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

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OBJECTIVE — To estimate direct medical costs of managing the complications of type 2 diabetes.

RESEARCH DESIGN AND METHODS — Costs were estimated for 15 diabetic complications by applying unit costs to typical resource-use profiles. Resource use and unit costs were estimated from many sources, including acute care discharge databases, clinical guidelines, government reports, fee schedules, and peer-reviewed literature. For each complication, the event costs are those associated with resource use that is specific to the acute episode and any subsequent care occurring in the 1st year. State costs are the annual costs of continued management. All costs are expressed in 1996 U.S. dollars.

RESULTS — As expected, the more severe or debilitating events, such as acute myocardial infarction ($27,630 event cost; $2,185 state cost), generate a greater financial burden than do early-stage complications, such as microalbuminuria ($62 event cost; $14 state cost). Yet, complications that are initially relatively low in cost (e.g., microalbuminuria) can progress to more costly advanced stages (e.g., end-stage renal disease, $53,659 state cost); therefore, minor complications should also be considered in any economic analysis of diabetes.

CONCLUSIONS — The recent literature has lacked cost estimates that may be readily translated into patient-level cost inputs for an economic model. Emerging therapies that may reduce the incidence of some diabetic complications will need to be scrutinized economically in today's cost-conscious environment. The cost estimates from this study provide one piece of the economic analysis needed to evaluate these new interventional therapies.

Approximately 8 million Americans are known to have diabetes. Every year, on average, 625,000 new cases of diabetes are diagnosed, and more than 178,000 deaths result from the disease and its related complications (1,2). Diabetes has been implicated as the underlying cause of 12% of all new cases of legal blindness, over one-third of new cases of end-stage renal disease (ESRD), and nearly half of nontraumatic lower-extremity amputations (LEAs) (1,3–6). Evidence has also shown that people with diabetes are two to four times more likely to die from heart disease or suffer a stroke (1). Managing these complications can be quite expensive.

Fortunately, there are emerging therapies designed to offer an alternative to standard therapies (e.g., insulin, sulfonylureas, other oral agents) which may improve glycemic control and help reduce the incidence of some complications. To assess the role of these new therapeutic regimens, it is important to have a comprehensive understanding of the economic implications of diabetes. To perform accurate economic analyses, it is necessary to have as recent and complete cost data as possible for relevant complications.

Although several frequently cited papers report on some aspect of the economic costs of diabetes (7–12), very few have taken a comprehensive account of the myriad costs specifically associated with its complications (10). Furthermore, the existing comprehensive cost estimates have been provided on an aggregate level (national-level spending rather than per-patient costs) that demonstrates the magnitude of the costs associated with the disease but may not be readily translated into patient-level cost inputs for an economic model (10). Although some studies have examined patient-level costs (7,9,11), they do so only for individual complications (7,11) or for specific aspects of care, such as hospitalization (9).

In developing an economic model of type 2 diabetes, the object was to estimate the average direct medical cost of managing selected complications of the disease. These complications were chosen based on those that were considered in a recent comprehensive epidemiological model of diabetes (13,14). As the perspective of the analysis is that of a payor with extensive responsibility for health care, only direct medical costs were included. Neither the economic model nor its results are discussed here, as this article addresses only one key aspect of this study—the initial and subsequent costs of managing the possible complications of diabetes. We present the data in a comprehensive manner so that researchers can examine the costs of all, or any one complication, on a per-patient basis.

RESEARCH DESIGN AND METHODS

— The complications considered were acute myocardial infarction (AMI), angina pectoris, ischemic stroke, transient ischemic attacks, nephropathy, retinopathy, symptomatic neuropathy, LEAs, foot ulcers, and hypoglycemia. Average per-patient total costs were estimated by applying unit costs to the likely course of treatment for each complication. Resource-use profiles appropriate for managing the complications of diabetes were derived from many sources, including state acute care discharge databases, clinical guidelines, published practice parameters, epidemiological studies, government reports, surveys, and peer-reviewed literature. References to both type 1 and type 2 diabetes were considered.

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Abbreviations: AMI, acute myocardial infarction; DCCT, Diabetes Control and Complications Trial; ESRD, end-stage renal disease; HHC, home health care; HMO, health maintenance organization; ICD-9, *International Classification of Diseases, Ninth Revision*; LEA, lower-extremity amputation; SNF, skilled nursing facilities; TIA, transient ischemic attack.

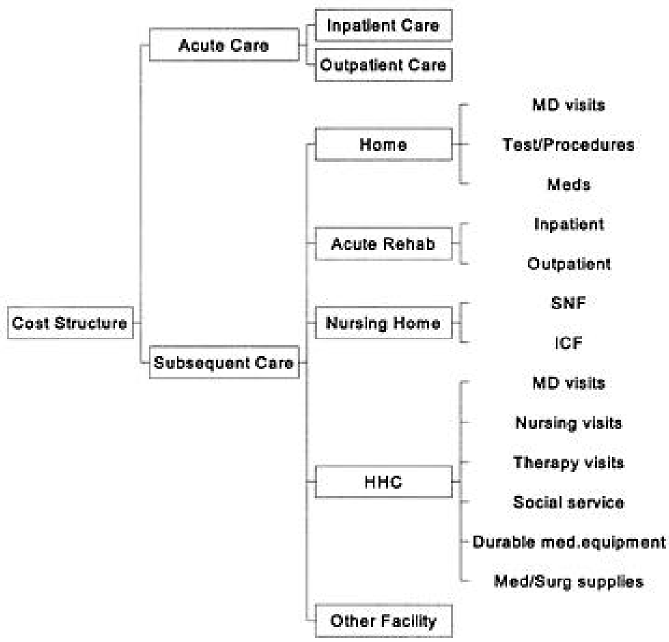

Figure 1—*Cost structure components. ICF, intermediate care facility.*

Figure 1 provides an overview of the cost structure used for all complications. The cost estimates are reported in terms of event and state costs. For the purpose of this analysis, a health state is defined as a permanently altered level of physical condition. A given complication is defined by its initial event and the subsequent health state. For example, the diagnosis of macular edema is the event that marks the onset of the health state characterized by this degree of retinopathy. Event costs are those associated with resource use that is specific to the defining clinical event (e.g., AMI, first leg amputation) occurring initially in the management of a given health state. All event cost estimates include both acute care (initial management in an inpatient or outpatient setting) and subsequent care rendered in the 1st year. Subsequent care may comprise subacute inpatient care (i.e., rehabilitation hospitals, skilled nursing facilities, intermediate care nursing facilities, chronic disease hospitals), home health care, outpatient therapy, physician visits, and diagnostic and therapeutic procedures depending on the complication addressed. The discharge disposition status from acute care was used to determine initial subsequent health care use.

State costs reflect annual resource use required beyond the 1st year for the ongoing management of the given health state and would apply while that particular health state is present for the remainder of the patient's life. All event and state costs that are reported for each complication are incremental to any recommended screening and prevention measures that take place as part of diabetes management, the costs of which are not included in this analysis.

Episodic events are those that can occur more than once and are potentially reversible, unlike other complications described thus far that alter a person's health state. Two complications fall into this category: foot ulcers and hypoglycemia. Given that these conditions are usually short term, only event costs are applicable.

Cost sources

Acute care inpatient profiles were developed for each complication from five state discharge databases (1995: Massachusetts, Florida; 1994: California, Maryland, North Carolina). The components of these profiles are presented in Fig. 2. Patients were identified by means of the *International Classification of Diseases, Ninth Revision* (ICD-9) coding (15). A population of 709,108 discharges of patients with type 1 or type 2 diabetes (principal or secondary ICD-9 diagnosis code of 250.00–250.93) was culled from a total of nearly 8 million discharges. A hierarchical identification method was used to identify specific populations for each complication from the pool of diabetic discharges. This method was used to avoid inflating the cost estimates of complications and to provide a representative cost for each stage of a potentially progressive complication. For example, if a patient during one admission had a diagnosis of diabetes with neurological manifestations (ICD-9: 250.60–250.63) and a foot ulcer (ICD-9: 707.1) resulting in wound debridement, the discharge was grouped to the foot ulcer complication population; however, if a patient with similar problems went on to

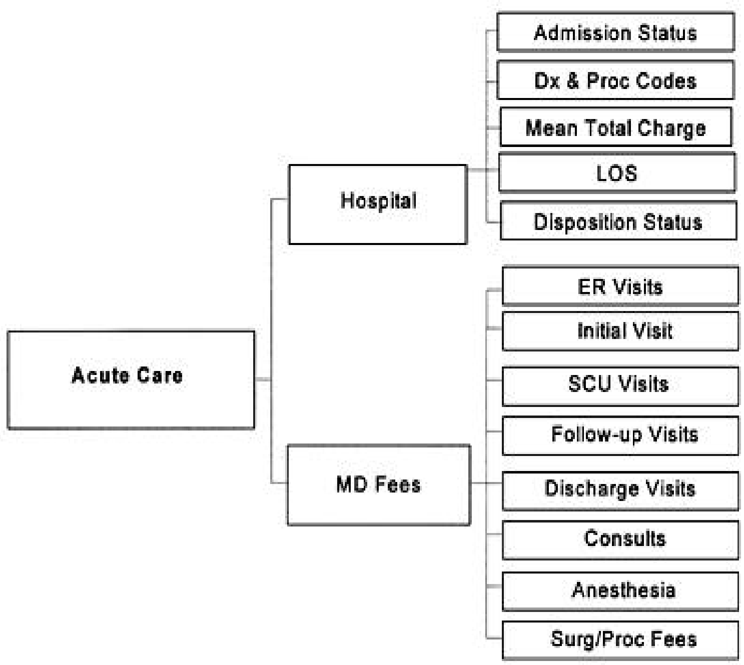

Figure 2—*Acute care cost-relevant elements. LOS, length of stay; SCU, special care unit.*

Table 1—*Acute inpatient hospital costs (including physician costs) by complication*

Complication	ICD-9 code	Discharges	Acute hospital cost (1996 U.S.$)
AMI	(410.00→410.91)	26,974	16,520
Angina	(413.0→413.9)	3,922	5,087
Ischemic stroke	(434.00→434.91, 436)	23,665	9,236
TIA	(435.9)	5,289	5,261
1st LEA	(84.10→84.17)	8,497	18,613
2nd LEA	(84.10→84.17)	8,497	19,071
Foot ulcers	(707.1)	8,317	9,910

Data are *n* or $. ICD-9 codes refer only to principal diagnoses. Only patients with a comorbid diagnosis of diabetes were included in the analyses.

have a leg amputation during the same admission, the discharge was grouped to the LEA pool. This methodology was used for all complications.

Acute care hospital costs include all accommodation, ancillary (e.g., pharmacy, laboratory), operating room, diagnostic and therapeutic procedures, and physician fees. *Physicians' Current Procedural Terminology* (CPT) codes (16) and Medicare fee schedules for 1996 were used to represent average costs for laboratory services, as well as physicians' procedure and visit fees. For consistency with the acute care databases, only fee schedules from Florida, Maryland, Massachusetts, North Carolina, and California were used. Because physician fees are not included in the discharge data and are not reported in the literature in sufficient detail by complication, it is necessary to develop an inpatient physician resource-use profile for each complication. Profiles were developed by creating a complex, complication-specific minimodel primarily based on length of stay, diagnosis and procedure codes, diagnosis related group (DRG) assignment, and other pertinent database elements. The physician cost profile was developed by building upon a baseline level of daily visits based on length of stay, adjusted for atypical days of care (e.g., discharge, surgery). To this baseline cost, fees were added to account for the differential use of more resource-intensive services for each complication, such as admission via the emergency room, stays in special care units, surgical procedures, anesthesia use, and consultations. As diagnostic procedures are often not coded in the databases, supplemental information from the literature was used when available (17).

Costs of skilled nursing facilities (SNF) and home health care (HHC) were taken from 1994 Medicare data (18). Diagnosis-specific costs were used where possible; however, some proxy diagnoses were used where more specific estimates were not available or appropriate. For example, the charges billed to Medicare for traumatic leg amputations were used to represent the SNF and HHC costs of an LEA. This decision was made because the postacute management of a leg amputation is likely to be similar regardless of the underlying cause for the amputation. Intermediate care nursing home facility costs were developed using published data from the Health Care Financing Administration and published nursing home reports (19–21). Acute rehabilitation and therapy costs are based on survey data. Durable medical equipment and supplies were derived from manufacturers' price lists, and medication costs were taken from the 1996 *Red Book* (22). Fees for outpatient office visits, tests, and procedures were taken from the Medicare fee schedules.

A conservative approach was taken in developing the cost profiles; therefore, some of the costs may be underestimated. In various areas of this economic analysis, there are aspects of the care of diabetic patients for which costs were unavailable. In such cases, costs were excluded rather than estimated based on pure assumption. There were other areas for which multiple, equally valid, sources provided conflicting data, in which case the more conservative estimate was used.

All event and state cost estimates are reported as costs in 1996 U.S. dollars. Where up-to-date values were not available, older estimates were inflated using the Medical Care Inflation Index (a component of the Consumer Price Index) supplied by the Federal Bureau of Labor Statistics for the month of January for each of the years 1990–1996. Any charges used as inputs were adjusted to costs by means of a cost-to-charge ratio. In the absence of a standard value, a ratio of 0.7 was assumed.

RESULTS

— Table 1 displays the acute inpatient hospital costs along with the size of the population analyzed and the identifying ICD-9 codes for complications for which hospital costs were a major component. The state and event costs for nonepisodic complications are provided in Table 2.

Cardiovascular events

The average event cost for an AMI was estimated to be $27,630, 60% of which was the cost related to the acute care hospitalization cost. In addition to the acute hospitalization, event costs include pre-admission ambulance/cardiopulmonary resuscitation care and all 1st-year subsequent care costs, including cardiac rehabilitation programs and cardiac-related medications (i.e., β-blockers, aspirin, ACE inhibitors, nitrates) (23–26). Although the costs related to coronary angiography, aortocoronary bypass grafts, and percutaneous transluminal coronary angioplasty are included in the acute care costs for those patients who had these procedures during their initial hospitalization, some patients accrue these costs after discharge. The cost of these procedures for the proportion of diabetic patients receiving them in the year subsequent to their initial hospital stay (20.5% angiography, 13.5% angioplasty, and 7% bypass surgery [25]) was also included in the event cost.

Average state costs of AMI were calculated to be $2,185 per patient per year. These included the cost of medications, physician visits, and monitoring cardiology tests (i.e., electrocardiogram and stress test). This also reflects the annual nursing-home care costs for the 2% of diabetic AMI patients who require permanent institutionalization.

Costs were estimated for diabetic patients with angina. Event costs included acute hospitalization, invasive procedures, medications, primary and consulting physicians, diagnostic procedures, and laboratory tests. The costs of acute hospitalization ($5,087) were applied only to those with unstable angina (24.6%) (27). The angina event cost was $2,477. The state costs ($1,082) for angina were composed of primary and consulting physician visits, medications, and monitoring cardiology tests.

Cerebrovascular events

Stroke is the major cost contributor for cerebrovascular events. Upon discharge from acute care, approximately 40% of diabetic patients suffering an ischemic stroke were transferred to some level of rehabilitative or subacute inpatient care, and another 13%

Table 2—*Event and state costs of nonepisodic complications*

Complication	Cost: Event cost (1996 U.S.$)	State cost (U.S.$ annualized)
Cardiovascular		
AMI	27,630	2,185
Angina	2,477	1,082
Cerebrovascular		
Ischemic stroke	40,616	9,255
TIA	6,204	45
Nephropathy		
Microalbuminuria	62	14
Gross proteinuria	69	23
ESRD	0*	53,659
Retinopathy		
Background retinopathy	0‡	57
Macular edema	1,100	57
Proliferative diabetic retinopathy	1,044	57
Blindness	0‡	3,486
Neuropathy		
Symptomatic neuropathy	218	—†
1st LEA	26,894	1,739
2nd LEA	27,132	—†

*Event costs were not calculated separately for ESRD as they are included in the composite state cost (see text). †Insufficient data available to estimate cost (see text). ‡No direct costs are attributable to this condition as an event (see text).

received HHC. Those patients who were receiving care in these settings before hospital admission were not included in these percentages to ensure that this subsequent care was attributed only to those in whom it represented a true incremental cost. To determine event and state costs for stroke, a previously developed model (28) was used.

An assumption was made that a transient ischemic attack (TIA) was truly transient, and thus no permanent residual disability would be considered in the economic analysis. This assumption was supported by the disposition status in the acute care databases as less than one-quarter of patients received either subacute inpatient or HHC upon discharge. The mean length of stay was 4.3 days compared with 8.8 days for ischemic stroke. TIA event costs included acute and subacute inpatient care, HHC, follow-up neurology visit, and daily aspirin therapy. No information, other than the recommendation of continued aspirin therapy, could be found for long-term follow-up of TIA patients; thus, only a daily regimen of aspirin was considered in determining the state costs.

Nephropathy

Screening for nephropathy was considered part of the management costs of diabetes and is not discussed here. The following cost estimates apply once diabetic nephropathy has been diagnosed. Diabetic nephropathy is classified into three progressive levels of severity: microalbuminuria, gross proteinuria, and ESRD. Physician visits and monitoring urine tests are the main components of the event costs for microalbuminuria ($62) and gross proteinuria ($69). Other interventions often recommended for gross proteinuria—such as protein-restricted diet and the discontinuation of smoking—were considered; but because none of these have measurable cost implications as isolated factors (29,30), only condition-appropriate urine tests were used to estimate the state costs of microalbuminuria ($14) and gross proteinuria ($23). Antihypertensive therapy, namely ACE inhibitors, was not included based on the position of the National Institutes of Health that there is insufficient evidence to recommend treatment with ACE inhibitors for prevention of progression of renal disease (31).

ESRD is defined as nephropathy requiring dialysis or renal transplant for the patient to survive. Most patients with ESRD, including 92% of dialysis patients and 90% of transplant recipients, are covered by a special program under the direction of Medicare (6). Data from this program were the basis of a 3-year cost-effectiveness study conducted to calculate average Medicare payments by ESRD treatment modality and etiology. The average annual Medicare payments for ESRD with diabetes as the primary cause are $53,659 per patient (in 1996 U.S. dollars) (6). This estimate includes all medical care received by the patient, not just those services required for the treatment of ESRD. For example, this estimate would include payments for a patient with an inpatient stay for a fractured hip as well as payments for hemodialysis sessions. As such, if this cost estimate were used for ESRD in a diabetic model, the costs relating to other complications should not be included, as it would constitute double-counting for those other complications.

Although this estimate does not represent the costs solely related to renal disease, it was used because it is the best available information for ESRD and is often used as a proxy for ESRD costs (13,32). Event costs were not calculated separately for ESRD because they are included in the composite described above.

Retinopathy

Diabetic retinopathy is defined by four stages of progression: background retinopathy (nonproliferative retinopathy), macular edema, proliferative retinopathy, and blindness.

The state cost ($57) of background retinopathy consists of a yearly comprehensive exam to monitor the disease. There is no associated event cost, as the American Diabetes Association reports that there is no commonly accepted therapy for the condition other than improved glycemic control (33). Screening for background retinopathy is considered part of diabetes management and, therefore, is not reported here.

The American Academy of Ophthalmology recommends that patients diagnosed with macular edema or proliferative retinopathy receive laser photocoagulation surgery, as well as diagnostic tests to guide laser treatment (34). Event costs ($1,100) for macular edema include an ophthalmology consultation, fluorescein angiography, focal photocoagulation, and one postsurgical follow-up visit. Event costs ($1,044) for proliferative retinopathy consist of pre- and postprocedure physician visits, color fundus photography, and panretinal (scatter) photocoagulation. Laser surgery and its corresponding costs are assumed to occur only once for patients diagnosed with macular edema or proliferative retinopathy. Both of these conditions imply state costs ($57) that consist of an additional monitoring visit per year.

The most recent information on the cost of blindness comes from a study of Medicaid and Medicare disability programs that cover this condition (35). After conversion to 1996 costs, the value of $3,486 was used as the state cost. Blindness for this purpose of the analysis is considered a permanent health state not precipitated by an acute event; therefore, no event cost was estimated.

Neuropathy

In this analysis, neuropathy is composed of three progressive levels: symptomatic neuropathy, first LEA, and second LEA. The components of the event cost ($218) of symptomatic neuropathy are electromyographic testing and neurological consult (36). Medications were not included in the event costs as there is little evidence that any drug therapy is useful for managing diabetic symptomatic neuropathy (37). Current treatments are palliative in nature, relieving symptoms of neuropathy rather than addressing the underlying nerve damage. No evidence of consensus was found to enable the creation of a representative medication profile. Therefore, rather than develop an arbitrary profile of managing symptoms, no cost was assumed as the state cost for symptomatic neuropathy.

For this study, an LEA is defined as one performed below the hip, as described in the Rochester (MN) Epidemiology Project (38). Although acute care inpatient costs were calculated for specific types of amputations through use of ICD-9 codes, other resource-use data for services, such as subsequent (postacute inpatient) care or prosthetic costs, are not reported at this level of detail in the literature. Final resource-use profiles were developed for only the most common levels of amputation (above-knee, below-knee, foot, and toe), and these levels were used proportionally to develop an overall LEA cost.

It has been reported that of diabetic patients with an LEA, approximately 50% will require a second LEA within 5 years of the initial amputation (39). Event costs for a first and second amputation were calculated separately. The acute hospitalization costs were estimated on a population of 8,500 diabetic LEA discharges from the acute state databases, but first versus second amputation could not be differentiated. The proportions of each type of amputation (e.g., toe, below the knee) were taken from the Rochester Epidemiology Project, and these differ for first versus second. Thus, using these proportions, the overall acute care cost for an initial LEA ($18,613) differs from that of a second LEA ($19,071). Revisions after the initial amputation, for the 15% to which they apply, also contribute to the event cost (40). Based on discharge data, 24% of patients with an LEA receive some form of rehabilitative or subacute inpatient care upon discharge from their initial acute stay, and another 21.5% receive HHC. For patients who are fitted for a prosthesis, the cost of the device was added to the event costs (38,41,42).

LEA also contributes to permanent disability in the diabetic population. Appropriate published data regarding annual health care costs subsequent to the initial event were not found; therefore, only costs related to nursing home care and management and refitting of the prosthetic device are included in the state costs—an acknowledged underestimation of the likely cost. In addition, the state cost of the second LEA is assumed to be zero because it was found that a low percentage of double amputees walk with the use of prostheses (5,41,43–45).

Diabetic foot ulcers

Foot ulcers are defined as those that heal without amputation or vascular surgery. Not all patients with foot ulcers require hospitalization; therefore, in calculating the event cost ($2,732) for foot ulcers, acute inpatient hospital costs were applied to only 20% of the diabetic foot ulcer population (46).

The mean acute hospital cost for foot ulcers includes hospital and physician costs for surgeries, such as wound debridement and skin grafting, but no vascular or amputation surgery. Also included in the event cost for those hospitalized were two follow-up office visits with a physician. As 24% of these patients require HHC (based on the inpatient databases' discharge disposition), 115 home health visits were added to these patients based on Medicare (18). For the 4.2% of patients discharged to an SNF with a foot ulcer complicated by osteomyelitis, Medicare data were also used to estimate subsequent care costs. The mean length of stay for treating foot ulcers, with and without osteomyelitis, was reported as 27.8 and 35.6 days, respectively (18).

Only outpatient care was included in the estimate for the 80% not hospitalized; however, as no published data were available on the overall cost of managing a foot ulcer on an outpatient basis, we relied on an article published in 1994 (46) that estimated treatment to include 4.5 physician visits on average. This is a conservative estimate, as supply costs are not included.

Hypoglycemia

An episode of hypoglycemia is defined, for costing purposes, as one in which the patient consumes resources. Three levels were considered: the mildest level is assumed to resolve with a glucagon injection and does not require the attention of medical personnel; the moderate level requires an emergency room visit and emergency room consult with a physician; the most severe level requires an inpatient stay to resolve, plus one follow-up visit with the patient's primary care physician. The proportion of third-level episodes (1%) was obtained from the Veteran's Affairs Cooperative Study (47), and the breakdown of the remaining two levels (28% level 2 and 71% level 1) was done according to the Diabetes Control and Complications Trial (DCCT) (48). Using a weighted average of these three levels and the resources estimated for each, the event cost of hypoglycemia was estimated to be $188.

CONCLUSIONS — Care related to diabetes comprised 14.6% of all U.S. health care expenditures in 1992 (12), and the total direct cost was $45.2 billion (49). This type of information is impressive, but is it meaningful to those who need to make decisions about interventions for diabetes?

Given the number of published articles on diabetes and the scope of the disease and its complications, it would be natural to assume that numerous sources of cost inputs for the purpose of an economic analysis would be available. We found, however, that there were no recent papers that provide comprehensive patient-level cost estimates for the majority of relevant diabetic complications.

In one article, for example, the total health care expenditures for a number of type 2 diabetes–related conditions were estimated to be $4.8 billion in 1986 (20). The estimates, by complication, were $3,849 million for circulatory disorders, $387 million for visual disorders, $240 million for neuropathy, $104 million for nephropathy, and $145 million for skin ulcers. Unfortunately, although the costs of many of the diabetes complications were estimated, they are now outdated. Furthermore, a patient-level estimate cannot be derived based on the methodology and sources used. An advantage of examining cost data on a per-patient, rather than on an aggregate, basis is that it provides estimates that can be used in disease models to inform health care decision-makers.

Glauber and Brown (11) estimated that cardiovascular disease directly accounted for at least $858,000 per 1,000 diabetic members in a health maintenance organization (HMO) in 1988. Because this estimate included diabetic patients with no cardiovascular disease, it is not the cost of managing cardiovascular disease per se. It depends on the prevalence of cardiovascular disease in that particular HMO. Also, the estimate is outdated.

Although we cite the deficiencies in the existing literature and believe our complication costs are more relevant for current economic analyses, we recognize the limitations of our estimates. A comprehensive examination of the cost of complications was undertaken, but there remains some uncertainty. Some complication costs are likely underestimated because their management was profiled based on guidelines due to a lack of published data on actual practice; however, it could also be argued that the use of guidelines could lead to an overestimation of resource use. Although clinical guidelines provide a possible forecast of costs to the health care system if closely followed, they may not be adhered to in clinical practice. With this in mind, we used them reluctantly, but we considered them to be a better option than mere assumption. This reasoning was also used when calculating the cost estimates for foot ulcer and LEA. As previously acknowledged in RESULTS, rather than assume a cost for those aspects of ongoing management for which there were no available data, we chose to underestimate, as care can vary substantially for these complications.

It should be remembered when viewing the state costs that they represent the annual cost of management for any year subsequent to the event, not a particular year. The estimates that are made may not apply well over time, but this is always an issue with estimates of any kind. Patients with diabetes do not spend a lot of time in each state, which reduces the time-dependence issue. Furthermore, the data we have do not provide any evidence of time dependence.

Limitations notwithstanding, the costs calculated for the diabetic complications presented in this paper provide comprehensive, up-to-date, U.S. cost estimates for most diabetic complications at a level that is functional for researchers and that does not exist in the current literature.

The DCCT showed that intensive insulin therapy could postpone, retard the progression, and/or reduce the occurrence of some type 1 diabetic complications (32). With 8 million diagnosed diabetic patients in the U.S., the chronic nature of the disease, and the potential for the development of multiple costly complications in any one patient, costs related to diabetes should be a major concern to those who are responsible for financing health care in the U.S. The complications of diabetes present a substantial economic burden. Obviously, efforts to delay or avoid complications would be beneficial not only to the patient, but also to the health care system. The costs provided here give one piece of the economic analysis that will need to be performed to evaluate new interventional therapies for diabetes.

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