Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and requires that many issues, beyond glycemic control, be addressed. A large body of evidence exists that supports a range of interventions to improve diabetes outcomes.

These standards of care are intended to provide clinicians, patients, researchers, payors, and other interested persons with the components of diabetes care, treatment goals, and tools to evaluate the quality of care. While individual preferences, comorbidities, and other patient factors may require modification of goals, targets that are desirable for most patients with diabetes are provided. These standards are not intended to preclude more extensive evaluation and management of the patient by other specialists as needed. For more detailed information, refer to Skyler (Ed.): Medical Management of Type 1 Diabetes and Zimmerman (Ed.): Medical Management of Type 2 Diabetes.

The recommendations included are diagnostic and therapeutic actions that are known or believed to favorably affect health outcomes of patients with diabetes. A grading system (Table 1), developed by the American Diabetes Association (ADA) and modeled after existing methods, was utilized to clarify and codify the evidence that forms the basis for the recommendations. The level of evidence that supports each recommendation is listed after each recommendation using the letters A, B, C, or E.

**CLASSIFICATION, DIAGNOSIS, AND SCREENING**

**Classification**

In 1997, the ADA issued new diagnostic and classification criteria. The classification of diabetes mellitus includes four clinical classes:

- Type 1 diabetes (results from β-cell destruction, usually leading to absolute insulin deficiency).
- Type 2 diabetes (results from a progressive insulin secretory defect on the background of insulin resistance).
- Other specific types of diabetes (due to other causes, e.g., genetic defects in β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas, drug or chemical induced).

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Description</th>
</tr>
</thead>
</table>
| A                 | Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered including:  
• Evidence from a well-conducted multicenter trial  
• Evidence from a meta-analysis that incorporated quality ratings in the analysis  
• Compelling nonexperimental evidence, i.e., “all or none” rule developed by Center for Evidence Based Medicine at Oxford*  
Supportive evidence from well-conducted randomized controlled trials that are adequately powered including:  
• Evidence from a well-conducted trial at one or more institutions  
• Evidence from a meta-analysis that incorporated quality ratings in the analysis  |
| B                 | Supportive evidence from well-conducted cohort studies  
• Evidence from a well-conducted prospective cohort study or registry  
• Evidence from a well-conducted prospective cohort study  
• Evidence from a well-conducted meta-analysis of cohort studies  
Supportive evidence from well-conducted case-control study |
| C                 | Supportive evidence from poorly controlled or uncontrolled studies  
• Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results  
• Evidence from observational studies with high potential for bias (such as case series with comparison to historical controls)  
• Evidence from case series or case reports  |
| D                 | Conflicting evidence with the weight of evidence supporting the recommendation |
| E                 | Expert consensus or clinical experience |

*Either all patients died prior to therapy and at least some survived with therapy, or some patients died without therapy and none died with therapy. Example: use of insulin in the treatment of diabetic ketoacidosis.
Table 2. Criteria for the diagnosis of diabetes*

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Symptoms of diabetes and a casual plasma glucose ≥200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss. OR</td>
</tr>
<tr>
<td>2. FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h. OR</td>
</tr>
<tr>
<td>3. 2-h post-glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization,4 using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.</td>
</tr>
</tbody>
</table>

*In the absence of unequivocal hyperglycemia with acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day. The OGTT is not recommended for routine clinical use, but may be required in the evaluation of patients with IFG (see text) or when diabetes is still suspected despite a normal FPG.

Table 3. Criteria for testing for diabetes in asymptomatic adult individuals

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Testing for diabetes should be considered in all individuals at age 45 years and above, particularly in those with a BMI ≥25 kg/m², and, if normal, it should be repeated at 3-year intervals.</td>
</tr>
<tr>
<td>2. Testing should be considered at a younger age or be carried out more frequently in individuals who are overweight (BMI ≥25 kg/m²) and have additional risk factors:</td>
</tr>
<tr>
<td>• are habitually physically inactive</td>
</tr>
<tr>
<td>• have a first-degree relative with diabetes</td>
</tr>
<tr>
<td>• are members of a high-risk ethnic population (e.g., African-American, Latino, Native American, Asian-American, Pacific Islander)</td>
</tr>
<tr>
<td>• have delivered a baby weighing &gt;9 lb or have been diagnosed with GDM</td>
</tr>
<tr>
<td>• are hypertensive (≥140/90 mmHg)</td>
</tr>
<tr>
<td>• have HDL cholesterol level ≤35 mg/dl (0.90 mmol/l) and/or a triglyceride level ≥250 mg/dl (2.82 mmol/l)</td>
</tr>
<tr>
<td>• have polycystic ovarian syndrome (PCOS)</td>
</tr>
<tr>
<td>• on previous testing, had IGT or IFG</td>
</tr>
<tr>
<td>• have other clinical conditions associated with insulin resistance (e.g., PCOS or acanthosis nigricans)</td>
</tr>
<tr>
<td>• have a history of vascular disease</td>
</tr>
</tbody>
</table>

*May not be correct for all ethnic groups.
Table 4. Testing for type 2 diabetes in children

- Criteria*
  - Overweight (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height)
  - Any two of the following risk factors:
    - Family history of type 2 diabetes in first- or second-degree relative
    - Race/ethnicity (Native American, African-American, Latino, Asian-American, Pacific Islander)
    - Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, or PCOS)
  - Age of initiation: age 10 years or at onset of puberty, if puberty occurs at a younger age
  - Frequency: every 2 years
  - Test: FPG preferred

*Clinical judgment should be used to test for diabetes in high-risk patients who do not meet these criteria.

tional screening by measuring the plasma or serum glucose concentration 1 h after a 50-g oral glucose load (glucose challenge test [GCT]) and perform a diagnostic OGTT on that subset of women exceeding the glucose threshold value on the GCT. When the two-step approach is used, a glucose threshold value ≥140 mg/dl identifies ~80% of women with GDM, and the yield is further increased to 90% by using a cutoff of ≥130 mg/dl.

Diagnostic criteria for the 100-g OGTT is as follows: ≥95 mg/dl fasting, ≥180 mg/dl at 1 h, ≥155 mg/dl at 2 h, and ≥140 mg/dl at 3 h. Two or more of the plasma glucose values must be met or exceeded for a positive diagnosis. The test should be done in the morning after an overnight fast of 8–14 h. The diagnosis can be made using a 75-g glucose load, but that test is not as well validated for detection of at-risk infants or mothers as the 100-g OGTT.

Low risk status requires no glucose testing, but this category is limited to those women meeting all of the following characteristics:
- Age <25 years
- Weight normal before pregnancy
- Member of an ethnic group with a low prevalence of GDM
- No known diabetes in first-degree relatives
- No history of abnormal glucose tolerance
- No history of poor obstetric outcome.

Recommendations
- The FPG is the preferred test to screen for and diagnose diabetes in children and nonpregnant adults. (E)
- Screen for diabetes in high-risk, asymptomatic, undiagnosed adults and children within the health care setting. (E)
- In those with pre-diabetes (IFG/IGT), lifestyle modification should be strongly recommended and progression of glycemic abnormalities followed by screening at least yearly. (A)
- Screen for diabetes in pregnancy using risk factor analysis and screening tests as noted; the OGTT is the preferred screening test in pregnancy. (E)

INITIAL EVALUATION

Glycemic control
Glycemic control is fundamental to the management of diabetes. Prospective randomized clinical trials such as the Diabetes Control and Complications Trial (DCCT)\textsuperscript{13} and the U.K. Prospective Diabetes Study (UKPDS)\textsuperscript{14,15} have shown that improved glycemic control is associated with sustained decreased rates of retinopathy, nephropathy, and neuropathy.\textsuperscript{16} In these trials, treatment regimens that reduced average A1C to ~7% (~1% above the upper limits of normal) were associated with fewer long-term microvascular complications; however, intensive control was found to increase the risk of severe hypoglycemia and weight gain.\textsuperscript{17,18} Epidemiological studies support the potential of intensive glycemic control in the reduction of CVD.\textsuperscript{13,18} Recommended glycemic goals for nonpregnant individuals are shown in Table 6. A major limitation to the available data are that they do not identify the optimum level of control for particular patients, as there are individual differences in the risks of hypoglycemia, weight gain, and other adverse effects. Furthermore, with multifactorial interventions, it is unclear how different components (e.g., educational interventions, glycemic targets, lifestyle changes, and pharmacological agents) contribute to the reduction of complications. There are no clinical trial data available for the effects of glycemic control in patients with advanced complications, the elderly (≥65 years of age), or young children (<13 years of age). Less stringent treatment goals may be appropriate for patients with limited life expectancies, in the very young or older adults, and in individuals with comorbid conditions. Severe or frequent hypoglycemia is an indication for the modification of treatment regimens, including setting higher glycemic goals. More stringent goals can be considered in individual patients based on epidemiological analyses that suggest that there is no lower limit of A1C at which further lowering does not reduce risk of complications. However, the absolute risks and benefits of lower targets are unknown.

Elevated postchallenge (2-h OGTT) glucose values have been associated with increased cardiovascular risk independent of FPG in some epidemiological studies. Postprandial plasma glucose (PPG) levels >140 mg/dl are unusual in nondiabetic individuals, although large evening meals can be followed by plasma glucose values up to 180 mg/dl.
ASSESSMENT OF GLYCEMIC CONTROL

Self-monitoring of blood glucose

The ADA’s consensus statements on SMBG provide a comprehensive review of the subject. Major clinical trials assessing the impact of glycemic control on diabetes complications have included SMBG as part of multifactorial interventions, suggesting that SMBG is a component of effective therapy. SMBG allows patients to evaluate their individual response to therapy and assess if glycemic targets are being achieved. Results of SMBG can be useful in preventing hypoglycemia and adjusting medications, medical nutrition therapy (MNT), and physical activity.

The frequency and timing of SMBG should be dictated by the particular needs and goals of the patients. Daily SMBG is especially important for patients treated with insulin to monitor for and prevent asymptomatic hypoglycemia. For most patients with type 1 diabetes and pregnant women taking insulin, SMBG is recommended three or more times daily. The optimal frequency and timing of SMBG for patients with type 2 diabetes is not known, but should be sufficient to facilitate reaching glucose goals. When adding to or modifying therapy, type 1 and type 2 diabetic patients should test more often than usual. The role of SMBG in stable diet-treated patients with type 2 diabetes is not known.

Because the accuracy of SMBG is instrument- and user-dependent, it is important for health care providers to evaluate each patient’s monitoring technique, both initially and at regular intervals thereafter. In addition, optimal use of SMBG requires proper interpretation of the data. Patients should be taught how to use the data to adjust food intake, exercise, or pharmacological therapy to achieve specific glycemic goals. Health professionals should evaluate at regular intervals the patient’s ability to use SMBG data to guide treatment.

Table 6. Summary of recommendations for adults with diabetes mellitus

<table>
<thead>
<tr>
<th>Glycemic control</th>
<th>A1C &lt;7.0%*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preprandial plasma glucose</td>
<td>90–130 mg/dl (5.0–7.2 mmol/l)</td>
</tr>
<tr>
<td>Peak postprandial plasma glucose</td>
<td>&lt;180 mg/dl (&lt;10.0 mmol/l)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>&lt;100 mg/dl (&lt;2.6 mmol/l)</td>
</tr>
<tr>
<td>Triglycerides†</td>
<td>&lt;150 mg/dl (&lt;1.7 mmol/l)</td>
</tr>
<tr>
<td>HDL</td>
<td>&gt;40 mg/dl (&gt;1.1 mmol/l)‡</td>
</tr>
</tbody>
</table>

Key concepts in setting glycemic goals:

- Goals should be individualized
- Certain populations (children, pregnant women, and elderly) require special considerations
- Less intensive glycemic goals may be indicated in patients with severe or frequent hypoglycemia
- More intensive glycemic goals may further reduce microvascular complications at the cost of increasing hypoglycemia
- Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals

*Referenced to a nondiabetic range of 4.0–6.0% using a DCCT-based assay.
†Current guidelines from the National Cholesterol Education Program Adult Treatment Panel III suggest that in patients with triglycerides ≥200 mg/dl, the “non-HDL cholesterol” (total cholesterol minus HDL) be utilized. The goal is ≤130 mg/dl.‡
‡For women, it has been suggested that the HDL goal be increased by 10 mg/dl.

There are now pharmacological agents that primarily modify PPG and thereby reduce A1C in parallel. Thus, in individuals who have premeal glucose values within target but who are not meeting A1C targets, consideration of monitoring PPG 1–2 h after the start of the meal and treatment aimed at reducing average PPG values <180 mg/dl may lower A1C.

For information on glycemic control for women with GDM, refer to the ADA position statement “Gestational Diabetes Mellitus.” For information on glycemic control during pregnancy in women with preexisting diabetes, refer to Medical Management of Pregnancy Complicated by Diabetes (3rd ed.).

Referral for diabetes management

For a variety of reasons, some people with diabetes and their health care providers do not achieve the desired goals of treatment (Table 6). In such instances, additional actions suggested include enhanced diabetes self-management education, comanagement with a diabetes team, change in pharmacological therapy, initiation of or increase in self-monitoring of blood glucose (SMBG), more frequent contact with the patient, and referral to an endocrinologist.

Recommendations

- Lowering A1C has been associated with a reduction of microvascular and neuropathic complications of diabetes. (A)
- Develop or adjust the management plan to achieve normal or near-normal glycemia with an A1C goal of <7%. (B)
- Lowering A1C may lower the risk of myocardial infarction and cardiovascular death. (B)
- Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness, perioperatively and following myocardial infarction. (B)
- Less stringent treatment goals may be appropriate for patients with a history of severe hypoglycemia, patients with limited life expectancies, very young children or older adults, and individuals with comorbid conditions. (E)
Recommendations

• SMBG is an integral component of diabetes therapy. (B)
• Include SMBG in the management plan. (E)
• Instruct the patient in SMBG and routinely evaluate the patient’s technique and ability to use data to adjust therapy. (E)

A1C

By performing an A1C test, health providers can measure a patient’s average glycemia over the preceding 2–3 months and, thus, assess treatment efficacy. A1C testing should be performed routinely in all patients with diabetes, first to document the degree of glycemic control at initial assessment and then as part of continuing care. Glycemic control is best judged by the combination of the results of the patient’s SMBG testing (as performed) and the current A1C result. The A1C should be used not only to assess the patient’s control over the preceding 2–3 months but also as a check on the accuracy of the meter (or the patient’s self-reported results) and the adequacy of the SMBG testing schedule. Table 7 contains the correlation between A1C levels and mean plasma glucose levels based on data from the DCCT.

Recommendations

• Perform the A1C test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control) and quarterly in patients whose therapy has changed or high-risk individuals.4–6

Table 7. Correlation between A1C level and mean plasma glucose levels

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>Mean plasma glucose (mg/dl)</th>
<th>Mean plasma glucose (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>135</td>
<td>7.5</td>
</tr>
<tr>
<td>7</td>
<td>170</td>
<td>9.5</td>
</tr>
<tr>
<td>8</td>
<td>205</td>
<td>11.5</td>
</tr>
<tr>
<td>9</td>
<td>240</td>
<td>13.5</td>
</tr>
<tr>
<td>10</td>
<td>275</td>
<td>15.5</td>
</tr>
<tr>
<td>11</td>
<td>310</td>
<td>17.5</td>
</tr>
<tr>
<td>12</td>
<td>345</td>
<td>19.5</td>
</tr>
</tbody>
</table>

MEDICAL NUTRITION THERAPY

MNT is an integral component of diabetes management and diabetes self-management education. A review of the evidence and detailed information can be found in the ADA technical review and position statement titled “Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications.”28,29 People with diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT. Goals of MNT that apply to all persons with diabetes are as follows:

• Attain and maintain recommended metabolic outcomes, including glucose and A1C levels; LDL cholesterol, HDL cholesterol and triglyceride levels; blood pressure; and body weight.
• Prevent and treat the chronic complications and comorbidities of diabetes. Modify nutrient intake and lifestyle as appropriate for the prevention and treatment of obesity, dyslipidemia, CVD, hypertension, and nephropathy.
• Improve health through healthy food choices and physical activity.
• Address individual nutritional needs, taking into consideration personal and cultural preferences and lifestyle while respecting the individual’s wishes and willingness to change.

Recommendations

• People with diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT. (B)

PHYSICAL ACTIVITY

ADA technical reviews on exercise in patients with diabetes have summarized the value of exercise in the diabetes management plan.30,31 Regular exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve well-being. Furthermore, regular exercise may prevent type 2 diabetes in high-risk individuals.

Recommendations

• A regular physical activity program, adapted to the presence of complications, is recommended for all patients with diabetes who are capable of participating. (B)

PREVENTION AND MANAGEMENT OF DIABETES COMPLICATIONS

I. CVD: management of risk factors and screening for coronary artery disease

CVD is the major cause of mortality for persons with diabetes. It is also a major contributor to morbidity and direct and indirect costs of diabetes. Type 2 diabetes is an independent risk factor for macrovascular disease, and its common coexisting conditions (e.g., hypertension and dyslipidemia) are also risk factors.

Studies have shown the efficacy of reducing cardiovascular risk factors in preventing or slowing CVD. Evidence is summarized in the following sections and reviewed in detail in the ADA technical reviews on hypertension, dyslipidemia, aspirin therapy, and smoking cessation and in the consensus statement on coronary heart disease (CHD) in people with diabetes.36 Emphasis should be placed on reducing cardiovascular risk factors, when possible, and clinicians should be alert for signs and symptoms of atherosclerosis.

A. Blood pressure control

Hypertension (blood pressure ≥140/90 mmHg) is a common comorbidity of diabetes, affecting 20–60% of people with diabetes, depending on age, obesity, and ethnicity. Hypertension is also a major risk factor for CVD and...
microvascular complications such as retinopathy and nephropathy. In type 1 diabetes, hypertension is often the result of underlying nephropathy. In type 2 diabetes, hypertension is likely to be present as part of the metabolic syndrome (i.e., obesity, hyperglycemia, dyslipidemia) that is accompanied by high rates of CVD.

Randomized clinical trials have demonstrated the incontrovertible benefit of lowering blood pressure to <140 mmHg systolic and <80 mmHg diastolic in persons with diabetes.\(^3^\)\(^7\)\(^3^\) Epidemiologic analyses show that blood pressures >120/80 mmHg are associated with increased cardiovascular event rates and mortality in persons with diabetes.\(^3^\)\(^9\) Therefore, a target blood pressure goal of <130/80 mmHg is reasonable if it can be safely achieved.

Although there are no well-controlled studies of diet and exercise in the treatment of hypertension in persons with diabetes, reducing sodium intake and body weight (when indicated), avoiding excessive alcohol consumption, and increasing activity levels have been shown to be effective in reducing blood pressure in nondiabetic individuals.\(^4^\)\(^0\) These nonpharmacological strategies may also positively affect glycemia and lipid control.

Lowering of blood pressure with regimens based on antihypertensive drugs including angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), \(\beta\)-blockers, diuretics, and calcium channel blockers, has been shown to be effective in lowering cardiovascular events. Several studies suggest that ACE inhibitors may be superior to dihydropyridine calcium channel blockers (DCCBs) in reducing cardiovascular events.\(^4^\)\(^1\)\(^\)\(^2\)

ACE inhibitors have been shown to improve cardiovascular outcomes in high cardiovascular risk patients with or without hypertension.\(^4^\)\(^3\)\(^4\) In patients with congestive heart failure, ACE inhibitors are associated with better outcomes when compared to ARBs. ARBs also improve cardiovascular outcomes in the subset of patients with hypertension, diabetes, and end-organ injury.\(^4^\)\(^5\) The compelling effect of ACE inhibitors or ARBs in patients with albuminuria or renal insufficiency provides additional rationale for use of these agents (see section II below).

The \(\alpha\)-blocker arm of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) was terminated after interim analysis showed that \(\alpha\)-blockers were substantially less effective in reducing congestive heart failure than diuretic therapy.\(^4^\)\(^6\) However, it should be noted that diuretics were not allowed in this arm of the trial.\(^4^\)\(^6\)

Before beginning treatment, patients with elevated blood pressures should have their blood pressure reexamined within 1 month to confirm the presence of hypertension unless the systolic blood pressure is \(\geq 160\) mmHg or the diastolic blood pressure is \(\geq 100\) mmHg, in which case, treatment should be immediately initiated. Patients with hypertension should be seen as often as needed until adequate blood pressure control is obtained and then seen as necessary. In these patients, other cardiovascular risk factors including hyperlipidemia, smoking, urinary albumin excretion (assessed before initiation of treatment), and glycemic control, should be carefully assessed and treated. Many patients will require three or more drugs to reach target goals.

**Recommendations**

**Screening and diagnosis**

- Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure \(\geq 130\) or diastolic blood pressure \(\geq 80\) mmHg should have blood pressure confirmed on a separate day. (E)
- Orthostatic measurement of blood pressure should be performed to assess for the presence of autonomic neuropathy. (E)

**Goals**

- Patients with diabetes should be treated to a systolic blood pressure <130 mmHg. (B)
- Patients with diabetes should be treated to a diastolic blood pressure <80 mmHg. (B)

**Treatment**

- Patients with a systolic blood pressure of 130–139 mmHg or a diastolic blood pressure of 80–89 mmHg should be given lifestyle and behavioral therapy alone for a maximum of 3 months and then, if targets are not achieved, in addition, should be treated pharmacologically. (E)
- Patients with hypertension (systolic blood pressure \(\geq 140\) or diastolic blood pressure \(\geq 90\) mmHg) should receive drug therapy in addition to lifestyle and behavioral therapy. (A)
- Initial drug therapy may be with any drug class currently indicated for the treatment of hypertension. However, some drug classes (ACE inhibitors, \(\beta\)-blockers, and diuretics) have been repeatedly shown to be particularly beneficial in reducing CVD events during the treatment of uncomplicated hypertension and are therefore preferred agents for initial therapy. If ACE inhibitors are not tolerated, ARBs may be used. Additional drugs may be chosen from these classes or another drug class. (A)
- If ACE inhibitors or ARBs are used, monitor renal function and serum potassium levels. (E)
- While there are no adequate head-to-head comparisons of ACE inhibitors and ARBs, there is clinical trial support for each of the following statements:
  - In patients with type 1 diabetes, with or without hypertension, with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A)
  - In patients with type 2 diabetes, hypertension, and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A)
• In those with type 2 diabetes, hypertension, macroalbuminuria (>300 mg/day), nephropathy, or renal insufficiency, an ARB should be strongly considered. (A)

• If one class is not tolerated, the other should be substituted. (A)

• In patients >55 years of age, with hypertension or without hypertension but with another cardiovascular risk factor (history of CVD, dyslipidemia, macroalbuminuria, smoking), an ACE inhibitor (if not contraindicated) should be considered to reduce the risk of cardiovascular events. (A)

• In patients with microalbuminuria or overt nephropathy, in whom ACE inhibitors or ARBs are not well tolerated, a non-DCCB or β-blocker should be considered. (C)

• In patients with a recent myocardial infarction, β-blockers, in addition, should be considered to reduce mortality. (A)

• In elderly hypertensive patients, blood pressure should be lowered gradually to avoid complications. (E)

• Patients not achieving target blood pressure on three drugs, including a diuretic, and/or patients with significant renal disease (see below) should be referred to a specialist experienced in the care of patients with hypertension. (E)

B. Lipid management

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities that contributes to higher rates of CVD. Lipid management aimed at lowering LDL cholesterol, raising HDL cholesterol, and lowering triglycerides has been shown to reduce macrovascular disease and mortality in patients with type 2 diabetes, particularly those who have had prior cardiovascular events.

In three secondary prevention studies using HMG (hydroxymethylglutaryl) CoA reductase inhibitors (statins), patients with diabetes achieved significant reductions in coronary and cerebrovascular events. 47–49 A primary prevention study using statins showed a similar trend of reduced events in the small number of patients with diabetes. 50 In two studies using the fibric acid derivative gemfibrozil, reductions in cardiovascular end points were also achieved. 51,52 In the Helsinki Heart Study, a primary prevention trial, a trend toward significant reductions in CHD events was observed in the small group of subjects with diabetes. 51 In the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT), a secondary trial, a significant reduction in events occurred with improved HDL and triglycerides and no change in LDL cholesterol. 52

Target lipid levels are shown in Table 6. MNT, increased physical activity, and weight loss should allow some patients to reach these lipid levels. Nutrition intervention should be tailored according to each patient’s age, type of diabetes, pharmacological treatment, lipid levels, and other medical conditions and should focus on the reduction of saturated fat, cholesterol, and transunsaturated fat intake. Glycemic control can also beneficially modify plasma lipid levels. In particular, triglycerides may be significantly reduced with optimal glucose lowering.

Pharmacological treatment is indicated if there is an inadequate response to lifestyle modifications and improved glucose control. The first priority of pharmacological therapy is to lower LDL cholesterol to a target goal of <100 mg/dl (2.60 mmol/l). For LDL lowering, statins are the drugs of choice. Statins raise HDL modestly, but a greater increase is usually achieved with fibrates. 53

In patients with LDL between 100 mg/dl (2.60 mmol/l) and 129 mg/dl (3.30 mmol/l), a variety of treatment strategies are available, including more aggressive nutrition intervention and pharmacological treatment with a statin. In addition, if the HDL is <40 mg/dl and the LDL is between 100 and 129 mg/dl, a fibric acid derivative might be used.

Niacin is the most effective drug for raising HDL but can significantly increase blood glucose, particularly at a high dose. 54 More recent studies demonstrate that at modest doses (750–2,000 mg/day), significant benefit with regards to LDL, HDL, and triglyceride levels are accompanied by modest changes in glucose that are generally amenable to adjustment of diabetes therapy. 55

Combination therapy, with a statin and a fibrate or statin and niacin, may be efficacious for patients needing treatment for all three lipid fractions, but this combination is associated with an increased risk for abnormal transaminase levels, myositis, or rhabdomyolysis.

Following the recommendations of the National Cholesterol Education Program’s Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents, LDL cholesterol should be lowered to ≤110 mg/dl (2.80 mmol/l) in children with cardiovascular risk factors in addition to diabetes. 56

Recommendations

General recommendations

• Lowering LDL cholesterol is associated with a reduction in cardiovascular events. (A)

• Lowering triglycerides and increasing HDL cholesterol are associated with a reduction in cardiovascular events. (B)

Goals

• Lower LDL cholesterol to <100 mg/dl (2.6 mmol/l) as the primary goal of therapy for adults. (B)

• Lower triglycerides to <150 mg/dl (1.7 mmol/l) and raise HDL cholesterol to >40 mg/dl (1.15 mmol/l). In women, an HDL goal 10 mg/dl higher may be appropriate. (C)

Screening

• In adult patients, test for lipid disorders at least annually and more often if needed to achieve goals. In adults with low-risk lipid values (LDL <100 mg/dl, HDL >60 mg/dl, triglycerides <150), repeat lipid assessments every 2 years. (E)

• In children >2 years of age, perform a lipid profile after diagnosis of diabetes and when glucose control has been
established. If values are considered low risk and there is no family history, assessments should be repeated every 5 years. (E)

Treatment
• MNT focusing on the reduction of saturated fat and cholesterol intake, weight loss, and increased physical activity has been shown to improve the lipid profile in patients with diabetes. (A)
• Patients who do not achieve lipid goals with lifestyle modifications require pharmacological therapy. (A)
• Statins should be used as first-line pharmacological therapy for LDL lowering. (A)
• Therapy with fibrates in patients with low HDL has been shown to reduce CVD rates and progression of carotid intimal medial progression. (A)
• When prescribing fibrates or niacin, in combination therapy with a statin, care is needed to minimize the risk of adverse effects. (E)

C. Anti-platelet therapy in diabetes
The use of aspirin in diabetes is reviewed in detail in the ADA technical reviews on aspirin therapy. Aspirin blocks thromboxane synthesis by acetylating platelet cyclo-oxygenase and has been used as a primary and secondary therapy to prevent cardiovascular events in diabetic and nondiabetic individuals. One large meta-analysis and several clinical trials demonstrate the efficacy of using aspirin as a preventive measure for cardiovascular events including stroke and myocardial infarction. Many trials have shown an ~30% decrease in myocardial infarction and a 20% decrease in stroke in a wide range of patients, including young and middle-aged patients, patients with and without a history of CVD, males and females, and patients with hypertension.

Dosages used in most clinical trials ranged from 75 to 325 mg/day. There is no evidence for a specific age at which to start aspirin, but at ages below 30 years, when the risk of CVD is low, there is no evidence of benefit of aspirin for primary prevention.

Clopidogrel has been demonstrated to reduce CVD rates in diabetic individuals. Adjunctive therapy in very high-risk patients or as alternative therapy in aspirin-intolerant patients should be considered.

Recommendations
• Use aspirin therapy (75–325 mg/day) in all adult patients with diabetes and macrovascular disease. (A)
• Consider beginning aspirin therapy (75–325 mg/day) for primary prevention in patients ≥40 years of age with diabetes and one or more other cardiovascular risk factors. (A)
• Do not use aspirin in patients <21 years of age because of the increased risk of Reye’s syndrome. (A)
• Consider aspirin therapy for patients between 30 and 40 years of age with other cardiovascular risk factors. (B)

D. Smoking Cessation
Issues of smoking in diabetes are reviewed in detail in the ADA technical review on smoking cessation. A large body of evidence from epidemiological, case-control, and cohort studies provides convincing documentation of the causal link between cigarette smoking and health risks. Studies of individuals with diabetes consistently found a heightened risk of morbidity and premature death associated with the development of macrovascular complications among smokers. Smoking is also related to the premature development of microvascular complications of diabetes and may have a role in the development of type 2 diabetes.

Recommendations
• Advise all patients not to smoke. (A)
• Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care. (B)

E. CHD screening and treatment
CHD screening and treatment are reviewed in detail in the ADA consensus statement on CHD in people with diabetes. To identify the presence of CHD in diabetic patients without clear or suggestive symptoms of coronary artery disease (CAD), a risk factor–based approach to the initial diagnostic evaluation and subsequent follow-up is recommended. At least annually, cardiovascular risk factors should be assessed. These risk factors include dyslipidemia, hypertension, smoking, a positive family history of premature coronary disease, and the presence of micro- or macroalbuminuria. Candidates for screening exercise stress (electrocardiogram [ECG]) include those with 1) typical or atypical cardiac symptoms; 2) an abnormal resting ECG; 3) a history of peripheral or carotid occlusive disease; 4) sedentary lifestyle, age >35 years, and plans to begin a vigorous exercise program; or 5) those with two or more risk factors noted above. There is, however, no current evidence that exercise testing in asymptomatic patients with risk factors improves prognosis. Patients with abnormal exercise ECG and patients unable to perform an exercise ECG require additional or alternative testing. Currently, stress nuclear perfusion and stress echocardiography are valuable next-level diagnostic procedures. A consultation with a cardiologist is recommended regarding further workup.

Recommendations
• Perform exercise stress testing in asymptomatic diabetic patients based on the criteria outlined above. Consider a risk factor–based strategy for the diagnosis of CAD that might include stress ECG and/or stress echocardiography and/or perfusion imaging. (E)
• Refer patients with signs and symptoms of CVD or with positive noninvasive test for CAD to a cardiologist for further evaluation. (E)
• In patients with treated congestive heart failu
heart failure, metformin use is contraindicated. The thiazolidinediones are associated with fluid retention, and their use can be complicated by the development of congestive heart failure. Caution in prescribing thiazolidinediones in the setting of known congestive heart failure or other heart diseases as well as in patients with preexisting edema or concurrent insulin therapy is required. (E)

II. Nephropathy screening and treatment
Diabetic nephropathy occurs in 20–40% of patients with diabetes and is the single leading cause of end-stage renal disease (ESRD). Persistent albuminuria in the range of 30–299 mg/24 h (microalbuminuria) has been shown to be the earliest stage of diabetic nephropathy in type 1 diabetes and a marker for development of nephropathy in type 2 diabetes. Microalbuminuria is also a well-established marker of increased CVD risk.60

While screening for microalbuminuria can be performed by three methods—1) measurement of the albumin-to-creatinine ratio in a random, spot collection; 2) 24-h collection with creatinine, allowing the simultaneous measurement of creatinine clearance; and 3) timed (e.g., 4-h or overnight) collection—the analysis of a spot sample for the albumin-to-creatinine ratio is strongly encouraged.72 The other two alternatives (24-h collection and a timed specimen) are rarely necessary. At least two of three tests measured within a 6-month period should show elevated levels before a patient is designated as having microalbuminuria. Abnormalities of albumin excretion are defined in Table 8.

Physicians may use the Levey modification of the Cockcroft and Gault equation to calculate estimated glomerular filtration rate (eGFR) from serum creatinine and stage the patient’s renal disease.72,73 The eGFR can easily be calculated by going to www.kidney.org/professionals/doi/gfr_calculator.cfm.

The role of annual microalbuminuria assessment is less clear after diagnosis of microalbuminuria and institution of ACE inhibitor or ARB therapy and blood pressure control. Many experts, however, recommend continued surveillance to assess both response to therapy and progression of disease.

For a complete discussion on the treatment of nephropathy, see the ADA’s position statement “Diabetic Nephropathy.”75

Recommendations

General recommendations
- To reduce the risk and/or slow the progression of nephropathy, optimize glucose control. (A)
- To reduce the risk and/or slow the progression of nephropathy, optimize blood pressure control. (A)

Screening
- Perform an annual test for the presence of microalbuminuria in type 1 diabetic patients with diabetes duration of $\geq$ 5 years and in all type 2 diabetic patients, starting at diagnosis. (E)

Treatment
- In the treatment of both micro- and macroalbuminuria, either ACE inhibitors or ARBs should be used. (A)
- While there are no adequate head-to-head comparisons of ACE inhibitors and ARBs, there is clinical trial support for each of the following statements:
  - In patients with type 1 diabetes, with or without hypertension, with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A)
  - In patients with type 2 diabetes, hypertension, and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A)
  - In patients with type 2 diabetes, hypertension, macroalbuminuria, and renal insufficiency (serum creatinine $>1.5$ mg/dl), ARBs have been shown to delay the progression of nephropathy. (A)
  - If one class is not tolerated, the other should be substituted. (E)

- With presence of nephropathy, initiate protein restriction to $\leq 0.8$ g · kg$^{-1}$ · day$^{-1}$ (~10% of daily calories), the current adult recommended dietary allowance for protein. Further restriction may be useful in slowing the decline of GFR in selected patients. (B)
- Use of DCCBs is less effective in slowing nephropathy progression compared with ARB therapy in those with diabetes with nephropathy and macroalbuminuria. (B)
- Consider the use of non-DCCBs or β-blockers in patients unable to tolerate ACE inhibitors and/or ARBs. (E)
- If ACE inhibitors or ARBs are used, monitor serum potassium levels for the development of hyperkalemia. (B)
- Consider referral to a physician experienced in the care of diabetic renal disease when the eGFR has fallen to $<60$ ml · min$^{-1}$ · 1.73 m$^{-2}$, or if difficulties occur in the management of hypertension or hyperkalemia. (B)

III. Diabetic retinopathy screening and treatment
Diabetic retinopathy is estimated to be the most frequent cause of new cases of...

**Table 8. Definitions of abnormalities in albumin excretion**

<table>
<thead>
<tr>
<th>Category</th>
<th>Spot collection (µg/mg creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>$&lt;$30</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>$30–299$</td>
</tr>
<tr>
<td>Macro (clinical) albuminuria</td>
<td>$\geq$300</td>
</tr>
</tbody>
</table>

Because of variability in urinary albumin excretion, two of three specimens collected within a 3- to 6-month period should be abnormal before considering a patient to have crossed one of these diagnostic thresholds. Exercise within 24 h, infection, fever, congestive heart failure, marked hyperglycemia, and marked hypertension may elevate urinary albumin excretion over baseline values.
blindness among adults aged 20–74 years.

For a detailed review of the evidence and further discussion, see the ADA’s technical review and position statement on this subject.76,90

Recommendations

General Recommendations

- Optimal glycemic control can substantially reduce the risk and progression of diabetic retinopathy. (A)
- Optimal blood pressure control can reduce the risk and progression of diabetic retinopathy. (A)
- Aspirin therapy does not prevent retinopathy or increase the risks of hemorrhage. (A)

Screening

- Patients with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 3–5 years after the onset of diabetes. (B)
- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes. (B)
- Subsequent examinations for type 1 and type 2 diabetic patients should be repeated annually by an ophthalmologist or optometrist who is knowledgeable and experienced in diagnosing the presence of diabetic retinopathy and is aware of its management. Examinations will be required more frequently if retinopathy is progressing. (B)
- When planning pregnancy, women with preexisting diabetes should have a comprehensive eye examination and should be counseled on the risk of development and/or progression of diabetic retinopathy. Women with diabetes who become pregnant should have a comprehensive eye examination in the first trimester and close follow-up throughout pregnancy and for 1 year postpartum. This guideline does not apply to women who develop GDM because such individuals are not at increased risk for diabetic retinopathy. (B)

Treatment

- Laser therapy can reduce the risk of vision loss in patients with high-risk characteristics. (A)
- Promptly refer patients with any level of macular edema, severe nonproliferative diabetic retinopathy, or any proliferative diabetic retinopathy to an ophthalmologist who is knowledgeable and experienced in the management and treatment of diabetic retinopathy. (A)

IV. Foot care

Amputation and foot ulceration are one of the most common consequences of diabetic neuropathy and a major cause of morbidity and disability in people with diabetes. Early recognition and management of independent risk factors can prevent or delay adverse outcomes.

The risk of ulcers or amputations is increased in people who have had diabetes >10 years, are male, have poor glucose control, or have cardiovascular, retinal, or renal complications. The following foot-related risk conditions are associated with an increased risk of amputation:

- Peripheral neuropathy with loss of protective sensation
- Altered biomechanics (in the presence of neuropathy)
- Evidence of increased pressure (erythema, hemorrhage under a callus)
- Bony deformity
- Peripheral vascular disease (decreased or absent pedal pulses)
- A history of ulcers or amputation
- Severe nail pathology.

For a detailed review of the evidence and further discussion, see the ADA’s technical review and position statement titled “Preventive Foot Care in Persons With Diabetes,”91,92

Recommendations

- A multidisciplinary approach is recommended for persons with foot ulcers and high-risk feet, especially those with a history of prior ulcer or amputation. (A)
- The foot examination can be accomplished in a primary care setting and should include the use of a Semmes-Weinstein monofilament, tuning fork, palpation, and a visual examination. (B)
- Educate all patients, especially those with risk factors or prior lower-extremity complications, about the risk and prevention of foot problems and reinforce self-care behavior. (B)
- Refer high-risk patients to foot care specialists for ongoing preventive care and life-long surveillance. (C)
- Refer patients with significant claudication for further vascular assessment and consider exercise and surgical options. (C)
- Perform a comprehensive foot examination annually on patients with diabetes to identify risk factors predictive of ulcers and amputations. Perform a visual inspection of patients’ feet at each routine visit. (E)

PREVENTIVE CARE

I. Preconception care

Overwhelming evidence supports the concept that malformations can be reduced or prevented by careful management of diabetes before pregnancy.

The goals of preconception care are to 1) integrate the patient into the management of her diabetes, 2) achieve the lowest A1C test results possible without excessive hypoglycemia, 3) assure effective contraception until stable and acceptable glycemia is achieved, and 4) identify, evaluate, and treat long-term diabetic complications such as retinopathy, nephropathy, neuropathy, hypertension, and CAD.

For further discussion, see the ADA’s technical review and position statement on this subject.99,100

Recommendations

- A1C levels should be normal or as close to normal as possible in an indi-
Individual patient before conception is attempted. (B)

• ACE inhibitors should be discontinued before pregnancy. (C)

• All women with diabetes and childbearing potential should be educated about the need for good glucose control before pregnancy. They should participate in family planning. (E)

• Women with diabetes who are contemplating pregnancy should be evaluated and, if indicated, treated for diabetic retinopathy, nephropathy, neuropathy, and CVD. (E)

• Among the drugs commonly used in the treatment of patients with diabetes, statins are pregnancy category X and should be discontinued prior to conception if possible. ACE inhibitors and ARBs are category C in the first trimester (maternal benefit may outweigh the fetal risk in certain situations), but category D in later pregnancy, and should generally be discontinued prior to pregnancy. Among the oral antidiabetic agents, metformin and acarbose are classified as category B and all others as category C; potential risks and benefits of oral antidiabetic agents in the preconception period must be carefully weighed, recognizing that sufficient data are not available to establish the safety of these agents in pregnancy. They should generally be discontinued in pregnancy. (E)

II. Immunization

Influenza and pneumonia are common, preventable infectious diseases associated with high mortality and morbidity in the elderly and in people with chronic diseases. The Centers for Disease Control’s Advisory Committee on Immunization Practices recommends influenza and pneumococcal vaccines for all persons over 65 years of age as well as for all persons of any age with diabetes.

For a complete discussion on the prevention of influenza and pneumococcal disease in people with diabetes, consult the technical review and position statement on this subject.104,105

Recommendations

• Annually provide an influenza vaccine to all diabetic patients 6 months of age or older. (C)

• Provide at least one lifetime pneumococcal vaccine for adults with diabetes. A one-time revaccination is recommended for individuals >64 years of age previously immunized when they were <65 years of age if the vaccine was administered >5 years ago. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and other immunocompromised states, such as postorgan transplantation. (C)

SPECIAL CONSIDERATIONS

I. Care of older adults with diabetes

Diabetes is an important health condition for the aging population; at least 15% of patients over the age of 65 years have diabetes. The number of older persons with diabetes can be expected to grow rapidly over the coming decades. Unfortunately, there are no long-term studies demonstrating the benefits of tight glycemic control in persons over 65 years of age. In approaching the elderly patient, a thoughtful individualized approach, consistent with the heterogeneity of the aging process, should be used. However, patients who can be expected to live long enough to reap the benefits of long-term glycemic control (10–20 years) and who are active, cognitively intact, and willing to undertake the responsibility of self-management should be encouraged to do so.

Older patients can be treated with the same drug regimens as younger patients, but special care is required in prescribing and monitoring drug therapy. Metformin is often contraindicated because of renal insufficiency or heart failure. Sulfonylureas and other insulin secretagogues can cause hypoglycemia. Insulin can also cause hypoglycemia as well as requiring good visual and motor skills and cognitive ability of the patient or a caregiver. Thiazolidinediones should not be used in patients with congestive heart failure (New York Heart Association Class III and IV). α-Glucosidase inhibitors are safe but may not be well tolerated and may not be effective as monotherapy. Drugs should be started at the lowest dose and titrated up gradually until targets are reached or side effects develop.

Cardiovascular risk reduction continues to be important as in younger patients; there is strong evidence from clinical trials of the value of treating hypertension in the elderly. There is less evidence for lipid-lowering and aspirin therapy, although diabetes patients have such an elevated risk for CVD that aggressive management of lipids and aspirin use when not contraindicated are probably reasonable interventions.

II. Children and adolescents

Approximately three-quarters of all newly diagnosed cases of type 1 diabetes occur in individuals younger than 18 years. Care of this group requires integration of diabetes management with the complicated physical and emotional growth needs of children, adolescents, and their families.

The incidence of type 2 diabetes in children and adolescents has been shown to be increasing. Although there are insufficient data to make definite recommendations, a recent ADA consensus statement provides guidance to the prevention, screening, and treatment of type 2 diabetes in young people. For further discussion, see the ADA consensus statement “Type 2 Diabetes in Children and Adolescents.”

Information should be supplied to the school or day care setting so that school personnel are aware of the diagnosis of diabetes in the student and of the signs, symptoms, and treatment of hypoglycemia.

For further discussion, see the ADA’s position statement “The Care of Children With Diabetes in the School and Day Care Setting.”