BMJ Open Comparison of biodegradable and durable polymer drug-eluting stents in acute coronary syndrome: a meta-analysis

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Correspondence to Dr Can Huang; huangcan413@csu.edu.cn ABSTRACT Objective To

Objective To compare the safety and effectiveness between biodegradable polymer drug-eluting stents (BP-DES) and durable polymer drug-eluting stents (DP-DES) in patients with acute coronary syndrome (ACS). **Design** Meta-analysis of randomised controlled trials (RCTs).

Primary and secondary outcome measures Major adverse cardiovascular events (MACEs) were considered the primary endpoint. Efficacy endpoints included target vessel revascularisation (TVR) and target lesion revascularisation (TLR). Safety endpoints included allcause death, cardiac death, target vessel myocardial infarction and stent thrombosis (ST).

Methods We searched PubMed, Medline, Embase and the Cochrane Controlled Register of Trials for comparative studies of BP-DES and DP-DES in patients with ACS from January 2000 to July 2021. Statistical pooling was performed to estimate incidence using a random-effects model with generic inverse-variance weighting. Risk estimates were computed with 95% Cls.

Results Eight articles with seven RCTs that compared BP-DES and DP-DES in patients with ACS were identified and included in the qualitative and quantitative analyses. There was no difference in the baseline characteristics. except for the number of smoking patients (OR: 1.13, 95% CI 1.03 to 1.24; p=0.008, I²=29%), which was significantly lower in the BP-DES group. The metaanalysis demonstrated that MACEs, efficacy endpoints and safety endpoints were similar between the groups at 1 vear. However, the incidence of total ST was significantly different between the BP-DES and DP-DES groups in the follow-up period (p=0.0001). Further analysis showed a statistically significant difference in MACEs (OR: 0.71, 95% CI 0.57 to 0.88; p=0.002, I²=0 %), TLR (OR: 0.71, 95% CI 0.51 to 1.01; p=0.05, I²=0%), TVR (OR: 0.70, 95% CI 0.52 to 0.94; p=0.002, I²=15%), total ST incidence $(OR: 0.59, 95\% CI 0.46 \text{ to } 0.77; p=0.0001, I^2=48\%)$ and ST incidence (OR: 0.63, 95% CI 0.47 to 0.85; p=0.002, I²=0%) over 2 years.

Conclusion This meta-analysis revealed that both stent types demonstrated excellent safety and efficacy profiles at 12 months. However, a slight increase in MACEs, TLR, TVR and ST incidence was observed in the DP-DES group over the 2-year follow-up period, suggesting that BP-DES may be more favourable when treating patients with ACS.

Trial registration number NCT00389220.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This meta-analysis included randomised controlled trials with long-term follow-ups.
- ⇒ The large sample size ensures adequate statistical power to detect even a small effect of interest.
- ⇒ Heterogeneity among the biodegradable polymer drug-eluting stents may distort the reported results.
- \Rightarrow The differences in the duration of dual antiplatelet therapy may influence clinical outcomes.

INTRODUCTION

Percutaneous coronary intervention (PCI) is the current standard of care for patients with coronary artery disease, particularly acute coronary syndrome (ACS).^{1 2} Unlike baremetal stents (BMS), drug-eluting stents (DES) use antiproliferative agents embedded in a polymer coating on the stent's surface, which inhibit neointimal hyperplasia to reduce the risk of restenosis.³ DES have substantially improved clinical outcomes; however, the first-generation durable polymer DES (DP-DES) were known to release sirolimus or paclitaxel, and were associated with similar risks of death and myocardial infarction compared with those of BMS beyond 1 year after implantation.⁴ Later, the second-generation DP-DES were confirmed to have lower restenosis rates than the first-generation devices and demonstrated reduced rates of stent thrombosis (ST).⁵ Recently, very late ST and neoatherosclerosis, with adverse clinical outcomes, have been observed with the second-generation DP-DES, which has improved the biocompatibility of the polymer.⁶ Late stent failure has been attributed to delayed endothelial healing secondary to a hypersensitivity reaction due to the DP.⁷

To address this potential limitation of DP-DES, biodegradable polymer DES (BP-DES) have been developed. Theoretically, BP-DES would lead to a reduction in vascular inflammation and a decreased risk of late



	В	P-DES		D	P-DES			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl		IV, Fixed, 95% Cl		
Antoinette de Waha 2015	62.5	12.1	291	63.1	12.6	206	5.5%	-0.60 [-2.81, 1.61]				
Hyo-Soo Kim 2021	63.1	11.1	1700	63	11.1	1713	48.6%	0.10 [-0.64, 0.84]				
Hyun Jong Lee 2015	64	14.08	171	63	14.08	536	4.6%	1.00 [-1.42, 3.42]				
Juan F Iglesias 2019	62.2	11.8	649	63.2	11.8	651	16.4%	-1.00 [-2.28, 0.28]				
Qi Zhang 2014	63.9	13.1	596	64.1	12.1	596	13.1%	-0.20 [-1.63, 1.23]				
Thomas Pilgrim 2016	61.3	12.4	211	61.7	12.7	196	4.5%	-0.40 [-2.84, 2.04]				
Yao-Jun Zhang 2015	62.9	11.7	280	62.8	11.7	293	7.3%	0.10 [-1.82, 2.02]				
Total (95% CI)			3898			4191	100.0%	-0.14 [-0.66, 0.38]		. 🕈		
Heterogeneity: Chi ² = 3.25,	df = 6 (P	= 0.78)); I ² = 0°	%					-10	-5 0		10
Test for overall effect: Z = 0.	.53 (P = I	0.60)							-10	BP-DES DP-DES	5	10

2) Sex (male)

	BP-DES DP-DES					Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl			
Antoinette de Waha 2015	214	291	149	206	7.0%	1.06 [0.71, 1.59]				
Hyo-Soo Kim 2021	1337	1700	1351	1713	43.9%	0.99 [0.84, 1.16]				
Hyun Jong Lee 2015	128	171	400	536	7.4%	1.01 [0.68, 1.50]				
Juan F Iglesias 2019	513	649	477	651	15.2%	1.38 [1.06, 1.78]	_ _			
Qi Zhang 2014	475	596	467	596	14.5%	1.08 [0.82, 1.43]	_			
Thomas Pilgrim 2016	170	211	151	196	4.6%	1.24 [0.77, 1.99]				
Yao-Jun Zhang 2015	215	280	210	293	7.3%	1.31 [0.90, 1.90]	+			
Total (95% CI)		3898		4191	100.0%	1.10 [0.99, 1.23]	◆			
Total events	3052		3205							
Heterogeneity: Chi ² = 5.85, c	if = 6 (P =	= 0.44);	l² = 0%							
Test for overall effect: Z = 1.8	81 (P = 0.	.07)					BP-DES DP-DES			

3) Body mass index

	BP	DES	5	DF	DES	5		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Hyo-Soo Kim 2021	25	3.2	1700	24.9	3.1	1713	74.0%	0.10 [-0.11, 0.31]	*
Juan F Iglesias 2019	26.9	4.3	649	26.8	4.3	651	15.1%	0.10 [-0.37, 0.57]	
Thomas Pilgrim 2016	27	4.3	211	27	4.3	196	4.7%	0.00 [-0.84, 0.84]	
Yao-Jun Zhang 2015	27.5	4.4	280	27.8	4.6	293	6.1%	-0.30 [-1.04, 0.44]	
T-4-1 (05% ON						0050	400.00	0.071.0.11.0.051	
Total (95% CI)			2840			2853	100.0%	0.07 [-0.11, 0.25]	
Heterogeneity: Chi ² = 1.0	09, df = 0	3 (P =	= 0.78);	l² = 0%					
Test for overall effect: Z =	= 0.76 (F	P = 0.		-2 -1 0 1 2					
	•• v		,						BP-DES DP-DES

4) Hypertension

	BP-D	ES	DP-DI	ES		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Antoinette de Waha 2015	142	291	110	206	7.8%	0.83 [0.58, 1.19]	
Hyo-Soo Kim 2021	1147	1700	1092	1713	41.7%	1.18 [1.02, 1.36]	
Hyun Jong Lee 2015	102	171	308	536	7.1%	1.09 [0.77, 1.55]	
Juan F Iglesias 2019	281	649	297	651	19.8%	0.91 [0.73, 1.13]	
Qi Zhang 2014	360	596	376	596	17.5%	0.89 [0.71, 1.13]	
Thomas Pilgrim 2016	102	211	98	196	6.2%	0.94 [0.63, 1.38]	
Yao-Jun Zhang 2015	360	280	376	293		Not estimable	
Total (95% CI)		3898		4191	100.0%	1.03 [0.94, 1.13]	•
Total events	2494		2657				
Heterogeneity: Chi ² = 7.92,	df = 5 (P =	= 0.16);	I ² = 37%				
Test for overall effect: $Z = 0.9$	57 (P = 0.	.57)					BP-DES DP-DES

Figure 1 Baseline characteristics and stent information of patients with acute coronary syndrome (ACS). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

5) Diabetes

	BP-DES DP-DES					Odds Ratio		Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl			
Antoinette de Waha 2015	56	291	34	206	4.3%	1.21 [0.75, 1.93]		_ _			
Hyo-Soo Kim 2021	747	1700	789	1713	59.0%	0.92 [0.80, 1.05]		•			
Hyun Jong Lee 2015	82	171	269	536	9.1%	0.91 [0.65, 1.29]					
Juan F Iglesias 2019	73	649	82	651	9.7%	0.88 [0.63, 1.23]					
Qi Zhang 2014	129	291	113	206	9.9%	0.66 [0.46, 0.94]					
Thomas Pilgrim 2016	30	211	27	196	3.2%	1.04 [0.59, 1.82]					
Yao-Jun Zhang 2015	55	280	46	293	4.8%	1.31 [0.85, 2.02]		+			
Total (95% CI)		3593		3801	100.0%	0.92 [0.83, 1.02]		•			
Total events	1172		1360								
Heterogeneity: Chi ² = 7.56, d	≴f=6(P=	= 0.27);	l² = 21%				0.01	0.1 1 10	100		
Test for overall effect: Z = 1.5	51 (P = 0.	13)					0.01	BP-DES DP-DES	100		

6) Dyslipidemia

	BP-DES DP-DES					Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl		
Antoinette de Waha 2015	119	291	109	206	9.1%	0.62 [0.43, 0.88]				
Hyo-Soo Kim 2021	1247	1700	1280	1713	41.0%	0.93 [0.80, 1.09]		•		
Hyun Jong Lee 2015	116	171	389	536	7.3%	0.80 [0.55, 1.16]				
Juan F Iglesias 2019	304	649	302	651	19.3%	1.02 [0.82, 1.27]		+		
Qi Zhang 2014	87	596	76	596	7.8%	1.17 [0.84, 1.63]				
Thomas Pilgrim 2016	110	211	101	196	6.0%	1.02 [0.69, 1.51]		+		
Yao-Jun Zhang 2015	152	280	176	293	9.5%	0.79 [0.57, 1.10]				
Total (95% CI)		3898		4191	100.0%	0.92 [0.83, 1.02]		•		
Total events	2135		2433							
Heterogeneity: Chi ² = 9.34, i	df = 6 (P =	= 0.16);	l² = 36%				0.01	0.1 1	10	100
Test for overall effect: $Z = 1.1$	66 (P = 0.	10)					0.01	BP-DES DP-DES	10	100

7) Smoking

	BP-DES DP-DES				Odds Ratio	Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H,	Fixed, 95% C	1	
Antoinette de Waha 2015	120	291	90	206	7.4%	0.90 [0.63, 1.30]		-		
Hyo-Soo Kim 2021	515	1700	475	1713	39.4%	1.13 [0.98, 1.31]		•		
Hyun Jong Lee 2015	65	171	228	536	8.2%	0.83 [0.58, 1.18]		-+		
Juan F Iglesias 2019	294	649	250	651	16.3%	1.33 [1.07, 1.66]		⊢ •-		
Qi Zhang 2014	257	596	223	596	15.1%	1.27 [1.01, 1.60]		-		
Thomas Pilgrim 2016	93	211	77	196	5.3%	1.22 [0.82, 1.81]		+		
Yao-Jun Zhang 2015	107	280	115	293	8.3%	0.96 [0.68, 1.34]		+		
Total (95% CI)		3898		4191	100.0%	1.13 [1.03, 1.24]		•		
Total events	1451		1458							
Heterogeneity: Chi ² = 8.51, (df = 6 (P =	= 0.20);	l² = 29%				0.01 0.1		10	100
Test for overall effect: Z = 2.0	64 (P = 0.	.008)						ES DP-DES		100

8) LVEF

	E	BP-DES		D	P-DES			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Antoinette de Waha 2015	0.47	0.1	291	0.48	0.12	206	7.6%	-0.01 [-0.03, 0.01]	
Hyo-Soo Kim 2021	0.587	0.104	1700	0.585	0.104	1713	42.1%	0.00 [-0.00, 0.01]	•
Hyun Jong Lee 2015	0.55	0.1481	171	0.5225	0.1407	536	4.9%	0.03 [0.00, 0.05]	
Juan F Iglesias 2019	0.49	0.11	649	0.484	0.112	651	18.7%	0.01 [-0.01, 0.02]	+
Qi Zhang 2014	0.5	0.12	596	0.49	0.17	596	10.6%	0.01 [-0.01, 0.03]	+
Thomas Pilgrim 2016	0.495	0.105	211	0.483	0.111	196	6.9%	0.01 [-0.01, 0.03]	+
Yao-Jun Zhang 2015	0.515	0.101	280	0.514	0.118	293	9.3%	0.00 [-0.02, 0.02]	+
Total (95% CI)			3898			4191	100.0%	0.00 [-0.00, 0.01]	•
Heterogeneity: Tau ² = 0.00;	Chi ² = 6	.80, df=	6 (P = 0	0.34); I ² =	12%				-0.2 -0.1 0 0.1 0.2
Test for overall effect: Z = 1.	.56 (P = I	0.12)							-0.2 -0.1 0 0.1 0.2 BP-DES DP-DES

Figure 2 Baseline characteristics and stent information of patients with acute coronary syndrome (ACS). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents; LVEF, left ventricular ejection fraction.

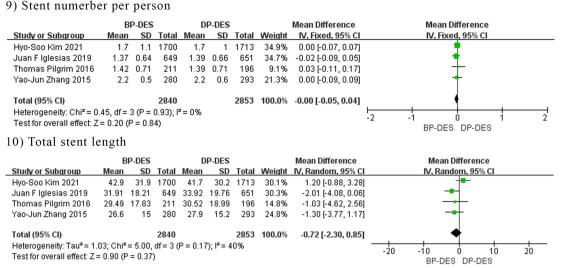


Figure 3 Baseline characteristics and stent information of patients with acute coronary syndrome (ACS). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents

stent-related complications due to the advantage of leaving the BMS only after complete drug elution and polymer degradation. BP-DES have been observed to reduce the rate of major adverse cardiac events (MACEs) compared with BMS⁸ and first-generation DP-DES.⁹ Studies of patients who underwent PCI revealed that the devicerelated outcomes were comparable between BP-DES and second-generation DP-DES.^{10–13} Thus, BP-DES would be expected to reduce the risk of ST-related MACEs beyond the first year compared with that of DP-DES. However, previous studies enrolled a significant proportion of stable angina patients. ACS confers an increased risk of adverse outcomes due to plaque characteristics, including culprit lesions, thrombus burden and persistent inflammation, compared with stable coronary artery diseases. ACS also increases the risk of delayed arterial healing and vessel remodelling,¹⁴ reflected by higher rates of incomplete stent strut coverage^{15 16} and malpositioning.¹⁷

Recently, many randomised trials have been performed to compare the efficacy and safety of DP-DES and BP-DES in patients with ACS who underwent PCI. In this metaanalysis, we aimed to summarise the studies comparing the two polymer technologies in patients with ACS and analyse the safety and effectiveness of these therapeutic options.

METHODS

Search strategy and registration

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was approved by the institutional review board of the Second Xiangya Hospital, Central South University. The protocol was registered with PROSPERO (CRD42021253412).

Based on the PRISMA statement, PubMed, Medline, Embase and the Cochrane Controlled Register of Trials databases were searched for comparative studies of BP-DES and DP-DES that were used in the treatment of patients with ACS who underwent PCI. The following search terms were used: "BP-DES," "biodegradable," "bioabsorbable," "bioabsorbable polymer drug-eluting stent," "biodegradable polymer drug-eluting stent," "DP-DES," "durable polymer," "durable polymer drug-eluting stent," "acute coronary syndrome," "ACS," "AMI," "Acute myocardial infarction," "Non ST segment elevation myocardial infarction," "ST segment elevation myocardial infarction," "NSTEMI," and "STEMI." We also reviewed prior meta-analyses and the reference lists of the original trials and reviewed articles to identify further studies. Only English language articles published in peer-reviewed journals from January 2000 to July 2021 were selected. Analyses were conducted by two independent reviewers.

Eligibility criteria

The inclusion criteria for this meta-analysis were as follows: (1) randomised controlled trials (RCTs) comparing BP-DES and DP-DES in the treatment of patients with ACS who underwent PCI; (2) data reporting patients' baseline characteristics, follow-up durations, outcomes at the primary, safety and efficacy endpoints; (3) mean follow-up time over 12 months; and (4) full-text articles.

The exclusion criteria for the meta-analysis were as follows: (1) duplications of samples and reports (evaluated by two independent reviewers); (2) case reports/ series; and (3) studies involving data from a national database.

Data extraction and outcome measurement

Two authors (HY and TW) systematically screened the titles and abstracts of publications retrieved using the search strategy to select studies that met the above inclusion criteria. Any disagreement regarding the eligibility of particular studies was resolved through discussion and involvement of a third author (ZW), when necessary. First, baseline characteristics, including the name

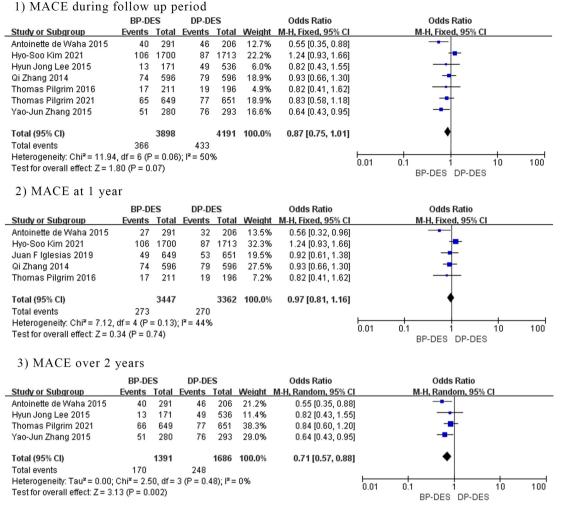


Figure 4 Primary endpoint: major adverse cardiac events (MACEs). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

of the first author, year of publication, study design, country of origin, number of patients, mean age of participants and mean duration of follow-up, were gathered from each included article. In addition, data on sex; body mass index; the presence of hypertension, diabetes, dyslipidaemia, chronic kidney disease, peripheral vessel disease or smoking; left ventricular ejection fraction (LVEF); number of stents per person; and total stent length were collected for evaluation of procedurerelated risks. MACEs were considered the primary endpoint. The efficacy endpoints included target vessel revascularisation (TVR) and target lesion revascularisation (TLR). In addition, all-cause death, cardiac death, target vessel myocardial infarction (TVMI), and ST were used as endpoints to evaluate the safety of BP-DES and DP-DES.

The Risk of Bias 2 tool was used to assess the quality of RCTs based on sequence generation; randomised group allocation; concealment; blinding of participants, personnel and outcome assessors; incomplete data; selectivity; outcome reporting; and other sources of bias (online supplementary material 1).¹⁸

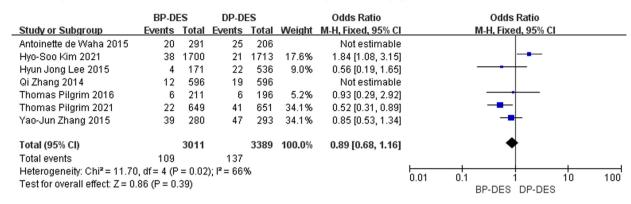
Data analysis and synthesis

Continuous variables were reported as the mean (SD), and categorical variables were expressed as numbers. Statistical pooling was performed to estimate incidence, according to a random-effects model with generic inversevariance weighting. We computed risk estimates with 95% CIs, using RevMan V.5.3 (The Cochrane Collaboration, The NordicCochrane Centre, Copenhagen, Denmark). Hypothesis testing for superiority was set at the two-tailed 0.05 level. Hypothesis testing for statistical homogeneity was set at the two-tailed 0.10 level and was based on the Cochran Q test, with I² values of 25%, 50% and 75% representing mild, moderate and severe heterogeneity, respectively.

RESULTS Search results

A total of 895 articles, written in English, were identified through the literature search. After an initial screening of the titles and abstracts, 803 articles were eliminated, as they were not related to the topic of this study. Following

1) Target vessel revascularization (TVR) during follow up period



2) Target vessel revascularization (TVR) at 1 year

	BP-DES DP-DES			ES		Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl		
Hyo-Soo Kim 2021	38	1700	21	1713	38.6%	1.84 [1.08, 3.15]				
Juan F Iglesias 2019	13	649	25	651	35.6%	0.51 [0.26, 1.01]				
Thomas Pilgrim 2016	6	211	6	196	25.7%	0.93 [0.29, 2.92]				
Total (95% CI)		2560		2560	100.0%	0.98 [0.40, 2.38]		-		
Total events	57		52							
Heterogeneity: Tau ² = 0.	46; Chi ² =	8.50, 0	df = 2 (P =	= 0.01);	l² = 76%		L 0.01	+ + + 0.1 1 10	100	
Test for overall effect: Z =	= 0.96)					0.01	BP-DES DP-DES	0 100		

3) Target vessel revascularization (TVR) over 2 years

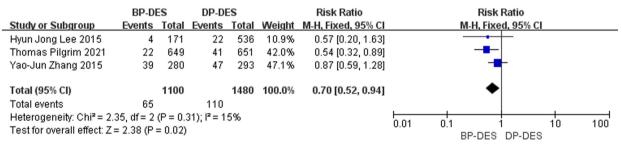


Figure 5 Target vessel revascularisation (TVR). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

the removal of these articles, 92 clinical studies and RCTs of the 2 polymers remained. After reading the full texts, 28 articles about ACS remained, with 20 articles including chronic and ACS. Finally, 8 articles, with 7 RCTs, comparing BP-DES and DP-DES in patients with ACS were identified and included in the qualitative and quantitative analyses.^{19–26} The follow-up duration ranged from 1 year to 5 years (online supplementary table 1 and online supplementary material 2).

General features of the trials

A total number of 8089 patients (3898 patients who were treated with BP-DES and 4191 patients who were treated with DP-DES) were included in this analysis. Further details about the quality of RCTs; total number of patients retrieved from each trial; publication years; countries of origin of the publications; centres in which the trials were performed; follow-up durations; risk factors; and primary, efficacy, and safety endpoints are listed in online supplementary table 2 and online supplementary material 2.

Patient characteristics

The baseline features of the patients are summarised in online supplemental table 2. The mean age of the patients who were treated by BP-DES ranged from 61.3 to 64 years, whereas the mean age of the patients who were treated by DP-DES ranged from 61.7 to 64.1 years. The proportions of male patients were above 70% in all included trials. There was no difference in age (mean difference (MD): 0.14, 95% CI -0.66 to 0.38; p=0.60, $I^2=0\%$), sex (male) (OR: 1.10, 95% CI 0.99 to 1.23; p=0.07, I²=0%), hypertension (OR: 1.03, 95% CI 0.94 to 1.13; p=0.57, I²=37%), dyslipidaemia (OR: 0.92, 95% CI 0.83 to 1.02; p=0.10, I²=36%), LVEF (MD: 0.00, 95% CI 0.00 to 0.01; p=0.12, I²=12%), body mass index (MD: 0.07, 95% CI -0.11 to 0.25; p=0.44, I²=0%), diabetes (OR: 0.92, 95% CI 0.83 to 1.02; p=0.13, $I^2=21\%$), total stent length (MD: -0.72, 95% CI -2.30 to -0.85; p=0.37, I²=40%) and in the number of stents per person (MD: -0.00, 95% CI -0.05 to 0.04; p=0.84, I²=0%) among patients who were

1) Target lesion revascularization(TLR) during follow up period

	BP-DES DP-DES				Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl		
Antoinette de Waha 2015	20	291	25	206	18.8%	0.53 [0.29, 0.99]	_ - ∎-		
Hyo-Soo Kim 2021	29	1700	16	1713	10.8%	1.84 [1.00, 3.40]	⊢		
Hyun Jong Lee 2015	3	171	12	536	3.9%	0.78 [0.22, 2.80]	· · · · · · · · · · · · · · · · · · ·		
Qi Zhang 2014	12	596	19	596	12.8%	0.62 [0.30, 1.30]	I —■+		
Thomas Pilgrim 2016	3	211	5	196	3.5%	0.55 [0.13, 2.34]	· · · · · · · · · · · · · · · · · · ·		
Thomas Pilgrim 2021	18	649	34	651	22.8%	0.52 [0.29, 0.93]	_ _ ₽_		
Yao-Jun Zhang 2015	39	280	47	293	27.3%	0.85 [0.53, 1.34]	· -•+		
Total (95% CI)		3898		4191	100.0%	0.78 [0.61, 1.00]	▶		
Total events	124		158						
Heterogeneity: Chi ² = 11.56	, df = 6 (P	= 0.07); l ² = 489	λ6					
Test for overall effect: $Z = 1$.	99 (P = 0.	.05)					BP-DES DP-DES		

2)Target lesion revascularization(TLR) at 1 year

	BP-D	ES	DP-DI	ES		Odds Ratio		Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% C	3		
Antoinette de Waha 2015	12	291	19	206	21.5%	0.42 [0.20, 0.89]					
Hyo-Soo Kim 2021	29	1700	16	1713	24.1%	1.84 [1.00, 3.40]					
Juan F Iglesias 2019	11	649	19	651	21.4%	0.57 [0.27, 1.21]					
Qi Zhang 2014	12	596	19	596	21.8%	0.62 [0.30, 1.30]					
Thomas Pilgrim 2016	3	211	5	196	11.2%	0.55 [0.13, 2.34]					
Total (95% CI)		3447		3362	100.0%	0.72 [0.40, 1.31]		-			
Total events	67		78								
Heterogeneity: Tau ² = 0.29;			= 4 (P = 0).02); I²	= 65%		0.01	0.1 1	10	100	
Test for overall effect: Z = 1.	U7 (P = 0.	29)						BP-DES DP-DES			

3) Target lesion revascularization(TLR) over 2 years

	BP-DES DP-DES						Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fi	xed, 95% (3	
Antoinette de Waha 2015	20	291	25	206	28.0%	0.53 [0.29, 0.99]			-		
Hyun Jong Lee 2015	3	171	12	536	5.8%	0.78 [0.22, 2.80]			•		
Thomas Pilgrim 2021	18	649	34	651	33.8%	0.52 [0.29, 0.93]			-		
Yao-Jun Zhang 2015	29	280	36	293	32.3%	0.82 [0.49, 1.39]		-	•		
Total (95% CI)		1391		1686	100.0%	0.64 [0.46, 0.87]		•			
Total events	70		107								
Heterogeneity: Chi ² = 1.85, (df = 3 (P :	= 0.60);	l² = 0%				L		-	-	400
Test for overall effect: $Z = 2$.	79 (P = 0	.005)					0.01	0.1 BP-DE	S DP-DE	10 S	100

Figure 6 Target lesion revascularisation (TLR). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

implanted with BP-DES or DP-DES. The meta-analysis demonstrated that the number of smoking patients (OR: 1.13, 95% CI 1.03 to 1.24; p=0.008, I^2 =29%) was significantly lower in the BP-DES group than that in the DP-DES group (figures 1–3).

Primary endpoint: MACEs reported during follow-up periods of 1–5 years, 1 year and over 2 years

MACEs, including all-cause death, recurrent myocardial infarction (MI), or any coronary repeat revascularisation involving TLR, TVR and non-TVR, were considered to be the primary endpoint of the trials. A meta-analysis indicated no statistically significant difference in the MACEs in a follow-up period ranging from 1 to 5 years between the two groups (OR: 0.87, 95% CI 0.75 to 1.01; p=0.07, $I^2=50\%$). Of the five studies that published

1-year outcomes, MACEs were not significantly different between the BP-DES and DP-DES groups (OR: 0.97, 95% CI 0.81 to 1.16; p=0.74, I²=44%). However, MACEs with follow-up periods of over 2 years were significantly lower in the BP-DES group (OR: 0.71, 95% CI 0.57 to 0.88; p=0.002, I²=0%) (figure 4).

Efficacy endpoint: TVR and TLR reported during follow-up periods of 1–5 years, 1 year and over 2 years

TLR and TVR were considered the efficacy endpoints of the trials. The meta-analysis indicated no statistically significant difference in TLR in the follow-up periods ranging from 1 to 5 years between the two groups (OR: 0.78, 95% CI 0.61 to 1.00; p=0.05, I²=48%). Among the five studies that published 1-year data, TLR was not significantly different between the BP-DES and DP-DES groups (OR:

1)All cause death during follow up period

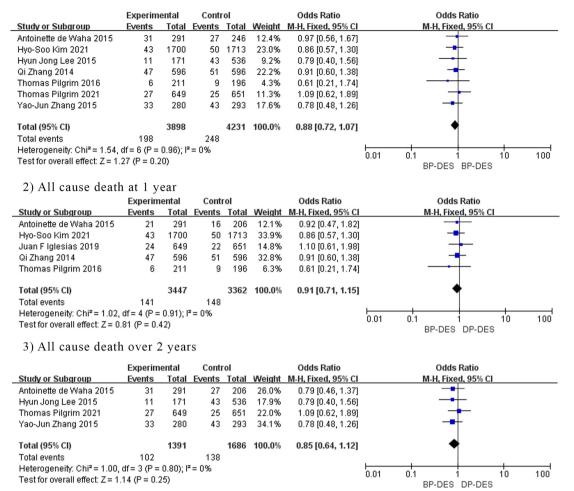


Figure 7 All-cause death. BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

0.72, 95% CI 0.40 to 1.31; p=0.29, I²=65%). The metaanalysis indicated no statistically significant difference in TVR in the follow-up periods ranging from 1 to 5 years (OR: 1.01, 95% CI 0.79 to 1.28; p=0.96, I²=46%) or in the three publications with 1-year follow-up periods (OR: 0.98, 95% CI 0.40 to 2.38; p=0.96, I²=76%). However, the difference in TLR was statistically significant in four RCT studies with follow-up periods of over 2 years (OR: 0.71, 95% CI 0.51 to 1.01; p=0.05, I²=0%), and the difference in TVR was also statistically significant in three RCT studies with follow-up periods of over 2 years (OR: 0.70, 95% CI 0.52 to 0.94; p=0.002, I²=15%), with values much lower in the BP-DES group (figures 5 and 6).

Safety endpoint: all-cause death, cardiac-related death, TVMI and ST over follow-up periods of 1–5 years, 1 year and over 2 years

All-cause death, cardiac-related death, TVMI and ST were considered the efficacy endpoints. The meta-analysis indicated no statistically significant difference between the two groups in all-cause death (OR: 0.88, 95% CI 0.72 to 1.07; p=0.20, I²=0%), cardiac-related death (OR: 0.89, 95% CI 0.71 to 1.12; p=0.32, I²=20%) and TVMI (OR: 0.73, 95% CI 0.53 to 1.01; p=0.05, I²=0%) over a follow-up

period ranging from 1 to 5 years. Of the five studies that published 1-year data, all-cause death, cardiac-related death and TVMI were also not significantly different between the BP-DES and DP-DES groups ((all-cause death, OR: 0.91, 95% CI 0.71 to 1.15; p=0.42, I²=0%), (cardiac-related death, OR: 0.96, 95% CI 0.74 to 1.26; p=0.79, $I^2=35\%$) and (TVMI, OR: 0.73, 95% CI 0.53 to 1.01; p=0.05, $I^2=0\%$). In the five studies with follow-up periods of over 2 years, similar findings were observed for the all-cause cardiac death, cardiac-related death and TVMI ((all-cause death, OR: 0.85, 95% CI 0.64 to 1.12; p=0.25, I²=0%), (cardiac-related death, OR: 0.77, 95% CI 0.56 to 1.17; p=0.12, $I^2=0\%$) and (TVMI, OR: 0.79,95% CI 0.51 to 1.22; p=0.28, I²=0%)) (figures 7–9). However, the total ST incidence, including the definite ST, probable ST and definite or probable ST incidence, was significantly different between the BP-DES and DP-DES groups during the follow-up period (OR: 0.59, 95% CI 0.46 to 0.77; p=0.0001, $I^2=48\%$). Further analysis revealed no difference in total ST for the 1-year follow-up (OR: 0.61, 95% CI 0.32 to 1.15; p=0.13, $I^2=72\%$), while the meta-analysis indicated a statistically significant difference in the total ST for the follow-up

	BP-DES DP-DES				Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl		
Antoinette de Waha 2015	20	291	21	206	14.3%	0.65 [0.34, 1.23]			
Hyo-Soo Kim 2021	38	1700	27	1713	16.4%	1.43 [0.87, 2.35]	+		
Hyun Jong Lee 2015	8	171	28	536	8.0%	0.89 [0.40, 1.99]			
Qi Zhang 2014	40	596	43	596	25.0%	0.93 [0.59, 1.45]			
Thomas Pilgrim 2016	3	211	9	196	5.7%	0.30 [0.08, 1.12]			
Thomas Pilgrim 2021	19	649	21	651	12.7%	0.90 [0.48, 1.70]	_		
Yao-Jun Zhang 2015	23	280	32	293	17.9%	0.73 [0.42, 1.28]			
Total (95% CI)		3898		4191	100.0%	0.89 [0.71, 1.12]	•		
Total events	151		181						
Heterogeneity: Chi ² = 7.50,	df = 6 (P =	= 0.28);	I² = 20%				- + + - + - + - + - + - + - + - + - +		
Test for overall effect: Z = 0.	99 (P = 0.	32)					BP-DES DP-DES		

2) cardiac death at 1 year

	BP-DES DP-DES			Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
Antoinette de Waha 2015	14	291	14	206	14.2%	0.69 [0.32, 1.49]]	
Hyo-Soo Kim 2021	38	1700	27	1713	24.0%	1.43 [0.87, 2.35]	」 _∎_	
Juan F Iglesias 2019	18	649	19	651	16.8%	0.95 [0.49, 1.82]		
Qi Zhang 2014	40	596	43	596	36.6%	0.93 [0.59, 1.45]		
Thomas Pilgrim 2016	3	211	9	196	8.4%	0.30 [0.08, 1.12]	i —•	
Total (95% CI)		3447		3362	100.0%	0.96 [0.74, 1.26]	↓ ♦	
Total events	113		112					
Heterogeneity: Chi ² = 6.14,	df = 4 (P =	= 0.19);	l² = 35%					÷,
Test for overall effect: Z = 0.							0.01 0.1 1 10 100 BP-DES DP-DES	,

3) cardiac death over 2 years

	BP-DES DP-DES		DP-DES		Odds Ratio		Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed	l, 95% Cl		
Antoinette de Waha 2015	20	291	21	206	27.0%	0.65 [0.34, 1.23]			-		
Hyun Jong Lee 2015	8	171	28	536	15.2%	0.89 [0.40, 1.99]					
Thomas Pilgrim 2021	19	649	21	651	24.0%	0.90 [0.48, 1.70]			_		
Yao-Jun Zhang 2015	23	280	32	293	33.8%	0.73 [0.42, 1.28]			-		
Total (95% CI)		1391		1686	100.0%	0.77 [0.56, 1.07]		•			
Total events	70		102								
Heterogeneity: Chi ² = 0.68,	df = 3 (P =	= 0.88);	l² = 0%					0.1 1			100
Test for overall effect: Z = 1.	55 (P = 0.	12)					0.01	BP-DES	11 DP-DES	1	100

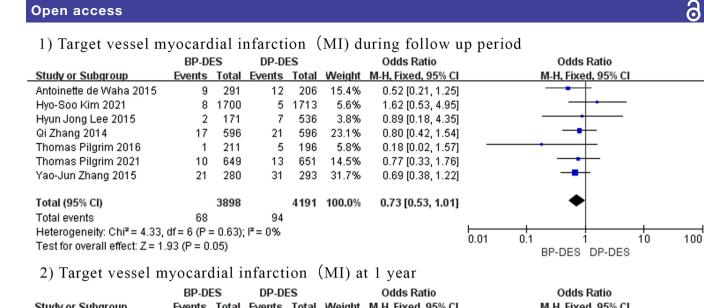
Figure 8 Cardiac-related death. BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

periods of over 2 years (OR: 0.63, 95% CI 0.47 to 0.85; p=0.002, $I^2=0\%$) (figure 10).

DISCUSSION

The choice of stent in patients undergoing PCI for ACS is debated. Coronary intervention with second-generation DP-DES generally reduces the need for revascularisation and improves mortality compared with BMS and first-generation DP-DES. Furthermore, the risk of late ST with DP-DES tends to off-set these benefits, as seen in registries and clinical trials comparing DP-DES to BMS.^{15 27} BP-DES was designed to leave only the BMS behind once the polymer completely bio-degraded after drug elution

and may represent an attractive solution for patients with ACS.²⁸ Prior meta-analyses have compared the clinical outcomes among BMS, DP-DES and BP-DES in patients with stable coronary artery disease, but no previous meta-analysis of RCTs and prospective trials directly compared clinical outcomes between BP-DES and DP-DES for the treatment of ACS. To our knowledge, this meta-analysis exclusively compared BP-DES to DP-DES. It included 7 trials representing 8089 patients with relatively long follow-up durations, ranging from 1 year to 5 years. BP-DES have been hypothesised to offer improved outcomes, mainly in the long term; however, several prior meta-analyses have demonstrated different outcomes with



	BP-DES DP-DES			Odds Ratio		Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95%	CI	
Antoinette de Waha 2015	9	291	12	206	23.6%	0.52 [0.21, 1.25]				
Hyun Jong Lee 2015	2	171	7	536	5.8%	0.89 [0.18, 4.35]			_	
Thomas Pilgrim 2021	10	649	13	651	22.1%	0.77 [0.33, 1.76]				
Yao-Jun Zhang 2015	21	280	31	293	48.5%	0.69 [0.38, 1.22]				
Total (95% CI)		1391		1686	100.0%	0.68 [0.45, 1.01]		•		
Total events	42		63							
Heterogeneity: Chi ² = 0.57, (df = 3 (P =	= 0.90);	l² = 0%				0.1 1	10	100	
Test for overall effect: $Z = 1.6$	89 (P = 0.	06)					0.01	BP-DES DP-DE		100

3) Target vessel myocardial infarction (MI) over 2 year

	BP-D	BP-DES DP-DES		Odds Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% CI	
Antoinette de Waha 2015	7	291	8	206	20.0%	0.61 [0.22, 1.71]			
Hyo-Soo Kim 2021	8	1700	5	1713	10.9%	1.62 [0.53, 4.95]			
Juan F Iglesias 2019	5	649	6	651	13.0%	0.83 [0.25, 2.75]			
Qi Zhang 2014	17	596	21	596	44.7%	0.80 [0.42, 1.54]			
Thomas Pilgrim 2016	1	211	5	196	11.3%	0.18 [0.02, 1.57]			
Total (95% CI)		3447		3362	100.0%	0.79 [0.51, 1.22]		•	
Total events	38		45						
Heterogeneity: Chi ² = 3.61,	df = 4 (P =	= 0.46);	l² = 0%						10 100
Test for overall effect: Z = 1.	08 (P = 0	28)		0.01	0.1 1 BP-DES DP-DES	10 100			

Figure 9 Target vessel myocardial infarction (MI). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

BP-DES compared with DP-DES in patients undergoing PCI. Bangalore *et al* observed that BP-DES were associated with higher mortality than DP-DES beyond 1 year of follow-up.²⁹ El-Hayek *et al* demonstrated no significant difference in mortality between these stent types.⁶ In our study, there were no significant differences in MACEs, all-cause death, cardiac-related death, TVMI, TVR or TLR at a follow-up period of 1 year and no significant differences in all-cause death, cardiac death or TVMI at a follow-up period of over 2 years. However, at a follow-up of over 2 years, MACEs, TVR and TLR were significantly lower in the BP group than those in the DP group. Pilgrim *et al* observed higher all-cause mortality among patients treated with BP-DES than with DP-DES in the BIOSCI-ENCE trial; they also observed comparable all-cause

mortality rates among patients treated with BP-DES and DP-DES in the BIOSTEMI trial with a 2-year follow-up.⁶ Iannaccone *et al* observed that BP-DES might decrease the risk of ischaemic events in selected high-risk subgroups of patients, although the two DES stents share the same safety factors for patients in high-anatomical-risk settings like left main disease.³⁰ Together, these findings suggest that BP-DES share similar outcomes in terms of MACEs (all-cause death, cardiac-related death, TVMI, TVR and TLR) during a 1-year follow-up and might show significantly improved clinical outcomes over a 2-year follow-up.

ST is defined as a thrombotic occlusion of a coronary stent³¹ and is a major complication. The risk of ST, particularly late ST (occurring beyond 30 days), remains one of the major concerns limiting the use of DES in

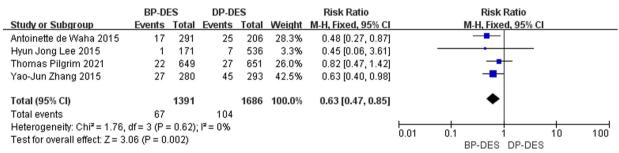
1) Stent thrombosis during follow up period

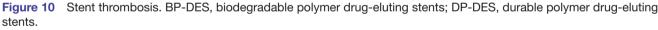
	BP-DES DP-DES		Odds Ratio		Odds Ratio						
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixe	d, 95% Cl		
Antoinette de Waha 2015	17	291	25	206	18.8%	0.45 [0.24, 0.86]					
Hyo-Soo Kim 2021	12	1700	6	1713	4.1%	2.02 [0.76, 5.40]		-+			
Hyun Jong Lee 2015	1	171	7	536	2.3%	0.44 [0.05, 3.64]					
Qi Zhang 2014	11	596	21	596	14.1%	0.51 [0.25, 1.08]		-			
Thomas Pilgrim 2016	7	211	23	196	15.8%	0.26 [0.11, 0.62]	_				
Thomas Pilgrim 2021	22	649	27	651	17.8%	0.81 [0.46, 1.44]			_		
Yao-Jun Zhang 2015	27	280	45	293	27.2%	0.59 [0.35, 0.98]					
Total (95% CI)		3898		4191	100.0%	0.59 [0.46, 0.77]		•			
Total events	97		154								
Heterogeneity: Chi ² = 11.58,	df = 6 (P	= 0.07); I ² = 489	Хо			L L L L L L L L L L L L L L L L L L L			10	100
Test for overall effect: Z = 3.8	87 (P = 0.	.0001)						BP-DES	DP-DES	10	100

2) Stent thrombosis at 1 year

	BP-DES DP-DES				Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl	
Antoinette de Waha 2015	13	291	24	206	21.2%	0.35 [0.18, 0.71]			
Hyo-Soo Kim 2021	12	1700	6	1713	17.0%	2.02 [0.76, 5.40]			
Juan F Iglesias 2019	21	649	22	651	22.6%	0.96 [0.52, 1.76]			
Qi Zhang 2014	11	596	21	596	20.6%	0.51 [0.25, 1.08]			
Thomas Pilgrim 2016	7	211	23	196	18.6%	0.26 [0.11, 0.62]			
Total (95% CI)		3447		3362	100.0%	0.61 [0.32, 1.15]		-	
Total events	64		96						
Heterogeneity: Tau ² = 0.38;	$Chi^2 = 14$				100				
Test for overall effect: Z = 1.	53 (P = 0		0.01	0.1 1 10 BP-DES DP-DES	100				

3) Stent thrombosis over 2 years





the treatment of ACS.³² Early-generation DP-DES were associated with increased rates of very late (>1 year) ST compared with BMS. It was hypothesised that the mechanism underlying late ST with first DP-DES in ACS was related to adverse reactions with the DP,³³ and the use of more biocompatible polymers has been associated with a reduction in ST in high-risk patients.⁹ In the LEADERS trial, the rate of very late ST was lower with the use of the BP-DES than that with DP-DES.³⁴ Our data demonstrated that both BP-DES and DP-DES have similar risks of ST beyond 1 year. However, BP-DES are associated with a significantly reduced risk of ST at a follow-up of over 2 years compared with DP-DES (OR: 0.64, 95% CI 0.46 to 0.88; p=0.006, I²=0%). In contrast, Kim *et al* observed that the incidence of ST by groups demonstrated numerically lower rates in the DP-DES group (0.1%) than those in the BP-DES group and that all late ST cases occurred in those receiving thick-strut BP-DES stents. They proposed that no meaningful differences in terms of ST could be identified

between the different polymer technologies by intravascular imaging and that the association of polymer technology and the risk of the ST was difficult to prove.^{20 35 36} Therefore, it may be hypothesised that BP-DES result in improved arterial healing, which not only minimises the risk of ST, but also improves the long-term durability of the antirestenotic efficacy in the long term, although the two groups have a similar risk of ST beyond 1 year.

Limitations

The present study had several limitations. First, this study included RCTs and shares the limitations of original studies. Second, BP-DES are a heterogeneous group of stents, differing in stent platform thickness, time to complete degradation of the polymer and drug-elution kinetics. DP-DES are equally heterogeneous groups. Innaccone *et al* observed that lower strut thickness would have a positive clinical outcome, thereby reducing ST and TLRs.³⁷ We were unable to match the stents with regards

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to the strut thickness. Consequently, the reported results may not be generalisable to all stents from the respective group. Third, over 6 months of dual antiplatelet therapy (DAPT) was provided to the patients in our study, including those in RCTs. D'Ascenzo *et al* observed a similar rate of MACEs between durable and BPs, irrespective of DAPT length, and the DAPT duration seems to partially impact the risk of adverse events of different types of stents during follow-up.³⁸ Thus, we remain concerned that the duration differences of DAPT may influence the clinical outcomes.

CONCLUSION

In this meta-analysis comparing BP-DES to DP-DES in patients with ACS who underwent PCI, the data indicated that both polymer types demonstrated excellent safety and efficacy profiles at 1 year. There was a slightly increased incidence of MACEs, TLR, TVR and ST in the DP-DES group in the follow-up period of over 2 years, suggesting that BP-DES may be more favourable for treating patients with ACS. These findings should be confirmed by longterm follow-ups in RCT trials.

Data availability statement

No additional data is available.

Patient and public involvement

We did not require patient and public involvement, as this is a meta-analysis, and no new patients were enrolled in the study.

Contributors CH, ZW and HY developed the idea of the study, participated in its design and coordination and helped draft the manuscript. TL and TW contributed to the acquisition and interpretation of data. YZ and YL provided a critical review and substantially revised the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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