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Economic Evaluation

The Cost of Hypoglycemia Associated With Type 2 Diabetes Mellitus in Taiwan

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ABSTRACT

Objectives: To quantify the incremental burden of patients with type 2 diabetes mellitus (T2DM) and a hypoglycemic event in Taiwan using the National Health Insurance Research Database. **Methods:** Data from 2000 through 2013 with an index period of 2001 through 2012 from the National Health Insurance Research Database's 2-million-patient sample were used. Using a nested case-control study design, patients were indexed if they reported a diagnosis of T2DM during the index period. Patients with T2DM with a hypoglycemic event (defined by *International Classification of Diseases, Ninth Revision, Clinical Modification* codes) during the index period were identified. Patients with T2DM without a hypoglycemic event were included to form a 4:1 (controls to cases) matched cohort on the basis of age, sex, the Charlson Comorbidity Index, and the T2DM diagnosis date. Both cohorts were followed up for 1 year after the hypoglycemic event and had their treatment utilization, resource utilization, and healthcare costs measured. **Results:** A total of 144 213 patients with T2DM were identified, with 3 651 (2.5%) recording a hypoglycemic event. Before matching, patients with T2DM with a hypoglycemic event were, on average, older (64.2 vs 56.6) and had higher mean CCI scores (2.4 vs 1.9) than did patients with T2DM without a hypoglycemic event. After matching, patients with T2DM and a hypoglycemic event incurred an additional $1353 in average direct healthcare costs during the 1 year of follow-up compared with the matched cohort. Patients with T2DM with hypoglycemia also spent an additional 5.9 days in the hospital during the follow-up period compared with the matched cohort. **Conclusions:** Patients with hypoglycemic events, on average, experienced a substantially higher economic burden than did their counterparts without a hypoglycemic event during the same period.
Keywords: Hypoglycemia, resource utilization, Taiwan, type 2 diabetes mellitus

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Introduction

Current treatment guidelines for patients with type 2 diabetes mellitus (T2DM) recommend that the optimization of glycemic control is a critical strategy to limit diabetes-related complications, limit their deleterious effects on morbidity and mortality, and improve patient outcomes.[1–4] Nevertheless, a barrier to achieving this goal is the development of, or the perceived risk of developing, hypoglycemia, which is a common adverse event experienced by patients and is often associated with treatment.[5] Hypoglycemia is associated with its own related comorbidities, including fall-related fractures and cardiovascular events and has been cited as increasing the risk of dementia, all of which can reduce quality of life and life expectancy.[6–8] In addition, older patients, particularly those older than 65 years, are more likely to experience hypoglycemic events requiring assistance.[9] Therefore, an event of hypoglycemia, or the fear of it, can have an impact on not only a patient's quality of life but also their ability to achieve glycemic control, particularly if clinical inertia develops or patients reduce compliance with their treatment plan to avoid an event.[1]

Hypoglycemic episodes have varying levels of severity. Mild episodes, limited to tachycardia and sweating, may be tolerated and may not require medical attention. Severe hypoglycemia, however, is almost always symptomatic, may require assisted medical treatment, and can result in serious consequences such as injury, unconsciousness, seizures, myocardial ischemia, and coma.[1,9–11] Therapy includes restoring blood glucose levels and treating symptoms, with glucagon recommended for severe cases.[12]

For patients receiving antidiabetic treatment for their T2DM, glucose-lowering medications that increase circulating insulin in a

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glucose-independent manner, such as insulin and sulfonylurea therapy, are the most common cause of hypoglycemia.[13] Despite providing glycemic control through careful titration, a common limitation of the use of these antidiabetic medicines, particularly in intensive glucose-lowering therapy regimens, is an increased risk for hypoglycemia. A recent analysis of emergency department (ED) visits resulting from insulin-related hypoglycemia found that errors, in meal-time planning, insulin administration, insulin formulation or delivery device, or dose, were the precipitating factors of the ED visits.[14] Therefore, although the treatment paradigm for T2DM includes more options than ever before with the availability of many different classes of medications, the risk of hypoglycemia persists. Consequently, patient education of their disease, treatment, and hypoglycemia risk remains an important consideration when choosing the type of medication, delivery system, and individualized glycemic target for patients with T2DM.

Overall, the prevalence of T2DM in Asia is increasing. Similarly, in Taiwan the prevalence of T2DM is rising, with estimates increasing from 5.79% in 2000 to 11.8% in 2015.[15,16] In 2004, a Taiwanese study estimated the incidence of severe hypoglycemia in T2DM hospital admissions to be 7.4%.[17] Chen et al[18] found that ED visits of Taiwanese patients with T2DM with hypoglycemia increased 5-fold between 2000 and 2010, with higher rates of severe hypoglycemia reported in women, patients older than 65 years, and patients living in rural areas.

Studies have demonstrated that patients experiencing hypoglycemic events may suffer negative impacts in health-related quality of life and life expectancy, incur additional costs, and use more healthcare resources than those without hypoglycemic events.[19–21] A US costing study estimated the total economic burden of hypoglycemia to be $1.84 billion in 2009.[22] In 2004 and 2008, the mean per visit cost in the United States for an inpatient admission and ED visit associated with a hypoglycemic event was estimated to be $17 564 and $1 387, respectively.[23] For Taiwan, no recent studies assessing the cost of hypoglycemia in patients with T2DM have been identified. As such, this study aimed to estimate the incremental healthcare resource utilization (HCRU) and direct healthcare costs attributable to hypoglycemic events in patients with T2DM compared with a matched cohort of patients with T2DM without hypoglycemia, using information from a nationally representative health insurance claims database in Taiwan.

Methods

Data Source

Taiwan launched its single-payer national health insurance program in 1995 and currently covers 99.9% of its population. Participating patients have a comprehensive benefit package with ambulatory care, inpatient care, and prescription drug, among other resources, all covered by the government. All healthcare claims for within the health system are coded into a system and recorded in a longitudinal database with records for each patient beginning in 2000. These patient records are de-identified and made available for research in several different databases by the Health and Welfare Data Science Center, the National Health Insurance Administration, and the Ministry of Health and Welfare.[24] The databases include basic demographic information; diagnosis and procedure codes using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*); and outpatient, inpatient, and pharmacy expenditures. The representative sample size of this longitudinal database provides an ideal platform for analyzing chronic diseases such as diabetes, and several recent studies examining patient populations with T2DM have used the National Health Insurance Research Database.[25,26] This study used a representative 2-million-patient sample derived from all beneficiaries in Taiwan's National Health Insurance program. The 2 million patients were randomly sampled in 2010, and the database includes all their longitudinal claims records. For this study, data from 2000 through 2013 were analyzed. The study received approval from the Joint Institutional Review Board.

Study Design

The primary objective of this study was to estimate the direct all-cause HCRU and healthcare costs attributable to hypoglycemic events in Taiwanese patients with T2DM in the 1-year period after the event. Using a nested case-control study design, these costs were compared with those attributable to a matched cohort of patients with T2DM without hypoglycemia over the same follow-up period, to assess if any incremental costs were incurred. Secondary objectives included describing the patient profile of T2DM with hypoglycemic events and understanding the T2DM medications used by patients with hypoglycemic events.

A retrospective database analysis was undertaken using data over a study period from January 1, 2000, through December 31, 2013. An index period from January 1, 2001, through December 31, 2012, was used in the analysis, which was the period in which patients were identified with a diagnosis of T2DM. The index date, which fell within the index period, was the date on which patients with T2DM were identified as being diagnosed with a hypoglycemic event. The 1-year period pre-index and postindex dates served as the screening and follow-up periods, respectively (Fig. 1).

Study Population

This study first identified Taiwanese patients with T2DM during the index period, using *ICD-9-CM*.[27] Patients with T2DM were included in the analysis if they had:

1. either 1 inpatient visit or 2 or more outpatient visits (separated by at least 30 days) with a diagnosis of T2DM (*ICD-9-CM* of 250.x0 and/or 250.x2) and
2. a minimum of 12 months of continuous medical services and pharmaceutical enrollment before and after their date of T2DM diagnosis.

Patients were excluded from the study if they:

1. were younger than 18 years,
2. had a hypoglycemic event (*ICD-9-CM* code 251.0, 251.1, or 251.2) in the 12 months before their date of T2DM diagnosis, or
3. had a diagnosis of type 1 diabetes mellitus (*ICD-9-CM* code 250.x1 and/or 250.x3), secondary diabetes (*ICD-9-CM* code 249.xx), or gestational diabetes (*ICD-9-CM* code 648.8x) at any time during the study period.

After the identification of the eligible patients with T2DM, these patients were examined for the presence of a hypoglycemic event during the index period. A hypoglycemic event was defined as an inpatient or outpatient visit with a diagnosis

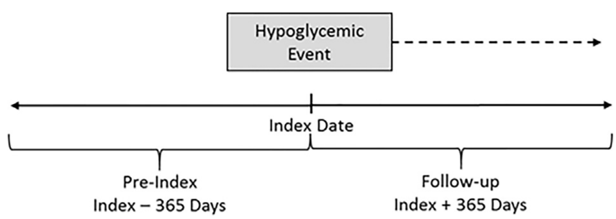

Fig. 1 – Overview of study period outlining index date and 1-y pre-index and postindex periods.

(*ICD-9-CM* code 251.0, 251.1, or 251.2). Hypoglycemic events included all levels of severity as long as they were available in the database and they were not classified by severity in this claims-based database without clinical markers. Patients with both a T2DM diagnosis and a hypoglycemic event in the index period were indexed into the study on the date of the hypoglycemic event (index date). The 1-year pre-index date was used as a screening period to ensure patients had a minimum of 12 months of continuous medical services and pharmaceutical enrollment before the index date. The 1-year follow-up period postindex date was used to track the HCRU and direct medical costs that the identified patients with T2DM incurred.

A matched cohort was then derived using propensity scoring methods, which matched in a 4:1 ratio (controls to cases) patients in a T2DM cohort without hypoglycemic events to a cohort of patients with T2DM with hypoglycemic events.[28] Matching was based on age, sex, the Charlson Comorbidity Index (CCI), and the date of the first T2DM diagnosis in the study period. Patients in the matched cohort were given an index date corresponding to the date of the hypoglycemic event for their counterparts to eliminate bias due to changing treatment patterns over time and seasonal effects on resource utilization and healthcare spending.

The analysis resulted in 2 patient cohorts: (1) patients with T2DM with a hypoglycemic event during the index period and (2) a matched cohort of patients with T2DM without hypoglycemic events matched to those with hypoglycemic events over the same index period.

Statistical Analysis

For both cohorts, baseline demographic and patient characteristics, including the presence of comorbidities commonly reported with T2DM, were assessed. Demographic information was measured at the index date, which included information on age and sex. Patient comorbidities were measured in the 12 months before patients' first T2DM diagnosis. Patients were classified as having an included comorbidity if they had a claim for an inpatient or ambulatory care expenditure accompanied by an *ICD-9-CM* code for any of the included comorbidities. The CCI[29] and the Adapted Diabetes Complications Severity Index (aDCSI)[30] were included in the comorbidity analysis. The 2 cohorts were assessed to identify any differences between the 2 groups.

The use of antidiabetic medications in the 365 days of follow-up postindex date was measured for each cohort. Medication use was grouped by class and included the biguanides, sulfonylurea, dipeptidyl peptidase 4 inhibitors, thiazolidinediones, α-glucosidase inhibitors, basal insulins, premixed insulins, and prandial insulin classes.

HCRU and direct healthcare costs were also measured in the 365 days of follow-up postindex date. Both HCRU and direct healthcare costs were all-cause and not diabetes-specific. The recorded HCRU measurements included the number of hospital admissions, hospital days, ED visits, and outpatient visits. Direct healthcare costs included outpatient costs, inpatient costs, and ED costs. These costs covered all costs within the database and were further split into medication and nonmedication costs for each of the categories. Medication costs included any type of pharmacy claim for patients, whereas nonmedication costs included all other potential costs such as procedures, laboratory tests, ward usage, and/or medical materials, among others. Medication use, HCRU, and direct healthcare costs of the 2 cohorts were then compared to assess whether incremental costs were incurred by the patient group with hypoglycemic event.

All costs were converted to, and are presented in, 2018 US dollars, using an exchange rate of Taiwanese new dollar (NT$) 1 = $0.032.[31] SAS software version 9.4 (SAS Institute, Cary, NC) was used in the management and analysis of data.

Results

A total of 144 213 patients with T2DM were included in the analysis (Fig. 2). Of these patients, 3651 (2.5%) recorded a hypoglycemic event within the index period. The remaining 140 562 (97.5%) patients were those with T2DM and without a hypoglycemic event during the index period, and they were used to derive the matched cohort, which consisted of 14 604 patients. Table 1 presents the baseline demographic and clinical characteristics for the hypoglycemia cohort and the matched and unmatched nonhypoglycemia cohorts. Compared with the nonmatched cohort of patients with T2DM and no hypoglycemic event, patients with hypoglycemia were, on average, older (64.2 years vs 56.6 years) and had higher mean CCI (2.4 vs 1.9) and aDCSI (0.4 vs 0.2) scores.

Treatment Utilization Postindex

The treatment utilization rates for patients 1 year after the index date are presented in Table 2. Overall, patients in the hypoglycemic event cohort recorded higher utilization of every included T2DM class of medication than did the matched nonhypoglycemic event cohort. For both cohorts, sulfonylureas, followed by biguanides and prandial insulins, were the most commonly used T2DM medications. Although the overall use of basal insulin across both groups was low, patients with a hypoglycemic event were 6 times more likely to use basal insulin than their matched nonhypoglycemic counterparts (1.8% vs 0.3%). This trend held true for each insulin type: patients with hypoglycemic events were 4.6 times more likely to use premixed insulin (5.1% vs 1.1%) and 3.1 times more likely to use a prandial insulin (27.5% vs 9.0%).

Resource Utilization

All measured categories of resource utilization during the 1-year period after the index date were significantly higher for patients with a hypoglycemic event than for the matched nonhypoglycemic event cohort (Table 3) (*P*<.001). Mean hospital admissions, hospital days, and ED visits for patients with a hypoglycemic event were more than double the matched cohort's. On average, during the 1-year follow-up period, patients with a hypoglycemic event used an additional 5.9 days in the hospital, 0.5 ED visits, and 2.2 outpatient visits compared with the matched nonhypoglycemic event cohort.

Direct Healthcare Costs

Direct healthcare costs for the 1-year postindex date are presented in Table 4. All measured cost categories were significantly higher for the cohort of patients with a hypoglycemic event compared with their matched counterparts (*P*<.001). The mean total all-cause direct healthcare cost was $3454 for the hypoglycemic event cohort compared with $2101 for the matched nonhypoglycemic event cohort, with the incremental difference of $1353 resulting from higher inpatient ($752), medication ($350), outpatient ($203), and ED ($49) costs. When averaged across the 144 213 patients with TD2M included in the analysis, the mean incremental cost attributed to hypoglycemia during the 1-year follow-up period was $34 per patient with TD2M.

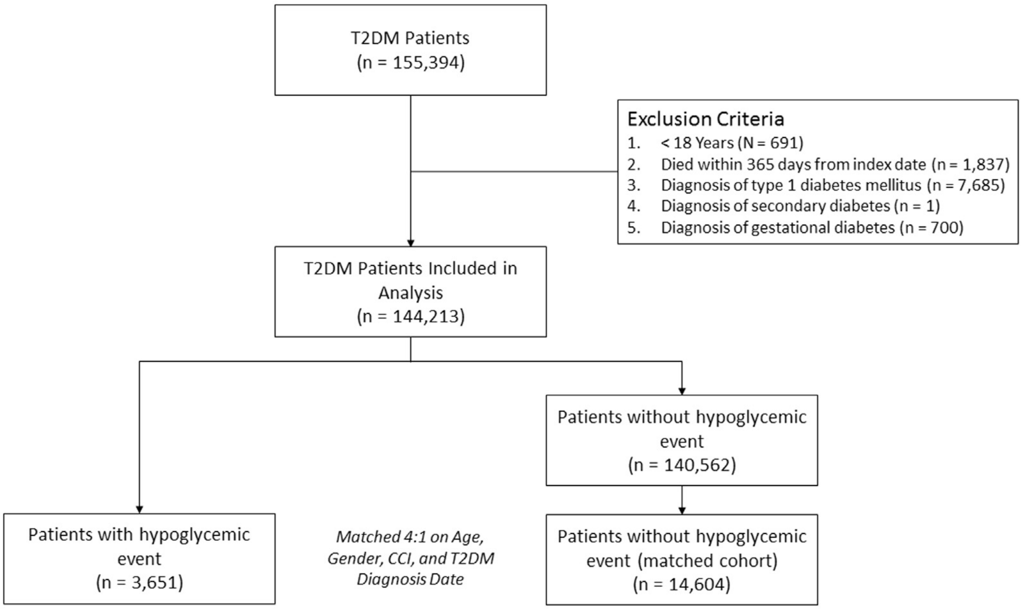

Fig. 2 – Patient selection. CCI, Charlson Comorbidity Index; T2DM, type 2 diabetes mellitus.

Discussion

This analysis is a retrospective cohort study undertaken on a large population-based sample of a claims-based database. The study used a 2-million-patient sample from the National Health Insurance Research Database of Taiwan to identify patients with T2DM with and without hypoglycemic events. To our knowledge, this is the first study of the HCRU and healthcare costs of patients with T2DM with hypoglycemia in Taiwan. Results demonstrated that patients with T2DM recording a hypoglycemic event were more likely to be older and had higher mean CCI and aDCSI scores than patients with T2DM without a reported hypoglycemic event. Demographic trends of patients with T2DM with and without hypoglycemic events were consistent between our analysis and the studies by Hsiao and Chien[17] and Chen et al.[18]

Of the patients with T2DM included in our study, 2.5% had a hypoglycemic event resulting in an inpatient or outpatient encounter and associated claim over the study period. Comparisons with our study are difficult because of differences in study design, setting, and patient population in the literature. Our study did not limit inclusion to patients on medication to control their glucose levels as other studies have. This may have resulted in a significant portion of the patient population not having a hypoglycemic event because of lack of T2DM medication and thus may have lowered our hypoglycemic event rate. The study by Chen et al[18] in Taiwan examined the incidence of hypoglycemia and found a similar number of patients as in our study, despite a small difference in study time frame. The study included 3184 patients with T2DM with a hypoglycemic event over 11 years compared with our 3651 patients over 12 years. The hospital-based

Table 1 – Baseline demographic and clinical characteristics.

Characteristic	Patients with T2DM without hypoglycemia (N = 140 562)	Patients with T2DM without hypoglycemia (matched cohort) (N = 14 604)	Patients with T2DM with hypoglycemia (N = 3651)
Age (y), mean ± SD	56.6 ± 13.1	63.9 ± 12.5	64.2 ± 12.6
Sex, n (%)			
Male	73 483 (52.1)	7665 (52.5)	1921 (52.6)
Female	67 443 (47.9)	6939 (47.5)	1730 (47.4)
Comorbidities, n (%)			
Cardiovascular disease	3724 (2.6)	668 (4.6)	190 (5.2)
Nephropathy/CKD	4314 (3.1)	802 (5.5)	249 (6.8)
Neuropathy	5513 (3.9)	703 (4.8)	228 (6.2)
Retinopathy	3927 (2.8)	448 (3.1)	235 (6.4)
Obesity	8 (0.0)	1 (0.0)	1 (0.0)
Depression	4194 (3.0)	490 (3.4)	122 (3.3)
CCI, mean ± SD	1.9 ± 1.3	2.4 ± 1.6	2.4 ± 1.6
aDCSI, mean ± SD	0.2 ± 0.5	0.3 ± 0.6	0.4 ± 0.8

aDCSI, Adapted Diabetes Complications Severity Index; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; T2DM, type 2 diabetes mellitus.

Table 2 – Treatment utilization during follow-up.

Treatment	Patients with T2DM without hypoglycemia (matched cohort), n (%) (N = 14 604)	Patients with T2DM with hypoglycemia, n (%) (N = 3651)
Biguanides	5516 (37.8)	2298 (62.9)
Sulfonylureas	6295 (43.1)	2736 (74.9)
DPP-4 inhibitors	95 (0.7)	62 (1.7)
Thiazolidinediones	579 (4.0)	343 (9.4)
α-Glucosidase inhibitors	680 (4.7)	387 (10.6)
Basal insulins	46 (0.3)	64 (1.8)
Premixed insulin	166 (1.1)	185 (5.1)
Prandial insulins	1313 (9.0)	1003 (27.5)

DPP-4, dipeptidyl peptidase 4; T2DM, type 2 diabetes mellitus.

retrospective analysis conducted by Hsiao and Chien[17] found an incidence rate of 7.4% for severe (loss of consciousness or a major alteration of mental status requiring assistance) hypoglycemia in Taiwan. The relative small sample size of this study (n = 1195), use of a single institution, and demographic characteristics of the sample may have influenced the results.

A study using the Medstat MarketScan claims (pharmacy and medical) database in the United States found a similar incidence of patients experiencing a hypoglycemic event using *ICD-9-CM* codes, with 3.5% of the sample having a medical encounter for hypoglycemia.[23] This study, however, had a shorter period (2004 to 2008), and a period similar to our study could have resulted in a higher rate.

The results of this analysis demonstrate that patients with a hypoglycemic event had higher mean direct all-cause resource utilization and healthcare costs in the 1-year period after the hypoglycemic event compared with their matched non-hypoglycemic event T2DM counterparts.

Our results are in line with those of other claims-based database analyses of the resource use and costs of T2DM with hypoglycemic events. The study by Williams et al[19] of an administrative claims data set in the United States found an increase in mean all-cause ambulatory visits for confirmed patients with hypoglycemia versus patients without hypoglycemia, as well as higher all-cause and diabetes-related healthcare costs. In this study, the incremental cost incurred by patients with T2DM in the year after a recorded hypoglycemic event compared with a matched nonhypoglycemic T2DM cohort was estimated to be $1353. This equates to an incremental cost of $34 per patient with T2DM, which is in line with the $14 to $96 in estimated per patient with T2DM costs attributed to hypoglycemic events in the study conducted by Foos et al[32] in the United States. A study by Jönsson et al[33] of hypoglycemia in Sweden estimated the direct cost per year of mild, moderate, and severe hypoglycemic events as €26 ($30), €334.70 ($382), and €2806.80 ($3200), respectively. In the Swedish study, moderate and severe events were those requiring medical attention and were most similar to the events in our study. The combined costs of moderate and severe events reported in the study by Jönsson et al align with the incremental cost of $1353 for patients with hypoglycemia in our study.

The average incremental cost of $1353 associated with hypoglycemia in patients with T2DM that we found was consistent with those found in other disease areas. In a study of osteoporotic fractures among postmenopausal women in Taiwan, those with vertebral fractures incurred, on average, between NT$ 36 807 ($1178) and NT$ 50 118 ($1604) in additional costs, depending on age, during the first year after their fracture compared with those without hip fractures.[34] Those with wrist fractures incurred an additional NT$ 20 724 ($663) to NT$ 30 232 ($967) depending on their age when compared with postmenopausal women without wrist fractures. A study comparing patients with and without ankylosing spondylitis found that patients with ankylosing spondylitis averaged $1353 in incremental costs when compared with patients without ankylosing spondylitis.[35]

These results have important implications for T2DM stakeholders in Taiwan. As shown in previous studies, patients with hypoglycemic events often become more tentative in their glycemic management, which can influence long-term outcomes of the disease.[1,13] This is in addition to the lower health-related quality of life caused by hypoglycemia.[19–21] The implementation of increased patient education and individual glycemic control thresholds can reduce the risk of hypoglycemia and should be considered by stakeholders. Payers are also carrying the high burden of hypoglycemia, as seen by the estimated incremental cost ($1353) incurred in the year after a hypoglycemic event. With an estimated 3651 patients having 1 hypoglycemic episode over the 12-year period in this analysis, the incremental cost per year was estimated to be $411 755 for the sample of 2 million. This is considered a conservative estimate because hypoglycemia is often recurrent in patients; therefore, it is likely that the actual cost of hypoglycemia over the study period was higher. When evaluating the budget impact and/or cost effectiveness of existing and new medications for T2DM, payers must also consider their hypoglycemic profile. This study will allow payers to understand the costs associated with hypoglycemia and better understand the economic implications of T2DM treatment regimens. Finally, physicians play an important role in the selection of T2DM management. The proper management of these patients and careful selection of T2DM medication could potentially save significant costs and resources in the future. Despite all the recent advances in medications to achieve glycemic control, a significant unmet need is still present to eliminate hypoglycemic events.

This study has several limitations. First, this study was undertaken on a sample of a claims-based database and only hypoglycemic events associated with a claim were included. These

Table 3 – All-cause HCRU 1-y postindex.

Resource	Patients with T2DM without hypoglycemia (matched cohort), mean ± SD (N = 14 604)	Patients with T2DM with hypoglycemia, mean ± SD (N = 3651)	*P* value	Incremental*
Hospital admissions	0.48 ± 1.08	1.00 ± 1.52	<.001	0.52
Hospital days	4.87 ± 30.11	10.79 ± 41.89	<.001	5.92
ED visits	0.50 ± 1.36	1.02 ± 2.50	<.001	0.52
Outpatient visits	29.48 ± 21.29	31.63 ± 22.63	<.001	2.15

ED, emergency department; HCRU, healthcare resource utilization; T2DM, type 2 diabetes mellitus.
* Mean difference between the hypoglycemia and the matched nonhypoglycemia cohorts.

Table 4 – All-cause direct healthcare costs ($) 1-y postindex.

Direct healthcare cost	Patients with T2DM without hypoglycemia (matched cohort) (N = 14 604)		Patients with T2DM with hypoglycemia (N = 3651)		P value	Incremental mean cost*
	Mean ± SD	Median	Mean ± SD	Median		
Outpatient costs						
Medication costs	471 ± 890	8655	670 ± 938	488	<.001	199
Other costs†	671 ± 1432	12 639	873 ± 2015	458	<.001	203
Inpatient costs						
Medication costs	134 ± 900	0	283 ± 1316	0	<.001	149
Other costs†	773 ± 3412	0	1524 ± 4363	0	<.001	752
ED costs						
Medication costs	5 ± 41	0	8 ± 37	0	<.001	3
Other costs†	48 ± 175	0	97 ± 215	0	<.001	49
Total costs						
Medication costs	610 ± 1336	319	960 ± 1712	603	<.001	350
Other costs†	1491 ± 3900	518	2494 ± 5149	901	<.001	1003
Total direct costs	2101 ± 4658	940	3454 ± 6170	1642	<.001	1353

ED, emergency department; T2DM, type 2 diabetes mellitus.
* Mean difference between the hypoglycemia and matched nonhypoglycemia cohorts.
† Other costs are all nonmedication claims. These costs include all costs outside of pharmacy costs, such as outpatient and inpatient services (diagnosis and service charges) and outpatient and inpatient orders (procedures, medical services, etc).

restrictions may have underestimated the number of hypoglycemic events in Taiwan because more mild events not requiring an interaction with a healthcare professional would have not been included. Second, the database does not include any indirect costs such as absenteeism/presenteeism or patient-reported outcomes to measure changes in quality of life. Third, this study was conducted before the availability of data for glucagon-like peptide-1 receptor agonist and sodium glucose cotransporter-2 inhibitor therapies, which may influence patient medication choices and thus hypoglycemic rates. Another limitation of our study is that only the cost associated with the first hypoglycemic event has been considered. Hypoglycemic events may recur in patients over time. Therefore, the actual cost of hypoglycemia in Taiwan is likely to be higher than that reported in the present study. Several possible study extensions could be undertaken to better understand the burden of hypoglycemia in Taiwan. An examination of the treatment regimens associated with hypoglycemic events to understand the risk of hypoglycemia for each of the T2DM treatment regimens would aid in patient selection of the appropriate regimen. A study following patients who experience a hypoglycemic event for a longer period of time could help identify the types of adjustments made to the treatment regimen and possible differences in long-term mortality or morbidity between patients with and those without hypoglycemic events. Finally, a study could be undertaken to examine the indirect costs and impact to quality of life in patients with hypoglycemic events.

Conclusions

Our study shows an economic and healthcare resource burden associated with hypoglycemia over a 1-year follow-up period. Compared with a matched cohort without hypoglycemia, patients with hypoglycemia incurred more medication costs, outpatient costs, inpatient costs, ED costs, hospital admissions, hospital days, ED visits, and outpatient visits. These findings confirm that the burden of hypoglycemia in T2DM in Taiwan is consistent with that in the rest of the world. The choice of treatment regimen and patient education could potentially lower the risk of hypoglycemia and reduce the related burden.

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