Reducing Cardiovascular Disease Risk in Patients with Type 2 Diabetes: A Message from the National Diabetes Education Program

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Although cardiovascular disease accounts for 65 percent of deaths in persons with type 2 diabetes, patients’ awareness of cardiovascular disease risk factors remains low. Opportunities to modify risks for coronary events, strokes, and other patient-oriented clinical outcomes often are missed. To improve outcomes among the 17 million Americans with diabetes, the National Diabetes Education Program (NDEP) has begun a campaign promoting the “ABCs” of diabetes care: A1C level, Blood pressure, and Cholesterol level. By increasing patient awareness of the link between diabetes and heart disease, family physicians can encourage patients to take medications (including aspirin), stop smoking, lower blood pressure, and lower cholesterol and blood glucose levels. (Am Fam Physician 2003;68:1569-74,1577-8. Copyright© 2003 American Academy of Family Physicians.)

A patient information handout on cardiovascular disease and diabetes, adapted from the National Diabetes Education Program, is available on page 1577.

See page 1461 for definitions of strength-of-evidence levels.

See editorial on page 1500.

Scope of the Problem

Approximately 4.2 percent of the U.S. population has diabetes. However, this statistic understates the true prevalence of the disease because another 2 percent of the population likely has undiagnosed diabetes. Unfortunately, type 2 diabetes is becoming even more common. Between 1990 and 1998, the age-adjusted prevalence rose by 33 percent, and in persons aged 30 to 39, the prevalence rose by 76 percent. Currently, 20.1 percent of persons age 65 or older have type 2 diabetes. This new epidemic disproportionately affects racial and ethnic minority populations; 13 percent of non-Hispanic black adults, 10.2 percent of Hispanic/Latino–American adults, and 15.1 percent of American Indian and native Alaskan adults have type 2 diabetes.

The disease is characterized by insulin resistance and is commonly associated with the “metabolic syndrome” of central obesity, high levels of free fatty acids, high triglyceride levels, high low-density lipoprotein (LDL) levels, low high-density lipoprotein (HDL) levels, and hypertension. These factors substantially increase the risk for atherosclerosis. However, the increased cardiovascular disease risk in
patients with diabetes is independent of body mass index or blood pressure.9

Over the past 30 years, there has been a 27 percent decrease in age-adjusted heart disease mortality in women without diabetes. In contrast, women with diabetes had a 23 percent increase.10 Men and women with type 2 diabetes have the same risk for a coronary event as persons without diabetes who have already had such an event.11

Persons with diabetes and hypertension also have a greater risk for cerebrovascular disease, stroke, and chronic heart failure. Smokers with hypertension and diabetes have a three-fold increase in the prevalence of peripheral vascular disease and a 3.5-fold increase in cerebrovascular disease.12,13

**Rationale for Risk Reduction**

Intensive treatment of diabetes can reduce substantially the risk for developing complications14,15 (Table 1).16-20 Improving blood glucose levels and lowering blood pressure can reduce the frequency of microvascular complications such as blindness, amputation, and end-stage renal disease. The United Kingdom Prospective Diabetes Study (UKPDS) found that lowering the A1c level by a mean of 0.9 percent for a median follow-up of 10 years after diagnosis of type 2 diabetes was associated with relative risk reduction of 12 percent for any diabetes-related end point (P = .029), 25 percent for microvascular end points (P = .0099), 16 percent for myocardial infarction (P = .052), 24 percent for cataract extraction (P = .046), 21 percent for retinopathy at 12 years (P = .015), and 33 percent for albuminuria at 12 years (P = .000054). Epidemiologic evaluation of the same data suggests that greater reductions may be possible.16 [Evidence level B, observational study]

Blood pressure reduction has a similar and larger effect on clinical outcomes. In the UKPDS, tight blood pressure control (144/82 mm Hg [n = 758] compared with an average blood pressure of 154/87 mm Hg [n = 390]) reduced the relative risk for any diabetes-related end point by 24 percent (P = .0046), diabetes-related deaths by 32 percent (P = .019), stroke by 44 percent (P = .013), microvascular disease by 37 percent (P = .0092), heart failure by 56 percent (P = .0043), retinopathy progression by 34 percent (P = .0038), and deterioration of vision by 47 percent (P = .0036) after nine years.17 [Evidence level A, randomized controlled trial (RCT)]

The Hypertension Optimal Treatment study18 randomized patients to three diastolic treatment goals: 80, 85, and 90 mm Hg. Patients with hypertension who did not have diabetes had similar rates of cardiovascular events at all three blood pressures. However, the 1,500 patients with diabetes had a 51 percent reduction in cardiovascular events, including myocardial infarction and cardiovascular death, at 80 mm Hg compared with 90 mm Hg. Patients with a goal of 80 mm Hg also did significantly better than patients with a goal of 85 mm Hg, suggesting that a small improvement in blood pressure can yield a big improvement in health. These findings led to a lower recommended blood pressure (130/80 mm Hg) level in patients with diabetes than the
level recommended for nondiabetic patients with high blood pressure.21

Findings from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial22 indicate that in diabetic and nondiabetic study participants, a thiazide diuretic was superior to an angiotensin-converting enzyme (ACE) inhibitor for several cardiovascular disease outcomes and superior to a calcium channel blocker for preventing development of heart failure. In patients with type 2 diabetes, ACE inhibitors provide substantial benefits,21 including a 25 to 30 percent reduced risk for heart attack, stroke, or cardiovascular death; markedly lower rates of stroke, fatal and nonfatal myocardial infarction, and other cardiovascular deaths; and prevention of nephropathy progression.23 Beta blockers and ACE inhibitors have been shown to reduce mortality and risk for a second heart attack in patients with diabetes.24

Persons with diabetes commonly have elevated triglyceride levels, reduced HDL levels, and an LDL fraction with a greater proportion of small, dense, atherogenic LDL particles.25 The National Cholesterol Education Program recommends that all patients with type 2 diabetes lower their LDL cholesterol level below 100 mg per dL (2.6 mmol per L), whether or not they have heart disease.26

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[Evidence level C, consensus/expert guidelines] Studies using 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) clearly have shown that rigorous lipid reduction therapy can reduce the risk for cardiovascular disease in persons with diabetes.27-29 Statins can lower cholesterol levels significantly and reduce the incidence of stroke, coronary artery disease, and cardiovascular mortality.30,31 Fibrates can lower triglyceride levels and increase HDL cholesterol lev-

### TABLE 1
Summary of Diabetes Risk-Reduction Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Measure evaluated</th>
<th>Relative risk reduction in eye disease</th>
<th>Relative risk reduction in kidney disease</th>
<th>Relative risk reduction in cardiovascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK Prospective Diabetes Study16,17</td>
<td>A1c reduction of 0.9% Blood pressure of 144/82 mm Hg compared with average blood pressure of 154/87 mm Hg</td>
<td>Retinopathy, 21% Cataract extraction, 24% Retinopathy progression, 34% Vision deterioration, 47%</td>
<td>Albuminuria, 33% N/A</td>
<td>Myocardial infarction, 16% Stroke, 44% Heart failure, 56%</td>
</tr>
<tr>
<td>Hypertension Optimal Treatment Study18</td>
<td>Diastolic treatment goal: 80 mm Hg Ramipril in patients with diabetes</td>
<td>N/A</td>
<td>N/A</td>
<td>Cardiovascular events, 51% Stroke, myocardial infarction, or cardiovascular death, 25 to 30% Cardiovascular death, 48%</td>
</tr>
<tr>
<td>Heart Outcomes Prevention Evaluation Study19</td>
<td>Captopril in patients with diabetes</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Captopril Prevention Project20</td>
<td>Captopril in patients with diabetes</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

Information from references 16 through 20.
However, the foundation of any treatment should be appropriate lifestyle changes. Daily aspirin intake reduced vascular events by about 25 percent in patients who had previous myocardial infarction, stroke, transient ischemic attack, or cardiovascular disease; patients with diabetes had risk reductions comparable to those of nondiabetic patients. About 38 vascular events per 1,000 diabetic patients (standard deviation, 12) would be prevented if patients were treated with aspirin as a secondary prevention strategy.

**Action Plan to Treat Risk Factors**

A proactive management plan should include patient-centered goals for controlling hypertension, lipid levels, and glycemia (*Table 2*). Risk-factor reduction that involves the patient in therapeutic decision-making, self-management to control risk factors, monitoring treatment effectiveness, and maintaining lifestyle changes can improve outcomes. The involvement of nurses, dietitians, and other such team members enables this approach. Optimal control of blood glucose levels, lipid levels, and blood pressure usually requires regular physical activity and a diet designed to reduce sodium intake, alter lipid patterns, lower blood glucose levels, and induce weight loss. Drug therapy is indicated if the response to altered diet and exercise is inadequate.

Several types of glucose-lowering drugs are available: insulin secretagogues (e.g., sulfonylureas, benzoic acid, D-phenylalanine); inhibitors of hepatic glucose production and insulin sensitizers (e.g., metformin [Glucomet], glitazones); drugs that delay glucose absorption; and glucagon-like peptide 1 (GLP-1) receptor agonists. Each type of drug targets different metabolic pathways to achieve glucose control.

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**Table 2**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Goal</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycemia</td>
<td>(\text{HbA1c} &lt; 7) percent, preprandial plasma glucose level 90 to 130 mg per dL (5 to 7.2 mmol per L), or postprandial plasma glucose level &lt; 180 mg per dL (10 mmol per L)</td>
<td>Diet, exercise, oral medications, insulin</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Blood pressure (\leq 130/80) mm Hg</td>
<td>Diet, exercise, thiazide diuretics, ACE inhibitors, other antihypertensives as needed to reach goal blood pressure</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>LDL cholesterol (\leq 100) mg per dL (2.6 mmol per L); HDL cholesterol &gt; 40 mg per dL (1 mmol per L) in men, &gt; 50 mg per dL (1.3 mmol per L) in women; triglycerides &lt; 150 mg per dL (1.7 mmol per L)</td>
<td>Diet, exercise, cholesterol-lowering medications</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>Smoking cessation</td>
<td>Physician counseling, smoking cessation programs, medications</td>
</tr>
<tr>
<td>Vascular events</td>
<td>Prevention</td>
<td>Diet, exercise, daily aspirin, glucose control, blood pressure control, ACE inhibitors, beta blocker after MI</td>
</tr>
<tr>
<td>Obesity</td>
<td>Reduced BMI</td>
<td>Diet, exercise, medications, obesity surgery</td>
</tr>
</tbody>
</table>

ACE = angiotensin-converting enzyme, LDL = low-density lipoprotein, HDL = high-density lipoprotein, MI = myocardial infarction, BMI = body mass index.
absorption (e.g., acarbose [Precose], miglitol [Glycet], voglibose [not currently available in the United States]); and insulin.

A1c values should be used to monitor blood glucose levels and guide therapy toward target levels. Lipid-lowering therapy should be considered in patients with diabetes and dyslipidemia, particularly in those with coronary artery disease. Thiazide diuretics provide effective drug therapy for hypertension.22 ACE inhibitors can prevent or delay diabetes-associated renal and cardiovascular disease.13,23 Smoking cessation and aspirin therapy also are important variables that contribute to risk reduction.

Final Comment

In focus groups conducted throughout the United States, participants with diabetes demonstrated a significant lack of awareness of the link between diabetes and cardiovascular disease.2 In a national survey of 2,008 patients with diagnosed diabetes, 68 percent did not consider cardiovascular disease to be a serious complication, 52 percent did not consider themselves at risk for heart attack or stroke, and 60 percent did not consider themselves at risk for high cholesterol levels or high blood pressure. Few respondents could name methods of reducing their risk for heart attack or stroke, such as taking prescription medications (18 percent), lowering cholesterol levels (8 percent), smoking cessation (7 percent), reducing blood pressure (5 percent), and taking aspirin (1 percent).1

To address this lack of awareness, the NDEP has enlisted the support of the American Academy of Family Physicians and other key organizations to help bring about improvements in the key areas addressed in its campaign. For information about “Be Smart About Your Heart: Control the ABCs of Diabetes—A1c, Blood Pressure and Cholesterol,” visit the NDEP Web site (www.ndep.nih.gov).

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