Type 1 Diabetes Treatment Guideline

Major Changes as of May 2017 ................................................................. 2
Prevention ........................................................................................................... 2
Screening ................................................................................................................ 2
Diagnosis .................................................................................................................. 2
Treatment .................................................................................................................. 3
  Risk-reduction goals ................................................................................................. 3
  Glucose control goals ............................................................................................... 3
  Lifestyle modifications and non-pharmacologic options .............................................. 4
  Pharmacologic options for blood glucose control ...................................................... 5
  Pharmacologic options that are not recommended .................................................. 6
Follow-up and Monitoring .......................................................................................... 7
  Periodic monitoring of conditions and complications ................................................ 7
  Recommended immunizations .................................................................................. 8
Comorbidities ............................................................................................................. 8
  Depression screening ............................................................................................... 8
  ASCVD prevention .................................................................................................. 8
  Hypertension management ....................................................................................... 8
Evidence Summary ................................................................................................... 9
References .................................................................................................................. 12
Guideline Development Process and Team .............................................................. 14

**Last guideline approval:** May 2017

**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.

This evidence-based guideline was developed by **Kaiser Permanente Washington (KPWA)**. It was adapted from the 2016 Kaiser Permanente National Guideline, as well as the 2015 U.S. Preventive Services Task Force Diabetes Guideline.
Major Changes as of May 2017

<table>
<thead>
<tr>
<th>New</th>
<th>Previous</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glucose targets</strong> are now 80–130 mg/dL.</td>
<td>Glucose targets were 70–120 mg/dL.</td>
</tr>
<tr>
<td>A new section on <strong>preconception counseling and contraception</strong> has been added.</td>
<td>—</td>
</tr>
</tbody>
</table>

Prevention

While it is possible to identify patients who are at increased risk of developing type 1 diabetes through autoantibody and genetic testing, this is currently being done in research settings. 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 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>
<tr>
<td></td>
</tr>
<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. This guideline recommends avoiding the term pre-diabetes because not all patients with IGT and/or IFG will develop diabetes.

Patients with type 1 diabetes most commonly present with abrupt onset of symptoms and may not be overweight. Diabetic ketoacidosis also can be 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 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 the Diabetes Team (use REF DIABETES).

**Risk-reduction goals**

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

**Table 2. Selected cardiac risk factors and goals for risk reduction for patients with diabetes**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>Lower than 130/80 mm Hg</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>Lower than 100 mg/dL</td>
</tr>
<tr>
<td>Hemoglobin A1c (HbA1c)</td>
<td>Lower than 7.0%</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
<td>80–130 mg/dL</td>
</tr>
</tbody>
</table>

1 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**

**Table 3. Ideal glucose targets**

<table>
<thead>
<tr>
<th>Timing</th>
<th>Target 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before meals</td>
<td>80–130 mg/dL</td>
</tr>
<tr>
<td>2 hours post-meals</td>
<td>160 mg/dL</td>
</tr>
<tr>
<td>Bedtime</td>
<td>80–130 mg/dL</td>
</tr>
<tr>
<td>3 a.m.</td>
<td>80–130 mg/dL</td>
</tr>
</tbody>
</table>

1 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

For information on nursing management of patients with type 1 diabetes, see Nursing Protocol 131 on the KPWA staff intranet.

**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/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 guidelines (for adults and for children and adolescents) for recommendations and further information.

**Living Well Workshops**

Six-week workshops are offered both in person for Living Well with Chronic Conditions and Living Well with Diabetes, and online (currently only for chronic conditions). 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®.

**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 .chronicdiseasedmtype1sickdayplan in Epic.
- 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 < 7.0% 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 .dmsimplescale 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 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)
## Follow-up and Monitoring

### 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, patient 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 with evidence of retinopathy should be screened annually. Patients without 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>
</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 greater than 30 mcg/mg. Two positive tests, ideally 3–6 months apart, are diagnostic for microalbuminuria.

² For foot-ulcer risk definitions, see “Foot care,” p. 4.

³ 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.
Recommended immunizations

<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</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 B²</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>

¹ See the CDC Recommended Adult Immunization Schedule for more detailed information.
² 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 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 Atherosclerotic Cardiovascular Disease (ASCVD) guidelines for primary prevention and secondary prevention for details.

Hypertension management
See the Hypertension Guideline.
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


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 ≥ 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).
References


Rosenstock J, Hollander P, Bhargava A, et al. Similar efficacy and safety of LY2963016 insulin glargine and insulin glargine (Lantus®) in patients with type 2 diabetes who were insulin-naive or previously treated with insulin glargine: a randomized, double-blind controlled trial (the ELEMENT 2 study). *Diabetes Obes Metab.* 2015 Aug;17(8):734-741.


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 May 2017.

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

Clinical expert: Avantika Waring, MD, Program Chief, Diabetes Care
CI&P clinician lead: David K. McCulloch, MD, Medical Director, Clinical Improvement
Guideline coordinator: Avra Cohen, RN, MN, Clinical Improvement & Prevention
Said Adjao, MD, MPH, Epidemiologist, Clinical Improvement & Prevention
Karen Aitken, ARNP, MSN, BC-ASM, Diabetes Program
Meredith Cotton, RN, MSN, CDE Diabetes Program
Dan Kent, PharmD, CDE, Pharmacy Administration
Sophia Malik, MD, Resident
Kathryn Ramos, Patient Engagement Team, Clinical Improvement & Prevention
Lesley Richardson, MD, Consultative Internal Medicine
Timothy Scholes, MD, Family Medicine
Rosemary Schreoter, MD, Family Medicine
Ann Stedronsky, Clinical Publications, Clinical Improvement & Prevention
Kay Tucker, RN, Diabetes Team

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.