


RESEARCH ARTICLE

Biodegradable polymer versus second-generation durable polymer drug-eluting stents in patients with coronary artery disease: A meta-analysis

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Abstract

Aims: Biodegradable polymer drug-eluting stents (BP-DES) were developed in hopes of reducing the risk of stent thrombosis. The comparison of this new stent platform with second-generation durable polymer drug-eluting stents (DP-DES) has not been well described. We, therefore, performed a meta-analysis to evaluate the safety and efficacy profiles of BP-DES versus second-generation DP-DES in patients with coronary artery disease.

Methods and Results: Electronic database searches were conducted, from their dates of inception to June 2018, to identify randomized controlled trials (RCTs) comparing patients with either BP-DES or second-generation DP-DES. Risk estimates were expressed as risk ratios (RRs) with 95% confidence intervals (CIs). We also performed a landmark analysis beyond 1 year and sensitivity analyses based on different variables. A total of 24,406 patients from 19 RCTs were included in the present meta-analysis. There were no significant differences between BP-DES and second-generation DP-DES for the risks of definite or probable stent thrombosis (RR 0.88; 95% CI, 0.69–1.12; $P = 0.29$), myocardial infarction (RR 0.97; 95% CI, 0.86–1.09; $P = 0.59$), cardiac death (RR 1.08; 95% CI, 0.92–1.28; $P = 0.34$), all-cause death (RR 1.02; 95% CI, 0.91–1.13; $P = 0.77$), target lesion revascularization (RR 1.05; 95% CI, 0.94–1.17; $P = 0.38$), and target vessel revascularization (RR 1.05; 95% CI, 0.95–1.16; $P = 0.36$). Similar outcomes were observed regardless of anti-proliferative drug and duration of dual antiplatelet therapy (all $P > 0.05$).

Conclusion: Our findings demonstrate similar safety and efficacy profiles between BP-DES and second-generation BP-DES, with comparable rates of stent thrombosis.

KEYWORDS

biodegradable polymer, coronary artery disease, drug-eluting stents, durable polymer, meta-analysis

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1 | INTRODUCTION

Drug-eluting stents (DES) have revolutionized the treatment of coronary artery disease in patients undergoing percutaneous coronary intervention (PCI). Advances in coronary stent technology have continually improved on patient outcomes through the refinement of design and component materials.¹ These sequential stent platforms have included bare metal stents (BMS), durable polymer drug-eluting stents (DP-DES), and biodegradable polymer drug-eluting stents (BP-DES). The first generation of DP-DES were introduced to reduce the risk of in-stent restenosis and subsequent target lesion revascularization associated with BMS.² However, first-generation DP-DES were found to have an increased risk of very late stent thrombosis (> 12 months) compared with BMS.³ This adverse event has been related to polymer-induced hypersensitivity reaction, incomplete strut re-endothelialization, stent malapposition, and accelerated neoatherosclerosis.⁴ Consequently, a second generation of DP-DES were developed, with novel anti-proliferative drugs, more biocompatible polymer coatings, and thinner metal alloy struts made possible by the use of cobalt-chromium or platinum-chromium in place of stainless steel.⁵ Second-generation DP-DES were shown to reduce the risk of very late stent thrombosis associated with first-generation DP-DES.⁶ However, concerns regarding the potential thrombogenicity of the durable polymer coating have remained, resulting in recommendations for dual antiplatelet agents to be continued for longer periods following DP-DES implantation.⁷

BP-DES were developed in the hope of providing a similar safety profile to that of BMS (reduced risk of stent thrombosis), while maintaining the efficacy profile of DP-DES (reduced risk of target lesion revascularization). The polymer coating of BP-DES degrades over two to nine months, and simultaneously releases controlled amounts of the anti-proliferative drug.⁸ The proposed benefit of BP-DES is the eventual absence of a foreign material in the vessel wall, in which there is a lower possibility for residual inflammation and, therefore, a reduced risk of very late stent thrombosis.⁹ There have been suggestions that BP-DES require a shorter duration of dual antiplatelet therapy (DAPT) than DP-DES.¹⁰ It is important to ensure that any potential safety benefits are not offset by the loss of efficacy (prevention of restenosis) through changes to the elution profile of the drug.¹¹ Therefore, we performed a meta-analysis of randomized controlled trial published to date to gain an evidence-based understanding of the safety and efficacy profiles of BP-DES versus second-generation DP-DES.

2 | METHODS

2.1 | Search strategy

Our meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹² We conducted electronic database searches using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), American College of Physicians (ACP) Journal Club, and Database of Abstracts of Reviews of

Effectiveness (DARE) from their dates of inception to June 2018. To identify potentially relevant studies, we used the following keywords or MeSH terms: “randomized controlled trial”, “drug-eluting stent”, “durable polymer”, “permanent polymer”, “everolimus-eluting stent”, “zotarolimus-eluting stent”, “biodegradable polymer”, “bioabsorbable polymer”, “bioresorbable polymer”, “biolimus-eluting stent”, “sirolimus-eluting stent”, and “stent thrombosis”. The reference lists of retrieved articles were evaluated using the inclusion and exclusion criteria.

2.2 | Selection criteria

The present meta-analysis included studies that had a randomized design. We included studies comparing patients with either BP-DES or second-generation DP-DES (Table 1). The BP-DES included biolimus-, everolimus-, and sirolimus-eluting stents. The second-generation DP-DES included everolimus- and zotarolimus-eluting stents. Studies evaluating sirolimus- and paclitaxel-eluting stents were not included, as these are first-generation DP-DES. For duplicate studies, only the most recent reports with greatest number of patients and length of follow-up were included for quantitative assessment. We limited the electronic database searches to studies involving human subjects. We excluded conference abstracts, editorials, case reports, and review articles due to the possibility of publication bias and duplication of results.

2.3 | Data extraction and critical appraisal

We extracted data from texts, tables, and figures. Two independent investigators (JJW and JAW) reviewed each retrieved article for eligibility at the title or abstract level. The senior author (DB) resolved any discrepancies between the two investigators by discussion and consensus. Each included study was evaluated using the Cochrane Collaboration risk of bias tool³² (see supplementary table).

2.4 | Outcomes

The primary outcome was definite or probable stent thrombosis, which was defined by the Academic Research Consortium (ARC).³³ The secondary outcomes were myocardial infarction, cardiac death, all-cause death, target lesion revascularization, and target vessel revascularization. All outcomes were extracted at the longest follow-up available and at 5 years of follow-up.

2.5 | Statistical analysis

Risk ratios (RRs) with 95% confidence intervals (CIs) were used for summary statistics and risk estimates to compare patients receiving either BP-DES or second-generation DP-DES. The Z test was used to derive *P* values. The χ^2 test was used to assess heterogeneity between studies. The I^2 statistic was used to assess total variation across studies, with values greater than 50% considered as significant heterogeneity.³² The Mantel-Haenszel fixed-effects model was used because there was no substantial heterogeneity between studies. Risk of publication bias was assessed using funnel plots and statistical tests.³⁴ We performed a landmark analysis beyond 1 year of follow-up to evaluate late safety and efficacy outcomes. To assess the extent

TABLE 1 Study characteristics

Study	Year	Patient (n)		DAPT (months)	Follow-up (months)	Anti-proliferative drug	
		BP-DES	DP-DES			BP-DES	DP-DES
BASKET-PROVE II ¹³	2015	765	765	12	24	Biolimus	Everolimus
BIOFLOW II ¹⁴	2015	298	154	6	12	Sirolimus	Everolimus
BIOFLOW V ¹⁵	2017	884	450	12	12	Sirolimus	Everolimus
BIO-RESORT ¹⁶	2016	2,341	1,173	6	12	Everolimus, Sirolimus	Zotarolimus
BIO-SCIENCE ¹⁷	2016	1,063	1,056	12	24	Sirolimus	Everolimus
CENTURY II ¹⁸	2014	551	550	6	9	Sirolimus	Everolimus
COMPARE II ¹⁹	2017	1,795	912	12	60	Biolimus	Everolimus
DESSOLVE II ²⁰	2015	123	61	6	9	Sirolimus	Zotarolimus
EVERBIO II ²¹	2015	80	80	6	9	Biolimus	Everolimus
EVOLVE FHU ²²	2013	193	98	6	24	Everolimus	Everolimus
EVOLVE II ²³	2015	846	838	6	12	Everolimus	Everolimus
ISAR-TEST 4 ²⁴	2016	1,299	652	6	60	Sirolimus	Everolimus
LONG-DES V ²⁵	2014	245	255	12	12	Biolimus	Everolimus
NEXT ²⁶	2018	1,283	1,285	3	60	Biolimus	Everolimus
PRISON IV ²⁷	2017	165	165	12	12	Sirolimus	Everolimus
Separham ²⁸	2011	100	100	12	12	Biolimus	Everolimus
SORT OUT VI ²⁹	2015	1,497	1,502	12	12	Biolimus	Zotarolimus
TARGET I ³⁰	2013	227	231	12	12	Sirolimus	Everolimus
Xu ³¹	2011	168	156	6	24	Sirolimus	Zotarolimus

BP-DES = biodegradable polymer drug-eluting stents; DAPT = dual antiplatelet therapy; DP-DES = durable polymer drug-eluting stents.

to which variables might influence the risk estimate of each outcome, we performed sensitivity analyses based on different variables: BP-DES anti-proliferative drug (biolimus, everolimus, or sirolimus); DP-DES anti-proliferative drug (everolimus or zotarolimus); and duration of DAPT (6 months or 12 months). We conducted statistical analyses using RevMan Version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen).

3 | RESULTS

3.1 | Study selection and patient population

Figure 1 illustrates the study selection process in the present meta-analysis. We identified 1,298 references through electronic database searches. After removing duplicate studies, we retrieved 1,126 potentially relevant articles. After applying the inclusion and exclusion criteria, we included 19 RCTs¹³⁻³¹ in the present meta-analysis, comprising data for 24,406 patients randomized to receive PCI with either BP-DES ($n = 13,923$) or second-generation DP-DES ($n = 10,483$). Table 1 summarizes the study characteristics of the included trials in the present meta-analysis. Patients randomized to receive BP-DES were treated with either biolimus-, sirolimus-, or everolimus-eluting stent. Patients randomized to receive second-generation DP-DES were treated with either everolimus- or zotarolimus-eluting stent.

The RCTs were assessed to be of high quality using the Cochrane Collaboration risk of bias tool.³⁵ All trials had a multicenter design, with a median follow-up of 12 months. The trials clearly identified the patient population, and defined the outcomes. In four trials,^{13,21,26,30} the main limitation was the lack of blinding of outcomes. One trial²⁴

included a third comparison arm of patients randomized to receive first-generation DP-DES. Another trial²¹ included a third comparison arm of patients randomized to receive bioresorbable vascular scaffolds. We excluded data from these third comparison arms because we deemed it irrelevant to our research question. The funnel plots showed no evidence of publication bias (see supplementary figures).

3.2 | Patient and procedural characteristics

Table 2 summarizes the baseline characteristics of the included trials in the present meta-analysis. The enrolled patients had a weighted mean age of 64.7 ± 10.7 years for those receiving BP-DES and 64.9 ± 10.6 years for those receiving second-generation DP-DES. Overall, the two comparison groups had similar proportions of male patients and with diabetes mellitus, hypertension, hyperlipidemia, current smoking, previous myocardial infarction, previous procedure (PCI or coronary artery bypass grafting), clinical presentation (stable/unstable angina or non-/ST-elevation myocardial infarction), and target vessel location (left anterior descending, left circumflex, or right coronary artery) (all $P > 0.05$). However, the proportion of patients with previous PCI was significantly higher in those receiving BP-DES than those receiving second-generation DP-DES (26.4% vs 26.2%; $P = 0.03$).

3.3 | Safety and efficacy outcomes

Nineteen trials¹³⁻³¹ reported definite or probable stent thrombosis (ST) in 24,274 patients. There was no significant difference between patients with BP-DES and those with second-generation DP-DES for the risk of definite or probable ST (1.0% vs 1.2%; RR 0.88; 95% CI, 0.69-1.12; $P = 0.29$; $I^2 = 0\%$; Figure 2). Nineteen trials¹³⁻³¹ reported

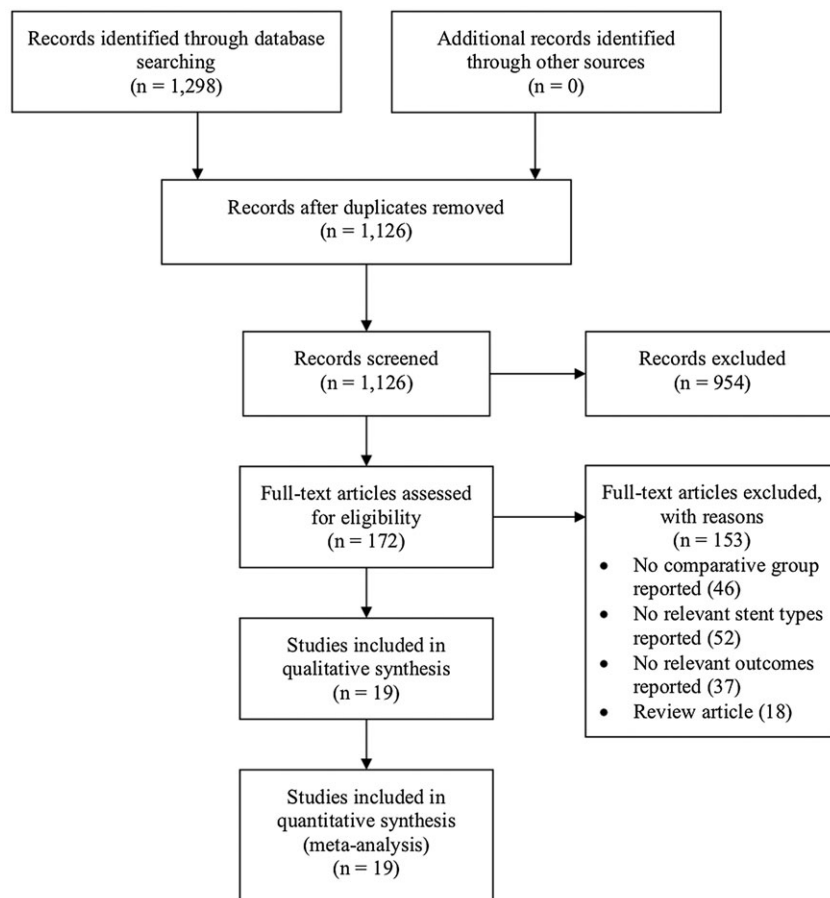


FIGURE 1 Flow diagram of study selection process

TABLE 2 Baseline characteristics

Baseline characteristic	BP-DES	DP-DES	RR or WMD (95% CI)	P Value ^a
Age (years)	64.7 ± 10.7	64.9 ± 10.6	-0.14 (-0.42 to 0.13)	0.30
Male	10,385/13,923 (74.6)	7,928/10,483 (75.6)	0.99 (0.98 to 1.00)	0.17
Diabetes mellitus	3,575/13,923 (25.7)	2,720/10,482 (25.9)	1.02 (0.97 to 1.06)	0.47
Hypertension	8,900/13,923 (63.9)	6,841/10,483 (65.3)	1.00 (0.98 to 1.02)	0.76
Hyperlipidemia	7,470/12,128 (61.6)	6,060/9,571 (63.3)	1.00 (0.98 to 1.02)	0.70
Current smoking	3,607/13,693 (26.3)	2,719/10,297 (26.4)	1.00 (0.96 to 1.05)	0.89
Previous MI	2,837/12,977 (21.9)	2,009/9,545 (21.0)	1.02 (0.97 to 1.08)	0.38
Previous PCI	3,224/12,204 (26.4)	2,501/9,553 (26.2)	1.05 (1.01 to 1.10)	0.03
Previous CABG	866/11,257 (7.7)	648/8,971 (7.2)	0.98 (0.89 to 1.07)	0.62
Clinical presentation				
Stable angina	5,657/12,418 (45.6)	4,383/9,237 (47.5)	0.99 (0.96 to 1.02)	0.44
Unstable angina	2,017/10,064 (20.0)	1,475/7,410 (19.9)	1.02 (0.97 to 1.08)	0.46
NSTEMI	2,550/9,736 (26.2)	1,879/7,045 (27.7)	0.99 (0.94 to 1.04)	0.70
STEMI	2,056/9,491 (21.7)	1,372/6,790 (20.2)	1.04 (0.98 to 1.11)	0.21
Target vessel location				
LAD	6,562/14,704 (44.6)	5,147/11,589 (44.4)	1.02 (0.99 to 1.05)	0.16
LCx	3,590/14,704 (24.4)	2,905/11,589 (25.1)	0.97 (0.93 to 1.01)	0.14
RCA	4,825/14,704 (32.8)	3,827/11,589 (33.0)	1.00 (0.97 to 1.04)	0.88

Values are n/N (%) or mean ± SD; BP-DES = biodegradable drug-eluting stents; CABG = coronary artery bypass grafting; DP-DES = durable polymer drug-eluting stents; LAD = left anterior descending artery; LCx = left circumflex artery; MI = myocardial infarction; NSTEMI = non-ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; RR = risk ratio; STEMI = ST-elevation myocardial infarction; WMD = weighted mean difference; ^aP value for Z test.

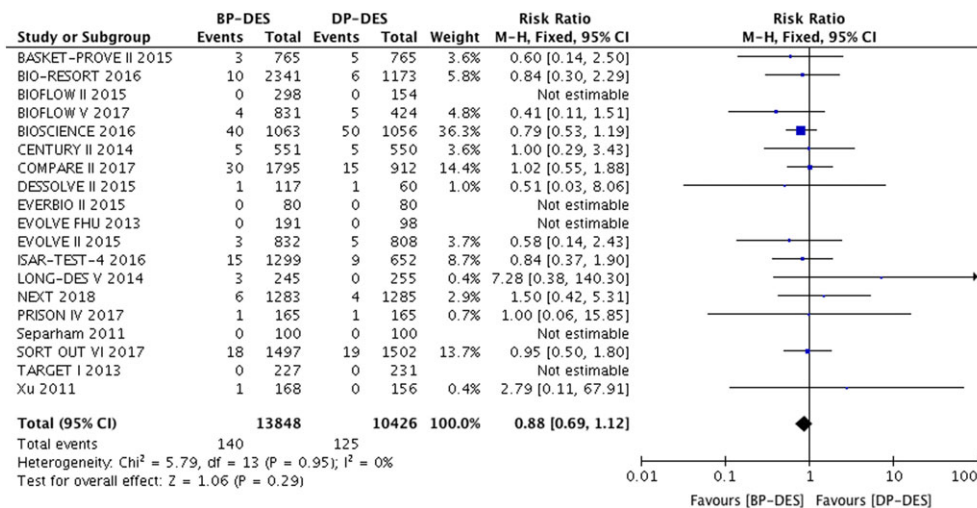


FIGURE 2 Risk of definite or probable stent thrombosis. BP-DES = biodegradable polymer drug-eluting stents. DP-DES = durable polymer drug-eluting stents. M-H = Mantel-Haenszel

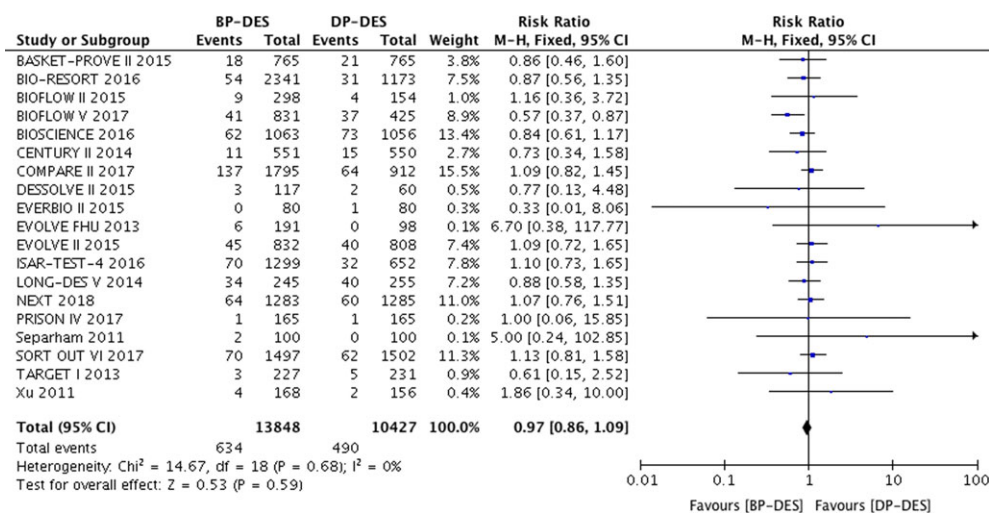


FIGURE 3 Risk of myocardial infarction. BP-DES = biodegradable polymer drug-eluting stents. DP-DES = durable polymer drug-eluting stents. M-H = Mantel-Haenszel

myocardial infarction (MI) in 24,275 patients. There was no significant difference between patients with BP-DES and those with second-generation DP-DES for the risk of MI (4.6% vs 4.7%; RR 0.97; 95% CI, 0.86–1.09; $P = 0.59$; $I^2 = 0\%$; Figure 3). Nineteen trials^{13–31} reported cardiac death in 24,279 patients. There was no significant difference between patients with BP-DES and those with second-generation DP-DES for the risk of cardiac death (2.4% vs 2.2%; RR 1.08; 95% CI, 0.92–1.28; $P = 0.34$; $I^2 = 0\%$; Figure 4). Eighteen trials^{13–27,29–31} reported all-cause death in 24,084 patients. There was no significant difference between patients with BP-DES and those with second-generation DP-DES for the risk of all-cause death (5.5% vs 5.4%; RR 1.02; 95% CI, 0.91–1.13; $P = 0.77$; $I^2 = 0\%$; Figure 5). Seventeen trials^{14–27,29–31} reported target lesion revascularization (TLR) in 22,543 patients. There was no significant difference between patients with BP-DES and those with second-generation DP-DES for the risk of TLR (5.5% vs 5.2%; RR 1.05; 95% CI, 0.94–1.17; $P = 0.38$; $I^2 = 22\%$; Figure 6). Seventeen trials^{13–23,25–30} reported target vessel

revascularization (TVR) in 21,999 patients. There was no significant difference between patients with BP-DES and those with second-generation DP-DES for the risk of TVR (6.3% vs 6.3%; RR 1.05; 95% CI, 0.95–1.16; $P = 0.36$; $I^2 = 4\%$).

Table 3 summarizes the safety and efficacy outcomes in different subgroups. At 5 years of follow-up, there were no significant differences between patients with BP-DES and those with second-generation DP-DES for the risks of definite or probable ST, MI, cardiac death, all-cause death, TLR, and TVR (all $P > 0.05$). Similarly, our landmark analysis beyond 1 year of follow-up showed no significant differences between patients with BP-DES and those with second-generation DP-DES for all outcomes (all $P > 0.05$). Our sensitivity analysis based on BP-DES anti-proliferative drug (biolimus, everolimus, or sirolimus), DP-DES anti-proliferative drug (everolimus or zotarolimus), and duration of DAPT (6 months or 12 months) showed no significant differences between patients with BP-DES and those with second-generation DP-DES for all outcomes (all $P > 0.05$).

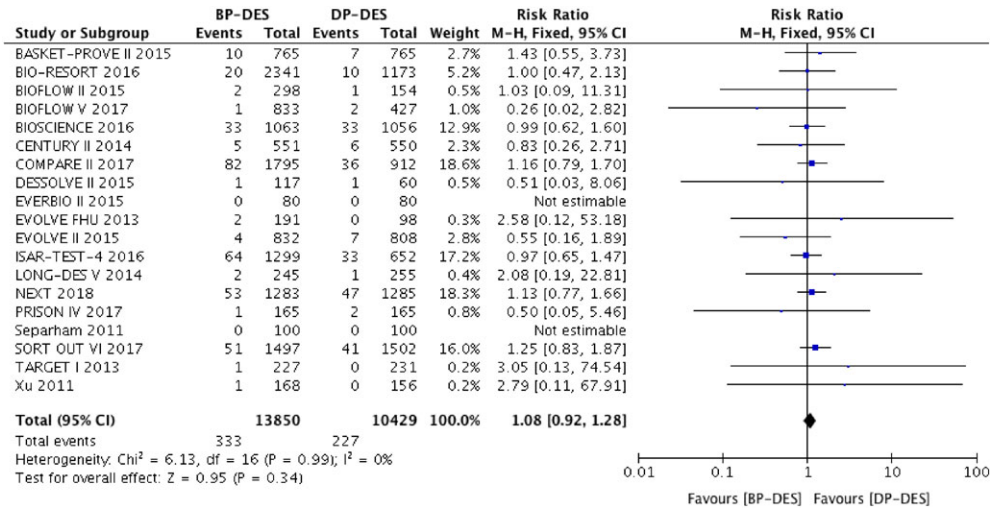


FIGURE 4 Risk of cardiac death. BP-DES = biodegradable polymer drug-eluting stents. DP-DES = durable polymer drug-eluting stents. M-H = Mantel-Haenszel

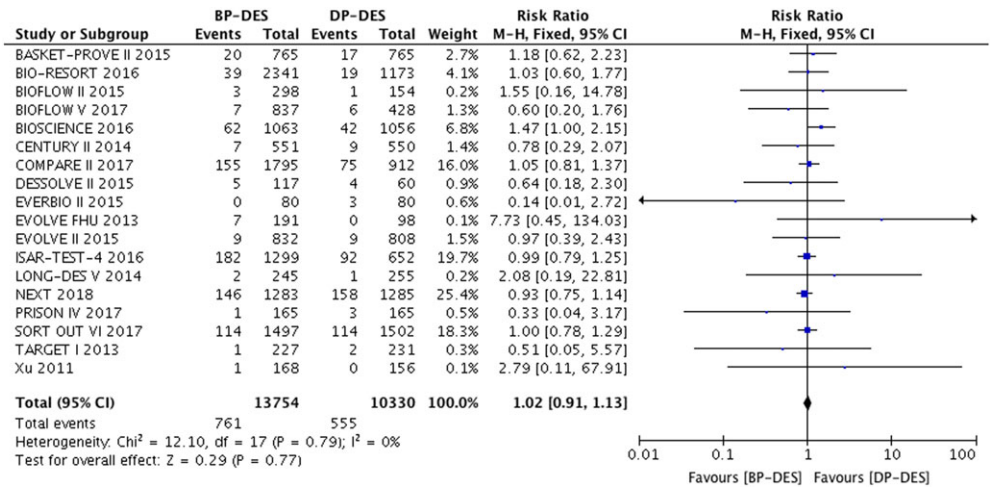


FIGURE 5 Risk of all-cause death. BP-DES = biodegradable polymer drug-eluting stents. DP-DES = durable polymer drug-eluting stents. M-H = Mantel-Haenszel

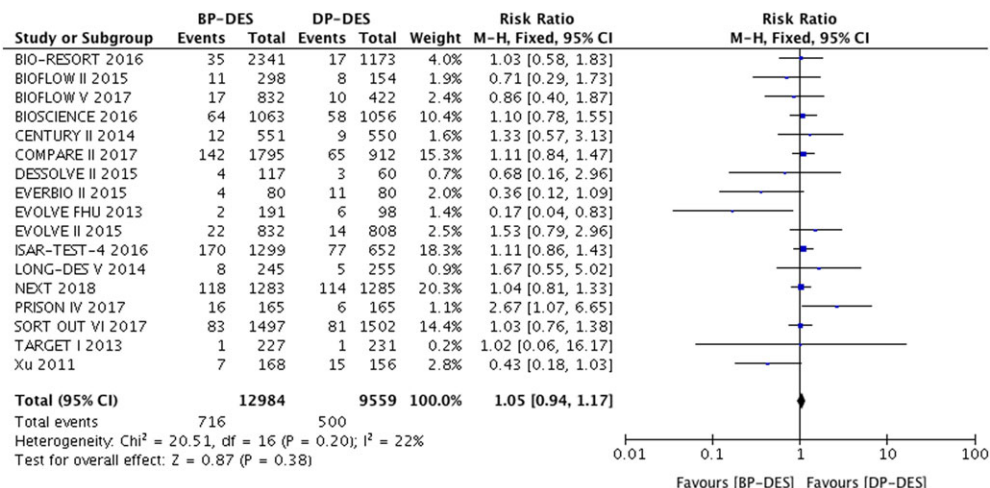


FIGURE 6 Risk of target lesion revascularization. BP-DES = biodegradable polymer drug-eluting stents. DP-DES = durable polymer drug-eluting stents. M-H = Mantel-Haenszel

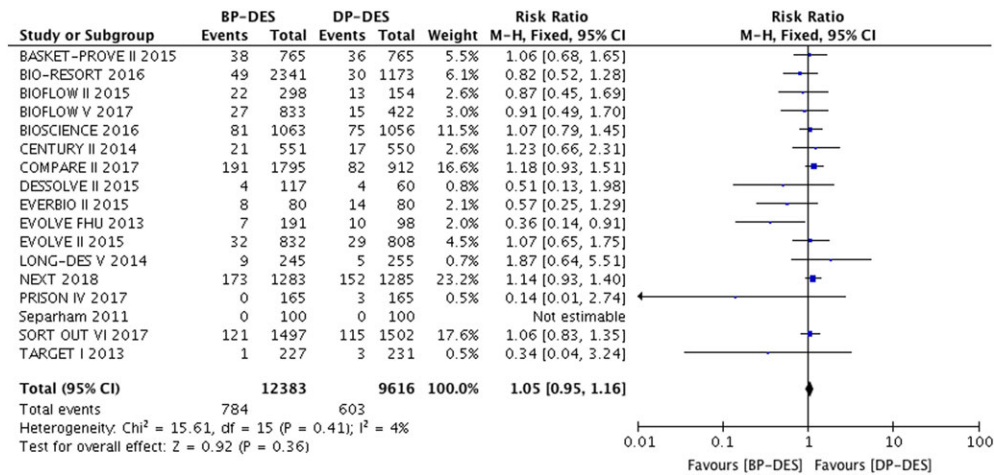


FIGURE 7 Risk of target vessel revascularization. BP-DES = biodegradable polymer drug-eluting stents. DP-DES = durable polymer drug-eluting stents. M-H = Mantel-Haenszel

TABLE 3 Safety and efficacy outcomes

Analysis	Definite or probable ST	MI	Cardiac death	All-cause death	TLR	TVR
Outcomes at longest follow-up	0.88 (0.69 to 1.12)	0.97 (0.86 to 1.09)	1.08 (0.92 to 1.28)	1.02 (0.91 to 1.13)	1.05 (0.94 to 1.17)	1.05 (0.95 to 1.16)
Outcomes at 5 years	0.92 (0.57 to 1.49)	1.10 (0.89 to 1.35)	1.07 (0.83 to 1.38)	1.03 (0.88 to 1.20)	1.06 (0.91 to 1.24)	1.16 (0.98 to 1.37)
Landmark analysis beyond 1 year	1.24 (0.57 to 2.74)	1.07 (0.79 to 1.45)	1.10 (0.83 to 1.46)	0.92 (0.76 to 1.11)	1.17 (0.94 to 1.45)	1.21 (0.98 to 1.51)
Sensitivity analysis						
BP-DES anti-proliferative drug						
Biolimus	1.05 (0.71 to 1.55)	1.05 (0.89 to 1.23)	1.19 (0.96 to 1.49)	0.99 (0.86 to 1.13)	1.04 (0.89 to 1.21)	1.11 (0.98 to 1.26)
Everolimus	0.72 (0.29 to 1.78)	1.02 (0.74 to 1.41)	0.88 (0.45 to 1.74)	1.18 (0.72 to 1.94)	1.02 (0.67 to 1.57)	0.82 (0.58 to 1.14)
Sirolimus	0.80 (0.58 to 1.09)	0.84 (0.70 to 1.01)	0.96 (0.74 to 1.26)	1.05 (0.88 to 1.25)	1.07 (0.90 to 1.26)	0.95 (0.78 to 1.16)
DP-DES anti-proliferative drug						
Everolimus	0.83 (0.63 to 1.10)	0.95 (0.83 to 1.08)	1.04 (0.85 to 1.28)	1.06 (0.93 to 1.22)	1.07 (0.94 to 1.21)	1.07 (0.94 to 1.20)
Zotarolimus	0.93 (0.55 to 1.57)	1.04 (0.80 to 1.34)	1.19 (0.84 to 1.68)	1.00 (0.80 to 1.25)	0.94 (0.74 to 1.21)	0.98 (0.79 to 1.21)
Duration of DAPT						
6 months	0.84 (0.51 to 1.39)	1.02 (0.82 to 1.27)	0.95 (0.69 to 1.30)	0.99 (0.81 to 1.21)	0.98 (0.81 to 1.18)	0.85 (0.67 to 1.08)
12 months	0.83 (0.64 to 1.09)	0.95 (0.82 to 1.11)	1.10 (0.90 to 1.34)	1.05 (0.92 to 1.19)	1.11 (0.96 to 1.27)	1.08 (0.94 to 1.23)

Values are risk ratio (95% confidence interval); BP-DES = biodegradable polymer drug-eluting stent; DAPT = dual antiplatelet therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention; ST = stent thrombosis; TLR = target lesion revascularization; TVR = target vessel revascularization.

4 | DISCUSSION

In the present meta-analysis of 19 RCTs, we investigated the safety and efficacy profiles of BP-DES versus second-generation DP-DES in a total of 24,406 patients with coronary artery disease. Our findings showed no significant differences between the two stent platforms for the risks of definite or probable ST, MI, cardiac death, all-cause death, TLR, and TVR at longest follow-up available and on landmark analysis beyond 1 year of follow-up. These results suggest that BP-DES confer no detectable safety and efficacy advantages over second-generation DP-DES.

Second-generation DP-DES were initially developed to overcome the late safety and efficacy concerns with the preceding generation of devices. A meta-analysis³⁶ of 6,789 patients reported that

second-generation DP-DES had significantly reduced rates of ST (RR 0.35; 95% CI, 0.21–0.60; $P = 0.0001$), MI (RR 0.57; 95% CI, 0.45–0.73; $P < 0.00001$), and TLR (RR 0.59; 95% CI, 0.47–0.73; $P < 0.00001$) compared with first-generation DP-DES. Despite these improved outcomes, the new generation of devices are still limited by issues of long-term safety and efficacy. A prospective cohort study³ of 4,212 patients receiving second-generation DP-DES showed that the annual incidence rate of very late ST was 0.6% during a follow-up of four years.

The potential chronic inflammatory stimulus of the polymer coating ultimately led to the design of BP-DES in an attempt to reduce the risk of very late ST associated with DP-DES.⁵ The biodegradable nature of the polymer coating was thought to improve vascular healing response by reducing platelet aggregation and inflammatory

cell adhesion.³⁷ However, this benefit was not realized in the present meta-analysis, which found no significant difference between BP-DES and second-generation DP-DES for the risk of definite or probable ST at 5 years of follow-up and on landmark analysis beyond 1 year of follow-up. Similarly, a meta-analysis³⁸ of 13,480 patients showed no significant difference between BP-DES and first-generation DP-DES for the risk of definite or probable ST. Some animal studies^{39,40} demonstrated higher rates of inflammation associated with biodegradable polymers than durable polymers. The attenuated benefit of BP-DES may be explained by this chronic inflammatory process associated with the degradation of the polymer coating.

The polymer coatings in different BP-DES dissolve at various rates, including 2 months for the Synergy everolimus-eluting stent (Boston Scientific, Natick, Massachusetts) and 9 months for the Nobori biolimus-eluting stent (Terumo, Shibuya, Tokyo), which might result in differing safety and efficacy profiles.⁴¹ However, our sensitivity analysis based on BP-DES anti-proliferative drug (biolimus, everolimus, or sirolimus) found comparable rates of safety and efficacy outcomes between BP-DES and second-generation DP-DES. The lack of heterogeneity for all outcomes, including definite or probable ST, suggested that the demonstrated lack of benefit is consistent across different stent platforms. Furthermore, our sensitivity analysis based on DP-DES anti-proliferative drug (everolimus or zotarolimus) showed similar rates of safety and efficacy outcomes between BP-DES and second-generation DP-DES. This finding is consistent with a meta-analysis⁴² of 13,218 patients, which reported no significant differences between BP-DES and second-generation durable polymer everolimus-eluting stents for the risks of definite or probable ST (odds ratio [OR] 1.11; 95% CI, 0.92–1.13; $P = 0.28$), MI (OR 1.04; 95% CI, 0.84–1.28; $P = 0.72$), and TVR (OR 1.11; 95% CI, 0.92–1.33; $P = 0.28$).

BP-DES have been proposed to allow a shorter duration of DAPT due to improved vascular healing response in the stented segment.⁴³ In light of this theoretical advantage, BP-DES might offer a valuable therapeutic option to patients at high risk of bleeding or deemed unsuitable for prolonged use of DAPT, with minimal penalty in terms of safety and efficacy outcomes.⁴⁴ In fact, the latest American College of Cardiology/American Heart Association (ACC/AHA) guidelines⁴⁵ have shortened the recommended duration of DAPT from 12 months to 6 months following DES implantation. Our sensitivity analysis based on duration of DAPT (6 months or 12 months) demonstrated equivalent rates of safety and efficacy outcomes between BP-DES and second-generation DP-DES, thereby supporting the ACC/AHA recommendations for DES, with no additional advantages realized with BP-DES. The degradation of the polymer coating was thought to reduce the risk of very late ST in patients with BP-DES compared to those with DP-DES.⁹ However, this benefit was not realized in our sensitivity analysis, which found no significant differences in safety and efficacy outcomes between the two stent platforms at 5 years of follow-up and on landmark analysis beyond 1 year of follow-up.

We reduced the risk of bias by combining data from RCTs only. The number of patients in each comparison arm would have increased if we used less stringent inclusion and exclusion criteria. However, the absence of significant heterogeneity across the included studies suggested that risk estimates were unlikely to change by the inclusion of observational studies. There were limitations in our meta-analysis that

should be acknowledged. As with any meta-analysis, our study was based on aggregate data and, therefore, shared the possible limitations of the original studies, which in many cases compared stents with different anti-proliferative drugs, durations of DAPT, and lengths of follow-up. We attempted to address this source of bias by performing sensitivity analyses based on these variables. The present meta-analysis summarized the results of 19 RCTs, with a median follow-up of 12 months. Extension of follow-up beyond this time point in the original studies remains crucial to assessing late safety and efficacy outcomes of BP-DES once the polymer has been completely degraded. Further RCTs with abbreviated duration of DAPT and long-term follow-up in larger number of patients are necessary to assess the purported benefits of BP-DES.

5 | CONCLUSIONS

In summary, our findings demonstrated that BP-DES have similar safety and efficacy profiles to second-generation DP-DES, with comparable rates of definite or probable ST. Other safety and efficacy outcomes were equivalent between the two stent platforms.

FUNDING

None declared.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Wu JJ, Way JAH, Roy P, et al. Biodegradable polymer versus second-generation durable polymer drug-eluting stents in patients with coronary artery disease: A meta-analysis. *Health Sci Rep.* 2018;1:e93. <https://doi.org/10.1002/hsr2.93>