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

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Cardiovascular disease is responsible for 65 percent of deaths in persons with type 2 diabetes. However, awareness of cardiovascular disease risk factors among patients with diabetes remains low, resulting in missed opportunities to lower risks for coronary events and strokes. The National Diabetes Education Program has begun a campaign to increase patient participation in risk-reduction practice s by promoting the "ABCs" of diabetes care: A_{1c} level, *B*lood pressure, and *C*holesterol 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.

Although cardiovascular disease accounts for 65 percent of deaths in persons with type 2 diabetes,[1] 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.[2,3] 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: A_{1c} level, *B*lood pressure, and *C*holesterol level.

NDEP is jointly sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases and the Centers for Disease Control and Prevention; NDEP works in partnership with more than 200 professional and consumer organizations. Its goal is to reduce the morbidity and mortality associated with diabetes and its complications. NDEP views family physicians as crucial partners because 80 percent of patients with diabetes are treated by primary care physicians.[4]

ACF *This article exemplifies the AAFP 2003 Annual Clinical Focus on prevention and health promotion.*

> **See editorial on page 1500.**

Scope of the Problem

Approximately 4.2 percent of the U.S. population has diabetes.[1] However, this statistic understates the true prevalence of the disease because another 2 percent of the population likely has undiagnosed diabetes.[5] 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.[6] Currently, 20.1 percent of persons age 65 or older have type 2 diabetes.[7] 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.[7]

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.[8] 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 complications[14,15] (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 A_{1c} 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 study[18] 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

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level recommended for nondiabetic patients with high blood pressure.[21]

Findings from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial[22] 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[19]; markedly lower rates of stroke, fatal and nonfatal myocardial infarction, and other cardiovascular deaths[20]; 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] [Evidence level A, RCT]

Persons with diabetes commonly have elevated triglyceride levels, reduced HDL levels,

> *Intensive treatment of diabetes can reduce substantially the risk for developing complications.*

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] [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

Trial	Measure evaluated	Relative risk reduction in eye disease	Relative risk reduction in kidney disease	Relative risk reduction in cardiovascular disease
UK Prospective Diabetes Study[16,17]	A_{1C} reduction of 0.9% Blood pressure of 144/82 mm Hg compared with average blood pressure of 154/87 mm Hg	Retinopathy, 21% Cataract extraction, 24% Retinopathy progression, 34 Vision deterioration, 47%	Albuminuria, 33% N/A	Myocardial infarction, 16% Stroke, 44% Heart failure, 56%
Hypertension Optimal Treatment Study[18]	Diastolic treatment goal: 80 mm Hg	N/A	N/A	Cardiovascular events, 51%
Heart Outcomes Prevention Evaluation Study[19]	Ramipril in patients with diabetes	N/A	N/A	Stroke, myocardial infarction, or cardiovascular death, 25 to 30%
Captopril Prevention Project[20]	Captopril in patients with diabetes	N/A	N/A	Cardiovascular death, 48%

Information from references 16 through 20.

TABLE 2
Interventions to Reduce Cardiovascular Events

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

ACE = angiotensin-converting enzyme, LDL = low-density lipoprotein, HDL = high-density lipoprotein, MI = myocardial infarction, BMI = body mass index.

els.[12] 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.[32] 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)*.[33] 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 [Glucophage], glitazones); drugs that delay glucose

absorption (e.g., acarbose [Precose], miglitol [Glycet], voglibose [not currently available in the United States]); and insulin.

A_{1c} 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).[3]

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—A_{1c}, *B*lood Pressure and *C*holesterol," visit the NDEP Web site (www.ndep.nih.gov).

REFERENCES

1. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Diabetes Public Health Resource. Statistics: Diabetes Surveillance, 1999. Accessed August, 2003 at: www.cdc.gov/diabetes/statistics/survl99/chap5/figure1.htm.
2. Hager Sharp Inc. Comprehensive Care Campaign: formative research with primary care providers and people with diabetes. Washington, D.C.: Hager Sharp Inc., 2001.
3. Merz CN, Buse JB, Tuncer D, Twillman GB. Physician attitudes and practices and patient awareness of the cardiovascular complications of diabetes. J Am Coll Cardiol 2002;40:1877-81.
4. Hiss RG, Greenfield S. Forum Three: Changes in the U.S. health care system that would facilitate improved care for non-insulin-dependent diabetes mellitus. Ann Intern Med 1996;124:180-3.
5. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998;21:518-24.
6. Mokdad AH, Ford ES, Bowman BA, Nelson DE, Engelgau MM, Vinicor F, et al. Diabetes trends in the U.S.: 1990-1998. Diabetes Care 2000;23:1278-83.
7. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Diabetes Public Health Resource. Prevalence of diabetes among people aged 20 years or older. Accessed August, 2003 at: www.cdc.gov/diabetes/pubs/estimates.htm#prev3.
8. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 1988;37:1595-607.
9. Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Lee ET, Welty TK, et al. Impact of diabetes on cardiac structure and function: the strong heart study. Circulation 2000;101:2271-6.
10. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA 1999;281:1291-7.
11. Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, Howard BV, et al. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation 1999;100:1134-46.
12. Papademetriou V, Narayan P, Rubins H, Collins D, Robins S. Influence of risk factors on peripheral and cerebrovascular disease in men with coronary artery disease, low high-density lipoprotein cholesterol levels, and desirable low-density lipoprotein cholesterol levels. HIT Investigators. Department of Veterans Affairs HDL Intervention Trial. Am Heart J 1998;136:734-40.
13. Folsom AR, Szklo M, Stevens J, Liao F, Smith R, Eckfeldt JH. A prospective study of coronary heart disease in relation to fasting insulin, glucose, and dia-

betes. The Atherosclerosis Risk in Communities (ARIC) Study. Diabetes Care 1997;20:935-42.

14. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977-86.

15. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352:837-53.

16. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405-12.

17. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ 1998;317:703-13.

18. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998; 351:1755-62.

19. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and the MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000;355:253-9.

20. Niskanen L, Hedner T, Hansson L, Lanke J, Niklason A, CAPPP Study Group. Reduced cardiovascular morbidity and mortality in hypertensive diabetic patients on first-line therapy with an ACE inhibitor compared with a diuretic/beta-blocker–based treatment regimen: a subanalysis of the Captopril Prevention Project. Diabetes Care 2001;24:2091-6.

21. American Diabetes Association. Treatment of hypertension in adults with diabetes. Diabetes Care 2003;26(suppl):S80-2.

22. Appel LJ. The verdict from ALLHAT—thiazide diuretics are the preferred initial therapy for hypertension. JAMA 2002;288:3039-42.

23. Nielsen FS, Rossing P, Gall MA, Skott P, Smidt UM, Parving HH. Impact of lisinopril and atenolol on kidney function in hypertensive NIDDM subjects with diabetic nephropathy. Diabetes 1994;43: 1108-13.

24. Brenner BM, Cooper ME, de Zeeuw D, Keane WF,

Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001;345:861-9.

25. American Diabetes Association. Management of dyslipidemia in adults with diabetes. Diabetes Care 2000;23(Suppl 1):S57-60.

26. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.

27. Goldberg RB, Mellies MJ, Sacks FM, Moye LA, Howard BV, Howard WJ, et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent events (CARE) trial. The Care Investigators. Circulation 1998;98:2513-9.

28. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 1996;335:1001-9.

29. Haffner SM, Alexander CM, Cook TJ, Boccuzzi SJ, Musliner TA, Pedersen TR, et al. Reduced coronary events in simvastatin-treated patients with coronary heart disease and diabetes or impaired fasting glucose levels: subgroup analyses in the Scandinavian Simvastatin Survival Study. Arch Intern Med 1999;159:2661-7.

30. Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). BMJ 1998;316:823-8.

31. Laakso M, Lehto S, Penttila I, Pyorala K. Lipids and lipoproteins predicting coronary heart disease mortality and morbidity in patients with non-insulin-dependent diabetes. Circulation 1993;88:1421-30.

32. Collaborative overview of randomised trials of antiplatelet therapy—I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ 1994;308:81-106.

33. Abbate SL. Expanded ABCs of diabetes. Clin Diabetes 2003;21:128-33.