Direct Medical Costs of Incident Complications in Patients Newly Diagnosed With Type 2 Diabetes in China

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ABSTRACT

Introduction: Reliable country-specific incidence and cost data on diabetes-related complications are essential inputs for the projections of the economic burden of diabetes. The aim of this study was to provide patient-level cost estimates of managing and treating complications in patients newly diagnosed with type 2 diabetes mellitus (T2DM) in China.

Methods: Patients newly diagnosed with T2DM in the Tianjin Urban Employee Basic Medical Insurance Claims database between 2008 and 2015 were identified and followed up. The cumulative incidence and descriptive costs of certain macrovascular and microvascular complications were examined. A generalized estimating equations model was used to estimate the immediate- and long-term costs for the incident complication in quarterly intervals, controlling for demographics and the confounding effects of comorbid complications.

Results: A total of 114,847 newly diagnosed patients were identified (mean age 56.9 years, 45.5% women). After 7 years, 80.8% of the patients at risk had developed nephropathy and 75.7% had developed neuropathy. The immediate additional costs were highest for myocardial infarction during the quarterly interval that the complication first occurred (China yuan [CNY] 19,633), and the long-term costs were highest for stroke in the quarterly intervals of subsequent years (CNY 1087). The expected costs for all complications were calculated and presented as costs per quarterly interval and per year for different age and sex subgroups.

Conclusions: Managing complications results in substantial costs to the Chinese healthcare system. Our study contributes towards quantifying the economic burden and supports the parametrization of economic models of diabetes in China.

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Key Summary Points

Why carry out this study?

The aim of this study was to provide patient-level cost estimates of managing and treating complications in patients newly diagnosed with type 2 diabetes mellitus in China.

Reliable country-specific cost data of diabetes-related complications are essential inputs for the projections of economic burden and economic evaluation models.

What was learned from the study?

Estimates of the cumulative incidence and individual-level costs of all chronic complications were determined.

Immediate additional costs were highest for myocardial infarction and stroke, and the long-term costs were highest for stroke and peripheral vascular disease.

This comprehensive set of incidence and cost data of diabetes-related complications will facilitate projections of the economic burden and economic evaluations for diabetes-related health interventions in China.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to: https://doi.org/10.6084/m9.figshare.13186808.

INTRODUCTION

Diabetes is a serious threat to global health, currently affecting more than 463 million people worldwide, of whom 116.4 million live in China [1]. Type 2 diabetes mellitus (T2DM) accounts for more than 90% of all diabetes cases. Uncontrolled diabetes leads to a number of macrovascular (cardiovascular and cerebrovascular) and microvascular (nephropathy, diabetic foot, and retinopathy) complications, which contribute still further to a reduced quality of life, premature mortality, increased need for health care, and considerable healthcare expenditures [1, 2]. According to the International Diabetes Federation (IDF), the total diabetes-related health expenditure worldwide is projected have reached USD 760 billion in 2019, with diabetes-related complications being the key cost drivers [1]. China spent an estimated USD 109.0 billion on managing and treating diabetes and its complications in 2019, second only in expenditure to the USA (USD 294.6 billion) [1].

Diabetes-related complications are the key drivers of the economic burden of diabetes. Numerous studies have measured the direct medical costs of diabetes-related complications, although with high between-study variability in data sources, complications of interest, cost measures, among others. To date, published studies in China have always estimated heathcare costs as the average costs per hospitalization for a certain event, or as the cost differences between patients with and without a specific complication [3–6]. A comprehensive set of cost estimates for different complications that take into account medication use and inpatient/outpatient medical services among patients with diabetes based on one single data source is highly recommended [7–10]. Such reliable country-specific cost data on diabetes-related complications are also essential inputs for the projections of the economic burden of diabetes and for economic evaluation models, such as the Center for Outcomes Research (CORE) Diabetes Model, and the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model [11, 12].

Another important issue in published studies relates to the estimation of costs of diabetes-related complications as these complications are always comorbid within the same patient. It is therefore challenging to estimate the independent economic impact of each complication

on direct medical costs. In 2018, Katharina Kähm et al. addressed this need by controlling for the confounding effects of comorbid complications within each patient and published the cost estimates of incident complications in patients with T2DM using one health insurance database in Germany [13]. Inspired by this study, the aim of the present study was to provide reliable individual-level cost estimates of managing and treating major diabetes-related complications in patients newly diagnosed patients with T2DM in China.

METHODS

Data Source

This was a population-based cohort study which used data on enrollees enrolled in the Urban Employee Basic Medical Insurance (UEBMI) Claims database of Tianjin, China, between 2008 and 2015. Tianjin is a Northern Chinese municipality with 15.6 million inhabitants in 2019 and was ranked seventh among the 31 provinces/municipalities of mainland China in terms of gross domestic product (GDP) per capita in 2019 [14, 15]. Mandatory participation in the UEBMI is planned for all employees and retirees of both public and private companies in all of the provinces/municipalities, including Tianjin; in 2015, about 5.2 million people were enrolled in the UEBMI in Tianjin. The analytical sample in this study was a random sample of all enrollees. The de-identified data extracted included patient-level demographic information, medical claims of inpatient and outpatient service, pharmacy claims, and related medical and medication costs. The Tolerability and Ethics Committee at the School of Pharmaceutical Science and Technology, Tianjin University, waived the requirement of ethics approval for the current study. Informed consent was not required due to the retrospective nature of this study.

Study Population

Adults individuals (aged $\geq$ 18 years) who had been newly diagnosed with T2DM according to the 10th Revision of the International Classification of Diseases (ICD-10) codes E11 and had made one inpatient claim or $\geq$ 2 outpatient claims ($\geq$ 30 days apart) between 1 January 2009 and 31 December 2014 were identified. The date of the first T2DM-related diagnosis (index claim) was defined as the index date. Patients were required to have continuous enrollment for at least 12 months preceding the index date (baseline period) and have no diabetes-related claims during the baseline period. Patients who had any diagnosis of type 1 diabetes mellitus (ICD-10 E10) or gestational diabetes mellitus (ICD-10 O24) during the research period were excluded from the analysis. Included patients were followed up from the index date to death, discontinuation, or the end of 2015.

Identification of Complications

Macrovascular and microvascular complications, including cardiovascular disease, cerebrovascular disease, peripheral vascular disease, foot disease, nephropathy, retinopathy, and neuropathy were examined in this study. The list of complications and the corresponding ICD-10 codes are presented in Electronic Supplementary Material [ESM] Table 1; these complications were identified based on the published literature and confirmed with clinical experts before being applied to the patient [16–19]. Certain cardiovascular and cerebrovascular events, including angina, myocardial infarction (MI), chronic heart failure, arrhythmia, stroke, and transient ischemic attacks (TIA) were analyzed further (ESM Table 1). Following consultation with clinical experts, the acute macrovascular complications (events), including MI and stroke, were only identified in inpatient claims with corresponding primary diagnoses. TIA was identified in inpatient and outpatient claims with the corresponding primary diagnoses. The other complications were identified in both inpatient and outpatient claims with either primary or secondary diagnoses.

Statistical Analysis

Baseline characteristics captured during the 12-month baseline period included patient demographics (age, gender), Charlson Comorbidity Index (CCI) score, and comorbidities (hypertension and dyslipidemia). CCI is a weighted index developed to measure comorbid conditions that takes into account both the number and the seriousness of comorbid diseases. Nineteen comorbidities, including MI, congestive heart failure, peripheral vascular disease, among others, were considered, with each condition assigned a weight from 1 to 6 points; these weights were summed to produce the CCI for each patient [20]. The prevalence of examined complications at baseline was also investigated.

The cumulative incidence of examined complications during the follow-up period was calculated by using the number of incident cases for each complication divided by the number of patients who were at risk for that complication during each follow-up year. The incident cases were identified as patients who were newly diagnosed with the specific complication, with related diagnoses absent during the baseline period. Patients who were at risk for the specific complication were patients who were followed up during the given year, excluding patients who had died, were lost to follow-up, or had previously related diagnoses.

Direct medical costs for the examined complications were calculated from the Chinese healthcare system perspective, including the medication and medical costs paid by both the medical insurance and patients. Patients who were newly diagnosed with a certain complication during the follow-up period were included in the corresponding cost analysis. For each incident complication case, the follow-up periods were divided into quarters, with each 90 days (a quarter) considered to be an interval during which the onset of the complication was taken into account. The quarters were consecutively numbered, starting with #0 and ending with #28, with #0 being the prior quarters without a certain complication, #1 being the quarter during which the complication first occurred (onset of complication), and #2 to #28 being the following quarterly intervals. The remaining follow-up time of < 90 days was not analyzed. Mean costs per quarter for each complication were estimated.

A generalized estimating equations (GEE) model was further constructed to estimate the independent costs of each complication on patients, controlling for the demographics and confounding effects of comorbid complications for each patient. Variables, including age, sex, presence of complications at baseline, and occurrence of different complications, were included in the model. Certain cardiovascular and cerebrovascular diseases, such as MI and stroke, were also included in the model, with 'cardiovascular disease' or 'cerebrovascular disease' excluded due to high correlations. A gamma distribution and a log-link function were used in the GEE model taking into account the non-normal distribution of costs, in accordance with recommendations in the literature [5, 19]. The coefficients were back-transformed to the ordinal scale using an exponential function to obtain the cost estimates. The costs of each complication were first estimated in the quarterly interval in which the complication occurred (quarter #1), then in the following quarters within the first year (quarters #2 to #4), and finally in subsequent quarters in following years (quarters #5 to #28). Specifically, the immediate costs of each complication refer to the additional costs in the quarter during which the complication first occurred (quarter #1). The costs within the first year of onset for each complication refer to the costs incurred in quarter #1, plus three times ($3 \times$) the average quarterly costs of the following quarters within the first year (quarters #2 to #4). Annual costs in the follow-up years were further calculated as four times ($4 \times$) the average quarterly costs among subsequent quarters (quarters #5 to #28) [13]. Detailed information on the models can be found in ESM Statistical Appendix. All statistical analyses were conducted using Stata version 13.1 (StataCorp, College Station, TX, USA).

RESULTS

Patient Selection and Baseline Characteristics

A search of the UEBMI Claims database identified 145,885 patients diagnosed with T2DM between 2009 and 2014. After excluding patients who were previously diagnosed with T2DM during the baseline period and patients who had received a diagnosis of type 1 diabetes or gestational diabetes mellitus during the research period, there remained 114,847 patients newly diagnosed with T2DM who were included in the study (Fig. 1). The mean (standrd deviation [SD]) age of this study population was 56.9 (12.4) years, and 45.5% were female (Table 1). The mean (SD) CCI of the total study cohort was 2.0 (1.4), with 54.2% of patients comorbid with hypertension and 34.1% comorbid with dyslipidemia. Diabetes-related complications and their prevalence among the study cohort at baseline: were nephropathy (9.0%), cardiovascular disease (6.7%), neuropathy (6.3%), cerebrovascular disease (3.8%), retinopathy (3.7%), peripheral vascular disease (3.4%), and foot disease (0.5%).

Cumulative Incidence for Complications

Table 2 presents the cumulative incidence of developing complications over the follow-up period. After 7 years the cumulative incidence was highest for nephropathy (80.8%), followed by neuropathy (75.7%) and peripheral vascular disease (64.7%). For certain cardiovascular and cerebrovascular disease complications, after 7 years the cumulative incidence was highest for angina (30.1%), arrhythmia (22.8%), stroke (16.7%) and chronic heart failure (16.5%).

Direct Medical Costs

The descriptive costs for quarters before and after the onset of certain complications are given in Table 3. Costs in the quarter during which the complication first occurred (quarter #1) were highest for cerebrovascular disease (China yuan [CNY] 18,162), followed by

cardiovascular disease (CNY 9340), foot disease (CNY 8044), and peripheral vascular disease (CNY 7721), and relatively lower for nephropathy, neuropathy, and retinopathy, ranging from CNY 6256 to CNY 6715. The costs decreased in quarters #2 for all complications and then increased slowly in the subsequent quarters. Regarding cardiovascular and cerebrovascular disease, the costs in quarters #1 were highest for MI (CNY 44,419), stroke (CNY 23,168), and chronic heart failure (CNY 17,804). The number of patients included in corresponding quarterly intervals (e.g., 31,203 patients were analyzed in quarter #0 for cardiovascular disease) are given in ESM Table 2.

The estimated coefficients and predicted cost differences obtained from the GEE model are given in Table 4. The intercept of CNY 2350 presents the costs for a male patient aged 50–59 years without any complications for a 3-month period. Costs increased steadily with age, and costs for women were slightly less than those for men. Patients with a history of complications appeared to have higher costs relative to those who did not experience any complication, with the additional costs varying between CNY 53 and CNY 2142 per quarter. The immediate costs, i.e., the additional costs in the quarters that the complications occurred, were highest for MI (CNY 19,633), followed by stroke (CNY 9959), and chronic heart failure (CNY 4215), with the costs for other complications ranging from CNY 784 for foot disease to CNY 1766 for TIA. The long-term additional costs were highest for stroke, with an increase of CNY 1716 in the quarters within the first year (i.e., #2 to #4) and of CNY 1087 in quarters of following years (i.e., #5 to #28). The expected costs in quarterly intervals and years for subgroups comprised of patients of different age and sex were also calculated and the results are presented in ESM Table 3. As an example we take the costs of stroke among 50- to 59-year-old men. Their stroke-related additional costs in the year of onset are CNY 24,507 (CNY 12,309 + 3 × CNY 4066), and the annualized costs in following years are CNY 13,746 (CNY 3437 × 4) (ESM Table 3).
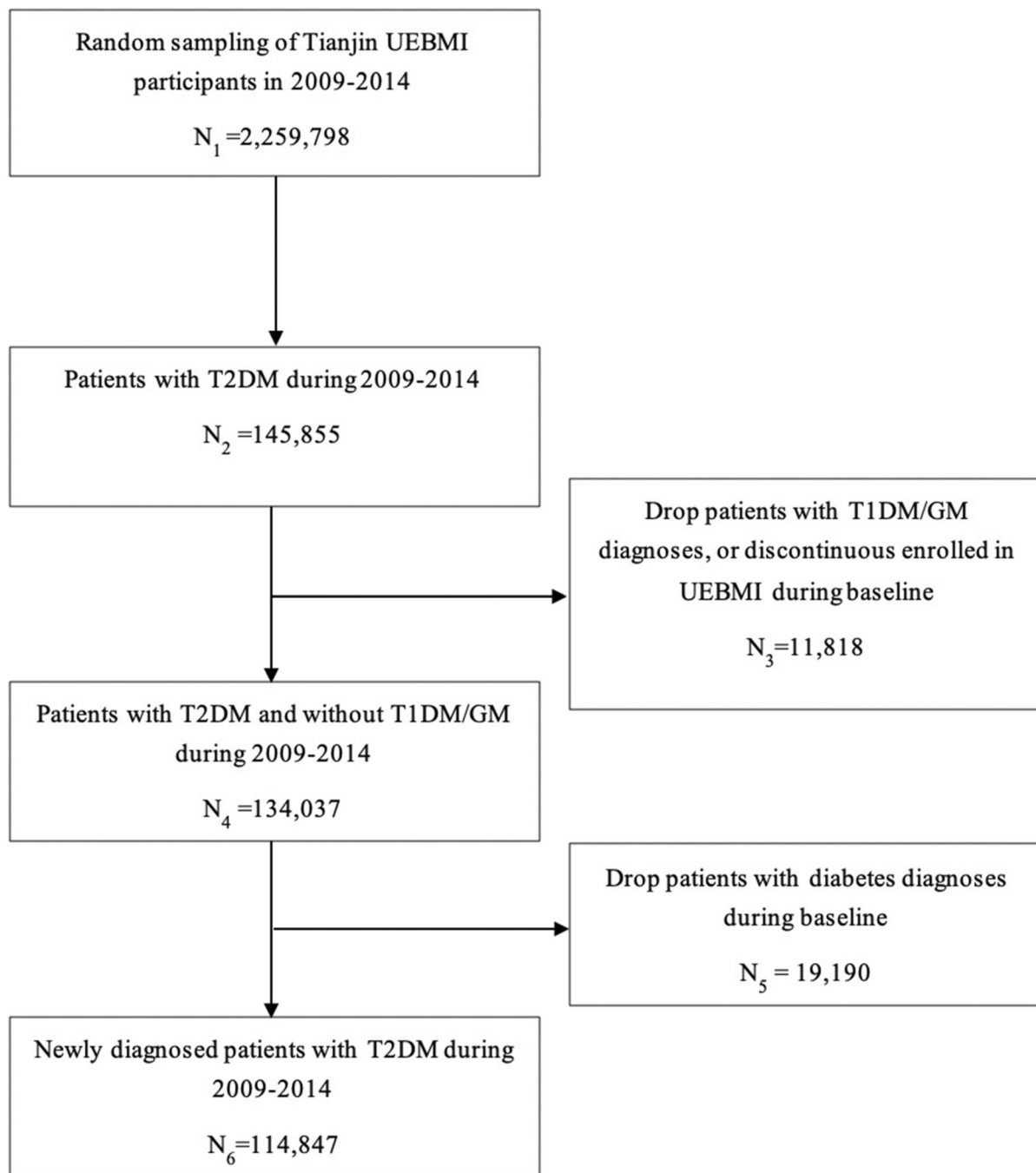
Fig. 1 Flow chart of patient selection. *GM* Gestational diabetes, *T1DM/T2DM* type 1/type 2 diabetes mellitus, *UEBMI* Urban Employee Basic Medical Insurance

DISCUSSION

In this study we estimated the cumulative incidence and individual-level costs of chronic complications in patients with T2DM in China. This study differs from previous studies whose aim was to estimate the cost differences between patients with and without one or

Table 1 Baseline characteristics of the study population

Baseline characteristics	Patients with newly diagnosed T2DM ($N = 114{,}847$)
Demographic characteristics	
Age, years	56.9 ± 12.4
Age group, years	
< 40	9751 (8.5%)
40,50)	17,468 (15.2%)
50,60)	42,668 (37.2%)
60,70)	27,080 (23.6%)
70,80)	13,213 (11.5%)
≥ 80	4667 (4.1%)
Female	52,288 (45.5%)
Charlson Comorbidity Index[a]	2.0 ± 1.4
Comorbidity	
Hypertension	62,270 (54.2%)
Dyslipidemia	39,122 (34.1%)
Chronic complications	
Cardiovascular disease	7750 (6.7%)
Angina	3122 (2.7%)
Myocardial infarction	524 (0.5%)
Chronic heart failure	1602 (1.4%)
Arrhythmia	3180 (2.8%)
Cerebrovascular disease	4337 (3.8%)
Stroke	3486 (3.0%)
Transient ischemic attacks	917 (0.8%)
Peripheral vascular disease	3948 (3.4%)
Foot disease	664 (0.5%)

Table 1 continued

Baseline characteristics	Patients with newly diagnosed T2DM ($N = 114{,}847$)
Nephropathy	10,298 (9.0%)
Retinopathy	4208 (3.7%)
Neuropathy	7220 (6.3%)

Values in table are presented as the mean ± standard deviation (SD) or as a number with the percentage in parentheses

T2DM Type 2 diabetes mellitus

[a] Charlson Comorbidity Index (CCI) is a weighted index developed to measure comorbid conditions that takes into account both the number and the seriousness of the comorbid diseases. Nineteen comorbidities were included in the index. Each condition was assigned a weight from 1 to 6. These weights were summed to produce the CCI score for each patient. Myocardial infarct, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, and diabetes have a score of 1 point. Hemiplegia, moderate or severe renal disease, diabetes with end organ damage, any tumor, leukemia, and lymphoma have a score of 2 points. Moderate or severe liver disease has a score of 3 points. Metastatic solid tumor and acquired immune deficiency syndrome have a score of 6 points

several specific complications, in that it has determined the net incremental costs of all common diabetes-related complications following the occurrence of corresponding complications. This information will be very useful as inputs into economic evaluations and economic burden projections among patients with T2DM in China.

We found that the majority of patients with T2DM were at risk for being newly diagnosed with chronic complications within 7 years, with nephropathy, neuropathy, peripheral vascular disease, and cardiovascular disease being the most common complications. More than 10% of these patients had diabetes-related complications at baseline, which indicates that people may have had diabetes-related complications prior to receiving a diagnosis of diabetes. In

Table 2 Cumulative incidence of complications during follow-up period

Complications	Years from index date[a]						
	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)	6 (%)	7 (%)
Cardiovascular disease	10.2	18.3	25.6	32.6	39.6	45.9	51.9
Angina	4.4	8.4	12.5	16.8	21.4	25.9	30.1
Myocardial infarction	0.2	0.4	0.6	0.9	1.3	1.6	2.2
Chronic heart failure	2.2	4.1	6.1	8.2	10.4	13.2	16.5
Arrhythmia	3.9	7.2	10.2	13.4	16.5	19.7	22.8
Cerebrovascular disease	3.4	6.3	9.1	12.0	15.0	18.3	21.7
Stroke	2.5	4.7	7.0	9.4	11.8	14.3	16.7
Transient ischemic attacks	1.1	2.1	3.1	4.0	5.2	6.5	8.0
Peripheral vascular disease	18.4	26.3	38.6	46.2	52.9	59.0	64.7
Foot disease	5.1	8.4	11.6	14.4	17.0	19.4	21.6
Nephropathy	32.3	47.8	58.5	66.4	72.5	76.9	80.8
Retinopathy	16.4	26.8	36.3	44.5	51.6	57.5	62.1
Neuropathy	27.6	40.9	51.2	59.3	66.2	71.7	75.7

Cumulative incidence is defined as the number of incident cases for each complication divided by the number of patients who were at risk for that complication during each follow-up year, and is presented as a percentage for that year

[a] Index date was defined as the date of the first T2DM-related diagnosis (index claim)

general, our estimates are higher than those in epidemiology data published in developed countries, including the UK [21], the USA [22], and Germany [23], even given the similar or even younger mean ages in these study populations. Definitions and/or diagnoses criteria of complications were not standardized in these earlier study, which is why we clarified the identification process in detail, including the ICD codes and primary or secondary diagnoses criteria we used. Ethnic variations may also exist in the development of diabetes-related complications. It has been suggested that Asian populations are at higher risk of developing kidney disease and macrovascular disease, such as stroke [24, 25].

Most of the published epidemiological studies in China have focused on existing patients instead of incident patients and have estimated the prevalence of chronic diabetes-related complications instead of the cumulative

incidence, primarily due to limitations in terms of data sources [26–28]. It is therefore challenging to directly compare our incidence estimates with those of these previous studies in China. For example, the prevalence of stroke was 15.6% among patients with prevalent diabetes according to Duan et al., while the corresponding cumulative incidence for stroke in our study was 2.5% for the first year following confirmed diabetes diagnoses, 7% after 3 years, and 16.7% after 7 years [26].

Compared with baseline quarters, the occurrence of diabetes-related complications increased the healthcare costs substantially in the quarter during which the complication occurred, and also continued to increase costs in subsequent quarters. Similar results were also observed in the USA [29] and German [13] studies. Acute and severe complications, including MI and stroke, were associated with a high peak in the incident quarter, while chronic

Table 3 Distribution of direct medical costs before and after onset of chronic complications in quarterly intervals (in China yuan)

Complications	Quarterly intervals[a]								
	#0	#1	#4	#8	#12	#16	#20	#24	#28
Cardiovascular disease	4643	9340	5103	5774	6173	6408	7295	7526	7714
Angina	4657	7964	5010	5877	6309	6189	6795	6874	8868
Myocardial infarction	4648	44,419	6151	5853	5031	6121	11,196	10,065	3090
Chronic heart failure	6199	17,804	7596	7444	7511	7659	9214	9278	7007
Arrhythmia	4578	6099	4774	5480	6006	6305	6652	6978	6458
Cerebrovascular disease	4377	18,162	6392	7051	7486	7884	8145	8726	6146
Stroke	4678	23,168	7446	7834	8279	8558	8406	9487	5911
Transient ischemic attacks	4139	7719	4516	5180	5769	6341	7557	6562	7790
Peripheral vascular disease	3899	7721	6061	6513	6800	7484	7905	8420	7837
Foot disease	5176	8044	6962	7126	7399	7804	8198	8682	9864
Nephropathy	3188	6256	5043	5643	6210	6856	7486	8521	7818
Retinopathy	4118	6637	6061	6483	6826	7552	7782	8609	8288
Neuropathy	3418	6715	5352	5857	6278	6889	7426	8093	8691

[a] The follow-up periods were divided into quarters, with each 90 days (a quarter) considered to be an interval during which the onset of the complication was taken into account. The quarters were consecutively numbered, starting with #0 and ending with #28, with #0 being the prior quarters without a certain complication, #1 being the quarter during which the complication first occurred (onset of complication), and #2 to #28 being the following quarterly intervals

disease, such as retinopathy, nephropathy, or foot complication, was associated with relatively slight peak. We also found that women had lower healthcare costs than men and that the total costs peaked among patients aged between 70 and 80 years. However, we did not consider the interactions between age, sex, and presence of complications, the existence of which has been implied by a previous study conducted in Germany [13].

Direct comparisons of the cost estimates reported in this study and those reported in previous studies in other countries may have limited value due to the various treatment patterns and healthcare systems across different countries. The published studies based on the Chinese population with diabetes have paid more attention to the costs per complication-related hospitalization or to the cost differences between prevalent diabetes patients with a

different number of complications (e.g., 0, 1, 2+), and did not provide the sex- and age-specific net additional costs of each common chronic diabetes complication. For example, a cross-sectional study published in 2018 reported that the total annual costs were highest for diabetic foot (USD 5207, around CNY 35,512), while the costs for stroke were USD 1724 (around CYN 11,758) [30]. In comparison, in our study the additional costs for foot disease among male patients aged 60 to 70 years were CNY 12,288 for the first year and CNY 11,390 for the second and following years (ESM Table 3), and those for stroke were CNY 25,976 in the first year year and CNY 14,570 for the second and following years .

Our findings should be interpreted with caution. First, given the unavailability of national longitudinal claims database in China, we used the Tianjin UEBMI claims database to

Table 4 Effects of chronic type 2 diabetes mellitus complications on direct medical costs per quarter in the generalized estimating equations model with gamma distribution and a log-link function

Variable	Coefficient (SE)	Exp (coefficient)	ΔCost (CNY)
Constant	7.76*** (0.01)	2350	–
Sex: female (Reference = male)	− 0.04*** (0.01)	0.96	− 83
Age group (Reference = 50–59 years)			
< 40	− 0.07*** (0.01)	0.93	− 164
40–50	− 0.10*** (0.01)	0.9	− 233
60–70	0.06*** (0.01)	1.06	141
70–80	0.07*** (0.01)	1.07	160
≥ 80	0.06*** (0.01)	1.06	136
Baseline complications (Reference = no)			
Angina	0.03 (0.03)	1.03	78
Myocardial infarction	0.40*** (0.05)	1.49	1155
Chronic heart failure	0.43*** (0.04)	1.53	1248
Arrhythmia	0.00*** (0.03)	1.00	0
Stroke	0.65*** (0.02)	1.91	2142
Transient ischemic attacks	0.02 (0.05)	1.02	53
Peripheral vascular disease	0.27*** (0.02)	1.31	737
Foot disease	0.17*** (0.04)	1.18	432
Nephropathy	0.39*** (0.02)	1.48	1126
Retinopathy	0.12*** (0.02)	1.13	310
Neuropathy	0.15*** (0.02)	1.16	368
Death	0.57*** (0.04)	1.77	1820
Onset of complications (Reference = no)			
Angina			
Quarter of onset of complication	0.56*** (0.02)	1.74	1746
Quarters #2 to #4	0.03** (0.01)	1.03	68
Quarters #5 to #28	0.03** (0.01)	1.04	83
Myocardial infarction			
Quarter of onset of complication	2.24*** (0.04)	9.36	19,633
Quarters #2 to #4	0.41*** (0.05)	1.51	1202
Quarters #5 to #28	0.05 (0.04)	1.06	133
Chronic heart failure			
Quarter of onset of complication	1.03*** (0.02)	2.79	4215

Table 4 continued

Variable	Coefficient (SE)	Exp (coefficient)	ΔCost (CNY)
Quarters #2 to #4	0.29*** (0.02)	1.34	788
Quarters #5 to #28	0.21*** (0.02)	1.24	557
Arrhythmia			
Quarter of onset of complication	0.32*** (0.02)	1.37	873
Quarters #2 to #4	0.00 (0.01)	1.00	9
Quarters #5 to #28	0.02 (0.01)	1.02	52
Stroke			
Quarter of onset of complication	1.66*** (0.02)	5.24	9959
Quarters #2 to #4	0.55*** (0.02)	1.73	1716
Quarters #5 to #28	0.38*** (0.01)	1.46	1087
Transient ischemic attacks			
Quarter of onset of complication	0.56*** (0.02)	1.75	1766
Quarters #2 to #4	− 0.02 (0.02)	0.98	− 54
Quarters #5 to #28	− 0.01 (0.02)	0.99	− 32
Peripheral vascular disease			
Quarter of onset of complication	0.50*** (0.01)	1.65	1523
Quarters #2 to #4	0.30*** (0.01)	1.35	823
Quarters #5 to #28	0.31*** (0.01)	1.36	855
Foot disease			
Quarter of onset of complication	0.29*** (0.01)	1.33	784
Quarters #2 to #4	0.18*** (0.01)	1.20	470
Quarters #5 to #28	0.13*** (0.01)	1.14	337
Nephropathy			
Quarter of onset of complication	0.46*** (0.01)	1.58	1370
Quarters #2 to #4	0.27*** (0.01)	1.31	737
Quarters #5 to #28	0.28*** (0.01)	1.33	767
Retinopathy			
Quarter of onset of complication	0.31*** (0.01)	1.36	838
Quarters #2 to #4	0.21*** (0.01)	1.24	559
Quarters #5 to #28	0.22*** (0.01)	1.25	592
Neuropathy			
Quarter of onset of complication	0.42*** (0.01)	1.52	1212

Table 4 continued

Variable	Coefficient (SE)	Exp (coefficient)	ΔCost (CNY)
Quarters #2 to #4	0.12*** (0.01)	1.13	295
Quarters #5 to #28	0.11*** (0.01)	1.12	272

CNY China yuan, *SE* standard error

**, ***Significant at **$P < 0.01$ and ***$P < 0.001$

estimate the China-specific cumulative incidence and individual-level costs of chronic complications in patients with T2DM. Our estimates may be relatively higher than the average costs in China since Tianjin is a more economically developed region (GDP per capita in 2019: CNY 90,371) compared with the national average level (GDP per capita in 2019: CNY 70,892) [14, 15]. The UEBMI is also relatively superior to other social medical insurance plans in China, such as the Urban Resident Basic Medical Insurance, in terms of its lower deductible and higher reimbursement rate. Second, some diseases, such as cardiovascular and cerebrovascular disease, may occur prior to the diagnosis of diabetes, which means part of the costs might not have been caused by diabetes. Thirdly, we also acknowledge the limitations resulting from the use of medical claims data, including potential misclassifications of diagnoses and lack of clinical variables, such as blood glucose, lipid and blood pressure control. The impact of clinical markers on the occurrences of complications should be investigated in future studies. Lastly, severe complications, such as endo-organ renal disease, retinopathy resulting in blindness, and amputation of limbs, were included in the corresponding disease category and were not analyzed separately. The sample sizes of these severe complications were very small in our database due to relatively limited follow-up period or diabetes duration.

CONCLUSIONS

In conclusion, the present study shows that healthcare costs increase substantially in the quarter during which the diabetes-related

complication occurs and that these continue to increase, with smaller differences between subsequent years. Our findings will provide support for future economic research and economic modelling conducted among patients with T2DM in China, which will further guide evidence-based clinical and policy decision-making.

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study are not publicly available as this was a retrospectively observational study using the de-identified medical claims data.

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