

# Type 1 Diabetes Treatment Guideline

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**Last guideline approval:** March 2021

**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.

# Interim Update September 2021

**Annual monitoring of estimated glomerular filtration rate (eGFR)** is now recommended for all patients with diabetes to be in compliance with the HEDIS® Kidney Health Evaluation for Patients with Diabetes (KED) measure. Previously, microalbumin/creatinine ratio was the only recommended lab test for monitoring kidney health.

## Changes as of March 2021

Following scheduled review, the KP Washington Type 1 Diabetes Guideline team determined that there were no outstanding evidence gaps and re-approved the guideline with only minor changes to content. The KPWA guideline is in alignment with current KP National clinical guidance.

## Prevention

While it is possible to use autoantibody and genetic testing to identify patients at increased risk of developing type 1 diabetes, this is currently being done in research settings only. There is no evidence-based strategy for preventing type 1 diabetes.

## Screening

Due to low population prevalence, screening for type 1 diabetes is not recommended.

## 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.

Test	Results	Interpretation
HbA1c	6.5% or higher	Diabetes
	5.7–6.4%	Impaired glucose tolerance <sup>1</sup>
	Lower than 5.7%	Normal
Random plasma glucose	200 mg/dL or higher	Diabetes
	140–199 mg/dL	Impaired glucose tolerance <sup>1</sup>
	Lower than 140 mg/dL	Normal
Fasting plasma glucose	126 mg/dL or higher	Diabetes
	100–125 mg/dL	Impaired glucose tolerance <sup>1</sup>
	Lower than 100 mg/dL	Normal

<sup>1</sup> 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.

Although patients with type 1 diabetes most commonly present with abrupt onset of symptoms and weight loss, type 1 diabetes can occur in patients at any age and weight. Diabetic ketoacidosis is also a frequent initial presentation.

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 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.

<b>Table 2. Selected cardiac risk factors and goals for risk reduction for patients with diabetes</b>	
<b>Risk factor</b>	<b>Goal</b>
Blood pressure	Lower than 140/90 mm Hg
LDL cholesterol	Lower than 100 mg/dL
Hemoglobin A1c (HbA1c)	Lower than 7.0% <sup>1</sup>
Fasting blood glucose	80–130 mg/dL
<sup>1</sup> While a target HbA1c of lower than 7.0% is ideal, it may not be achievable for all patients. Any progress should be encouraged. For frail elderly patients, a target HbA1c of 7.0–9.0% is reasonable.	

### Glucose control goals

<b>Table 3. Ideal glucose targets</b>	
<b>Timing</b>	<b>Target <sup>1</sup></b>
Before meals	80–130 mg/dL
2 hours post meals	160 mg/dL
Bedtime	80–130 mg/dL
3 a.m.	80–130 mg/dL
<sup>1</sup> Evaluate for hypoglycemia. Regardless of whether the target is met, it is important to ask patients about hypoglycemia occurring at any time of day or night.	

## Lifestyle modifications and non-pharmacologic options

### Diet and physical activity

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 patients with type 1 diabetes, carbohydrate counting is the best way to keep tight control of blood sugar levels. Kaiser Permanente Washington offers several resources to help patients with meal planning, including [“Sample meals for carbohydrate counting”](#) and [“Carbohydrate examples for sick days”](#) from the “Living Well with Diabetes” series (Resource Line order numbers 404 and 343, respectively), as well as more detailed carbohydrate counting information on [Healthwise](#).

For additional 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.

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

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<sup>2</sup>].) 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.

### Better Choices, Better Health® workshop

The Better Choices, Better Health web-based workshop lasts 6 weeks, but there's no set time to participate. Participants log on for activities 2 to 3 times each week at their convenience and, once the workshop is over, they can join an ongoing moderated self-management community, Healthier Living Alumni, to reinforce the skills gained during the workshop.

This workshop improves outcomes for patients with ongoing health conditions, such as diabetes, as participants experience fewer symptoms, get more exercise, have better medication adherence, are more active partners in their health care, and spend less time in the hospital. This program is offered to patients free of charge. Use .avsBCBH to refer patients to the program. Patients can register at <https://enroll-kpwa1.selfmanage.org/>. 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 glucose monitoring and control. The following information and help is available:

- The pamphlet "[Living Well with Type 1 Diabetes: Taking care of yourself when you're sick](#)" is available online and can be ordered (#337) from the Resource Line, or use SmartPhrase **.dmttype1sickdayplan**.
- Pharmacy staff can help with selecting sugar-free cold medicines and cough syrups.

## Preconception counseling and contraception

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](#).

## Pharmacologic options for blood glucose control

The long-term goal of insulin treatment is to prevent complications by maintaining blood glucose levels as close to normal as possible.

The aggressiveness of therapy should be individualized based on HbA1c goals and the patient's ability to engage in self-management. Selected populations may have better clinical results with less aggressive regimens (e.g., very young children, older adults, people with a history of severe hypoglycemia, and those with limited life expectancies or comorbid conditions).

## Recommended physiologic insulin replacement schedule

Insulin management for type 1 diabetes typically includes basal insulin such as glargine (Lantus) and rapid-acting insulin such as lispro (Humalog). Consider using the SmartPhrases **.dmsimpleyscale** and **.dmsophscale** ("sophisticated") for rapid-acting insulin dosing instructions.

- While a once-daily glargine dose can be given at any time of day, administration in the morning is preferable. Some patients may require two doses of glargine daily.
- For patients with type 1 diabetes who have difficulty affording glargine, NPH is a reasonable and less expensive alternative. Glargine is associated with lower HbA1c and less hypoglycemia than NPH.

All patients should engage in the following self-management activities:

- Monitoring blood sugar before breakfast (fasting), before lunch, before dinner, and before bed to identify a pattern.
- Counting and recording carbohydrates.
- Recalling and recording possible influencing factors for specific blood glucose readings.
- Adjusting insulin doses in response to given glucose patterns.
- Coordinating attention to diet, exercise, and insulin therapy.
- Responding appropriately to hypoglycemia.

Consider consultation with the KP Washington Diabetes Team.

Patients should review their glucose patterns every 3–7 days and adjust insulin doses as needed. Insulin doses of greater than 50 units should be split into two separate injections, given at different sites.

## Insulin adjustments in response to planned variations in eating or exercise patterns

**Diet**—Calculate the carbohydrate content of the meal, and adjust the insulin dose based on the carbohydrate ratio that was prescribed (e.g., 1 unit for each 15 g of carbohydrate). The actual ratio of insulin units to grams of carbohydrate may vary in individuals from 1 unit/5 g of carbohydrate to 1 unit/20 g of carbohydrate.

**Exercise**—Insulin requirements may change by up to 50% during periods of exercise. Patients should monitor their glucose level before, during, and after exercise to determine the effects on their glucose levels. If the effects of the exercise are predictable, insulin doses can be adjusted.

**Stress**—Whether due to physical injury, infection or illness, iatrogenic use of steroids, or psychological factors, stress causes an increase in hormones that antagonize insulin (and thus increases glucose unless adjustments are made). Although stress usually causes glucose to rise, some people become more agitated and active during stress, leading to a drop in glucose.

## Continuous subcutaneous insulin infusion (insulin pumps and pods)

Motivated patients with type 1 diabetes of at least 6 months' duration who are having difficulty with glucose control and experiencing frequent hypoglycemia 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 in order 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 implementing 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.

- Amylinomimetics—pramlintide (Symlin)
- Insulin analogs—insulin detemir (Levemir) (PA for children)
- Inhaled insulin (Afrezza) – rapid acting insulin

## Referral to Nursing for Chronic Disease Management

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

For patients with type 1 diabetes who are not a goal and have agreed to work with an RN, use **REF Clinical Nursing Services: CDM**. Referral to a clinical pharmacist is not available for patients with type 1 diabetes, but is an option for patients with type 2 diabetes.

Use the job aid: CDM Referral Decision Support Tool (on the KPWA staff intranet) to help determine if your patient could benefit from RN care management interventions.

# Follow-up and Monitoring

## Periodic monitoring of conditions and complications

Table 4. Periodic monitoring of conditions and complications		
Condition/complication	Tests	Frequency
Elevated blood pressure	BP taken with appropriate size cuff using optimal technique.	Every visit.
Blood glucose control	HbA1c.	Every 3 months until the target level is reached; thereafter, patient should be monitored at least every 12 months.
Foot ulcers	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.	Patients at <b>very high risk</b> <sup>2</sup> should be seen every 3 months by a wound care nurse.  Patients at <b>increased risk</b> <sup>2</sup> and <b>average risk</b> <sup>2</sup> should be screened annually.
Kidney health	Microalbumin/creatinine ratio <sup>1</sup> and Estimated glomerular filtration rate (eGFR).	Annually.
Retinopathy	Dilated eye exam by a trained eye services professional <b>or</b> Nondilated digital photography followed by a comprehensive exam for those who test positive.	Patients <b>with</b> evidence of retinopathy should be screened annually.  Patients <b>without</b> evidence of retinopathy should be screened every 2 years. <sup>3</sup>
Electrolyte and chemistry abnormalities	Serum creatinine <b>and</b> Serum potassium.	At least annually.
Lipohypertrophy or lipodystrophy <sup>4</sup>	Examine insulin injection sites or infusion set insertion sites.	At initial visit and at least annually.
<p><sup>1</sup> 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 greater than 30 mcg/mg. Two positive tests, ideally 3–6 months apart, are diagnostic for microalbuminuria.</p> <p><sup>2</sup> For foot-ulcer risk definitions, see “Foot care.”</p> <p><sup>3</sup> Annual screening is not recommended because the benefits of more frequent screening are marginal: For every 1,000 people 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.</p> <p><sup>4</sup> Lipohypertrophy or lipodystrophy can interfere with efficient insulin absorption.</p>		

## Recommended immunizations

Source: [CDC Recommended Adult Immunization Schedule by Medical Condition and Other Indications \(2021\)](#)

Table 5. Recommended immunizations for patients with diabetes	
Immunization	Frequency
Influenza	<ul style="list-style-type: none"><li>Annually by the end of October.</li><li>Injectable vaccine recommended. Avoid LAIV (FluMist).</li></ul>
Pneumococcal polysaccharide	<ul style="list-style-type: none"><li>One dose PPSV-23 between ages 19 and 64 years.</li><li>Age 65 years and older, one dose of PCV-13, plus another dose of PPSV-23 at appropriate intervals.</li></ul>
Hepatitis B	<ul style="list-style-type: none"><li>Three-dose series for ages 19 to 59 years.</li><li>Ages 60 years and older, depending on risk.</li></ul>

## Comorbidities

### Depression screening

Screen for depression by using the [Annual Mental Health Questionnaire](#). 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](#) for additional guidance. Patients with major depression can be treated in Primary Care or offered a referral to Mental Health and Wellness 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 diabetes who have hypertension (BP > 140/90 mm Hg). See the ASCVD guidelines for [primary prevention](#) and [secondary prevention](#) 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 1 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

- Kaiser Permanente National Adult Diabetes Clinical Practice Guidelines, 2020.
- Siu AL; U.S. Preventive Services Task Force. Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med.* 2015 Dec 1;163(11):861-868.

## KPWA evidence review

The guideline team reviewed additional evidence in the following areas:

- Use of HbA1c to diagnose diabetes
- Pharmacologic treatment for controlling glucose
- Screening

## 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 using HbA1c of 6.5% or higher and FPG of 126 mg/dL or higher as the cut-points for diabetes, results showed that there is 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).

## Pharmacologic treatment for controlling blood glucose

### Rapid-acting insulin analogs versus regular insulin

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

### Insulin detemir

A meta-analysis of RCTs compared insulin detemir versus NPH insulin in people with type 1 diabetes and found no significant difference in HbA1c levels; however, a slight reduction was found in the risk of severe and nocturnal hypoglycemia in favor of insulin detemir. There was no data available regarding the long-term safety of insulin detemir (Singh 2009).

### Biosimilar insulins with basal insulins

Two multinational RCTs (Blevins 2015, Rosenstock 2015) were critically appraised. The primary outcome of each study was to demonstrate the non-inferiority of LY IGLar (biosimilar insulin) over IGLar (basal insulin); non-inferiority margins were 0.4% and 0.3%. 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% in the studies. In the study that enrolled type 1 diabetes patients (Blevins 2015), patients were randomized to either LY IGLar once daily or IGLar once daily with mealtime insulin lispro; whereas in the study that enrolled type 2 diabetes patients (Rosenstock 2015), patients who were previously treated with IGLar or  $\geq 2$  oral antihyperglycemic drugs were randomized to either LY IGLar once daily or IGLar once daily.

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 diabetes and type 2 diabetes.

### **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.

### **Continuous glucose monitoring (CGM) systems**

Three studies, including two RCTs (Beck 2017, Lind 2017) and one meta-analysis (Benkhadra 2016), were reviewed. The RCTs assessed the effects of CGM with the use of multiple daily insulin injections on type 1 diabetes. The primary outcome was the change in HbA1c at 12 and 24 weeks in one RCT (Beck 2017) and the difference in HbA1c at 26 and 69 weeks in the second RCT (Lind 2017). Follow-up was up to 69 weeks (Lind 2017). Sample size ranged from 142 to 158 and baseline characteristics were similar across groups; mean age: 45–48 years; HbA1c: 8.6–8.7%; mean duration of diabetes: 19–22 years; self-reported number of self-monitoring blood glucose tests per day and the use of non-insulin glucose-lowering medication were similar. Patients were randomized to CGM or self-monitoring of blood glucose (SMBG). Patients in the SMBG group monitored their glucose level 4 times per day.

Both RCTs found a statistically significant change in HbA1c from baseline (-0.6%; 95% CI, -0.8% to -0.3%;  $p < 0.001$  [Beck 2017]); (-0.43%; 95% CI, -0.57 to -0.29%;  $p < 0.001$  [Lind 2017]). The change favored CGM. A reduction of 0.3% was clinically meaningful (Lind 2017). The meta-analysis (Benkhadra 2016), wherein the majority of the RCTs assessed CGM with the use of insulin pumps, also found a statistically significant overall change in HbA1c in adults (-0.258%; 95% CI, -0.464 to -0.052;  $p=0.014$ ). However, heterogeneity was high.

Glycemic variability and the time or percentage of time spent in hypoglycemic range were lower in patients on CGM than in patients in the SMBG group. The findings were inconsistent in the time or percentage of time spent in hyperglycemia. Time spent in euglycemic range and treatment satisfactions were higher in the CGM group. No significant differences in adverse events were reported. The definitions of hypoglycemia, hyperglycemia and euglycemia ranges varied between studies. The meta-analysis showed no statistically significant difference in time spent in hypoglycemia (Benkhadra 2016).

Main limitations included small sample size, short follow-up periods, the open-label nature of the RCTs, and low to moderate risk of bias. Based on precision, directness, consistency and risk of bias, the strength of the evidence is deemed moderate. Overall, moderate evidence shows that continuous glucose monitoring system with the use of multiple daily insulin injection or the use of an insulin pump may be more effective on HbA1c in adults with type 1 diabetes than self-monitoring blood glucose in the short term. The technology is safe. Studies with longer follow-up are warranted.

## 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.

### Neuropathy

There is fair evidence that diabetic foot screening prevents adverse outcomes. One RCT (McCabe 1998) 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. 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. A cohort study investigated the optimum screening interval by grade of retinopathy and found that for patients at low risk for retinopathy, a 2-year screening interval was not associated with increased risk (Misra 2009).

#### **Nonmydriatic digital stereoscopic retinal imaging**

A 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 has 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).

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# Guideline Development Process and Team

## Development process

The Type 1 Diabetes 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 March 2021.

## Team

The Type 1 Diabetes Treatment Guideline development team included representatives from the following specialties: endocrinology, nursing, and pharmacy.

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