in the clinic

Type 2 Diabetes

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It is nearly impossible to be a practicing internist in the United States and have a day of clinical work pass without encountering at least 1 patient with type 2 diabetes. Currently, over 20 million Americans and over 150 million persons worldwide have type 2 diabetes. Models estimate that this number will nearly double by the year 2050 so that about one third of adult Americans will have the disease. Unfortunately, although researchers are gaining new insights into the pathophysiology of the disease, including its genetic basis, and therapeutic options are expanding, many people with type 2 diabetes develop complications of the disease. A recent national analysis of diabetes care in the United States shows that despite improvements in processes of care and intermediate outcomes over the past decade, there remains much room for improvements in diabetes care. Among adult Americans with diabetes, 2 in 5 have suboptimal lipid control, 1 in 3 has poor blood pressure control, and 1 in 5 has poor glycemic control.

### Diagnosis

#### What are the diagnostic criteria for type 2 diabetes in nonpregnant adults?

Type 2 diabetes is often present at least 4 to 7 years before diagnosis. Definitive diagnosis of type 2 diabetes is important because it allows attempts to improve glycemic control and to implement other interventions to improve clinical outcomes. Clinicians should confirm the diagnosis with laboratory testing when a patient presents with symptoms compatible with type 2 diabetes (polyuria, polydipsia, and unexplained weight loss), with evidence of possible diabetes complications (vision problems, retinopathy, impotence, renal dysfunction, peripheral neuropathy, acanthosis nigricans, or frequent infections), or with elevated incidental blood glucose levels (≥126 mg/dL fasting or ≥200 mg/dL nonfasting). A fasting plasma glucose level that is 126 mg/dL or greater and is confirmed on repeated testing on another day is the current American Diabetes Association (ADA) preferred criterion for diagnosis (Table 1).

#### What alternative diagnoses should clinicians consider when a patient presents with hyperglycemia?

The differential diagnosis for type 2 diabetes is limited and includes type 1 diabetes, diabetes insipidus, and maturity-onset diabetes of the young. Clinicians should consider type 1 diabetes when patients are younger than 30 years of age, have ketosis on presentation, or have a family history of diabetes.

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### Table 1: Diagnostic Tests For Diabetes

<table>
<thead>
<tr>
<th>Test</th>
<th>Threshold Value</th>
<th>Recommended Follow-up</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose (FPG)</td>
<td>≥126 mg/dL suggests diabetes</td>
<td>· Confirm by repeated test on another day</td>
<td>· Time since last meal easily defined</td>
<td>· Less convenient to draw than a random glucose level</td>
</tr>
<tr>
<td></td>
<td>100–125 mg/dL suggests prediabetes</td>
<td></td>
<td>· Preferred American Diabetes Association criterion for diagnosis</td>
<td></td>
</tr>
<tr>
<td>Random plasma glucose</td>
<td>≥200 mg/dL in setting of symptoms indicates diabetes</td>
<td>· Confirm with FPG or OGTT performed on another day</td>
<td>· Convenient</td>
<td>· Lower sensitivity and specificity than other tests</td>
</tr>
<tr>
<td>2-h oral glucose tolerance test (OGTT)</td>
<td>≥200 mg/dL diagnostic for diabetes</td>
<td>· Confirm with FPG on another day</td>
<td>· None</td>
<td>· Least acceptable test for diagnosis</td>
</tr>
<tr>
<td></td>
<td>140–199 mg/dL suggests prediabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycosylated hemoglobin</td>
<td>Hemoglobin A1c value &gt;6% is suggestive of diabetes but not diagnostic</td>
<td>· Perform confirmatory testing with fasting glucose or OGTT measurement</td>
<td>· Convenient</td>
<td>· No universally implemented standard</td>
</tr>
</tbody>
</table>

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Diagnosis continued

Type 2 diabetes is common, and clinicians should consider the diagnosis when patients present with symptoms or signs of the disease or its complications. Fasting plasma glucose levels greater than 126 mg/dL on 2 occasions at least 1 day apart confirm the diagnosis and have the advantage of being relatively convenient to measure. However, random plasma glucose levels and oral glucose tolerance testing can also be used to establish the diagnosis of type 2 diabetes. Other forms of diabetes are much less common than type 2 diabetes, but clinicians should consider these alternatives and endocrinology consultation when the clinical picture is unclear.

CLINICAL BOTTOM LINE

Screening

Should we screen for type 2 diabetes?
The natural history of type 2 diabetes includes an asymptomatic phase that is detectable only through screening or incidental testing. Because complications can occur before clinical symptoms, some groups advocate screening all primary care patients for the disease. However, no direct evidence proves that screening improves health outcomes. Further research is needed to define the effect of delaying the onset of frank diabetes on long-term outcomes and resource utilization and to determine whether there are potential harms of early treatment in patients with diabetes identified through screening. In the absence of such evidence, there is a lack of consensus about whether to screen all primary care patients, regardless of their underlying risk. Organizations have tended to advocate focusing screening on patients at high risk for diabetes or its complications.

Which patients are likely to benefit most from diabetes screening?
Several evidence-based guidelines advocate focusing screening efforts on patients with elevated risk for type 2 diabetes (Table 2), particularly those with cardiovascular disease, hypertension, or dyslipidemia.

Intensive glycemic control in people with type 2 diabetes reduces intermediate markers of microvascular complications but has not been convincingly shown to reduce end-organ complications or macrovascular disease. Yet fair evidence from observational studies and a decision model suggests that detecting diabetes improves estimates of cardiovascular risk and provides an opportunity for earlier and more aggressive interventions, such as more aggressive hypertension and lipid control, to reduce cardiovascular events in patients with type 2 diabetes and those who have had a myocardial infarction.

Table 2: Diabetes Screening Guidelines

<table>
<thead>
<tr>
<th>Date</th>
<th>Organization (Reference)</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| 2006  | American Diabetes Association\(^1^3\) | · For adults who do not have diabetes risk factors, consider screening every 3 y starting at age 45 y, particularly if body mass index >25 kg/m\(^2\)  
· Screen adults <45 y of age if they are overweight and have another diabetes risk factor |
| 2003  | U.S. Preventive Services Task Force\(^1^4\) | · There is insufficient evidence to recommend for or against routine screening of asymptomatic adults  
· Fair evidence supports screening adults with hypertension or hyperlipidemia |
| 2003  | Canadian Diabetes Association\(^1^5\) | · Evaluate all patients for type 2 diabetes risk annually  
· Screen patients without diabetes risk factors every 3 y starting at age 40 y  
· Consider earlier, more frequent screening for patients with diabetes risk factors |

Patients with diabetes should be screened for common diabetes complications. Although currently available guidelines (Table 2) differ in their recommendations for screening of patients with average cardiovascular risk and the ages at which to begin screening, they generally agree that clinicians should screen for diabetes in patients with elevated risk for cardiovascular disease. ◆

Screening... Pending direct evidence of the benefits of early treatment for patients with type 2 diabetes identified through routine screening, screening for diabetes seems prudent for middle-aged patients with risk factors for cardiovascular disease, such as hypertension or dyslipidemia. Professional groups differ with respect to recommendations for screening in people without elevated cardiovascular risk.

Can we prevent type 2 diabetes?
Before people develop type 2 diabetes, they almost always have “prediabetes.” This condition is defined by hyperglycemia that does not meet the diagnostic criteria for diabetes. Whether this condition is called “impaired fasting glucose” or “impaired glucose tolerance” depends on whether the hyperglycemia was detected on measurement of fasting plasma glucose levels or an oral glucose tolerance test. Both impaired fasting glucose and impaired glucose tolerance are risk factors for future diabetes and cardiovascular disease. Patients with prediabetes should undergo monitoring and should modify their risk factors for diabetes and cardiovascular disease if possible.

In addition to observational studies, clinical trials document that dietary changes and regular exercise prevent or delay the development of overt diabetes in individuals at high risk for the disease, such as those with prediabetes.

In a randomized, controlled trial that involved 522 overweight Finnish patients with impaired glucose tolerance (mean age, 55 years), an intervention aimed at a 5% reduction in weight decreased the incidence of newly diagnosed type 2 diabetes over 3 years from 23% to 11%. The intervention involved personal counseling sessions to encourage a reduction in total and saturated fat intake to less than 30% and 10% of energy consumed, respectively; an increase in fiber intake; and moderate exercise for at least 30 minutes per day.

The Diabetes Prevention Project, a randomized, controlled trial that involved 3234 U.S. patients with prediabetes (mean age, 51 years; mean body mass index, 34 kg/m²), showed that a lifestyle modification program aimed at a 7% weight loss reduced the cumulative incidence of diabetes over 3 years from 29% to 14% compared with placebo. The lifestyle intervention involved personal and group counseling sessions to encourage a low-calorie, low-fat diet and at least 150 minutes of moderate exercise (such as brisk walking) per week.

In a randomized, controlled trial that involved 577 Chinese adults with impaired glucose tolerance randomly assigned to diet, exercise, both, or neither, the incidence of diabetes over 6 years was 68% among persons in the “neither” group, 44% in the diet group, 41% in the exercise group, and 46% in the “both” group. All 3 interventions resulted in statistically significant reductions in the progression to diabetes.

Clinical trials also show that certain medications can prevent type 2 diabetes in high-risk patients. In the medication arm of the Diabetes Prevention Project, the trial that involved 3234 patients with prediabetes, metformin (850 mg twice daily) reduced the cumulative incidence of diabetes from 29% to 22% over...
Prevention continued
3 years. This reduction was significant but smaller than that observed with the lifestyle intervention in this trial.

In the randomized, double-blind, international Study to Prevent Non–Insulin-Dependent Diabetes Mellitus, which involved 1429 patients with impaired glucose tolerance, acarbose (100 mg three times daily) reduced the incidence of diabetes from 42% to 32% compared with placebo. The relative risk reduction over 3 years was 25%.

The DREAM trial (Diabetes Reduction Assessment with ramipril and rosiglitazone Medication) is a multinational study that, using a 2-by-2 factorial design, randomized 5269 adults without previous cardiovascular disease but with impaired fasting glucose, impaired glucose tolerance, or both to rosiglitazone 8 mg per day or placebo and to rosiglitazone up to 15 mg per day or placebo. After a median 3 years, 11.6% of patients who received rosiglitazone developed diabetes or died compared with 26.0% of patients who received placebo (hazard ratio, 0.40 [95% CI, 0.35 to 0.46]). In addition, patients who received rosiglitazone were more likely to achieve normoglycemia than patients in the placebo group (50.5% vs. 30.3%; P<0.001). Cardiovascular event rates were statistically similar in both groups. Patients in the ramipril group did not have a significantly reduced incidence of diabetes or death, but these patients were more likely to have regressed to normoglycemia than were those receiving placebo (42.5% vs. 38.2%; P=0.001).

What should the initial evaluation of patients with newly diagnosed type 2 diabetes include?
The initial evaluation of a patient with newly diagnosed type 2 diabetes should include a detailed history, physical examination, and laboratory tests to establish baseline values of glycemic control, to assess risk factors for complications, and to screen for existing diabetes complications.

What are the components of nondrug therapy for patients with type 2 diabetes?
Diet and exercise with optimization of body weight are the cornerstones of the management of type 2 diabetes.

In a study of patients with newly diagnosed type 2 diabetes, diet initially improved hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) levels by 2.25 percentage points\textsuperscript{22}. However, control deteriorated over time and most patients eventually required drug therapy.

A meta-analysis of 14 randomized trials that compared exercise with no exercise and involved a total of 377 patients with type 2 diabetes showed that exercise significantly improved glycemic control, reduced visceral adipose tissue, and reduced plasma triglycerides even in the absence of weight loss\textsuperscript{23}. Physicians should initiate diet and exercise regimens as the first line of treatment for type 2 diabetes unless severe hyperglycemia necessitates immediate drug therapy. Even when drug therapy is necessary, diet and exercise remain essential components of diabetes management. Physicians need to recognize that no single diet applies to all patients with type 2 diabetes; instead, they should offer education about sensible dietary principles and an individualized strategy for optimization of body mass index.

What is the role of home glucose monitoring for patients with type 2 diabetes?
Physicians should consider home blood glucose testing for patients with type 2 diabetes. Although no studies have assessed whether home blood glucose monitoring leads to more favorable outcomes for patients receiving oral therapy, home monitoring can be helpful to guide oral medication adjustment, is essential for sensible adjustment of insulin dosage, and is valuable in determining whether symptoms are due to hypoglycemia or hyperglycemia. Urine glucose control is a helpful indicator of adequate blood glucose control. Patients with type 2 diabetes who require intensive blood glucose control should have frequent monitoring of urine glucose and be educated about the symptoms of hypoglycemia and hyperglycemia.

Initial Laboratory Evaluation of Patients with Type 2 Diabetes
- Fasting blood glucose level
- Glycosylated hemoglobin level
- Fasting lipid profile
- Serum electrolyte, blood urea nitrogen, and creatinine levels
- Urine dipstick for overt proteinuria, with confirmation of positive result. If no dipstick proteinuria, screen for microalbuminuria with a spot urinary albumin–creatinine ratio (>30 mg albumin/g creatinine is positive result)
- Electrocardiography

Prevention… High-quality evidence supports the recommendation of regular exercise, weight loss, and reduction in total and saturated dietary fat for patients with blood glucose levels that are higher than normal but that do not meet the diagnostic criteria for diabetes (prediabetes). In some circumstances, evidence supports the use of pharmacologic therapy (metformin, acarbose, or rosiglitazone) to reduce a patient’s risk for type 2 diabetes. Clinicians should consider one of these interventions when they identify patients as having prediabetes.

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glucose testing is not recommended because it does not adequately reflect current glycemic status.

Patients should generally test before a meal to reflect fasting glucose levels as closely as possible. However, measurement of postprandial levels may be informative, particularly for patients with elevated glycosylated hemoglobin values despite normal fasting glucose levels. Some experts now advocate postprandial monitoring to limit after-meal glucose excursions on the basis of observational data suggesting that postprandial glucose levels are associated with a degree of cardiovascular risk independent of fasting glucose levels24–25. Currently, however, the only studies that show improved outcomes with interventions based on postprandial glucose levels have been done in patients with gestational diabetes.

What target for glycemic control should physicians aim for in patients with type 2 diabetes?

Quality improvement efforts often define an HbA1c value less than 7% as optimal control. It is clear that “tight” glycemic control reduces the risk for microvascular diabetic complications22,26, and recent evidence shows that control also reduces the risk for macrovascular complications in type 1 diabetes27. However, tight control may not benefit patients with a limited life expectancy, substantial comorbidity, or a high risk for adverse hypoglycemic events. Clinicians and patients should consider these factors when setting targets for control.

When should the treatment of type 2 diabetes include drugs?

If diet and exercise fail to achieve the desired level of glycemic control, pharmacologic intervention is indicated. Patient characteristics and preferences should be used to set treatment goals in the initial choice of pharmacologic agent. In patients with severe hyperglycemia or marked symptoms, pharmacologic therapy may begin at the time of diagnosis. Some suggest that patients with fasting glucose levels greater than 250 to 300 mg/dL are reasonable candidates, although there are no clear data in this area. Patient preferences and

### Table 3: Oral Drug Therapies for Treating Type 2 Diabetes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Hemoglobin A1c Reduction</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides (metformin)</td>
<td>- Suppresses hepatic glucose production</td>
<td>- 1%–2%</td>
<td>- No weight gain</td>
</tr>
<tr>
<td></td>
<td>- Decreases intestinal absorption of glucose</td>
<td></td>
<td>- Gastrointestinal side effects</td>
</tr>
<tr>
<td></td>
<td>- Improves insulin sensitivity</td>
<td></td>
<td>- Increase in risk for lactic acidosis (avoid if creatinine level &gt; 1.4 mg/dL in women and &gt; 1.5 mg/dL in men, decompensated congestive heart failure, liver failure, or heavy alcohol use)</td>
</tr>
<tr>
<td>Sulfonylureas (glimipide, glipizide, glyburide, acetohexamide, chlorpropamide)</td>
<td>- Increases pancreatic secretion of insulin</td>
<td>- 1%–2%</td>
<td>- Possible initial weight gain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Potential for hypoglycemia</td>
</tr>
<tr>
<td>Thiazolidinediones (rosiglitazone and pioglitazone)</td>
<td>- Increases sensitivity to insulin</td>
<td>- 1%–2% as monotherapy or when added to other agents</td>
<td>- Weight gain and edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Avoid in New York Heart Association class III or class IV heart failure</td>
</tr>
<tr>
<td>α-glucosidase inhibitors (acarbose and miglitol)</td>
<td>- Decreases postprandial hyperglycemia by reducing gastrointestinal carbohydrate absorption</td>
<td>- 0.5%–1.0%</td>
<td>- Gastrointestinal side effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Acarbose contraindicated in cirrhosis and requires liver function monitoring</td>
</tr>
<tr>
<td>Meglitinides (repaglinide and nateglinide)</td>
<td>- Increases pancreatic secretion of insulin through a different glucose-binding site than used by sulfonylureas</td>
<td>- 0.5%–2%</td>
<td>- Compared with sulfonylureas: Shorter onset of action and half-life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Greater decrease in postprandial glucose level</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Lower risk for hypoglycemia</td>
</tr>
</tbody>
</table>
**How should physicians select therapies for a patient from among the many oral drug therapies available for type 2 diabetes?**

Table 3 provides information on oral drug therapies for treating type 2 diabetes. Given the minimal differences in efficacy and the limited data on long-term outcomes, use of oral agents should be based on patient preference, provider familiarity, and consideration of such issues as side effects and costs. Clinicians should consult with the patient and balance maximization of efficacy with minimization of weight gain, patient effort, hypoglycemia, other side effects, and cost.

Metformin and sulfonylureas are the mostly commonly used first-line agents. For overweight patients, metformin is often the preferred initial therapy since it causes less weight gain and is associated with a lower rate of hypoglycemia than other agents. Sulfonylureas are a reasonable first choice for patients who are not very overweight, since these agents are associated with initial weight gain.

For obese patients who do not tolerate metformin or have renal insufficiency or another contraindication to metformin, thiazolidinediones are an alternative. Other alternatives include the nonsulfonylurea insulin secretagogues (nateglinide and repaglinide) and the α-glucosidase inhibitors (acarbose and miglitol) administered before meals. They may be good choices for patients with irregular mealtimes, but they are more expensive than other oral diabetes drugs.

Most patients with diabetes have worsening glycemic control over time and are likely to need medication adjustment. When glucose control deteriorates with an oral agent, clinicians should consider increasing the dose, but the response to escalating from submaximal to maximal doses, particularly for metformin and sulfonylureas, is usually limited.

When glucose can no longer be controlled with a single oral agent, adding another oral agent with a different mechanism of action may help. The best-studied oral-agent combination is sulfonylurea compounds plus metformin, an approach that addresses both insulin deficiency and insulin resistance. Other combinations in common use are sulfonylurea compounds plus either α-glucosidase inhibitors or thiazolidinediones, and combinations of various insulin-sensitizing agents, such as biguanides and thiazolidinediones. Aggressive combination oral treatment may delay the need for insulin in patients with advancing type 2 diabetes, an option that may be preferable to many patients. Combination medications (low doses of sulfonylurea plus metformin, metformin plus a glitazone, and glitazone plus sulfonylurea) are available, but there is limited evidence on improvements in effectiveness or safety with these treatment options.

**When should physicians consider insulin therapy for patients with type 2 diabetes?**

Patients who do not achieve adequate glycemic control with a combination of oral medications are candidates for insulin treatment. Other indications include:

- New diagnosis with severe, symptomatic hyperglycemia
- Comorbid illness, such as myocardial infarction, infection, or renal or hepatic disease, that

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**General Advice about Diet and Exercise for Patients with Type 2 Diabetes**

**Diet**
- Stress the importance of moderation
- Base calorie recommendations on the goal of achieving near-ideal body weight. A reasonable starting formula for weight maintenance is as follows: 10 calories per pound of current body weight, plus 20% for sedentary patients; 33% for those who engage in light physical activity; 50% for those who are moderately active; and 75% for heavily active patients
- Advise patient to avoid saturated fats
- Encourage regular meal schedule, particularly if patient is receiving insulin
- Inform patient that frequent, small meals might aid in weight loss and control of blood glucose levels
- Advise patient to choose complex carbohydrates (e.g., whole grains, cereals) over simple sugars (e.g., sweets).

**Exercise**
- Individualize exercise regimen, consider current level of activity, living situation, and comorbid conditions
- Consider beginning with 15 min of low-impact aerobic exercise 3 times per week for patients who can exercise and gradually increasing the frequency and duration to 30–45 min of moderate aerobic activity 3–5 d per week
- Caution patients receiving drug therapy about hypoglycemia during and after exercise

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### Table 4: Onset and Mechanisms of Action of Various Types of Insulin*

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Onset and Mechanisms of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lispro/aspart Glulisine</td>
<td>Very short acting; onset of action within 15 min; peak action, 30–90 min; maximum, 5 h</td>
</tr>
<tr>
<td>Regular</td>
<td>Short acting; onset of action within 1 h; duration, typically 4–8 h; maximum, 12 h</td>
</tr>
<tr>
<td>NPH</td>
<td>Intermediate acting; onset within 2–3 h; duration, typically 8–12 h; maximum, 24 h</td>
</tr>
<tr>
<td>Lente</td>
<td>Intermediate acting; onset within 2–3 h; duration, typically 8–12 h; maximum, 24 h</td>
</tr>
<tr>
<td>Glargine</td>
<td>Long acting up to 24 h</td>
</tr>
<tr>
<td>Ultralente</td>
<td>Longest acting up to 28 h</td>
</tr>
</tbody>
</table>

* NPH = neutral protamine Hagedorn.

Regular and long acting (usually NPH); concentrations vary.

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**Evaluation & Treatment continued**

makes control difficult with oral medications
- Pregnancy
- Intolerance to oral medication.

Many different forms of insulin are available; all act directly on glucose metabolism (see Table 4)[30]. The starting dose for insulin varies widely and may be determined by weight-based algorithms. Randomized, controlled trials of different insulin regimens show that insulin can improve hemoglobin A\textsubscript{1c} values by 1% to 2%, but there is no documented advantage of dosing insulin more than twice daily in type 2 diabetes[30]. Side effects include hypoglycemia and weight gain.

Insulin therapy may be combined with oral therapy to better achieve target glucose control. Options for combination therapy with insulin and oral agents include bedtime insulin (glargine or neutral protamine Hagedorn [NPH]) plus daytime sulfonylurea or bedtime insulin (glargine or NPH) plus metformin. Patients may discontinue other diabetes therapy before beginning these regimens. Glucose monitoring is essential to titrate the insulin dose to a morning fasting glucose level of 80 to 120 mg/dL.

After discontinuation of previous therapy, start with a dose of 0.10 to 0.15 U/kg divided into 2 daily doses (or with meals), then adjust dosages (typically in 10% increments at 1-week intervals) based on results of home glucose monitoring. Metformin and glitazones can be continued for their insulin-sensitizing and insulinsparing effects.

**What other options are available if control is inadequate on traditional oral drugs or insulin?**

If glycemic control remains inadequate, consider using either of these agents.

In 2005, the U.S. Food and Drug Administration (FDA) approved pramlintide for use with mealtime insulin when control is inadequate despite optimal insulin dosing. Exenatide is not for use with insulin.

**Pramlintide**

Pramlintide is a synthetic form of the hormone amylin, which is produced by the β cells in the pancreas along with insulin. Prescription should be as follows:

- Begin pramlintide at a dose of 60 μg subcutaneously just before each major meal.
- Reduce the dose of rapid-acting, short-acting, or fixed-mix premeal insulin by 50% to avoid risk for hypoglycemia.
- Monitor blood glucose frequently before and after meals and at bedtime.
- If the patient has no nausea, increase maintenance dose to 120 μg; if nausea develops and persists, decrease to 60 μg.
- When pramlintide dose is stabilized, adjust insulin dose to optimize.

In a multicenter, randomized, controlled trial, 538 insulin-treated patients with type 2 diabetes were given various doses of pramlintide or placebo for 52 weeks. In the 150-μg pramlintide group, 48% of patients achieved a reduction in both HbA\textsubscript{1c} and body weight from baseline to week 52 compared with 16% of patients on placebo[32].

In a similar study of 656 patients receiving insulin or insulin combined with metformin or a sulfonylurea, treatment with pramlintide, 120 μg twice daily, led to an HbA\textsubscript{1c} value less than 8% in 46% of patients compared with 28% of those receiving placebo. Patients in the
In October 2006, the FDA approved sitagliptin as a monotherapy adjunct to diet and exercise or for use in combination with metformin or thiazolidinediones. Sitagliptin, a dipeptidyl peptidase 4 (DPP-4) inhibitor, is the first drug in a new class of oral therapy for type 2 diabetes. DPP-4 inhibitors block the breakdown of proteins that stimulate insulin synthesis and release when blood glucose rises. Further data, especially about long-term safety, is needed to determine the role of sitagliptin in the treatment of type 2 diabetes.

A randomized, controlled trial assigned 521 patients age 27 to 76 years with a mean baseline HbA1c of 8.1% in a 1:2:2 ratio to receive placebo, sitagliptin 100 mg once daily, or sitagliptin 200 mg once daily. After 18 weeks, HbA1c was significantly reduced with sitagliptin at both doses compared with placebo (placebo-subtracted HbA1c reduction, 0.60% for 100 mg and –0.48% for 200 mg).14

What are the novel therapeutic options on the horizon for patients with type 2 diabetes?

The FDA approved inhaled insulin in January 2006, providing patients with an alternative to injection as a mechanism of insulin delivery by enabling patients to breathe insulin into their lungs by using a special device.35

A 2005 study involving 309 patients with type 2 diabetes who were taking oral drugs and had poorly controlled diabetes compared the results among those randomly assigned to continue taking the oral drugs, to add inhaled insulin to the pills before meals, or to stop taking the pills and take only inhaled insulin before meals. After 12 weeks, HbA1c level was most improved in the group that took inhaled insulin with the pills, second most improved in the group that took only inhaled insulin, and worst in the group that took only pills. The patients in the inhaled insulin groups experienced more mild weight gain, episodes of low blood glucose levels, and mild cough.35

Whether patients will continue to show improved blood glucose levels or have side effects if they used inhaled insulin for longer periods is not known. It is also unclear how inhaled insulin compares with injected insulin over the long term. Injected insulin currently allows for finer dose adjustments than does inhaled insulin.
Table 5: Antihypertensive Agents in Type 2 Diabetes*

<table>
<thead>
<tr>
<th>Antihypertensive Agent</th>
<th>Notes</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td>· ADA and ACP advocate as first-line agent</td>
<td>· Cardioprotective · Renoprotective</td>
<td>· Relatively expensive · Caution with advanced renal failure</td>
</tr>
<tr>
<td>ARBs</td>
<td>· ADA and ACP advocate as second-line agent</td>
<td>· Cardioprotective · Renoprotective</td>
<td>· Expensive · Caution with advanced renal failure</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>· Use in patients with known CAD</td>
<td>· Cardioprotective · Most are inexpensive</td>
<td>· Can mask hypoglycemia · May be associated with weight gain and metabolic abnormalities</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>· Often used in combination with other agents to achieve blood pressure targets · ACP advocates as first-line agent</td>
<td>· May reduce CHF · Inexpensive · Cardioprotective</td>
<td>· May elevate blood glucose levels</td>
</tr>
<tr>
<td>α-Blockers</td>
<td>· Use only if target blood pressure cannot be reached with other agents</td>
<td>· Can help alleviate symptoms of benign prostatic hypertrophy</td>
<td>· Do not protect against CHF · Generally must be used with other agent</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>· Use if target blood pressure cannot be reached with ACE inhibitors, ARBs, and thiazides</td>
<td>· Some evidence suggests this class is cardioprotective</td>
<td>· Appear to offer less cardioprotection than other antihypertensive agents</td>
</tr>
</tbody>
</table>

*ACE = angiotensin-converting enzyme; ACP = American College of Physicians; ADA = American Diabetes Association; ARB = angiotensin-receptor blocker; CAD = coronary artery disease; CHF = congestive heart failure.

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**In addition to therapies aimed at glycemic control, what therapies should physicians consider to reduce the complications of type 2 diabetes?**

Patients with hypertension should receive aggressive antihypertensive therapy to a blood pressure target <130/80 mm Hg. Some experts recommend <125/75 if proteinuria is present. Randomized controlled trials support the use of angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker therapy for patients with type 2 diabetes regardless of blood pressure level. Physicians should consider comorbidity, efficacy, and side effects when choosing antihypertensive agents (see Table 5).

Patients with known cardiovascular disease should receive lipid-lowering agents. For primary prevention of cardiovascular disease, patients with diabetes who are 40 years or older and have at least one additional cardiovascular risk factor should receive lipid-lowering therapy regardless of low-density lipoprotein cholesterol level. Statins are generally the agents of choice, except for patients with low levels of both high-density lipoprotein and high triglycerides in whom fibrates with or without a statin may be a reasonable option. Caution is needed when combining statins and fibrates.

Physicians should consider aspirin 75 to 325 mg/day for all patients who have type 2 diabetes age >40 years, ≥1 additional risk factor, and no specific contraindication.

A variety of pharmacologic agents are effective in treating the symptoms of diabetic neuropathy (see Table 6).

---

### Table 6: Therapies To Decrease Neuropathy Symptoms

<table>
<thead>
<tr>
<th>Agent</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic</td>
<td>· Randomized, controlled trial (RCT) evidence shows effectiveness in neuropathic pain</td>
</tr>
<tr>
<td>antidepressants</td>
<td>· Start with small bedtime dose (25 mg of nortriptyline) and titrate up</td>
</tr>
<tr>
<td></td>
<td>· Watch for anticholinergic side effects</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>· Recently approved by the U.S. Food and Drug Administration for diabetic neuropathy</td>
</tr>
<tr>
<td></td>
<td>· Recommended dosage is 60 mg/d</td>
</tr>
<tr>
<td></td>
<td>· Not appropriate if patient has liver disease or substantial alcohol use</td>
</tr>
<tr>
<td>Capsaicin cream</td>
<td>· RCTs show effectiveness in reducing pain and increasing function</td>
</tr>
<tr>
<td></td>
<td>· May cause burning sensation</td>
</tr>
<tr>
<td>Antiepileptic</td>
<td>· Carbamazepine or gabapentin in patients unable to tolerate above options</td>
</tr>
<tr>
<td>agents</td>
<td>· RCTs support effectiveness</td>
</tr>
</tbody>
</table>

---

How frequently should physicians see patients with type 2 diabetes, and what should physicians include in follow-up visits?

While no direct evidence suggests the ideal frequency of follow-up for patients with type 2 diabetes, expert opinion and the recommended frequency of monitoring HbA1c levels and other aspects of routine diabetes care suggest that quarterly visits are prudent (see Table 7).

When should generalist physicians consult specialists to assist in the care of patients with type 2 diabetes?

Meta-analyses have shown that diabetes education is effective in improving knowledge, skill, self-care behaviors, psychosocial outcomes, and metabolic control. Data from randomized, controlled trials show that evaluation by a dietitian leads to improved glycemic control.

Endocrinology consultation can be helpful when the diagnosis is uncertain, management is complicated, glycemic control is elusive (persistent hyperglycemia, recurrent hypoglycemia, or ketoacidosis), or if the patient is pregnant or is contemplating pregnancy.

Nephrology consultation is prudent when a patient’s glomerular filtration rate has decreased to <30 mL/min per 1.73 m², proteinuria persists, blood pressure control is difficult, or hyperkalemia occurs.

Cardiology consultation is appropriate for patients with cardiovascular symptoms or abnormal electrocardiography or stress test results.

Ophthalmology evaluation is recommended annually. Less frequent evaluation may be considered in the setting of repeated normal examinations.

Podiatry consultation is helpful when orthotic footwear is necessary to correct deformities and prevent foot ulcers.

Evaluation & Treatment continued

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<table>
<thead>
<tr>
<th>Issue</th>
<th>Actions</th>
<th>How Often?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycemic control</td>
<td>- Ask about diet, exercise, results of home monitoring, and medications. Adjust medications.</td>
<td>- Each visit (at least quarterly)</td>
</tr>
<tr>
<td></td>
<td>- Check hemoglobin A1c values</td>
<td>- Quarterly</td>
</tr>
<tr>
<td>Weight control</td>
<td>- Weigh patient. Ask about diet and exercise.</td>
<td>- Each visit</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>- Ask about diet, smoking, and cardiac events in family members</td>
<td>- Each visit</td>
</tr>
<tr>
<td>complications</td>
<td>- Measure blood pressure, examine heart and peripheral pulses</td>
<td>- Each visit</td>
</tr>
<tr>
<td></td>
<td>- Measure lipid levels</td>
<td>- Annually, or more frequently to monitor therapy</td>
</tr>
<tr>
<td></td>
<td>- Consider performing other cardiac testing</td>
<td>- If patient has symptoms; has abnormal findings on examination or electrocardiography; or is sedentary and &gt;35 y of age and plans vigorous exercise</td>
</tr>
<tr>
<td></td>
<td>- Adjust therapy to achieve target lipid levels and blood pressure</td>
<td>- Each visit</td>
</tr>
<tr>
<td>Vision complications</td>
<td>- Ask about visual acuity, central vision loss, and eye pain</td>
<td>- At least annually; each visit once problem exists</td>
</tr>
<tr>
<td></td>
<td>- Have specialist conduct eye examination</td>
<td>- At least annually; each visit once problem exists</td>
</tr>
<tr>
<td>Neurologic complications</td>
<td>- Ask about burning, tingling, numbness in extremities</td>
<td>- At least annually; each visit once problem exists</td>
</tr>
<tr>
<td></td>
<td>- Conduct neurologic examination with monofilament testing</td>
<td>- At least annually; each visit once problem exists</td>
</tr>
<tr>
<td>Nephrologic</td>
<td>- Perform urinalysis; measure electrolytes, blood urea nitrogen, and creatinine; test urine for microalbuminuria</td>
<td>- At least annually, more frequently once problem exists</td>
</tr>
<tr>
<td>complications</td>
<td>- Examine for periodontal disease, skin infection, and foot infection</td>
<td></td>
</tr>
<tr>
<td>Infectious</td>
<td>- Ask about infections, including skin, dental, foot, genitourinary</td>
<td></td>
</tr>
<tr>
<td>complications</td>
<td>- Have specialist conduct eye examination</td>
<td></td>
</tr>
<tr>
<td>Patient education</td>
<td>- Advocate diet, exercise, monitoring, and medication adherence</td>
<td>- Each visit</td>
</tr>
</tbody>
</table>

Treatment... Diet and exercise are the cornerstones for achieving glycemic control in patients with type 2 diabetes, and clinicians should stress the importance of lifestyle modification regardless of whether patients also require pharmacologic therapy. However, most patients with type 2 diabetes eventually require drug therapy to control glucose levels. Given the numerous oral and insulin-based therapies available and the limited data comparing 1 oral agent or combination of oral agents to another, clinicians should consider effectiveness, potential side effects, comorbid conditions, costs, and patient preferences when selecting treatment regimens for glycemic control.

CLINICAL BOTTOM LINE

Endocrinology consultation can be helpful when the diagnosis is uncertain, management is complicated, glycemic control is elusive (persistent hyperglycemia, recurrent hypoglycemia, or ketoacidosis), or if the patient is pregnant or is contemplating pregnancy.

Nephrology consultation is prudent when a patient’s glomerular filtration rate has decreased to <30 mL/min per 1.73 m², proteinuria persists, blood pressure control is difficult, or hyperkalemia occurs.

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Podiatry consultation is helpful when orthotic footwear is necessary to correct deformities and prevent foot ulcers.
What measures do U.S. stakeholders use to evaluate the quality of care for patients with type 2 diabetes?

In April 2005, The Ambulatory Care Quality Alliance (AQA) released a set of 26 health care quality indicators for use in quality improvement efforts, public reporting, and pay-for-performance programs (www.ambulatory-qualityalliance.org). In May 2005, the Centers for Medicare & Medicaid Services (CMS) endorsed the development of these indicators. Of the 26 indicators, 6 focus on the care of patients with diabetes (see Table 8). Three of the 6 diabetes-related indicators measure processes of care (HbA1c measurement, lipid measurement, and eye examination by an eye specialist) and 3 measure intermediate outcomes (HbA1c, blood pressure, and low-density lipoprotein cholesterol levels). It is important that clinicians be aware of these measures. AQA selected these measures because they have been linked to better clinical outcomes for patients with diabetes. Over the coming years, Medicare and other payers will increasingly link reimbursement to physician performance with respect to these quality indicators.

In addition to the 6 AQA measures, the CMS Physician Focused Quality Initiative’s Doctors’ Office Quality-Information Technology project (www.doqit.org) advocates the additional diabetes-related performance measures shown in Table 9.

What do professional organizations recommend regarding the care of patients with type 2 diabetes?

As noted in the preceding section on screening, several organizations offer recommendations about screening for type 2 diabetes. In addition, evidence-based guidelines are available to guide clinicians in the care of patients with the disease. A comprehensive listing of available guidelines is available through the National Guideline Clearinghouse (www.guidelines.gov). The following summarizes recently developed guidelines related to the care of type 2 diabetes.

American Diabetes Association

Every January, the ADA releases standards of diabetes care to provide clinicians, patients, and other stakeholders with tools to help in the provision and evaluation of diabetes care. These standards address a broad range of issues in diabetes spanning...
from prevention to treatment for type 1, type 2, and gestational diabetes mellitus in a variety of settings. Complete ADA guidelines are available at www.diabetes.org/for-health-professionals-and-scientists/cpr.jsp.

American College of Physicians
The American College of Physicians (ACP) conducted systematic reviews of the evidence to develop guidelines on the management of hypertension and lipids in patients with type 2 diabetes, which were published in 2003 and 2004, respectively (Lipids: www.annals.org/cgi/reprint/138/7/587.pdf; and Hypertension: www.annals.org/cgi/reprint/140/8/644.pdf).

American Association of Clinical Endocrinologists
The most recent guidelines for the management of diabetes mellitus from the American Association of Clinical Endocrinologists (AACE) are contained in the AACE System of Intensive Diabetes Self-Management—2002 Update. These guidelines include 3 phases. Phase 1 addresses the initial assessment of patients following the diagnosis of diabetes. Phase 2 addresses interim assessments of patients with diabetes. Phase 3 addresses ongoing assessment of the complications of diabetes and strategies for encouraging maintenance of patient enthusiasm for intensive control. The AACE guidelines include specific recommendations regarding the frequency of follow-up and specific components of physical, psychosocial, and laboratory examinations. The AACE guideline is summarized at www.guideline.gov/summary/summary.aspx?ss=15&doc_id=3172&nbr=002398&string=AACE+AND+guideline.

What tools are available to help clinicians adhere to performance standards?

Patient Registries
A registry is a system for tracking information about a specific group of patients. The Centers for Disease Control and Prevention (CDC) and the Bureau of Primary Health Care have developed several disease-specific electronic registries, including one for patients with diabetes, which are available free of charge. There are hardware, software, and staffing considerations for practices interested in using electronic registries. The CDC has developed a registry assessment tool to enable specific practices to evaluate the resources necessary to implement these registries (www.healthdisparities.net).

Flow Charts
Even practices that do not have the resources to implement electronic patient registries can avail themselves of “low-tech” tools to promote care in accordance with published, evidence-based recommendations. Such care will improve outcomes for patients with type 2 diabetes. In addition, the

Table 9: Additional Doctors’ Office Quality–Information Technology Diabetes–Related Quality Indicators

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine protein testing</td>
<td>· Denominator is all patients with diabetes age 18–75 y · Measurement interval is the last 15 mo</td>
<td>· Percentage of patients with ≥1 test for microalbuminuria during the measurement year or those who had evidence of existing nephropathy, microalbuminuria, or albuminuria</td>
</tr>
<tr>
<td>Foot examination</td>
<td>· Denominator is all patients with diabetes age 18–75 y · Measurement interval is the last 15 mo · Excludes patients with bilateral lower-extremity amputation</td>
<td>· Percentage of eligible patients receiving ≥1 complete foot examination (visual inspection, sensory examination with monofilament, and pulse examination)</td>
</tr>
</tbody>
</table>

Other Evidence-Based Clinical Guidelines Related to Type 2 Diabetes
Other organizations have developed guidelines relevant to specific elements of the care of patients with type 2 diabetes.

Eye Care
American Academy of Ophthalmology
Available at www.aao.org/professionals/doqi/guidelineindex.cfm

Lipid Control
National Cholesterol Education Program—Adult Treatment Panel III
Available at www.nhlbi.nih.gov/guidelines/cholesterol/index.htm

Hypertension
National Heart, Lung, and Blood Institute
Available at www.nhlbi.nih.gov/guidelines/hypertension/jncintro.htm

Nephropathy
National Kidney Foundation
Available at www.kidney.org/professionals/doqi/guidelineindex.cfm

provision and documentation of such care will increasingly influence physician reimbursement over the coming years as pay for performance becomes a reality in the United States.

Reminder systems have been shown to improve the rates at which physicians provide recommended services. While electronic reminder systems can be particularly powerful, many physicians practice in settings in which electronic medical records and other high-technology systems are not yet available. Some evidence from a demonstration project done by the Diabetes Physician Committee of the Medical Society of Delaware suggests that “low-tech” paper flow sheets can also be effective in improving the rates of recommended care among patients with type 2 diabetes. Flow charts can remind physicians and other caregivers about recommended interventions. In addition, they can help to improve documentation of the provision of recommended care, which is important since many third parties consider the absence of documentation to indicate that a service was not rendered.

Many flow sheets are available, some locally developed and others developed by such organizations as the American Medical Association’s Physician Consortium for Performance Improvement. The end of this section provides an example of a flow chart that focuses on the major performance measures discussed above and also provides space for noting current therapy. The ACP welcomes physicians to use or adapt this flow sheet for use in their own practices. A PDF file is available for free download at www.annals.org/intheclinic/.

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**in the clinic**

**Tool Kit**

**Type 2 Diabetes**

**Chart Stickers**

Reminder systems are built into many electronic health records but can also be implemented in practices without such systems. The ACP will provide Order Reminder and Check Results chart stickers that physicians and their staff can use to promote compliance with recommendations (www.acponline.org/provate/abimpim/diabetes/practicetools.html).

**Diabetes Flow Sheet**

To download an electronic copy of the flow sheet that appears at the end of this section for duplication and use in your office, go to www.annals.org/intheclinic/. Foot Examination Chart, Exercise Prescription, Patient Self-Management Check List, Worksheet, and Goal Contract (www.annals.org/intheclinic/)

**Patient Education Brochures**

ACP Special Reports are patient education brochures about conditions, including diabetes. Brochures (in packs of 100) are available free to ACP members at www.acponline.org/catalog/campaign/special.htm.

Coming soon...Living with Diabetes is a practical guide for patients with diabetes that the ACP Foundation is developing in collaboration with health literacy experts, physicians, and patients with diabetes. The guide is designed for patients to use in concert with provider-delivered education. It will be available free to ACP members. Check www.foundation.acponline.org in April 2007.

**Smoking Cessation Assistance**

www.cdc.gov/tobacco/pubs1.htm#quit

**Standard Orders Worksheet**

Create a customized worksheet of standing orders for patients with diabetes (www.acponline.org/private/abimpim/diabetes/standing orders.html).

**Tools To Promote Evidence-Based Immunization**

Obtain reminders, wallet cards, vaccine records, posters, and educational flyers (www.acponline.org/aii/tools.htm).

**Web Resources for Patients with Type 2 Diabetes**

- American Diabetes Association: www.diabetes.org
- State-Based Diabetes Prevention and Control Programs: www.cdc.gov/diabetes/states/index.htm
- American Association of Diabetes Educators: www.aadenet.org

# Type 2 Diabetes Care Flow Sheet

**Patient Name:**  
**Date of Birth:**

## DIET AND EXERCISE

<table>
<thead>
<tr>
<th>Weight/BMI</th>
<th>frequency: every visit</th>
<th>target: BMI &lt;24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet counseling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise counseling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking cessation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## AQA MEASURES

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>frequency: every 3-4 months</th>
<th>target: &lt;7%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>frequency: every visit</td>
<td>target: &lt;130/80</td>
</tr>
<tr>
<td>Lipids tested</td>
<td>frequency: yearly</td>
<td>target: LDL &lt;100mg/dL (lower is better)</td>
</tr>
</tbody>
</table>

## COMPLICATIONS MONITORING

<table>
<thead>
<tr>
<th>Microalbumin</th>
<th>frequency: yearly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialist eye exam</td>
<td>frequency: yearly</td>
</tr>
<tr>
<td>Foot exam</td>
<td>frequency: yearly</td>
</tr>
</tbody>
</table>

## DIABETES MEDICATIONS

<table>
<thead>
<tr>
<th>Aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE or ARB</td>
</tr>
<tr>
<td>β-Blocker</td>
</tr>
<tr>
<td>Statin</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

## MEDICATIONS TO DECREASE RISK FOR CARDIOVASCULAR COMPLICATIONS

<table>
<thead>
<tr>
<th>Aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE or ARB</td>
</tr>
<tr>
<td>β-Blocker</td>
</tr>
<tr>
<td>Statin</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

## IMMUNIZATIONS

<table>
<thead>
<tr>
<th>Influenza</th>
<th>frequency: every year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>frequency: every 6-10 years</td>
</tr>
</tbody>
</table>
1. A 67-year-old obese (body mass index, 34 kg/m²) man has had type 2 diabetes mellitus for the past 8 years. The disease was originally diagnosed on the basis of a routine fasting plasma glucose level of 156 mg/dL and responded well to initiation of a nutrition and exercise plan. The hemoglobin A1c (HbA1c) value decreased of a nutrition and exercise plan. The mg/dL and responded well to initiation routine fasting plasma glucose level of 156 was originally diagnosed on the basis of a mellitus for the past 8 years. The disease HbA1c value increased to 8.1%; therapy months of nutrition therapy and a 5.5-kg (12-lb) weight loss. After 2 years, the HbA1c value increased to 8.1%; therapy with glyburide, with dosage titrated up to 10 mg/d, was started. The HbA1c value then decreased to 6.6% and remained less than 7% until 1 year ago. At that time the patient noted a 7-kg (15-lb) weight gain and some symptoms of distal paresthesias. The HbA1c value had increased to 7.7%. The patient is counseled to intensify diet and exercise to lose 7 kg (15 lb).

What is the most appropriate additional intervention at this time?
A. Add repaglinide therapy before breakfast and dinner
B. Increase the glyburide dose to 10 mg twice daily
C. Discontinue glyburide therapy and begin metformin therapy
D. Add metformin to current glyburide therapy
E. Switch from glyburide therapy to glipizide therapy

2. A 32-year-old man presents for follow-up evaluation after he was found to have a fasting plasma glucose level of 132 mg/dL as part of a preemployment physical examination. He is concerned that he will be labeled as having diabetes. His mother has a history of type 2 diabetes, and his father has a history of hypertension. He is active and works out at the gym for 45 minutes 3 times weekly. He has never been overweight. He does not have polyuria, polyphagia, or polydipsia, and his vision has been fine. His only symptom is mild fatigue.

The patient is 173 cm (68 inches) tall and weighs 90 kg (198 lb); her body mass index is 34 kg/m². The random plasma glucose level is 135 mg/dL. A 75-g glucose tolerance test shows a fasting plasma glucose level of 112 mg/dL and a 2-hour value of 178 mg/dL.

What is the next step in management?
A. Measure HbA1c
B. Obtain a random blood glucose measurement
C. Measure fructosamine
D. Repeat plasma glucose concentration after an 8-hour fast
E. Reassure the patient that he does not have diabetes

3. A 27-year-old asymptomatic Hispanic American woman is evaluated for risk of diabetes mellitus. She developed gestational diabetes with her first pregnancy, which ended successfully 12 months ago. She has a strong family history of type 2 diabetes mellitus.

On physical examination, she is 165 cm (64 inches) tall and weighs 90 kg (198 lb); her body mass index is 34 kg/m². The random plasma glucose level is 135 mg/dL. A 75-g glucose tolerance test shows a fasting plasma glucose level of 112 mg/dL and a 2-hour value of 178 mg/dL.

What is the next step in the management of this patient?
A. Repeat the glucose tolerance test in 1 year
B. Begin thiazolidinedione therapy
C. Begin acarbose therapy
D. Begin metformin therapy
E. Begin intensive lifestyle intervention

4. A 58-year-old man presents with a 4-year history of type 2 diabetes found by incidental blood glucose testing. He is 183 cm (72 inches) tall and weighs 95 kg (210 lb). He takes metformin, 1000 mg/d, and glyburide, 10 mg/d, but he continues to have home blood glucose values greater than 200 mg/dL. The HbA1c value is 9.6%. He has no microvascular or macrovascular complications.

What is the next step in management?
A. Begin a low-carbohydrate diet
B. Increase glycyluride dosage
C. Increase metformin dosage
D. Begin pioglitazone therapy
E. Begin basal insulin therapy

5. A 58-year-old black man has had hypertension for 5 years. He has maintained a blood pressure of 135/85 mm Hg with the use of hydrochlorothiazide, 25 mg/d. Laboratory assessment reveals a serum sodium level of 141 mEq/L, serum potassium level of 4.1 mEq/L, and fasting plasma glucose level of 132 mg/dL. These values are confirmed on remeasurement several days later.

What is the most appropriate management of this patient’s hypertension?
A. Continue the current therapy, with a target blood pressure less than 140/90 mm Hg
B. Discontinue hydrochlorothiazide therapy and begin ramipril therapy
C. Add amlodipine to hydrochlorothiazide therapy
D. Add ramipril to hydrochlorothiazide therapy
E. Increase the hydrochlorothiazide dose to 50 mg/d

6. A 45-year-old woman presents for an annual physical examination. Her medical history is significant only for mild arthritis and type 2 diabetes that is well-controlled with metformin, 500 mg twice daily. She has no history of hypertension and does not smoke. She has no personal or family history of heart disease. She exercises daily and follows a low-fat diet. Laboratory evaluation reveals a serum total cholesterol level of 220 mg/dL, a high-density lipoprotein cholesterol level of 42 mg/dL, and a triglyceride level of 185 mg/dL. The calculated low-density lipoprotein cholesterol level is 141 mg/dL.

What is the next step in management?
A. Continue current diet and exercise program
B. Start low-carbohydrate diet
C. Start therapy with an hydroxy-methylglutaryl coenzyme A reductase inhibitor (a statin)
D. Start therapy with nicotinic acid
E. Start therapy with a bile acid sequestrant

Questions are from the ACP’s Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers or to purchase the complete MKSAP program.