. DPP-4-i was assessed as monotherapy and as combination therapy with other antidiabetic medications.

Limitations: The number of events was small for statistical analysis. The definitions of MACE varied across studies; there were reliability issues and the post hoc design (except in studies that evaluated linagliptin and alogliptin) may have affected the results; the cardiovascular risk status of patients in some...
studies was lacking; the follow-up period was short (2 years), raising the concern of long-term outcomes (one study assessed 4 years outcomes); and the standard care that patients received might have affected the findings.

However, a statistically significant increased risk of MACE was not observed. The evidence is of low quality.

**SGLT2 inhibitors**

Five meta-analyses of RCTs (Monami 2016, Palmer 2016, Sonesson 2016, Tang 2016, Su 2016) assessed the cardiovascular outcomes of SGLT2 inhibitors. Although comparisons were made between SGLT2 inhibitors and other antidiabetic agents, the main comparison was SGLT2 inhibitor versus placebo. Canagliflozin, dapagliflozin, empagliflozin, ipragliflozin, luseogliflozin, and tofogliflozin were assessed. Sample size ranged from 5,936 to 120,000 adults. Duration of diabetes was > 10 years; mean follow-up was < 2 years (but up to 5.4 years); some patients had established cardiovascular disease or history of CV disease and others did not. Patients had background treatment in most studies. Demographics and baseline characteristics were not different across groups. While most of the studies reported favorable CV outcomes and all-cause mortality for SGLT2 inhibitors, the biggest meta-analysis concluded there was no difference in CV risk and all-cause mortality between SGLT2 inhibitors and placebo or active controls. For non-fatal stroke, one meta-analysis reported that SGLT2 inhibitors significantly increased the risk of stroke whereas another one reported no difference.

The EMPA-REG OUTCOME was a randomized, double-blind, Phase 3 trial that assessed the safety of empagliflozin compared to placebo for 7,020 patients with type 2 diabetes and established cardiovascular disease (Monami 2016). Empagliflozin has been shown to reduce CV and overall mortality when added to standard glucose-lowering agents (i.e., metformin, insulin, and sulfonylureas), and treatment with empagliflozin resulted in a 38% relative risk reduction (2.2% absolute risk reduction) in cardiovascular deaths. However, empagliflozin’s effect on MI is not significant and clinical benefit in the setting of primary prevention for CVD is still unknown.

Compared to each other, no statistically significant difference in CV outcomes among individual medications was reported. The most frequently reported adverse event was genital infection.

The main limitations were short follow-up, variability of study populations, and small number of events. Moderate- to high-quality evidence shows conflicting results on the risk of CV events and all-cause mortality in the short term (< 2 years).

**Thiazolidinediones (TZDs)**

Insufficient evidence precludes conclusions about the comparative effectiveness of TZDs on cardiovascular outcomes in adults with type 2 diabetes.

**Insulin pump therapy**

A randomized controlled trial (Aronson 2016) that enrolled 331 patients compared insulin pump therapy and multiple daily injections (MDI) in patients with type 2 diabetes. The authors reported that compared with multiple daily injections, pump therapy was more effective in reducing HbA1c and total daily insulin dose over 12 months in patients with type 2 diabetes. No major adverse events were reported. However, the results should be interpreted with caution, and the overall risk of bias is high. Precision of study: precise; directness: direct outcomes were assessed. Overall, the evidence is of moderate quality.

**Biosimilar insulins with basal insulins**

Two multinational RCTs (Blevins 2015, Rosenstock 2015) were critically appraised. The primary outcome was to demonstrate the non-inferiority of LY IGlar over IGlar (0.4% and 0.3% non-inferiority margin). Sample sizes ranged from 535 (all type 1 diabetes) to 756 (all type 2 diabetes) patients. Baseline characteristics were similar across groups in each study. The mean HbA1c was 7.7% and 8.3%, respectively, in the studies. In the study that looked at type 1 diabetes (Blevins 2015), patients were randomized to either LY IGlar once per day or IGlar once-daily with mealtime insulin lispro, whereas in the study that looked at type 2 diabetes (Rosenstock 2015), patients who were previously treated with IGlar or ≥ 2 oral antihyperglycemic drugs were randomized to either once-daily LY IGlar or IGlar. Patients were followed for 24 weeks for the primary outcome. However, the follow-up for safety was 52 weeks in
one study (Blevins 2015). In both studies, HbA1c decreased in both groups from baseline to 24 weeks (even at 52 weeks), but the improvement was marked in patients receiving LY IGlar. This suggests that LY IGlar was non-inferior to IGlar on the change of HbA1c at both the 0.4 and 0.3% non-inferiority margins. However, the results were not statistically significant. In addition, there were no statistically significant differences in the following outcomes: proportions of patients achieving target HbA1c < 7%, fasting plasma glucose, self-monitored blood glucose, daily mean blood glucose, and basal insulin dose. Adverse events were similar; the most common were hypoglycemia, nasopharyngitis, upper respiratory tract infection, and diarrhea.

Moderate evidence shows no statistically significant difference in glucose control between LY IGlar (biosimilar insulin) and IGlar in patients with type 1 or type 2 diabetes.

U-500 or U-300 and U-100 insulin

There is no new evidence to suggest that more concentrated insulins (U-500 or U-300) in patients with type 2 diabetes with insulin resistance result in better glycemic control compared to U-100 insulin.

Insulin degludec versus U-100 insulin

Two meta-analyses (Einhorn 2015, Rodbard 2013), two RCTs (Kumar 2016, Onda 2016), and one retrospective study (Ghosal 2016) assessed the outcomes of IDeg in comparison to IGlar. The Einhorn meta-analysis investigated the effects of IDeg among patients who achieved good glycemic control, and the Rodbard meta-analysis assessed similar outcomes in patients requiring high insulin dose. The meta-analyses included 12 RCTs. One of the RCTs was a pilot study with insufficient power. Sample size was up to 3,000 patients and baseline characteristics were similar between groups. Patients were followed for ≤ 1 year. Some patients received concomitant oral agents including metformin, DPP-4I, pioglitazone, and SU. One study compared IDegAsp versus IGlar and another study compared IDeg followed by IGlar versus IGlar followed by IDeg.

Limitations included differences in populations, short follow-up periods, bias related to the open label design of some trials, and failure to specify the exact concentration of IGlar given to patients.

Moderate evidence shows conflicting results between IDeg and IGlar in terms of hypoglycemic events, fasting plasma glucose, and insulin dose. However, IDeg may lower nocturnal hypoglycemic incidence (moderate evidence). There is no statistically significant difference in HbA1c reduction between IDeg and IGlar (moderate evidence). In terms of cardiovascular effects, there is insufficient evidence to assess the cardiovascular outcomes of insulin degludec compared to U-100 insulin.

Bariatric surgery and type 2 diabetes with obesity

Bariatric surgery versus medical treatment in type 2 diabetes patients with obesity

Two meta-analyses (Rohde 2016, Yan 2016) and three RCTs were reviewed (Cummings 2016, Ding 2015, Schauer 2017). These compared bariatric surgery versus medical management in patients with type 2 diabetes who were obese. Bariatric surgery included laparoscopic adjustable gastric band (LAGB), RYGB, and duodenal-jejunal bypass sleeve (DJBS). Medical management included diet modifications; medications for controlling hyperglycemia, dyslipidemia, and hypertension; weight management; decreasing energy intake; and increasing physical activity.

Baseline characteristics were similar across studies. HbA1c ranged from 7.9 to 10.5%; BMI: > 27 kg/m² including morbid obesity; duration of diabetes was up to 13 years; age varied from 20 to 64 years; cardiovascular risk factors; follow-up ranged from 1 to 5 years; only one study (included in the meta-analysis) followed patients for 5 years; one RCT (Schauer 2017) also followed patients for 5 years. Diabetes-related complications were not marked.

RYGB or LAGB was found to be more effective than medical treatment in type 2 diabetes remission (one meta-analysis and 2 RCTs). RYGB or LAGB was more effective than medical management in reduction of cardiometabolic risk factors such as BMI, waist circumference, serum lipida, blood pressure, quality of life, and use of medications (although the very small sample size study reported no significant difference
in quality of life). However, one RCT with small sample size found no statistically significant difference in cardiometabolic risk factors. No major adverse events were reported.

The major limitation was the duration of the trials, wherein an investigation of end-organ damage could not be performed.

Overall, moderate evidence shows that RYGB or LAGB is more effective than medical treatment in glycemic control, type 2 diabetes remission and reduction of cardiometabolic risk factors in the short to medium term (1–5 years). There is insufficient evidence for patients with BMI < 35 kg/m².

**Bariatric surgery versus medical treatment in type 2 diabetes patients with obesity on end-organ complications**

- **Diabetic retinopathy:** One RCT (Schauer 2017) and a number of non–randomized controlled studies (Abbatini 2013, Johnson 2013, Miras 2015, Zakaria 2016) reported conflicting evidence for the effects of bariatric surgery on diabetic retinopathy in the short term; in the long term, there is no statistically significant difference between surgery and medical treatment.
- **Diabetic nephropathy:** Based on one RCT (Schauer 2017) with moderate quality and a number of retrospective studies (Amor 2013, Brethauer 2013, Carlsson 2013, Iaconelli 2011, Johnson 2013), results are conflicting.
- **Diabetic neuropathy:** Evidence is limited; a firm conclusion cannot be made.
- **Cardiovascular:** Low to moderate evidence (Chen 2016, Ding 2015, Douglas 2015, Ricci 2015, Yan 2016) shows that bariatric surgery may decrease the risk of hypertension and macrovascular complications. More trials are warranted to determine the effects on stroke.
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Guideline Development Process and Team

Development process
The Type 2 Diabetes Screening and Treatment Guideline was developed 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 April 2019.

Team
The Type 2 Diabetes Screening and Treatment Guideline development team included representatives from the following specialties: endocrinology and pharmacy.

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Guideline coordinator: Avra Cohen, RN, MN, Clinical Improvement & Prevention
Meredith Cotton, RN, MSN, CDE, Diabetes Program
Dan Kent, PharmD, CDE, Pharmacy Administration
Ann Stedronsky, Clinical Publications, Clinical Improvement & Prevention
Amber Sweeny, RN, MSN, Diabetes Program

Disclosure of conflict of interest
Kaiser Permanente 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.