

The Challenge of Diabetes Management

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The treatment of type 2 diabetes in a managed care setting was the topic of discussion at a roundtable symposium recently hosted by *The American Journal of Managed Care* in Aspen, Colorado. This topic has many facets. Diabetes is among the most prevalent of chronic diseases. In the United States, it affects 7.8% of adults older than 20 years and 18.8% of those older than 60 years.¹ An estimated 25% of the entire Medicare budget is spent on those with diabetes, and 10% of all healthcare dollars is allocated to the treatment of diabetic patients.² The total cost of diabetes in 1997 exceeded \$98 billion in the United States.³

Although there have been marked decreases in the incidence of hypertension, hyperlipidemia, and heart disease, both the prevalence and incidence of diabetes continue to increase.^{4,7} There is also little evidence that the rate of complications caused by diabetes is decreasing. Diabetes remains the leading cause of blindness in people between 18 and 65 years of age. It results in 42% of end-stage renal disease and is the cause of more than half of lower-extremity amputation. Diabetes is the sixth leading cause of death from disease.³ People with diabetes have a 2- to 3-fold increased risk of cardiovascular disease.⁸

Managing diabetes well is a matter of national urgency. In some respects, it typifies the opportunities and the hazards of treating any chronic disease in a modern managed care environment.

Four broad influences affect diabetes-related care today: the explosion of scientific information that provides a far better understanding of the disease as well as many new therapeutic options, the evidence that good care matters, the formidable cost of diabetes treatment and optimal management, and the cost consciousness of managed care today.

Four decades ago, many clinicians were not aware that most people with diabetes secrete some endogenous insulin and actually produce more than the normal amount.⁹ Insulin resistance has become central to our understanding of type 2 diabetes.¹⁰ In the past decade, there has been an emphasis on insulin resistance as a concomitant condition with (and perhaps a cause of) accelerated atherosclerosis in those with diabetes.

A series of oral antidiabetic agents have now been made available. At least theoretically, those oral agents act at each level of carbohydrate dysmetabolism in diabetes: the variety of sulfonylureas (as well as repaglinide), enhance pancreatic insulin secretion, metformin reduces the uncontrolled hepatic glucose output that worsens hyperglycemia, thiazolidinediones specifically enhance insulin sensitivity at the tissue level, and α -glucosidase inhibitors slow carbohydrate absorption from the gut.¹¹⁻¹⁴ New insulins, new insulin delivery systems, new glucose monitoring capabilities, and a wealth of psychosocial and educational research are further

examples of the advancement of diabetes research in recent years.

Another topic of interest involves the risk factors (in addition to the blood glucose level) associated with type 2 diabetes. Dyslipidemia, high blood pressure, and smoking increase the risk of cardiovascular disease, which in turn increases the risk of diabetes.

Does treatment really matter? There is incontrovertible evidence that good diabetes care matters a great deal. Results of the Diabetes Control and Complications Trial (DCCT)¹⁵ confirmed relatively uncontrolled and experiential information indicating that intensive glycemic control in patients with type 1 diabetes affects the rate at which chronic complications develop. The most remarkable DCCT finding emphasized the dramatic link between control and complications. Each of the microvascular complications—retinopathy, nephropathy, and neuropathy—was significantly reduced when the average blood glucose level in the intensive control group was approximately 155 mg/dL for 6 years.

Results of the United Kingdom Prospective Diabetes Study (UKPDS), a larger, longer, and less tightly controlled study of type 2 diabetes, indicated the same conclusion. Microvascular complications in that older cohort of patients were linked to glycemic control.¹⁶ A variety of studies have indicated that the total cardiovascular event rate, which indicates large-vessel disease, is directly correlated with glycemic control.¹⁷ Among the most dramatic findings of the UKPDS was the effect of blood pressure control on cardiovascular events in those with diabetes.^{18,19}

The secondary treatment of established complications has also advanced. Annual retinal examinations are indicated because laser photocoagulation is so successful in treating advanced retinopathy.²⁰ Angiotensin-converting enzyme

inhibitors used in the treatment of hypertension or proteinuria slow the progress of nephropathy.²¹ Diabetes education, medical nutrition therapy, prophylactic use of aspirin, vaccines that protect against flu and pneumonia, and symptomatic treatment of neuropathic pain have been proven effective. Kidney or combined kidney and pancreas transplantation for the treatment of end-stage renal disease, coronary bypass surgery, and peripheral vascular surgery are also major advances in treatment.

The problem attendant to this increased understanding of diabetes, the expanded therapeutic options, and the proven efficacy of good diabetes care is cost. It is true that preventing late-stage complications is less expensive in the long run than treating them. But because people shift health plans regularly, the incentive for prevention declines and it is clear that good diabetes care is expensive short term. The cost of new oral agents ranges from approximately \$40 to \$180 per month. Glucose strips may cost another \$30 to \$90 per month. Eye examinations, medical nutrition therapy, and foot care are additional expenses. The per-capita expenditure for an individual with diabetes in 1997 was \$10,071 versus \$2669 for a person without diabetes (a 3.8-fold increase in treatment cost).³ The penalty to a payer of adverse selection (having more than the fair share of people with diabetes) is therefore considerable.

Whether the factors of diabetes care (the explosion of knowledge, the opportunities for treatment, the proof of benefit from good treatment, and the cost of treatment) create a situation that imprisons and frustrates those with diabetes or whether there is a positive solution to providing better care for people with chronic disease remains to be seen. The premise of this roundtable symposium was the latter: that the challenges of treating diabetes present an opportunity for implementing the very best in managed care.

ACRONYM LIST

The following acronyms appear in the pages of this Special Report supplement:

4S	Scandinavian Simvastatin Survival Study
ACCORD	Angioplastie Coronaire CORvasal Diltiazem
ACE	Angiotensin-converting enzyme
ADA	American Diabetes Association
AFCAPS/ TexCAPS	Air Force/Texas Coronary Atherosclerosis Prevention Study
ALLHAT	Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial
ALT	Alanine aminotransferase
BARI	Bypass Angioplasty Revascularization Investigation
BMI	Body mass index
CARE	Cholesterol and Recurrent Events
CME	Continuing medical education
DCCT	Diabetes Control and Complications Trial
DPP	Diabetes Prevention Program
EWA	Estrogen in Women with Atherosclerosis study
FDA	Food and Drug Administration
FPG	Fasting plasma glucose
GAP	Glycohemoglobin Assessment Program
Ghb	Glycosylated hemoglobin
GITS	Gastrointestinal therapeutic system
HbA1c	Hemoglobin A1c
HDL	High-density lipoprotein
HEDIS	Health Plan Employer Data and Information Set
HERS	Heart and Estrogen-progestin Replacement Study
HMO	Health maintenance organization
HOPE	Heart Outcomes Prevention Evaluation study
LDL	Low-density lipoprotein
MI	Myocardial infarction
MRFIT	Multiple Risk Factor Intervention Trial
NCEP	National Cholesterol Education Program
NCQA	National Committee on Quality Assurance
PMPM	Per member per month
PPAR	Peroxisome proliferator-activated receptor
QUEST	Quality, utilization, effectiveness, statistically tabulated
UGDP	University Group Diabetes Program
UKPDS	United Kingdom Prospective Diabetes Study
VA	Veterans' Administration
VAS	Visual analogue scale
VLDL	Very low-density lipoprotein

This roundtable brought together a small group of people with special expertise. In the first presentation, Anne L. Peters, MD, Associate Clinical Professor at UCLA School of Medicine, summarized our current understanding of insulin resistance. She emphasized that insulin resistance is part of the tangled web of risk factors including diabetes, obesity, genetics, coagulation, and dyslipidemia that can trigger atherosclerosis or thrombosis. Dr. Peters combined a review of the pathophysiologic factors and treatment options for patients with insulin resistance with her own clinical experiences in treating that condition.

To provide further insight into this critical research area, *AJMC* interviewed John B. Buse, MD, PhD, Associate Professor in the Department of Medicine at the University of North Carolina. You can find Dr. Buse's comments, which are related to insulin resistance and treatment with thiazolidinediones, in the interview at the end of this supplement.

In the second presentation, Ronald B. Goldberg, MD, of the Diabetes Research Institute at the University of Miami School of Medicine, reviewed the evidence linking cardiovascular risk to diabetes. He focused on results of the large clinical trials that have tested the efficacy of modifying those risk factors.

In the final presentation, Bruce Steffens, MD, Senior Vice President and Chief Medical Officer of John Deere Health Care, Inc., reviewed his organization's pioneering efforts to manage its 20,000 members with diabetes. The Deere experience reminds us of the value of practical, achievable goals.

Diabetes is a model subject for enlightened managed care. It is manageable, and management makes a difference. A rational

sequencing of care and care intensity in which hemoglobin A1c is the marker for glycemia can be formulated, and other risk factors can be monitored routinely. The reasonable intensity of level of care varies from basic screening and observation to (in a minority of patients) complex insulin delivery regimens. The rewards of success could be great, both medically and economically.

... REFERENCES ...

1. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults. *Diabetes Care* 1998;21:518-524.
2. Diabetes Research Working Group. *Conquering Diabetes: A Strategic Plan for the 21st Century*. Bethesda, MD: National Institutes of Health;1999:2. NIH publication 99-4398.
3. American Diabetes Association. Economic consequences of diabetes mellitus in the U.S. in 1997. *Diabetes Care* 1998;21:296-308.
4. Burt VL, Cutler JA, Higgins M, et al. Trends in the prevalence, awareness, treatment and control of hypertension in the adult U.S. population: Data from the Health Examination Surveys, 1960-1991. *Hypertension* 1995;26:60-69.
5. Johnson CL, Rifkind BM, Sempos CT, et al. Declining serum total cholesterol levels among U.S. adults: The National Health and Nutrition Examination Surveys. *JAMA* 1993;269:3002-3008.
6. Pell S, Fayerweather WE. Trends in the incidence of myocardial infarction and in associated mortality and morbidity in a large employed population, 1957-1983. *N Engl J Med* 1985;312:1005-1011.
7. Centers for Disease Control and Prevention. *Diabetes Surveillance*, 1997. Atlanta, GA: US Department of Health and Human Services;1997:15-36.
8. Goldberg RB. Cardiovascular disease in diabetic patients. *Med Clin North Am* 2000;84:81-93.
9. Yallow RS, Berson SA. Assay of plasma insulin in human subjects by immunological methods. *Nature* 1959;184:1648.
10. Haffner SM, Miettinen H. Insulin resistance implications for type II diabetes mellitus and coronary heart disease. *Am J Med* 1997;103:152-162.
11. DeFronzo RA. Pharmacologic therapy for type 2 diabetes mellitus. *Ann Intern Med* 1999;131:281-303.
12. Klip A, Leiter LA. Cellular mechanism of action of metformin. *Diabetes Care* 1990;13:696-704.
13. Nolan JJ, Ludvik B, Beerdsen P, Joyce M, Olefsky J. Improvement in glucose tolerance and insulin resistance in obese subjects treated with troglitazone. *N Engl J Med* 1994;331:1188-1193.
14. Campbell LK, White JR, Campbell RK. Acarbose: Its role in the treatment of diabetes mellitus. *Ann Pharmacother* 1996;30:1255-1262.
15. The Diabetes Control and Complications Trial (DCCT) 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.
16. 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;352:837-853.
17. Turner RC, Millns H, Neil HAW, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study. *BMJ* 1998;316:823-828.
18. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study (UKPDS) Group. *BMJ* 1998;317:703-713.
19. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. *BMJ* 1998;317:713-720.
20. American Diabetes Association. Position Statement: Diabetic Retinopathy. *Diabetes Care* 1999;22(suppl 1):S70-S73.
21. Hebert LA, Bain RP, Verme D, et al. Remission of nephrotic range proteinuria in type I diabetes. Collaborative Study Group. *Kidney Int* 1994;46:1688-1693.