ORIGINAL RESEARCH

Glycemic control and diabetes-related health care costs in type 2 diabetes; retrospective analysis based on clinical and administrative databases

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Background: Diabetes is one of the most prevalent chronic diseases, and its prevalence is predicted to increase in the next two decades. Diabetes imposes a staggering financial burden on the health care system, so information about the costs and experiences of collecting and reporting quality measures of data is vital for practices deciding whether to adopt quality improvements or monitor existing initiatives. The aim of this study was to quantify the association between health care costs and level of glycemic control in patients with type 2 diabetes using clinical and administrative databases.

Methods: A retrospective analysis using a large administrative database and a clinical registry containing laboratory results was performed. Patients were subdivided according to their glycated hemoglobin level. Multivariate analyses were used to control for differences in potential confounding factors, including age, gender, Charlson comorbidity index, presence of dyslipidemia, hypertension, or cardiovascular disease, and degree of adherence with antidiabetic drugs among the study groups.

Results: Of the total population of 700,000 subjects, 31,022 were identified as being diabetic (4.4% of the entire population). Of these, 21,586 met the study inclusion criteria. In total, 31.5% of patients had very poor glycemic control and 25.7% had excellent control. Over 2 years, the mean diabetes-related cost per person was: €1291.56 in patients with excellent control; €1545.99 in those with good control; €1584.07 in those with fair control; €1839.42 in those with poor control; and €1894.80 in those with very poor control. After adjustment, compared with the group having excellent control, the estimated excess cost per person associated with the groups with good control, fair control, poor control, and very poor control was €219.28, €264.65, €513.18, and €564.79, respectively.

Conclusion: Many patients showed suboptimal glycemic control. Lower levels of glycated hemoglobin were associated with lower diabetes-related health care costs. Integration of administrative databases and a laboratory database appears to be suitable for showing that appropriate management of diabetes can help to achieve better resource allocation.

Keywords: diabetes mellitus, glycemic control, HbA_{1c}, health expenditure

Introduction

Diabetes is one of the most prevalent chronic diseases. The estimated prevalence of diabetes in the world population was 6.6% in 2010, and this number is projected to increase to 7.8% by 2030.[1] The condition commonly progresses to include microvascular and macrovascular complications.[2,3] Development of diabetes-related complications is related to glycemic control.[4] Diet and pharmacological treatment play a central role in the management of diabetes. However, according to the World Health Organization, only 50% of diabetic patients in developed countries comply with drug treatment.[5,6]

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In addition, the National Health and Nutrition Examination Survey reported that only 37% of patients with diabetes have adequate disease control.[7] In addition to its adverse effects on health and quality of life, diabetes also imposes a staggering financial burden on the health care system. The total cost of diabetes care is 2.3 times the cost of care for nondiabetic patients.[8] In Italy, direct costs for people with diabetes amount to about 9 billion Euros per year, representing nearly 9% of the national health expenditure.[9] Oglesby et al found that diabetes-related costs were 16% and 20% lower for patients with good control (glycated hemoglobin [HbA_{1c}] $\leq$7%) compared with those having fair control (HbA_{1c} >7%–9%) and poor control (HbA_{1c} >9%).[10] Menzin et al reported that patients with a mean HbA_{1c} $\geq$10% had higher diabetes-related hospital costs than those with a mean HbA_{1c} <7%.[11] Other data suggest that diabetes-related complications and consequent costs may be increased in patients with therapy targeted to very tight glycemic control.[12]

Estimates of the direct medical costs attributed to diabetes are essential to be able to assess the financial burden of the disease and plan for future health care needs. In addition, because type 2 diabetes is potentially preventable,[13] estimates of medical expenditure are needed to assess the full economic effect of programs aimed at prevention of the disease. The data used to determine these policies are based either on disease registries clinical information or on administrative data. The former often involve population samples and are time-consuming and expensive to collect, whereas the latter have been used successfully as a source of information for diabetes monitoring.[14,15]

The aim of this study was to quantify the relationship between health care costs attributable to diabetes and level of glycemic control by cross-linkage of various large clinical and administrative databases in order to increase our understanding of the management of diabetes and be able to make informed policy decisions.

Materials and methods
Data source
The study was based on administrative databases maintained by two local health units in Italy; Arezzo in Tuscany and Ravenna in Emilia-Romagna, representing a population of about 700,000 subjects. Using the Territorial Pharmacy Database, local health units routinely measure the volume of expenditure generated by dispensing of drugs to enrollees. The data available in each prescription claim include the patient's national health number, the prescribing physician's number, the anatomical-therapeutic-chemical (ATC) code

of the drug dispensed, the number of packs dispensed, the number of units per pack, the dose, the unit cost per pack, and the prescription date. Using the anonymous alphanumeric code allocated to each citizen by the local health unit as a unique identifier to guarantee patient privacy, this database is linked with the Hospital Direct Drugs Distribution Registry, which contains the same data as the Territorial Pharmacy Database: the Beneficiaries' Database, listing patient demographic characteristics, ie, date of birth, gender, place of residence, physician license number, start and end of registration dates and the date of death; the Hospital Discharge Database, which includes all hospitalization data, with the principal and secondary discharge diagnosis codes classified according to the International Classification of Diseases, Ninth Revision (ICD9CM), and the diagnosis-related group code; the Outpatient Service Registry, which includes all laboratory investigations, instrumental tests, and specialist checkups requests, and the dates on which these were performed; the Clinical Laboratory File, which records the test results of all laboratory tests performed. Universal health care coverage in Italy means that the information contained in these databases is complete and comprehensive, and has been used in previous epidemiological studies.[16] The Italian Ministry of Health reports that these archives are 100% complete and 95% accurate.[17] No identifiers related to patients were provided to the researchers. The ethics committees for the local health units approved the study.

Cohort definition
This was a retrospective cohort study, which included subjects identified as diabetic if, between January 1, 2009 and December 31, 2009, they had at least two prescriptions of antidiabetic drugs (ATC code A10), and/or at least one fasting glucose determination over 126 mg/dL, and/or at least one hospitalization with a discharge diagnosis of diabetes (ICD9CM code 250), and/or at least one outpatient service with an exemption for diabetes. The date of the first prescription of antidiabetic medication, date of glucose determination, hospital discharge, and/or outpatient service was defined as the index date. The clinical characteristics of the patients enrolled in this study were investigated for the one-year period before the index date. A two-year study period, starting from the index date, was evaluated for each patient. Patients were excluded if they were younger than 45 years, if they had only one determination of HbA_{1c} in the first or the second year of the study, if they had moved to another local health unit, or if they had died during the study period.

Subjects enrolled were defined as: dyslipidemic based on the presence of at least two prescriptions of lipid-lowering drugs (ATC code C10) and/or at least one hospitalization with a primary or secondary diagnosis of metabolic syndrome (ICD9CM code 277.7) or disorder of lipid metabolism (ICD9CM code 272); as hypertensive based on the presence of at least two prescriptions of antihypertensive drugs (ATC code C02, C03, C07, C08, C09) and/or a hospitalization with a primary or secondary diagnosis of hypertensive disease (ICD9CM code 401–405); as affected by a previous major cardiovascular event based on the presence of at least one hospitalization with a primary or secondary diagnosis of ischemic heart disease (ICD9CM code 410–414), heart failure (ICD9CM code 428), cerebrovascular disease (ICD9CM code 430–438), or arterial disease (ICD9CM code 440–442); as affected by a cardiovascular disease if they had a previous hospitalization for a cardiovascular event and/or had prescriptions for drugs acting on the renin-angiotensin system (ATC code C09A, C09B), antiplatelet drugs (ATC code B01AC06), beta-blockers (ATC code C07), and/or antiplatelet drugs. The Charlson comorbidity index was also calculated for each patient by summing the assigned weights for all comorbid conditions evaluated in the one-year period before the index date.[18] In addition, for the purposes of analysis, all HbA_{1c} measurements available during the follow-up period were identified. HbA_{1c} is a widely used marker of glycemic control that reflects the average glycemic level during the past 2–3 months. As in previous studies, the target HbA_{1c} was defined as ≤7%.[19] Enrolled patients were subdivided into five cohorts according to target HbA_{1c} values achieved: excellent (≥80%), good (60%–79%), fair (40%–59%), poor (20%–39%), and very poor (<20%). We also grouped patients without any determination of HbA_{1c}.

Adherence with antidiabetic medication

Adherence was determined using the medication possession ratio (MPR). The MPR reflects the proportion of days during which the enrollee possesses a supply of medication.

$$MPR = \frac{\text{Sum of days' supply for all but the last filling of antidiabetic medication}}{\text{Total number of days between first and last refill}}$$

For enrollees on multiple antidiabetic medications, the MPR reported was calculated as the mean of the MPR calculated for each drug. We excluded the number of days spent by the patients in an institutionalized care setting, such as hospital, from the MPR calculation. Because the Territorial

Pharmacy Database does not include data for drug dose, the mean daily dose of the prescribed drugs was defined according to the recommended dose reported in "L'Informatore Farmaceutico" for 2010.[20] Patients were defined as adherent with antidiabetic medication if their MPR was ≥80%.

Cost of illness

Cost of illness was measured using two different methods, ie, cohorts of people based on the percentage of HbA_{1c} levels ≤7%, as previously described, or the first and last HbA_{1c} measurement during the study period. Disease-related health care costs evaluated in the study period included: costs of antidiabetic medication dispensed by the Territorial and Hospital Pharmacy; costs due to hospitalizations for fatal and nonfatal hypertensive disease (ICD9CM code 401–405); ischemic heart disease (ICD9CM code 410–414), heart failure (ICD9CM code 428), cerebrovascular disease (ICD9CM code 430–438), arterial disease (ICD9CM code 440–442), and diabetes (ICD9CM code 250); costs of laboratory/instrumental tests for HbA_{1c}, glycemia, complete blood count, lipid panel, and albumin to creatinine ratio; and costs for specialist visits and eye examinations. Drug costs were evaluated using the National Health Service purchase price. Hospitalization costs were determined using the diagnosis-related group tariff. The cost of instrumental and laboratory tests was defined according to the tariffs applied by the Emilia-Romagna and Tuscany regions. The currency reference used was the Euro (€).

Statistical analysis

Quantitative variables are presented as the mean ± standard deviation. One-way analysis of variance was used to compare the means for the quantitative variables. Associations between categoric variables were tested using the Pearson χ^2 test. A generalized linear model with an identity link function and a gamma distribution was used to estimate the association between health care costs and level of glycemic control.[21] To control for confounding, we included in the model factors including age, gender, Charlson comorbidity index, coexisting illnesses (such as hypertension, dyslipidemia, and cardiovascular disease), and adherence level. Age was categorized as ≤65 or >65 years; the Charlson score was grouped into three categories based on distribution of scores, ie, ≤1, 2–3, ≥4; and adherence level was categorized based on the MPR value and grouped into three categories, ie, poor adherence (MPR <40%), fair adherence (MPR 40% to <80%), or good adherence (MPR ≥80%). Two-tailed P-values < 0.05 were considered to be statistically significant, and all statistical
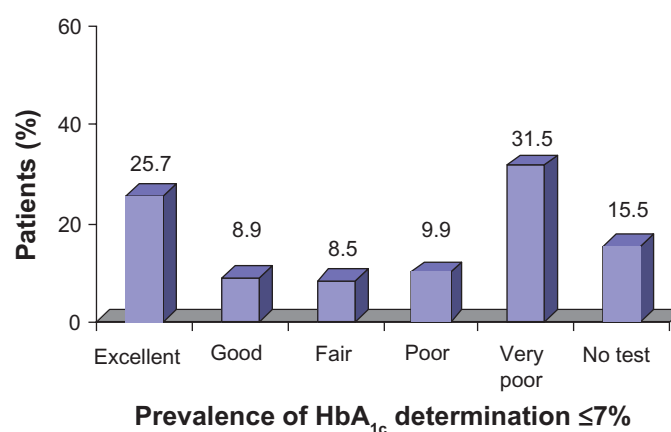
Figure 1 Prevalence of diabetic patients with different levels of glycemic control.

analyses were conducted using Stata software version 12.1 (Stata Corporation, College Station, TX, USA).

Results

Of the total study population of 700,000 subjects, 31,022 (4.4% of the entire population) were identified as diabetic. Of these, 9436 were excluded (1481 for being younger than 45 years; 5980 for having only one determination of HbA$_{1c}$ in the first or second year of the study; and 1975 because they died or moved to another local health unit). We identified six cohorts of patients using HbA$_{1c}$ levels (Figure 1). In total, 6807 patients (31.5%) had very poor HbA$_{1c}$ control, 5540 (25.7%) had excellent control, and 3337 (15.5%) did not have any determination of HbA$_{1c}$ during the 2 years of the study. Patient characteristics are reported in Table 1. Patients without HbA$_{1c}$ determinations were more frequently older than those with HbA$_{1c}$ determinations, and had less concomitant illness and cardiovascular disease.

Worst is the glycemic control level, higher is the median value as well as the number of HbA$_{1c}$ tests performed

during the study period (Table 2). Table 3 and Figure 2 show glycemic control expressed as HbA$_{1c}$ ≤7% in relation to the number of antidiabetic drugs prescribed for each patient. There were 2046 patients (9.5% of the entire study population) with no prescriptions for antidiabetic medication, 7633 patients (35.4%) with prescriptions for one drug, 6204 (28.7%) with prescriptions for two drugs, and 5703 (26.4%) with prescriptions for three or more drugs. The majority (53.6%) of untreated patients did not have any HbA$_{1c}$ measurements recorded. In contrast, the number of treated patients without HbA$_{1c}$ determinations was very low, ranging from 18.7% to 4.2%. Moreover, in the group of patients with excellent control, 39.6% maintained their target HbA$_{1c}$ level successfully using a single drug whereas subjects with very poor control failed to maintain their target HbA$_{1c}$ level despite intensification of treatment (56.1% were prescribed more than two drugs).

The rate of adherence with antidiabetic medication (Table 4) was significantly different in the six cohorts of

Table 1 Characteristics of enrolled patients

	Glycemic control level							P-value
	Excellent	Good	Fair	Poor	Very poor	No test	Total	
n	5540	1924	1844	2134	6807	3337	21,586	
Mean age (years)	69.3	69.2	69.2	69.5	69.1	71.5	69.6	<0.001
Male gender (%)	55.2	51.8	51.5	53.7	47.7	54.7	52.1	<0.001
Charlson comorbidity index (%)								<0.001
≤1	71.3	71.0	71.4	68.9	65.7	62.3	67.9	
2–3	24.9	25.7	25.0	26.8	30.5	32.9	28.2	
≥4	3.8	3.2	3.6	4.3	3.9	4.8	3.9	
Dyslipidemia (%)	49.4	54.2	53.0	54.5	56.4	29.2	49.7	<0.001
Hypertension (%)	77.0	76.7	76.5	77.4	75.2	72.8	75.8	<0.001
Previous CV hospitalization (%)	6.2	5.8	7.5	6.6	6.6	7.4	6.6	0.105
CV disease (%)	31.9	31.1	34.3	32.8	35.4	30.3	33.0	<0.001

Abbreviation: CV, cardiovascular.

Table 2 Number of determinations and median values for HbA₁c

	Glycemic control level					*P*-value
	Excellent	**Good**	**Fair**	**Poor**	**Very poor**	
HbA$_{1c}$ median value % (IQR)	6.4 (0.5)	6.9 (0.3)	7.1 (0.3)	7.4 (0.5)	8.2 (1.1)	<0.001
HbA$_{1c}$ determination, mean number (SD)	4.5 (2.2)	5.0 (2.3)	5.1 (2.5)	5.3 (2.6)	5.5 (2.6)	<0.001

Abbreviations: HbA$_{1c}$, glycated hemoglobin; IQR, interquartile range; SD, standard deviation.

diabetic patients, being 6.7%–4.6% in <40% and 64.7%–60.1% in ≥80%.

Total health care costs were calculated to be €30,433,264.79 and the mean cost per patient was €1557.49. The mean cost calculated per patient according to the prevalence of HbA$_{1c}$ ≤7% (Table 5) showed a progressive and significant increase correlating with a progressive decrease in control of HbA$_{1c}$, from €1291.56 in patients with excellent control to €1894.80 in patients with very poor control. Patients without any HbA$_{1c}$ tests showed the lowest mean cost at €859.90. Older age, presence of hypertension, dyslipidemia, cardiovascular disease, and uncontrolled HbA$_{1c}$ were factors that contributed significantly to increased health care costs in these patients (Table 6).

We also analyzed health care costs according to the first and last HbA$_{1c}$ levels recorded during the study period (Table 7). The intervals between the first and last HbA$_{1c}$ determinations were similar in all cohorts, and in the range of 17.1–18.4 months. The mean cost per patient increased progressively in patients with stable HbA$_{1c}$ <7%, 7.1%–8%, 8.1%–9%, and >9%. There was an increment in mean health care costs in patients with worsening control of HbA$_{1c}$. Analysis of the different components of health care costs (Table 8) showed that the progressive incremental cost was mainly because of antidiabetic drugs, hospitalizations for diabetes-related problems, and use of outpatient services.
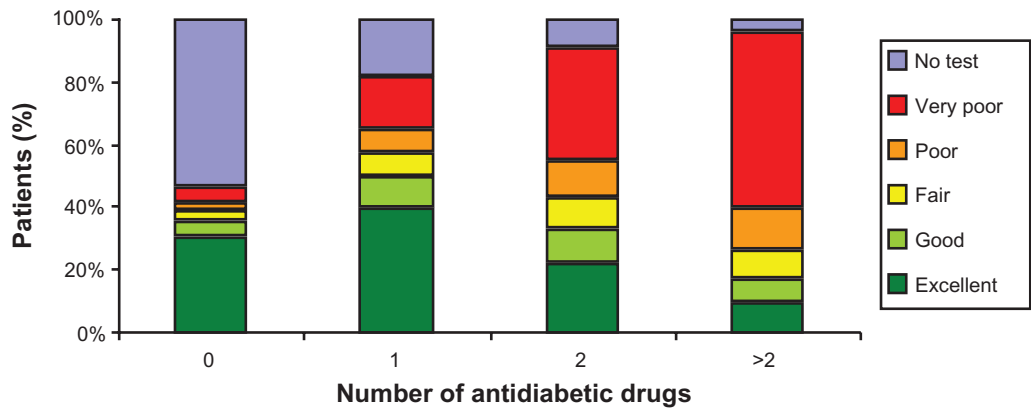
Table 3 Number of antidiabetic drugs prescribed in the different cohorts of diabetic patients

Glycemic control level	Antidiabetic drugs prescribed (n)							
	0		**1**		**2**		**>2**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Excellent	617	30.2	3023	39.6	1379	22.2	521	9.1
Good	103	5.0	739	9.7	657	10.6	425	7.5
Fair	70	3.4	619	8.1	599	9.7	556	9.7
Poor	44	2.2	580	7.6	748	12.1	762	13.4
Very poor	116	5.7	1244	16.3	2250	36.3	3197	56.1
No test	1096	53.6	1428	18.7	571	9.2	242	4.2
Total	2046	100.0	7633	100.0	6204	100.0	5703	100.0

Discussion

Diabetes registries have been used for years to evaluate clinical care provided by health systems,[22] and are usually created from administrative data, such as those for hospital discharge diagnoses and pharmaceutical claims.[23,24] The availability of detailed clinical data, including real-time laboratory test results, has improved the ability to build more sophisticated and accurate diabetes registries that capture more precisely defined cohorts of individuals with diabetes. With regard to laboratory tests, we selected plasma glucose and HbA$_{1c}$ levels to create the linkage with clinical and administrative databases. In addition to antidiabetic medication, we used three further criteria to identify diabetic patients, and documented a diabetes prevalence of 4.4%, which makes our cohort comparable with the entire Italian population.[25] Moreover, these criteria enabled identification of 9.5% of subjects who were not treated with antidiabetic medication. About half of these untreated subjects did not have any determination of HbA$_{1c}$, while the majority of the remaining subjects had excellent HbA$_{1c}$ control. This apparently conflicting profile could be because: firstly, the presence in this cohort of a high percentage of subjects defined as diabetic on the basis of a single determination of fasting plasma glucose >126 mg/dL, which might be considered the weakest of the criteria we used; secondly, the inability of this analysis to capture diet and exercise habits, which have been shown to have a positive impact on glycemic control. The importance of the criteria used for inclusion in such registries is not trivial. For example, in a sample of residents of Ontario, Canada, Harris et al showed that the prevalence of diabetes ranged from 5% to 12% depending on which combinations of laboratory, pharmacy, and diagnosis data were used.[26] To determine the quality of control of diabetes in clinical practice, we subdivided our patients into five cohorts according to the percentage of HbA$_{1c}$ levels ≤7% during the two-year study period. HbA$_{1c}$ concentration is a good indicator of glycemic control during the previous 8–12 weeks and is used as the standard biomarker for the efficacy of glycemic

Figure 2 Prevalence of different levels of glycemic control in diabetic patients categorized according to number of antidiabetic drugs prescribed.

management because it correlates well with development of microvascular complications and also (albeit to a lesser extent) macrovascular complications, according to a large epidemiological study.[27,28] The treatment guidelines for patients with type 2 diabetes that existed during the study period recommended a target HbA$_{1c}$ level of ≤7%,[29] although the National Institute for Health and Clinical Excellence has more recently recommended a target HbA$_{1c}$ level of ≤7.5%.[30] Despite these recommendations, most patients still do not achieve their target HbA$_{1c}$ level in general practice.[7,31] Among our diabetic patients with HbA$_{1c}$ determinations, only 25.7% had excellent control of diabetes (median HbA$_{1c}$ 6.4%) and 8.9% had good control (6.9%), while 31.5% had very poor control (8.2%). Of note is that more than 60% of patients in each of our study cohorts showed ≥80% adherence with antidiabetic medication, which is greater than the adherence figures reported by the World Health Organization,[6] and indicates that the quality of glycemic control decreases with increasing numbers of antidiabetic prescriptions. Other authors have documented significant differences in the use of diabetic medication at different levels of HbA$_{1c}$ control.[10] In order to quantify the association between health care costs attributable to diabetes and quality of control of diabetes in clinical practice, we used two different calculation methods, ie, one

based on the percentage of HbA$_{1c}$ levels ≤7% and the other based on the first and the last determinations of HbA$_{1c}$. Using the first method, we identified five cohorts. Patients with very poor HbA$_{1c}$ control (less than 20% of HbA$_{1c}$ determinations ≤7%) showed a cost per year increment of 46.7% (€947.40) compared with those having excellent control (more than 80% of HbA$_{1c}$ determinations ≤7%) who had a cost per year of €645.78. Our findings using this method of analysis highlight the significant differences in cost associated with each of the five levels of glycemic control. Even patients considered to have fair glycemic control, ie, HbA$_{1c}$ 7.1%–9%, had significantly higher total and prescription costs attributable to diabetes than patients with excellent glycemic control.

Using the second method, we identified sixteen cohorts of patients. Those with a first-last HbA$_{1c}$ determination >9% compared with those with a first-last HbA$_{1c}$ determination ≤7% showed an annual cost increment of 63.2% (€1042.37 versus €638.67, respectively). In general, we found a significant cost increment when the HbA$_{1c}$ increased during the follow-up period independent of the initial level, whereas decreasing HbA$_{1c}$, although advantageous in the short-term, did not significantly change costs. Our findings also indicate that a modest (around 1%) incremental worsening of HbA$_{1c}$ resulted

Table 4 Adherence to antidiabetic medication in different cohorts of diabetic patients

Adherence to antidiabetic drugs*	Glycemic control level													
	Excellent		Good		Fair		Poor		Very poor		No test		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<40%	330	6.7	94	5.2	82	4.6	101	4.8	306	4.6	221	6.4	1134	5.8
40%–79%	1636	33.2	590	32.4	544	30.7	658	31.5	2142	32.0	802	31.3	6372	32.6
≥80%	2957	60.1	1137	62.4	1148	64.7	1331	63.7	4243	63.4	1218	62.3	12034	61.6
Total	4923	100.0	1821	100.0	1774	100.0	2090	100.0	6691	100.0	2241	100.0	19540	100.0

Note: *P < 0.001.

Table 5 Health care costs in different cohorts of diabetic patients

	Glycemic control level						
	Excellent	Good	Fair	Poor	Very poor	No test	Total
Patients (n)	4923	1821	1774	2090	6691	2241	19,540
Total (€)	6,358,342.03	2,815,248.53	2,810,142.19	3,844,394.14	12,678,098.98	1,927,038.92	30,433,264.79
Mean (€)	1291.56 ± 3301.27	1545.99 ± 3535.66	1584.07 ± 3453.53	1839.42 ± 3743.26	1894.80 ± 3773.76	859.90 ± 2693.76	1557.49 ± 3509.89

in greater health care costs and increased resource utilization in the two-year study period. However, modest incremental improvements in HbA_{1c} control may not be sufficient to reduce costs in a meaningful way. The amount of antidiabetic medication prescribed, number of outpatient attendances, and frequency of hospitalizations for diabetes-related reasons contributed to the increased costs. Other researchers have found that reduction of HbA_{1c} to ≤7% was associated with a 30% decrease in expenditure on long-term health care, and patients with HbA_{1c} ≤8% had a lower likelihood of hospitalization.[10,32,33] This mixed-methods assessment of the cost and issues surrounding quality of measurement of glycemic control and use in primary care practices yielded interesting results. The data we collected enabled estimation of costs per patient in a context more easily understood by payers and policymakers.

Table 6 Multivariate regression analysis

	B	(95% CI for B)		P-value
Constant	362.04	294.97	470.07	<0.001
Age >65 years	280.33	277.51	446.57	<0.001
Male gender	296.03	204.26	356.39	<0.001
Charlson comorbidity index^				
2–3	−21.01	−87.87	45.85	0.538
>3	267.93	−13.91	549.78	0.062
Hypertension*	281.65	191.51	371.79	<0.001
Dyslipidemia*	346.85	259.19	434.50	<0.001
Cardiovascular disease*	2102.80	1631.75	2573.85	<0.001
Adherence level**				
<40%	63.11	−14.21	140.43	0.110
40%–79%	−128.67	−211.05	−46.29	0.002
Glycemic control level***				
Good	219.28	75.25	363.30	0.003
Fair	264.65	117.03	412.27	<0.001
Poor	513.18	345.13	681.23	<0.001
Very poor	564.79	456.35	673.23	<0.001
No test	−151.24	−235.09	−67.38	<0.001

Notes: ^Reference, Charlson index ≤ 1; *reference, no treatment or no diagnosis of cardiovascular disease; **reference, adherence level ≥ 80%; ***reference, excellent control. Constant is the expected health care cost when all the covariates have been set to their reference values.
Abbreviations: B, regression coefficient; CI, confidence interval.

The findings of the present study must be interpreted in light of some limitations. First, the analyses were performed using the databases of two local health units located in the north-center of Italy. Although these databases were deemed to cover the area of the local health units adequately, the results may not be generalizable to other populations. Second, the analysis only included subjects receiving antidiabetic medication, so it is unknown if all of our study subjects had a formal diagnosis of type 2 diabetes. However, we excluded subjects younger than 45 years of age to minimize the risk of inclusion of subjects with type 1 diabetes, which is common practice in retrospective analyses of databases.[34,35] Menzin et al found a higher prevalence of patients with type 1 diabetes in the younger age groups.[11] Third, we did not examine place of residence, which could confound the association between glycemic control and diabetes-related health care costs. Fourth, we were unable to define time since initial diagnosis, a factor that may influence response to antidiabetic medication, level of glycemic control, and costs. Fifth, we only considered subjects receiving oral antidiabetic drugs or a combination of oral agents and insulin. Future work using alternative approaches, eg, based on type of medication that subjects require, may be of interest. Sixth, we did not consider costs related to other therapies (eg, lipid-lowering or antihypertensive medication) or hospitalizations for any other reason, which are both factors that may contribute to underestimation of the cost per patient. Finally, the two-year study period was too short to evaluate cardiovascular morbidity and total mortality. In conclusion, our study shows that cross-linkage between various clinical and administrative databases is critical for successfully implementing systems of care that are value-based. To be adopted and embraced fully, systems must be applicable to patient care across payment sources and must have adequate patient volumes in order to identify patient characteristics influencing costs and be able to estimate the expected costs of quality improvement or deterioration. Our results indicate that glycemic control (ie, HbA_{1c} level) is a useful surrogate not only for diabetes-related complications but also for the associated health care costs.

Table 7 Mean cost per patient in different cohorts of diabetic patients determined according to the levels of first and last HbA$_{1c}$ determination performed during the study

Last HbA$_{1c}$ level	Baseline HbA$_{1c}$ level			
	≤7.0	>7.0 to ≤8.0	>8.0 to ≤9.0	>9
≤7	1277.35 ± 3226.27	1675.57 ± 4046.27	2037.18 ± 4625.92	1896.18 ± 3684.02
>7.0 to ≤8.0	1512.66 ± 3678.53	1487.79 ± 3035.17	1839.75 ± 3555.66	2281.92 ± 4725.64
>8.0 to ≤9.0	1776.12 ± 4355.22	2032.54 ± 4543.08	1844.87 ± 3146.61	2136.09 ± 3938.02
>9.0	2176.66 ± 4194.85	2086.86 ± 3312.51	2322.20 ± 3955.73	2084.75 ± 3579.18

Abbreviation: HbA$_{1c}$, glycated hemoglobin.

Table 8 Distribution of health care costs

	Stable HbA$_{1c}$ levels				
	≤7.0	>7.0 to ≤8.0	>8.0 to ≤9.0	>9	Total
n	5221	2492	849	699	9261
Antidiabetic drugs					
Total (€)	1,257,794.82	1,091,827.00	630,897.08	582,377.94	3,562,896.84
Mean (€)	240.91 ± 319.79	438.13 ± 453.18	743.11 ± 687.62	833.16 ± 818.60	384.72 ± 496.07
CV hospitalizations					
Total (€)	3,640,317.44	1,695,460.00	582,458.05	510,201.86	6,428,437.42
Mean (€)	697.25 ± 2873.34	680.36 ± 2614.14	686.05 ± 2796.09	729.90 ± 3068.32	694.14 ± 2813.92
Hospitalizations for diabetes					
Total (€)	309,145.94	240,148.00	521,60.71	146,214.79	747,669.48
Mean (€)	59.21 ± 665.68	96.37 ± 1211.42	61.44 ± 679.75	209.18 ± 1107.53	80.73 ± 883.71
Outpatient services					
Total (€)	1,474,236.30	763,007.50	293,648.87	230,290.28	2,761,182.99
Mean (€)	282.37 ± 234.73	306.18 ± 201.29	345.88 ± 212.00	329.46 ± 233.71	298.15 ± 225.02
Total					
Total (€)	6,681,494.50	3,790,443.00	1,559,164.71	1,469,084.87	13,938,048.51
Mean (€)	1279.73 ± 3140.15	1521.04 ± 3073.86	1836.47 ± 3133.04	2101.70 ± 3589.82	1505.03 ± 3356.97

Abbreviations: HbA$_{1c}$, glycated hemoglobin; CV, cardiovascular.

Disclosure

The authors declare no conflicts of interest in this work.

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