Lifetime Costs of Complications Resulting From Type 2 Diabetes in the U.S.

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OBJECTIVE — To model the lifetime costs associated with complications of type 2 diabetes.

RESEARCH DESIGN AND METHODS — A cohort of 10,000 patients with diabetes was simulated using a model based on existing epidemiological studies. Complication rates were estimated for various stages of macrovascular disease, nephropathy, retinopathy, neuropathy, and hypoglycemia. At the beginning of the simulation, patients were assumed to have been treated for 5 years and have a mean HbA_{1c} of 8.4. From the U.K. Prospective Diabetes Study, it was estimated that on current therapies, the HbA_{1c} would drift upward on average 0.15% per year. Direct medical costs of managing each complication were estimated (in 2000 U.S. dollars) from all-payor databases, surveys, and literature.

RESULTS — Macrovascular disease was estimated to be the largest cost component, accounting for 85% of cumulative costs of complications over the first 5 years. The costs of complications were estimated to be $47,240 per patient over 30 years, on average. The management of macrovascular disease is estimated to be the largest cost component, accounting for 52% of the costs; nephropathy accounts for 21%, neuropathy accounts for 17%, and retinopathy accounts for 10% of the costs of complications.

CONCLUSIONS — The complications of diabetes account for substantial costs, with management of macrovascular disease being the largest and earliest. If improving glycemic control prevents complications, it will reduce these costs.

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Diabetes affects an estimated 10.2 million Americans (1). A study by the American Diabetes Association (ADA) estimated the direct costs of diabetes to be $44.1 billion in 1997 (2), and as the prevalence of diabetes has been increasing, the demand for medical care will continue to increase (3–6). As a result of evidence that intensive blood glucose control can reduce the risk of microvascular complications (7), ADA guidelines indicate that glycemic control is an important goal of treatment (8). Postprandial hyperglycemia, which is a determinant of glycemia (9–11), and the degree of albuminuria (12,13) are associated with an increased risk of cardiovascular disease and death. Unfortunately, although hypoglycemic agents achieve an initial reduction, glycemic levels tend to drift upward over time (14–16). Moreover, many patients are not reaching the recommended treatment goals (17).

In this study, we provide estimates of the costs of managing the complications of diabetes over time. We relate these costs to the level of glycemia and also explore the impact of its upward drift. The impact of other risk factors, such as hypertension and hypercholesterolemia, is also taken into account. Although specific strategies for managing diabetes, including pharmacologic treatments, are not addressed, these estimates provide a basis for performing those economic analyses.

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Abbreviations: ADA, American Diabetes Association; ESRD, end-stage renal disease; UKPDS, U.K. Prospective Diabetes Study.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

Model

The model (Fig. 1) simulates patients with type 2 diabetes from diagnosis to death (18), including the occurrence of macrovascular complications (stroke, transient ischemic attack, myocardial infarction, and angina) and various levels of the progressive complications (nephropathy, retinopathy, and neuropathy), which start at the mildest level but can develop into major complications. For example, nephropathy has three levels: microalbuminuria, gross proteinuria, and end-stage renal disease (ESRD). Progressive complications are assumed to be irreversible, although there is now some evidence that this may not always be the case. Episodic complications such as hypoglycemia and foot ulcers are also considered. These are reversible, and it is assumed that an episode resolves within the modeling cycle. A patient can have this type of complication multiple times. During each annual cycle, the patient is exposed to the complication risks, which are determined by the assigned characteristics, including glycemia (measured in terms of HbA_{1c}). No specific assumption about the correlation of risks is made.

Using a Monte Carlo technique, each hypothetical patient is assigned characteristics based on distributions of age, race, sex, cholesterol, smoking, and systolic blood pressure (Table 1). The sex and race distributions were those of incident cases of clinically diagnosed type 2 diabetes in U.S. citizens aged 25–74 years (19,20), as were the distributions of cholesterol, smoking, and systolic blood pressure (21,22). The age distribution reflects U.S. clinical practice (23). Patients with onset of diabetes after 74 years of age were not included because of the low complication rate and the lack of natural history data. During a premodel period of

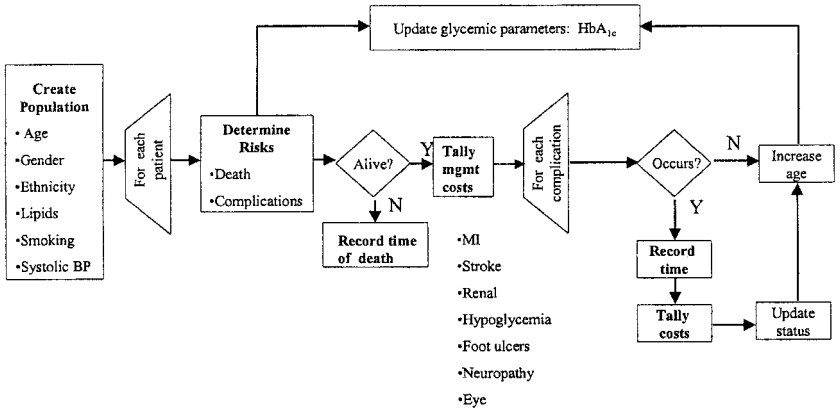

Figure 1—*Schematic representation of model.*

5 years, the patients were allowed to accumulate complications, but no costs from managing these complications were considered. The HbA_{1c} level was set at 8.4% at the start. From the U.K. Prospective Diabetes Study (UKPDS), it was estimated that despite therapy, the HbA_{1c} would increase an average of 0.15 percentage points per year (14).

Face validity of this model was established via review by clinical experts and health authorities. In addition, previous analyses have been peer-reviewed (18). Technical accuracy was ascertained by implementing the model in two different ways and comparing the results, as well as by performing extreme-value sensitivity analyses to study its behavior. Unexpected model behavior, or programming errors, were identified and resolved. Predictive validity was assessed by comparing predictions with the source data and other independently obtained results (7,24). The model yields comparable results to those of the UKPDS patients in the intensive and conventional treatment groups in terms of relative risk over 10 years for all-cause mortality and for microvascular disease or retinopathy at 12 years.

Table 1—*Baseline inputs to the model*

Parameter	Value
Age (years)	
25–34	0.4
35–44	14.4
45–54	22.6
55–64	18.4
65–74	44.2
Female (%)	55
Ethnicity (%)	
White	70
African-American	20
Hispanic-American	5
Native American	2.5
Asian	2.5
HbA_{1c}	
Baseline level (%)	8.4
Upward drift (%/year)	0.15

Risks of complications

Microvascular risks were estimated from the best available data and all depended on HbA_{1c}. Risk gradients observed in the Diabetes Control and Complications Trial (25) were applied to type 2 diabetes (24, 26, 27), an accepted assumption (28–30) confirmed by the UKPDS (7). Data from the Rochester Epidemiology Project were used for the ESRD estimates (31) as well as those for lower-extremity amputation (32). Retinopathy risks were estimated from the Wisconsin Epidemiologic Study of Diabetic Retinopathy (33).

Macrovascular risks were estimated based on a Framingham Heart Study equation that includes coefficients for age, sex, systolic blood pressure, smoking status, total cholesterol level, and HDL cholesterol level (24). These risks are not directly dependent on glycemia but are linked indirectly, given the known association with nephropathy (13,34–36).

The risk of death is obtained by adjusting the age- and sex-dependent mortality of the general population by the relative risk associated with diabetes (24). An additional adjustment is made if nephropathy develops (12,37,38).

Costs

The direct medical costs (in 2000 U.S. dollars) of treating each complication were estimated, excluding the routine costs of managing diabetes (such as home monitoring or supplies) and preventive screening. All event costs include acute care (initial management in inpatient or outpatient setting) and subsequent care in the first year, consisting of subacute inpatient care (i.e., rehabilitation, skilled and intermediate care nursing facilities, chronic hospitals), home health care, outpatient therapy, physician visits, and diagnostic and therapeutic procedures. State costs reflected annual resource use beyond the first year.

Inpatient resource use was derived from five all-payor databases (39–43). Outpatient services were estimated from government and other published reports, ambulatory care and emergency room databases, clinical practice guidelines, provider survey data, and the literature (44–51). The costs of physician visits and laboratory tests were obtained from corresponding 2000 Medicare fee schedules. Full methodological details have been published elsewhere (52). The cost for ESRD reflects only management of the renal disease itself and not all medical care for patients with ESRD. Cost-to-charge ratios were used as appropriate.

Analyses

The mean cost of each type of complication over 30 years was calculated by summing each patient's costs and dividing by the total number simulated, thus reflecting all patients (not just survivors). Simulations were also performed at different initial HbA_{1c} levels and with various levels of HbA_{1c} drift and delay in its initiation, singly and jointly. No discounting was applied because these analyses do not compare one treatment with another.

RESULTS — Patients who had type 2 diabetes for 5 years before entering the model with an average HbA_{1c} level of 8.4%, which then increases an average of 0.15 percentage points per year, are expected to accrue, on average, $47,240 for managing complications over 30 years. The management of macrovascular disease is estimated to be the largest cost component, costing $24,330 or 52% of the costs. Nephropathy accounts for 21%, neuropathy accounts for 17%, and retinopathy accounts for 10%.

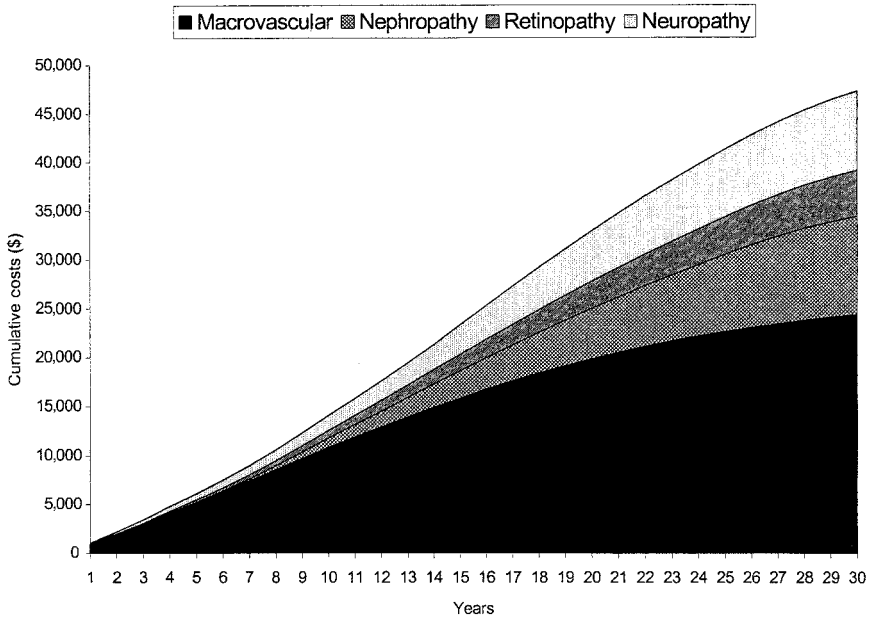

Figure 2—*Estimated cumulative cost (average per patient) of managing complications of type 2 diabetes according to type of complication.*

The cumulative cost estimates indicate that macrovascular disease is expected to be the largest cost component at all time points (Fig. 2). Moreover, macrovascular disease is an important determinant of cost at an earlier time than the microvascular complications, accounting for 85% of the cumulative costs over the first 5 years and 77% over the first decade.

A key factor in the development of complications, and consequently of their costs, is the level of glycemia. For example, with an initial HbA_{1c} level of 7.5%, the 30-year cost is estimated to be $40,801; with an initial HbA_{1c} level of 8.0%, the 30-year cost is $44,145; with an initial HbA_{1c} level of 8.5%, the 30-year cost is $47,943; with an initial HbA_{1c} level of 9.0%, the 30-year cost increases to $51,554. Macrovascular disease remained the largest cost component. The impact of changes in the drift over time was also examined (Fig. 3). If onset of the annual drift of 0.15 percentage points is delayed by 1 year, the 30-year costs decrease 3%. If, in addition, the annual drift is only 0.13%, the costs decrease by 6%, and if the annual drift were as low as 0.075%, the costs decrease by 14%.

The joint impact on 30-year cost estimates of HbA_{1c} level at the start of the model and average annual drift is summarized in a contour plot in Fig. 4. Each contour line going from left to right represents a $1,000 increment in the 30-year cost estimates. Points along a line have a similar cost implication. For example, similar cost estimates were obtained if the initial HbA_{1c} level was 7.5% with a mean annual drift of 0.14% or a combination of 8.0% at baseline and 0.10% drift per year. This contour plot indicates that for a baseline HbA_{1c} of 9%, when the annual drift was reduced by one-third, from 0.15 to 0.10 percentage points, then the cost estimate decreased ~7%. In addition, a decrease in baseline HbA_{1c} from 9 to 8%, despite an annual drift of 0.15 percentage points, was associated with a 14% decrease in the costs of managing complications.

CONCLUSIONS— The management of complications generates substantial costs in type 2 diabetes. Macrovascular disease is the major component of these costs, and they are incurred much earlier than those due to managing microvascular complications. Therefore, reduction of the risks of macrovascular complications should also ease the costs of complications. Whether this results in net savings will depend on the cost of the treatment strategy used to achieve the lower risks. This strategy should address risk factors for cardiovascular disease such as smoking, high blood pressure, and hypercholesterolemia; it is not yet certain that improved glycemic control will also help, but recent epidemiological evidence suggests that macrovascular disease is related to postprandial glucose (53).

This simulation of the course of the disease demonstrates the dependency of costs of treating diabetes-related complications on glycemic level—at both the starting point and the degree of deterioration over time. The costs increase considerably with relatively small increases in

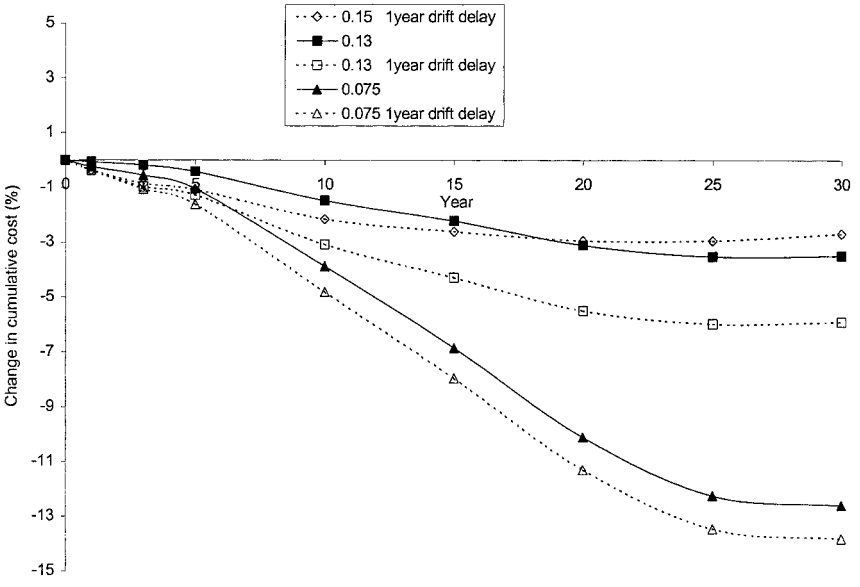

Figure 3—*Relative change in cumulative cost for HbA_{1c} various combinations of annual upward drift and delay in onset of the drift compared with the base case of a drift of 0.15% starting immediately.*

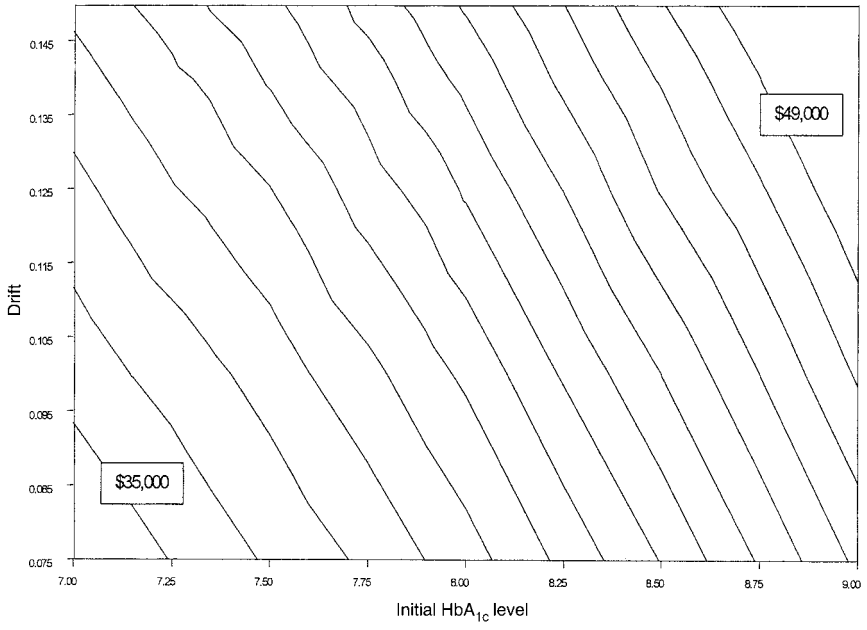

Figure 4—*Impact of HbA_{1c} levels at the start of the model and average annual drift on 30-year cost estimates (each contour line represents a $1,000 increment in 30-year cost, starting from $35,000 at the lower left corner and going to $49,000 at the upper right corner).*

HbA_{1c}, and these escalate faster at higher levels. Moreover, the rate at which glycemia increases over time has an important effect.

There is evidence that, in practice, many patients do not currently achieve or sustain the level of glycemic control (HbA_{1c} <7%), blood pressure, or cholesterol levels recommended by the ADA. For example, in one study of patients with type 2 diabetes treated with oral agents, 38% achieved the target level of <7%, but 42% of patients had levels >8%. Our analysis shows that, apart from the potential devastating health consequences, this failure to control hyperglycemia has a major economic impact. Therefore, it is important economically to reduce complication rates by reviewing HbA_{1c} control and introducing changes to the health care processes to ensure that appropriate additions to drug therapy are made promptly so the ADA limits are more frequently achieved and maintained.

Several important assumptions were made for these analyses. Two key assumptions were that complication rates and survival are related to glycemic levels. The relation between HbA_{1c} and the risk of developing microvascular complications has been convincingly demonstrated in the Diabetes Control and Complications Trial (25) and confirmed in type 2 diabetes by the UKPDS (7,54). Several studies support our assumption that survival is dependent on age and sex as well as the patient's nephropathy state (13,37,38). Similarly, the degree of albuminuria has been found to predict the development of cerebrovascular and cardiovascular disease (13,34–36). Patients with type 2 diabetes also present other important risk factors for cardiovascular disease, such as high blood pressure and cholesterol levels, and these were considered in the model using data on U.S. patients with diabetes.

Complications have been shown to be an important component of the excess direct medical costs of treating patients with diabetes (4). Additional support for our analyses is provided by the finding that the costs of managing complications over 10 years were actually found to be reduced in patients with type 2 diabetes receiving intensive treatment rather than conventional therapy (55). Other shorter-term studies have also concluded that the costs of medical care are increased if HbA_{1c} levels exceed 7% (5) or 8% (56) and that a reduction from a baseline level of HbA_{1c} of 10% by at least 1% or more that was sustained over 2 years is associated with lower costs (6,18).

As macrovascular disease costs arise early and represent the major component of lifetime costs, this study supports the initiatives by the National Diabetes Education Program to promote awareness of the benefits of optimizing blood pressure and cholesterol levels as well as blood glucose levels (57). Improving control of known risk factors for cardiovascular disease has an enormous potential for reducing the risk of developing complications and lowering health care costs associated with those complications. The net economic impact will depend on the costs of these treatment strategies, which may use more resources than conventional therapy.

This study evaluated the impact of various degrees of glycemia on the long-term costs of managing complications. These estimates show that favorable changes in risk factors may offset at least some of the costs of the required treatment interventions to achieve the optimal glycemic, blood pressure, or cholesterol levels.

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