



The Association Between Poor Glycemic Control and Health Care Costs in People With Diabetes: A Population-Based Study

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OBJECTIVE

To analyze the differences in health care costs according to glycemic control in people with type 2 diabetes.

RESEARCH DESIGN AND METHODS

Data on health care resource utilization from 100,391 people with type 2 diabetes were extracted from the electronic database used at the Catalan Health Institute. Multivariate regression models were carried out to test the impact of glycemic control (HbA_{1c}) on total health care, hospital admission, and medication costs; model 1 adjusted for a variety of covariates, and model 2 also included micro- and macrovascular complications. Glycemic control was classified as good for HbA_{1c} <7%, fair for ≥7% to <8%, poor for ≥8% to <10%, and very poor for ≥10%.

RESULTS

Mean per patient annual direct medical costs were €3,039 ± 6,581 Euros (€). Worse glycemic control was associated with higher total health care costs: compared with good glycemic control, health care costs increased by 18% (509.82) and 23% (€661.35) in patients with very poor and poor glycemic control, respectively, when unadjusted and by €428.3 and €395.1, respectively, in model 2. Medication costs increased by 12% in patients with fair control and by 28% in those with very poor control (model 2). Patients with poor control had a higher probability of hospitalization than those with good control (5% in model 2) and a greater average cost when hospitalization occurred (€811).

CONCLUSIONS

Poor glycemic control was directly related to higher total health care, hospitalization, and medication costs. Preventive strategies and good glycemic control in people with type 2 diabetes could reduce the economic impact associated with this disease.

Type 2 diabetes has become a major public health problem, with the incidence and prevalence rates steadily increasing over the past three decades, especially in low- and middle-income countries (1). Apart from the large number of associated chronic complications and disability, type 2 diabetes is also an important cause of premature deaths. Furthermore, there continues to be changes in the demographics of people with type 2 diabetes, health care use and delivery patterns, technology, medical costs, and other social conditions that affect the economic burden associated with type 2

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diabetes (1–3). Previous research indicates that medical costs per person are much higher in people with type 2 diabetes than in the general population, due mainly to the increased use of hospital resources caused by the complications of the disease (4–12). In fact, having type 2 diabetes is associated with substantially higher lifetime medical expenditures despite being associated with reduced life expectancy (5).

Several studies have related poor glycemic control to higher health care cost (12,13) and have suggested that interventions that improve glycemic control can be cost-effective, because health care expenses increase exponentially when control worsens and the age of the patient increases (14–16). In a recent meta-analysis of quality-improvement interventions addressed to lower HbA_{1c}, these measures appeared to be a fair-to-good value depending on society's willingness to pay for improvements in health (17).

Given the importance of type 2 diabetes control, some studies have been conducted in Europe specifically to evaluate the costs associated with the control of glycated hemoglobin (6–9,11,12). However, population studies based on big databases are scarce (10–12). Furthermore, only a few studies have compared health care costs among people with diabetes according to different degrees of glycemic control in Europe (8,11). However, these studies have some limitations that may impede their generalizability: both are from a managed care health care system (based on a health insurance system similar to the case in the U.S.), and one of them is actually limited to hospitalization costs (11). Overall, there is a lack of large population studies that evaluate health care costs according to different degrees of glycemic control that are generalizable to European countries with a National Health System (NHS). Such studies may help facilitate resource-allocation decisions based on interventions that benefit the most both clinically and economically. This is especially pertinent in countries with an NHS, which are generally encountering significant financial pressures.

To address this gap in the evidence, the current study aims to elucidate if there are differences in annual health care costs considering the degree of glycemic control in a population-based cohort of >100,000 people with type 2 diabetes from the

perspective of an NHS that covers the majority of the population in a Mediterranean area (Catalonia, Spain). We also performed additional analyses on hospital admission and medication costs.

RESEARCH DESIGN AND METHODS

Design and Inclusion Criteria

This was a cross-sectional study designed to estimate and compare the costs of people with type 2 diabetes according to glycemic control as measured by glycated hemoglobin (HbA_{1c}). All patients attended the Catalan Health Institute (ICS), were aged 31–90 years diagnosed with type 2 diabetes (ICD-10 codes E11 and E14), and had at least one HbA_{1c} measurement during 2011.

All variables recorded during 2011 were entered in the study following the same criteria reported in previous studies (18). Spain invested 9.0% of its gross domestic product in health care. Health care is organized in Spain in a framework of an NHS mainly financed by general taxes and based on the principles of universality, free access, and equity (19). From an organizational point of view, it has two main levels: national and regional. Regional governments are responsible for the management of 90% of public health expenditures. The ICS is the main provider of primary health care services in Catalonia. It manages 470 primary care teams caring for 5.8 million citizens, ~83% of the Catalan population. All ICS primary care professionals (~15,000) use the same computerized medical record program (eCAP) created and managed by the institution itself.

Data were extracted from the Information System for the Development of Research in Primary Care (SIDIAP) database, which is intended for use in research and includes the eCAP medical records of all patients in the ICS (20).

Variables Collected

To estimate the health care resource utilization, we used the SIDIAP^Q subpopulation, which is composed of patients cared for in the primary care centers with the best clinical records (21) and includes data from 1,878,816 of the 5.8 million patients registered in the parent SIDIAP database. The SIDIAP^Q is a subdatabase generated through a record quality index that was created by comparing the prevalence of acute and chronic diseases in the parent database (observed cases)

with the prevalence in the literature (expected cases) to permit the selection of centers with high-quality data. It has been previously validated to be highly representative of the population of Catalonia in terms of geographical, age, and sex distributions (21). This information was supplemented with data registered in the Spanish Minimum Basic Data Set of Hospital Admissions (Conjunto Mínimo Básico de Datos de Altas Hospitalarias) (22), which records all hospital admissions in Catalonia. The Conjunto Mínimo Básico de Datos follows the recommendations of the European Minimum Basic Data Committee and contains information on clinical records and discharge reports from hospitals. However, it does not have information about medical emergencies, including hypoglycemia or visits to the hospital outpatient services.

The analysis included health care direct costs of people with type 2 diabetes using the NHS. Data on private health care costs for the people with diabetes themselves or for their relatives were not available.

The main independent variable of the analysis was glycemic control, measured by HbA_{1c}. It is a continuous variable expressed as a percentage of millimoles per mole, with 5.7% as the maximum value indicating a normal HbA_{1c} level in a person without diabetes (23) and 6.5% as a threshold for the diagnosis of diabetes (3). Glycemic control (HbA_{1c}) was measured using the last recorded value of the year. According to HbA_{1c} levels, four categories were generated: good glycemic control for HbA_{1c} <7% (the usual goal for most patients); fair control for HbA_{1c} ≥7% to <8% (8% as a upper limit for older, frail, or comorbid patients); poor glycemic control for HbA_{1c} ≥8% to <10%; and very poor control for HbA_{1c} ≥10% (usually, the threshold at which insulinization is the preferred option for most patients) (18,23). Because the risk of developing micro- and macrovascular complications is, among others, associated with poor glycemic control (24,25), we included dichotomous variables for the following scenarios: whether the individuals with type 2 diabetes had no vascular complications, only microvascular complications (i.e., retinopathy, neuropathy, and albuminuria or renal failure), only macrovascular complications (i.e., coronary heart disease, heart failure, stroke, and peripheral arteriopathy), or both

micro- and macrovascular complications. We additionally considered whether the individuals had hypertension or hypercholesterolemia.

Type 2 diabetes duration was divided into categories (<2 years, from 2 to 5 years, from 5 to 10 years, and >10 years).

We also included sociodemographic factors, such as age, in groups (younger than 45 years, 45–55 years, 55–65 years, 65–80 years, and older than 80 years), and sex. Information was also available on lifestyle factors such as smoking and BMI. For smoking, we generated three categories: never smoked, current smokers, and people who have ever smoked but have quit smoking. We calculated the BMI value based on the recorded weight and height. BMI was divided into four categories: obese (BMI ≥ 30 kg/m²); overweight (BMI 25–30 kg/m²); normal weight (BMI 19–25 kg/m²); and underweight (BMI <19 kg/m²).

Supplementary Table 1 provides a detailed description of each variable included in the analysis.

Cost Calculation

Annual direct costs were analyzed by adding primary care visits, referrals of patients from primary care physicians (gatekeepers) to specialist care, hospitalizations, diagnostic tests, all medications for any health problem billed to the NHS, dialysis treatment, and use of self-monitoring test strips.

To calculate annual health care costs, we used the prices established in the Official Bulletin of the Catalan Government (DOGC) for 2012 (26). All costs are expressed in Euros (€) at 2011 prices. For this, the prices set by the Department of Health were adjusted to 2011 values by subtracting 0.9% to account for inflation (27).

The costs of hospital admissions were obtained using the Diagnosis-Related Group patient classification system (28) published in the DOGC and weighted by level of hospital complexity (high, medium, and low). For medications, the retail price was used based on the pharmacy billing information. As information on the type and amount of self-monitoring test strips used by each person with diabetes was not available, we used the mean annual cost per patient accounted in each primary care team. For the cost of dialysis, the mean frequency was estimated to be three sessions a week. As information on the type of dialysis

used for each patient was not available, the cost of each session was weighted according to local use (20% peritoneal dialysis and 80% hemodialysis) (29) using the prices established by the DOGC.

The total health care costs were calculated as follows: every resource used by each individual was identified, quantified, and multiplied by the unit cost of each resource. This procedure yielded the total resource cost per individual as well as the overall cost for each study population (HbA_{1c}: <7%, $\geq 7\%$ to <8%, $\geq 8\%$ to <10%, and $\geq 10\%$).

Statistical Analysis

Three outcome measures were used in the current study: total health care costs, hospitalization costs, and medication costs. Hospitalization and medication costs were analyzed separately because they represented the vast majority of the total health care cost.

The impact of glycemic control, and the other independent variables, on total health care costs was estimated using a generalized linear model (GLM). GLMs have a greater capability for identifying model effects as statistically significant when the data are not normally distributed, and therefore, GLMs have frequently been used for recent health care cost analyses, given the skewed distribution of costs (30). GLMs are empirical transformations of the classical ordinary least square regression model, which specifies the conditional mean function directly. Specifically, GLMs do not require a transformation scale, but a response distribution of one of the exponential family of distributions (normal, Poisson, γ , binomial, and inverse Gaussian), which relates the mean of the response to a scale on which the model effects combine additively. According to the Modified Park Test, the chosen family was the γ distribution for modeling health care costs in our analysis.

Two subsets of regression models were performed, depending on whether type 2 diabetes duration was introduced as a categorical variable or continuous variable. Within each set of regression models, we performed two regression models: in model 1, we included age, sex, type 2 diabetes duration, HbA_{1c} categories, BMI categories, having hypertension, total cholesterol >200 mg/dL, and smoking habits. Subsequently, micro- and macrovascular complications were introduced in a second regression model.

Different models were applied according to the distribution of hospitalization and medication costs. A two-part model (31) was used for assessing the impact of glycemic control and the other independent variables on hospitalization costs because $\sim 86\%$ of the sample had no hospital admission registered. The first part of the two-part model was a probit regression model with a dichotomous dependent variable, which represented hospitalization costs and took value 1 if the individual had hospitalization costs >0 and 0 otherwise. After using probit estimation techniques, the second part of the two-part model was performed only for the subsample with hospitalization costs >0. A GLM with γ distribution and identity link was used for the second part of the two-part model, as it was for total health care costs. When modeling medication costs, we applied a GLM with γ distribution and log link.

As a sensitivity analyses, multivariate interquartile analyses were also performed to complement the main analysis. For health care costs, quantile regressions at the 25th, 50th, and 75th percentile were estimated. For hospitalization and medication costs, 50th quantile regressions were run. All results are shown adjusted by other explanatory and control variables (i.e., age, sex, diabetes duration, vascular complications, etc.).

RESULTS

Descriptive: Sample Characteristics and Health Care Costs

The baseline characteristics of the study population are summarized in Supplementary Table 2. Within the whole sample, 60.1% of patients were older than 65 years, were slightly more likely to be men (48% were female), and had a mean type 2 diabetes duration of 7 years. More than half of the study population was obese (56%), $\sim 70\%$ were hypertensive, and almost two-thirds had never smoked (64%). Overall, 64% of the whole study population with type 2 diabetes had no micro- or macrovascular complications, while 16% had both types of vascular complications.

Some differences were observed by glycemic control group. Almost two-thirds (62.5%) of the individuals with very poor glycemic control (HbA_{1c} $\geq 10\%$) were 65 years old or younger, whereas in the good control group (HbA_{1c} <7%), a

similar percentage of patients (63%) was older than 65 years of age. The proportion of people with no vascular complications and any vascular complication by age group and HbA_{1c} level is shown in Supplementary Table 3. Overall, 68% of patients with good glycemic control (HbA_{1c} <7%) had no microvascular complications, decreasing to 58% in patients with very poor glycemic control (HbA_{1c} ≥10%). In addition, as levels of HbA_{1c} worsened, subjects were more likely to suffer from microvascular complications (18% in the group with very poor glycemic control vs. 8% in the good glycemic control group). In contrast, the prevalence of macrovascular complications decreased as glycemic control got poorer (Supplementary Table 2).

The mean general annual cost per person with type 2 diabetes was €3,039 (SD 6,581), increasing as the level of glycated hemoglobin worsened: €2,843 (SD 6,233), €3,102 (SD 7,293), €3,504 (SD 6,549), and €3,353 (SD 6,520) in the cohorts with glycemic control values of HbA_{1c} <7%, ≥7% to <8%, ≥8% to <10%, and ≥10%, respectively (Table 1). The component with the greatest weight on the overall cost in all groups was hospitalization, followed by any medication costs and primary care visits. Those three-category expenditures were lower in subjects with optimal glycemic control and increased across the different cohorts. As complementary information, Supplementary Table 4 reports the total health care costs for each complication.

Table 2 shows the regression results for the overall sample. When vascular complications were omitted (model 1), individuals with fair glycemic control (HbA_{1c} ≥7% to <8%) were associated with higher total health care costs, which increased by €147.8 compared with the good glycemic control group (HbA_{1c} ≤7%). Such increases reached their maximum in those with very poor glycemic control (HbA_{1c} ≥10%), whose health care costs were €582.3 higher than the good control group. Moreover, compared with the group who had type 2 diabetes for <2 years, for those subjects with type 2 diabetes for 2–5 years, 5–10 years, and >10 years, health care costs were higher by €162.6, €520.2, and €1,039, respectively. When micro- and macrovascular complications were included in the model (model 2), individuals with fair glycemic control (HbA_{1c} ≥7% to <8%) were still significantly associated with higher total health care costs, which increased by €127.5. The largest increase in costs

was observed in the very poor glycemic control group, whose health care costs were €428.3 higher than in the good control cohort. Similar changes occurred for type 2 diabetes duration, which were still significant but with lower coefficients. For example, having type 2 diabetes for >10 years was associated with higher health care costs of €738.7 compared with people with type 2 diabetes for <5 years. With respect to having any vascular complication, compared with none, health care costs were higher by €1,516 for those having any macrovascular complication, by €844.1 for those suffering from microvascular complications, and by €2,091 for those with both types.

Table 3 shows the regression results for hospital admission costs. People with poor glycemic control (HbA_{1c} between 8 and 10%) were significantly associated with a higher probability of hospitalization (7.93% for the first part of model 1; 5.0% for the first part of model 2). Conditional on having been admitted to hospital, only having an HbA_{1c} level between 8 and 10% was significantly related to higher hospitalization costs of €927.5 (second part, model 1). When micro- and macrovascular complications were included in the model (second part of the two-part model, model 2), individuals whose glycemic control was between 8 and 10% were still significantly associated with higher hospitalization costs (5% higher than individuals with good control), and the hospital costs were also higher (€811.1).

Table 4 shows that in model 1, the group with fair glycemic control (HbA_{1c} between 7 and 8%) was associated with higher medication costs, which increased by 13.2 percentage points compared with good glycemic control (HbA_{1c} <7%). Such differences became larger in the group with very poor glycemic control (HbA_{1c} >10%), with medication costs being 33.6% higher compared with the good control group. In model 2, medication costs in the group with fair glycemic control increased by 11.9%, whereas in the very poor glycemic control group, medication costs were 28.1 percentage points higher.

Results from the quantile regressions can be found in Supplementary Tables 5–7. Compared with the previous results explained, quantile regressions confirm the significances of the different variables, including glycemic control, diabetes duration, and micro- and macrovascular

complications significantly related to health care (and hospitalizations and medication) costs. Coefficients are not comparable because GLMs are performed around the mean, and quantile regressions are performed around the median.

CONCLUSIONS

In the current study, we have described the annual costs (total health care costs, hospital admission costs, and medication costs) according to glycemic control in people with type 2 diabetes. We report significant differences among groups with different levels of HbA_{1c}, regardless of the cost component analyzed. In general, the percentage of patients with microvascular complications is greater in the categories of worse glycemic control (32). In addition, our work shows that, even after controlling for the presence of micro- and macrovascular complications, a worse glycemic control is associated with higher total health care costs: compared with good glycemic control, health care costs increased by 18% (€509.82), 23% (€661.35), and 9% (259.37€) in individuals with very poor (HbA_{1c} >10%), poor (HbA_{1c} between 8 and 10%), and fair (HbA_{1c} between 7 and 8%) glycemic control, respectively, when unadjusted; and by €428.3, €395.1, and €127.5, respectively, when adjusted in the full model (model 2). Moreover, the positive associations between those variables and health care costs are confirmed by the results obtained in the sensitivity analyses performed. However, according to our results and in line with a previous publication by our group, the youngest group of subjects (younger than 45 years of age) had poorer glycemic control than older groups (older than 80 years of age); macrovascular complications increase with increasing age and with duration of diabetes (33), and therefore, the differences in macrovascular complications in the good and very poor glycemic groups may be related to the age of the subjects.

The potential strength of this study is based on the large number of patients and that all of the included variables were obtained from a high-quality database (a subset of data from the primary care centers with best records) in real clinical practice. In this regard, it is worth emphasizing that only a few population studies have analyzed the differences in health

Table 1—Mean per patient annual direct medical costs (in 2011 €)

	Patients with HbA _{1c} (N = 100,391)	HbA _{1c} <7% (N = 54,395)	7% ≥ HbA _{1c} < 8% (N = 24,994)	8% ≥ HbA _{1c} < 10% (N = 16,286)	HbA _{1c} ≥10% (N = 4,716)	Patients without HbA _{1c} (N = 26,419)
Total costs	3,038.76 (6,580.76)	2,842.95 (6,233.06)	3,102.32 (7,292.54)	3,504.30 (6,548.69)	3,352.77 (6,520.38)	3,381.14 (12,049.61)
GP						
consultations	607.52 (553.98)	585.24 (540.96)	620.52 (549.74)	654.01 (581.80)	635.16 (610.29)	460.94 (548.53)
Hospitalization	1,203.58 (6,082.86)	1,131.46 (5,705.22)	1,197.99 (6,865.55)	1,396.55 (6,041.79)	1,398.63 (6,012.60)	1,681.00 (11,214)
Referrals to specialist care	123.59 (164.85)	119.45 (160.32)	126.83 (164.75)	131.76 (177.93)	125.88 (168.44)	81.58 (142.35)
Tests	14.72 (39.39)	14.44 (38.87)	15.66 (40.85)	14.45 (38.68)	13.94 (39.48)	9.76 (33.82)
Self-monitoring test strips	49.95 (11.72)	49.89 (11.63)	50.23 (11.90)	49.85 (11.76)	49.44 (11.64)	50.46 (12.03)
Medications	930.07 (986.09)	825.59 (938.43)	989.08 (999.08)	1,154.61 (1,052.55)	1,046.94 (1,046.14)	905.79 (1,276.16)
Dialysis	34.16 (949.78)	43.44 (1,076.27)	23.53 (773.46)	25.90 (822.35)	11.91 (578.20)	147.49 (1,982.07)

Data are mean (SD). GP, general practitioner.

costs associated with glycemic control in people with type 2 diabetes (10,11). Our results reinforce the previous results of these studies, identifying a negative association between glycemic control and health care costs. However, a cost comparison with other countries is difficult to perform due to methodological differences (population vs. sample of a health care organization, population vs. patients recruited in specialized care or hospitals, and cutoff points of glycemic level), to differences among health care systems and the clinical practices used among

them, and to differences in cost structures and unit costs (prices and rates) of the different health systems (9–11,13–17). Additionally, depending on the richness and comprehensiveness of the database used, the included cost items may differ among studies. An advantage of our study over others is that we were able to disentangle the association between glycemic control and hospitalization and medication costs separately.

One limitation of this study, although common to all studies using population-based databases, is the incompleteness

of some clinical variables. First, ~20% of patients with diabetes had no HbA_{1c} measurement; the absence of any HbA_{1c} value in the database was an exclusion criterion given the scope of our analyses in which the target study population consisted of people with diabetes with at least one HbA_{1c} measurement who were followed by a general practitioner. However, we tested whether individuals with diabetes and with missing HbA_{1c} values had higher health care costs, and the results showed that people with no HbA_{1c} measurement incurred, on average, €345 more in total health care costs than the sample used in this study due to the higher costs of hospitalization and dialysis. This difference might be, at least in part, explained by the fact that these subjects were followed by hospital specialists not using the same electronic clinical record system, which resulted in the absence of this information in the SIDIAP database. However, we have insufficient evidence to postulate whether these patients with missing values are more likely to have high HbA_{1c} levels and therefore cannot make any conclusions regarding this group with missing values. Additionally, we have used only one HbA_{1c} measurement (i.e., the last recorded).

Secondly, we did not use the entire SIDIAP database but a subsample (SIDIAP^Q), which has the most complete medical histories. While this may be regarded as a possible limitation, we have found that the SIDIAP^Q database is representative of the entire population of Catalonia (the northeastern region of Spain) in terms of geographic and demographic characteristics (21). Moreover, we

Table 2—Results from the GLM regression with γ distribution and identity link on total costs

Variables	Model 1	Model 2
Diabetes duration categories (reference: 0–2 years)		
2–5 years	162.6*** (44.74)	127.9*** (41.71)
5–10 years	520.2*** (48.19)	347.9*** (43.78)
>10 years	1,039*** (66.19)	738.7*** (60.68)
HbA _{1c} categories (reference: HbA _{1c} <7%)		
7% ≥ HbA _{1c} < 8%	147.8*** (42.21)	127.5*** (39.11)
8% ≥ HbA _{1c} < 10%	527.0*** (58.04)	395.1*** (52.64)
HbA _{1c} ≥10%	582.3*** (95.64)	428.3*** (86.16)
Complications (reference: no complications)		
Macrovascular complications		1,516*** (97.51)
Microvascular complications		844.1*** (69.74)
Both types		2,091*** (83.61)
Observations ^a	90,874	90,874
AIC	17.947	17.892
BIC	–1,001,518	–1,006,790
Log-likelihood	–866,376.45	–863,723.18

SEs are given in parentheses. Model 1 adjusted for age (in categories), sex, BMI (in categories), hypertension and hypercholesterolemia, and smoking habits. Model 2 adds to model 1 whether the individual has any micro- or macrovascular complications or both. Reference categories: diabetes duration of <2 years, HbA_{1c} <7% (models 1 and 2), and no vascular complications (model 2). AIC, Akaike information criterion; BIC, Bayesian information criterion. ***P < 0.01. ^aOnly individuals with complete data for all lifestyle factors (and any other variable included in the regressions) were included the analyses (i.e., 90,874 patients in both models 1 and 2 out of 100,391 patients from the whole patient cohort).

Table 3—Results from the two-part model on hospitalization costs

Variables	First-part probit of two-part model, model 1	Second-part GLM with γ distribution and identity link of two-part model, model 1	First-part probit of two-part model, model 2	Second-part GLM with γ distribution and identity link of two-part model, model 2
Diabetes duration categories (reference: 0–2 years)				
2–5 years	0.0529*** (0.0177)	147.6 (369.3)	0.0462*** (0.0178)	106.1 (362.0)
5–10 years	0.100*** (0.0161)	773.4** (339.1)	0.0791*** (0.0162)	568.3* (333.2)
>10 years	0.191*** (0.0175)	1,215*** (373.7)	0.151*** (0.0177)	910.9** (371.1)
HbA _{1c} categories (reference: HbA _{1c} <7%)				
7% \geq HbA _{1c} < 8%	0.0103 (0.0124)	109.9 (268.4)	–0.000905 (0.0124)	87.46 (262.6)
8% \geq HbA _{1c} < 10%	0.0793*** (0.0144)	927.5*** (330.3)	0.0500*** (0.0146)	811.1** (323.6)
HbA _{1c} \geq 10%	0.169*** (0.0243)	843.6 (552.1)	0.126*** (0.0246)	636.8 (541.8)
Complications (reference: no complications)				
Macrovascular complications			0.297*** (0.0173)	1,733*** (388.8)
Microvascular complications			0.201*** (0.0162)	974.5*** (357.5)
Both types			0.358*** (0.0138)	2,323*** (320.1)
Constant	–1.688*** (0.0369)	4,521*** (693.5)	–1.677*** (0.0370)	4,404*** (690.8)
Observations	90,874	13,837	90,874	13,837
AIC		20.06		20.04
BIC		–117,709.7		–117,854.6
Log-likelihood	–38,835.91	–138,739.50	–38,424.52	–138,652.77

SEs are given in parentheses. Model 1 adjusted for age (in categories), sex, BMI (in categories), hypertension and hypercholesterolemia, and smoking habits. Model 2 adds to model 1 whether the individual has any micro- or macrovascular complications or both. Reference categories: diabetes duration of <2 years, HbA_{1c} <7% (models 1 and 2), and no vascular complications (model 2). AIC, Akaike information criterion; BIC, Bayesian information criterion. **P* < 0.1; ***P* < 0.05; ****P* < 0.01.

included only people with full data in every variable included in the statistical analysis, which might lead to an underestimation of the relationship between

glycemic control and health care costs. Further analyses could aim to disentangle the reverse pathway among some of the variables included by using instrumental

variables to get rid of endogeneity issues that could be present in the associations analyzed in the current study, as some relevant variables might have been omitted. Finally, the costs of ambulatory hospital services and medical emergencies, including hypoglycemia, were not recorded. Hospital outpatient services are more frequent in patients with advanced complications. However, those patients are still seen by the primary care doctor, at which time multiple comorbidities (not only diabetes) are also followed up. Moreover, the cost of ambulatory medical visits in the Spanish national public health system is very low, having a very minor impact in terms of health care costs in comparison with other cost components that are indeed included in the database and, hence, in the current analysis (6,12). Regarding hypoglycemia, it was clearly underreported as a health problem in the eCAP system (0.8% of patients; data not shown); thus, the impact of the treatment of this complication on the number of visits and the use of other resources and the cost could not be analyzed. Despite being evident that medication and good prevention is necessary to

Table 4—Results from the GLM regression with γ distribution and log link on treatment costs

Variables	Model 1	Model 2
Diabetes duration categories (reference: 0–2 years)		
2–5 years	0.148*** (0.0122)	0.140*** (0.0122)
5–10 years	0.313*** (0.0112)	0.284*** (0.0112)
>10 years	0.430*** (0.0125)	0.375*** (0.0126)
HbA _{1c} categories (reference: HbA _{1c} <7%)		
7% \geq HbA _{1c} < 8%	0.132*** (0.00907)	0.119*** (0.00908)
8% \geq HbA _{1c} < 10%	0.308*** (0.0107)	0.275*** (0.0108)
HbA _{1c} \geq 10%	0.336*** (0.0182)	0.281*** (0.0183)
Complications (reference: no complications)		
Macrovascular complications		0.384*** (0.0135)
Microvascular complications		0.270*** (0.0121)
Both types		0.552*** (0.0107)
Observations	90,874	90,874
AIC	15.56	15.52
BIC	–1,012,478	–1,016,589
Log-likelihood	–751,214.62	–749,055.06

SEs are given in parentheses. Model 1 adjusted for age (in categories), sex, BMI (in categories), hypertension and hypercholesterolemia, and smoking habits. Model 2 adds to model 1 whether the individual has any micro- or macrovascular complications or both. Reference categories: diabetes duration of <2 years, HbA_{1c} <7% (models 1 and 2), and no vascular complications (model 2). AIC, Akaike information criterion; BIC, Bayesian information criterion. ****P* < 0.01.

achieve an optimal glycemic control, it cannot be ignored that cases of severe hypoglycemia are not uncommon in patients treated with insulin or sulfonylureas (34–36). This implies that the mean costs in this study could be underestimated (1,6,7). In a recent Spanish study, the estimated mean direct cost of an episode of severe hypoglycemia was €702, and episodes that required hospital treatment accounted for 49% of the total costs (35). In addition, the inclusion of emergencies would increase the cost difference depending more on the type of treatment (especially in insulin-treated patients) than the degree of glycemic control (37).

The prevalence of type 2 diabetes is a serious issue of pandemic level in Western countries and a great economic burden for health care systems (1–3,5–7). Therefore, it is necessary to develop new efficient therapy strategies, together with appropriate prevention measures, to manage type 2 diabetes and associated risk factors. The importance of good control of type 2 diabetes has been reported in several studies conducted in the U.S. and Europe (9,16,17). It is clear that preventive measures promoted by primary health care professionals and good care of hyperglycemia, among other steps, should be included as routine (12).

These findings suggest that achieving an HbA_{1c} target value indicative of good glycemic control (<7%) could result not only in better patient outcomes but also in even more considerable health care savings and reduced health care resource utilization. Therefore, any improvement in glycemic control—for instance, from poor (>8%) to fair (7 to 8%)—could result in benefits from both a clinical perspective and an economic point of view. Based on these results, the great challenge is to identify for each type of patient the interventions that allow a more efficient use of resources, achieving a good glycemic control and an improvement of health in the short, medium, and long term (38). The question is complex because the answer will depend on the type of patient (39), the degree of the HbA_{1c}, the personal and contextual circumstances of diabetes management, and even the available resources of the health care system, because a cost-effective intervention in one country might not be borne in another country (40). Finally, this study yields results supporting the use of glycemic control as a surrogate

measure not only for the risk of diabetes-related complications, but also health care utilization and costs attributable to diabetes.

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