



OPEN

Biodegradable polymer everolimus-eluting stents versus contemporary drug-eluting stents: a systematic review and meta-analysis

Juntao Yin¹, Yang Li¹, Yangyang Chen², Chaoyang Wang^{3,4}✉ & Xiaoyong Song⁵✉

In spite of similar efficacy and safety in pilot studies, compared with the contemporary durable polymer drug-eluting stent (DP-DES), the bioabsorbable polymer drug-eluting stent (BP-DES) may be more superior in promoting blood vessel healing. We sought to compare the safety and efficacy of everolimus-eluting BP-DES (BP-EES) with contemporary DP-DES through a meta-analysis. We performed this meta-analysis to provide further evidence of the safety and efficacy of BP-EES. Medline, Embase and the Cochrane library databases were searched for randomized controlled trials comparing clinical efficacy and safety of BP-EES versus contemporary DP-DES. Fifteen RCTs with a total of 15,572 patients were selected. The rate of MACE was 9.4% in patients receiving BP-EES and 7.3% receiving DP-EES (RR 1.13, 95% CI 0.99–1.29, $p = 0.05$; $I^2 = 46\%$). TLF and MI were also similar in both groups. Based on the available data, this review demonstrates that BP-EES displays a clinically comparable efficacy and safety profile to that of contemporary DP-DES at years of follow-up in patients undergoing PCI.

Abbreviations

BP-DES	Bioabsorbable polymer drug-eluting stent
BP-EES	Bioabsorbable polymer everolimus-eluting stent
CI	Confidence intervals
CoCr	Cobalt chromium
DP	Durable polymer
DP-DES	Durable polymer drug-eluting stent
ISR	In-stent restenosis
ITT	Intention-to-treat
MACE	Major adverse cardiovascular event
MD	Mean differences
MI	Myocardial infarction
non-TLR TVR	Non-target lesion revascularization target vessel revascularization
PCI	Percutaneous coronary intervention
PLGA	Poly-lactide-co-glycolide
RCT	Randomized Controlled Trial
RR	Risk Ratio
ST	Stent thrombosis
TLF	Target-lesion failure
TLR	Target lesion revascularization
TVR	Target vessel revascularization

¹Department of Pharmacy, Huaihe Hospital, Henan University, Kaifeng, China. ²Department of Cardiology, Huaihe Hospital, Henan University, Kaifeng, Henan, China. ³Department of General Surgery, Huaihe Hospital, Henan University, Kaifeng, Henan, China. ⁴Evidence-Based Medicine Center, Department of Medicine, Henan University, Kaifeng 475000, Henan, China. ⁵Department of Pharmaceutics, School of Pharmacy, Henan University, Kaifeng 475000, Henan, China. ✉email: pharmayjt@sohu.com; 10200119@vip.henu.edu.cn

VLST	Very late stent thrombosis
ZES	Zotarolimus eluting stent

Implantation of drug-eluting stent (DES) that consists of a metal platform and a polymer coating with controlled release of antiproliferative agent has become the standard approach for percutaneous coronary intervention (PCI)^{1,2}. Although the DES implantation could reduce the rate of restenosis, the lifelong presence of a durable polymer (DP) in a coronary artery could result in persistent arterial inflammation, delayed vessel healing, and occasionally increases the risk of severe complications such as stent thrombosis (ST), very late stent thrombosis (VLST), myocardial infarction (MI)³ and in-stent restenosis (ISR)⁴. These shortcomings had driven stent iterations incorporating DES with biodegradable coatings (BP-DES) that leave only bare metal scaffolds after polymer resorption, and raised the obvious question of whether the development of BP-DES will improve outcomes. Compared with contemporary DP-DES, BP-DES have comparable clinical outcomes^{5,6}. The potential influence of other factors on the outcomes, such as polymer coatings composition and scaffolds strut thickness⁷, has been the focus of controversy^{8,9}. It is worth noting that the strut thickness of existing BP-DES varies significantly, which may be partly the cause that BP-DES fails to show superiority over DP-DES^{10,11}. Because thinner stent struts could reduce the incidence of in-stent restenosis (ISR) and target lesion revascularization (TLR)¹², Nowadays, novel BP-DES have uncoated struts and the struts are only half as thick as that of the contemporary BP-DES³. BP-EES, a novel thin-strut (74–79 µm) platinum chromium alloy stent, delivers abluminal everolimus from an ultrathin poly-lactide-co-glycolide (PLGA) biodegradable polymer¹³.

Results from several recently published randomized controlled trials (RCTs) are inspiring, showing that PCI with BP-EES or DP-DES is of similar outcomes^{14,15}. In this meta-analysis of RCTs, we made efforts to assess the clinical efficacy and safety of BP-EES versus contemporary DP-DES.

Methods

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines¹⁶.

Search strategy. A systematic literature search was conducted by two authors independently using MEDLINE, Embase, and the Cochrane Library from inception to January 15, 2022 for RCTs comparing BP-EES with latest generation DP-DES. The search keywords were as follows: “everolimus” AND “stent” AND “biodegradable polymer” OR “bioresorbable polymer” OR “bioabsorbable polymer”.

Eligibility criteria. Eligibility criteria were developed in accordance with the PICOS approach¹⁷. To perform this meta-analysis, in which all enrolled RCTs had been published, we used the PRISMA 2020 27-item checklist¹⁸. No restrictions on language, year, or study design were imposed, and the search strategy complied with the PRESS Guidelines¹⁹. Retrieve and carefully manual search the list of references for the original paper to identify other relevant studies.

Data extraction and quality assessment. Two investigators (JY and CW) independently reviewed the eligibility of retrieved articles. Discrepancy will be resolved through consultation with a third independent investigator (XS). Pre-specified data were extracted from each enrolled study including: study design and duration, demographic and clinical characteristics of the study population, and duration of follow-up. Outcomes of interest including cardiac death, ST, MI, TLR, TLF, all-cause mortality, vessel restenosis, and MACE, were extracted as counts and percentages and recorded according the intention-to-treat (ITT) principle.

Two authors (JY and XS) independently assessed risk of bias (ROB) using the Cochrane risk of bias tool version 2.0 for RCTs²⁰. All conflicts were resolved through discussion. The Robvis web application was used to produce and visualize relevant plots²¹. Authors JY and CW conducted the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) independently via the GRADEpro GDT web application and resolved conflicts through discussion²².

Data synthesis and analysis. Baseline risk factors and outcomes were reported as pooled proportions or mean differences (MD) with 95% confidence intervals (CI). Random effect model was selected to calculate the pooling relative risk (RR) and its 95% CI²³. If no statistical heterogeneity was present, a fixed-effect model was used to pool data. However, if there was heterogeneity (I^2 ranging from 50 to 75%), a random-effects model was used to pool data.

Heterogeneity among trials was evaluated using the I^2 statistic and the Chi² test²⁴. I^2 values of < 25%, 25–50% and > 50% correspond to low, moderate and high levels of heterogeneity, respectively. For the Chi² test, a P value of 0.10 was considered statistically significant. We investigated potential explanations for heterogeneity by visually inspecting the forest plot. Funnel plots were used to calculate publication bias when two or more trials were enrolled. Statistical significance for hypothesis test was set at the level of 0.05. The Review Manager 5.4 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020) was used to synthesize the data on an ITT basis.

Results

Study selection and characteristics. A PRISMA flowchart illustrates the selection process and the number of articles, with reasons included for why studies were excluded at each step of the meta-analysis 47 (Fig. 1). Fifteen RCTs met our inclusion criteria^{2,13,25–37}. Some data are from shorter follow-up time of the same study^{25,31}

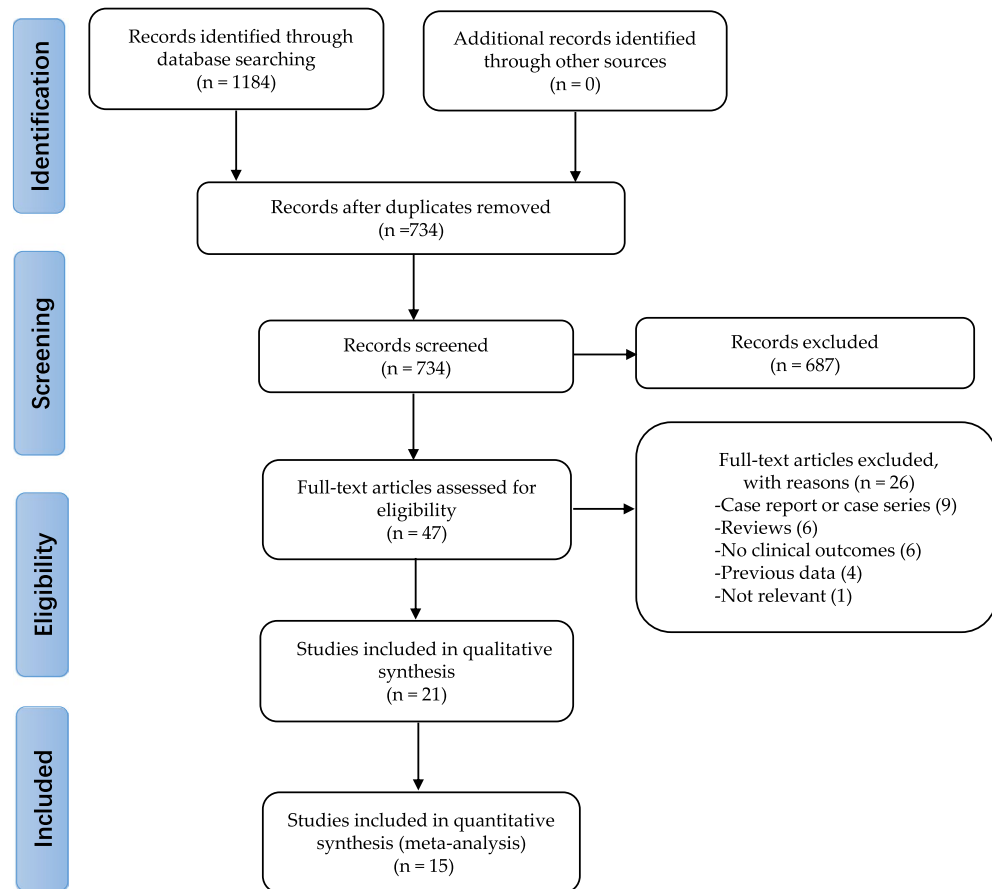


Figure 1. The flowchart of the database search and study selection.

or from a single center in a multi-center study^{13,36–38}. Therefore, a total of ten RCTs with 15,572 patients were included in the final analysis. Among these patients, 5290 were randomized to receive a BP-EES, and 10,282 patients to receive a DP-DES (DP-EES (n = 2440) and DP-zotarolimus eluting stent (ZES) (n = 1438). Unfortunately, we cannot determine how many of the other 6404 people in a study received either of the two DP-DES)²⁷. Characteristics of included trials and stent used are presented in Table 1.

Patients characteristics on the included trials are presented in Table 2. No difference was found in age (pooled mean, 61.2 vs. 61.4 years, $p = 0.69$), male sex (73.8 vs. 72.2%, $p = 0.42$), smoking habit (28.9 vs. 30.5%, $p = 0.30$), diabetes (26.7 vs. 26.8%, $p = 0.78$), hypertension (66.0 vs. 67.3%, $p = 0.96$), dyslipidaemia (59.3 vs. 60.0%, $p = 0.46$), or unstable angina (26.6 vs. 27.0%, $p = 0.74$). Patients who received DP-DES had a higher prevalence of prior MI (18.6 vs. 21.9%, $p < 0.001$) compared with BP-EES. Table 2 also present procedural characteristics and there was no difference among treated vessels.

Risk of bias was predominately low across all studies except in regards to performance bias (Fig. 2). The individual items of the risk of bias are presented in Fig. 3.

Primary outcome TLF. Target-lesion failure (TLF), a composite endpoint of cardiac death, MI, and clinically indicated TLR, represent a safety and efficacy outcome³⁸. Study-level outcomes at longest available follow-up for MACE, the individual components of MACE and TLR are summarized in Table 3. TLF was comparable between patients intervened with BP-EES and DP-DES (8.8% vs. 6.8%; RR 1.09, 95% CI 0.95–1.24; $I^2 = 9\%$) (Fig. 4). The rate of MACE was 9.4% in patients receiving BP-EES and 7.3% receiving DP-EES (RR 1.13, 95% CI 0.99–1.29; $I^2 = 46\%$) (Fig. 5). The rate of TLR was also comparable between patients intervened with BP-EES and DP-DES (4.4% vs. 4.1%, RR 1.09, 95% CI 0.90–1.32; $I^2 = 10\%$) (Fig. 6).

Secondary outcomes MI, cardiac death and ST. The meta-analysis showed no significant difference between BP-EES and DP-DES in MI (5.9% vs. 4.4%; RR 1.14, 95% CI 0.96–1.35; $I^2 = 0\%$) (Fig. S1), ST (1.2% vs. 0.8%; RR 1.63, 95% CI 1.00–2.66; $I^2 = 7\%$) (Fig. S2), cardiac mortality (1.3% vs. 1.4%, RR 0.82, 95% CI 0.58–1.15; $I^2 = 0\%$) (Fig. S3), All-cause death (2.8% vs. 2.3%, RR 0.94, 95% CI 0.74–1.18; $I^2 = 0\%$) (Fig. S4), or Target vessel failure (11.5% vs. 4.1%, RR 1.26, 95% CI 0.51–3.12; $I^2 = 98\%$) (Fig. S5). There was no significant difference between BP-EES and DP-DES in Target vessel revascularization (7.3% vs. 6.4%, RR 0.89, 95% CI 0.64–1.25;

Study/ first author	Number of patients (N)		DAPT Duration (months)	Follow-up (months)	BP-EES characteristics					DP-DES characteristics			
	BP-EES	DP-DES			Stent	Strut Thickness (μm)	Scaffoldmaterial	Drug release (months)	Polymer biodegradation (months)	Stent	Strut thickness (μm)	Drug	Scaffold material
Baber 2020	491	4990	> 12	15	Synergy	74	Pl-Cr	3	4	Xience V Resolute Integrity Resolute Onyx Promus Element	81 91 81 or 90 81	Everoli- mus zotaroli- mus zotaroli- mus Everoli- mus	Co-Cr Co-Cr Co-Cr Pl-Cr
Birgelen 2016	1172	1173	> 6	12	Synergy	74	Pl-Cr	3	4	Resolute Integrity	91	zotaroli- mus	Co-Cr
Buiten 2020	252	265	> 6	24	Synergy	74	Pl-Cr	3	4	Resolute Integrity	91	zotaroli- mus	Co-Cr
Chevalier 2016	335	166	> 6	24	Absorb	150	PLLA and PDLLA	24	36	Xience V	81	Everoli- mus	Co-Cr
Han 2017	205	207	> 6	12	Synergy	74	Pl-Cr	3	4	Promus Element	81	Everoli- mus	Pl-Cr
Kereiakes 2017	1322	686	> 12	36	Absorb	150	PLLA and PDLLA	24	36	Xience V	81	Everoli- mus	Co-Cr
Kereiakes 2019	846	838	> 12	60	Synergy	74	Pl-Cr	3	4	Promus Element	81	Everoli- mus	Pl-Cr
Meredith 2018	92	98	> 6	60	Synergy	74	Pl-Cr	3	4	Promus Element	81	Everoli- mus	Pl-Cr
Onuma 2016	261	130	> 12	24	Absorb	150	PLLA and PDLLA	24	36	Xience V	81	Everoli- mus	Co-Cr
Xu 2018	236	235	> 12	36	Absorb	150	PLLA and PDLLA	24	36	Xience V	81	Everoli- mus	Co-Cr

Table 1. Characteristics of the included trials and stent used. *BP-EES* biodegradable polymer everolimus-eluting stent(s), *Co-Cr* cobalt-chromium, *DAPT* dual-antiplatelet therapy, *DP-DES* durable polymer drug-eluting stent(s), *PDLLA*, poly(D,L-lactide), *Pl-Cr* latinumchromium, *PLLA* poly(L-lactide), *SS* stainless steel.

Baseline characteristics	No. of studies	BP-EES	DP-DES	<i>p</i> value	<i>I</i> ²	Fixed-effects estimates
Age, years	10	61.2 ± 10.3	61.4 ± 10.2	0.69	38%	0.83 [0.62, 1.06]
Male	10	73.8 ± 4.35	72.2 ± 3.3	0.42	47%	1.02 [0.98, 1.06]
Smoking habit	8	28.9 ± 14	30.5 ± 14	0.30	0%	0.97 [0.92, 1.03]
Diabetes	10	26.7 ± 7.7	26.8 ± 6.9	0.78	0%	1.01 [0.95, 1.07]
Hypertension	10	66.0 ± 13.5	67.3 ± 12.3	0.96	23%	1.00 [0.97, 1.03]
Dyslipidaemia	9	59.3 ± 22.4	60.0 ± 23.3	0.46	0%	0.99 [0.96, 1.02]
Prior myocardial infarction	10	18.6 ± 7.6	21.9 ± 8.8	< 0.0001	2%	0.85 [0.79, 0.92]
Unstable angina	9	26.6 ± 17.4	27.0 ± 16.8	0.74	14%	0.99 [0.91, 1.07]
Treated vessels						
LAD	10	46.8 ± 5.8	45.5 ± 6.4	0.42	0%	1.02 [0.98, 1.06]
Cx	9	24.5 ± 5.2	26.8 ± 3.9	0.07	21%	0.93 [0.87, 1.01]
RCA	10	33.6 ± 6.6	32.1 ± 5.4	0.19	3%	1.03 [0.98, 1.08]
Left main	4	3.8 ± 4.2	4.2 ± 4.6	0.28	0%	0.86 [0.65, 1.13]
Reference vessel diameter, mm	6	2.7 ± 0.1	2.7 ± 0.1	0.54	0%	0.76 [0.62, 1.19]
Minimal lumen diameter, mm	6	0.8 ± 0.1	0.8 ± 0.1	0.92	48%	1.02 [0.84, 1.21]
Total lesion length, mm	5	14.8 ± 1.2	14.6 ± 1.1	0.34	32%	0.95 [0.80, 1.17]
Stenosis diameter	5	70.8 ± 5.9	70.2 ± 5.4	0.08	39%	0.79 [0.58, 1.03]
Stent length, mm	4	26.9 ± 8.9	26.9 ± 9.1	0.16	20%	0.97 [0.78, 1.05]

Table 2. Patients and procedural characteristics. Bold values showing statistical significant difference. Values are proportions, mean differences or RR with 95% confidence intervals (in parentheses). *BP-EES* biodegradable polymer everolimus-eluting stent, *DP-DES* durable polymer drug-eluting stent, *CI* confidence interval, *CABG* coronary artery bypass grafting, *PCI* percutaneous coronary intervention, *LAD* left anterior descending artery, *Cx* circumflex artery, *RCA* right coronary artery.

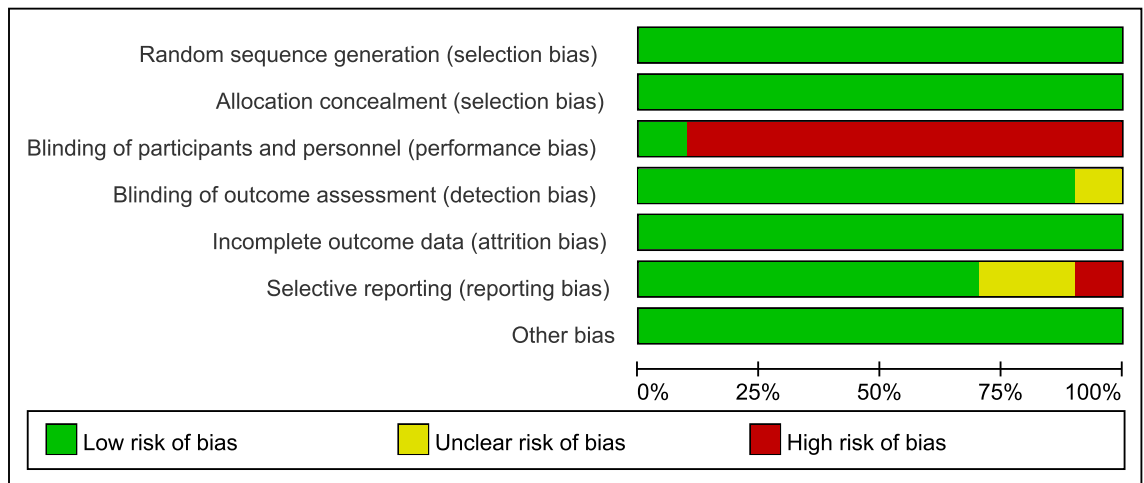


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

$I^2 = 62%$) (Fig. S6). Again, no significant difference was noted between BP-EES and DP-DES in non-target lesion revascularization target vessel revascularization (non-TLR TVR) (2.7% vs. 2.6%, RR 0.77, 95% CI 0.38–1.56; $I^2 = 65%$) (Fig. S7).

Discussion

Prior meta-analysis³⁹ demonstrated no significant difference in clinical outcomes at one-year follow-up in patients treated with BP-EES (only include the *Synergy*[™] stent) or DP-DES. This current meta-analysis is the largest sample size meta-analysis comparing BP-EES to contemporary DP-DES, which involves 15 RCTs with 15,772 patients' years of follow-up. In our meta-analysis, we demonstrated that both BP-EES and contemporary DP-DES had similar safety and efficacy profiles in patients with obstructive coronary artery disease. Although there was numerical increase in TVR and reduction in cardiac mortality with BP-EES, there was no statistically significant difference, with regard to the low rates in both groups. There was no significant difference in TLR, MI, ST or TLF, MACE when comparing BP-EES with contemporary DP-DES. In addition to BP-EES, the biolimus-eluting *Nobori* stent and bioresorbable Sirolimus-eluting *MiStent*, have shown similar difference in TLR and ST compared with contemporary DP-DES^{40,41}.

Interestingly, while there was a trend for less TVR associated with BP-EES in several studies^{2,13,28,29}, this meta-analysis of all available RCTs showed no significant difference between BP-EES and contemporary DP-DES. The outcomes, while demonstrating no superiority of BP-EES, suggest that the BP-EES is not inferior to newer, widespread used DP-DES. Furthermore, considering ST with the *Absorb*[™] (*Abbott Vascular*) bioresorbable vascular scaffold^{42,43}, these data do not cause BP-EES safety concerns. Current generation DP-DES with superior antiproliferative drug, pharmacokinetic release profile, stent, and strut thickness, demonstrating better efficacy compared with previous generation stents^{11,44}, remains the benchmark for comparison. However, durable polymer coating in these stents might lead to chronic arterial inflammation and incomplete endothelialization, resulting in delayed vascular healing and nidus for ST and VLST⁴⁵. Indeed, whether BP-DES can improve clinical efficacy when compared with newer DP-DES has been a controversial topic⁴⁶ and may be affected by other factors, such as polymer composition and strut thickness⁷. Some research has further developed approaches to meet challenges in the design of polymeric drug delivery systems⁴⁷. It is obvious that there is significant variability in the strut thickness of available BP-DES, which may account for the efficacy inconsistency between BP-DES and DP-DES^{48,49}. This inconsistency may be also associated with the biocompatible polymer of contemporary DP-DES and subsequent improvements in safety and efficacy, which counteract the benefits of BP⁷. Newer generation ultra-thin strut BP-DES (strut thickness < 70 μm) could cause a 16% reduction in incidence of TLF driven by lower rates of MI and ST^{12,50}. Additionally, the advantages of thin or ultra-thin stents BP-DES, which can reduce platelet aggregation and inflammatory cell adhesion^{51,52}, may be very helpful in certain clinical situations, such as small-vessel PCI or in-stent restenosis.

The current meta-analysis cannot show a significantly reduced risk of late ST/VLST between BP-DES and DP-DES. Eight of the ten trials included in the study (including two 5-years and two 3-years) present a follow-up for more than two-year post implantation. Previous RCTs and meta-analyses demonstrated that BP-DES were associated with lower incidence of late ST/VLST compared with either bare metal stents or first generation DES⁵³. Furthermore, recent studies have shown lower rates of ST in the newer generation cobalt chromium (CoCr) and PtCr durable polymer (polyvinylidene fluoride) EES than other DP-DES, early BP-DES and bare metal scaffolds^{54,55}. Eventually, a large sample size RCT of the CoCr EES vs. the *Nobori*[™] (*Terumo*) BP-DES showed comparable long-term outcomes between both stents⁵⁶. These obvious discrepancies may be partly due to the design difference of BP-DES platform⁶. Many factors, such as metal alloys, stent strut thickness, polymer composition, and distribution, may affect the time course of biodegradable polymer and scope of endothelial stent coverage, as well as the function and maturation of endothelial cells^{7,57}. These aspects emphasize that device specific analysis is more important than stent category.

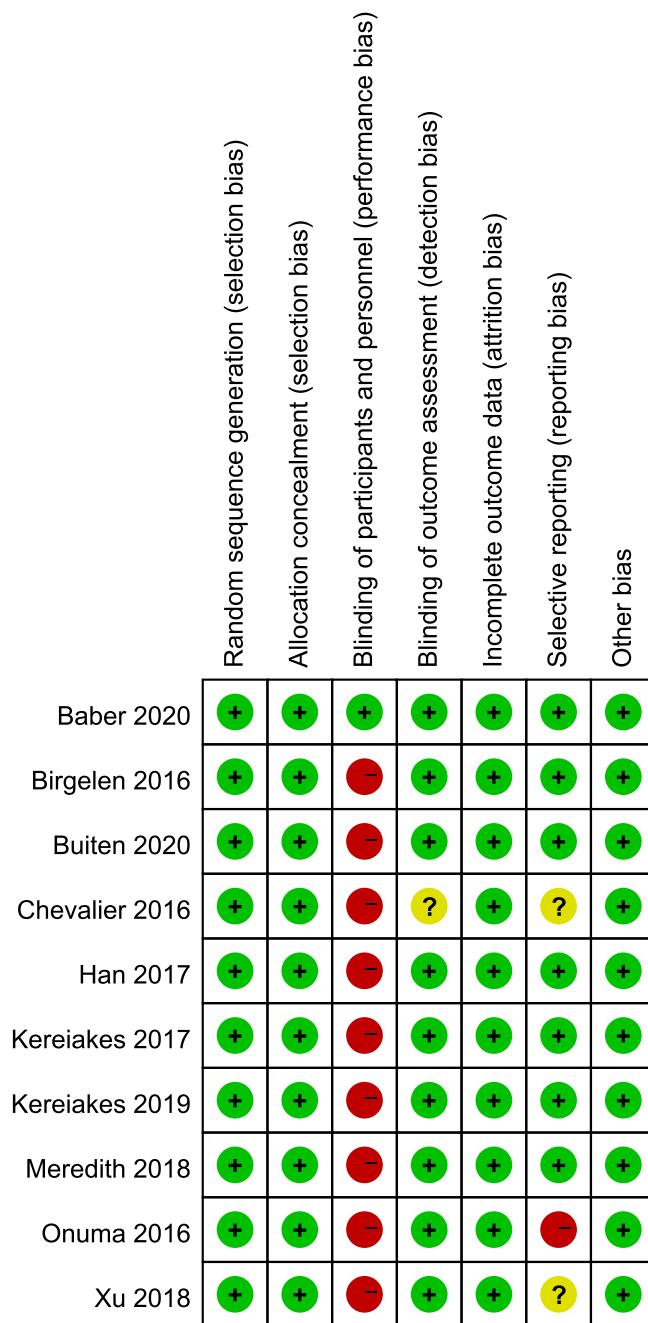


Figure 3. Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.

This paper, like any meta-analysis, also shares the limitations of original research. First, we can access no information on the duration of DAPT, which may influence the clinical outcomes. Second, this is a study-level meta-analysis, so it is impossible to investigate the role of several confounders at the patient level. Third, we grouped all types of DP-DES into a control group, which may cause potential heterogeneity. However, our subgroup analysis has no significant interaction between the two different types of device. The small number of DP-ZES subgroup studies may limit results of subgroup analysis, and reliability of the conclusions may be decreased by moderate heterogeneity of some secondary outcome analysis.

Since we included only RCTs and used all available study data, the likelihood of publication bias seems low. Although this meta-analysis included 15 RCTs with 15,772 patients, it may still be insufficient to assess minor difference in the incidence of rare adverse events such as ST/VLST.

Analysis (no. of trials included)	TVR RR (95% CI)	Cardiac death RR (95% CI)	MI RR (95% CI)	Definite/probable ST RR (95% CI)
Outcomes at 1 year (2)	0.72 [0.45, 1.17]	1.00 [0.42, 2.40]	0.88 [0.54, 1.44]	0.73 [0.25, 2.20]
Outcomes at the longest follow-up (8)	0.95 [0.64, 1.41]	0.79 [0.55, 1.15]	1.18 [0.99, 1.42]	1.63 [1.01, 2.64]
Landmark analysis beyond 1 year (8)	0.95 [0.64, 1.41]	0.79 [0.55, 1.15]	1.18 [0.99, 1.42]	1.63 [1.01, 2.64]
Subgroup analysis				
BP-EES strut thickness				
Thin struts (6)	0.64 [0.39, 1.06]	0.76 [0.51, 1.12]	1.03 [0.83, 1.28]	0.80 [0.45, 1.43]
Thick struts (4)	1.40 [1.08, 1.82]	1.07 [0.53, 2.19]	1.34 [1.01, 1.77]	3.07 [1.46, 6.46]
DP eluting drug				
Everolimus (7)	1.10 [0.81, 1.48]	0.82 [0.56, 1.21]	1.19 [0.99, 1.44]	1.66 [1.01, 2.72]
Zotarolimus (2)	0.53 [0.22, 1.25]	0.83 [0.40, 1.71]	0.89 [0.58, 1.38]	0.79 [0.30, 2.12]
DAPT duration				
≥ 6 months (5)	0.53 [0.33, 0.85]	0.96 [0.49, 1.89]	0.94 [0.64, 1.38]	1.01 [0.43, 2.36]
≥ 12 months (5)	1.24 [1.03, 1.50]	0.78 [0.53, 1.16]	1.20 [0.99, 1.45]	1.64 [0.98, 2.74]

Table 3. Cardiac outcomes. *MI* myocardial infarction, *RR* risk ratio, *ST* stent thrombosis, *TVR* target vessel revascularization, other abbreviations as in Table 1.

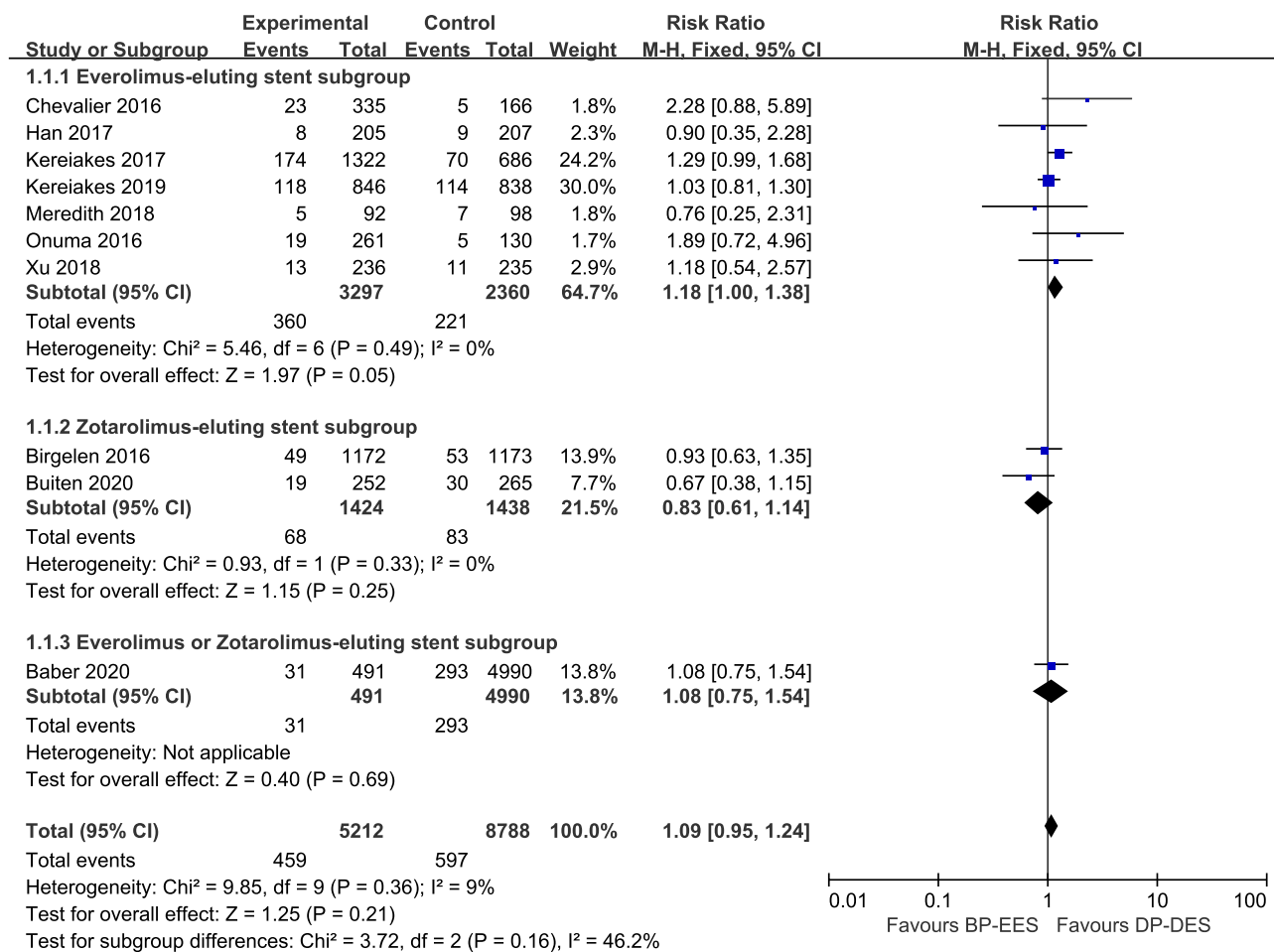


Figure 4. The pooled RR of target-lesion failure between patients intervened with BP-EES and DP-DES with subgroup analysis.

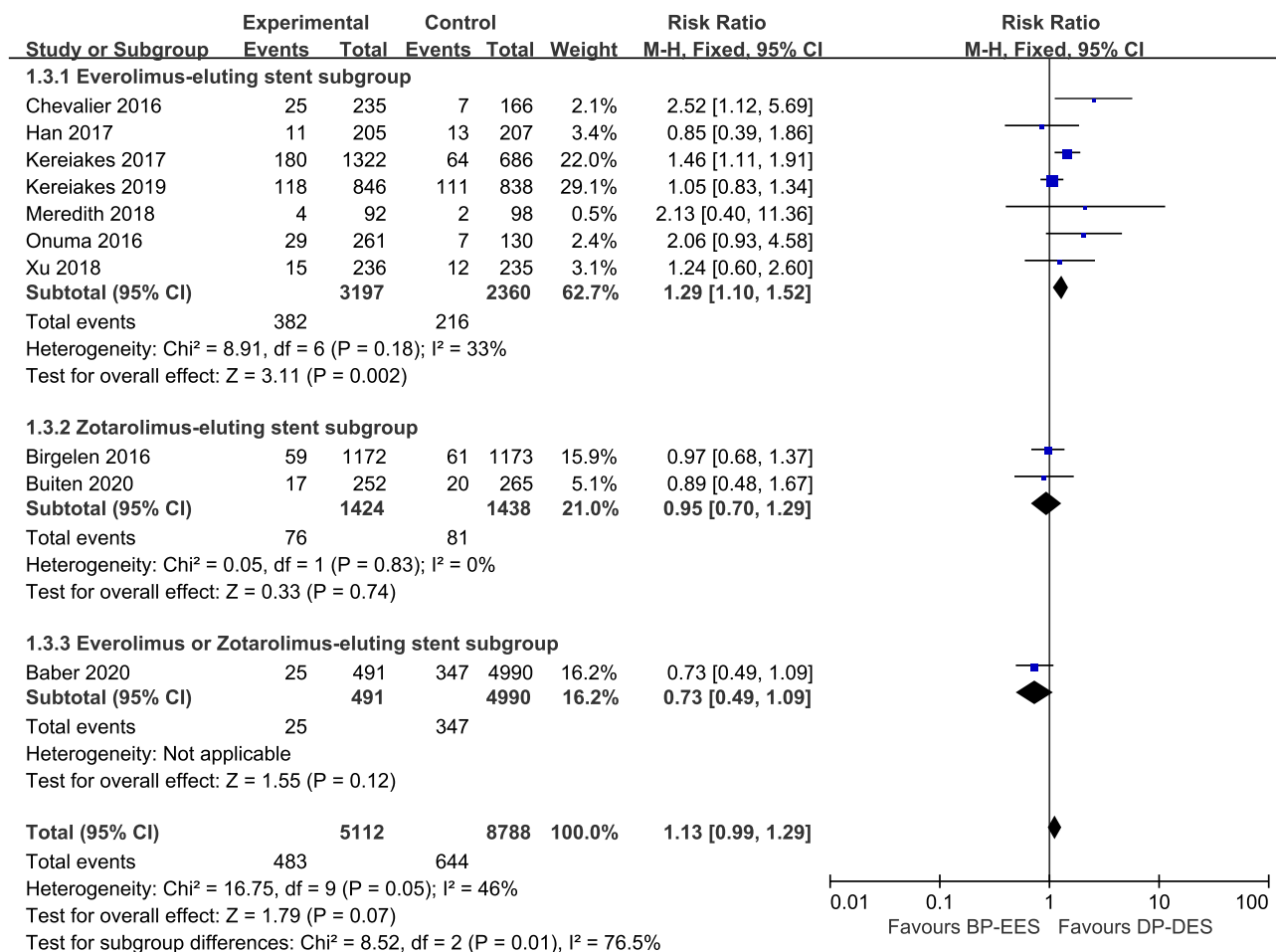


Figure 5. The pooled RR of major adverse cardiovascular event between patients intervened with BP-EES and DP-DES with subgroup analysis.

Conclusions

In this meta-analysis comparing BP-EES with contemporary DP-DES, no significant differences in clinical outcomes were found between the two platforms, which suggests that the safety and efficacy of BP-EES are comparable to contemporary DP-DES.

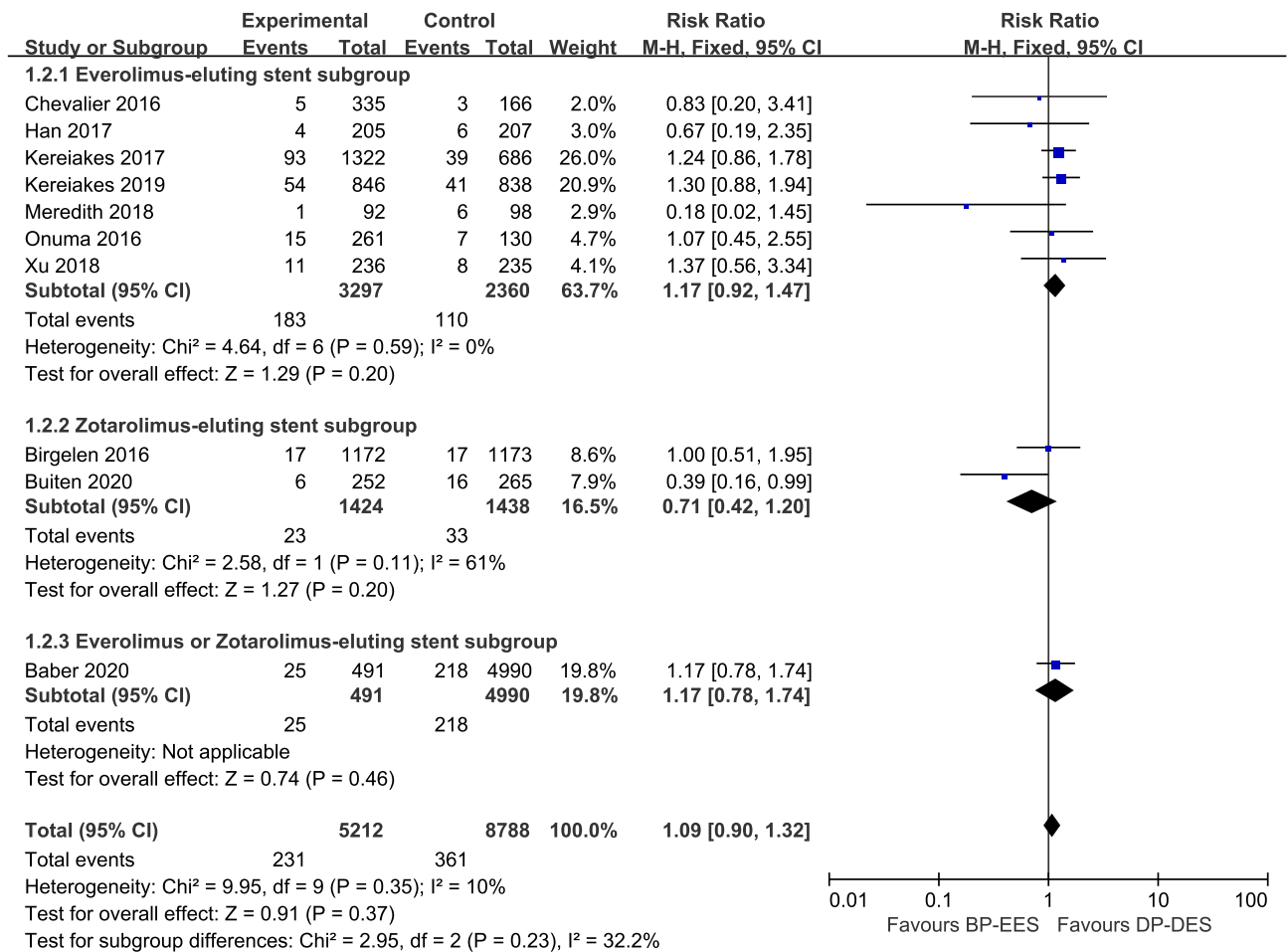


Figure 6. The pooled RR of target lesion revascularization between patients intervened with BP-EES and DP-DES with subgroup analysis.

Data availability

The present study is a meta-analysis of published randomized trials. All data used for analyses are presented in the manuscript.

Received: 18 August 2022; Accepted: 19 December 2022

Published online: 31 January 2023

References

- Kelly, C. R. *et al.* Long-term safety and efficacy of platinum chromium everolimus-eluting stents in coronary artery disease: 5-year results from the PLATINUM trial. *JACC Cardiovasc. Interv.* **10**, 2392–2400. <https://doi.org/10.1016/j.jcin.2017.06.070> (2017).
- von Birgelen, C. *et al.* Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): A three-arm, randomised, non-inferiority trial. *Lancet* **388**, 2607–2617. [https://doi.org/10.1016/s0140-6736\(16\)31920-1](https://doi.org/10.1016/s0140-6736(16)31920-1) (2016).
- Byrne, R. A., Stone, G. W., Ormiston, J. & Kastrati, A. Coronary balloon angioplasty, stents, and scaffolds. *Lancet* **390**, 781–792. [https://doi.org/10.1016/s0140-6736\(17\)31927-x](https://doi.org/10.1016/s0140-6736(17)31927-x) (2017).
- Tocci, G. *et al.* Blood pressure levels at the time of percutaneous coronary revascularization and risk of coronary in-stent restenosis. *Am. J. Hypertens.* **29**, 509–518. <https://doi.org/10.1093/ajh/hpv131> (2016).
- El-Hayek, G. *et al.* Meta-analysis of randomized clinical trials comparing biodegradable polymer drug-eluting stent to second-generation durable polymer drug-eluting stents. *JACC Cardiovasc. Interv.* **10**, 462–473. <https://doi.org/10.1016/j.jcin.2016.12.002> (2017).
- Iglesias, J. F. *et al.* Orsiro cobalt-chromium sirolimus-eluting stent: present and future perspectives. *Expert Rev. Med. Devices* **14**, 773–788. <https://doi.org/10.1080/17434440.2017.1378091> (2017).
- Palmaz, J. C., Bailey, S., Marton, D. & Sprague, E. Influence of stent design and material composition on procedure outcome. *J. Vasc. Surg.* **36**, 1031–1039. <https://doi.org/10.1067/mva.2002.129113> (2002).
- Trimukhe, R., Vani, P., Patel, A. & Salgotra, V. Safety and performance of the EverPro(TM) everolimus-eluting coronary stent system with biodegradable polymer in a real-world scenario. *World J. Cardiol.* **12**, 615–625. <https://doi.org/10.4330/wjc.v12.i12.615> (2020).
- Iannaccone, M. *et al.* Comparison of bioresorbable vs durable polymer drug-eluting stents in unprotected left main (from the RAIN-CARDIOGROUP VII Study). *BMC Cardiovasc. Disord.* **20**, 225. <https://doi.org/10.1186/s12872-020-01420-5> (2020).
- Matsuda, H. *et al.* Midterm clinical impacts of biodegradable polymer everolimus-eluting stents compared with durable polymer everolimus-eluting stents: A 3-year propensity-matched study. *J. Interv. Cardiol.* <https://doi.org/10.1155/2020/2869303> (2020).

11. Pilgrim, T. *et al.* Biodegradable-versus durable-polymer drug-eluting stents for STEMI: final 2-year outcomes of the BIOSTEMI trial. *JACC Cardiovasc. Interv.* **14**, 639–648. <https://doi.org/10.1016/j.jcin.2020.12.011> (2021).
12. Bangalore, S., Toklu, B., Patel, N., Feit, F. & Stone, G. W. Newer-generation ultrathin strut drug-eluting stents versus older second-generation thicker strut drug-eluting stents for coronary artery disease. *Circulation* **138**, 2216–2226. <https://doi.org/10.1161/circulationaha.118.034456> (2018).
13. Meredith, I. T. *et al.* Final five-year clinical outcomes in the EVOLVE trial: A randomised evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting stent. *EuroIntervention* **13**, 2047–2050. <https://doi.org/10.4244/eij-d-17-00529> (2018).
14. Kereiakes, D. J. *et al.* Efficacy and safety of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent: The EVOLVE II randomized trial. *Circ. Cardiovasc. Interv.* **8**, e002372. <https://doi.org/10.1161/circinterventions.114.002372> (2015).
15. Kereiakes, D. J. *et al.* Clinical outcomes following implantation of thin-strut, bioabsorbable polymer-coated, everolimus-eluting SYNERGY stents. *Circ. Cardiovasc. Interv.* **12**, e008152. <https://doi.org/10.1161/CIRCINTERVENTIONS.119.008152> (2019).
16. Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med.* **6**, e1000097. <https://doi.org/10.1371/journal.pmed.1000097> (2009).
17. Namin, S., Zhou, Y., Neuner, J. & Beyer, K. The role of residential history in cancer research: A scoping review. *Soc. Sci. Med.* **270**, 113657. <https://doi.org/10.1016/j.socscimed.2020.113657> (2021).
18. Rethlefsen, M. L. *et al.* PRISMA-S: An extension to the PRISMA statement for reporting literature searches in systematic reviews. *Syst. Rev.* **10**, 39. <https://doi.org/10.1186/s13643-020-01542-z> (2021).
19. McGowan, J. *et al.* PRESS peer review of electronic search strategies: 2015 guideline statement. *J. Clin. Epidemiol.* **75**, 40–46. <https://doi.org/10.1016/j.jclinepi.2016.01.021> (2016).
20. Sterne, J. A. C. *et al.* RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ* **366**, l4898. <https://doi.org/10.1136/bmj.l4898> (2019).
21. McGuinness, L. A. & Higgins, J. P. T. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Res. Synth. Methods* **12**, 55–61. <https://doi.org/10.1002/jrsm.1411> (2021).
22. Schünemann, H., Guyatt, G. & Oxman, A. GRADE handbook for grading quality of evidence and strength of recommendations: The GRADE Working Group. 2013. guidelinedevelopment.org/handbook, Updated October 2013. Accessed December (2018).
23. Higgins, J. P. *et al.* The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* **343**, d5928. <https://doi.org/10.1136/bmj.d5928> (2011).
24. Higgins, J. P., Thompson, S. G., Deeks, J. J. & Altman, D. G. Measuring inconsistency in meta-analyses. *BMJ* **327**, 557–560. <https://doi.org/10.1136/bmj.327.7414.557> (2003).
25. Meredith, I. T. *et al.* Six-month IVUS and two-year clinical outcomes in the EVOLVE FHU trial: A randomised evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting stent. *EuroIntervention* **9**, 308–315. <https://doi.org/10.4244/EIJV9I3A52> (2013).
26. Arroyo, D. *et al.* Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds: Two-year clinical outcomes of the EVERBIO II trial. *Int. J. Cardiol.* **243**, 121–125. <https://doi.org/10.1016/j.ijcard.2017.05.053> (2017).
27. Baber, U. *et al.* Safety and efficacy of the bioabsorbable polymer everolimus-eluting stent versus durable polymer drug-eluting stents in high-risk patients undergoing PCI: TWILIGHT-SYNERGY. *Catheter. Cardiovasc. Interv.* **97**, 63–71. <https://doi.org/10.1002/ccd.28995> (2020).
28. Buiten, R. A. *et al.* Three contemporary thin-strut drug-eluting stents implanted in severely calcified coronary lesions of participants in a randomized all-comers trial. *Catheter. Cardiovasc. Interv.* **96**, E508–e515. <https://doi.org/10.1002/ccd.28886> (2020).
29. Han, Y. *et al.* A randomised comparison of biodegradable polymer- and permanent polymer-coated platinum-chromium everolimus-eluting coronary stents in China: The EVOLVE China study. *EuroIntervention* **13**, 1210–1217. <https://doi.org/10.4244/eij-d-17-00271> (2017).
30. Kereiakes, D. J. *et al.* 3-Year clinical outcomes with everolimus-eluting bioresorbable coronary scaffolds: The ABSORB III trial. *J. Am. Coll. Cardiol.* **70**, 2852–2862. <https://doi.org/10.1016/j.jacc.2017.10.010> (2017).
31. Kereiakes, D. J. *et al.* Efficacy and safety of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent: The EVOLVE II Randomized Trial. *Circ. Cardiovasc. Interv.* **8**, e002372. <https://doi.org/10.1161/CIRCINTERVENTIONS.114.002372> (2015).
32. Kereiakes, D. J. *et al.* Clinical outcomes following implantation of thin-strut, bioabsorbable polymer-coated, everolimus-eluting SYNERGY stents: Final 5-year results of the EVOLVE II randomized trial. *Circ. Cardiovasc. Qual. Outcomes* **12**, e008152. <https://doi.org/10.1161/CIRCINTERVENTIONS.119.008152> (2020).
33. Kimura, T. *et al.* Final 5-year results in randomized Japanese patients implanted with a thin-strut, bioabsorbable, polymer-coated, everolimus-eluting SYNERGY stent (from the EVOLVE II study). *Circ. Rep.* **3**, 9–17. <https://doi.org/10.1253/circrep.CR-20-0114> (2020).
34. Meredith, I. T. *et al.* Primary endpoint results of the EVOLVE trial: A randomized evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent. *J. Am. Coll. Cardiol.* **59**, 1362–1370. <https://doi.org/10.1016/j.jacc.2011.12.016> (2012).
35. Chevalier, B. *et al.* Randomised comparison of a bioresorbable everolimus-eluting scaffold with a metallic everolimus-eluting stent for ischaemic heart disease caused by de novo native coronary artery lesions: the 2-year clinical outcomes of the ABSORB II trial. *EuroIntervention* **12**, 1102–1107. https://doi.org/10.4244/eijy16m08_01 (2016).
36. Onuma, Y. *et al.* Two-year clinical, angiographic, and serial optical coherence tomographic follow-up after implantation of an everolimus-eluting bioresorbable scaffold and an everolimus-eluting metallic stent: insights from the randomised ABSORB Japan trial. *EuroIntervention* **12**, 1090–1101. https://doi.org/10.4244/eijy16m09_01 (2016).
37. Xu, B. *et al.* Comparison of everolimus-eluting bioresorbable vascular scaffolds and metallic stents: Three-year clinical outcomes from the ABSORB China randomised trial. *EuroIntervention* **14**, e554–e561. <https://doi.org/10.4244/eij-d-17-00796> (2018).
38. Lou, Y. *et al.* Five-year outcomes of biodegradable polymer drug-eluting stents versus second-generation durable polymer drug-eluting stents: A meta-analysis of randomized controlled trials. *Cardiovasc. Drugs Ther.* **33**, 557–566. <https://doi.org/10.1007/s10557-019-06912-x> (2019).
39. Picard, F. *et al.* Comparison of the biodegradable polymer everolimus-eluting stent with contemporary drug-eluting stents: A systematic review and meta-analysis. *Int. J. Cardiol.* **278**, 51–56. <https://doi.org/10.1016/j.ijcard.2018.11.113> (2019).
40. Kufner, S. *et al.* Ten-year clinical outcomes from a trial of three limus-eluting stents with different polymer coatings in patients with coronary artery disease. *Circulation* **139**, 325–333. <https://doi.org/10.1161/circulationaha.118.038065> (2019).
41. Kaiser, C. *et al.* Long-term efficacy and safety of biodegradable-polymer biolimus-eluting stents: Main results of the Basel Stent Kosten-Effektivitäts Trial-PROspective Validation Examination II (BASKET-PROVE II), a randomized, controlled noninferiority 2-year outcome trial. *Circulation* **131**, 74–81. <https://doi.org/10.1161/circulationaha.114.013520> (2015).
42. Ali, Z. A. *et al.* Three-year outcomes with the absorb bioresorbable scaffold: Individual-patient-data meta-analysis from the absorb randomized trials. *Circulation* **137**, 464–479. <https://doi.org/10.1161/circulationaha.117.031843> (2018).
43. Pradhan, A., Vishwakarma, P., Vankar, S. & Sethi, R. “The unpredictable ABSORB” - Very late stent thrombosis of bioresorbable vascular scaffold. *Heart Views* **20**, 65–69. https://doi.org/10.4103/heartviews.Heartviews_18_19 (2019).
44. Bavishi, C. *et al.* Efficacy and safety of everolimus and zotarolimus-eluting stents versus first-generation drug-eluting stents in patients with diabetes: A meta-analysis of randomized trials. *Int. J. Cardiol.* **230**, 310–318. <https://doi.org/10.1016/j.ijcard.2016.12.116> (2017).

45. Gatto, P. *et al.* Incomplete stent apposition and very late stent thrombosis after everolimus eluting stent implantation and dual antiplatelet therapy interruption. A case of OCT guided therapy. *Int. J. Cardiol.* **180**, 52–54. <https://doi.org/10.1016/j.ijcard.2014.11.207> (2015).
46. Kang, S. H. *et al.* Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-eluting stents: A systematic review and Bayesian approach network meta-analysis. *Eur. Heart J.* **35**, 1147–1158. <https://doi.org/10.1093/eurheartj/ehv570> (2014).
47. Browe, D. P. *et al.* Characterization and optimization of actuating poly(ethylene glycol) diacrylate/acrylic acid hydrogels as artificial muscles. *Polymer (Guildf)* **117**, 331–341. <https://doi.org/10.1016/j.polymer.2017.04.044> (2017).
48. Akinapelli, A. *et al.* Current state of bioabsorbable polymer-coated drug-eluting stents. *Curr. Cardiol. Rev.* **13**, 139–154. <https://doi.org/10.2174/1573403x12666161222155230> (2017).
49. Toong, D. W. Y. *et al.* Bioresorbable polymeric scaffold in cardiovascular applications. *Int. J. Mol. Sci.* **21**, 3444. <https://doi.org/10.3390/ijms21103444> (2020).
50. Rigatelli, G. *et al.* Feasibility, safety and long-term outcomes of complex left main bifurcation treatment using the nano-inverted-t stenting: A multicentre prospective registry. *Int. J. Cardiovasc. Imaging* **37**, 1107–1119. <https://doi.org/10.1007/s10554-020-02106-x> (2021).
51. Koppa, T. *et al.* Thrombogenicity and early vascular healing response in metallic biodegradable polymer-based and fully bioabsorbable drug-eluting stents. *Circ. Cardiovasc. Interv.* **8**, e002427. <https://doi.org/10.1161/circinterventions.115.002427> (2015).
52. Ochijewicz, D., Tomaniak, M., Opolski, G. & Kochman, J. Inflammation as a determinant of healing response after coronary stent implantation. *Int. J. Cardiovasc. Imaging* **37**, 791–801. <https://doi.org/10.1007/s10554-020-02073-3> (2021).
53. Kandzari, D. E. *et al.* Ultrathin bioresorbable-polymer sirolimus-eluting stents versus thin durable-polymer everolimus-eluting stents for coronary revascularization: 3-year outcomes from the randomized BIOFLOW V trial. *JACC Cardiovasc. Interv.* **13**, 1343–1353. <https://doi.org/10.1016/j.jcin.2020.02.019> (2020).
54. Palmerini, T. *et al.* Long-term safety of drug-eluting and bare-metal stents: Evidence from a comprehensive network meta-analysis. *J. Am. Coll. Cardiol.* **65**, 2496–2507. <https://doi.org/10.1016/j.jacc.2015.04.017> (2015).
55. Koni, E. *et al.* Five-year comparative efficacy of everolimus-eluting vs. resolute zotarolimus-eluting stents in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *J. Clin. Med.* **10**, 1278. <https://doi.org/10.3390/jcm10061278> (2021).
56. Natsuaki, M. *et al.* Final 3-year outcome of a randomized trial comparing second-generation drug-eluting stents using either biodegradable polymer or durable polymer: NOBORI biolimus-eluting versus XIENCE/PROMUS everolimus-eluting stent trial. *Circ. Cardiovasc. Interv.* **8**, 815–818. <https://doi.org/10.1161/circinterventions.115.002817> (2015).
57. Stevens, J. R., Zamani, A., Osborne, J. I. A., Zamani, R. & Akrami, M. Critical evaluation of stents in coronary angioplasty: a systematic review. *Biomed. Eng. Online* **20**, 46. <https://doi.org/10.1186/s12938-021-00883-7> (2021).

Author contributions

J.T.Y., C.Y.W., Y.L. and X.Y.S. conceptualised and designed the study. Y.L. and Y.Y.C. collected, selected, and analysed the data. J.T.Y., Y.L. and C.Y.W. drafted the manuscript. C.Y.W. and X.Y.S. revised the manuscript.

Funding

This research was funded by Science and Technology Department of Henan Province (Grant Number 112102310306) and Science and Technology Bureau of Kaifeng (Grant Number 119).

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-022-26654-5>.

Correspondence and requests for materials should be addressed to C.W. or X.S.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2023