

# Cost of Cardiovascular Disease Events in Patients With and Without Type 2 Diabetes and Factors Influencing Cost: A Retrospective Cohort Study

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## Research Article

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## Abstract

**Background:** Cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) are non-communicable diseases that impose a significant economic burden on healthcare systems, particularly in low- and middle-income countries. The purpose of this study was to evaluate the hospital treatment cost for cardiovascular disease events (CVDEs) in patients with and without diabetes and identify factors influencing cost.

**Method:** We conducted a retrospective, cross-sectional study using administrative data from three public tertiary hospitals in Malaysia. Data for hospital admissions between 1 March 2019 and 1 March 2020 with International Classification of Diseases 10th Revision (ICD-10) codes for acute myocardial infarction (MI), ischaemic heart disease (IHD), hypertensive heart disease, stroke, heart failure, cardiomyopathy, and peripheral vascular disease (PVD) were retrieved from the Malaysian Disease Related Group (Malaysian DRG) Casemix System. Patients were stratified by T2DM status for analyses. Multivariate logistic regression was used to identify factors influencing treatment costs.

**Results:** Of the 1,183 patients in our study cohort, approximately 60.4% had type 2 diabetes. The most common CVDE was acute MI (25.6%), followed by IHD (25.3%), hypertensive heart disease (18.9%), stroke (12.9%), heart failure (9.4%), cardiomyopathy (5.7%) and PVD (2.1%). Nearly two-thirds (62.4%) of the patients had at least one cardiovascular risk factor, with hypertension being the most prevalent (60.4%). The treatment cost for all CVDEs was RM 4.8 million and RM 3.7 million in the T2DM and non-T2DM group, respectively. IHD incurred the largest cost in both groups, constituting 30.0% and 50.0% of the total CVDE treatment cost for patients with and without T2DM, respectively. Predictors of high treatment cost included male gender, minority ethnicity, IHD diagnosis and severity level.

**Conclusion:** This study provides real-world cost estimates for CVDE hospitalisation and quantifies the combined burden of two major non-communicable disease categories at the public health provider level. Our results confirm that CVDs are associated with substantial health utilisation in both T2DM and non-T2DM patients.

## Background

Non-communicable diseases (NCDs), namely cardiovascular disease (CVD) and diabetes, continue to be a major public health concern worldwide. CVDs constitute the leading cause of global mortality, accounting for 17.9 million deaths or nearly one third of all deaths in the world [1]. Of these deaths, approximately 85% are due to ischaemic heart disease (IHD) and stroke [1].

The global burden of CVD-related death and disability have risen over the past two decades, largely due to the combined effects of population growth, ageing, and the rising epidemic of CVD risk factors. Prevalent cases of total CVDs have increased by 93% from 271 million in 1999 to 523 million in 2019. Trends for disability-adjusted life years (DALYs) due to CVDs have also risen, with years lived with disability doubling from 17.7 million to 34.4 million over the same duration [2]. This phenomenon represents a significant challenge that must be urgently addressed as it places immense strain on healthcare systems.

Diabetes represents yet another significant driver behind the escalating burden of NCDs. An estimated 537 million adults aged 20–79 have diabetes, which translates to a global prevalence of 10.5% in this age group [3]. Diabetes has long been known as an independent risk factor for CVD and is a common precursor to a cardiovascular event. Up to one third (32.2%) of all patients with diabetes have CVD, and one in ten (9.9%) individuals with diabetes meet their demise due to CVD complications [4]. The most prevalent form of diabetes is type 2 diabetes mellitus (T2DM), which accounts for 96.0% of diabetes cases and a staggering 95.4% diabetes DALYs worldwide [5]. According to the World Health Organization, DALYs from diabetes have surged by more than 80% between 2000 and 2019 [6]. By 2050, the disease could affect more than 1.31 billion individuals and prevalence rates are predicted to surpass 20% in many parts of the world by the end of the period [5].

The burden of NCDs is especially pronounced in low- and middle-income countries (LMICs). Over three quarters of CVD deaths and more than 80% of diabetes cases occur in LMICs [1, 7]. Malaysia has the highest prevalence of diabetes in Southeast Asia. In Malaysia, up to 3.9 million (18.3%) adults aged 18–79 are affected by diabetes and more than half are unaware that they have diabetes [8]. According to the Malaysia Burden of Disease report, approximately 75% of DALYs are attributable to NCDs, with IHD, diabetes and stroke being the top three burden contributors [9, 10]. In 2017, the total direct healthcare costs for CVD and diabetes were RM 3.9 billion and RM 4.4 billion, respectively – at least triple the cost for cancer (RM 1.3 billion). These included costs for hospitalization, outpatient visits, medications, laboratory tests, allied health, and medical consumables [11].

The health and economic burden associated with CVD in people with T2DM not only impacts affected individuals and their families, but also imposes substantial costs on healthcare providers at the societal level. To date, limited work has been done to appraise the direct treatment costs of both NCD categories combined in LMICs [12, 13, 14, 15]. Current available data comparing financial health expenditures for CVDs in patients with and without T2DM are mainly derived from Western populations and conducted in high-income countries [16, 17, 18, 19, 20, 21, 22].

Understanding the impact of CVD on hospitalisation costs for patients with and without T2DM is crucial to inform resource allocation for disease surveillance, prevention and treatment, particularly in LMIC settings where access to healthcare services is often limited and the epidemiological burden of these conditions is substantial. To this end, we conducted a retrospective administrative database analysis to determine the

hospitalisation costs incurred due to cardiovascular disease events (CVDEs) among diabetic versus non-diabetic patients in Malaysia. In addition, we sought to describe the type and incidence of CVDEs, length of stay (LoS), and CVD risk factors influencing the incremental cost of acute CVDE care in local public health setting.

## Methods

This was a retrospective cross-sectional study using administrative data from three public tertiary hospitals (Hospital Sultan Idris Shah Serdang, Hospital Putrajaya, and Hospital Tuanku Jaafar Negeri Sembilan) in Malaysia. These hospitals were selected based on their strategic location in the central region of Peninsular Malaysia and for their large catchment areas, where a high influx of admissions related to CVDEs can be anticipated.

The primary objective of this study was to determine the hospital treatment cost for CVDEs in patients with and without T2DM. The secondary objective was to identify factors influencing treatment cost in these patients.

The primary data source was clinical and costing data extracted from the Malaysian Diagnosis Related Group (Malaysian DRG) Casemix System. A casemix system is a structured framework designed to classify patients with similar clinical characteristics and resource utilisation patterns into relatively homogeneous costing groups [23]. The most widely known example of a casemix system is the Diagnosis Related Group (DRG) classification system, where each DRG describes a cluster of patients with related diagnoses incurring similar treatment costs for an episode of care [24].

In Malaysia, the Malaysian DRG Casemix System serves as a useful health management tool for budgeting and quality assurance monitoring [25]. To date, it has been implemented in 148 public hospitals for tracking inpatient expenditure. The Malaysian DRG system routinely collects patient variables such as patient age and sex, primary and secondary diagnoses, LoS, procedures performed, discharge status, and cost of services. Outputs generated include treatment cost per disease according to the DRG, estimated treatment cost for inpatient service care, workload metrics, and health facility efficiency index [26].

Figures 1 and 2 illustrate the Malaysian DRG design components and system workflow to calculate treatment costs [27, 28]. The system requires input of two important sets of information: (i) the patient's demographic and encounter information, and (ii) clinical data [28]. When patients are discharged from the hospital, relevant information obtained from case notes generated during the episode of care are manually keyed into the system. Each patient care episode is then assigned to a DRG code. In the Malaysian DRG system, DRG codes are made up from a combination of diagnosis and procedure codes defined by the International Classification of Diseases 10th Revision (ICD-10) and International Classification 9th Revision Clinical Modification (ICD-9-CM) codes, respectively. Each CVDE is rated using a three-tiered Severity of Illness (Sol) Index (increasing in severity from Level I to III) derived based on an aggregation of health dimensions to reflect the total burden of illness and intensity of resource consumption for a patient [28]. This is determined using discharge records and scored based on the presence of complications and comorbidities, number of procedures, dependency on life support procedures, and other prognostic indicators (for example, age). A DRG code is then generated and assigned to a hospital tariff according to the cost group weight [27].

Data pertaining to hospital admissions between 1 March 2019 and 1 March 2020 were retrieved from the Malaysian DRG Casemix System. The index date for each patient was defined as the date on which an ICD-10 code for a principal diagnosis of CVDE was identified. The pre-index period was defined as 12 months before the index hospital admission date. Figure 3 illustrates the study design and schema. All Malaysian patients aged  $\geq 18$  who were hospitalised with a principal diagnosis defined by ICD-10 codes for acute myocardial infarction (MI), IHD, hypertensive heart disease, stroke, heart failure, cardiomyopathy, and peripheral vascular disease (PVD) were included in the study (see Appendix A for ICD-10 codes). Patients were excluded if they had a history of cancer, COVID-19 infection, hepatitis B or C, human immunodeficiency virus or major psychiatric illness. Eligible patients were assessed for T2DM status (Appendix B) and CVD risk factors (Appendix C) by extracting the relevant ICD-10 codes in the one-year pre-index period. Additional clinical information not captured by the Malaysian DRG Casemix System, such as T2DM duration and glycated haemoglobin measurement (HbA1c), were retrieved from the patient's medical records and case notes. The DRG codes for CVDEs of interest were then extracted according to the ICD-10 codes of interest and grouped to determine the cost of treatment (Appendix D).

We used numbers and percentages for categorical variables and mean  $\pm$  standard deviation (SD) for continuous variables. Non-normally distributed data were presented as median and data range (minimum and maximum range). Cost analyses included cost per CVDE and total cost per year for CVDEs. All costs are expressed in Malaysian Ringgit (RM) for the financial year FY2020 from 1 March 2019 to 1 March 2020 (average exchange rate is 1 USD = RM 4.20 for 2020). Patients were stratified and analysed according to T2DM status. As treatment costs did not conform to normal distribution, we used the Mann Whitney test for inter-group comparison between T2DM and non-T2DM patients. A Chi-square test of independence was conducted to determine the relationship between independent variables and cost. Multivariate analysis using binary logistic regression was used to determine predictors of high CVDE cost among T2DM and non-T2DM patients. Data analyses were conducted using Microsoft Excel and SPSS Software version 26.0. A P value of  $< 0.05$  was considered statistically significant.

## Results

A total of 4,643 admission records between 1 March 2019 and 1 March 2020 with CVDE as the principal diagnosis were identified from the Malaysian DRG Casemix System from these three hospitals. Using random sampling technique, we selected and screened 1192 patients for eligibility. Of these, a final sample size of 1,183 patients were included for analyses. Table 1 provides an overview of the patients' demographic and clinical characteristics. Overall, the mean age of patients admitted for CVDE was 58.6 years. The youngest patient was 18 years old while the oldest patient was 91 years old. The most common CVDE diagnosis was acute MI (25.6%), followed by IHD (25.3%), hypertensive heart disease (18.9%), stroke (12.9%), heart failure (9.4%). CVDE admissions were less commonly for cardiomyopathy (5.7%) and PVD (2.1%). The mean (average) LoS was 4.8 days. A longer average LoS was observed in patients with more complex illness (5.6 days for Severity III versus 4.4 days for Severity I). Nearly two-thirds (62.4%) of all patients who were admitted for a CVDE had at least one CVD risk factor. The most frequent risk factor was hypertension (60.4%), followed by PVD (17.8%), dyslipidaemia (10.1%), and previous stroke (6.9%).

Table 1  
Patient demographic and clinical characteristics

	CVDE patients	CVDE patients with T2DM	CVDE patients without T2DM
Total, N (%)	1183 (100)	715 (100)	468 (100)
Age, mean (years ± SD)	58.6 ± 13.2	59.1 ± 12.8	58 ± 13.7
Gender			
Male	778 (65.8)	425 (59.4)	353 (75.4)
Female	405 (32.2)	290 (40.6)	115 (24.6)
Ethnicity			
Malay	763 (64.5)	487 (68.1)	276 (59.0)
Chinese	185 (15.6)	80 (11.2)	105 (22.3)
Indian	235 (19.9)	148 (20.7)	87 (18.6)
Age category (years)			
18–29	18 (1.5)	14 (2.0)	4 (0.9)
30–39	83 (7.0)	50(7.3)	31(6.6)
40–49	184 (15.6)	113 (15.8)	71 (15.2)
50–59	312 (26.4)	176(24.6)	136 (29.1)
60–69	336 (28.4)	207 (29.0)	129 (27.6)
≥ 70	250 (21.1)	153 (21.4)	97 (20.7)
Type of CVDE			
Acute MI	303(25.6)	151 (21.1)	152 (32.5)
IHD	300 (25.3)	129 (18.0)	171 (36.5)
Hypertensive HD	224 (18.9)	186 (26.0)	3.8 (8.1)
Stroke	153 (12.9)	91 (12.7)	62 (13.2)
Heart failure	111 (9.4)	91 (12.7)	20 (4.3)
Cardiomyopathy	67 (5.7)	47 (6.6)	20 (4.3)
PVD	25 (2.1)	20 (2.8)	5 (1.1)
Outcome of admission			
Discharged well	1113 (94.1)	662 (92.6)	451 (96.4)
Death	70 (5.9)	53 (7.4)	17 (3.6)
Severity level			
Severity I	306 (26.0)	174 (24.3)	134 (28.6)
Severity II	530 (44.8)	354 (49.5)	176 (37.6)
Severity III	345 (29.2)	187 (26.2)	158 (33.8)
Average LoS (days ± SD)			
Severity I	4.71 ± 3.51	4.87 ± 3.72	3.85 ± 1.93
Severity II	5.06 ± 3.85	5.22 ± 3.98	3.7 ± 2.00
Severity III	6.98 ± 7.38	6.68 ± 6.9	8.07 ± 8.99
Presence of CVD risk			
All variables are reported as frequency and percentage unless otherwise specified. CVDE = cardiovascular disease event; IHD = ischaemic heart disease; MI = myocardial infarction; HD = heart disease; PVD = peripheral vascular disease; LoS = length of stay; T2DM = type 2 diabetes mellitus; SD = standard deviation.			

	CVDE patients	CVDE patients with T2DM	CVDE patients without T2DM
Yes	738 (62.4)	453 (63.4)	285 (60.9)
No	445 (37.6)	262 (36.6)	183 (39.1)
Number of CVD risks			
1	644 (54.4)	406 (56.9)	238 (50.7)
2	91 (7.7)	46 (6.4)	45 (9.6)
≥ 3	12 (1)	7 (1.0)	5 (1.1)
Type of CVD risk			
Hypertension	714 (60.4)	482 (67.5)	232 (49.5)
Dyslipidaemia	119 (10.1)	62 (8.6)	57 (12.2)
PVD	211 (17.8)	210 (29.4)	1 (0.3)
Stroke	82 (6.9)	60 (8.4)	22 (5.9)
All variables are reported as frequency and percentage unless otherwise specified. CVDE = cardiovascular disease event; IHD = ischaemic heart disease; MI = myocardial infarction; HD = heart disease; PVD = peripheral vascular disease; LoS = length of stay; T2DM = type 2 diabetes mellitus; SD = standard deviation.			

## Incidence of CVDE in T2DM and non-T2DM patients

Approximately 60.4% of patients with CVDE had underlying T2DM. Compared with non-T2DM patients, the cohort with T2DM were slightly older, were comprised of more women and had a higher prevalence of CVD risk factors. Nearly half (48.7%, n = 348/714) of patients with T2DM had a duration of diabetes of ≤ 5 years. Data for HbA1c was available for 351 patients. Three quarters of these patients (75.2%) had a HbA1c greater than 7.0%. The proportion of patients with T2DM who did not survive their admission was twice as high compared with those without T2DM (7.4% versus 3.2%, respectively).

We found differing CVDE frequencies between T2DM and non-T2DM patients. Within the T2DM group, the most common type of CVDE was hypertensive heart disease (26.0%), followed by acute MI (21.1%) and IHD (18.0%). In the non-T2DM group, the predominant type of CVDE was IHD (36.5%), followed by acute MI (32.5%) and stroke (13.2%). Over 60% of patients had at least one CVD risk factor, with hypertension being the most prevalent in both the T2DM and non-T2DM groups. Patients with T2DM were more frequently affected by PVD (29.4%) as opposed to those without T2DM (0.3%). In contrast, patients without T2DM (12.2%) were more likely to have dyslipidaemia compared with their T2DM counterparts (8.4%).

## Cost of CVDE in T2DM and non-T2DM patients

Table 2 shows the total and individual costs for CVDE treatment in T2DM and non-T2DM patients. The overall expenditure (total cost for all cases) for inpatient CVDE treatment was approximately RM 8.4 million. Patients with T2DM incurred a higher cost in excess of RM 1.1 million, about 30% higher than the amount incurred by patients without T2DM. Despite the higher overall cost incurred by T2DM patients, the median cost per case (or cost per episode of CVDE care) was slightly lower (RM5,452.63) compared to non-T2DM patients (RM6,941.30). IHD incurred the highest cost: up to RM 1.4 million in the T2DM group and RM1.8 million in the non-T2DM group. This constituted 30.0% and 50.0% of the total CVDE treatment cost for patients with and without T2DM, respectively. The median cost per case for IHD was RM 8,364.65, more than double the cost for acute MI or stroke. The higher cost for IHD could be attributed to resource-intensive procedures, such as percutaneous coronary intervention and coronary bypass grafting, resulting in increased average LoS and cost per case for the provider (Table 3).

Table 2  
 Cost of CVDE treatment in T2DM and non-T2DM patients for FY2020

Diagnosis	CVDE with T2DM					CVDE without T2DM				
	N	Median cost per case (RM)	Minimum cost (RM)	Maximum cost (RM)	Total cost for all cases (RM)	N	Median cost per case (RM)	Minimum cost (RM)	Maximum cost (RM)	Total cost for all cases (RM)
Acute MI	151	4,608.38	2,989.98	16,373.72	874,388.08	152	4,649.53	2,989.98	14,197.31	941,588.78
IHD	129	8,364.65	3,235.20	106,357.88	1,415,411.24	171	8,364.65	3,545.80	106,357.88	1,837,803.52
Hypertensive HD	186	5,440.91	2,573.20	9,946.92	1,021,690.43	38	4,740.02	2,789.78	9,477.31	206,964.00
Stroke	91	4,521.59	2,989.98	100,790.23	582,047.77	62	4,521.59	2,989.98	9,860.14	314,731.73
Heart failure	91	5,440.91	2,573.20	17,462.31	495,503.89	20	5,756.94	3,954.56	100,790.23	206,582.14
Cardiomyopathy	47	5,452.63	3,827.03	14,197.31	276,592.20	20	6,371.82	3,147.64	10,847.26	127,034.15
PVD	20	5,090.46	3,472.18	14,943.43	119,962.18	6	5,149.68	3,235.20	8,364.65	30,898.08
Total	715	5,452.63	2,573.20	106,357.88	4,785,595.79	468	6,941.30	2,789.78	106,357.88	3,658,555.47
CVDE = cardiovascular disease event; T2DM = type 2 diabetes; FY = financial year; MI = myocardial infarction; IHD = ischaemic heart disease; HD = heart disease; PVD = peripheral vascular disease.										

Table 3  
Cost per case (CPC) and average length of stay (LoS) per DRG code

DRG code	DRG details	Cases, n (%)	CPC (RM)	Average LoS (days)
<b>Cardiovascular Disease Events (n = 614)</b>				
<b>Coronary artery disease</b>		228 (19.3)		
5531	Without complication	69 (30.3)	3,954.56	3.80
5532	With complication	128 (56.2)	4,521.59	4.00
5533	With major complication	31 (13.5)	7,121.32	5.20
<b>Vascular disorder and injuries</b>		105 (8.9)		
5611	Without complication	34 (32.3)	5,440.91	5.50
5612	With complication	63 (60.0)	5,708.21	5.80
5613	With major complication	8 (7.7)	8,672.86	8.70
<b>Heart failure and shock</b>		94 (7.9)		
5571	Without complication	30 (31.9)	4,740.02	4.50
5572	With complication	3 (3.2)	4,690.69	4.60
5573	With major complication	61 (64.9)	5,805.67	5.60
<b>Nonspecific cerebrovascular disorder</b>		63 (5.3)		
1651	Without complication	15 (23.8)	4,608.38	4.70
1652	With complication	35 (55.5)	5,452.63	5.70
1653	With major complication	13 (20.6)	8,153.81	8.50
<b>Ischaemic cerebrovascular disease</b>		59 (4.9)		
1551	Without complication	7 (11.8)	2,989.98	3.60
1552	With complication	39 (66.1)	3,235.20	3.90
1553	With major complication	13 (22.0)	6,278.19	7.80
<b>Atherosclerosis</b>		21 (1.8)		
5521	Without complication	13 (61.9)	6,898.62	3.50
5522	With complication	5 (23.8)	6,928.42	3.80
5523	With major complication	3 (14.2)	11,008.35	5.30
<b>Myocardial disease</b>		19 (1.6)		
5541	Without complication	4 (21.0)	6,889.68	4.70
5542	With complication	10 (52.6)	6,941.30	4.60
5543	With major complication	5 (26.4)	9,477.31	6.80
<b>Cardiac arrhythmia and conduction disorder</b>		11 (0.9)		
5561	Without complication	3 (27.3)	3,722.52	3.10
5562	With complication	6 (54.5)	4,598.89	3.80
5563	With major complication	2 (18.2)	5,960.91	4.80
<b>Cardiac arrest, unexplained</b>		9 (0.8)		
5593	With major complication	9 (100)	9,389.25	8.30
<b>Hypertension</b>		5 (0.4)		
5511	Without complication	1 (20.0)	2,849.30	3.30

DRG = Disease Related Group; CVDE = cardiovascular disease event; RFA = radiofrequency ablation.



DRG code	DRG details	Cases, n (%)	CPC (RM)	Average LoS (days)
<b>Cardiovascular Disease Events (n = 614)</b>				
5512	With complication	1 (20.0)	3,168.96	3.60
5513	With major complication	3 (60.0)	4,342.06	4.80
<b>Procedures related to CVDE (n = 341)</b>				
<b>Percutaneous coronary intervention</b>		315 (26.6)		
5041	Without complication	57 (18.0)	7,753.10	3.20
5042	With complication	103 (32.7)	8,364.65	3.50
5043	With major complication	155 (49.3)	9,860.14	3.60
<b>Coronary bypass procedure</b>		10 (0.8)		
5001	Without complication	2 (20.0)	106,357.88	16.80
5002	With complication	1 (10.0)	102,400.48	18.30
5003	With major complication	7 (70.0)	100,790.23	22.70
<b>Electrophysiology study or RFA and pacemaker insertion</b>		5 (0.3)		
5062	With complication	2 (40.0)	10,847.26	4.20
5063	With major complication	3 (60.0)	14,197.31	5.20
<b>Other circulatory system operating room procedure</b>		3 (0.2)		
5101	Without complication	1 (33.3)	3,391.62	3.50
5102	With complication	2 (66.7)	4,510.08	4.30
<b>Other vascular procedure</b>		4 (0.2)		
5091	Without complication	1 (25.0)	3,582.61	3.80
5092	With complication	2 (50.0)	4,749.74	4.00
5093	With major complication	1 (25.0)	11,275.83	9.30
<b>Spinal cord and spinal canal procedure</b>		1 (0.1)		
1051	Without complication	1(100.0)	7,740.05	8.60
	Vein ligation and stripping	1 (0.1)		
5081	Without complication	1(100.0)	4,203.07	2.90
<b>Other respiratory system operating room procedure</b>		2 (0.1)		
4011	Without complication	1 (50.0)	6,853.90	6.70
4013	With major complication	1 (50.0)	21,649.81	18.40
DRG = Disease Related Group; CVDE = cardiovascular disease event; RFA = radiofrequency ablation.				

For the T2DM group, median per case showed an incremental increase with each additional CVD risk factor (Table 4). On the other hand, cost per case was highest in non-T2DM patients with 2 CVD risk factors and lowest for those with three or more risk factors. The cost per case for each CVD risk factor of interest can be found in Table 5. The median cost per case when hypertension and hyperlipidaemia were present were similar in both groups. However, a higher median cost per case was incurred by patients with T2DM if they also had a history of prior IHD or concomitant PVD.

Table 4  
Cost of CVDE management by number of CVD risk factors

Number of CVD risk factors	CVDE with T2DM				CVDE without T2DM			
	N	Median cost (RM)	Minimum cost (RM)	Maximum cost (RM)	N	Median cost (RM)	Minimum cost (RM)	Maximum cost (RM)
1	429	4,376.78	2,341.75	66,413.89	183	4,376.78	2,531.11	53,757.11
2	45	7,118.00	2,683.25	9,970.46	45	7,118.00	2,683.25	860,411.00
≥ 3	7	8,604.11	4,232.30	53,757.11	5	2,683.25	2,508.80	7,118.00

CVDE = cardiovascular disease event; CVD = cardiovascular disease; T2DM = type 2 diabetes.

Table 5  
Cost of CVDE treatment in T2DM and non-T2DM patients with cardiovascular risks of interest

Cardiovascular risk	CVDE with T2DM				CVDE without T2DM			
	N	Median cost (RM)	Minimum cost (RM)	Maximum cost (RM)	N	Median cost (RM)	Minimum cost (RM)	Maximum cost (RM)
Hypertension	482	4,377.00	2,342.00	66,414.00	233	4,743.44	2,509.00	53,757.00
Hyperlipidaemia	151	7,118.00	2,683.00	53,757.00	57	7,118.00	2,509.00	8,604.00
IHD	180	9,173.98	2,738.71	68,685.24	137	8,528.57	3,119.45	53,757.11
Stroke	60	4,363.76	2,509.00	53,757.00	NA	NA	NA	NA
PVD	210	4,405.31	2,342.00	8,604.00	917	2,907.44	2,907.00	2,907.00

CVDE = cardiovascular disease event; T2DM = type 2 diabetes; IHD = ischaemic heart disease; PVD = peripheral vascular disease; NA = not available.

## Factors influencing cost of CVDE treatment

The median CVDE cost calculated for patients with T2DM (RM5,452.63) was used to as the threshold for categorising treatment cost level (low versus high). As shown in Table 6, the cost of CVDE treatment was significantly associated with gender, outcome of admission, type of CVDE, Sol Index level, T2DM status, and CVD risk factors. Age, ethnicity, duration of diabetes, and HbA1c level did not significantly influence treatment costs. Certain factors were significantly correlated with CVDE treatment cost in patients with T2DM patients (Table 7). These factors included male gender, age, admission for IHD, outcome of admission, and the presence of CVD risk. For patients without T2DM, only two factors significantly correlated with treatment costs: the type of CVDE and the Sol Index level.

Table 6  
Association between patient characteristics and total cost (N = 1183)

Variable	Cost		$\chi^2$	df	p-value
	Low, n (%)	High, n (%)			
Gender			7.863	1	0.005*
Male	316 (40.6)	462 (59.4)			
Female	199 (49.1)	206 (50.9)			
Ethnicity			5.64	2	0.06
Malay	350 (45.9)	413 (54.1)			
Chinese	68 (36.8)	117 (63.2)			
Indian	97 (41.3)	138 (58.7)			
Age category (years)			7.09	5	0.214
18–29	10 (55.6)	8 (44.4)			
30–39	41 (49.4)	42 (50.6)			
40–49	70 (38.0)	114 (62.0)			
50–59	126 (135.8)	186 (59.6)			
60–69	151 (44.9)	185 (55.1)			
≥ 70	117 (46.8)	133 (53.2)			
Type of CVDE			186.593	6	<0.001*
Acute MI	162 (53.5)	141 (46.5)			
IHD	31 (10.3)	269 (89.7)			
Hypertensive heart disease	118 (52.7)	106 (47.3)			
Stroke	95 (66.6)	58 (37.9)			
Heart failure	63 (56.8)	48 (43.2)			
Cardiomyopathy	31 (46.3)	36 (53.7)			
Peripheral vascular disease	15 (60)	10 (40.0)			
Outcome of admission			11.213	1	0.001*
Discharged well	498 (44.7)	615 (55.3)			
Death	17 (24.3)	53 (75.7)			
Severity level			358.01	2	<0.001*
Severity I	215 (69.8)	93 (30.2)			
Severity II	293 (55.3)	237 (44.7)			
Severity III	7 (2.0)	338 (98.0)			
Diabetes status			11.064	1	0.001*
Yes	339 (65.8)	376 (56.3)			
No	176 (34.2)	292 (43.7)			
Diabetes duration (years)			8.199	4	
0–5	166 (47.7)	182 (52.3)			
6–10	55 (42.0)	76 (58.0)			
11–15	59 (48.4)	63 (51.6)			

CVDE = cardiovascular disease event; MI = myocardial infarction; IHD = ischaemic heart disease; HbA1c = glycated haemoglobin; CV = cardiovascular.

Variable	Cost		$\chi^2$	df	p-value
	Low, n (%)	High, n (%)			
16–20	42 (54.5)	35 (45.5)			
≥ 20	24 (66.7)	12 (33.3)			
HbA1c level (%)			4.554	3	0.206
0.0–6.5	28 (48.3)	30 (51.7)			
6.6–7.0	15 (11.6)	14 (17.4)			
7.1–8.0	19 (21.5)	35 (64.8)			
≥ 8.0	78(37.1)	132 (62.9)			
Presence of CV risk factor			21.469	1	< 0.001*
Yes	283 (55.0)	455 (68.1)			
No	232 (45.0)	213 (31.9)			
CVDE = cardiovascular disease event; MI = myocardial infarction; IHD = ischaemic heart disease; HbA1c = glycated haemoglobin; CV = cardiovascular.					

Table 7  
Association between patient characteristics and cost among T2DM and non-T2DM patients (N = 1183)

Variables	CVDE with T2DM (n = 715)					CVDE without T2DM (n = 496)				
	Cost, n (%)		$\chi^2$	df	Pvalue	Cost		$\chi^2$	df	Pvalue
	Low	High				Low	High			
Gender			2.101	1	0.147			3.764	1	0.052
Male	192 (56.6)	233 (62.0)				124 (70.5)	229 (78.4)			
Female	147 (43.4)	143 (38.0)				52 (29.5)	63 (21.6)			
Ethnicity			6.385	3	0.094			1.739	3	0.649
Malay	235 (69.3)	245 (65.2)				108 (61.4)	166 (56.8)			
Chinese	34 (10.0)	46 (12.2)				34 (19.3)	71 (24.3)			
Indian	64 (18.9)	84 (22.3)				33 (18.8)	54 (18.5)			
Others	6 (1.8)	1 (0.3)				1 (0.6)	1 (0.3)			
Age category (years)			18.477	5	0.002*			5.747	5	0.332
18–29	16 (4.7)	5 (1.3)				5 (2.8)	2 (0.7)			
30–39	33 (9.7)	15 (4.0)				22 (12.5)	28 (9.6)			
40–49	41 (12.1)	61 (16.2)				35 (19.9)	58 (19.9)			
50–59	94 (27.7)	111 (29.5)				39 (22.2)	81 (27.7)			
60–69	100 (29.5)	120 (31.9)				42 (23.9)	72 (24.7)			
≥ 70	55 (16.2)	64 (17.0)				33 (18.8)	51 (17.5)			
Type of CVDE			83.717	6	<0.001			98.463	6	<0.001
Acute MI	84 (24.8)	67 (17.8)				78 (44.3)	74 (25.3)			
IHD	15(4.4)	114 (30.3)				16 (9.1)	155 (53.1)			
Hypertensive HD	97(28.6)	89 (23.7)				21 (11.9)	17 (5.8)			
Stroke	54 (15.9)	37 (9.8)				41 (23.3)	21 (7.2)			
Heart failure	54 (15.9)	37 (9.8)				9 (5.1)	11 (3.8)			
Cardiomyopathy	23 (6.8)	47 (6.6)				8 (4.5)	12 (4.1)			
PVD	12 (3.5)	20 (2.9)				3 (1.7)	2 (0.7)			
Outcome of admission			12.023	1	0.001*			1.490	1	0.222
Discharged well	326 (96.2)	336 (89.4)				172 (97.7)	279 (95.5)			
Death	13 (3.8)	40 (10.6)				4 (2.3)	13 (4.5)			
Severity level			201.77	2	<0.001*			136.836	2	<0.001*
Severity I	133 (39.2)	41 (10.9)				82 (46.6)	52 (17.8)			
Severity II	201 (59.3)	153 (40.7)				92 (52.3)	84 (28.8)			
Severity III	5(1.5)	182 (48.4)				2 (1.1)	156 (53.4)			
Presence of CVD risk factor			29.226	1	<0.001*					
Yes	180 (53.1)	273 (72.6)								
No	159 (46.9)	103 (27.4)								
Duration of diabetes (years)			6.869	4	0.231					

CVDE = cardiovascular disease event; T2DM = type 2 diabetes; MI = myocardial infarction; IHD = ischaemic heart disease; HD = heard disease; PVD = peripheral vascular disease; CVD = cardiovascular disease; HbA1c = glycated haemoglobin.

Variables	CVDE with T2DM (n = 715)			CVDE without T2DM (n = 496)						
	Cost, n (%)		$\chi^2$	df	Pvalue	Cost		$\chi^2$	df	Pvalue
	Low	High				Low	High			
0–5	161 (47.5)	192 (51.1)								
6–10	61 (18.0)	81 (21.5)								
11–15	60 (17.7)	58 (15.4)								
16–20	28 (8.3)	27 (28.9)								
≥ 20	28 (8.3)	18 (4.8)								
HbA1c level (%)			4.502	3	0.217					
0.0–6.5	15 (17.4)	21 (12.8)								
6.6–7.0	10 (11.6)	9(5.5)								
7.1–8.0	11 (12.8)	23 (14.0)								
≥ 8.0	50 (58.1)	111 (67.7)								

CVDE = cardiovascular disease event; T2DM = type 2 diabetes; MI = myocardial infarction; IHD = ischaemic heart disease; HD = heard disease; PVD = peripheral vascular disease; CVD = cardiovascular disease; HbA1c = glycated haemoglobin.

For multivariate logistic regression analysis, we included nine variables for initial modelling: age, sex, ethnicity, type of CVDE, Sol Index level, and CVD risk. Among these, we identified four variables – gender, ethnicity, type of CVDE and Sol Index level, to be significant. Results for determinants of high treatment cost are shown in Table 8. Females were less likely to incur high CVDE costs compared to males (odds ratio [OR] = 0.66; 95% confidence interval [CI] 0.47–0.93, P = 0.017). Other ethnicities, for example Eurasians, Chindians, and indigenous peoples (Orang Asli), were significantly less likely to incur high treatment costs for CVDE (OR = 0.03; 95% CI 0.003–0.382, P = 0.007). Patients with Sol Index Level II (moderate disease burden) were twice as likely to incur high treatment costs, and this risk increased 262 times higher for patients with Sol Index Level III (high disease burden). Additionally, patient who were admitted with diagnosis of IHD had a 12-fold greater risk for incurring high costs compared with those with acute MI.

Table 8  
Multivariate logistic regression analysis

	$\beta$	SE	Wald	Adjusted odds ratio	95% CI		P value
					Lower	Upper	
<b>Gender</b>							
Male				1			
Female	-0.416	0.174	5.686	0.660	0.469	0.929	0.017
<b>Ethnicity</b>							
Malay			9.315	1			0.025
Chinese	0.333	0.245	1.848	1.395	0.863	2.256	0.174
Indian	0.036	0.216	0.028	1.037	0.679	1.585	0.867
Others	-3.461	1.275	7.363	0.031	0.003	0.382	0.007
<b>Severity level</b>							
Level I			128.509	1			< 0.01
Level II	1.006	0.197	26.09	2.734	1.859	4.022	< 0.01
Level III	5.57	0.497	125.842	262.405	99.16	694.397	< 0.01
<b>Type of CVDE</b>							
Acute MI			125.293	1			< 0.01
IHD	2.49	0.258	93.174	12.056	7.272	19.987	< 0.01
Hypertensive HD	-0.035	0.248	0.019	0.966	0.594	1.570	0.889
Stroke	-0.461	0.264	3.051	0.631	0.376	1.058	0.081
Heart failure	-0.047	0.314	0.022	0.954	0.515	1.767	0.881
Cardiomyopathy	0.438	0.345	1.614	1.550	0.788	3.048	0.204
PVD	0.005	0.54	0	1.005	0.349	2.899	0.992
SE = standard error; CI = confidence interval; CVDE = cardiovascular disease event; MI = myocardial infarction; IHD = ischaemic heart disease; HD = heart disease; PVD = peripheral vascular disease.							

## Discussion

This retrospective, cross-sectional study conducted at three public tertiary hospitals in Malaysia provides evidence regarding the epidemiological, clinical, and economic impact of CVDEs in hospitalised patients with and without T2DM. Malaysia is classified as an upper middle-income country with a total population of 32.7 million people [29]. Healthcare is organised as a two-tiered system consisting of a tax-funded public sector and a fee-for-service private healthcare system [30]. The former provides universal health coverage through a network of government health facilities that caters to the bulk (~ 65%) of the population [31]. Public healthcare is heavily subsidised by the government, with patients paying a nominal fee for inpatient and outpatient services [32]. For example, patients are only charged RM 3 (~ USD 0.70, USD 1 = RM 4.20) for a third-class ward, inclusive of inpatient treatment and ward fees. Sustainability of this healthcare system relies on proficient fiscal management to maintain affordability and quality of care.

In our study, T2DM was present in 60.4% of CVDE patients. This figure was higher than those reported in most studies [33, 34, 35, 36, 37, 38, 39]. Available data indicate a wide range of diabetes prevalence among patients with CVD, between 20–30% in the Western countries [33], 20–60% in China, India and Southeast Asia [34, 35, 36, 37, 38, 39], and nearly 70% in the Middle East [40]. The reasons for the large proportion of patients with T2DM in our cohort may be due to the selection of patients from hospitals in urbanised areas, where risk factors for developing T2DM such as sedentary lifestyle, unhealthy diets, and obesity are prevalent.

The mortality rate among CVDE patients with T2DM in our cohort was twice as high as for patients without T2DM. Previous studies have consistently reported an elevated risk of incident CVDs and premature deaths in patients with T2DM, and these risks are amplified when patients have a history of both T2DM and prior CVDE, in contrast to those with T2DM or prior CVDE alone [16, 42, 43, 44]. As such, patients with T2DM who

have survived a CVDE constitute a particularly vulnerable to recurrent events and increased healthcare expenditure.16 Implementing secondary prevention strategies that prioritise intensified cardioprotective interventions are imperative for these patients.

Studies have shown that patients with diabetes consume more healthcare resources [45, 46, 47], and incur 2.3 times more in hospitalisation cost than the general population [47]. In our T2DM cohort, total treatment cost for all CVDEs exceeded those of the non-T2DM group but the median cost per case in patients with T2DM was lower than in non-T2DM patients. This may be explained by the high proportion of T2DM patients with recently diagnosed or early-stage diabetes, where almost half of the T2DM cohort had a disease duration of  $\leq 5$  years. The non-T2DM group were pre-dominantly male and had a greater proportion of patients with severity Level III illness compared with the T2DM cohort.

We identified four variables predicting high treatment cost for CVDEs. Patients with the following risk profile are likely to incur treatment costs in excess the median threshold: male gender, non-minority ethnicity, IHD diagnosis, and Sol Index Level II. The gender differences in CVDE treatment costs may be attributed to biological and behavioural factors affecting predisposition and disease onset [48]. Premenopausal women experience a higher degree of cardio protection than men of similar age and have a more favourable blood pressure and lipid profile. In addition to that, women are more inclined to exhibit behaviours that lower the risk of CVDs. Studies indicate that they are more likely than men to be non-smokers [49], abstain from or drink less alcohol [50], and adopt healthy eating habits [51]. They also have higher participation in preventive health checks for CVDs and are more likely to seek care early in the disease process [52].

We acknowledge several limitations inherent to the design of our study. Administrative data sources are prone to coding errors, which can lead to incorrect assignment of the DRG codes and inaccurate cost estimations. We have taken steps to address these limitations by selecting audited sites, and have used additional data sources, such as patient medical records and case notes, to ensure a sufficient level of clinical data. In the present study, only costs per episode of care were examined. Therefore, we are unable to draw conclusions regarding lifetime costs or outcomes which will be done from longitudinal data over years. Last but not least, although our dataset was drawn from a demographically diverse, multicentre cohort, our results have limited generalisability. Patients admitted to tertiary hospitals typically require specialised and complex care, so our findings may not be representative of the treatment cost across all of Malaysia.

## Conclusion

This study provides real-world cost estimates for CVDE hospitalisation and quantifies the combined burden of two major NCDs categories at the public health provider level. Results confirm that CVDs are associated with substantial health utilisation in both T2DM and non-T2DM patients. Additional allocation of resources for intensified and targeted public health interventions may be justified to reduce CVD risk factors and to contain public health expenditure. The findings from this study may be used for future health technology assessments and economic modelling.

## Abbreviations

CVD	: Cardiovascular Disease
CVDE	: Cardiovascular Disease Event
DALY	: Disability-Adjusted Life Year
ICD-9-CM	: International Classification of Diseases, 9th Revision, Clinical Modification
ICD-10	: International Classification of Diseases, 10th Revision
IHD	: Ischaemic Heart Disease
LMIC	: Low- and Middle-Income Country
LoS	: Length of Stay
MI	: Myocardial Infarction
NCD	: Non-Communicable Disease
PVD	: Peripheral Vascular Disease
Sol	: Severity of Illness
T2DM	: Type 2 Diabetes Mellitus

## Declarations



## Ethics Approval and Consent to Participate

This study obtained ethics and research approval from the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR-21-01958-1WS) and the Research Ethics Committee, Hospital Canselor Tuanku Muhriz (FF-2021-349).

## Consent for Publication

Not applicable.

## Availability of Data and Materials

The datasets analysed during this study are available from the corresponding author on reasonable request.

## Competing interests

The authors declare that they have no competing interests.

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## Authors' Contributions

SEWP contributed to the conception and design of the study; NAK was involved in data collection, analysis and interpretation of data, and the drafting of the manuscript; ZH, NA and MRS reviewed and revised the study protocol, result and final manuscript. All authors read and approved the final draft of the manuscript. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editor (ICMJE) and did not receive any payment related to the development of the proposal and final report of this CVDE study. SEWP from UKM provided the writing, technical and editorial support which was funded by Boehringer Ingelheim (Malaysia) Sdn Bhd (BI) and BI was given the opportunity to review the manuscript for medical and scientific accuracy as well as intellectual property consideration.

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## Figures

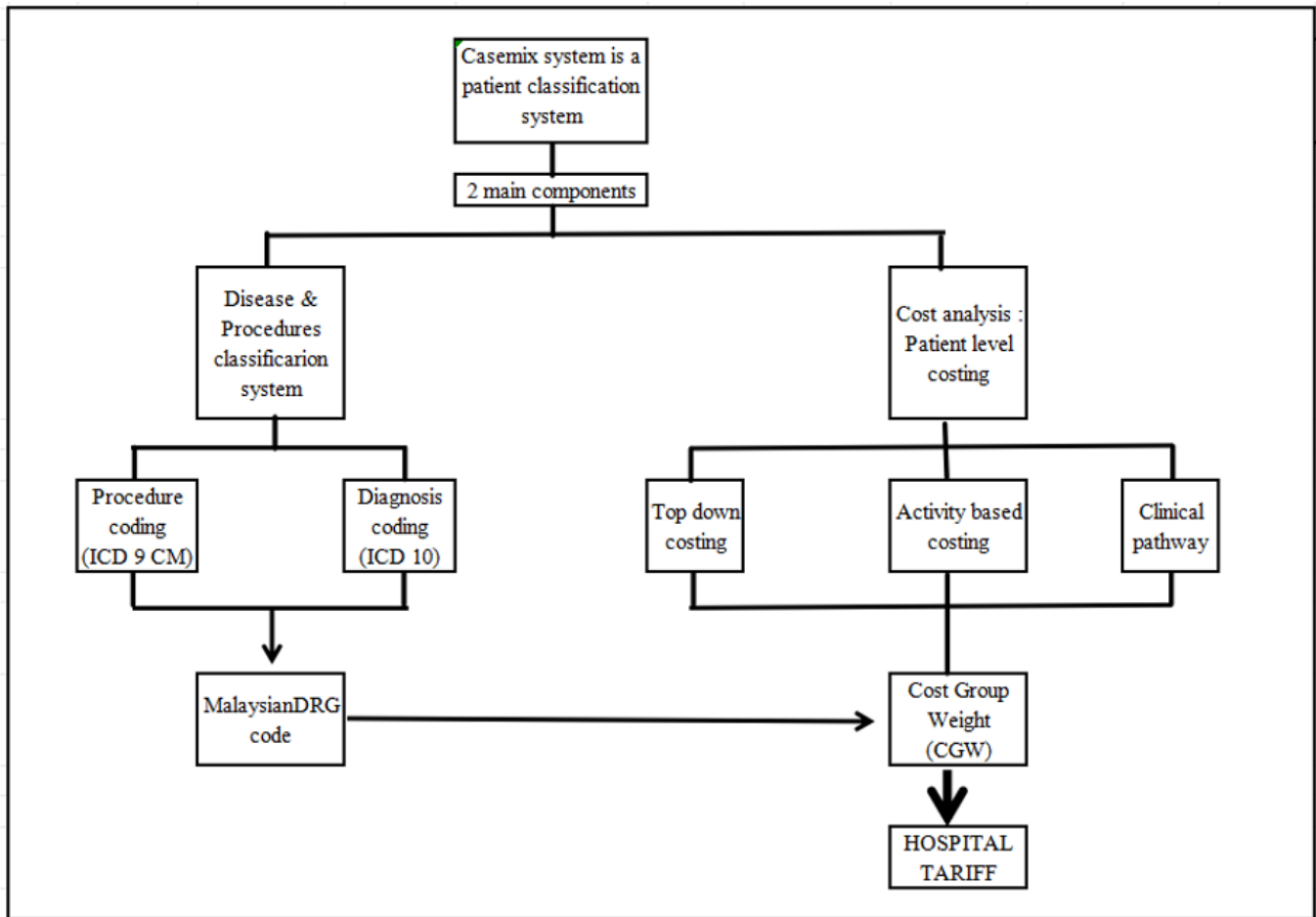


Figure 1

Design components of the Malaysian DRG Casemix System

ICD-10 = International Classification of Diseases 10<sup>th</sup> Revision; MY-DRG = Malaysian Diagnosis Related Group. Reproduced with permission from Zafrah *et al.* 2018 [27].

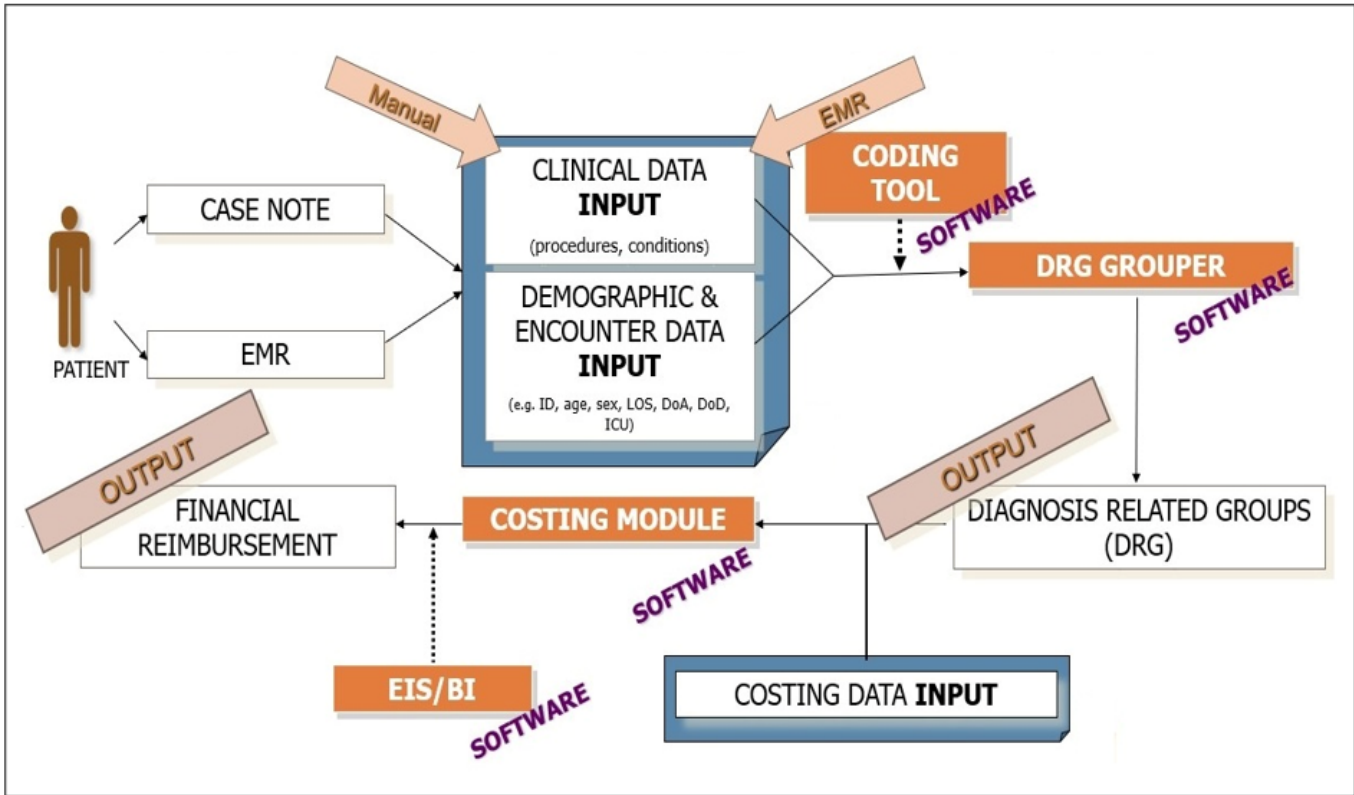


Figure 2

The Malaysian DRGCasemix System workflow

EMR = electronic medical record; EIS = Executive information system; BI = business intelligence; ID = identification; LOS = length of stay; DoA = date of admission; DoD = date of discharge; ICU = intensive care unit; DRG = diagnosis related group. Reproduced with permission from Ministry of Health Malaysia MyHEALTH Portal [28].

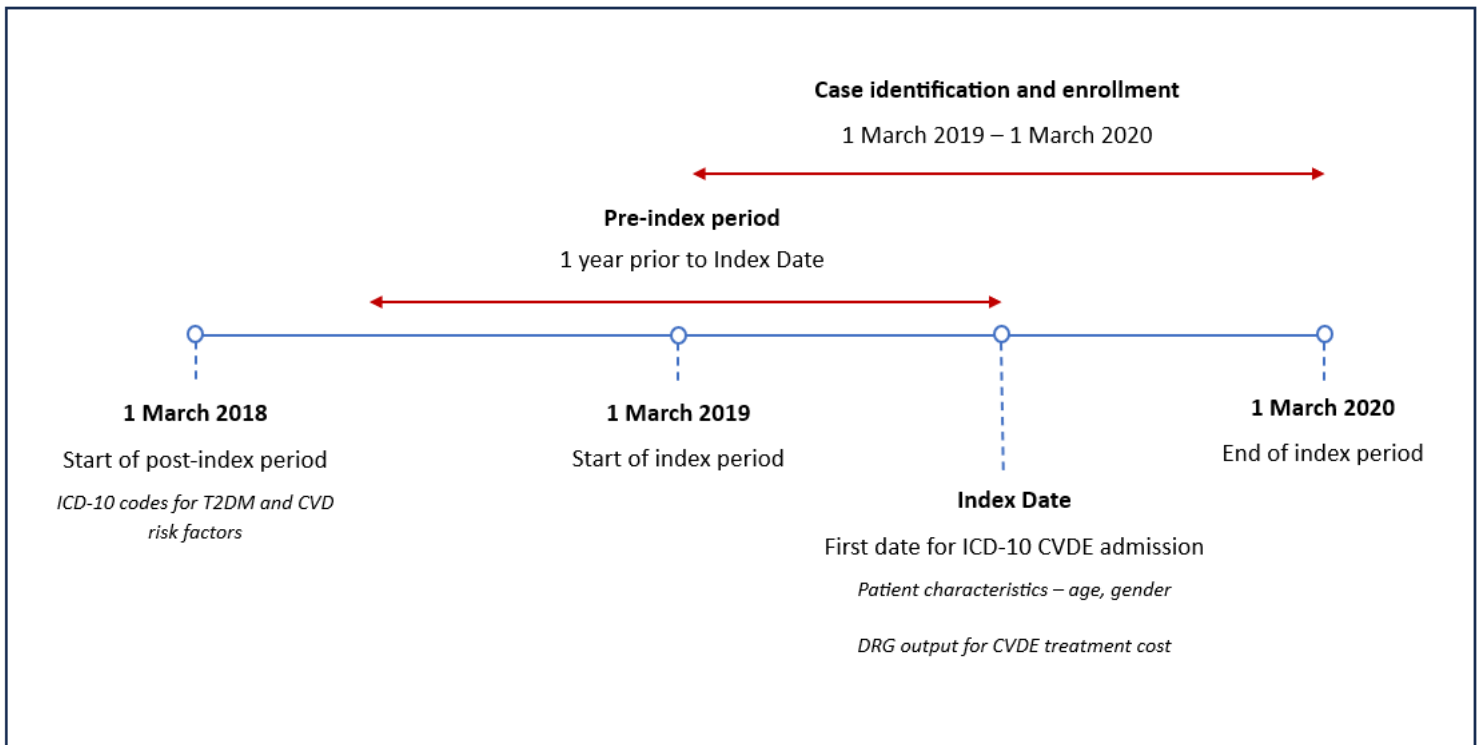


Figure 3

## Study design and schema

ICD-10 = International Classification of Diseases 10<sup>th</sup> Revision; T2DM = type 2 diabetes mellitus; CVD = cardiovascular disease; CVDE = cardiovascular disease event; ; DRG = diagnosis related group.

## Supplementary Files

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