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Estimating Quality of Life Decrements Due to Diabetes Complications in the United States:

the Health Utility Index (HUI) Diabetes Complication Equation

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Abstract

Objective—Health utility decrements associated with diabetes complications are essential for calculating quality-adjusted life years (QALYs) in patients for use in economic evaluation of diabetes interventions. Previous studies mostly focused on assessing the impact of complications on health utility at event year based on cross-sectional data. This study aimed to separately estimate health utility decrements associated with current and previous diabetes complications.

Research Design and Methods—The Health Utilities Index Mark 3 (HUI-3) was used to measure health utility in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial (N=8,713). Five macrovascular complications (myocardial infarction (MI), congestive heart failure (CHF), stroke, angina, and revascularization surgery (RS)) and three microvascular complications (nephropathy (renal failure), retinopathy (severe vision loss), and neuropathy (severe pressure sensation loss)) were included in a set of alternative modelling approaches including ordinary least squares (OLS) model, fixed effects model and random effects model to estimate the complication-related health utility decrements.

Results—All macrovascular complications were associated with decrements of HUI-3 scores: MI (event year: −0.042, successive years: −0.011), CHF (event year: −0.089, successive years: −0.041), stroke (event year: −0.204, successive years: −0.101), angina (event year: −0.010, successive years: −0.032), revascularization (event year: −0.038, successive years: −0.016) (all $p < 0.05$). For microvascular complications, severe vision loss (−0.057), and severe pressure sensation loss (−0.066) were significantly associated with decrements of HUI-3 scores (both $p < 0.05$). Hypoglycemia (both severe and symptomatic) was found to be associated with a 0.036 decrement of health utility at event year, and a 0.033 decrement of health utility at successive years. Results from OLS model are preferred for supporting microsimulation model while fixed effects model are preferred to describe direct health impacts from complications.

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Conclusions—Macrovascular and microvascular complications caused QALY decrements in patients with type 2 diabetes. While only part of total impaired QALY is experienced during the event year, further QALY decrements for successive years were quite substantial.

Keywords

Quality Adjusted Life Year; Economic Evaluation; Impact of Complication; Diabetes

Introduction

The quality-adjusted life year (QALY) has been widely adopted in economic evaluation to assess the benefit of interventions across health outcomes. This metric combines data on preferences for being in a particular health state with data on length of time in that state (1–4). The application of QALYs have also been acknowledged by several organizations as recommend practice (5; 6) and they are widely accepted as a reference standard in cost-effectiveness analyses (7–10). For example, the National Institute for Health and Clinical Excellence (NICE) in England requires the use of QALYs for health technology assessment research (5). A health utility score, which is used for calculating QALYs, is a preference-based score indexed at zero and one, where a score of zero represents death a score of one represents perfect health (4). A variety of direct and indirect methods have been developed to measure this index. The direct methods commonly measure health utility based on eliciting preferences using tools such as a visual analogue scale (VAS)(11), a time trade-off (TTO) (12), or a standard gamble (SG)(1). Indirect methods rely on standardized preference-based measures, including the EuroQol (EQ)-5D (13; 14), the Health Utilities Index (HUI) (15), the Quality of Well-Being Scale (6), and the Short Form 6D (SF-6D)(16).

Economic evaluation of diabetes-related intervention relies heavily on health utility as an outcome measurement for the effect of chronic illness, treatments, and short/long-term disabilities on patients' life quality (17; 18). As the progression of diabetes is associated with a variety of complications (e.g., myocardial infarction and stroke), it is necessary to estimate their impacts (i.e., decrements) on health utility scores in order to aggregate these disease endpoints into a single measure to compare cost-effectiveness ratios. Several studies have estimated health utility decrements related to diabetes complications (19–28). For example, Coffey et al. estimated health utility scores associated with antidiabetic medications, complications, and comorbidities among 1,257 type 2 diabetes using the Quality of Well-Being Index (19). In addition, Clarke et al. (20) estimated health utility scores based on 3,192 type 2 diabetes patients from the United Kingdom Prospective Diabetes Study (UKPDS) using the EQ-5D questionnaire. Zhang et al. (29) estimated a set of utility decrements for diabetes complications based on the baseline data collected from 7,327 diabetes patients in the Translating Research into Action for Diabetes (TRIAD) trial, using the EQ-5D questionnaire.

However, most of those studies were based on cross-sectional data (19-23; 25; 26; 29) comparing the differences in health utility between those with and without a history of complication. With the exception of the study by Clarke et al.(20), none have differentiated the successive impact of cardiovascular events in later years from the current events. An

increasing number of studies have shown that most macrovascular events have both an initial impact as well as long lasting effects on quality of life (30; 31). This study aims to separate contemporaneous and long-lasting health utility decrements associated with complications among type 2 diabetes patients.

Methods

Data Source

Data from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial were used in this study. The ACCORD trial is one of the largest multicenter trials conducted in type 2 diabetes patients from the United States. 10,251 enrollees were randomly recruited using established criteria designed to identify type 2 diabetes patients at high risk for CVD. Risk was estimated by either presence of clinical CVD or, for patients without CVD history, a high likelihood of CVD suggested by evidence from the past 2 years (e.g., microalbuminuria) or presence of two or more factors that increase CVD risks (e.g. LDL-c >130 mg/dl). More details can be found in the original ACCORD study report (32). The trial tested three potential strategies for lowering the risk of major cardiovascular events: intensive blood glucose control, intensive blood pressure control, and optional treatments for lipids control. The ACCORD trial actively tracked five major cardiovascular outcomes: myocardial infarction (MI), congestive heart failure (CHF), stroke, angina, and revascularization surgery (32). It also recorded the progression of nephropathy (renal failure defined as dialysis, renal transplantation, or rise of serum creatinine >291.72 μ mol/L in absence of an acute reversible cause, assessed every 4 months), retinopathy (i.e., vision loss defined as a Snellen fraction <20/200, assessed every 2 years), and neuropathy (loss of light touch measured by a 10g force monofilament test, assessed every year). The ACCORD study used the protocol-defined vision loss (i.e., Snellen fraction <20/200, assessed every 2 year), renal failure (defined as dialysis, renal transplantation, or rise of serum creatinine >291.72 μ mol/L in absence of an acute reversible cause, assessed every 4 months), and severe pressure sensation loss (defined as loss of light touch measure by 10g force monofilament test, assessed every year) as key measurements for each microvascular complication type. The definitions of the microvascular complications in the ACCORD trial have been detailed elsewhere (33). Only the first encounter for each complication type was record in the ACCORD trial. Baseline characteristics, including the history of CVD events, were based on patient self-reports at scheduled clinical visit (34). For individuals with a history of CVD at baseline we included follow-up years in the study as “successive years.” Adverse events (e.g., hypoglycemia) were recorded periodically during the follow-up period, along with information on values of biomarkers, physical/mental conditions, and health-related quality of life scores. We limited our study to enrollees of the ACCORD trial with complete records for the five cardiovascular outcomes and three of the microvascular outcomes: renal failure, vision loss, and loss of light touch. The ACCORD trial started its recruitment in January 2001 (35).

Health Utility Measurement

The Health Utility Index Mark 3 (HUI-3) was used to measure health utility in this study (15; 36; 37). The value of the HUI-3 multi-attribute utility score varies from -0.36 to 1,

where 1 represents perfect health, 0 represents death, and a negative index score indicates a health state considered to be worse than death. In order to collect a HUI-3 score for each individual, the HUI-15Q was administered at baseline, 12 months, 36 months, 48 months, and study exit. The HUI-15Q is a self-administered, 15-item instrument that covers 8 attributes (vision, speech, hearing, dexterity, ambulation, cognition, emotion, and pain), with 5 or 6 levels per attribute. After collecting patients' responses on each attribute, the HUI-3 score was calculated by ACCORD study personnel using a multiplicative weighting function, where each level of an attribute was assigned a corresponding multiplier as is standard in computing HUI-3 scores (15). The applied HUI-15Q instrument can also generate HUI-2 and HUI-3 single-attribute utility scores as well as HUI2 multi-attribute utility scores.

Descriptive Statistics

Means and proportional distributions of demographic characteristics (age, gender, race, and education), the presence of biomarkers or other health indicators (smoking, depression, diabetes duration, body mass index (BMI), HbA1c, systolic Blood Pressure (SBP), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL)), and the presence of diabetes related-complications (MI, stroke, CHF, angina, revascularization, vision loss, and foot ulcers) are presented in Table 1.

Our study separated the impact of complications on health utility into contemporaneous effects that occur in the event year and historical effects that accumulate over successive years. For each diabetes complication, we categorized the target population into three groups: 1) individuals without a history of the complication before the current year and who did not encounter the complication in the current year, 2) individuals without a history of the complication before the current year but who encountered the complication in the current year, 3) individuals with a history of the complication. To estimate the contemporaneous unadjusted utility decrement for a particular event we compared the average HUI-3 score between group 2 and group 1. We then applied a Wilcoxon Rank Sum Test to draw statistical inference for the observed difference. We estimated unadjusted utility decrements for historical years using the same method but comparing groups 3 and 1. Due to the small proportion of respondents with microvascular events, we did not separate the impact of microvascular complications into event year and historical years.

Modelling Strategies

To estimate the marginal impacts of these complications while controlling for other factors we applied three modelling strategies: an Ordinary Least Squares (OLS) model, a fixed effects model, and a random effects model. In the OLS model, three sets of covariates were included. The first set of covariates comprised controls for events that occurred in the current year, including a full set of indicators for presence of macrovascular events (MI, stroke, CHF, angina, and revascularization), microvascular events (renal failure, severe vision loss, and severe pressure sensation loss) and hypoglycemia. The second set of covariates was a set of indicators for the history of each event, including macrovascular events and hypoglycemia. The last set of covariates controlled for demographic characteristics including age at which diabetes was first diagnosed, gender, an indicator for having a college

degree, being a current smoker, body mass index (BMI), and duration of diabetes. In the fixed effect model, due to a lack of HUI-3 measurements at years after primary endpoints of the ACCORD trial, we only estimated the impact of each complication type at the event year while controlling for several time-varying demographic characteristics. We also estimated a random effects model using the same model specification as fixed effects model and conducted a Hausman test to compare the appropriateness of the fixed and random effects models. Data were aggregated yearly, and years with HUI-3 measurements (i.e., the 1st year, the 3rd year, and the 4th year) were used to fit the model. The event year was defined as the year the event occurred, and successive years were defined as years after an event occurred. No data imputations were conducted. Standard errors were clustered at the individual level to account for serial correlation in health status. More details can be found in Appendix 1. To address the truncation of HUI-3 score at 1 (perfect health), we estimated a Tobit regression as a sensitivity analysis.

Results

Our sample consisted of a total of 8,713 patients from the ACCORD trial. Their baseline characteristics are summarized in Table 1. The mean age of the included population was 62.61 years, 39% were females and racial distribution was 18.7% black, 7% Hispanic, 62.3% white, and 12% other. In our sample 26.8% received a college degree, 13.8% were current smokers, and 23% had a history of depression. Based on BMI records, 8.4% of the included population had normal weight (BMI: 18–25), 29.4% were overweight (BMI: 25–30), and 62.2% were obese (BMI >30). The average diabetes duration was 10.55 years (S.D. = 7.47). 12.9% of the study population had a history of vision loss, and 1.4% had a history of foot ulcers. The mean HbA1c was 8.27% (S.D. = 0.93%), systolic blood pressure (SBP) was 135.99 mmHg (S.D. = 15.87 mmHg), low density lipoprotein cholesterol (LDL) was 105.06 mg/dl (S.D. = 32.67 mg/dl), and high density lipoprotein cholesterol (HDL) was 41.94 mg/dl (S.D. = 11.2 mg/dl). The percentage of the population with a history of MI was 15%, angina was 11.2%, CHF was 4.1%, stroke was 5.5%, and revascularization was 21.7% at baseline.

Table 2 presents the unadjusted mean utility scores for individuals with diabetes-related complications at event year and successive years. Utility decrements for individuals with contemporaneous MI (0.08), CHF (0.16), stroke (0.21), angina (0.06), revascularization surgery (0.06), renal failure (0.04), severe vision loss (0.08), and severe pressure sensation loss (0.10) were observed when compared with individuals without a history of complications. Aside from renal failure, all utility decrements were found to be statistically significant ($p < 0.05$). Utility decrements for individuals with a history of MI (0.04), CHF (0.08), stroke (0.12), angina (0.04), and revascularization surgery (0.04) were observed when compared to individuals with no complication history (all comparisons $p < 0.05$). Utility decrements were also observed for individuals having had a symptomatic hypoglycemia event at the current year (0.07), a severe hypoglycemia event at the current year (0.05), a history of symptomatic hypoglycemia (0.09), and a history of severe hypoglycemia (0.05) (all $p < 0.01$).

Table 3 presents point estimates of the OLS regression. Except for angina and renal failure, all diabetes complications reported in the ACCORD trial had statistically significant impacts (i.e., $p < 0.05$) on health utility scores: MI (event year: -0.042 , successive years: -0.011), CHF (event year: -0.089 , successive years: -0.041), stroke (event year: -0.204 , successive years: -0.101), angina (only at successive years: -0.032), revascularization (event year: -0.038 , successive years: -0.016), severe vision loss (event and successive year: -0.057), severe pressure sensation loss (event and successive year: -0.066), and hypoglycemia (event year: -0.036 , successive years: -0.033). We have also identified several demographic characteristics which have significant impacts on health utility: age at diagnosis (-0.002 per year, $p < 0.01$), being female (-0.043 , $p < 0.01$), not having a college degree (-0.051 , $p < 0.01$), being a current smoker (-0.054 , $p < 0.01$), having a high BMI (-0.007 per unit, $p < 0.01$), and having a longer diabetes duration (-0.005 per year, $p < 0.01$) were associated with lower health utility scores. Hispanics (-0.045 , $p < 0.01$) and whites (-0.019 , $p < 0.01$) were also associated with lower health utility scores when compared to blacks (all $p < 0.05$). An OLS model with interaction terms between events and event histories has also been estimated (see Appendix 4). Results from the Tobit model are presented in Appendix 5.

Because the Hausman test ($p < 0.001$) indicated that a fixed effects model was more appropriate than a random effects model, the results from the fixed effects regression model are presented in Table 4, and the results from a random effects model are presented in Appendix 6. According to the fixed effects model, stroke at event year (-0.202 , $p < 0.01$), CHF at event year (-0.067 , $p < 0.01$), severe vision loss (-0.039 , $p < 0.01$), and severe pressure sensation loss (-0.024 , $p < 0.01$) were found to be associated with lower health utility scores.

Discussion

Our study, which uses data from a large, US-based type 2 diabetes trial, has developed the first longitudinal measure of HUI-3 decrements for diabetes complications where impacts for those conditions are separated into onset-year impacts and further long-lasting impacts that carry over successive years. We measured each complication's impact on patients' HUI-3 after controlling for age, gender, race, education, and diabetes duration. For example, a cost-effectiveness study exploring the impacts of an intervention that reduces the risk of stroke, would save 0.204 health utility units in the year a stroke is avoided, followed by a further reduction of 0.101 for following years. The decrements estimated from our equation relating HUI-3 scores and complicating conditions can be used to update health utility scores in several widely-used diabetes simulation models such as the CORE (38) or CDC-RTI models(39).

Among all macrovascular complications that were found to have a significant impact on patients' health utility, the largest impact was found for stroke, followed by CHF, MI, revascularization, and angina. In addition, the impact of macrovascular events at the event year was usually greater than their impact at the successive years. After the initial health decline, there were some following health effects, but those were much lower than the initial quality of life hit. Our HUI diabetes complication equation separated these two effects in a single equation, which could improve economic evaluation with QALY measures. One important finding from our study is that symptomatic hypoglycemia and severe

hypoglycemia had similar impacts on patients' health utility in both the onset year (-0.036) and over the course of following years (-0.033). This finding is in concordance with our prior study which found hypoglycemia had both a direct impact on health and was associated with a fear of further hypoglycemia (40).

Our model found lower health utilities in individuals who were female, were older, had a higher BMI, did not complete college, and had a longer duration of diabetes. These patterns are consistent with previous findings (20; 29). Our estimation of the impact of stroke and CHF was similar to those found by Ping et al. (29), where history of stroke and CHF were associated with roughly 0.1 and 0.04 utility unit decrements. Our study provides additional information on concurrent impacts of stroke (-0.204) and CHF (-0.089), which were roughly twice as large as the impact of those conditions that carried into successive years (stroke: -0.101 , CHF: -0.041). In addition, our estimation on the impact of angina (-0.032) and severe vision loss (-0.057) was similar to the finding in Sullivan et al. (36). While the impact of renal failure was found to have no statistically significant impact in our study, unlike both Ping et al. (29) and Sullivan et al. (36), this may be a product of our smaller sample size. The estimated impact of MI at event year and successive years were both lower than the findings in Clarke et al. (20). While the reason for this inconsistency may be differences between the US and the UKPDS populations, it could also be attributed to improvements in how medical technology mitigates the impacts of MI between the Clarke et al. study era (1970) (20) and our own (2001).

Compared to the EQ-5D, the most commonly used instrument for measuring health utility in the diabetes population, with 5 health dimensions, our study used the HUI-3 instrument, which measures health utility based on a different set of eight health attributes. Previous work has suggested a discordance between these two utility measurements (41). Thus, estimating a set of utility decrements based on HUI-3 scores expands the available utility decrements to allow researchers to use the HUI-3 for assessing the health utility impacts of diabetes interventions. Some consistent patterns have been identified between our study and previous studies (20; 29; 36). For example, Stroke was associated with the largest health utility decrement among all diabetes-related complications, and the macrovascular complications all have successive impacts on health utility at later years after disease onset. However, health utility scores associated with each complication vary across studies. Several possible reasons that might contribute to this variation are: 1) the instruments used to measure health utility vary in their underlying valuation systems and descriptions of health states (25), and there is no evidence to support using one instrument over another, 2) health utilities differ across countries as the preference weights for each health state may be influenced by cultural norms (42; 43), and 3) different modelling approaches with differences in included covariates could also influence the estimation results.

We utilized a fixed effects model to address the bias caused by time-invariant, unobservable covariates. Due to the aforementioned data limitation, the model cannot provide estimates of health utility decrements at successive years after a complication. For health utility decrements at the event year, the fixed effect model provided estimations mostly consistent with the OLS model: stroke (OLS: -0.204 vs fixed effect: -0.202), CHF (OLS: -0.089 vs fixed effect: -0.067), severe vision loss (OLS: -0.057 vs fixed effect: -0.039), and severe

pressure sensation loss (OLS:−0.066 vs fixed effect:−0.024). The fixed effect model identified fewer statistically significant variables compared to the OLS model, possibly due to a reduced statistical power associated with this modelling strategy. We encourage researchers who seek estimates of direct health impacts from events to refer to the results from the fixed effect model, and those who intend to use the HUI-3 diabetes complication equation to support microsimulation to refer to the results from the OLS model, because OLS model includes more covariates. In addition, we provided a separate fixed effect model estimating the impacts of cardiovascular outcomes: Major Adverse Cardiovascular Events (MACE), which were defined as a composite of nonfatal MI, nonfatal stroke, and CVD death, and microvascular outcomes, which were defined as a composite of renal failure, retinal photocoagulation, and vitrectomy to treat retinopathy, (see Appendix 7).

Limitations

The study contains several limitations. First, the HUI-3 score was collected periodically according to the ACCORD trial scheduled visits, instead of right after the onset of events. In other words, it is possible that an event occurred at the beginning of the year and the HUI-3 score was collected at the end of that year. Thus, the estimated impact of each macrovascular event at the event year may only represent a portion of the total impact on health utility in the first year after the event. Second, the ACCORD population was an older population with generally long diabetes durations and escalated cardiovascular risks at baseline. Although our utility equation controlled for age at diagnosis and duration of diabetes, whether the utility scores estimated from ACCORD can be generalized to the larger US population requires further evaluation. Third, due to the small number of renal failure events, we failed to estimate a health decrement that was statistically distinguishable from zero. The estimated impact of renal failure (−0.024) in our study was lower than estimations from previous studies. For example, Ping et al.(29) reported a health decrement of −0.6 for renal failure. Fourth, for computation tractability, we assumed a constant utility decrement across all successive years after an event. An alternative strategy could model a trajectory of utility decrements that are large in the first one or two years after an event, and then become weaker over the following years. Unfortunately, due to the lack of sufficient data to estimate these detailed variations, we were unable to estimate an impact model with this more complex trajectory. This issue may impact studies using our equation to support short term economic evaluation. Lastly, the multiplicative weighting function used to calculate the HUI-3 score in the ACCORD study was a scoring algorithm based on a random sample of the general population in a city of Canada, which might not be generalizable to the US-population. This potential bias could be addressed in the future if US-based weights could be applied by the ACCORD study coordinating center to the HUI-15Q questionnaire.

Conclusion

Our study quantified the magnitude of impacts for each macrovascular and microvascular diabetes complication on patients' quality of life. While only part of total impaired QALY is experienced during the event year, further QALY decrements for successive years were quite substantial. The health utility equation estimated in this study could help researchers to improve economic evaluations within diabetes related fields.

Data Availability Statement

The datasets used for this study are publicly available and can be accessed through the National Heart, Lung, and Blood Institute (44).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Hui Shao researched the data and wrote the first draft of the manuscript. Shuang Yang analyzed the data. Vivian Fonseca provided knowledge from the physician perspective. Stoecker Charles helped with interpreting the statistical results. Lizheng Shi designed the study and managed the project flow. All authors contributed to the discussion and reviewed/edited the manuscript.

Dr. Hui Shao is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1

Baseline characteristics of the individuals (N=8,713)

Characteristics	Proportion (%) or mean	SE
Age (years)		
18–64	66.8	0.5
>65	33.2	0.5
Mean	62.6	0.1
Gender		
Male	61.0	0.5
Female	39.0	0.5
Race		
Black	18.7	0.4
Hispanic	7.0	0.3
Other	12.0	0.3
White	62.3	0.5
Education		
Lower than College	73.2	0.5
College graduates and above	26.8	0.5
Current Smoker		
No	86.2	0.4
Yes	13.8	0.4
Depression		
No	77.0	0.5
Yes	23.0	0.5
Body Mass Index (BMI)		
18–25 (normal weight)	8.4	0.3
25–30 (overweight)	29.4	0.5
>30(obese)	62.2	0.5
Mean	32.16	0.1
Time since diagnosis (years)		
<5	21.8	0.4
5–10	29.2	0.5
11–15	22.9	0.5
>15	26.1	0.5
Mean	10.55	0.1
Vision Loss	12.9	0.4
Foot Ulcer	1.4	0.1
HbA1c (%)	8.27	0.0
Systolic Blood Pressure (mmHg)	135.99	0.2
Low-density lipoprotein (mg/dl)	105.06	0.4
High-density lipoprotein (mg/dl)	41.94	0.1
Cardiovascular History		

Characteristics	Proportion (%) or mean	SE
Myocardial Infarction	14.99	0.4
Angina	11.24	0.3
Congestive heart failure	4.07	0.2
Stroke	5.52	0.2
Revascularization Surgery	21.67	0.4
Microvascular History		
Renal Failure	0.51	0.001
Severe vision loss	1.96	0.002
Severe pressure sensation loss	3.46	0.002

Table 2.

Unadjusted HUI3 by diabetes-related complications for type 2 diabetes patients

Health States	HUI-3 Score		Difference	P value
	Mean	SD		
Macrovascular Complications (No condition: reference)	0.72	0.26		
Myocardial infarction (Event)	0.64	0.29	-0.08	<0.001
Myocardial infarction (History)	0.68	0.28	-0.04	<0.001
Congestive heart failure (Event)	0.55	0.29	-0.16	<0.001
Congestive heart failure (History)	0.63	0.28	-0.08	<0.001
Stroke (Event)	0.51	0.31	-0.21	<0.001
Stroke (History)	0.60	0.30	-0.12	<0.001
Angina (Event)	0.65	0.28	-0.06	<0.001
Angina (History)	0.67	0.29	-0.04	<0.001
Revascularization Surgery (Event)	0.66	0.27	-0.06	<0.001
Revascularization Surgery (History)	0.68	0.27	-0.04	<0.001
Microvascular Complications (No condition: reference)	0.71	0.26	0.00	
Renal Failure	0.67	0.29	-0.04	0.099
Severe vision loss	0.63	0.30	-0.08	<0.001
Severe pressure sensation loss	0.62	0.31	-0.10	<0.001
Hypoglycemia (No condition: reference)	0.71	0.26		
Symptomatic (Event)	0.64	0.30	-0.07	<0.001
Symptomatic (History)	0.62	0.29	-0.09	<0.001
Severe (Event)	0.66	0.28	-0.05	<0.001
Severe (History)	0.66	0.28	-0.05	<0.001
Number of individuals	8,713			
Number of observations	21,045			

Compare individuals encountered the event at current year to individuals never encountered the event.

Compare individuals with a history of event to individuals without a history of event.

Table 3.

Estimated coefficients for OLS regression model

Variables	Coefficient	SE	95% CI		p Value
			Lower	Upper	
Macrovascular Complications					
Myocardial Infarction Event	-0.042	0.016	-0.074	-0.010	0.010
Myocardial Infarction History	-0.011	0.006	-0.022	0.001	0.064
Stroke Event	-0.204	0.035	-0.272	-0.136	<0.001
Stroke History	-0.101	0.008	-0.117	-0.086	<0.001
Congestive Heart Failure Event	-0.089	0.022	-0.132	-0.047	<0.001
Congestive Heart Failure History	-0.041	0.010	-0.060	-0.022	<0.001
Angina Event	-0.010	0.021	-0.051	0.032	0.653
Angina History	-0.032	0.006	-0.043	-0.020	<0.001
Revascularization Event	-0.038	0.011	-0.060	-0.016	<0.001
Revascularization History	-0.016	0.005	-0.026	-0.006	0.002
Microvascular Complications					
Renal Failure	-0.024	0.016	-0.056	0.008	0.142
Severe vision loss	-0.057	0.009	-0.074	-0.040	<0.001
Severe pressure sensation loss	-0.066	0.007	-0.080	-0.053	<0.001
Hypoglycemia Event	-0.036	0.010	-0.056	-0.016	<0.001
Hypoglycemia History	-0.033	0.011	-0.054	-0.011	0.003
Demographic Characteristics					
Age at diagnosis -52 years	-0.002	0.000	-0.002	-0.001	<0.001
Female	-0.043	0.004	-0.050	-0.036	<0.001
Race (ref=black)					
Hispanic	-0.045	0.008	-0.060	-0.029	<0.001
Others	-0.010	0.007	-0.022	0.003	0.148
White	-0.019	0.005	-0.029	-0.010	<0.001
Education above college	0.051	0.004	0.043	0.059	<0.001
Current smoker	-0.054	0.006	-0.066	-0.042	<0.001
BMI-32	-0.007	0.000	-0.007	-0.006	<0.001
Diabetes duration	-0.005	0.000	-0.005	-0.004	<0.001
Intercept	0.800	0.023			
Number of individuals	87,13				
Number of observations	21,045				

Table 4.

Estimated coefficients for fixed effect regression model

Variables	Coefficient	SE	95% CI		p Value
			Lower	Upper	
Macrovascular Complications					
Myocardial Infarction Event	-0.018	0.018	-0.054	0.017	0.31
Stroke Event	-0.202	0.039	-0.278	-0.126	<0.001
Congestive Heart Failure Event	-0.067	0.023	-0.113	-0.021	0.004
Angina Event	0.043	0.027	-0.010	0.095	0.109
Revascularization Event	-0.013	0.013	-0.039	0.013	0.332
Microvascular Complications					
Renal Failure	-0.029	0.021	-0.069	0.012	0.165
Severe vision loss	-0.039	0.012	-0.063	-0.016	0.001
Severe pressure sensation loss	-0.024	0.009	-0.042	-0.006	0.009
Hypoglycemia Event	0.016	0.012	-0.008	0.039	0.188
Hypoglycemia History	0.012	0.014	-0.016	0.040	0.404
Demographic Characteristics					
Current smoker	0.001	0.009	-0.018	0.019	0.922
BMI	0.001	0.001	-0.001	0.003	0.360
Time level fixed effects (ref=1st year)					
3rd year	-0.016	0.003	-0.022	-0.010	<0.001
4th year	-0.017	0.003	-0.024	-0.010	<0.001

Hausman Test P value <0.001