



An Economic Evaluation of the Relationship Between Glycemic Control and Total Healthcare Costs for Adults with Type 2 Diabetes: Retrospective Cohort Study

Kristina S. Boye · Jay P. Bae · Vivian T. Thieu · Maureen J. Lage

Received: August 21, 2023 / Accepted: October 31, 2023 / Published online: December 1, 2023
© The Author(s) 2023

ABSTRACT

Introduction: Glycemic control is associated with better outcomes among individuals with type 2 diabetes (T2D). This research examines total US all-cause medical costs for adults with T2D with recommended glycemic control (HbA1c < 7%) compared to poor glycemic control (HbA1c ≥ 7%).

Prior presentation This manuscript is based upon research which was presented at the American Diabetes Association, 83rd Scientific Session in San Diego, CA, June 23–26, 2023.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s13300-023-01507-0>.

K. S. Boye · J. P. Bae · V. T. Thieu
Eli Lilly and Company, Lilly Corporate Center,
Indianapolis, IN 46225, USA

K. S. Boye
e-mail: boye_kristina_secnik@lilly.com

J. P. Bae
e-mail: bae_jay@lilly.com

V. T. Thieu
e-mail: thieu_vivian_thuyanh@lilly.com

M. J. Lage (✉)
HealthMetrics Outcomes Research, 28 Riverside
Lane, Madison, CT 06443, USA
e-mail: maureen.j.lage@gmail.com

Methods: The study used administrative claims data linked to HbA1c laboratory test results from January 1, 2015 through June 30, 2021 to identify adults with T2D with a recorded HbA1c test. Patients with recommended glycemic control at index date were propensity score matched to patients with poor glycemic control. General linear models and two-part models were used to compare all-cause outpatient, drug, acute care and total costs for 1 year post index date.

Results: The study included 59,830 propensity-matched individuals. Results indicate that recommended glycemic control, compared to poor glycemic control, was associated with statistically significantly lower all-cause acute care (\$23,868 ± \$21,776 vs. \$24,352 ± \$22,223), drug (\$10,277 ± \$14,671 vs. \$10,540 ± \$14,928), and total medical costs (\$41,381 ± \$42,757 vs. \$42,054 ± \$43,422) but significantly higher outpatient costs (\$7290 ± \$12,028 vs. \$7026 ± \$11,587) (all $p < 0.0001$). Sensitivity analyses examined results based upon alternative HbA1c thresholds of ≤ 6.5% and < 8%. Results were generally robust to alternative HbA1c thresholds, with higher HbA1c thresholds associated with higher all-cause total costs as well as increased savings for having HbA1c below threshold.

Conclusions: Glycemic control was associated with significantly lower all-cause total, drug, and acute care medical costs. Given the high prevalence of T2D in the USA, our results

suggest potential economic benefits associated with glycemic control for healthcare providers.

Keywords: Costs; Economic evaluation; Glycemic control; HbA1c; Retrospective; Type 2 diabetes

Key Summary Points

Why carry out this study?

Glycemic control is associated with improved microvascular and macrovascular outcomes among individuals with T2D.

This study examines the all-cause total medical costs for suboptimal glycemic control (HbA1c \geq 7%) compared to recommended glycemic control (HbA1c $<$ 7%).

What was learned from the study?

The findings revealed that individuals whose index HbA1c was below the ADA target for glycemic control (HbA1c $<$ 7%) had substantially lower 1-year all-cause total medical costs relative to patients with above-target hyperglycemia (HbA1c \geq 7%).

The findings were also consistent when examining higher or lower HbA1c targets, and suggest economic benefits associated with glycemic control.

that the condition is relatively prevalent. An estimated 11.3% of US adults have diabetes currently [3], and the frequency of the disease is forecasted to increase to 17.9% by 2060 [4].

Previous research has shown that glycemic control is associated with reduced diabetes-related medical costs [5]. In addition, previous clinical trials have shown that glycemic control is associated with reductions in diabetes-related complications. Long-term follow-up of the cohorts from the UK Prospective Diabetes Study (UKPDS) demonstrated that individuals with T2D who received intensive antihyperglycemic therapy during the study had a decreased risk of most microvascular complications and significant long-term reductions in myocardial infarctions [6]. As a result of these and other clinical trials, the American Diabetes Association (ADA) suggested the HbA1c goal for non-pregnant adults in general should be $<$ 7% [7]. Such a goal has been shown to reduce microvascular and neuropathic complications. Furthermore, intensive glycemic control has also been shown to be associated with long-term reductions in cardiovascular risk if the reduction in HbA1c is obtained soon after a diagnosis of diabetes [8].

Given that glycemic control may be associated with reductions in both microvascular and macrovascular complications, the present study sought to quantify the economic impact of glycemic control for individuals with T2D. In particular, this retrospective study examines the hypothesis that glycemic control may be associated with reduced all-cause total medical costs. The results of this research may be used to quantify the economic benefits associated with glycemic control.

INTRODUCTION

Diabetes is associated with a substantial economic burden in the USA. In 2017, the direct medical costs of the disease came to an estimated \$237 billion, while the total costs amounted to \$327 billion [1]. The majority of these costs can be ascribed to type 2 diabetes (T2D), which accounts for 90–95% of all cases of diagnosed diabetes [2]. One of the reasons the overall medical costs of diabetes are so high is

METHODS

The analyses were conducted using de-identified Market Clarity data from Optum[®]. The data were obtained from administrative health insurance claims for members located across the USA. The approximately 17–19 million lives covered in this database were all insured via large commercial and Medicare Advantage health plans. The data were fully de-identified

and Health Insurance Portability and Accountability Act (HIPAA) compliant. For this study, the dataset supplied longitudinal information on patient demographics, coverage eligibility, inpatient and outpatient services, outpatient prescription fills, payments, and laboratory test results. Data for this study covered the period from January 1, 2015 through June 30, 2021, and permission to access the data was obtained from Optum[®]. The data for this study are available from Optum[®] but restrictions apply to the availability of these data, which were used under license for the current study. Given the use of retrospective and de-identified data, ethics committee approval was not required.

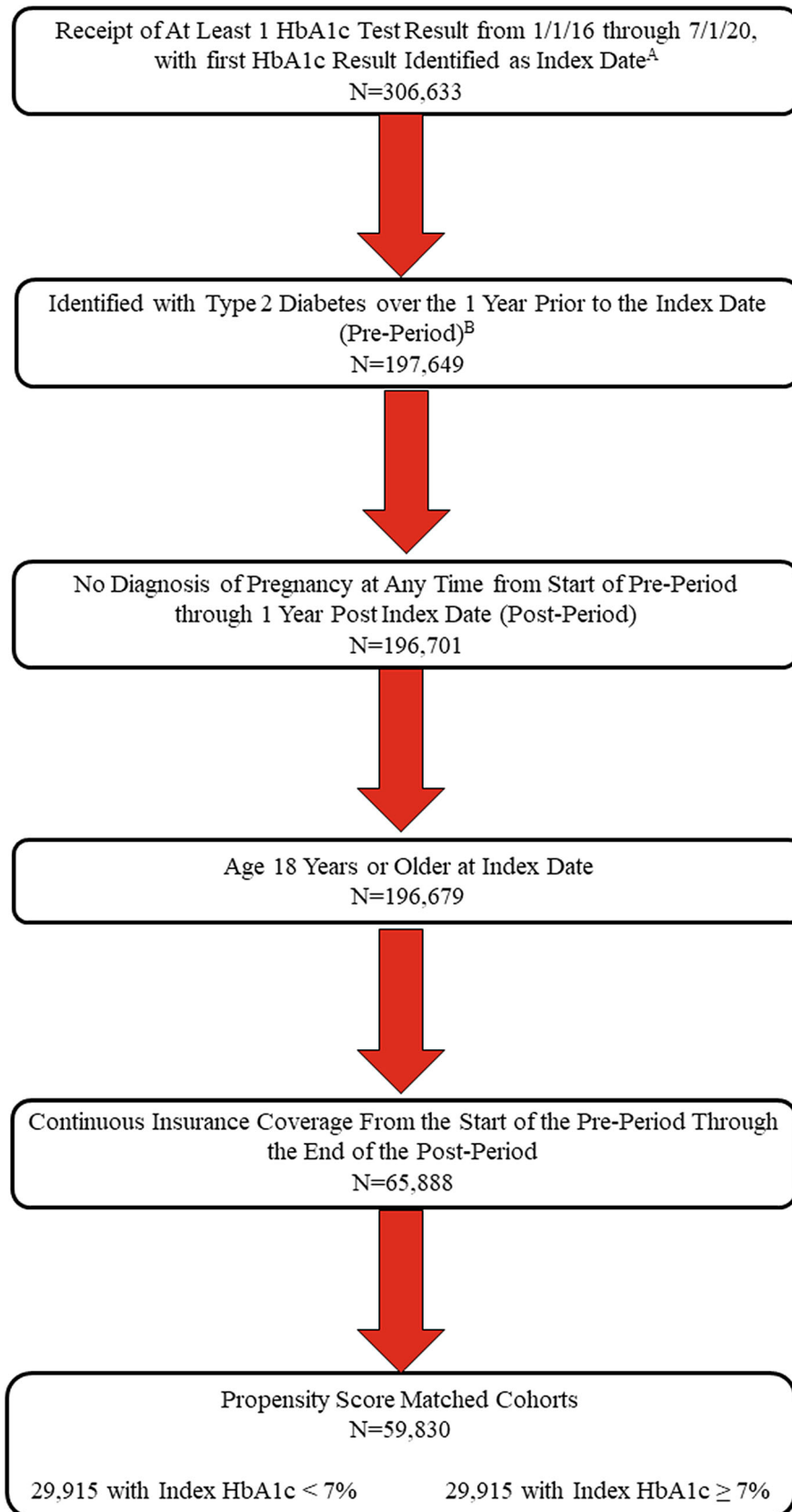
Patients were required to have at least one recorded HbA1c result at any time from January 1, 2016 through July 1, 2020 (the identification window). For each patient, the date of the first such HbA1c result was identified as the index date. Patients were also required to have had T2D during the 12 months prior to the index date (the pre-period) based upon receipt of two or more diagnoses of T2D and no receipt of any diagnoses of type 1 diabetes. Patients were excluded from the analyses if they were younger than age 18 years on the index date or were diagnosed with gestational diabetes or pregnancy at any time from the start of the pre-period through 1 year after the index date (the post-period). The selection of a 1-year post-period is consistent with economic models which update risks and outcomes annually [9, 10]. Finally, in order to ensure complete records of diagnoses, costs, and resource utilization, all patients were required to be insured continually from the start of the pre-period through the end of the post-period.

The primary outcome of interest was annual all-cause total healthcare costs. Consistent with previous research, costs were calculated as the sum of standard costs, copayments, and deductibles [11, 12]. In addition, costs were subcategorized into outpatient, acute care (inpatient and emergency room), and drug costs. All cost measures were expressed as average per-patient annual costs in 2021 US dollars, as adjusted for inflation by the medical component of the Consumer Price Index [13].

Consistent with ADA guidelines, which suggest that a target of HbA1c < 7% is appropriate for many nonpregnant adults with T2D [7], recommended glycemic control was defined as HbA1c < 7%, and patients were grouped on the basis of whether or not they met that HbA1c target on the index date. The analyses employed propensity score matching and multivariable analyses which controlled for patient demographics and baseline clinical characteristics. Specifically, propensity score matching (PSM) was used to match the group with HbA1c < 7% to the cohort with index HbA1c \geq 7%, utilizing a greedy nearest neighbor match without replacement and a specified caliper distance of 0.2 [14]. Covariates included in the PSM model were patient age, sex, race, ethnicity, region of residence, and year of index date. The final sample after PSM consisted of 59,830 patients. Figure 1 illustrates how each of the study inclusion and exclusion criteria affected sample size.

Given the PSM matched cohort, multivariable analyses were used to examine the relationship between index HbA1c and all-cause healthcare costs. Specifically, given the skewed nature of cost data, generalized linear models (GLM) with gamma distribution and log link [15] were used to examine all-cause total costs, outpatient costs, and drug costs, while all-cause acute care costs were examined using a two-part model. In this two-part model, the first step examined the probability of having an acute care visit and the second step estimates acute care costs for individuals with such a visit [16]. In the multivariable models, costs were estimated using the method of recycled predictions, with standard errors calculated from 1000 bootstrap iterations [17].

The multivariable analyses of all-cause costs controlled for patient demographics and pre-period characteristics, including general health, comorbidities, resource utilization, and medication use. Patient demographic information included age, sex, race, ethnicity, and region of residence. Patient general health and comorbidities were measured using the Diabetes Complications Severity Index (DCSI) and the adjusted Charlson Comorbidity Index (CCI). The DCSI is scored on a scale of 0–13, with



◀ **Fig. 1** Study inclusion–exclusion criteria and sample size. ^AIdentification window time frame of January 1, 2016 through July 1, 2020 determined by the duration of the data (January 1, 2015–June 30, 2021) and the requirement of 1-year pre- and post-periods. ^BIdentification of type 2 diabetes (T2D) based upon receipt of two or more diagnoses of T2D and no receipt of any diagnoses of type 1 diabetes

higher scores assigned to patients with a larger number and/or more severe levels of the following diagnoses: retinopathy, neuropathy, nephropathy, cerebrovascular disease, cardiovascular disease, peripheral vascular disease, and metabolic disease [18]. Meanwhile, the CCI creates a composite morbidity score that reflects mortality risk based upon the presence of any of 19 comorbidities, with individual comorbidities given a score between 1 and 6 [19]. In this study, myocardial infarction, peripheral vascular disease, and diabetes with or without complications were omitted from the calculation of the adjusted CCI either because they applied to all individuals (e.g., diabetes) or because they were included in the DCSI. For example, the CCI condition of myocardial infarction was omitted in our measurement of the CCI since it is captured as a cardiovascular complication in the DCSI. In addition, the comorbidities of anxiety and depression, which are not included in either the CCI or DCSI, were included as covariates. Resource utilization was measured by indicator variables capturing whether the individual visited a cardiologist, endocrinologist, nephrologist, or ophthalmologist in the pre-period, as well as the number of pre-period visits to a family practitioner or internist. Pre-period medication use was used as an additional proxy for disease severity and overall health and was measured by the number of classes of prescriptions filled for insulin, non-insulin glucose-lowering agents (GLAs), and non-GLA medication prescriptions filled. Insulin was subgrouped into basal, bolus and premixed classes, while non-insulin GLAs consisted of alpha-glucosidase inhibitors, amylin analogues, dipeptidyl peptidase IV inhibitors, glucagon-like peptide 1 receptor agonists, meglitinides, metformin,

sulfonylureas, sodium-glucose cotransporter 2 inhibitors, and thiazolidinediones.

In addition to the multivariable analyses, unadjusted descriptive statistics were summarized for the cohort across index HbA1c thresholds ($< 7\%$ or $\geq 7\%$) post matching. Differences in continuous variables across groups were examined using *t* statistics, while differences in categorical variables were examined using chi-square statistics. All analyses were conducted using SAS, version 9.4 (Cary, NC), and a *P* value < 0.05 was considered, a priori, to be statistically significant.

RESULTS

Table 1 provides descriptive statistics for the cohort after PSM. Results indicate that the average patient was 69.7 years old (standard deviation [SD] 11.1 years) and that the cohort consisted of more females (51.0%) than males (49.0%). The majority of patients were white (71.1%), non-Hispanic (75.9%), and residents of the Southern (35.2%) or Midwestern (32.6%) regions of the USA. After matching, significant differences remained between the two cohorts, with patients below HbA1c threshold at index date found to be significantly older, more likely to be female, more likely to be Hispanic, and less likely to be white. However, the absolute value of the standardized difference for all covariates, except for age, included in PSM was < 0.1 after matching, the absolute value of the standardized difference of the mean propensity score was 0.16, and the ratio of variances between the individuals with HbA1c below target to those with index HbA1c at or above target was 1.05 (see Supplementary Table 1). All of these results suggest balance between the two cohorts [20, 21].

Figure 2 illustrates the results of the multivariable analyses that examined differences in annual total medical costs associated with index HbA1c $< 7\%$ compared to $\geq 7\%$. Individuals who achieved the HbA1c target of $< 7\%$ were found to have significantly lower all-cause total costs, drug costs, and acute care costs, but significantly higher all-cause outpatient costs. Specifically, annual total medical costs were

Table 1 Descriptive statistics

	All patients (<i>N</i> = 59,830) <i>N</i> (%) or mean ± SD	Index HbA1c < 7% (<i>N</i> = 29,915)	Index HbA1c ≥ 7% (<i>N</i> = 29,915)	<i>p</i> value
Patient demographics (measured at baseline)				
Age (mean ± SD)	69.7 ± 11.1	70.6 ± 11.2	68.8 ± 10.9	< 0.0001
Sex <i>N</i> (%)				< 0.0001
Female	30,499 (51.0)	15,741 (52.6)	14,758 (49.3)	
Male	29,296 (49.0)	14,158 (47.3)	15,138 (50.6)	
Unknown	35 (0.1)	16 (0.1)	19 (0.1)	
Race <i>N</i> (%)				0.0045
Asian	1472 (2.5)	769 (2.6)	703 (2.3)	
African–American	8710 (14.6)	4473 (15.0)	4237 (14.2)	
White	42,548 (71.1)	21,091 (70.5)	21,457 (71.7)	
Other/Unknown	7100 (11.9)	3582 (12.0)	3518 (11.8)	
Ethnicity <i>N</i> (%)				0.0176
Hispanic	5426 (9.1)	2618 (8.8)	2808 (9.4)	
Non-Hispanic	45,425 (75.9)	22,754 (76.1)	22,671 (75.8)	
Unknown	8979 (15.0)	4543 (15.2)	4436 (14.8)	
Region <i>N</i> (%)				< 0.0001
Midwest	19,480 (32.6)	9325 (31.2)	10,155 (33.9)	
Northeast	8196 (13.7)	4231 (14.1)	3965 (13.3)	
South	21,090 (35.2)	10,783 (36.0)	10,307 (34.5)	
West	9248 (15.5)	4658 (15.6)	4590 (15.3)	
Other/unknown	1816 (3.0)	918 (3.1)	898 (3.0)	
Pre-period general health and comorbidities				
Adjusted CCI (mean ± SD)	0.6 ± 0.8	0.6 ± 0.8	0.5 ± 0.8	< 0.0001
DCSI score (mean ± SD)	1.5 ± 1.4	1.5 ± 1.4	1.5 ± 1.4	< 0.0001
Anxiety <i>N</i> (%)	7459 (12.5)	4074 (13.6)	3385 (11.3)	< 0.0001
Depression <i>N</i> (%)	9715 (16.2)	5151 (17.2)	4564 (15.3)	< 0.0001
Pre-period resource use <i>N</i> (%)				
Cardiologist	24,896 (41.6)	12,942 (43.3)	11,954 (40.0)	< 0.0001
Endocrinologist	7173 (12.0)	2886 (9.6)	4287 (14.3)	< 0.0001
Nephrologist	5625 (9.4)	2880 (9.6)	2745 (9.2)	0.0586
Ophthalmologist	22,695 (37.9)	11,579 (38.7)	11,116 (37.2)	0.0001

Table 1 continued

	All patients (<i>N</i> = 59,830) <i>N</i> (%) or mean ± SD	Index HbA1c < 7% (<i>N</i> = 29,915)	Index HbA1c ≥ 7% (<i>N</i> = 29,915)	<i>p</i> value
# of family practice/internist visits (mean ± SD)	7.0 ± 7.8	7.2 ± 8.1	6.7 ± 7.3	< 0.0001
Pre-period medication use (mean ± SD)				
# of classes of insulin prescribed	0.3 ± 0.6	0.1 ± 0.4	0.5 ± 0.7	< 0.0001
# of classes of non-insulin prescribed	1.1 ± 1.0	0.9 ± 0.9	1.4 ± 1.1	< 0.0001
# of non-GLAs prescribed	9.2 ± 6.2	9.3 ± 6.3	9.0 ± 6.1	< 0.0001
Index HbA1c (mean ± SD)				
HbA1c	7.3 ± 1.5	6.2 ± 0.5	8.4 ± 1.5	< 0.0001

CCI Charlson Comorbidity Index, *DCSI* Diabetes Complications Severity Index, *GLA* glucose-lowering agent, *SD* standard deviation

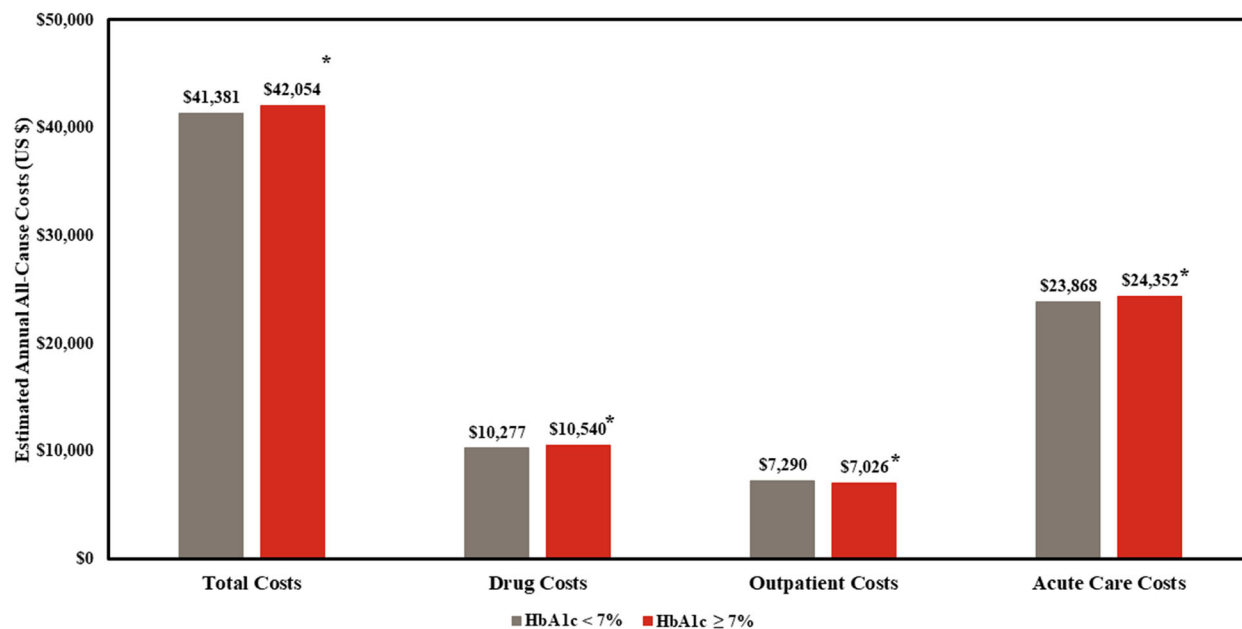


Fig. 2 Association between index HbA1c and annual total medical costs. **p* < 0.0001; *N* = 59,830. Results from multivariable analyses of propensity score matched cohorts

that control for patient characteristics, pre-period general health and comorbidities, pre-period resource use, and pre-period medication use

estimated to be \$41,381 for individuals with HbA1c < 7% (SD \$42,757), compared to

\$42,054 for individuals with HbA1c ≥ 7% (SD \$43,422) (*P* < 0.0001). In addition to having

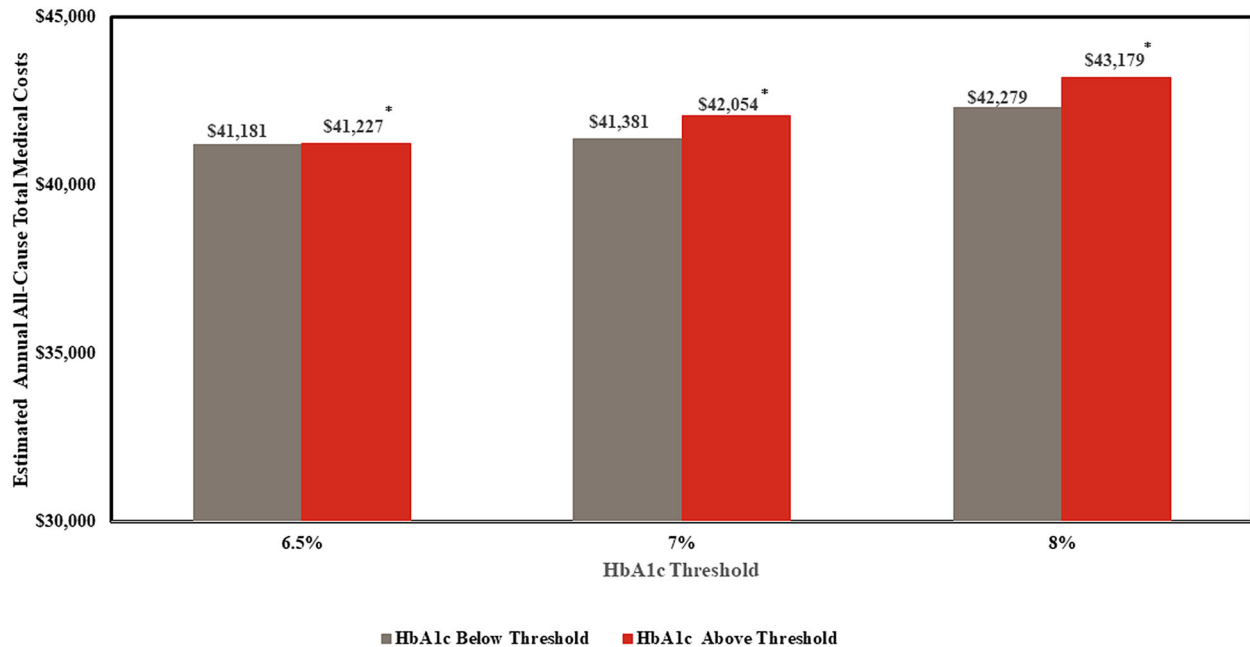


Fig. 3 Estimated annual total medical costs for alternative HbA1c thresholds. *Difference in cost for patients below threshold significantly lower compared to costs for patients above threshold ($p < 0.0001$). Thresholds are $\leq 6.5\%$ vs. $> 6.5\%$ ($N = 50,402$); $< 7\%$ vs. $\geq 7\%$ ($N = 59,830$); and $\leq 8\%$ vs. $> 8\%$ ($N = 30,082$). Results from multivariable analyses of propensity score matched cohorts that

control for patient characteristics, pre-period general health and comorbidities, pre-period resource use, and pre-period medication use. Results indicate that, at all thresholds, lower HbA1c is associated with statistically significantly lower annual diabetes-related total costs. In addition, as the HbA1c threshold increases, annual diabetes-related total costs increase

significantly lower total medical costs, lower HbA1c was also associated with statistically significantly lower all-cause acute care costs ($\$23,868 \pm \$21,776$ vs. $\$24,352 \pm \$22,223$; $P < 0.0001$) and drug costs ($\$10,277 \pm \$14,671$ vs. $\$10,540 \pm \$14,928$; $P < 0.0001$). In contrast, all-cause outpatient costs were significantly higher for individuals with HbA1c below threshold compared to those with HbA1c at or above threshold ($\$7290 \pm \$12,028$ vs. $\$7026 \pm \$11,587$; $P < 0.0001$).

As a test of the sensitivity of the results, all analyses were examined using alternative HbA1c thresholds. In these analyses, targets of $\leq 6.5\%$ and $< 8\%$ were informed by expert guidelines and clinical trials [7, 22–24]. The results from the multivariable analyses which examined annual all-cause total costs are provided in Fig. 3, while component costs are given in Table 2. As Fig. 3 and Table 2 show, at all thresholds, those who achieved the HbA1c

target had significantly lower mean all-cause total healthcare costs. For example, annual total medical costs were, on average, \$46, \$673, and \$900 lower for patients with HbA1c $\leq 6.5\%$, $< 7\%$, and $< 8\%$, respectively, compared to patients above such targets. Given our cohorts, these differences amount to \$1,159,246, \$20,132,795, and \$13,536,900 lower annual total medical costs for patients below HbA1c targets of 6.5%, 7%, and 8%, respectively. Furthermore, costs increased as the HbA1c threshold increased. In all cases, all-cause outpatient costs remained significantly higher for individuals who were below HbA1c threshold compared to those with HbA1c at or above threshold. As an additional sensitivity analysis, the study was re-examined, omitting the time period associated with COVID-19 [25]. As with the other sensitivity analyses, the findings remain unchanged with all-cause outpatient costs significantly higher for individuals below

Table 2 All-cause total medical component costs at alternative HbA1c thresholds

	Index HbA1c ≤ 6.5% (N = 25,201)	Index HbA1c > 6.5% (N = 25,201)
HbA1c threshold of 6.5% (N = 50,402)		
All-cause total medical component costs (mean ± SD)		
Drug*	\$9640 ± \$14,328	\$9923 ± \$14,672
Outpatient*	\$7476 ± \$12,210	\$7303 ± \$11,836
Acute care*	\$24,048 ± \$20,983	\$23,886 ± \$20,818
	Index HbA1c < 8% (N = 15,041)	Index HbA1c ≥ 8% (N = 15,041)
HbA1c threshold of 8% (N = 30,082)		
Diabetes-related component costs (mean ± SD)		
Drug*	\$11,064 ± \$15,193	\$11,482 ± \$15,668
Outpatient*	\$7185 ± \$10,713	\$6838 ± \$10,117
Acute care*	\$24,219 ± \$23,255	\$25,239 ± \$24,302

Results from multivariable analyses of propensity score matched cohorts which control for patient characteristics, pre-period general health and comorbidities, pre-period resource use, and pre-period medication use

SD standard deviation

*Indicates statistically significant differences between the two groups ($p < 0.0001$)

HbA1c threshold and all-cause acute care, drug, and total costs significantly lower for individuals below target HbA1c.

DISCUSSION

This study compared the annual all-cause total medical costs of patients with index HbA1c < 7% to costs for patients with index HbA1c ≥ 7% in the year immediately following the glycemic measurement. The results indicate that recommended glycemic control is associated with significantly lower all-cause total, acute care, and drug costs and significantly higher all-cause outpatient costs.

Results revealed that, after matching, significant differences remained between the two cohorts. For example, female sex, identification as non-Hispanic, and older age were all associated with being more likely to have HbA1c below target. Such results are consistent with research which has found that older patients [26] and white individuals, compared to Latino individuals, are more likely to be adherent to

diabetes regimens [27]. In contrast, previous research has found that men are more likely than women to achieve glycemic control [28].

The present findings are consistent with prior research examining the relationship between glycemic control and medical costs. For example, previous research showed that, for individuals in Spain, worse glycemic control was associated with higher hospitalization, medication, and primary care costs, as well as higher total healthcare costs [29]. In addition, a study from Brazil found lower total costs, medication costs, and costs of consultations for individuals with HbA1c ≤ 7% (vs. > 7%) and lower total costs and medication costs for individuals with HbA1c ≤ 8% (vs. > 8%) [30]. Another study found that glycemic control was associated with significantly lower diabetes-related total, acute care, outpatient, and drug costs [5]. In that study, diabetes-related outpatient costs were significantly lower for individuals with HbA1c below target, while in the present study, all-cause outpatient costs were significantly higher. Higher all-cause outpatient

costs concurrent with lower all-cause total costs support previous evidence that better outpatient healthcare leads to earlier diagnosis and interventions and lowers the likelihood of acute care and more expensive treatments [31]. It should be noted that the annual costs found in this study are generally higher than found in previous research. For example, research which also utilized Optum data found that, in the years 2014–2016, individuals newly diagnosed with T2D without any comorbidities had estimated annual costs of \$3365, while individuals with T2D and dominant comorbid conditions had estimated annual costs of \$38,168 [32]. In addition to the later study period leading to higher estimated costs, the cohort in the current research is older compared to the study discussed above and the current study did not limit the cohort exclusively to individuals newly diagnosed with T2D. Results suggest that the cost estimates found in this study are generally consistent with prior research which has focused on individuals with T2D and comorbidities.

Results of the sensitivity analyses revealed that at higher HbA1c thresholds, mean all-cause total medical costs increased. This finding is consistent with research conducted in at a government institution in Saudi Arabia which found that total annual direct medical costs significantly increased when comparing individuals with HbA1c < 7%, HbA1c \geq 7% and < 9%, and HbA1c \geq 9% ($p < 0.001$) [33]. In addition, previous research has found that individuals with T1D or T2D whose HbA1c decreased had first-year average annual healthcare costs that were 24% lower and second-year annual healthcare costs 17% lower, compared to those whose HbA1c stayed the same or increased [34]. Similarly, a retrospective study which utilized US health plan administrative data linked to HbA1c values found that a 1% decrease in HbA1c was associated with a 2% reduction in all-cause total medical costs [35].

The findings of the current study must be interpreted within the context of the limitations. One limitation is that insurance claims describe only commercially insured patients, which may limit the generalizability of the findings. Second, the use of claims data

precluded studying, or controlling for, body mass index, or other potentially important confounders. In addition, the study design precluded measuring and controlling for duration of diabetes. Third, as a result of inconsistencies in the timing of HbA1c tests across individuals, this study required only one HbA1c test result. As a result, the study was unable to examine time in range and changes in HbA1c over time. Fourth, while the analyses control for classes of GLAs utilized, they do not examine the relationship between method of drug delivery or glucose monitoring and glycemic control. Finally, these claims-based analyses focused on statistical significance rather than clinical significance, and associations rather than causation.

CONCLUSION

This study examined associations between glycemic control and annual all-cause total medical costs among a population of US adults with T2D. The findings revealed that individuals whose index HbA1c was below the ADA recommendation for glycemic control (HbA1c < 7%) had substantially lower 1-year all-cause total medical costs relative to patients with poor glycemic control (HbA1c \geq 7%). An examination of component costs revealed that, although those with HbA1c < 7% had significantly higher outpatient costs, those outpatient costs were more than offset by lower annual all-cause acute care and drug costs. Results were generally robust to alternative HbA1c thresholds, with the difference in costs between those below target and those above target increasing when examining higher HbA1c thresholds. Given the relatively high prevalence of T2D [3], results from both the primary and sensitivity analyses suggest potential cost savings for healthcare payers associated with maintaining HbA1c at or below target.

Medical Writing/Editorial Assistance The authors thank Patricia Nespore for her assistance in the drafting of the manuscript. Support for this assistance was funded by HealthMetrics Outcomes Research.

Author Contributions. All authors made substantial contributions to the conception and design of the research study. Maureen J Lage performed analyses and wrote the first draft of the manuscript. The authors Kristina S Boye, Jay P Bae and Vivian T Thieu critically revised the draft manuscript for important intellectual content. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

Funding. All funding for this study, including payment of the journal's rapid service fee, was provided by Eli Lilly and Company who reviewed all work prior to submission.

Data Availability. Market Clarity data used for this study are available via licensing agreement.

Declarations

Conflict of Interest. The authors Jay P Bae, Kristina S Boye and Vivian T Thieu are employees and shareholders of Eli Lilly and Company and conducted this research as part of their employment. Maureen J Lage was compensated by Eli Lilly and Company for her work on this research.

Ethical Approval. The data were fully de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant. Given the use of de-identified and retrospective data, institutional review board approval was not required.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's

Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. American Diabetes Association. Economic costs of diabetes in the US in 2017. *Diabetes Care*. 2018;41(5):917–28.
2. Centers for Disease Control and Prevention. Diabetes Fast Facts. 2023. <https://www.cdc.gov/diabetes/basics/quick-facts.html>. Accessed 24 Apr 2023.
3. Centers for Disease Control and Prevention. By the numbers: diabetes in America. 2022. <https://www.cdc.gov/diabetes/health-equity/diabetes-by-the-numbers.html>. Accessed 24 Apr 2023.
4. Lin J, Thompson TJ, Cheng YJ, et al. Projection of the future diabetes burden in the United States through 2060. *Popul Health Metr*. 2018;19:9.
5. Boye KS, Lage MJ, Thieu VT. The association between HbA1c and 1-year diabetes-related medical costs: a retrospective claims database analysis. *Diabetes Ther*. 2022;13(2):367–77.
6. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359(15):1577–89.
7. ElSayed NA, Aleppo G, Aroda VR, et al. 6. Glycemic targets: standards of care in diabetes—2023. *Diabetes Care*. 2023;46(Suppl1):S97–110.
8. Skyler JS, Bergenstal R, Bonow RO, et al. Intensive glycemic control and the prevention of cardiovascular events: implications of the ACCORD, ADVANCE, and VA diabetes trials: a position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association. *Diabetes Care*. 2009;32(1):187–92.
9. Pollock RF, Norrbacka K, Boye KS, Osumili B, Valentine WJ. The PRIME Type 2 Diabetes Model: a novel, patient-level model for estimating long-term clinical and cost outcomes in patients with type 2 diabetes mellitus. *J Med Econ*. 2022;25(1):393–402.

10. McEwan P, Foos V, Palmer JL, et al. Validation of the IMS CORE diabetes model. *Value Health*. 2014;17(6):714–24.
11. Li G, Zhang L, DiBernardo A, et al. A retrospective analysis to estimate the healthcare resource utilization and cost associated with treatment-resistant depression in commercially insured US patients. *PLoS ONE*. 2020;15(9):e0238843.
12. Joish VN, Zhou FL, Preblich R, et al. Estimation of annual health care costs for adults with type 1 diabetes in the United States. *J Manag Care Spec Pharm*. 2020;26(3):311–8.
13. U.S. Bureau of Labor Statistics. Consumer price index for all urban consumers: medical care services in the U.S. city average, series id CUUR0000SAM2, CUUS0000SAM2. 2023. <https://www.bls.gov/data/>. Accessed 24 Apr 2023.
14. Austin PC. A comparison of 12 algorithms for matching on the propensity score. *Stat Med*. 2014;33(6):1057–69.
15. Barber J, Thompson S. Multiple regression of cost data: use of generalised linear models. *J Health Serv Res Policy*. 2004;9(4):197–204.
16. Smith VA, Maciejewski ML, Olsen MK. Modeling semicontinuous longitudinal expenditures: a practical guide. *Health Serv Res*. 2018;53(Suppl 1):25–47.
17. Kleinman LC, Norton EC. What's the risk? A simple approach for estimating adjusted risk measures from nonlinear models including logistic regression. *Health Serv Res*. 2009;44:288–302.
18. Glasheen WP, Renda A, Dong Y. Diabetes Complications Severity Index (DCSI) update and ICD-10 translation. *J Diabetes Compl*. 2017;31(6):1007–13.
19. Glasheen WP, Cordier T, Gumbina R, Haugh G, David J, Renda A. Charlson Comorbidity Index: ICD-9 update and ICD-10 translation. *Am Health Drug Benefits*. 2019;12(4):188–97.
20. Stuart EA. Matching methods for causal inference: a review and a look forward. *Stat Sci*. 2010;25(1):1–21.
21. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28(25):3083–107. <https://doi.org/10.1002/sim.3697>.
22. Heller SR. A summary of the ADVANCE trial. *Diabetes Care*. 2009;32:S357–61.
23. National Committee for Quality Assurance (NCQA). HEDIS measures and technical resources: comprehensive diabetes care (CDC). 2023. <https://www.ncqa.org/hedis/measures/comprehensive-diabetes-care/>. Accessed 24 Apr 2023.
24. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm - 2020 executive summary. *Endocr Pract*. 2020;26(1):107–39.
25. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *New Engl J Med*. 2020;382(10):929–36.
26. Kirkman MS, Rowan-Martin MT, Levin R, et al. Determinants of adherence to diabetes medications: findings from a large pharmacy claims database. *Diabetes Care*. 2015;38(4):604–9.
27. Fernández A, Quan J, Moffett H, et al. Non-adherence to newly prescribed diabetes medications among insured Latino and white patients with diabetes. *JAMA Intern Med*. 2017;177(3):371–9.
28. Kautzky-Willer A, Kosi L, Lin J, Mihaljevic R. Gender-based differences in glycemetic control and hypoglycaemia prevalence in patients with type 2 diabetes: results from patient-level pooled data of six randomized controlled trials. *Diabetes Obes Metab*. 2015;17(6):533–40.
29. Mata-Cases M, Rodríguez-Sánchez B, Mauricio D, et al. The association between poor glycemetic control and health care costs in people with diabetes: a population-based study. *Diabetes Care*. 2020;43(4):751–8.
30. Henriques RS, Steimbach LM, Baptista DR, et al. Direct costs of type 2 diabetes: a Brazilian cost-of-illness study. *Int J Technol Assess Health Care*. 2018;34(2):180–8.
31. Amadeo K. How Preventive care lowers health care costs. 2022. <https://www.thebalancemoney.com/preventive-care-how-it-lowers-aca-costs-3306074>. Accessed 24 Apr 2023.
32. Lin P, Pope E, Zhou FL. Comorbidity type and health care costs in type 2 diabetes: a retrospective claims database analysis. *Diabetes Ther*. 2018;9:1907–18.
33. Almutairi N, Alkharfy KM. Direct medical cost and glycemetic control in type 2 diabetic Saudi patients. *Appl Health Econ Health Policy*. 2013;11(6):671–5.

-
34. Bansal M, Shah M, Reilly B, Willman S, Gill M, Kaufman FR. Impact of reducing glycated hemoglobin on healthcare costs among a population with uncontrolled diabetes. *Appl Health Econ Health Policy*. 2018;16(5):675–84.
 35. Lage MJ, Boye KS. The relationship between HbA1c reduction and healthcare costs among patients with type 2 diabetes: evidence from a U.S. claims database. *Curr Med Res Opin*. 2020;36(9):1441–7.