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## Excess Hospitalization Expenses Attributable to Type 2 Diabetes Mellitus in Singapore

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### ABSTRACT

**Objectives:** To estimate the excess hospitalization expenses attributable to type 2 diabetes mellitus (T2DM) in a high-income Asian country from the health system perspective and the patient perspective. **Methods:** Electronic medical records from a tertiary academic hospital in Singapore from 2012 to 2013 were used to create propensity score-matched cohorts with and without T2DM on the basis of their entry characteristics. A two-part model was then used to control for remaining differences between the cohorts. Excess cost due to diabetes was defined as the difference in hospital expenses between a patient with diabetes and a matched patient without diabetes. As part of the sensitivity analysis, a two-part model without matching and different matching algorithms were used to obtain the range of hospitalization expenses attributable to patients with T2DM. Balance of covariates after matching was investigated. All costs were presented in 2013 US dollars. **Results:** Mean adjusted excess hospital expense of one hospital visit attributable to diabetes was

approximately \$1007 and \$113 from the health system perspective and the patient perspective, respectively. For the cohort of patients with T2DM in Singapore, this amounts to a total average expenditure of \$117 million and \$13 million from the health system perspective and the patient perspective, respectively. **Conclusions:** Hospitalization expenses from diabetes result in a significant cost to the health care system in Singapore. Nevertheless, the excess burden of hospitalization on patients is mitigated significantly by cost sharing, which may reduce financial incentives to avert admissions through preventive care, which is largely out-of-pocket.

**Keywords:** cost, diabetes, excess, hospitalization, matching.

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### Introduction

Diabetes is a costly chronic disease that affects more than 520 million (about 10.5%) of the world population [1,2]. Recent estimates from the International Diabetes Federation showed that global annual health expenditure attributable to diabetes in 2015 ranged from US \$673 billion to US \$1197 billion (12%–21% of total global health expenditure) [3]. The bulk of this expenditure is due to direct medical costs [4], whereas the largest component of direct medical costs is hospital inpatient care [5,6].

To date, however, most published findings have focused on the total direct medical cost incurred by patients with diabetes, rather than on the incremental direct medical cost of a patient with diabetes compared with one without diabetes. There are two estimation techniques that are widely used in diabetes cost-of-illness (COI) studies—the disease-attributable cost approach and the incremental cost approach that uses matching or regression. Studies that investigate the effect of these estimation techniques have concluded that the incremental cost approach would result

in a “higher, and likely more exact,” estimation of such costs [4,7,8] relative to the disease-attributable cost approach. On the basis of a recent systematic review on the economic burden of type 2 diabetes mellitus (T2DM) [4], most COI studies in high-income countries examined the direct medical cost of diabetes without using control groups, likely overestimating the direct cost of diabetes. In addition, the same study found that studies conducted in high-income countries usually take on the societal or health system perspective and do not consider the patient perspective, which has important implications for the incidence of the cost burden [4].

In this article, we demonstrate the value of addressing these two important gaps in the literature, using a rich data set from Singapore, a high-income country with a rapidly increasing burden of diabetes. By using a regression-adjusted matching incremental cost approach, we seek to provide a more accurate estimation of the excess hospitalization expenses attributable to patients with T2DM and address the following research questions:

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1. From the health system perspective, how much more would a hospital visit cost a patient with diabetes compared with a patient without diabetes?
2. From the patient perspective, how much more would a patient pay out-of-pocket when contrasting the scenario in which he or she has diabetes and does not have diabetes?

## Methods

### Subjects and Database

A matched case-control cross-sectional study was conducted using electronic medical records (EMRs) from the National University Hospital, a 1225-bed academic tertiary care hospital in Singapore. The study sample was extracted from the hospital EMRs, which contain information on all clinical services, consumables, supplies, drugs, and their corresponding financial data and diagnoses. This study was approved by the National Healthcare Group Domain-Specific Review Board (protocol no. 2015/00091).

Patients with T2DM, who were citizens or permanent residents of Singapore and aged 21 years and older between 2012 and 2013, were identified from the EMRs by the presence of an *International Classification of Diseases, Ninth Revision, Clinical Modification* code of 250.x, except 250.x1 and 250.x3; an *International Classification of Diseases, Tenth Revision, Australian Modification* code of E11.x for T2DM; or a prescription of insulin or oral hypoglycemic agents from January 2005 to December 2013. Patients with type 1 diabetes mellitus or gestational diabetes were excluded. Patients without T2DM were classified under “controls.”

### Estimation of Excess Hospitalization Expenses

Hospitalization expenses consisted of the cost of health services consumed during hospitalization such as the cost of ward, prescriptions, laboratory investigations, physicians' fees, and medical devices from 2012 to 2013. More specifically, hospitalization expenses from the health system perspective were derived from the gross amount that a patient would have to pay after tax and without any subsidies or insurance payouts. Hospitalization expenses from the patient perspective referred to the amount the patient had to pay out-of-pocket.

The excess costs generated by patients with diabetes during one inpatient visit were then calculated by estimating the difference in hospital expenses between a patient with diabetes and a patient without diabetes who was matched by the covariates, which would be described in the following section.

Excess hospitalization expenses of one inpatient visit that would be attributable to diabetes in Singapore were then estimated by multiplying the prevalence of diabetes in Singapore (11.3% [9]), the diabetes hospital admission rate in Singapore (431.6 per 100,000 residents [10]), and the number of Singapore residents (3,844,751 residents [11]) in 2013. All costs are in 2013 US dollars (US \$1 = SGD1.2653) [12].

### Regression-Based Matching

Matching is sometimes preferred over traditional regression models because only untreated groups that are similar to the treated group are used, whereas the latter does not make it clear when it would be unlikely to separate the treatment effect from other differences between the groups [13]. Nevertheless, a hybrid methodology (regression-adjusted matching), which involves

both regression and matching, exists and has been used in health economic evaluation but not in diabetes COI studies; regression-adjusted matching can decrease finite sample bias and increase efficiency relative to matching along [14].

Matching was conducted on the basis of propensity scores because it alleviates the increasing difficulty faced when identifying an exact match between case and controls as the number of observable characteristics to match increases. In this study, the “treatment” is T2DM and the probability of T2DM was obtained through a logistic regression based on the patient's entry characteristics (or characteristics of patient during the first inpatient admission in the study period): age; sex; ethnicity (Chinese, Malay, Indian, or others); year and month of all inpatient admissions (patients with multiple admissions had their admissions analyzed as unique admissions); whether patient died during this admission; admission type (inpatient, emergency, day surgery, or endoscopy); ward type (private or subsidized); 21 major diagnostic categories, which are grouped from the diagnosis-related group codes, excluding pregnancy and newborns; and six comorbidities unrelated to diabetes (chronic obstructive pulmonary disease, liver disease, cancer, rheumatic disease, peptic ulcer disease, and AIDS/HIV).

The six comorbidities were selected from the Charlson comorbidity index and Elixhauser comorbidity index because they were not related to diabetes [15,16]. This is important because including conditions related to diabetes will cause a downward bias in estimates of diabetes-related expenses because the proportion of diabetes-related expenses that is attributable to diabetes-attributable conditions (e.g., cardiovascular disease and renal disease) would not be allocated to diabetes [7].

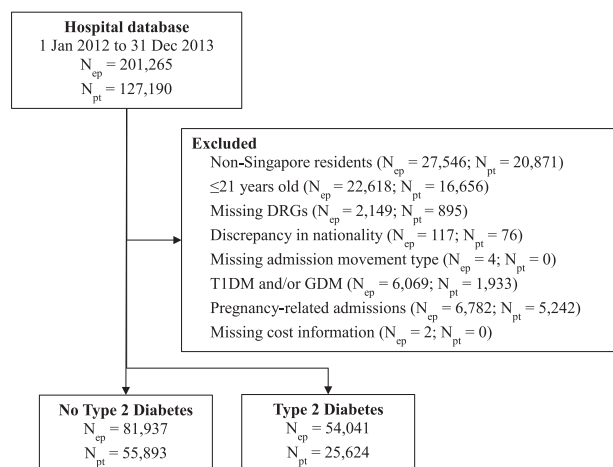
In the matching algorithm, replacement was considered while a common support condition was adopted to ensure that the distribution of the propensity scores of patients with and without T2DM was located in the same domain, whereas ties (case was matched to their nearest neighbor and also to controls with identical propensity scores) were kept under the recommendation of Abadie and Imbens [17]. Balance between the case and control groups was assessed by comparing the reduction in bias in the means of the covariates before and after matching [18]. All matching procedures were performed using the PSMATCH2 package [19].

To control for remaining differences between the cohorts after matching [20], a two-part model that used the propensity score as a predictor was used on the matched data after the matching process. Because some patients incurred zero medical expenses while some incurred extremely high expenses, a two-part model was used in favor of a generalized linear model. The first part consists of logistic regression that estimates the probability of incurring medical expenses, whereas the second part consists of a generalized linear model with logarithmic link function and gamma distribution to estimate the conditional expenditures among those with positive expenditures.

### Sensitivity Analysis

As part of the sensitivity analysis, different commonly used matching algorithms were considered because there are no guidelines on the type of matching algorithm to use in such a study. The following matching algorithms were considered:

1. 1-to-1 optimal nearest-neighbor matching;
2. 1-to-2 optimal nearest-neighbor matching;
3. 1-to-1 greedy nearest-neighbor matching within a caliper distance of 0.000001; and
4. 1-to-1 optimal nearest-neighbor matching within a caliper distance of 0.000001.



**Fig. 1 – Flowchart of patients included in or excluded from study. DRG, diagnosis-related group; GDM, gestational diabetes mellitus; N<sub>ep</sub>, number of episodes; N<sub>pt</sub>, number of patients; T1DM, type 1 diabetes mellitus.**

A two-part model without matching (or a regression-based model) was also used as part of the sensitivity analysis because this was a common methodology used in the published literature.

In addition, length of stay (LOS;  $\leq 7$  days or  $> 7$  days), which is not part of the entry characteristics, was also included in the two-part model because patients with diabetes tend to have longer LOS than do patients without diabetes [21]. All analyses were conducted using Stata version 14.2 (StataCorp, College Station, TX), and an *a priori*  $\alpha$  value of 0.05 was used for all statistical tests.

## Results

A total of 81,937 episodes and 54,041 episodes were identified from the EMRs for patients without T2DM and patients with T2DM, respectively, from January 1, 2012, to December 31, 2013 (Fig. 1). The characteristics of the cohorts before and after matching are presented in Table 1.

On the basis of the results presented in Table 2, the unadjusted mean excess hospital expense that was attributable to diabetes was \$2505 from the health system perspective and \$292 from the patient perspective. The mean excess hospital expense from the two-part model without matching or controlling for LOS was \$878 and \$49 from the health system perspective and the patient perspective, respectively (model M02), whereas controlling for LOS would result in an estimate of \$584 and \$16 from the health system perspective and the patient perspective, respectively (model M03).

The matching algorithm that gave the best balance of covariates was the 1-to-1 optimal matching with caliper distance of 0.000001 (median bias after matching = 0.4 and mean bias after matching = 0.5). On the basis of the matching algorithm that gave the best balance of covariates and the regression-adjusted matching model that excluded the LOS (model M10), mean excess hospital expense attributable to diabetes was \$1007 from the health system perspective and \$113 from the patient perspective. The excess hospital expenses incurred by the diabetes population in Singapore would be \$117 million and \$13 million

from the health system perspective and the patient perspective, respectively, in 2013. If the LOS was included (model M11), this estimate would decrease to \$935 from the health system perspective and to \$96 from the patient perspective. The excess hospital expenses incurred by the diabetes population in Singapore would then be \$109 million and \$11 million from the health system perspective and the patient perspective, respectively, in 2013.

## Discussion

On the basis of the regression-adjusted method, the mean hospital expenses were about \$1007 and \$113 from the health system perspective and the patient perspective, respectively. This estimate from the health system perspective was comparable with (although similar to) the estimate from a local study that reported a mean direct medical cost (estimated using a disease-attributable approach) of SGD1237.20 (or US \$910) in 2010 [5]. One other possible reason for the higher estimate when matching was used is that before matching, patients without diabetes tend to stay in the private (hence higher cost) wards, but this event disappeared after matching as the controls were matched to the cases.

Overall, the hospitalization costs attributable to diabetes are substantial, but the excess burden of hospitalization on patients is mitigated significantly by cost sharing. Although this suggests that potentially vulnerable households are largely protected from the financial risk of hospitalization due to diabetes, there may be other unintended consequences. Most of the primary care in Singapore takes place in the private sector, which is mostly paid for out-of-pocket [22]. Such asymmetry in financial protection in favor of treatment but not prevention may result in poor incentives for preventative care, leading eventually to higher overall health care expenditures.

A key strength of this study is that diabetes-attributable conditions were not controlled for or matched (e.g., included as part of a comorbidity score) because this could lead to an underestimation of diabetes-attributable costs. Furthermore, complementing matching methods with regression analysis reduces bias due to covariate differences and controls for “small remaining differences and increase efficiency of estimates” [23].

Nevertheless, this study has limitations inherent to the source data. First, there could be an underestimation of patients with T2DM if the patients were not admitted because of diabetes-related conditions (usually patients with mild diabetes symptoms). To address this issue, patients with prescriptions of insulin or oral hypoglycemic agents were included if they did not have an *International Classification of Diseases* code related to type 1 diabetes or gestational diabetes. In addition, the mean excess hospital expense estimated in this study heavily depends on the degree to which the matched control group is an accurate representation of the counterfactual of what patients with T2DM would have spent if they did not have T2DM. On the basis of the sensitivity analysis, the largest difference in mean excess hospital expense obtained among the regression-adjusted matching models from the model with the best balance of covariates after matching, regardless of its perspective, was less than \$350. Hence, the results obtained in this study are likely to be robust. Further research could involve the data analysis of other public hospitals to obtain a more accurate value of this excess hospitalization cost between a patient with T2DM and one without.

**Table 1 – Characteristics of patients without and with T2DM before and after matching.**

Characteristic	Unmatched (n = 135,978)			Matched* (n = 29,927)		
	No T2DM (n = 81,937)	T2DM (n = 54,041)	P value <sup>†</sup>	No T2DM (n = 14,491)	T2DM (n = 15,436)	P value <sup>†</sup>
Age (y), mean ± SD	51.4 ± 17.8	66.4 ± 13.4	<0.001	63.0 ± 13.2	64.6 ± 12.9	<0.001
Sex, n (%)			<0.001			<0.001
Female	39,317 (48.0)	22,612 (41.8)		6,238 (43.0)	6,146 (39.8)	
Male	42,620 (52.0)	31,429 (58.2)		8,253 (57.0)	9,290 (60.2)	
Ethnicity, n (%)			<0.001			<0.001
Chinese	60,550 (73.9)	34,787 (64.4)		12,384 (85.5)	12,881 (83.4)	
Malay	9,944 (12.1)	9,314 (17.2)		1,176 (8.1)	1,416 (9.2)	
Indian	6,724 (8.2)	6,421 (11.9)		637 (4.4)	778 (5.0)	
Others	4,719 (5.8)	3,519 (6.5)		294 (2.0)	361 (2.3)	
Died during this admission, n (%)	1,118 (1.4)	1,474 (2.7)	<0.001	128 (0.9)	157 (1.0)	0.234
Admission type, n (%)			<0.001			<0.001
Inpatient	10,894 (13.3)	5,629 (10.4)		896 (6.2)	969 (6.3)	
Emergency	31,943 (39.0)	38,784 (71.8)		7,709 (53.2)	10,363 (67.1)	
Day surgery	27,943 (34.1)	6,931 (12.8)		3,640 (25.1)	2,831 (18.3)	
Endoscopy	11,157 (13.6)	2,697 (5.0)		2,246 (15.5)	1,273 (8.2)	
Ward type, n (%)			<0.001			<0.001
Private	21,644 (26.4)	5,377 (9.9)		1,330 (9.2)	1,111 (7.2)	
Subsidized	60,293 (73.6)	48,664 (90.1)		13,161 (90.8)	14,325 (92.8)	
Admission period, n (%)			<0.001			0.108
January 2012	2,800 (3.4)	2,105 (3.9)		413 (2.9)	513 (3.3)	
February 2012	3,128 (3.8)	2,248 (4.2)		519 (3.6)	593 (3.8)	
March 2012	3,206 (3.9)	2,247 (4.2)		531 (3.7)	576 (3.7)	
April 2012	3,112 (3.8)	2,219 (4.1)		548 (3.8)	538 (3.5)	
May 2012	3,394 (4.1)	2,338 (4.3)		588 (4.1)	611 (4.0)	
June 2012	3,242 (4.0)	2,236 (4.1)		602 (4.2)	670 (4.3)	
July 2012	3,520 (4.3)	2,417 (4.5)		638 (4.4)	724 (4.7)	
August 2012	3,293 (4.0)	2,191 (4.1)		572 (3.9)	599 (3.9)	
September 2012	2,950 (3.6)	2,129 (3.9)		500 (3.5)	579 (3.8)	
October 2012	3,403 (4.2)	2,276 (4.2)		603 (4.2)	608 (3.9)	
November 2012	3,259 (4.0)	2,220 (4.1)		546 (3.8)	613 (4.0)	
December 2012	3,073 (3.8)	2,299 (4.3)		555 (3.8)	583 (3.8)	
January 2013	3,690 (4.5)	2,287 (4.2)		611 (4.2)	663 (4.3)	
February 2013	3,191 (3.9)	1,998 (3.7)		517 (3.6)	572 (3.7)	
March 2013	3,563 (4.3)	2,260 (4.2)		619 (4.3)	715 (4.6)	
April 2013	3,746 (4.6)	2,317 (4.3)		629 (4.3)	678 (4.4)	
May 2013	3,782 (4.6)	2,378 (4.4)		630 (4.3)	689 (4.5)	
June 2013	3,566 (4.4)	2,251 (4.2)		619 (4.3)	649 (4.2)	
July 2013	4,191 (5.1)	2,418 (4.5)		810 (5.6)	750 (4.9)	
August 2013	3,774 (4.6)	2,221 (4.1)		621 (4.3)	655 (4.2)	
September 2013	3,568 (4.4)	2,332 (4.3)		736 (5.1)	750 (4.9)	
October 2013	3,839 (4.7)	2,487 (4.6)		764 (5.3)	826 (5.4)	
November 2013	3,656 (4.5)	2,452 (4.5)		794 (5.5)	772 (5.0)	
December 2013	2,991 (3.7)	1,715 (3.2)		526 (3.6)	510 (3.3)	
Length of stay, n (%)			<0.001			<0.001
≤7d	75,706 (92.4)	43,663 (80.8)		13,092 (90.3)	13,059 (84.6)	
>7 d	6,231 (7.6)	10,378 (19.2)		1,399 (9.7)	2,377 (15.4)	
Major diagnostic categories, n (%)			<0.001			<0.001
Endocrine, nutritional, and metabolic system	1,310 (1.6)	3,074 (5.7)		175 (1.2)	248 (1.6)	
Nervous system	4,363 (5.3)	4,570 (8.5)		1,244 (8.6)	1,581 (10.2)	
Eye	6,141 (7.5)	3,353 (6.2)		2,180 (15.0)	1,672 (10.8)	
Ear, nose, mouth, and throat	9,372 (11.4)	2,124 (3.9)		637 (4.4)	632 (4.1)	
Respiratory system	5,002 (6.1)	4,753 (8.8)		1,014 (7.0)	1,152 (7.5)	
Circulatory system	4,785 (5.8)	13,178 (24.4)		2,233 (15.4)	3,916 (25.4)	
Digestive system	16,887 (20.6)	6,041 (11.2)		3,333 (23.0)	2,499 (16.2)	
Hepatobiliary system and pancreas	2,154 (2.6)	1,798 (3.3)		189 (1.3)	233 (1.5)	
Musculoskeletal system and connective tissue	7,765 (9.5)	3,129 (5.8)		909 (6.3)	913 (5.9)	

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**Table 1 – continued**

Characteristic	Unmatched (n = 135,978)			Matched* (n = 29,927)		
	No T2DM (n = 81,937)	T2DM (n = 54,041)	P value <sup>†</sup>	No T2DM (n = 14,491)	T2DM (n = 15,436)	P value <sup>†</sup>
Skin, subcutaneous tissue, and breast	5,806 (7.1)	1,993 (3.7)		490 (3.4)	442 (2.9)	
Kidney and urinary tract	4,467 (5.5)	5,069 (9.4)		1,011 (7.0)	1,170 (7.6)	
Male reproductive system	1,097 (1.3)	425 (0.8)		80 (0.6)	86 (0.6)	
Female reproductive system	3,823 (4.7)	365 (0.7)		244 (1.7)	117 (0.8)	
Blood and blood-forming organs and immunological disorders	1,125 (1.4)	742 (1.4)		85 (0.6)	112 (0.7)	
Myeloproliferative diseases and disorders	1,131 (1.4)	389 (0.7)		49 (0.3)	61 (0.4)	
Infectious and parasitic diseases and disorders	1,312 (1.6)	968 (1.8)		144 (1.0)	156 (1.0)	
Mental diseases and disorders	1,134 (1.4)	358 (0.7)		67 (0.5)	55 (0.4)	
Alcohol/drug use or induced mental disorders	132 (0.2)	43 (0.1)		9 (0.1)	11 (0.1)	
Injuries, poison, and toxic effect of drugs	1,507 (1.8)	556 (1.0)		96 (0.7)	91 (0.6)	
Burns	30 (0.0)	10 (0.0)		0 (0.0)	3 (0.0)	
Factors influencing health status	2,594 (3.2)	1,103 (2.0)		302 (2.1)	286 (1.9)	
Comorbidities unrelated to diabetes, n (%)						
Chronic obstructive pulmonary disease	2,217 (2.7)	2,335 (4.3)	<0.001	447 (3.1)	498 (3.2)	0.484
Liver disease	968 (1.2)	1,397 (2.6)	<0.001	82 (0.6)	118 (0.8)	0.035
Cancer	6,326 (7.7)	3,432 (6.4)	<0.001	440 (3.0)	551 (3.6)	0.01
Rheumatic disease	346 (0.4)	286 (0.5)	0.005	24 (0.2)	32 (0.2)	0.404
Peptic ulcer disease	722 (0.9)	620 (1.1)	<0.001	73 (0.5)	78 (0.5)	0.985
AIDS/HIV	122 (0.1)	42 (0.1)	<0.001	7 (0.0)	9 (0.1)	0.708

T2DM, type 2 diabetes mellitus.  
 \* Matched cohort based on the propensity score matching algorithm with the best balance.  
 † P values were obtained from  $\chi^2$  and t tests.

**Table 2 – Mean (and SD) excess hospital expenses of one hospital visit that is attributable to T2DM (in 2013 US dollars).**

Model	Median bias after matching*	Mean bias after matching*	Health system perspective			Patient perspective		
			No T2DM	T2DM	Difference	No T2DM	T2DM	Difference
M01	NA	NA	3227 ± 25	5731 ± 55	2505 ± 61	790 ± 6	1082 ± 10	292 ± 12
M02	NA	NA	3835 ± 28	4714 ± 35	878 ± 43	889 ± 6	939 ± 6	49 ± 9
M03	NA	NA	4049 ± 28	4632 ± 32	584 ± 36	901 ± 5	917 ± 6	16 ± 7
M04	0.6	1.0	4340 ± 39	5606 ± 51	1265 ± 58	933 ± 7	1039 ± 8	107 ± 10
M05	0.6	1.0	4646 ± 39	5662 ± 47	1016 ± 47	959 ± 6	1026 ± 6	67 ± 8
M06	0.6	0.9	4288 ± 37	5602 ± 49	1314 ± 55	929 ± 7	1039 ± 8	110 ± 9
M07	0.6	0.9	4575 ± 37	5565 ± 45	991 ± 44	952 ± 6	1022 ± 6	70 ± 7
M08	0.4	0.6	3447 ± 58	4325 ± 72	878 ± 77	809 ± 11	893 ± 12	84 ± 15
M09	0.4	0.6	3605 ± 46	4377 ± 55	772 ± 51	812 ± 9	882 ± 9	69 ± 12
M10	0.4	0.5	3383 ± 49	4389 ± 64	1007 ± 71	768 ± 9	881 ± 11	113 ± 13
M11	0.4	0.5	3485 ± 38	4420 ± 47	935 ± 45	775 ± 7	870 ± 9	96 ± 10

Note. M01: TPM (unadjusted); M02: TPM (adjusted with entry characteristics); M03: TPM (adjusted with entry characteristics and LOS); M04: 1-to-1 optimal matching + TPM (adjusted with entry characteristics); M05: 1-to-1 optimal matching + TPM (adjusted with entry characteristics and LOS); M06: 1-to-2 optimal matching + TPM (adjusted with entry characteristics); M07: 1-to-2 optimal matching + TPM (adjusted with entry characteristics and LOS); M08: 1-to-1 greedy matching with caliper distance of  $10^{-6}$  + TPM (adjusted with entry characteristics); M09: 1-to-1 greedy matching with caliper distance of  $10^{-6}$  + TPM (adjusted with entry characteristics and LOS); M10: 1-to-1 optimal matching with caliper distance of  $10^{-6}$  + TPM (adjusted with entry characteristics); M11: 1-to-1 optimal matching with caliper distance of  $10^{-6}$  + TPM (adjusted with entry characteristics and LOS).

LOS, length of stay; NA, not applicable; T2DM, type 2 diabetes mellitus; TPM, two-part model.

\* Before matching, median bias was 3.1, whereas mean bias was 12.3.



## Conclusions

Given that other aspects of direct costs such as outpatient costs as well as indirect costs were excluded from this analysis, the total costs attributable to T2DM will be even more burdensome to the society and will likely be increasingly taxing to the society as the prevalence of diabetes increases in the future.

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