# ACE/AACE CONSENSUS CONFERENCE ON THE IMPLEMENTATION OF OUTPATIENT MANAGEMENT OF DIABETES MELLITUS: CONSENSUS CONFERENCE RECOMMENDATIONS

*ACE/AACE Diabetes Recommendations Implementation Writing Committee:*

*Harold E. Lebovitz, MD, FACE, Chair,*
*Mary M. Austin, MA, RD, CDE, Lawrence Blonde, MD, FACP, FACE,*
*Jaime A. Davidson, MD, FACE, Stefano Del Prato, MD,*
*James R. Gavin III, MD, PhD, Yehuda Handelsman, MD, FACP, FACE,*
*Paul S. Jellinger, MD, MACE, Philip Levy, MD, FACE,*
*Matthew C. Riddle, MD, FACE, Victor L. Roberts, MD, MBA, FACP, CDE, FACE,*
*and Linda M. Siminerio, RN, PhD, CDE*

**Abbreviations:**
**AACE** = American Association of Clinical Endocrinologists; **A1C** = hemoglobin A1c; **ACE** = American College of Endocrinology; **DCCT** = Diabetes Control and Complications Trial; **EDIC** = Epidemiology of Diabetes Interventions and Complications; **IGT** = impaired glucose tolerance; **IMT** = intima-media thickness; **SMBG** = self-monitoring of blood glucose

## INTRODUCTION

Among the more than 20 million Americans who have diabetes, approximately 30% of the cases are undiagnosed (1). An additional 42 million people in the United States have pre-diabetes (impaired glucose tolerance [IGT], impaired fasting glucose, or both), a condition that often leads to diabetes if it is not treated (1).

The dramatic 41% increase in prevalence of diabetes during the 1990s was characterized by a shift to a younger age at onset. The prevalence of diabetes increased more than 70% in the age-group 30 to 39 years (1).

The longer the duration of poorly controlled diabetes, the greater the risk for development of vascular complications, including retinopathy, end-stage kidney disease, neuropathy, and coronary artery disease. These complications are not only debilitating but also expensive. In 2002, health-care costs for diabetes in the United States surpassed $132 billion (1). These costs were primarily related to the treatment and consequences of complications of diabetes (2).



Several large prospective studies have shown that intensive treatment of diabetes can decrease the chronic complications associated with this disease (3-6). There seems to be no glycemic threshold for reduction of complications; the lower the hemoglobin A1c (A1C) level, the lower the rate of occurrence of diabetes-related complications (7).

Advances in pharmacologic therapies and new treatment technologies can facilitate reduction of blood glucose values in patients with diabetes to near-normal and achieve glycemic goal levels recommended in current practice guidelines. Nevertheless, the management of patients with diabetes in the United States has actually worsened during the past decade (8). Data from the National Health and Nutrition Examination Survey III in 1994 showed that only 44% of patients with type 2 diabetes achieved an A1C level of less than 7% (9). By the year 2000, this proportion actually decreased to 37% (10). Recently, at an American Association of Clinical Endocrinologists (AACE) meeting, a report on the state of diabetes health showed that, in a study of 157,000 Americans in 39 states, two-thirds of the subjects with type 2 diabetes had A1C values above the American College of Endocrinology (ACE) goal for glycemic control of 6.5% or less (American College of Endocrinology/American Association of Clinical Endocrinologists. State of Diabetes in America: Striving for Better Control. Available at: http://www.aace.com/pub/StateofDiabetes/stateofdiabetes.php). Clearly, more aggressive and comprehensive application of these available treatment options, supported by diabetes education, is needed.

On January 31, 2005, ACE and AACE convened a 2-day consensus conference to review current research and address questions relevant to the treatment of diabetes. The conference brought together US and international diabetes researchers, clinical and educational experts, and

national organizations to focus on improving diabetes care. This report is a follow-up of the 2001 ACE/AACE Glycemic Control Consensus Conference, addressing the implementation of those glycemic goals. The conference focused on answering six questions:

**1. Are we in the medical community intervening early enough to address glycemic control and insulin resistance in glucose-intolerant states?**

No. Numerous studies have shown that significant cardiovascular disease may develop years before the clinical onset of diabetes (7,11,12). In epidemiologic studies, hyperglycemia has been found to have a strong association with the subsequent development of cardiovascular disease. In the absence of an intervention, IGT, characterized by postprandial hyperglycemia, often progresses to type 2 diabetes.

Additionally, recent data from the Epidemiology of Diabetes Interventions and Complications (EDIC) Study (13), a follow-up analysis of the Diabetes Control and Complications Trial (DCCT) (3), demonstrate the importance of early intervention to lower blood glucose levels aggressively to decrease complications years later. In the EDIC Study (13), the 2 original DCCT treatment cohorts (intensive and conventional glycemic control groups) were evaluated for A1C, retinal and renal complications, and cardiovascular events yearly after the conclusion of the DCCT in 1993. Glycemic control no longer differed substantially (A1C ~8.1%) between the 2 original DCCT treatment groups beginning at year 4 of follow-up to the publication date. Patients who had been intensively treated during the DCCT study period, however, showed significant decreases in risk for nephropathy, retinopathy, and cardiovascular complications in comparison with study subjects from the conventional treatment arm at years 5 through 8 of follow-up. In essence, the benefits of early intensive treatment during the DCCT extended well beyond the time of the intensive therapy, an indication that the vascular system has a "metabolic memory" for previous glycemic control.

Sufficient data are available to support the recommendation of intervention to prevent progression of IGT to type 2 diabetes. Targeted screening should be performed at age 30 years for populations at high risk for the development of diabetes (Table 1). The 2-hour oral glucose tolerance test is the most sensitive method for detection and is the recommended screening procedure. Large randomized controlled studies have shown the effectiveness of lifestyle interventions in preventing the progression of IGT to type 2 diabetes; for example, a 58% reduction in the incidence of type 2 diabetes was demonstrated in both the Diabetes Prevention Program (14) and the Finnish Diabetes Prevention Study (15).

Clinical trials have also shown several pharmacologic agents to be effective in reducing IGT conversion to type 2 diabetes. Such investigations include the Diabetes Prevention Program (metformin, troglitazone) (14), the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (acarbose) (16), Troglitazone in the Prevention of Diabetes (troglitazone) (17), and Xenical in the Prevention of Diabetes in Obese Subjects (orlistat) (18). Although troglitazone, a thiazolidinedione, is no longer available, several other thiazolidinediones with similar properties are being studied. Patients with IGT frequently have increased cardiovascular risk factors. Treatment of these risk factors is necessary to reduce the occurrence of cardiovascular events. Epidemiologic studies have shown postchallenge hyperglycemia to be a strong independent risk factor for cardiovascular disease. Thus, another potential benefit of treating the hyperglycemia associated with IGT may be the subsequent reduction of cardiovascular disease. The Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (16) showed that targeting postprandial hyperglycemia with use of an α-glucosidase inhibitor delayed the progression from IGT to type 2 diabetes and was asso-

**Table 1**
**Risk Factors for the Development of Diabetes**

| |
|---|
| Family history of diabetes |
| Cardiovascular disease |
| Overweight or obesity |
| Sedentary lifestyle |
| Latino/Hispanic, African American, Asian American, Native American, or Pacific Islander ethnicity |
| Previously identified impaired glucose tolerance or impaired fasting glucose |
| Hypertension |
| Increased levels of triglycerides, low concentrations of high-density lipoprotein cholesterol, or both |
| History of gestational diabetes |
| Delivery of a baby weighing more than 9 pounds (4.1 kg) |
| Polycystic ovary syndrome |

ciated with a significant reduction in clinical cardiovascular events. Highlighting this finding is not an endorsement of use of nonapproved pharmacologic therapy in patients with IGT but simply an acknowledgment of the first interventional trial that demonstrated the potential for decreasing clinical cardiovascular events by targeting postprandial blood glucose levels.

Current recommendations for the diagnosis and treatment of diabetes are adequate (19). Studies have found that, when current glycemic goals are achieved early, beta cells are preserved (17). Furthermore, early glycemic control in patients with diabetes has been shown to yield residual long-term benefits in reducing vascular complications (13). Nevertheless, reports have indicated that clinicians often are reluctant to follow these recommendations; the result is a substantial delay in intensive treatment.

**2. Is A1C the most important measure of glycemic control? What is the effect of glycemic excursions on the development and progression of complications?**

The A1C value, which is the sum of both fasting and postprandial glucose excursions during a 2- to 3-month period, is considered by many authorities to be the "gold standard" (albeit imperfect) for assessing long-term glycemic control. A recent study by Monnier et al (20) showed that the relative contributions of postprandial glucose and fasting glucose to A1C elevations in patients with type 2 diabetes are dependent on the A1C level; the lower the A1C value, the greater the postprandial contribution. In contrast, the higher the A1C level, the greater the contribution of the fasting glucose. Therefore, controlling both fasting and postprandial glucose levels at all times is necessary to achieve the A1C target. The closer the A1C level approaches to target values, the greater the emphasis needs to be placed on controlling the postprandial glucose excursions.

A key limitation of using A1C as a measure of glycemic control is the lack of timeliness. Of even more importance, A1C values do not provide information to the physician or patient about glucose excursions throughout the day. Hence, self-monitoring of blood glucose (SMBG) is needed to assess short-term glucose control and make appropriate and timely changes in patient treatment regimens.

Use of SMBG is particularly valuable in identifying and assessing postprandial glucose excursions in patients. As previously mentioned, epidemiologic data have shown that postchallenge hyperglycemia is associated with cardiovascular disease risk (12). Experimental data have suggested mechanisms by which postprandial glucose "spikes" cause oxidative stress and adversely affect endothelial function (21-23). In a recent study by Esposito et al (22), postprandial hyperglycemia was assessed as a possible risk factor for cardiovascular disease in patients with type 2 diabetes. Results from that study showed that reductions in postprandial hyperglycemia were associated with regression of carotid intima-media thickness (IMT), a known surrogate marker for coronary artery atherosclerosis (22).

**3. Are the current glycemic targets achievable?**

Yes. ACE glycemic targets have been achieved in clinical practice and by a significant number of subjects in some reported studies (24,25). Persistent titration of appropriate therapies can achieve glycemic targets without unacceptable hypoglycemic episodes. Medical nutrition therapy and lifestyle interventions are the cornerstones of all treatment regimens. Early use of combination pharmacologic therapies (combinations of orally administered agents, orally administered agents plus insulin, or orally administered agents in conjunction with incretin mimetics) along with medical nutrition therapy and lifestyle interventions is more effective in achieving and maintaining glycemic targets than are monotherapies. Other therapies should be added when glycemia begins to exceed the established targets. Current ACE targets for glycemic control are as follows:

- A1C ≤6.5%
- Fasting/preprandial plasma glucose <110 mg/dL
- 2-hour postprandial plasma glucose <140 mg/dL

Early use of insulin therapy is frequently needed for timely achievement of glycemic goals. In type 2 diabetes, glycemic targets may be achieved by use of basal insulin plus orally administered agents or basal-bolus insulin regimens; premixed insulin preparations can be used in special situations. Basal-bolus insulin regimens or insulin pump therapy is indicated for all patients with type 1 diabetes.

Insulin therapy should be tailored to minimize hypoglycemic events. Hypoglycemia is less of a risk in patients with type 2 diabetes than in those with type 1 diabetes. Use of insulin analogues has been shown to reduce the incidence of hypoglycemia. As recommended in the AACE glycemic guidelines (19), glycemic targets and therapy should be individualized to meet the needs and conditions of each patient.

In patients with diabetes, insulin resistance, and the metabolic syndrome, treatment with a combination of insulin and orally administered agents for insulin resistance is frequently helpful. This approach can lower the insulin dose required and improve many of the nontraditional cardiovascular risk factors.

**4. How important is glycemic control in reducing macrovascular complications?**

It is likely quite important. As discussed in the foregoing material, epidemiologic data (5,6) and evidence from experimental trials by Esposito et al (22) demon-

strate a relationship between glycemia and cardiovascular disease. Epidemiologic and interventional data from the United Kingdom Prospective Diabetes Study (5,6) show that improved glycemic control decreases the rate of macrovascular events. Data from the DCCT/EDIC Study substantiate that early and aggressive glycemic control reduces the risk for both microvascular complications and macrovascular disease (26). At 8 years of follow-up, study subjects who had been treated conventionally during the DCCT had significantly greater carotid IMT, a proven surrogate marker for atherosclerosis, and a significantly higher rate of coronary artery calcification than did those treated intensively despite similar A1C levels (26). Data presented at the 2005 annual meeting of the American Diabetes Association and published in the *New England Journal of Medicine* in December 2005 showed that after 13 years the intensively treated DCCT group had significantly fewer (57% reduction) clinical cardiovascular events than did the conventionally treated group from the DCCT. A similar long-term follow-up of the United Kingdom Prospective Diabetes Study cohorts revealed that intensive glucose control significantly reduced the frequency of myocardial infarctions. Moreover, experimental studies have reported a strong relationship between glycemic control, particularly postprandial glucose levels, and a reduction in carotid IMT (21-23).

## 5. How can current therapies and interventions be implemented to achieve glycemic control?

### *Clinical Strategies*

Effective intervention begins with an uncompromising insistence to treat to target. This management approach involves early initiation of appropriate therapies in conjunction with timely and persistent titration of dosages in order to achieve established glycemic targets.

Because diabetes is primarily a self-managed disease, patient education in self-management skills is essential for implementing interventions. An effective program involves acquisition of self-management knowledge and skills, which translate into behavioral changes. Initial and ongoing self-management education must be made available to all patients with diabetes (27,28).

In addition, SMBG is a critical resource for the management of diabetes. When performed with sufficient frequency, SMBG readings enable patients and their health-care professionals to make informed decisions about lifestyle choices and adjustments in pharmacologic therapy. SMBG can also provide ongoing feedback to patients about their nutrition and physical activity. Thus, it is a very important educational tool.

### *Systems Strategies*

A key obstacle, however, to implementing effective interventions is a lack of supportive health-care systems. Too often, a fragmented health-care delivery system is a major contributor to suboptimal care. Such a system lacks clinical information capabilities, frequently duplicates services, and is poorly structured to deliver long-term care for chronic conditions.

Chronic care models that are focused on both outcomes and prevention have been developed and proposed as viable alternatives to our current health-care systems to address these problems (28). Implementation of new models often necessitates innovative approaches and system changes. For example, the International Diabetes Center in Minneapolis, Minnesota, has pioneered the use of group education in an effort to reach more people with diabetes. This educational approach was shown to be as effective as traditional one-on-one education, but at substantial cost savings (30). Another innovative approach used by the International Diabetes Center was the provision of group diabetes education at the worksite of a major employer. This intervention had a positive effect on metabolic and educational outcomes.

Similarly, redesigning systems to accommodate diabetes education in primary care practices in western Pennsylvania had a positive influence on behavioral and metabolic outcomes (31,32). Several other organizations have implemented elements of a chronic care model to improve diabetes care processes and outcomes in community, worksite, and primary care practice settings and have thereby achieved positive results. Integrating a multifaceted approach to improving diabetes care has been shown to optimize outcomes.

The elements of a chronic care model include the following factors: decision support, clinical information systems, self-management education, and delivery system redesign (28). In an effort to help health-care professionals organize their diabetes care, the National Diabetes Education Program recently launched an online resource: www.betterdiabetescare.nih.gov. This Web site should help users design and implement more effective health-care delivery systems for patients with diabetes.

## 6. What resources are available to support more widespread implementation of the glycemic guidelines?

### *Guidelines*

Evidence-based guidelines are a necessary component of effective chronic disease programs. Although many organizations have developed practice guidelines, they are frequently not implemented in practice for various reasons. Studies done at the University of Pittsburgh Medical Center demonstrated that interventions that included prompts, reminders, and timely laboratory results helped physicians to increase utilization of established evidenced-based guidelines, with a positive effect on patient care and outcomes (31). Guidelines should always be easily accessible at the point of care (for example, in examination rooms, on patient medical records, and on office computers and personal digital assistants).

### *Clinical Information Systems*

Clinical information systems help facilitate adherence to guidelines by providing all members of the health-care team with timely access to data. Examples of information systems include electronic medical records and disease-specific patient databases or registries. These systems facilitate risk stratification, application of risk-specific interventions to improve diabetes care, and outcome evaluation. Use of such systems can enable health-care professionals to improve outcomes for their patients with diabetes and gain information on performance and results.

### *Other Resources*

Many organizations conduct live diabetes-related educational programs. Other educational resources, including Web-based educational programs, teleconferences, medical journals, magazines, and newsletters, reinforce these educational efforts, as do books, manuals, and audiovisual materials. Many resources can be located through the Web sites of diabetes-related organizations and the National Diabetes Clearinghouse Table 2.

Increasingly, educational materials for patients with diabetes have become available on organizational Web sites.

**Table 2**
**Selected Useful Diabetes-Related Web Sites**

*Web sites that publish, aggregate, or help translate diabetes-related guidelines*
- American Association of Clinical Endocrinologists (www.aace.com)
- American Association of Diabetes Educators (www.diabeteseducator.org)
- American Diabetes Association (www.diabetes.org)
- Centers for Disease Control and Prevention (www.cdc.gov/diabetes)
- Council for the Advancement of Diabetes Research and Education (www.cadre-diabetes.org)
- International Diabetes Federation (www.idf.org)
- Lawson Wilkins Pediatric Endocrine Society (www.lwpes.org)
- National Diabetes Education Program (www.ndep.nih.gov)
- National Guideline Clearinghouse (www.guideline.gov)
- National Institute of Diabetes and Digestive and Kidney Diseases (www.niddk.nih.gov)
- Texas Diabetes Council (www.dshs.state.tx.us/diabetes)

*Web sites with information that can help enhance patient adherence to lifestyle choices and pharmacologic therapy*
- AACE Power of Prevention (http://www.powerofprevention.com)
- American Association of Clinical Endocrinologists/American College of Endocrinology (www.aace.com)
- American Association of Diabetes Educators (www.diabeteseducator.org)
- American Diabetes Association (www.diabetes.org)
- American Dietetic Association (www.eatright.org/Public/NutritionInformation/92.cfm)
- Lawson Wilkins Pediatric Endocrine Society (www.lwpes.org)
- MedlinePlus (www.medlineplus.gov)
- National Diabetes Education Program (www.ndep.nih.gov)
- National Diabetes Information Clearinghouse (http://diabetes.niddk.nih.gov/)
- National Institute of Diabetes and Digestive and Kidney Diseases (www.niddk.nih.gov)
- National Nutrient Database, US Department of Agriculture (www.nutrition.gov)

*Resources that can help clinicians answer clinical questions at the point of care*
- American Association of Clinical Endocrinologists/American College of Endocrinology (www.aace.com)
- American Diabetes Association (www.diabetes.org)
- Council for the Advancement of Diabetes Research and Education (www.cadre-diabetes.org)
- InfoPOEMS (www.infopoems.com)
- National Library of Medicine's PubMed (www.ncbi.nlm.nih.gov/entrez/query.fcgi)
- Physicians' Information and Education Resource (http://pier.acponline.org/info?hp)
- UpToDate (www.uptodate.com)

Such organizational Web sites provide extensive information about diabetes and may include daily tips, risk tests for diabetes and its complications, recipes, guidance for exercise, and even computer forums to receive information from health-care professionals or exchange information with other patients who have diabetes.

Electronic media have also been used to support follow-up education (33). Several computer-based interventions have been shown to be effective in improving physical activity levels and nutrition goals in people with diabetes (34). Computer-assisted programs that facilitate goal setting and self-management planning, available on an office kiosk with a touch-screen computer, have been shown to improve self-care skills (35). Similar applications are being included on diabetes-related Web sites or as software for personal computers and personal digital assistants. Web sites of the American Association of Diabetes Educators and the American Diabetes Association can help patients and health-care professionals locate programs and diabetes educators. A listing of selected diabetes-related Web sites is presented in Table 2.

## RECOMMENDATIONS

1. Detect and treat IGT for the purpose of preventing type 2 diabetes and potentially reducing cardiovascular disease:
   - Use currently recognized profiles to identify patients at risk for type 2 diabetes, and perform a 2-hour oral glucose tolerance test
   - Promptly initiate education and appropriate therapy for reduction of known risk factors

2. Adopt an uncompromising treat-to-target approach to achieve and maintain glycemic goals in patients with diabetes:
   - Initiate *early* treatment and persist with titration to achieve and maintain glycemic targets safely in patients with diabetes
   - Address postprandial glucose and fasting glucose levels to achieve target A1C safely
   - Minimize glucose excursions throughout the 24-hour period
   - Use *combination* pharmacologic therapy that is physiologic to address multiple disorders
   - Institute insulin therapy early when targets are not met
   - Combine pharmacologic treatment with medical nutrition therapy and other lifestyle interventions as initial therapy when appropriate

3. Promote the tools for patient self-management:
   - Allocate necessary resources to support the provision of patient-centered team care
   - Promote and provide diabetes education
   - Use SMBG to support therapeutic decisions and enhance patient education
   - Advocate system redesign to support a chronic care model in the treatment of diabetes

***ACE/AACE Diabetes Recommendations Implementation Task Force***
Jaime A. Davidson, MD, FACE, Chair
Lawrence Blonde, MD, FACP, FACE, Co-Chair
Paul S. Jellinger, MD, MACE, Co-Chair

***Medical Writer***
Christopher G. Parkin, MS

## REFERENCES

1. **Centers for Disease Control and Prevention.** Diabetes Fact Sheet. Available at: http://www.cdc.gov/diabetes/pubs/factsheet.htm. Accessed for verification December 13, 2005.
2. **Hogan P, Dall T, Nikolov P (American Diabetes Association).** Economic costs of diabetes in the US in 2002. *Diabetes Care*. 2003;26:917-932.
3. **Diabetes Control and Complications Trial Research Group.** The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977-986.
4. **Ohkubo Y, Kishikawa H, Araki E, et al.** Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract*. 1995; 28:103-117.
5. **UK Prospective Diabetes Study (UKPDS) Group.** Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33) [erratum in *Lancet*. 1999;354:602]. *Lancet*. 1998;352:837-853.
6. **Stratton IM, Adler AI, Neil HA, et al.** Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321:405-412.
7. **Khaw KT, Wareham N, Luben R, et al.** Glycated haemoglobin, diabetes, and mortality in men in the Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk). *BMJ*. 2001;322:15-18.
8. **Koro CE, Bowlin SJ, Bourgeois N, Fedder DO.** Glycemic control from 1988 to 2000 among U.S. adults diagnosed with type 2 diabetes: a preliminary report. *Diabetes Care*. 2004;27:17-20.
9. **Narayan KM, Gregg EW, Engelgau MM, et al.** Translation research for chronic disease: the case of diabetes. *Diabetes Care*. 2000;23:1794-1798.
10. **Saydah SH, Fradkin J, Cowie CC**. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA*. 2004;291:335-342.
11. **Coutinho M, Gerstein HC, Wang Y, Yusuf S.** The relationship between glucose and incident cardiovascular events: a metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care*. 1999;22:233-240.

12. **DECODE Study Group, European Diabetes Epidemiology Group.** Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and noncardiovascular diseases? *Diabetes Care*. 2003;26:688-696.
13. **Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group.** Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus. *JAMA*. 2002;287:2563-2569.
14. **Knowler WC, Barrett-Connor E, Fowler SE, et al (Diabetes Prevention Program Research Group).** Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393-403.
15. **Tuomilehto J, Lindstrom J, Eriksson JG, et al (Finnish Diabetes Prevention Study Group).** Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344:1343-1350.
16. **Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M (STOP-NIDDM Trial Research Group).** Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet*. 2002;359:2072-2077.
17. **Wolford JK, Yeatts KA, Dhanjal SK, et al.** Sequence variation in PPARG may underlie differential response to troglitazone. *Diabetes*. 2005;54:3319-3325.
18. **Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L.** XENical in the Prevention of Diabetes in Obese Subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients [erratum in *Diabetes Care*. 2004;27:856]. *Diabetes Care*. 2004;27:155-161.
19. The American Association of Clinical Endocrinologists medical guidelines for the management of diabetes mellitus: the AACE system of intensive diabetes self-management—2002 update. *Endocr Pract*. 2002;8(Suppl 1):40-82.
20. **Monnier L, Lapinski H, Colette C.** Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations with increasing levels of HbA(1c). *Diabetes Care*. 2003;26:881-885.
21. **Hanefeld M, Koehler C, Schaper F, Fuecker K, Henkel E, Temelkova-Kurktschiev T.** Postprandial plasma glucose is an independent risk factor for increased carotid intima-media thickness in non-diabetic individuals. *Atherosclerosis*. 1999;144:229-235.
22. **Esposito K, Giugliano D, Nappo F, Marfella R (Campanian Postprandial Hyperglycemia Study Group).** Regression of carotid atherosclerosis by control of postprandial hyperglycemia in type 2 diabetes mellitus. *Circulation*. 2004;110:214-219.
23. **Hanefeld M, Chiasson JL, Koehler C, Henkel E, Schaper F, Temelkova-Kurktschiev T.** Acarbose slows progression of intima-media thickness of the carotid arteries in subjects with impaired glucose tolerance. *Stroke*. 2004;35:1073-1078.
24. **Strowig SM, Aviles-Santa ML, Raskin P.** Improved glycemic control without weight gain using triple therapy in type 2 diabetes. *Diabetes Care*. 2004;27:1577-1583.
25. **Riddle MC, Rosenstock J, Gerich J (Insulin Glargine 4002 Study Investigators).** The Treat-to-Target Trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care*. 2003;26:3080-3086.
26. **Genuth S.** Insights from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study on the use of intensive glycemic treatment to reduce the risk of complications of type 1 diabetes. *Endocr Pract*. 2006;12(Suppl 1):34-41.
27. **Mensing C, Boucher J, Cypress M, et al (Task Force to Review and Revise the National Standards for Diabetes Self-Management Education Programs).** National standards for diabetes self-management education. *Diabetes Care*. 2000;23:682-689.
28. **Mulcahy K, Peeples M, Tomky D, Weaver T.** National Diabetes Education Outcomes System: application to practice. *Diabetes Educ*. 2000;26:957-964.
29. **Wagner EH, Austin BT, Von Korff M.** Improving outcomes in chronic illness. *Manag Care Q*. 1996;4:12-25.
30. **Rickheim PL, Weaver TW, Flader JL, Kendall DM.** Assessment of group versus individual diabetes education: a randomized study. *Diabetes Care*. 2002;25:269-274.
31. **Siminerio L, Zgibor J, Solano FX Jr.** Implementing the chronic care model for improvements in diabetes practice and outcomes in primary care: the University of Pittsburgh Medical Center experience. *Clin Diabetes*. 2004;22:54-58.
32. **Siminerio LM, Piatt G, Zgibor JC.** Implementing the chronic care model for improvements in diabetes care and education in a rural primary care practice. *Diabetes Educ*. 2005;31:225-234.
33. **Boucher JL, Pronk NP, Gehling EM.** Telephone-based lifestyle counseling. *Diabetes Spectrum*. 2000;13:190-192.
34. **McKay HG, King D, Eakin EG, Seeley JR, Glasgow RE.** The diabetes network Internet-based physical activity intervention: a randomized pilot study. *Diabetes Care*. 2001;24:1328-1334.
35. **Glasgow RE, Toobert DJ, Hampson SE.** Effects of a brief office-based intervention to facilitate diabetes dietary self-management. *Diabetes Care*. 1996;19:835-842.