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ESTIMATING THE COSTS OF MANAGING COMPLICATIONS OF TYPE 2 DIABETES MELLITUS IN MALAYSIA

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This study aimed to estimate current direct costs for managing type 2 diabetes mellitus (T2DM)-related complications including ischaemic heart diseases (IHD), myocardial infarction (MI), stroke, heart failure (HF), amputation, blindness, renal failure (RF) requiring haemodialysis (end-stage renal disease) and diabetic foot ulcer in the event year and subsequent year. Initially, diabetes-related complications are defined based on the Malaysian Clinical Practice Guidelines (CPGs) or published literatures while each resource unit was valued using local costing obtained from the public hospital or other sources. The interventions for the management of complications were supported by evidence in the Malaysian CPGs or local literature and confirmed by the physicians related to the field who are working at the public hospital. All costs were converted to the value of USD currency in the year 2016. On the whole, macrovascular diseases incurred the highest management cost with MI employing the highest management cost (USD4,528.37) in the event year, while the management of heart, failure disease incurs the highest management cost at USD524.79 for subsequent year management. End-stage renal disease was associated with the highest annual per-patient costs, with mean first year and subsequent year costs for haemodialysis estimated at USD9,905.37 and USD9,233.89. In studying the costs of managing of diabetes-related complications, these data are vital economic evaluation for diabetes interventions, particularly in managing complications to macrovascular and microvascular functions, as it contributes significantly to the economic burden in Malaysia's public healthcare; hence significantly affecting the proportion of the overall healthcare costs.

***Keywords*:** Type 2 diabetes mellitus, Diabetes-related complications, Cost, Macrovascular, Microvascular

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INTRODUCTION

Over the years, the prevalence of type 2 diabetes mellitus (T2DM) has been on the rise in Malaysia (Hussein *et al*. 2015). The prevalence of diabetes in Malaysia was 15.2% in 2011 (Mustapha and Azmi 2013), and it has increased by 2.3% over four years (Tee and Yap 2017). This trend poses significant burden to healthcare payers because it requires billions of dollars in care annually not only to manage the disease itself, but also to treat its macrovascular and microvascular complications. In Malaysia, RM1.4 billion (approximately USD0.33 billion [USD1:RM4.28]) is estimated to manage T2DM and its related complications in the public healthcare setting (Mustapha *et al*. 2017). This expense excludes the cost of managing complications in undiagnosed T2DM patients. The prevalence of undiagnosed T2DM patients is estimated to be at least 9.2% (Aris *et al*. 2015). It is believed that the risk factors for microvascular and macrovascular complications are markedly elevated for this group of patients and that diabetes complications are developing in this group (Harris and Eastman 2000). It is suspected that the total expenditure of managing diabetes complications is huge and possibly accounts for more than 50% of the total healthcare budget (Mustapha *et al*. 2017).

At health clinics serviced by family medicine specialists, the annual direct outpatient cost of diabetes per patient is RM1,281 (approximately USD299) (Mustapha *et al*. 2017). For public hospitals with or without specialists, the cost per admission in treating diabetes is nearly RM2,000 (approximately USD467) (Sharifa Ezat *et al.* 2009). Although many local studies have explored the cost of T2DM (Ibrahim, Aljunid and Ismail 2010; Mustapha *et al*. 2017; Rohana *et al.* 2007; Sharifa Ezat *et al*. 2009), none have explored the total direct medical costs of diabetes complications. Exploring the expenditure costs of managing these complications is vital because decision makers, like the Ministry of Health Malaysia must realise the severity of diabetes complications. Furthermore, exploring these costs, which are important inputs for cost-effectiveness analysis, is necessary to discern the numerous T2DM medications that have been launched into the market in the last 10 years. These medications claim to improve glycemic control and prevent acute life-threatening metabolic complications while reducing risks of morbidity and mortality associated with the development of long-term diabetes complications, yet there is scarce financially impactful information about this. The objective of study was to estimate the direct medical costs of complications management for T2DM patients in public healthcare facilities from onset to their subsequent years. The complications included in the study are ischaemic heart disease (IHD), myocardial infarction (MI), stroke, heart failure (HF), cardiovascular death, amputation, blindness, renal failure (RF) and foot ulcers.

METHODS

A bottom-up approach was used to estimate the costs of managing diabetes complications. Some diabetes complications (MI, stroke, HF and IHD) can occur suddenly. Whereas amputation, blindness, RF requiring haemodialysis and foot ulcer are not sudden-onset events. Therefore, the cost estimation pathways were slightly different (Table 1 and Table 2). To identify the costs of T2DM management, the T2DM medical conditions and complications were defined as either a directly retrieved clinical treatment pathway from the Malaysian Clinical Practice Guidelines (CPGs) or as a projected treatment pathway from literature and expert opinion. The frequency use of resources and interventions was then estimated based on the condition of the event and a micro-costing method was used to obtain the cost. Lastly, the estimation was confirmed with specialists who work in public healthcare services to avoid overcounting the use of resources and interventions.

Table 1: Costing pathway for the total cost in the event year of MI, stroke, HF and IH disease based on activity-based costing approach.

Event Year									
Unit of analysis	**Emergency management**		**Admission to hospital (in ward)**				**Follow up at outpatient clinic**		
Cost component	Diagnostic test	Medication	Hospitalisation	Procedure	Diagnostic test	Medication	Clinic visits	Diagnostic test	Medications
Unit resource	Number of diagnostic tests (Qd_e)	Number of unit (tablet, vial, ampoule, bottle) (Qm_e)	Days of hospital stay (Qh^w)	Number of procedures (Qp_w)	Number of diagnostic tests (Qd_w)	Number of unit (tablet, vial, ampoule, bottle) (Qm_w)	Number of visits (Qv_c)	Number of diagnostic tests (Qd_c)	Number of unit (tablet, vial, ampoule, bottle) (Qm_c)
Valuation of unit cost	Full patient pay tariff MOH ($\$d_e$)	Medicine price list from Procurement Unit ($\$m_e$)	MY-DRG® ($\$h_w$)	Full patient pay tariff MOH ($\$p_w$)	Full patient pay tariff MOH ($\$p_w$)	Medicine price list from Procurement Unit ($\$m_w$)	Full patient pay tariff MOH ($\$v_c$)	Full patient pay tariff MOH ($\$d_c$)	Medicine price list from Procurement Unit ($\$m_c$)
Cost calculation	$Qd_e \times \$d_e$	$Qm_e \times \$m_e$	$Qh_w \times \$h_w$	$Qp_w \times \$p_w$	$Qd_w \times \$d_w$	$Qm_w \times \$m_w$	$Qv_c \times \$v_c$	$Qd_c \times \$d_c$	$Qm_c \times \$m_c$
Total cost	Total cost of emergency management (TCEM) = $Qd_e \times \$d_e + Qm_e \times \$m_e$		Total cost of hospitalisation (TCH) = $Qh_w \times \$h_w + Qp_w \times \$p_w + Qd_w \times \$d_w + Qm_w \times \$m_w$				Total cost of outpatient (TCOP) = $Qv_c \times \$v_c + Qd_c \times \$d_c + Qm_c \times \$m_c$		
Total annual cost	Total annual cost = TCEM+ TCH+ TCOP								
Subsequent Event Year									
Unit of analysis	Follow up at outpatient clinic								
Cost component	Clinic visits			Diagnostic test			Medications		
Unit resource	Number of visits (Qv_c)			Number of diagnostic tests (Qd_c)			Number of unit (tablet, vial, ampoule, bottle) (Qm_c)		
Valuation of unit cost	Full patient pay tariff MOH ($\$v_c$)			Full patient pay tariff MOH ($\$d_c$)			Medicine price list from Procurement Unit ($\$m_c$)		
Cost calculation	$Qv_c \times \$v_c$			$Qd_c \times \$d_c$			$Qm_c \times \$m_c$		

Table 2: Costing pathway for the total cost in the event year of amputation, blindness, RF requiring hemodialysis and foot ulcer based on activity-based costing approach.

Event Year							
Unit of analysis	**Admission to hospital (in ward)**				**Follow-up at outpatient clinic**		
Cost component	Hospitalisation	Procedure	Diagnostic test	Medication	Clinic visits	Diagnostic test	Medications
Unit resource	Days of hospital stay (Qh^w)	Number of procedures (Qp_w)	Number of diagnostic tests (Qd_w)	Number of unit (tablet, vial, ampoule, bottle) (Qm_w)	Number of visits (Qv_c)	Number of diagnostic tests (Qd_c)	Number of unit (tablet, vial, ampoule, bottle) (Qm_c)
Valuation of unit cost	DRG Malaysia ($\$h_w$)	Full patient pay tariff MOH ($\$p_w$)	Full patient pay tariff MOH ($\$p_w$)	Medicine price list from Procurement Unit ($\$m_w$)	Full patient pay tariff MOH ($\$v_c$)	Full patient pay tariff MOH ($\$d_c$)	Medicine price list from Procurement Unit ($\$m_c$)
Cost calculation	$Qh_w \times \$h_w$	$Qp_w \times \$p_w$	$Qd_w \times \$d_w$	$Qm_w \times \$m_w$	$Qv_c \times \$v_c$	$Qd_c \times \$d_c$	$Qm_c \times \$m_c$
Total cost	Total cost of hospitalisation (TCH) = $Qh_w \times \$h_w + Qp_w \times \$p_w + Qd_w \times \$d_w + Qm_w \times \$m_w$				Total cost of outpatient (TCOP) = $Qv_c \times \$v_c + Qd_c \times \$d_c + Qm_c \times \$m_c$		
Total annual cost	Total annual cost = TCH+ TCOP						
Unit of analysis	Follow up at outpatient clinic						
Cost component	Clinic visits		Diagnostic test		Medications		
Unit resource	Number of visits (Qv_c)		Number of diagnostic tests (Qd_c)		Number of unit (tablet, vial, ampoule, bottle) (Qm_c)		
Valuation of unit cost	Full patient pay tariff MOH ($\$v_c$)		Full patient pay tariff MOH ($\$d_c$)		Medicine price list from Procurement Unit ($\$m_c$)		
Cost calculation	$Qv_c \times \$v_c$		$Qd_c \times \$d_c$		$Qm_c \times \$m_c$		
Total cost	Total cost of outpatient (TCOP) = $Qv_c \times \$v_c + Qd_c \times \$d_c + Qm_c \times \$m_c$						

The cost estimation for managing diabetes complications started with defining the complications either from literature (American Heart Association 2016; Boyd 2018; National Health Service (NHS) United Kingdom 2016; Rodger 2012) or from the CPGs (Basri *et al*. 2012; Jeyamalar *et al.* 2014; Ministry of Health Malaysia 2018; Zambahari *et al*. 2014) to help the researchers determine the procedures and resources required for the complications. We assumed patients who were diagnosed with IHD were admitted to hospital or healthcare institute, but they did not fulfill the diagnosis criteria of MI. On the other hand, amputation refers to minor amputation involving the removal of toes or feet. It can be considered as the removal of lower limbs in T2DM patients. RF treatment is defined as complication that requires haemodialysis to remove waste, restore the balance of electrolytes in their blood, and eliminate extra fluids from their body. The estimation cost started from the operation to create the arteriovenous fistula. We also assumed that the condition of the foot ulcer is superficial and non-limb threatening.

Defining the complications was followed by identifying the required and most frequently used healthcare services for complication management. This identification was based on the condition of the event described previously. These healthcare services included the services provided by outpatient clinics, emergency care, laboratory departments and hospital wards. These services are available in public healthcare and the present study was written from the perspective of a public healthcare provider. The frequency of use of these services, like the duration of hospital stays, was retrieved from the Malaysian Diagnosis Related Group (MY-DRG®) (Ministry of Health Malaysia 2013) and the types of laboratory tests and procedures used were retrieved from the Malaysian CPGs and literature. The frequency use of the laboratory tests and procedures (healthcare services) conducted were obtained from experts who work in a related field in a public hospital. A microcosting method was used; thus, the unit cost of each healthcare service needed to be identified. The unit cost of procedures, hospitalisations, and investigations were retrieved from the article 'Fees (Medical) (Cost of Services) Order 2014,' which was published by the Federal Government Gazette, while the pharmaceutical costs were derived from a public hospital purchase price list from 2015. Attributable costs were calculated by adding the direct enumeration and the monthly cost of every input consumed in the treatment of a complication in the event year and the subsequent year, including inpatient hospital stays, outpatient visits, tests, drugs and diagnostic and therapeutic procedures. The annual cost (Equation 1) of the event year and the subsequent year is the addition of the total cost of the consumed services used in that year for the treatment of the complication.

Equation 1

$$\text{Total cost} = \sum \text{number of units of each health service per year} \times \text{unit cost of the service}$$

Ethical Approval

This study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. The registration nomber is NMRR-17-3295-37360 (IIR).

RESULTS

Table 3 shows the cost estimation of diabetes complications in the event year and the subsequent year. The detail of quantity resource used for T2DM complications management

during event year can be found in Appendices 1, 2 and 3. Among both macrovascular and microvascular complications, RF requiring haemodialysis incurred the highest annual per-patient costs at RM39,659.45 (USD9,266.23). MI was the highest direct cost among all macrovascular complications and the second highest direct cost among all complications, as its management involved the highly expensive percutaneous coronary intervention (PCI) procedure. Complications with the lowest direct cost estimation in the subsequent year included amputation, blindness and foot ulcer, as monitoring and care happened during the episode of the event and further medical care was not necessary. The expenditure of cardiovascular death included all the expenditure during hospitalisation. Figure 1 shows the estimated unit costs of diabetes management and the treatment of complications in the event year. For RF management, it was found that haemodialysis (considered an outpatient investigation and procedure) was the biggest component in its management (> 80%).

Table 3: Cost-estimation of T2DM complications in the event year and subsequent year (annual per patient costs).

T2DM complications	Event year	Subsequent year
MI	RM19,381.43 (USD4,528.37)	RM1,802.40 (USD421.12)
Stroke	RM8,740.60 (USD2,042.20)	RM1,388.40 (USD312.71)
HF	RM5,032.71 (USD1,175.87)	RM2,246.10 (USD524.79)
IHD	RM3,788.31 (USD885.12)	RM1,802.40 (USD421.12)
Amputation	RM5,959.93 (USD1,392.51)	–
Blindness	RM2,387.00 (USD557.71)	–
RF with haemodialysis	RM42,394.97 (USD9,905.37)	RM39,521.52 (USD9,233.89)
Diabetic foot ulcer	RM316.12 (USD73.86)	–

In terms of procedures, patients experiencing blindness due to retinopathy were treated with photocoagulation and may have attended follow-up ophthalmology clinics up to three times in the event year. Patients with a foot ulcer or an amputation visited the orthopaedic department a minimum of two times after the event: before being discharged from the orthopaedic department and once the wound had recovered well. Patients with other complications followed-up every 4 months at the medical outpatient department during the event year and the subsequent year. Appendix 4 shows the laboratory investigation and the medications used for managing complications in the outpatient clinic setting.

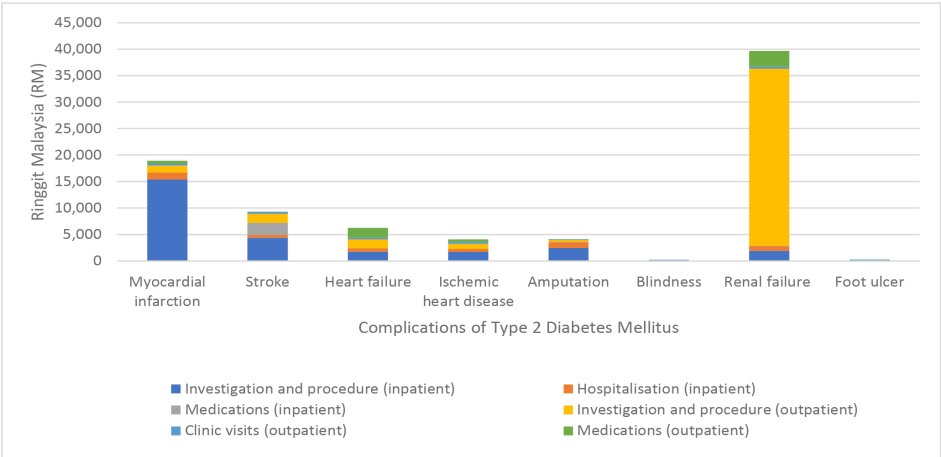

Figure 1: Estimated unit costs of diabetes management and treatment of complications in the event year.

DISCUSSION

The results of the present study will be useful for future policy and economic evaluation studies. The findings are similar to another published result (Todorova *et al*. 2012) which showed that in comparison to the management of other complications, the management of RF consumed the highest cost.

Yet the cost estimation in the present study was found to be higher than that of a local study, which may have been due to the employed methodology. Todorova *et al*. (2012) derived the direct costs of diabetes complications from three key opinion leaders in the field of T2DM in Malaysia and published literature. In the present study, the procedures and medications for all macrovascular T2DM complications were based on the recommendations of the Malaysian CPGs, which may have included a higher frequency of possible procedures, tests and medications for newly diagnosed patients. However, in a real clinical setting, not all procedures and management would be employed for the patients, thus contributing to the lower cost estimation in the Todorova et al. study, which lacked details of the approach and methodology in terms of cost estimation.

Two local studies (Mustapha and Azmi 2013; Nor Azlin *et al*. 2012) used the International Classification of Diseases (ICD) coding system to estimate the admission cost in government subsidised hospitals and reported lower cost estimations than that of the present study. Nor Azlin *et al*. (2012) estimated the cost of inpatient medical care due to stroke in a tertiary teaching hospital and the mean cost of care per patient per admission to be 50% lower than that of the present study. This may have been due to the use of alteplase (for stroke patients) in the present study, which contributed to 30% of the total estimated cost of stroke management. The preferred stroke management in Malaysia is to use streptokinase as the priority thrombolytic medication instead of alteplase, which was used at a rate of less than 0.0001 per 1,000 people per day in a public hospital (Chok and Chan 2017). Streptokinase is used eight times more often than alteplase, which indicates that fewer patients were using alteplase in the public healthcare setting. In the Nor Azlin *et al*.'s (2012) study, the cost of stroke was evaluated in the inpatient setting using a top-down

costing method that lacked a detailed approach including expenses for every drug use, thus, affecting the accuracy of their cost calculation. For instance, the total allocated costs were divided by the total units of inpatient days to obtain the cost of providing services on a per-patient, per-day stay basis. In practicality, the cost of thrombolytic agents can also be lower because thrombolytic agents must be administered within 3 to 4.5 hours of the onset of a stroke attack (Robinson, Zaheer and Mistri 2011), thereby disqualifying certain stroke patients.

Another study derived the admission cost of MI, stroke, IHD and RF from the medical record unit at the hospital level according to the Major Diagnostic Category (MDC) (Ministry of Health Malaysia 2013) and estimated it to be lower than that of the present study. Admission costs vary due to variances in the frequency use of procedures and laboratory tests that do not adhere to the recommendations of the CPGs. In the MY-DRG®, the case group weight for MI, stroke, IHD and HF is below 1, and RF has a case group weight that is the same as the average case (Ministry of Health Malaysia 2013). This shows that most of these cases are less complex and severe than average cases, thus requiring fewer procedures and management. The MDC for the cases was based on the possibility of principal diagnoses from the International Classification of Diseases, ninth revision (ICD-9), which means the code assignment process was unable to acutely assess patients' actual conditions. For instance, the RF in the MDC code 11101 includes a wide variety for RF with different severities and conditions, yet real costs may differ due to the varied procedures and management for each condition.

The estimated cost of HF in the present study was similar to that of the MY-DRG® (Ministry of Health Malaysia 2013), where the cost was estimated by retrieving data from the medical record unit and assigning every clinical case an ICD code. The hospitalisation cost of HF for a patient was estimated at RM2,700 (Ministry of Health Malaysia 2013), while the cost estimation per event year for HF in the present study was similar to that of the Mustapha *et al*.'s (2017) study, even though the study assessed the cost information from secondary data. In the present study, the cost of managing MI was markedly higher than the cost of the MY-DRG®, as the assignment of ICD code for MI cases may be disputable. For instance, ICD-9 was published in 1978 (Rouse 2014), and the first coronary angioplasty (or PCI) was developed in 1977 and was classified as other vascular procedures (codes 05211 and 05212) according to the ICD-9. Misspecification occurs when the primary diagnosis or order for laboratory tests and procedures is misaligned with the evidence found in the medical record (O'Malley *et al*. 2005). Misspecification will lead to issues with assigning correct codes, for example, whether the coder should classify the case as acute MI or as other vascular procedures. Therefore, the estimated cost of MI with PCI in the MY-DRG® was lower than that of the present study. Other local studies, like those of Todorova *et al*. (2012) and Mustapha *et al*. (2017), have also reported lower cost estimations for MI, which largely attributed to the method of defining complications in the present study. In the cost estimation of the present study, it was assumed that patients with MI were able to undergo PCI and that the PCI procedure was the biggest expenditure component in the management cost of MI, as found by another local study in which PCI consumables accounted for the biggest proportion of the total cost (Lee *et al*. 2017). Hence, the study estimated that the mean hospitalisation cost for a patient with PCI was between RM12,117 and RM16,289 (Lee *et al*. 2017), which was similar to the estimation in the present study.

The estimated cost of amputation in the present study was similar to that of a local study, as the estimated cost of amputation per patient per episode was less than RM6,000 (Mustapha *et al*. 2017). However, the MY-DRG® (Ministry of Health Malaysia 2013) has a higher cost estimation for amputation (~38% higher) per patient per admission due to the severity and complexity of each amputation case (Ministry of Health Malaysia 2013).

One of the T2DM complications that generates the highest costs is end-stage RF requiring haemodialysis. T2DM is 9 times more common than type 1 diabetes mellitus (Shahbazian and Rezaii 2013). Patients may develop end-stage RF after 20 to 30 years after diagnosis and 10 years after the onset of clinical nephropathy (Shahbazian and Rezaii 2013). This group of patients has a higher chance of developing other complications, such as cardiovascular disease or diabetic foot ulcer (Shahbazian and Rezaii 2013). This means that the estimation of expenditure for T2DM patients with end-stage RF requiring haemodialysis may be higher due to the group's higher risk of developing other complications.

In addition, having a risk of cardiovascular disease has a positive association with the haemoglobin A1c (HbA1c) level (Zhao *et al*. 2014). A study conducted in Louisiana found that a 1% increase of HbA1c was associated with a greater increase in the risk of cardiovascular disease, especially in white diabetic patients. A local study that recruited diabetic patients in several centres in the country found that the mean value of HbA1c was 8.66%, and this value exceeded the target of HbA1c suggested by the American Diabetes Association (< 7%) (Mafauzy, Hussein and Chan 2011). This shows a deterioration of mean HbA1c over a five-year period (2003 to 2008 from 7.82% to 8.66%) (Mafauzy, Hussein and Chan 2011). The study also found that 25.4% of patients experienced at least one of the severe late-onset complications, including legal blindness, MI, stroke and leg amputation, and that the event rate had also increased (Mafauzy, Hussein and Chan 2011). This indicates that the burden of managing diabetes complications increased over the year for the Malaysian government.

The cost estimation in the present study indicates that managing diabetes complications is high. Policy makers at the macrolevel should be aware of the burden of diabetes complications, and actions should be taken to improve the mean HbA1c level of T2DM patients. Policy makers should focus on preventing and controlling diabetes by making improvements to their patients' environment. Possible improvements include increasing screening for populations who are at an increased risk of developing diabetes (i.e. those with pre-diabetes), promoting a healthy lifestyle and implementing education and prevention programs (Bergman *et al*. 2012).

Although the strength of the present study is that it followed the recommended CPGs, for instance, confirming with the physicians the number of tests and procedures done and avoiding unaccounted procedures or tests for the management of the complications, a few limitations were identified. First, this study used the CPGs and literature to estimate the cost of management. Even though it confirmed the estimation with the specialists, the clinical practice on the ground may vary depending on availability in the practice facility, the physician's preference, and the patient's background and condition. Second, the present study did not include patient characteristics and behaviours that may affect costs for patients with T2DM complications. For instance, smoking and obesity have been shown to be associated with the development of cardiovascular disease and T2DM patients who smoke are associated with having higher healthcare costs than those who do not smoke (O'Sullivan *et al*. 2011). Although the data was not made available, this study tried to capture as much information as possible on the complications. Lastly, the present study did not track events that may have occurred after the initial indexed event year, as tracking multiple or subsequent events was beyond the scope of this study; thus, the cumulative costs for managing those complications was not reflected in this study. Patients who have a single cardiovascular event are at risk of experiencing subsequent events over their lifetime, which may be two different events, such as MI and stroke, or subsequent events occurring years after the initial event, such as MI followed by IHD. Again, this study did not account for this type of a scenario.

CONCLUSION

This study provides direct medical cost estimations for the management of T2DM complications. This shows that T2DM is associated with a substantial economic burden in Malaysia and that the management of T2DM complications is likely to consume a significant proportion of healthcare payers' overall financial budget. The cost data reported in this study will be a useful resource for future expenditure evaluations of T2DM in Malaysia.

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AVAILABILITY OF DATA AND MATERIALS

The datasets used and analysed in the study are available from the corresponding author on reasonable request.

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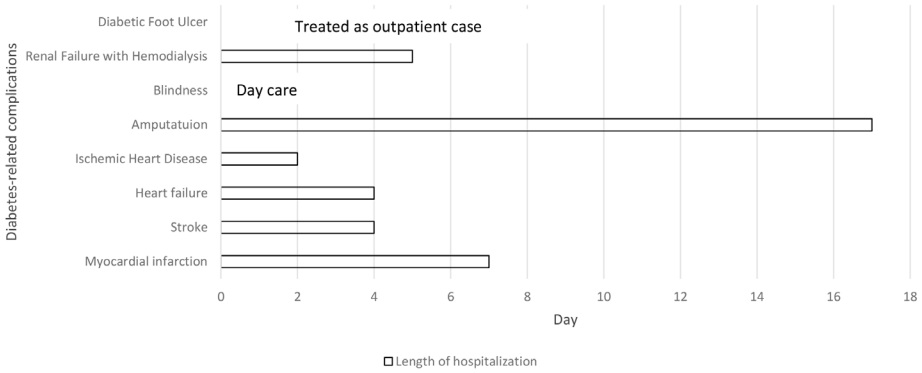
APPENDICES

Appendix 1: The average length of hospitalisation for type 2 diabetes mellitus complications based on MY-DRG®



Appendix 2: Number of times of laboratory investigation and procedure conducted in a single episode of hospitalization at event year

Laboratory Investigations and Procedure	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Renal Failure with Hemodialysis
ECG	III	III	I	III		
Chest X-ray	I		I	I		
Full blood count	I	I	I	I	I	I
Renal Profile	I	I	I	I	I	I
HbA1c					I	
Capillary blood sugar	I			I		
Troponin T	I		I	I		
CK-MB	I			I		
Fasting Blood glucose*	IIIIIII	IIII	I	II	IIIIIIIIIIIIIII	IIIII
Fasting Lipid Profile	I	I	I	I		I
Liver function test	I	I	I	I	I	I
Hep B	I					
Hep C	I					
HIV	I					
Clotting profile		I			I	
CT brain		I				
MRI Brain		I				
Echocardiogram	I	I	I	I		
Calcium phosphate serum test						I
Ultrasound kidney						I
PCI	I					

Laboratory Investigations and Procedure	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Renal Failure with Hemodialysis
Amputation below knee					I	
Catheter insertion central venous						I
Hemodialysis						II
*Fasting blood glucose repeated daily during hospitalization to assess patient's fasting glucose level						

Appendix 3: Medication costs for each complication during hospital stay at event year

Medications	Medication costs in T2DM Complications (RM)					
	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Renal Failure with Hemodialysis
Morphine 10mg/ml Inj	0.81			0.81		
Hydrocortisone 200mg Inj	5.80					
Alteplase 50mg/50ml Inj		2,232.91				
Frusemide 10mg/5ml Inj			19.29			
Fondaparinux 2.5mg/0.5ml Inj				64.88		
Ampicillin Sodium 1g& Sulbactam Sodium 500mg Inj					89.25	
Tramadol 50mg/ml Inj					47.94	
Iron Sucrose 200mg/5ml Inj						66.72
Aspirin 300mg Tab	0.14	0.14		0.14		
Cardipin 100mg Tab	0.49	0.28		0.14		
Clopidrogrel 75mg Tab	2.30			0.60		
Bisoprolol 2.5mg Tab	0.56			0.16		
Perindopril 4mg Tab	0.56			0.16		

Medications	Medication costs in T2DM Complications (RM)					
	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Renal Failure with Hemodialysis
Atorvastatin 40mg Tab	1.54	0.88		0.44		
Glyceryl Trinitrate 0.5mg Tab	0.56			0.16		
Isosorbide mononitrate SR 60mg Tab	2.31			0.66		
Trimetazidine 35mg Tab	0.84			0.24		
Pantoprazole 40mg Tab	1.12			0.32		
Digoxin 0.25mg Tab			0.25			
Ivabradine 5mg Tab			10.08			
Frusemide 40mg Tab						0.675
Folic acid 10mg Tab						0.05
Ferrous Fumarate 400mg Tab						1.90
Vitamin B Complex Tab						0.05
Calcium Carbonate 500mg Tab						1.05
Inj= Injection, Tab= Tablet						

Appendix 4: Number of times of laboratory investigation conducted and total medication costs in T2DM complications in outpatient at event year

Laboratory investigation and medications	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Blindness	Renal Failure with Hemodialysis	Foot ulcer
Number of times for laboratory investigation and procedure								
Full blood count	III	III	III	III	II	I	III	
Renal profile	III	III	III	III	II		III	

Laboratory investigation and medications	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Blindness	Renal Failure with Hemodialysis	Foot ulcer
Fasting blood glucose	III	III	III	III	II	I	III	I
Fasting lipid profile	III	III	III	III			III	
Liver function test	III	III	III	III	II		III	
HbA1c	I	I	I	I			I	
Fundus photography						I		
Laser photocoagulation						I		
Culture of clinical specimen								I
Calcium serum level							III	
Medication costs								
Cardipin 100mg Tab	25.20	25.2		25.20				
Clopidrogrel 75mg Tab	108.00			108.00				
Bisoprolol 2.5mg Tab	28.80			28.80				
Perindopril 4mg Tab	28.80			28.80				
Atorvastatin 40mg Tab	79.20	79.20		79.20				
Glyceryl Trinitrate 0.5mg Tab	28.80			28.80				
Isosorbide mononitrate SR 60mg Tab	118.80			118.80				
Trimetazidine 35mg Tab	43.20			43.20				
Pantoprazole 40mg Tab	57.60			57.60				
Digoxin 0.25mg Tab			22.50					
Ivabradine 5mg Tab			907.20					

Laboratory investigation and medications	Myocardial Infarction	Stroke	Heart Failure	Ischemic Heart Disease	Amputation	Blindness	Renal Failure with Hemodialysis	Foot ulcer
Frusemide 40mg Tab			32.40				48.60	
Folic acid 10mg Tab							3.60	
Ferrous Fumarate 400mg Tab							136.80	
Vitamin B Complex Tab							3.60	
Calcium Carbonate 500mg Tab							75.60	
Iron sucrose 200mg Inj							5,404.32	
Unasyn 375mg Tab					18.06			36.12
Tramadol 50mg Tab					1.68			

HbA1c= Hemoglobin A1c, Tab= Tablet, Inj= Injection