Direct medical costs of diabetes mellitus in the year of mortality and year before mortality

Authors: Carlos King Ho Wong, PhD[1], Fangfang Jiao, PhD[1], Eric Ho Man Tang, BSc[1], Thaison Tong, MSc[2], Praveen Thokala, PhD[2], Cindy Lo Kuen Lam, MD[1]

[1] Department of Family Medicine and Primary Care, The University of Hong Kong, Hong Kong

[2] Health Economics and Decision Science, School of Health and Related Research, The University of Sheffield, UK

Corresponding Author:

Dr. Carlos King Ho Wong[1]

Address: 3/F, Ap Lei Chau Clinic, 161 Ap Lei Chau Main Street, Ap Lei Chau, Hong Kong.

Tel: (+852) 2518-5688

Fax: (+852) 2814-7475

Email: carlosho@hku.hk

Running title: DM healthcare costs in mortality year and year before mortality

Abstract

Aims

Studies have shown that health service utilization often increases in few years immediately before death. Estimates of direct medical cost of diabetes mellitus (DM) in mortality year and the previous year is not well understood. This study aimed to report the health resource use and estimate the direct medical costs among DM patients in the year of mortality and the year before mortality.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dom.13253

Materials and Methods

We analysed a population-based, retrospective cohort study including all adults with DM diagnosis in Hong Kong between 2009 and 2013, and death between January 1, 2010 and December 31, 2013. Annual direct medical costs in year of mortality and year before mortality were determined by summing costs of health services utilized within the respective year. The costs were analysed by gender, the presence of co-morbidities, diabetic complications and primary cause of death.

Results

A total of 10,649 patients met the eligibility criteria for analysis. On average, the direct medical costs in the year of death were 1.947 times higher than those in the year before death. Male and female patients had similar costs in the year before mortality and mortality year. Patients with any diabetic complications had greater costs in the year of mortality and before mortality than those without.

Conclusions

This analysis provides new evidence on incorporating additional direct medical costs in the mortality year, and refining the structure of total cost estimates for use in costing and cost-effectiveness analyses of interventions for DM.

Manuscript Text

Introduction

Due to the population ageing, environmental and lifestyle changes, the global prevalence of diabetes mellitus (DM) in adults was 8.8% in 2015, and has been predicted to increase to 10.4% in 2040 [1]. The mean healthcare expenditure for each adult living with DM was US$1,583 in 2014, projecting an annual healthcare expenditure attributable to DM ranging between US$612-1,099 billion worldwide [2].

Direct medical costs have important implications for the implementation of health care interventions regarding the prevention of diabetes and diabetes-related complications. Estimations of the lifetime direct medical costs of DM quantifies economic burden and consequences to national healthcare services. A United States national retrospective study estimated lifetime medical expenditures for DM patients from diagnosis to death [3]. Results from UK Prospective Diabetes Prospective Study [4] reported that patients with diabetes-related complications incurred more annual direct medical costs than those without. Another study based on multiple data sources in the US reported the total number of deaths attributable to DM, and estimated the indirect cost due to early mortality [5]. The largest direct medical cost component was hospital inpatient care, followed by outpatient care and allied health care. Premature mortality attributed to DM equated to US$18.5 billion in 2012 [5]. Among 246,000 deaths in 2012 attributable to DM, about 55% and 28% of them had renal failure and cerebrovascular disease recorded as the primary causes of death, suggesting that high direct medical costs at mortality year may result from healthcare due to diabetes-related complications.

With prevailing number of co-existing morbidities or complications over the survival years, thereby leading to morbidity compression and drastic rise in healthcare resource use [6], the direct medical costs in the year of death was thought to be greater than those costs in the survival years. The time-to-death variable plays an important role in cost models for chronic diseases [7]. Although access to population-based database on healthcare utilization enables us to examine direct medical costs and their determinants, there have been no published studies that report direct medical costs in the year of death and compare them with costs in the survival years.

This study aimed to report the health resource utilization and estimate the direct medical costs among patients with DM in the year of mortality and the year before mortality. We examined the influence of the primary causes of death and the presence of diabetes-related complications on the direct medical costs, allowing for better projections of medical expenditures attributable to DM patients.

Materials and Methods

Study design and patient sampling

The population-based, retrospective cohort data, of those patients who had visited primary care general outpatient-clinics in Hong Kong Hospital Authority between August 1, 2008 and December 31, 2013, were extracted from Hospital Authority administrative database. Inclusion criteria of patients were 1) aged 18 and over; and 2) documented diagnosis of DM

(defined by the ICPC-2 codes T89/T90) on or before January 1, 2009. A cohort of 161,469 DM patients was selected based on aforementioned inclusion criteria. To assess the cost of mortality year and the year before mortality, only patients who died between Jan 1, 2010 and December 31, 2013 were included. A total of 10,649 DM patients dying between January 1, 2010 and December 31, 2013 were included in final data analysis of the mortality year cost estimation (Supplemental Figure 1). While the data inclusion period started from August 2008, patients who died between January 1, 2010 and 1 August 2010 were not utilized for the data analysis of the year before mortality cost estimation.

The International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) diagnosis codes were used to identify the primary cause of death, whereas the diabetes-related complications were identified by the International Statistical Classification of Diseases and Related Health Problems, 9th Revision, Clinical Modification (ICD-9-CM) and the International Classification of Primary Care, Version 2 (ICPC-2) codes as listed in Supplementary table 1 and Supplementary table 2.

Estimation of annual direct medical costs

This cost analysis adopted the same approach in a previous study [8]. Frequency of healthcare service utilization within Hospital Authority of each patient at the mortality year and the years before mortality were retrieved from the Hospital Authority administrative database. Cost items included general outpatient visits, specialist outpatient visits, emergency visits, and length of hospital stay at general ward, intensive care unit, and high dependency unit. The unit cost of each type of healthcare service was based on the price list for non-

eligible persons, published in 2013 Government Gazette and Hospital Authority Ordinance [9]. Annual direct medical costs were calculated for each patient as follows: annual direct medical costs = Σ number of unit of each healthcare service item x unit cost of respective healthcare service item.

Patient covariates

The covariates of the DM patients included gender, group of death age, ethnicity, type of diabetes, the presence of co-morbidities, the presence of diabetes-related complications, and the primary cause of death.

Death age was categorized into four groups: <65 years, 65-74 years, 75-84 years and ≥85 years. The ethnicity was divided into "Chinese" and "non-Chinese". Type of diabetes was identified by ICPC-2 codes "T89" for insulin dependent diabetes (Type I diabetes) and "T90" for non-insulin dependent diabetes (Type II diabetes). The level of co-morbidities was measured by the Charlson Comorbidity Index (CCI) [10]. The Charlson comorbidities for DM with and without chronic complications were excluded from the CCI calculation to avoid double-counting. Existence of each co-morbidity was scored and a final score was calculated by summing all the points. The CCI was categorized into four groups: 0, 1, 2 and ≥3.

Association between annual direct medical cost and the presences of nine diabetic complications (acute myocardial infarction, other ischemic heart disease, congestive heart failure, stroke, peripheral vascular disease, diabetic retinopathy, diabetic nephropathy, end-

stage renal disease, and diabetic foot ulcer) were tested. Other diabetes-related complications (amputation, lower limb ulcer, blindness, diabetic neuropathy and sight-threatening diabetic retinopathy) with low observation counts (<2%) were not controlled for regression analysis.

Because of the limited number of patients in some groups for primary causes of death, a total of seven groups including infectious and parasitic diseases, neoplasms, diseases of the circulatory system, diseases of the respiratory system, diseases of the digestive system, diseases of the genitourinary system, and others were divided.

Statistical analysis

Annual direct medical costs, their 95% confidence intervals and the proportion of the cost of hospitalization of patients with DM at 48-60 months before mortality, 36-48 months before mortality, 24-36 months before mortality, 12-24 months before mortality, and the mortality year were calculated.

Furthermore, healthcare resource use and annual direct medical costs at the year of mortality and the year before mortality (12-24 months before mortality) were analysed by the covariates, which are gender, age group, the presence of co-morbidities, the presence of diabetic complications (heart disease, stroke, diabetic nephropathy, or diabetic retinopathy), and primary cause of death.

Generalized linear models with an identity-link function and log-link function with gamma distribution were used to explore the associations of the annual direct medical costs. Both the

log-link function and identify-link function in the generalized linear model were used for estimations of direct medical costs, in line with previous costing study [8]. Coefficients, multipliers (exponential value of coefficient) and their corresponding 95% confidence intervals for each covariate were reported. In comparing the goodness-of-fit of generalized linear models with an identify-link and log-function, the mean absolute error (MAE) and the root-mean-square error (RMSE) of the each model were be calculated. A smaller MAE and RMSE indicate a better model fit.

All statistical analyses were performed using STATA version 13.0 (StataCorp LP, College Station, TX, USA). All significance tests were two-tailed and P values < 0.05 were taken to indicate statistical significance.

Results

Patient characteristics

A total of 10,649 patients with documented diagnosis of DM at least one year before mortality were identified. The mean death age of the patients was 79.4 (with S.D. 10.6) and the distribution of the gender was nearly fifty-fifty (with male 49.36% and female 50.64%). 96.69% of the patients were Chinese and nearly all of the patients were non-insulin dependent diabetes (99.88%). Nearly two-third of the patients (62.19%) suffered from at least one of diabetic complications and the most common primary cause of death was Neoplasms (28.41%) (Supplementary table 3).

Costs in the mortality year and years before mortality

Annual direct medical costs, their 95% confidence intervals and the proportion of the cost of hospitalization of patients with DM in the mortality year and the years before mortality are presented in Figure 1. The closer the mortality year, the higher the annual direct medical costs and the proportions of the hospitalization cost over the annual direct medical cost were. The average medical cost in the year of mortality doubled from US$11,807.0 (73.7% for hospitalization cost) to US$22,987.5 (78.4% for hospitalization cost) in the year of mortality (Figure 1). Given the costs in 48-60 months before mortality, 36-48 months before mortality and 24-36 months before mortality are roughly similar while the costs in 12-24 months before mortality and the mortality year are much higher, the detailed results are only presented for the year before mortality (12-24 months before death) and the year of mortality.

Utilization of healthcare services

Frequencies of healthcare services attendance for each patient in the year before mortality and in the year of mortality were measured, respectively. The mean number of general outpatient clinic and specialist outpatient clinic visits in the year before mortality were greater than that of in the mortality year (5.0 times and 4.7 times vs 2.4 times and 3.9 times, respectively). However, mean number of nights of hospital stay at general ward in the mortality year was much greater than that in the year before mortality (27.7 nights vs 13.8 nights). Mean number of nights of hospital stay at intensive care unit and critical care unit in the mortality year were also greater than that in the year before mortality (0.4 nights and 0.1 nights vs 0.1 nights and 0 nights respectively) (Table 1). Since unit costs of hospital stay at general ward, intensive care unit and high dependency unit were at least four times of that of

general outpatient clinic and specialist outpatient clinic visit [9], the annual direct medical cost in the mortality year was higher than that in the year before mortality.

Comparison of the annual direct medical cost by time and existence of covariates

Table 2 shows the influence of the patients' covariates on the annual direct medical cost.

The female patients had a similar medical cost compared with the male patients in the year before mortality (US$11,980.6 vs US$11,628.8; p=0.440) and in the mortality year (US$22,825.4 vs US$23,153.8; p=0.543). The medical costs were almost double in the mortality year compared to the year before for both male and female (Table 2).

Analysed by age group, the group with the highest cost in the year before mortality was patients aged 85 or above (US$12,172.1) and the group with the highest cost for the mortality year patients aged 65-74 (US$24,459.9). The medical costs in all age groups were nearly double in the mortality year (1.94 times for aged below 65; 2.27 times for aged 65-74; 1.97 times for aged 75-84; 1.76 times for aged 85 or above) (Table 2).

By ethnicity, higher medical costs were recorded for Chinese patients in both year before mortality and in the mortality year (US$11,992.6 and US$23,216.6 for Chinese patients; US$6,394.0 and US$16,304.5 for non-Chinese patients, respectively). The costs in the mortality year in two groups were doubled compared to the costs in the year before mortality (1.94 times for Chinese; 2.54 times for non-Chinese) (Table 2).

For type of diabetes, patients with non-insulin dependent diabetes had significantly higher medical costs in the mortality year than the year before mortality (US$22,988.8 vs US$11,819.2; $p<0.001$), but insignificantly higher costs for patients with insulin dependent diabetes in both years (US$23,789 vs US$14,525.9; $p=0.1236$) (Table 2).

Analysed by the levels of co-morbidities, the higher the CCI score, the higher medical cost in the mortality year. The medical cost in the mortality year was increased 1.5 times compared to the year before mortality, regardless of the CCI scores (1.96 times for score 0; 1.61 times for score 1; 2.17 times for score 2; 1.84 times for score 3 or above) (Table 2).

Patients with at least one of the diabetes-related complications had higher costs than those without both in the year of mortality (US$24,585.6 vs US$20,358.5) and the year before mortality (US$13,509.0 vs US$9,007.1). The medical costs in the mortality year were two times of the costs in the year before mortality (1.82 times for patients with any diabetic complications; 2.26 times for patients without diabetic complication) (Table 2).

The most costly primary cause of death in the year before mortality was diseases of the genitourinary system (US$16,696.4), whereas the most costly primary cause of death for the mortality year was certain infectious and parasitic diseases (US$32,989.0). The ratio of the costs in the mortality year to the costs in the year before mortality varied from 1.43 to 3.35 times (Table 2).

Association between the annual direct medical costs and patients' covariates

Table 3 and Table 4 show the estimated coefficients of the effect of covariates on direct medical costs of patients with DM using the generalized models with identify link and log link, respectively.

a) Fitting a generalized linear model using the identity link with gamma distribution

From table 3, the base case annual average medical cost was US$6,005.7 in the year before mortality (85-year-old or elder male patient without any diabetic complications died with other primary cause of death). Female DM patients were expected to cost US$531.5 more than male DM patients. The patients aged below 65 paid US$1,990.5 more while the patients aged 65-74 paid US$340.4 less compared to those aged 85 or above. Moreover, nearly all the presence of diabetes-related complications increased the direct medical cost. DM patients with diabetic foot were expected to cost US$9,055.0 more than the patients who do not. Patients with diabetic retinopathy would cost US$577.5 less than the patients who do not but the difference was not statistically significant. The patients that died due to diseases of the genitourinary system and diseases of the respiratory system would cost US$3,574.9 and US$5,097.1 more than patients with other primary cause of death respectively.

In the year of mortality, the base case annual average inpatient cost was US$8,283.1. The average medical cost of female patients was US$767.1 higher than that of male patients. DM patients aged 65-74 and aged 75-84 paid US$1,329.1 and US$1,143.2 more than the patients aged 85 or above respectively. The presence of any of the diabetes-related complications increased the direct medical cost (ranging between an increase of US$512.3 for the presence of acute myocardial infarction and an increase of US$13,479.0 for the presence of diabetic

foot). The patients that died due to certain infectious and parasitic diseases and neoplasms would cost US$18,218.2 and US$15,792.1 more than patients with other primary causes of death respectively.

b) Fitting a generalized linear model using the log link with gamma distribution

Table 4 presents the base case annual average medical cost was US$6,172.2 in the year before mortality (85-year-old or elder male patient without any diabetic complications died with other primary cause of death). Female DM patients had a higher cost than male patients with a multiplier 1.037. Compared with the patients aged 85 or above, all the patients in other age groups had higher costs (with multipliers 1.357, 1.060 and 1.060 for patients aged 65 below, 65-74 and 75-84 respectively). The most costly diabetic complication and the most costly primary cause of death were diabetic foot ulcer (with a multiplier 1.766) and diseases of the respiratory system (with multiplier 1.547), respectively.

At the year of mortality, the base case annual average medical cost was US$9,891.8. The cost of the female patients was higher than that of male patients (with a multiplier 1.020). Patients below 85 years old would cost more than the patients aged 85 or above (with multipliers 1.131, 1.164 and 1.099 for patients aged 65 or below, 65-74 and 75-84 respectively). All the presence of diabetic complications would have a positive relationship on the medical cost, where the most costly diabetic complication was diabetic foot ulcer (with a multiplier 1.660). The most costly primary cause of death is certain infectious and parasitic diseases (with a multiplier 2.369).

c) Goodness-of-fit of models

Both the MAE and RMSE of the generalized linear model using the identity link with gamma distribution are smaller than the generalized linear model using the log link with gamma distribution (The year before mortality – MAE: 13,171.4 vs 13,266.8, RMSE: 222.9 vs 260.1; The mortality year – MAE: 17,737.8 vs 17,877.9, RMSE: 223.8 vs 261.4). Therefore, the generalized linear model using the identity link with gamma distribution was preferred over that using the log-link with gamma distribution.

Discussions

To quantify burden of DM to healthcare provider, healthcare resource use and annual direct medical costs were estimated using routine administrative database in many developed countries such as US [3, 11], United Kingdom [4, 12], Denmark [13], Australia [14], Sweden [15], and Singapore [16]. Nevertheless, aforementioned studies primarily assessed the impact of diabetes-related complications on healthcare costs while the present study utilized the patient-level data within hospital administrative database, and reported the robust estimates of annual direct medical costs at mortality year and years before the mortality. Importantly, annual direct medical costs in the mortality year (US$22,987.5) were almost double of those in the year before mortality (US$11,807.0), echoing to the notion "the high cost of dying" [17] that the annual healthcare costs of those DM patients in their last year of life were greater than those of DM patients who survived. High costs in the mortality year were possibly due to the occurrence of diabetes-related complications. Evidence from diabetes models (e.g. UKPDS 82[18]) demonstrated that DM patients had higher probability of death in the first year of complication event. Healthcare costs of patients having complication event

(s) occurred in the first year were significantly greater than those of those without complication event occurred. Our costing analysis provided evidence on incorporating additional amounts into direct medical cost estimation in the mortality year, especially when a complication event occurs. Furthermore, the proportion of hospitalization cost increased with the decrease in life expectancy from 73.7% in the year before mortality to 78.4% in the year of mortality, indicating the switch of healthcare service utilization from primary care setting to hospital-based setting for those who had shorter life expectancy.

The present study investigated the association between annual direct medical cost and the patient characteristics. Based on regression results, substantial impacts of co-morbidities, diabetes-related complications and primary cause of death on annual direct medical costs were observed. Patients with presence of the diabetic ulcer foot had the highest incremental annual direct medical costs, with US$13,479.0 more than those who did not (in generalized linear model with identity link of gamma distribution) or 1.660 times more than those who did not (in generalized linear model with log link of gamma distribution). The costs associated with diabetic ulcer foot in the event and subsequent years were not derived in most of the costing analyses[3, 4, 12, 13, 16], whereas diabetic ulcer foot was part of the broad category such as peripheral circulatory complications[15] in one Swedish study. However, as demonstrated in current study, the diabetic foot ulcer was one of the most expensive diabetes-related complications, in line with previous retrospective cohort studies[8, 11, 14]. Besides, among types of primary death cause, DM patients who died because of certain infectious and parasitic diseases had the highest incremental annual direct medical costs in the mortality year (US$18,218.2). Of those, more than 80% patients (83.5%) died due to that category were classified as sepsis.

In light of healthcare resource use in public sector, DM patients in their mortality year had less utilization of outpatient visits and allied health professional visits than those in the year before mortality. Reciprocally, patients in the mortality year utilized more emergency visits and hospitalization in term of general wards and intensive care unit than those in the year before mortality. Towards the mortality year, DM patients relied on secondary care delivered by hospitals rather than primary care mainly delivered by outpatient clinics. In addition to age and composition of multi-morbidity, the time-to-death was determinants of healthcare utilization and direct medical costs in DM patients, supported by previous study [7]. Hence, healthcare utilization pattern presented in current study would help policy-makers to advocate the healthcare service planning and allocation according to life expectancy and time-to-death information of DM patients.

Another implication of our findings was significant increase in the healthcare costs in mortality year in comparison to those in the year before mortality. Differences in accrued health costs between the two years provided a strong argument for the refinement of the cost structure in costing and cost-effectiveness analysis of health interventions for DM. Conventionally, cost-effectiveness modelling assumed that the Hong Kong healthcare costs in DM patients were the same over the time horizon, and do not account for the differences in healthcare costs between the mortality and non-mortality years [19-22]. Therefore, evidence from this study supports the adjustment on direct medical costs in the mortality year and year before mortality in future cost-effectiveness analyses.

Limitations

Several limitations and assumptions must be acknowledged. Firstly, unit costs of healthcare service item were obtained from published documents at Hong Kong Government Gazette, whereby no temporal adjustment or inflation was taken into consideration. Each patient was assumed to have the same unit cost of healthcare service item, as a packaged price inclusive of consultation, investigations, prescribed medications, radiology, and other examinations during the clinic visit or hospital stay. Actual resource use for each healthcare service item, in term of human resource, equipment, consumables, and overhead, were assumed to be the same. As such, the annual direct medical costs in the death year and years before death might be biased, and valid for Hong Kong DM patients and for the time period when unit costs of healthcare service are still current. Secondly, current analysis estimated public healthcare utilization and corresponding annual direct medical cost attributable to DM patients, adopting government-based public healthcare provider perspective. Resource use in private sector and indirect costs based upon productivity losses were not taken into consideration. Finally, the cause of the healthcare resource use is an important issue for consideration. Especially for elderly DM patients, a proportion of healthcare resource use and costs might be unrelated to DM or diabetes-related complications However, our retrospective cohort data are not possible to differentiate the cause of the healthcare resources uses, and not possible to determine whether the healthcare resources uses are due to primary cause of death or diabetic complications.

Conclusions

The annual direct medical costs of DM patients in the mortality year were almost two times greater than those in the year before mortality. Healthcare costs in both the mortality year and the year before mortality were influenced by the presence of diabetes-related complications

and primary cause of death. This analysis provides new evidence on incorporating an additional direct medical cost in the mortality year, and refining the structure of total cost estimates for use in costing and cost-effectiveness analyses of health interventions for DM.

Acknowledgements

The authors wish to acknowledge the contributions of the RAMP-DM programme teams (including Ms Dorothy Lam and Mr Jackey Chan) and Statistics and Workforce Planning Department (including Ms Eva Tsui, Mr Peggo Lam and Mr Choi-Fan Yiu) at the Hong Kong Hospital Authority. Also, we would like to thank all Hospital Authority cluster coordinators and clinical staff in the Chronic Disease Management Programmes for working with our team in this study. Last but not least, the authors would like to express gratitude to Dr Claudia Geue, the University of Glasgow for helpful comments.

Funding sources

This study was funded by the Food and Health Bureau, the Government of the Hong Kong Special Administrative Region (EPC-HKU-2) and the Small Project Fund of the University of Hong Kong (201309176076).

Conflict of interest

Authors did not have potential conflict of interest.

References

[1] Ogurtsova K, da Rocha Fernandes JD, Huang Y, *et al.* IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017; **128**: 40-50

[2] da Rocha Fernandes J, Ogurtsova K, Linnenkamp U, *et al.* IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. Diabetes Res Clin Pract. 2016; **117**: 48-54

[3] Zhuo X, Zhang P, Barker L, Albright A, Thompson TJ, Gregg E. The lifetime cost of diabetes and its implications for diabetes prevention. Diabetes Care. 2014; **37**: 2557-2564

[4] Alva ML, Gray A, Mihaylova B, Leal J, Holman RR. The impact of diabetes-related complications on healthcare costs: new results from the UKPDS (UKPDS 84). Diabetic Medicine. 2015; **32**: 459-466

[5] American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013; **36**: 1033-1046

[6] Payne G, Laporte A, Deber R, Coyte PC. Counting Backward to Health Care's Future: Using Time-to-Death Modeling to Identify Changes in End-of-Life Morbidity and the Impact of Aging on Health Care Expenditures. Milbank Quarterly. 2007; **85**: 213-257

[7] de Meijer C, Koopmanschap M, d' Uva TB, van Doorslaer E. Determinants of long-term care spending: Age, time to death or disability? Journal of Health Economics. 2011; **30**: 425-438

[8] Jiao F, Wong CKH, Tang SCW, *et al.* Annual direct medical costs associated with diabetes-related complications in the event year and in subsequent years in Hong Kong. Diabetic Medicine. 2017; **34**: 1276-1283

[9] HKSAR. Hospital Authority Ordinance (Chapter 113) Revisions To List of Charges. 2013

[10] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of Chronic Diseases. 1987; **40**: 373-383

[11] Ramsey SD, Newton K, Blough D, McCulloch DK, Sandhu N, Wagner EH. Patient-level estimates of the cost of complications in diabetes in a managed-care population. Pharmacoeconomics. 1999; **16**: 285-295

[12] Clarke P, Gray A, Legood R, Briggs A, Holman R. The impact of diabetes-related complications on healthcare costs: results from the United Kingdom Prospective Diabetes Study (UKPDS Study No. 65). Diabetic Medicine. 2003; **20**: 442-450

[13] Sortsø C, Green A, Jensen PB, Emneus M. Societal costs of diabetes mellitus in Denmark. Diabetic Medicine. 2016; **33**: 877-885

[14] Clarke P, Leal J, Kelman C, Smith M, Colagiuri S. Estimating the cost of complications of diabetes in Australia using administrative health-care data. Value Health. 2008; **11**: 199-206

[15] Gerdtham UG, Clarke P, Hayes A, Gudbjornsdottir S. Estimating the Cost of Diabetes Mellitus-Related Events from Inpatient Admissions in Sweden Using Administrative Hospitalization Data. Pharmacoeconomics. 2009; **27**: 81-90

[16] Shuyu Ng C, Toh MP, Ko Y, Yu-Chia Lee J. Direct medical cost of type 2 diabetes in singapore. PLoS One. 2015; **10**: e0122795

[17] Scitovsky AA. "The high cost of dying": what do the data show? 1984. Milbank Q. 2005; **83**: 825-841

[18] Hayes AJ, Leal J, Gray AM, Holman RR, Clarke PM. UKPDS Outcomes Model 2: a new version of a model to simulate lifetime health outcomes of patients with type 2 diabetes mellitus using data from the 30 year United Kingdom Prospective Diabetes Study: UKPDS 82. Diabetologia. 2013; **56**: 1925-1933

[19] Chan CK, Gangwani RA, McGhee SM, Lian J, Wong DS. Cost-Effectiveness of Screening for Intermediate Age-Related Macular Degeneration during Diabetic Retinopathy Screening. Ophthalmology. 2015; **122**: 2278-2285

[20] Lian J, McGhee SM, Gangwani RA, *et al.* The impact of a co-payment on the cost-effectiveness of screening for diabetic retinopathy. J Public Health (Oxf). 2016; **38**: 782-792

[21] Lian J, McGhee SM, So C, *et al.* Five-year cost-effectiveness of the Patient Empowerment Programme (PEP) for type 2 diabetes mellitus in primary care. Diabetes Obes Metab. 2017; **19**: 1312-1316

[22] Jiao F, Fung CSC, Wan EYF, *et al.* Five-Year Cost-effectiveness of the Multidisciplinary Risk Assessment and Management Programme–Diabetes Mellitus (RAMP-DM). Diabetes Care. 2018; **41**: 250-257

Figure Legend

Figure 1: Average annual direct medical costs of patients with diabetes mellitus and proportion of the cost of hospitalization at 48-60 months before mortality, 36-48 months before mortality, 24-36 months before mortality, 12-24 months before mortality, and the mortality year. Error bars indicated their 95% confidence intervals.

Table 1: Annual healthcare service utilization in the mortality year and the year before mortality

Healthcare service (# of visits)	The year before mortality					The mortality year				
	Median	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**
General outpatient clinic	5.0	0.0	62.0	5.0	3.2	2.0	0.0	38.0	2.4	2.4
Specialist outpatient clinic	3.0	0.0	63.0	4.7	6.0	2.0	0.0	58.0	3.9	5.1
Accident and emergency	1.0	0.0	50.0	1.5	2.3	2.0	0.0	82.0	2.2	2.2
Allied health professionals										
Dietetics	0.0	0.0	4.0	0.0	0.2	0.0	0.0	3.0	0.0	0.1
Diabetic Retinopathy screening	0.0	0.0	4.0	0.2	0.4	0.0	0.0	5.0	0.1	0.3
Physiotherapy	0.0	0.0	11.0	0.0	0.1	0.0	0.0	2.0	0.0	0.0
Podiatry	0.0	0.0	5.0	0.0	0.1	0.0	0.0	3.0	0.0	0.1
Hospitalization (night)										
General ward	1.0	0.0	366.0	13.8	29.7	17.0	0.0	351.0	27.7	34.3
Intensive care unit	0.0	0.0	49.0	0.1	1.3	0.0	0.0	103.0	0.4	2.6
Critical care unit	0.0	0.0	34.0	0.0	0.6	0.0	0.0	43.0	0.1	0.9
High dependency unit	0.0	0.0	40.0	0.0	0.5	0.0	0.0	43.0	0.0	0.6

Table 2: Comparison of the direct medical costs between the existence of the covariates in the year before mortality and in the mortality year

	The year before mortality				The mortality year			
	N	**Mean** (US$)	**S.D.**	**95% C.I.**	**N**	**Mean** (US$)	**S.D.**	**95% C.I.**
Gender								
Male	5256	11628.8	22939.7	[11,008.5, 12,249.1]	5256	23153.8	28248.8	[22,389.9, 23,917.7]
Female	5393	11980.6	24081.4	[11,337.8, 12,623.5]	5393	22825.4	27521.7	[22,090.7, 23,560.1]
Age								
Below 65	1157	12030.2	26746.7	[10,487.4, 13,572.9]	1157	23297.3	32117.6	[21,444.7, 25,149.9]
65-74	1936	10770.5	22773.9	[9,755.5, 11,785.6]	1936	24459.9	29667.5	[23,137.6, 25,782.3]
75-84	4122	11926.9	24745.2	[11,171.3, 12,682.6]	4122	23498.9	28428.0	[22,630.8, 24,367.0]
85 or above	3434	12172.1	21152.0	[11,464.4, 12,879.8]	3434	21439.0	24366.7	[20,623.8, 22,254.3]
Ethnicity								
Chinese	10296	11992.6	23474.2	[11,539.1, 12,446.0]	10296	23216.6	27963.6	[22,676.4, 23,756.8]
Non-Chinese	353	6394.0	24362.0	[3,843.8, 8,944.2]	353	16304.5	24500.2	[13,739.9, 18,869.1]
Type of Diabetes†								
Insulin dependent	53	14525.9	34323.5	[5,065.2, 23,986.6]	53	23789.1	31351.4	[15,147.6, 32,430.6]
Non-insulin dependent	10636	11819.2	23535.9	[11,371.8, 12,266.5]	10636	22988.8	27888.2	[22,458.7, 23,518.9]
Charlson Comorbidity Index ‡								
0	3967	9324.7	22885.6	[8,612.3, 10,037.0]	3967	18238.2	28830.5	[17,340.7, 19,135.6]
1	1494	13982.9	27710.7	[12,576.6, 15,389.2]	1494	22559.4	27756.0	[21,150.8, 23,968.0]
2	3496	12234.6	21648.6	[11,516.7, 12,952.4]	3496	26494.4	27031.6	[25,598.0, 27,390.8]
3 or above	1692	14822.1	24115.3	[13,672.3, 15,972.0]	1692	27254.5	25663.9	[26,030.8, 28,478.2]
Diabetes-related complications								
Yes	6623	13509.0	25042.8	[12,905.7, 14,112.2]	6623	24585.6	29507.2	[23,874.8, 25,296.4]
No	4026	9007.1	20484.0	[8,374.2, 9,640.0]	4026	20358.5	24759.9	[19,593.4, 21,123.5]
Primary cause of death								
Certain infectious and parasitic diseases	334	9842.4	18227.8	[7,880.4, 11,804.3]	334	32989.0	37641.5	[28,937.5, 37,040.6]
Neoplasms	3025	11426.7	18764.1	[10,757.8, 12,095.6]	3025	27416.1	24781.2	[26,532.6, 28,299.5]
Diseases of the circulatory system	1966	8372.7	18911.2	[7,536.2, 9,209.2]	1966	15402.8	23707.1	[14,354.2, 16,451.4]
Diseases of the respiratory system	2835	15458.6	29209.1	[14,382.9, 16,534.2]	2835	27351.1	31036.2	[26,208.1, 28,494.0]
Diseases of the digestive system	333	10811.5	25426.0	[8,070.6, 13,552.4]	333	22106.9	29134.6	[18,966.2, 25,247.5]
Diseases of the genitourinary system	492	16696.4	30462.5	[13,998.0, 19,394.8]	492	26549.2	27586.1	[24,105.6, 28,992.7]
Others (including those who were incoded)	1664	9482.4	22507.9	[8,400.2, 10,564.7]	1664	13579.1	25076.1	[12,373.3, 14,784.8]

† Patients can be both insulin dependent and non-insulin dependent

‡ The Charlson comorbidities for DM with and without chronic complications were excluded from the CCI calculation to avoid double-counting.

Table 3: Effects of gender, age, diabetes-related complications, primary cause of death on annual direct medical costs (generalized linear model with identity link of gamma distribution)

	Total cost before the year of mortality		**Total cost at the year of mortality**	
	Coefficient (US$)	95% CI	Coefficient (US$)	95% CI
Independent variables				
Constant	6,005.7	[4,958.0 , 7,053.4]	8,283.1	[7,222.1 , 9,344.2]
Female (vs male)	531.5	[-164.1 , 1,227.1]	767.1	[-123.3 , 1,657.6]
Age (vs 85 or above)				
Below 65	1,990.5	[553.6 , 3,427.5]	-170.8	[-1,571.9 , 1,230.2]
65-74	-340.4	[-1,358.9 , 678.1]	1,329.1	[-41.8 , 2,700.1]
75-84	-208.4	[-1,037.7 , 620.9]	1,143.2	[123.0 , 2,163.3]
Presence of acute myocardial infarction	512.6	[-508.8 , 1,534.0]	512.3	[-897.7 , 1,922.4]
Presence of other ischemic heart disease	2,693.1	[1,460.7 , 3,925.4]	3,548.3	[2,095.7 , 5,000.8]
Presence of congestive heart failure	4,927.4	[3,401.4 , 6,453.4]	5,874.0	[4,299.5 , 7,448.5]
Presence of stroke	3,208.0	[2,268.1 , 4,147.9]	4,076.7	[3,029.8 , 5,123.6]
Presence of peripheral vascular disease	2,555.5	[-1,447.4 , 6,558.4]	2,984.3	[-1,021.9 , 6,990.4]
Presence of diabetic retinopathy	-577.5	[-1,843.1 , 688.1]	1,262.7	[-612.2 , 3,137.6]
Presence of diabetic nephropathy	4,661.0	[2,723.5 , 6,598.5]	7,834.9	[5,819.9 , 9,849.8]
Presence of end-stage renal disease	2,754.2	[1,201.0 , 4,307.4]	6,921.4	[4,962.2 , 8,880.6]
Presence of diabetic foot ulcer	9,055.0	[3,837.8 , 14,272.2]	13,479.0	[7,736.3 , 19,221.7]
Primary cause of death (vs others)				
Certain infectious and parasitic diseases	124.6	[-1,936.6 , 2,185.7]	18,218.2	[13,598.3 , 22,838.0]
Neoplasms	3,326.4	[2,190.1 , 4,462.7]	15,792.1	[14,304.8 , 17,279.3]
Diseases of the circulatory system	-3,214.7	[-4,199.5 , -2,230.0]	-2,188.8	[-3,281.0 , -1,096.6]
Diseases of the respiratory system	5,097.1	[3,735.2 , 6,459.1]	12,852.5	[11,358.9 , 14,346.1]
Diseases of the digestive system	1,517.9	[-863.8 , 3,899.6]	9,287.2	[6,149.7 , 12,424.7]
Diseases of the genitourinary system	3,574.9	[574.6 , 6,575.1]	6,441.1	[3,382.7 , 9,499.5]

Baseline represents a 85-year-old or elder male patient without any diabetic complications died with other primary cause of death

Table 4: Effects of gender, age, diabetes-related complications, primary cause of death on annual direct medical costs (generalized linear model with log link of gamma distribution)

	Total cost before the year of mortality				**Total cost at the year of mortality**			
	Coefficient (US$)	95% CI	Multiplier	95% CI	Coefficient (US$)	95% CI	Multiplier	95% CI
Independent variables								
Constant	8.728	[8.596 , 8.860]	NA	NA	9.199	[9.117 , 9.282]	NA	NA
Female (vs male)	0.036	[-0.045 , 0.117]	1.037	[0.956 , 1.124]	0.020	[-0.031 , 0.071]	1.020	[0.970 , 1.073]
Age (vs 85 or above)								
Below 65	0.305	[0.159 , 0.451]	1.357	[1.173 , 1.570]	0.123	[0.033 , 0.213]	1.131	[1.033 , 1.238]
65-74	0.058	[-0.064 , 0.180]	1.060	[0.938 , 1.198]	0.152	[0.076 , 0.228]	1.164	[1.079 , 1.256]
75-84	0.058	[-0.038 , 0.154]	1.060	[0.963 , 1.167]	0.094	[0.034 , 0.154]	1.099	[1.035 , 1.167]
Presence of acute myocardial infarction	-0.026	[-0.168 , 0.116]	0.974	[0.845 , 1.123]	0.031	[-0.057 , 0.120]	1.032	[0.945 , 1.127]
Presence of other ischemic heart disease	0.258	[0.144 , 0.373]	1.295	[1.155 , 1.451]	0.179	[0.107 , 0.251]	1.196	[1.113 , 1.286]
Presence of congestive heart failure	0.434	[0.317 , 0.550]	1.543	[1.373 , 1.734]	0.245	[0.172 , 0.318]	1.277	[1.187 , 1.374]
Presence of stroke	0.346	[0.257 , 0.434]	1.413	[1.293 , 1.544]	0.161	[0.105 , 0.217]	1.174	[1.110 , 1.242]
Presence of peripheral vascular disease	0.216	[-0.062 , 0.495]	1.241	[0.940 , 1.640]	0.137	[-0.037 , 0.312]	1.147	[0.963 , 1.366]
Presence of diabetic retinopathy	-0.014	[-0.165 , 0.138]	0.987	[0.848 , 1.148]	0.091	[-0.003 , 0.185]	1.095	[0.997 , 1.203]
Presence of diabetic nephropathy	0.378	[0.252 , 0.504]	1.459	[1.286 , 1.655]	0.288	[0.210 , 0.367]	1.334	[1.234 , 1.443]
Presence of end-stage renal disease	0.212	[0.087 , 0.337]	1.236	[1.091 , 1.400]	0.241	[0.163 , 0.319]	1.272	[1.177 , 1.375]
Presence of diabetic foot ulcer	0.569	[0.307 , 0.830]	1.766	[1.359 , 2.294]	0.507	[0.342 , 0.671]	1.660	[1.408 , 1.957]
Primary cause of death (vs others)								
Certain infectious and parasitic diseases	-0.014	[-0.257 , 0.230]	0.986	[0.773 , 1.258]	0.863	[0.710 , 1.015]	2.369	[2.034 , 2.760]
Neoplasms	0.331	[0.204 , 0.458]	1.392	[1.226 , 1.580]	0.807	[0.727 , 0.886]	2.240	[2.069 , 2.426]
Diseases of the circulatory system	-0.367	[-0.511 , -0.223]	0.693	[0.600 , 0.800]	-0.031	[-0.120 , 0.059]	0.970	[0.887 , 1.060]

Diseases of the respiratory system	0.436	[0.310 , 0.562]	1.547	[1.363 , 1.754]	0.686	[0.607 , 0.765]	1.986	[1.835 , 2.149]
Diseases of the digestive system	0.201	[-0.045 , 0.446]	1.222	[0.956 , 1.563]	0.533	[0.380 , 0.686]	1.704	[1.462 , 1.986]
Diseases of the genitourinary system	0.293	[0.076 , 0.511]	1.341	[1.079 , 1.666]	0.446	[0.309 , 0.582]	1.561	[1.362 , 1.790]

Baseline cost before the year of mortality = US$6,172.2 (95% CI: US$5,409.7 to US$7,042.3); Baseline cost at the year of mortality = US$9,891.8 (95% CI: US$9,108.3 to US$10,742.7), which represents a 85-year-old or elder male patient without any diabetic complications died with other primary cause of death; NA, Not Applicable;

Figure 1: Average annual direct medical costs of patients with diabetes mellitus and proportion of the cost of hospitalization at 48-60 months before mortality, 36-48 months before mortality, 24-36 months before mortality, 12-24 months before mortality, and the mortality year. Error bars indicated their 95% confidence intervals.