Type 1 Diabetes Treatment Guideline

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Last guideline approval: June 2015

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

The guideline team reviewed the 2013 Type 1 Diabetes Treatment Guideline, determined that there were no outstanding evidence gaps, and re-approved the guideline with no changes.

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>
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<tbody>
<tr>
<td>Test</td>
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<tr>
<td>HbA1c</td>
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<tr>
<td></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>

<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. Group Health 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 usually are not 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 diabetes experts in Consulting Internal Medicine or from David McCulloch, MD, diabetologist at Group Health.

### Risk-reduction goals

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

| Table 2. Selected cardiac risk factors and goals for risk reduction |
|-----------------------|-----------------------------|
| Risk factor             | Goal                        |
| Blood pressure         |                             |
| Age 79 or younger      | Lower than 140/90 mm Hg     |
| Age 80 or older        | Lower than 150/90 mm Hg     |
| With microalbuminuria (at any age) | Lower than 130/80 mm Hg   |
| LDL cholesterol        | Lower than 100 mg/dL        |
| Hemoglobin A1c (HbA1c) | Lower than 7% ¹              |
| Fasting blood glucose  | 80–120 mg/dL                |

¹ While a target HbA1c of lower than 7% is ideal, it may not be achievable for all patients. Any progress should be encouraged. For frail elderly patients, a target HbA1c of 7–9% is reasonable.

### Glucose control goals

| Table 3. Ideal glucose targets |
|-----------------------------|-----------------------|
| Timing                     | Target                |
| Before meals               | 70–120 mg/dL          |
| 2 hours post-meals         | 160 mg/dL             |
| Bedtime                    | 70–120 mg/dL          |
| 3 a.m.                     | 70–120 mg/dL          |
Lifestyle modifications and nonpharmacologic 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 personalized eating plans and interactive tools to help patients plan and assess food choices, see the U.S. Department of Agriculture’s Choose My Plate website (http://www.choosemyplate.gov).

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

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

Foot-ulcer risk definitions:

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

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

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

- The pamphlet “Living Well with Type 1 Diabetes: Taking Care of Yourself When You’re Sick” is available online and can be ordered (#337) from the Group Health Resource Line. Or use SmartPhrase .chronicdiseasedmtype1sickdayplan in Epic.
- Pharmacy staff can help with selecting sugar-free cold medicines and cough syrups.
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).

Simple insulin schedules

<table>
<thead>
<tr>
<th>Table 4. Recommended simple insulin schedules</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Once-daily schedules</strong></td>
</tr>
<tr>
<td>Glargine ¹ (100%)</td>
</tr>
<tr>
<td>N/A</td>
</tr>
<tr>
<td><strong>Twice-daily schedule</strong></td>
</tr>
</tbody>
</table>

¹ Prior Authorization (PA) for insulin glargine (Lantus) is not required for patients with type 1 diabetes but is required for those with type 2 diabetes.

² While NPH twice a day is reasonable (and less expensive) for some patients with type 1 diabetes, glargine is associated with lower HbA1c and less hypoglycemia.

Intensive insulin schedules

Intensive insulin management typically includes basal (long-acting) insulin such as glargine (Lantus) and bolus (fast-acting) insulin such as lispro (Humalog). Consider using the SmartPhrases .dmsimplescale and .dmsophscale.

Patients who are able to engage in the following self-management activities may be good candidates for intensive insulin regimens:

- Monitoring blood sugar before breakfast (fasting), before lunch, before dinner, and before bed to identify a pattern.
- Counting and recording carbohydrates. (See the pamphlet Living Well with Diabetes: Understanding 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 CIM and/or diabetologist David McCulloch, MD, for advice.
Note that blood glucose patterns should be reviewed by the patient every 3–7 days and adjusted as needed. Insulin doses of greater than 50 units should be split into two separate injections, given in 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 (up or down) 1 unit of insulin for each 15 g of carbohydrate by which the meal varies from a typical meal. (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 every 30 minutes during periods of exercise to determine the effects of exercise on their glucose level. If the effects of the exercise are predictable, insulin doses can be adjusted.

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

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

Motivated patients with type 1 diabetes for more than 1 year who are having difficulty controlling their blood glucose and having 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 Group Health’s Clinical Review Criteria and Medicare requirements in order to acquire and maintain use of a pump.

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

**Continuous glucose monitoring (CGM) systems**

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 with type 1 diabetes who have well documented frequent and/or severe hypoglycemia (blood glucose under 50 and/or patient has hypoglycemia unawareness) 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 Group Health formulary**; consider consultation with diabetologist David McCulloch, MD:

- 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>Hyperlipidemia</td>
<td>Fasting LDL</td>
<td>Annually</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>Dilated eye exam by a trained eye services professional or Nondilated digital photography followed by a comprehensive exam for those who test positive</td>
<td>Patients with evidence of retinopathy should be screened annually. Patients without evidence of retinopathy should be screened every 2 years 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 are diagnostic for microalbuminuria, ideally 3–6 months apart.

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 6. Recommended immunizations for patients with diabetes

<table>
<thead>
<tr>
<th>Immunization</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Annually, as early as possible when vaccine becomes available</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>• Once between ages 19 and 64 years</td>
</tr>
<tr>
<td></td>
<td>• Booster after age 65 years (at least 5 years after previous dose)</td>
</tr>
<tr>
<td>Hepatitis B</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’s Recommended Adult Immunization Schedule (http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf) 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 Group Health Depression Guideline for additional guidance. Patients with major depression can be treated in Primary Care or offered a referral to Behavioral Health Services for counseling and/or drug therapy.

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

Hypertension management
See the Group Health Hypertension Guideline.
Evidence Summary

Group Health developed the Type 1 Diabetes Treatment Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

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

Rapidly acting insulin analogs versus regular insulin

A Cochrane Library meta-analysis of RCTs published through September 2005 found a statistically significant reduction of HbA1c with short-acting insulin analogs compared with regular human insulin for patients with type 1 diabetes (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 with 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).

Continuous glucose monitoring systems

Results from a meta-analysis that included 22 RCTs and evaluated the effects of continuous glucose monitoring (CGM) compared with self-blood glucose monitoring (SBGM) found that there was limited evidence on the efficacy of CGM in children, adolescents, and adults with type 1 diabetes. The mean difference in HbA1c using real-time CGM compared with SBGM was -0.2% after 6 months of follow-up (Langendam 2012).

A recent RCT assessed the benefits of CGM with SMBG compared with SMBG alone in 146 children aged 4–9 years with type 1 diabetes. The mean change in HbA1c was -0.1% in both groups. Results from this study suggest that CGM does not reduce HbA1c in children aged 4–9 years (Mauras 2012).
**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


Guideline Development Process and Team

Development process
Group Health developed the Type 1 Diabetes Treatment Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

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

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

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

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