



Real-world cost-effectiveness of drug-eluting stents vs. bare-metal stents for coronary heart disease—A five-year follow-up study

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ABSTRACT

Objective: To evaluate the cost-effectiveness of using drug-eluting stents (DES) compared to bare-metal stents (BMS) for coronary heart disease (CHD).

Data sources/study setting: Data were obtained from the National Health Insurance Longitudinal Health Insurance Database, which contains claims data for 1,000,000 beneficiaries. The data were randomly sampled from all beneficiaries.

Study design: A retrospective claims data analysis.

Data collection/extraction methods: Patients with stable coronary heart disease who underwent coronary stent implantation from 2007 to 2008 were recruited and followed to the end of 2013. After a 2:1 propensity score matched by gender, age, stent number, and the Charlson comorbidity index (CCI), 852 patients with 568 stents in the BMS group and 284 stents in the DES group were included. The cumulative medical costs for both matched groups were estimated with the Kaplan-Meier Sample Average (KMSA), and then the incremental cost-effectiveness ratio (ICER) was estimated.

Principal findings: The ICER of DES vs. BMS was NT\$ 663,000 per cardiovascular death averted and NT\$ 238,394 per cardiovascular death or coronary event averted in five years from the insurer perspective.

Conclusion: Percutaneous coronary intervention (PCI) with DES was a more cost-effective strategy than PCI with BMS for CHD patients during the five-year follow-up.

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1. Introduction

Coronary heart disease (CHD) was the leading cause of death worldwide between 1995 and 2009. It caused approximately one of every five deaths in the United States in 2005 [1], and it has been

ranked as one of the top three leading causes of death in Taiwan since 2000, gradually increasing from 49.2 per 100,000 population in 2001, to 67.7 in 2010, and to 81.8 in 2015 [2–4]. Strategies for coronary artery revascularization include percutaneous coronary intervention (PCI) with coronary stenting and coronary artery bypass grafting (CABG).

Coronary stenting has emerged as an effective strategy to prevent restenosis of the coronary artery after the PCI. Re-establishment of the coronary blood flow, with the subsequent relief of symptoms, can be readily achieved in most patients. Drug-eluting stents (DESs) have been shown to reduce the rate of the target vessel revascularization (TVR) and the target lesion revascularization (TLR) compared with bare metal stents (BMSs). For these reasons, DESs have been widely used since their launch in 2003.

The Taiwan National Health Insurance (NHI) program, launched in 1995, is a mandatory, compulsory, single-payer social health

Abbreviations: DES, drug-eluting stents; BMS, bare-metal stents; CHD, coronary heart disease; CCI, Charlson comorbidity index; KMSA, Kaplan-Meier Sample Average; ICER, incremental cost-effectiveness ratio; PCI, Percutaneous coronary intervention; CABG, coronary artery bypass grafting; TVR, target vessel revascularization; TLR, target lesion revascularization; NHI, National Health Research Institutes National Health Insurance; WHO, World Health Organization; MACE, major adverse cardiovascular events.

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insurance system that covers 99.9% of the population [5]. The benefits package is comprehensive; all necessary medical services are covered. The benefits package includes inpatient and outpatient care, dental services, and traditional Chinese medicine, and it maintains a list of approximately 20,000 prescription drugs. The coverage of health technology is one of the leading factors that increases the costs of all health insurance plans. Taiwan regulates medical devices and pharmaceuticals under the same legislation. According to the National Health Act, to be eligible for NHI reimbursement, a new medical service must be proven to have both comparative effectiveness and cost-effectiveness for the NHI, after the manufacturers have received marketing approval from the TFDA [6]. After a product has been added to the reimbursement list by the BNHI, it can be used at any healthcare facility in Taiwan.

The diffusion and affordability of health technology is an emerging health policy issue of critical concern in developed and developing countries. To balance the technological adoption, patient needs, and budgets, balance billing was initiated in August 1999. In December 2006, the drug eluting stents was included as one of the balance billing items. The National Health Insurance provides the basic coverage (bare metal stent), and beyond that patients will have to pay the price differentials for better services (drug-eluting stent). Hence, patient can choose any kinds of stents, as long as they are willing to pay the price differences between the reimbursed prices for bare metal stent.

In Taiwan, the use of BMS and DES has gradually increased, with growth rates of 8% and 24%, respectively, between 2005 and 2008. After introducing balance billing, the number of claims soared from 521 (2006) to 14,311 (2010), and total claims reimbursements increased from NT\$15 million to NT\$300 million [7]. The NHI started to cover BMS in 1997, with the reimbursement price of NT\$54,000. Since then, the price has decreased dramatically to NT\$27,000 in 2006, and NT\$14,099 in 2016, primarily due to the monopoly purchasing power of the NHI. However, according to our survey, the price of DES ranged from approximately NT\$70,000 to NT\$90,000, and it decreased at a much lower rate than BMS did during our study period. The average out-of-pocket payment for balance billing was NT\$55,168. We expect that if DES were covered by the NHI, the price would significantly decrease.

The use of DESs has been demonstrated to be effective in reducing not only the risk of restenosis but also the incidence of repeated revascularization, compared with BMSs [8–11]. In our previous study, we demonstrated that the use of DES rather than BMS was associated with reduced cumulative coronary events and mortality in a multivariable proportional hazard regression model, after adjusting for age, sex, premium-based monthly salary, levels of hospital care, stent number, Charlson comorbidity index (CCI), medications, and acute coronary syndrome presentation in the index hospitalization [12].

To date, no population-based study has investigated differences in the medical costs of DES and BMS after the balance billing of DES in Taiwan and the corresponding cost-effectiveness. In addition, there has been no comprehensive analysis of the utilization of medical resources for patients with coronary stents. Thus, this study has attempted to compare the medical utilization and cost between patients with DES and those with BMS by analysing the population database.

2. Materials and method

2.1. Patients and study design

We conducted a retrospective cohort study based on the NHI program. Data were obtained from the National Health Research Institutes Longitudinal Health Insurance Database (LHID). The LHID

contains all original claims data for 1,000,000 beneficiaries, randomly sampled from the 2005 Registry of all Beneficiaries ($n = 25.68$ million) under the NHI program [13]. The time horizon of the whole study was 8 years, spanning from 2006 to 2013. Year 2006 was used as the washout period. Patients with stable coronary heart disease who had received coronary stent implantation between Jan. 2007 and Dec. 2008 were recruited and each patient was followed for five years. In total, 1038 patient visits for BMS and 568 patient visits for DES were included. Because there was no itemized payment information, we excluded self-paying patients. We also excluded patients who were not fresh cases. Patients who had received both BMS and DES during the same procedure or had been stented a year before were also excluded. Before matching, we included a total of 1188 patients, 789 patients with BMS and 399 with DES. After a 2:1 propensity score matched by gender, age, stent number, and the CCI, 852 patients with stenting were included in the study: 568 in the BMS group, and 284 in the DES group (Appendix 1). Large computerized de-identified databases derived from this system by the Bureau of National Health Insurance, Taiwan (BNHI) and maintained by the National Health Research Institutes, Taiwan, are provided to scientists in Taiwan for research purposes.

2.2. Medical cost and effectiveness

Costs were estimated from National Health Insurance payer's perspective and were reported in 2013 NT dollar. The resource utilization included the admission days, overall and heart disease related health care costs (inpatient and outpatient), overall and heart disease related follow-up clinic visits, and overall and heart disease related readmitted rates. We identified the heart disease related data using the diagnosis code for "diseases of the circulatory system" (ICD-9-CM code: 390~459), or the operating room procedure code for "operations on the cardiovascular system" (ICD-9-CM code: 35~39). The primary endpoint effectiveness was defined as the reduction of death, while the secondary endpoint was death or major adverse cardiac events, such as cardiac death, nonfatal myocardial infarction, and target vessel revascularization. MI was defined using the ICD-9-CM code: 410, as the principle diagnosis of admission, and confirmed by visits to the emergency department and utilizations of intensive care. Death was further identified by the National Death Registry.

2.3. Statistical analysis

Continuous variables were presented as the mean \pm standard deviation and were compared with Student's *t*-test. Categorical variables were presented as numbers and percentages and were compared using the Cochran-Mantel-Haenszel Chi-squared test. Clinical characteristics between the study groups (DES and BMS) were compared with the Chi-squared test for categorical variables and *t*-test for continuous variables, as appropriate. Log-linear regression was used to examine the effectors associated with the cardiovascular care expenditure. All statistical tests were two-tailed and were conducted using SAS 9.3 (SAS Institute Inc., Cary, North Carolina, USA) and SPSS 18 (SPSS Inc., Chicago, Illinois, USA). A *P* value of <0.05 was defined as being significant.

We estimated the cumulative medical cost for these two matched groups by conducting Kaplan-Meier Sample Average (KMSA) estimates [14,15]. Using this technique, the follow-up period for each patient was partitioned into one-year intervals, and the Kaplan-Meier estimates of the probability of survival were calculated. Medical costs were then calculated as the sum of the Kaplan-Meier estimates of the probability of survival to the beginning of each interval, multiplied by the corresponding estimates of costs, during the interval, being conditional on survival to the beginning of the interval [14,15]. Given that we have demonstrated

the survival benefit associated with DES compared with BMS for mortality and adverse coronary events [12], we further estimated the sensitivity analysis of the incremental cost-effectiveness ratio (ICER) of DES compared to BMS per death or coronary event averted. The average out-of-pocket payment for each DES was NT\$55,168, based on the information provided by the National Health Insurance Administration Ministry of Health and Welfare [16]. The out-of-pocket payment and a discount rate of 3.5% were used for the sensitivity analysis.

3. Results

The characteristics of patients with BMS and DES (before and after the propensity matching) are summarized in Table 1. After matching, both BMS and DES were balanced on all the covariates included in the PS model (standardized differences were smaller than 0.001). In both study groups, 23.6% were female and 76.4% were male, 48.2% ranged from 30 to 64 years of age, 51.8% were older than 65 years of age, and the mean patient age was 65 years. A total of 27.8% of patients had the lowest premium-based monthly salary (\leq NT\$19,200), 31.0% of patients had a monthly premium-based salary ranging from NT\$19,201 to NT\$21,900, and 41.2% of patients had the highest monthly premium-based salary of more than NT\$21,900. The percentages of 1, 2, and 3 implanted stents were 80.6%, 17.3%, and 2.1%, respectively, and the percentages of CCI scores of 0–1, 2, and >3 were 33.1%, 21.5%, and 45.4%, respectively.

3.1. Medical utilization of study population

Table 2 compares the health care utilization and outcomes of both study groups over a five-year period. The average number of outpatient visits was 32.3 in the DES group and 27.7 in the BMS group ($p=0.004$) in the first year, and the between-group difference in the number of outpatient visits decreased and was not significantly different in the second to the fifth follow-up years. In the first year, in the DES group, 12.7 outpatient visits were related to cardiovascular diseases and 10.8 visits were related to cardiovascular diseases in the BMS group ($p=0.0006$); these visits gradually dropped to 9.8 in the DES group and 8.6 in the BMS group in the second year ($p=0.04$) and 7.8 in the DES group and 8.2 in the BMS group in the fifth year ($p=0.41$); the total number of visits for the five-year follow-up period ($p=0.005$) was 43.8 in the DES group and 38.3 in the BMS group. Throughout the five-year follow-up period, the readmission rate for cardiovascular disease gradually decreased from the 1st year to the 5th year (75.6% in the DES group and 72.5% in the BMS group in five years). However, there was no significant between-group difference in the readmission rate.

The average length of hospital stay was five days in the DES group and 7.2 days in the BMS group ($p=0.0005$). The in-hospital mortality rate was not different between the BMS group (2.1%) and the DES group (0.7%) during index hospitalization. The cumulative mortality was significantly lower in the DES group (20.4%) than in the BMS group (28.3%). According to the Cox proportional regression analysis, DES was associated with a significantly lower mortality rate (hazard ration [HR] and 95% confidence interval [C.I.]: 0.67, 0.51–0.89) and lower cumulative coronary event rate (HR=0.65, 95% C.I.=0.49–0.99) than BMS (Table 2).

3.2. Cumulative medical cost and ICER

As shown in Appendix 2, using the KMSA estimates, with a discount rate of 3.5%, the DES group had higher cumulative outpatient, inpatient, and cardiovascular diseases related outpatient costs than the BMS group, with differences of NT\$77,0105, NT\$13,196, and NT\$25,3024, respectively. However, the DES group had a lower

cumulative inpatient cost related to cardiovascular disease, and the difference was NT\$ -25,437.

The ICER of DES vs. BMS was NT\$1,141,860 per death averted in five years and NT 1,176,946 per death or coronary event averted in five years. After including the average out-of-pocket cost (NT\$55,168) into the total expenditures, the ICER increased to NT\$1,840,190 per death averted in five years and NT\$ 1,707,404 per death or coronary event averted. However, the total costs included all disease treatments during the study period. The ICER of DES vs. BMS was NT\$ 663,000 per death related to cardiovascular disease averted and NT\$ 238,394 per cardiovascular death or coronary event averted in five years. Even after including the out-of-pocket cost (NT\$55,168), the ICER increased to NT\$1,361,331 per cardiovascular death averted and NT\$ 768,856 per cardiovascular death or coronary event averted in five years (Table 3).

The predictors for cardiovascular disease-related outpatient costs were stent type ($e\beta=1.35$; $p=0.001$), as well as the procedure to treat acute coronary syndrome (ACS). The predictors of cardiovascular disease-related inpatient costs were stent number (2 stents $e\beta=1.16$ $p<.001$) and CCI (score of 2 or ≥ 3 ; $p<.0001$) (Table 4).

Compared to patients with 1 stent, patients with 2 stents had a 1.16 times greater risk of having increased cardiovascular related costs. Compared to patients with a 0–1 point CCI score, patients with CCI scores of 2 points and ≥ 3 points had an increased risk of death, with HRs of 1.22 and 1.79, respectively.

4. Discussion

This study used propensity score matching to match baseline clinical characteristics of the studied populations identified in the NHRI LHID, and it followed patients' clinical events and resulting medical costs longitudinally. Through this process, the use of DES was found to be associated with a significantly lower incidence of death and coronary events five years after PCI, as well as lower five-year cumulative inpatient costs related to cardiovascular disease in Taiwan. The estimated ICER per death averted was NT\$1,141,861. If the cost included out-of-pocket expenses, the ICER was NT\$1,840,190 per death avoided in five years. If we only count the costs related to cardiovascular diseases, then the estimated ICER per death averted was NT\$663,000. If the cost also included out-of-pocket expenses, then the ICER was NT\$1,361,331 per death avoided in five years. Considering all cardiovascular deaths or coronary events avoided by using DES rather than BMS, the ICER was NT\$238,394 or NT\$768,856 with out-of-pocket expenses. The World Health Organization (WHO) recommended that an ICER between one and three times GDP per capita is cost effective, and in 2013, the GDP of Taiwan was NT\$1,957,287 ($652,429 \times 3$); therefore, our results suggest that DES for CHD, compared with BMS, may well be cost effective.

Numerous clinical trials have been conducted to investigate the effectiveness of DES vs. BMS in treating CHD. By synthesizing the results of these randomized controlled trials, previous systematic reviews and meta-analyses have demonstrated that DES was more effective than BMS in reducing major adverse cardiovascular events (MACE) for patients with stable CHD [17], unprotected left main CHD [18], and ST-segment-elevation myocardial infarction [19]. Moreover, in previous RCTs comparing DES with BMS, the ICER per QALY gain was more than US\$50,000 [20]. Therefore, it has been suggested that DES should be reserved for patients with complex CHD. Cohen et al. have investigated the cost-effectiveness of DES vs. bypass surgery for patients with complex CHD in the SYNTAX trial [21]. The authors suggested that DES was the economically superior strategy, compared with bypass surgery, for patients with left main coronary artery disease or a SYNTAX score of less than

Table 1
Patient Characteristics of BMS and DES Groups before and after Matching.

Variable	Before Matching		P value	Standardized mean difference	After Matching		P value	Standardized mean difference
	BMS (n = 789) N (%)	DES (n = 399) N (%)			BMS (n = 568) N (%)	DES (n = 284) N (%)		
Gender			0.84				1.0	
Female	218 (27.6%)	108 (27.1%)		0.013	134 (23.6%)	67 (23.6%)		0.000
Male	571 (72.4%)	291 (72.9%)		−0.013	434 (76.4%)	217 (76.4%)		0.000
Age			0.42				1.0	
30–64	368 (46.6%)	196 (49.1%)		−0.050	274 (48.2%)	137 (48.2%)		0.000
≥65	421 (53.4%)	203 (50.9%)		0.050	294 (51.8%)	147 (51.8%)		0.000
Premium-based monthly salary (\$NT)			<.001 ^a				1.0	
≤19,200	237(30.0%)	108(27.1%)		0.067	158 (27.8%)	79 (27.8%)		0.000
19,201~21,900	293(37.1%)	108(27.1%)		0.226	176 (31.0%)	88 (31.0%)		0.000
≥21,901	259(32.9%)	183(45.8%)		0.261	234 (41.2%)	117 (41.2%)		0.000
Disease Severity								
Stent number			0.03 ^a				1.0	
1	589 (74.7%)	272 (68.2%)		0.107	458 (80.6%)	229 (80.6%)		0.000
2	159 (20.2%)	94 (37.2%)		−0.077	98 (17.3%)	49 (17.3%)		0.000
≥3	41 (5.2%)	33 (8.3%)		−0.068	12 (2.1%)	6 (2.1%)		0.000
CCI (points)			0.02 ^a				1.0	
0–1	232 (29.4%)	151 (37.8%)		−0.174	188 (33.1%)	94 (33.1%)		0.000
2	188 (23.8%)	87 (21.8%)		0.049	122 (21.5%)	61 (21.5%)		0.000
≥3	369 (46.8%)	161 (40.4%)		0.131	258 (45.4%)	129 (45.4%)		0.000

BMS = Bare metal stent; DES = Drug-eluting stent; CCI = Charlson comorbidity index.

^a Chi-Square test.**Table 2**
Comparison of Medical Utilization and Outcome for BMS and DES Groups.

Variable	BMS (n = 568) N(%) /mean ± SD	DES (n = 284) N(%) /mean ± SD	p value	BMS (n = 568) N(%) /mean ± SD	DES (n = 284) N(%) /mean ± SD	p value
Outpatient Visits				Cardiovascular diseases Outpatient visit		
1 st year	27.7 ± 21.3	32.3 ± 22.5	*0.004 ^a	10.8 ± 6.9	12.7 ± 8.0	*.0006 ^a
2 nd year	27.9 ± 22.3	30.6 ± 23.5	0.11	8.6 ± 6.8	9.8 ± 8.0	*0.04 ^a
3 rd year	28.1 ± 22.0	28.5 ± 21.0	0.81	8.5 ± 7.0	8.8 ± 6.3	0.79
4 th year	27.4 ± 22.0	28.6 ± 20.2	0.47	8.0 ± 6.1	8.5 ± 6.9	0.3
5 th year	27.2 ± 25.3	27.0 ± 24.5	0.88	8.2 ± 6.8	7.8 ± 5.8	0.41
Total	118.3 ± 96.4	134.2 ± 93.6	*0.02 ^a	38.3 ± 26.5	43.8 ± 28.4	*0.005 ^a
Readmission Rates				Cardiovascular diseases Readmission rates		
1 st year	279 (49.1%)	138 (48.6%)	0.88	267 (47.0%)	129 (45.4%)	0.66
2 nd year	171 (34.4%)	103 (38.6%)	0.25	155(31.2%)	87 (32.6%)	0.69
3 rd year	153 (32.6%)	90 (35.4%)	0.45	141 (30.1%)	83 (32.7%)	0.47
4 th year	138 (30.1%)	73 (30.0%)	0.87	128 (28.0%)	68 (27.5%)	0.91
5 th year	134 (30.7%)	80 (33.3%)	0.49	122 (28.0%)	75 (31.3%)	0.37
Total	434 (76.4%)	222 (78.2%)	0.56	412 (72.5%)	214(75.6%)	0.38
Length of Stay	7.2 ± 11.9	5.0 ± 6.9	*0.0005 ^a			
Die during Hospitalization	12 (2.1%)	2 (0.7%)	0.16b ^b			
Cumulative mortality, N (%)			*0.004 ^c			
One year	71(12.5%)	17 (6.0%)				
Two years	99 (17.4%)	30 (10.6%)				
Three years	110 (19.4%)	37 (13.0%)				
Four years	132 (23.3%)	44 (15.5%)				
Five years	155 (28.3%)	58 (20.4%)				
Risk of mortality HR (95% CI)		0.67 (0.51–0.89)	*0.006 ^d			
Cumulative cardiovascular event rate, N (%)			*0.0387 ^c			
One year	47(8.3%)	5(1.8%)				
Two years	54(9.5%)	12(4.2%)				
Three years	63(11.1%)	17(6.0%)				
Four years	69(12.1%)	21(7.4%)				
Five years	77(13.6%)	29(10.2%)				
Risk of cardiovascular event HR (95% CI)		0.65(0.49–0.99)	*0.0442 ^d			

BMS = bare-metal stent; DES = drug-eluting stent; HR = hazard ratio; CI = confidence interval.

^a t-test.^b Fisher's exact test.^c Log-rank test.^d Cox Proportional Hazard Regression Model, based on different stent type.

Table 3
Sensitivity analysis of the incremental cost-effectiveness ratio (ICER) for per death reduced and death or coronary event reduced.

	Cost		Effect		ΔCost	ΔEffect	ICER
	DES	BMS	DES	BMS			
Total Treatment Cost Discounted 3.5%							
Death reduced	NT\$736,632	NT\$646,425	0.204	0.283	NT\$90,207	0.079	NT\$1,141,861
Death(+DES out-of-pocket NT\$55,168)	NT\$791,800	NT\$646,425	0.204	0.283	NT\$145,375	0.079	NT\$1,840,190
Death or coronary event reduced	NT\$713,462	NT\$591,060	0.255	0.359	NT\$122,402	0.104	NT\$1,176,942
Death or coronary event reduced (+DES out-of-pocket NT\$55,168)	NT\$768,630	NT\$591,060	0.255	0.359	NT\$177,570	0.104	NT\$1,707,404
Cardiovascular Treatment Related Cost (Discounted 3.5%)							
Death reduced	NT\$455,568	NT\$403,191	0.204	0.283	NT\$52,377	0.079	NT\$663,000
Death(+DES out-of-pocket NT\$55,168)	NT\$510,736	NT\$403,191	0.204	0.283	NT\$107,545	0.079	NT\$1,361,331
Cardiovascular Disease treatment costs Discounted 3.5%							
Death or coronary event reduced	NT\$439,719	NT\$414,926	0.255	0.359	NT\$24,793	0.104	NT\$238,394
Death or coronary event reduced (+DES out-of-pocket NT\$55,168)	NT\$494,887	NT\$414,926	0.255	0.359	NT\$79,961	0.104	NT\$768,856

DES = Drug-eluting stent.
Cost: Five years cumulative medical costs Effect: Five years cumulative mortality rate.

Table 4
Predictors of cardiovascular diseases related costs.

Variable	Outpatient		Impatient	
	e ^β	p (95% CI)	e ^β	p (95% CI)
Stent type				
BMS(reference)	1		1	
DES	1.35	<.001 (0.17-0.45)	0.97	0.57 (-0.12-0.07)
Sex				
Female(reference)	1			
Male	0.91	0.27 (-0.26-0.71)	1.01	0.82 (-0.10-0.12)
Age(yr) 1.00		0.18 (-0.01-0.002)	1.00	0.07 (-0.0003-0.008)
Insurance amount (NTD)				
≤19,200 (reference)	1		1	
19,201~21,900	1.11	0.27 (-0.08-0.28)	1.07	0.28 (-0.05-0.18)
≥21,901	1.10	0.28 (-0.07-0.26)	1.05	0.37 (-0.06-0.16)
Hospital level				
Medical center (reference)	1			
Non-medical center	1.02	0.79 (-0.12-0.16)	1.01	0.80 (-0.08-0.11)
Stent number				
1(reference)	1		1	
2	0.97	0.72 (-0.21-0.14)	1.16	*0.01 (0.03-0.26)
3	0.97	0.91 (-0.51-0.45)	1.27	0.13 (-0.07-0.55)
CCI				
0-1(reference)	1		1	
2	1.13	0.21 (-0.07-0.31)	1.22	*0.0019 (0.07-0.33)
≥3	1.16	0.08 (-0.02-0.31)	1.79	*<.0001 (0.47-0.69)
Procedure for ACS				
Yes (reference)	1		1	
No	1.19	0.01 (0.04-0.41)	0.98	0.66 (-0.11-0.07)

Dependent variable = log(heart related cost).
CCI = Charlson comorbidity index.
ACS = Acute coronary syndrome.

22.The cost effectiveness of DES vs. BMS has been studied in the Korean National Health Insurance Database [22]. In that study, Lee et al. demonstrated that the ICER was KRW256,315 (=NT\$7281)/per death avoided by using DES vs. BMS for CAD patients during four years of follow-up. The major limitation of the study was that the differences of the effectiveness between DES vs. BMS were not adjusted for some important confounders, such as income and/or disease severity and, therefore, might be overestimated. Kaiser et al. showed in a real world setting DES were more cost effective for elderly patients in specific high-risk groups such as the diabetics and small vessel disease and suggested DES than for all patients [23]. Using Taiwan NHRI LHID, the treatment strategy for CHD was at the discretion of physicians and patients and, therefore, reflects real-world practice. Usually, patients who have undergone bypass surgery in Taiwan had more complex CHD and were associated with a lower socio-economic status [24].

As a result, we focused the comparison between DES and BMS for CHD. Moreover, to account for possible confounders that might have influenced the effectiveness of different treatment strategies Our study suggests that even considering the inclusion of out-of-pocket expenses, DES may be a more cost-effective strategy than BMS for CHD. Moreover, most of our study population had a single vessel disease (Table 1), which suggested that DES could still be more cost-effective than BMS for patients with less complex CHD.

Previous studies have primarily used modelling simulation to evaluate the cost-effectiveness of DES compared to BMS in patients undergoing PCI. The advantages of our study were adopting the NHI claim data and using propensity score matching to ensure the equivalence between the DES and the BMS groups. Using real-world data for health technology assessment could provide timely and effective information to the government for local regulation decisions. In general, clinical original studies were more

interested in highlighting outcomes for different subgroups, but our study focused more on the policy implication for the reimbursement. Hence, we did not focus on analyzing the optimized cost-effectiveness results.

However, this study has some limitations. First, although we used a propensity-matching score to balance the baseline characteristics between the two groups, there might be some unmeasured confounders that could have affected the clinical outcomes associated with DES or BMS and that may have biased our evaluations of the comparative effectiveness. Second, the severity of CHD could not be assessed through angiography. In addition, we did not measure patients' potential quality of life improvement. Hence, a cost-utility approach was excluded due to lack of utility value.

Therefore, the characteristics of the coronary artery blockage could not be ascertained or explained. Nonetheless, we did adjust the comorbidity by using CCI scoring, which might have influenced the treatment and follow-up medical costs. Third, we could not confirm the site of coronary stent deployment. Therefore, it was unclear whether revascularization was at the same site for in-stent restenosis or for de-novo lesions.

Future studies, including those investigating patient quality of life (QoL) data, CHD severity, and the comparative arm of bypass surgery, may help to provide more comprehensive information relating to the decision making process.

5. Conclusions

Our study demonstrated that percutaneous coronary intervention (PCI) with DES was associated with better clinical outcomes and acceptable higher medical costs and, therefore, could be a more cost-effective strategy than BMS for patients with CHD. Based on the decreasing costs of the DES device, we suggest that the NHI should seriously consider fully reimbursing for DES instead of the current balance billing policy.

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Competing interests

The authors declare that they have no competing interests

Authors' contributions

HMC, HCL&CHC participated in the conception and design of the study, and interpretation and drafted the manuscript. LJC, TCC, SHS participated in data analysis and drafted the manuscript. All authors contributed interpretation of findings and preparing, reading, revising, and approving the manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.healthpol.2018.11.010>.

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