

Diabetes: The Next Chapter



Edmund Pezalla, MD, MPH

National Medical Director for Pharmacy Policy and Strategy, Aetna
President Emeritus, The Pharmacy and Therapeutics Society

Morbidity and mortality from type 2 diabetes continue to increase in the United States and worldwide.¹ Increasing prevalence is correlated with age, obesity, and sedentary lifestyles. Diabetes increases risk for both macrovascular and microvascular diseases such as renal failure, neuropathy, and coronary artery disease (CAD). Of great concern is the huge risk for mortality from CAD.² Persons with diabetes not only are at greater risk for CAD than nondiabetic persons, but also are at higher risk for dying from the disease.

According to the National Committee for Quality Assurance 2010 annual report, some progress has been made in managing glycosylated hemoglobin (A1C), but there are no data to suggest that this better management has translated into an appreciable decline in CAD morbidity or mortality.³

The problem is multifactorial. The incidence of diabetes is increasing. Morbidity and mortality remain high. Solutions have been difficult to develop.

Prevention or delay of development of diabetes has been recognized as a public health priority.⁴ However, effective population wide lifestyle modification programs are difficult to provide. Policy solutions are either indirect (eg, provision of more playgrounds) and therefore only partially effective, or direct but unpopular (eg, junk food tax). Employer and health plan solutions have had some success, but only on a small scale, and these solutions are not available to most consumers.

Pharmaceutical manufacturers have attempted to improve the situation by developing new drugs for weight loss or control, but have met with little success and some high-profile failures. Additionally, no drugs have been developed that clearly show preservation of beta cell function or reduction in insulin intolerance. This inability to impact 2 of the known biologic mechanisms in diabetes

has meant that we have been unable to develop a clear strategy for treating prediabetes except to promote weight loss and exercise.

Cardiovascular disease remains the single greatest cause of mortality in people with diabetes. In spite of therapies to reduce blood pressure and cholesterol, and attempts to control blood sugar as measured by A1C, diabetic patients are 2 to 4 times as likely to die from CAD than similar nondiabetic patients.⁵ Joint American Diabetes Association and American Heart Association guidelines recognize the need for specific treatments of lipid disorder and hypertension.⁶ These guidelines make specific recommendations for monitoring and treating these disorders, but the therapies clearly are not as effective in the diabetic population as they are in the general population.

Reduction in A1C has been associated with a reduction in CVD morbidity and mortality. However, hypoglycemia remains a serious barrier to tight control. In addition, many of the available medications provide limited reduction in A1C and are not sufficient alone or in combination to get all patients to goal. Even patients who reach a goal A1C of <7% continue to have a high rate of CVD.

Recent setbacks in pharmacologic therapy include the Food and Drug Administration (FDA) rejection of the New Drug Application for extended-release exenatide (Amylin's once-weekly Byetta) and FDA-imposed restrictions on the use of rosiglitazone. New drug introductions in all areas including diabetes, weight loss, and primary prevention of cardiovascular disease have been declining for decades.⁷

Compounding this decline in effective new therapies is a lack of clear guidelines for the use of existing technologies, tools, and pharmaceuticals. Existing practice guidelines, although thoughtful, have proved to be overly broad. The guidelines have been based on the best

available evidence, but we lack direct evidence that use of the guidelines will result in better outcomes.

Reorganization of our approach to diabetes is both necessary and possible. Although we cannot rely on pharmaceuticals alone, the failure of recent programs for glycemic control and weight loss may still result in discovery of new evidence regarding the biology and biochemistry of the disease and a deeper understanding of human neuroendocrine regulatory functions.

Development of specific treatment protocols similar to those for childhood leukemia and registry of patients will provide an opportunity to evaluate treatment strategies and allow us to make better use of existing tools and resources. Early detection and treatment are important, as evidenced by the United Kingdom Prospective Diabetes Study follow-up study.⁵

Adherence will remain an important issue. New developments in digital devices and the expansion of social networks hold the promise of empowering consumers to develop their own approaches to disease management. Collaborations between payers, pharmaceutical firms, and consumer groups will further this agenda.⁸

The federal government has launched significant public health efforts including educational campaigns. The Centers for Disease Control and Prevention–sponsored campaign *Managing Diabetes: It's Not Easy But It's Worth It* provides education, public service announcements, and other materials for consumers, doctors, pharmacists, and other healthcare practitioners. This campaign stresses the need for early detection, continued monitoring, and adherence to recommended drug, diet, and exercise regimens.⁴

To support these public health efforts, we need to develop systems for monitoring outcomes, including morbidity and mortality, on a national basis. The Centers for

Disease Control and Prevention continue to move ahead in this area.⁴

In summary, diabetes will continue to be a serious public health problem. Although our current approach has not made major inroads with respect to long-term outcomes for the diabetic population, we have the tools to make an impact on the incidence of the disease, as well as improve secondary prevention of cardiovascular mortality.

Author Affiliation: From Aetna, Hartford, CT.

Author correspondence to: Edmund Pezalla, MD, MPH, National Medical Director for Pharmacy Policy and Strategy, Aetna, 151 Farmington Ave, RE52, Hartford, CT 06156. E-mail: pezallae@aetna.com.

REFERENCES

1. The National Institute of Diabetes and Digestive and Kidney Diseases, National Diabetes Information Clearinghouse. National diabetes statistics, 2007. <http://diabetes.niddk.nih.gov/dm/pubs/statistics/index.htm>. Accessed November 10, 2010.
2. Fox CS, Sullivan L, D'Agostino RB Sr, Wilson PW; Framingham Heart Study. The significant effect of diabetes duration on coronary heart disease mortality: the Framingham Heart Study. *Diabetes Care*. 2004;27(3):704-708.
3. National Committee for Quality Assurance. *The State of Healthcare Quality Report*. 14th ed. Washington, DC: NCQA; 2010. www.ncqa.org/.../state%20of%20health%20care/2010/SOHC%202010%20-%20Full2.pdf. Accessed November 10, 2010.
4. Centers for Disease Control and Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2007. <http://www.cdc.gov/diabetes/pubs/factsheet07.htm>. Accessed November 10, 2010.
5. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359(15):1577-1589.
6. Buse JB, Ginsberg HN, Bakris GL, et al; American Heart Association; American Diabetes Association. Primary prevention of cardiovascular disease in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. *Diabetes Care*. 2007;30(1):162-172.
7. The Future of Drug Development: advancing clinical trial design. *Nature Reviews: Drug Discovery*. 2009; 8:949-957. <http://www.nature.com/nrd/journal/v8/n12/abs/nrd3025.html> doi:10.1038/nrd3025 4. Accessed December 3, 2010.
8. Novo Nordisk. National Changing Diabetes Program. http://www.novonordisk-us.com/documents/promotion_page/document/hcdp_splash.asp. Accessed November 10, 2010. 