Catheterization and Cardiovascular Interventions

WILEY

REVIEW OPEN ACCESS

Long-Term (5-Years) Outcomes of Current Drug-Eluting Stents in Percutaneous Coronary Intervention: A Network Meta-Analysis of Randomized Controlled Trials

Aman Goyal[1] | Humza Saeed[2] | Sonia Hurjkaliani[3] | Yusra Mashkoor[3] | Abdullah[2] | Gauranga Mahalwar[1] | Ankur Kalra[4,5] | Grant W. Reed[6]

[1]Department of Internal Medicine, Cleveland Clinic Foundation, Cleveland, Ohio, USA | [2]Department of Internal Medicine, Rawalpindi Medical University, Rawalpindi, Punjab, Pakistan | [3]Department of Internal Medicine, Dow University of Health Sciences, Karachi, Pakistan | [4]Department of Cardiology, Franciscan Health, Lafayette, Indiana, USA | [5]Krannert Cardiovascular Research Center, Indiana University School of Medicine, Indianapolis, Indiana, USA | [6]Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA

Correspondence: Grant W. Reed (REEDG2@ccf.org)

Received: 20 February 2025 | **Revised:** 25 May 2025 | **Accepted:** 29 May 2025

Funding: The authors received no specific funding for this work.

Keywords: cardiac death | drug-eluting stents | myocardial infarction | network meta-analysis | stent thrombosis | target lesion failure | target lesion revascularization

ABSTRACT

Background: Various drug-eluting stents (DES) are currently used for percutaneous coronary intervention (PCI). However, long-term trials reveal inconsistent results in head-to-head comparisons.

Aims: To conduct a network meta-analysis of relevant trials to assess the performance of different DES currently used in PCI.

Methods: We systematically searched major databases for randomized controlled trials (RCTs) reporting 5-year outcomes of currently used DES and conducted a network meta-analysis using a frequentist random-effects model with odds ratios (ORs) as effect measures. DES were ranked by P-scores across several outcomes, with definite/probable stent thrombosis as the primary outcome. Statistical analyses were conducted in R software (v4.4.1), with significance set at $p < 0.05$.

Results: Twenty-nine RCTs involving 46,502 patients were included in the analysis. Six currently used DES—Orsiro, Xience, Resolute, Nobori/BioMatrix, Synergy, and Promus—were analyzed. All comparisons showed nonsignificant results for outcomes at 5-year follow-up. Synergy ranked highest for definite/probable stent thrombosis ($p = 0.85$), all-cause mortality ($p = 0.76$), cardiac death ($p = 0.87$), and target vessel revascularization ($p = 0.91$). Promus ranked best for any myocardial infarction (MI) ($p = 0.86$), target lesion revascularization ($p = 0.93$), and target vessel-related MI ($p = 0.73$). Nobori/BioMatrix ranked highest for target lesion failure ($p = 0.80$). The newer generation Biofreedom stent also showed nonsignificant results but was excluded from the main analysis due to the availability of 5-year outcomes from only one study. Global and local inconsistencies were nonsignificant for all outcomes and comparisons.

Conclusion: The analysis revealed no significant differences in 5-year outcomes among the various DES. However, Synergy and Promus performed best for key outcomes such as stent thrombosis, mortality, and MI, suggesting their potential for favorable performance in clinical practice.

Abbreviations: BMS, bare-metal stents; CAD, coronary artery disease; DAPT, dual antiplatelet therapy; DES, drug-eluting stents; DM, diabetes mellitus; PCI, percutaneous coronary intervention; RCTs, randomized controlled trials; STEMI, ST-elevation myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization; TV-related MI, target vessel-related myocardial infarction.

1 | Introduction

Drug-eluting stents (DES) are specialized stents used in procedures such as angioplasty that release medication to prevent the narrowing or re-blockage of arteries [1]. The stents are coated with drugs that inhibit cellular proliferation, reducing the risk of restenosis. DES is commonly used to treat coronary artery disease (CAD), improve blood flow, and reduce symptoms such as chest pain and shortness of breath [2]. Since their introduction, DES have revolutionized the management of CAD, offering a more durable solution compared with bare-metal stents (BMS) by minimizing the need for repeat interventions [3]. The development of DES began in the early 2000s as an improvement on BMS, which had high restenosis rates due to excessive tissue growth within the stent [4]. The first generation of DES introduced a polymer coating embedded with antiproliferative drugs, released gradually to prevent scar tissue formation [5]. Over the years, advances in stent design, drug formulation, and polymer technology have led to the evolution of second and newer-generation DES, offering improved safety and efficacy, as well as reduced complications like thrombosis [5].

DES is now widely used across the globe, with a significant portion of stenting procedures involving drug-eluting variants. In clinical practice, it is a cornerstone for the management of atherosclerotic heart disease, as endorsed by international guidelines. The European Society of Cardiology (ESC) [6] and the American College of Cardiology (ACC) [7] recommend DES for patients undergoing percutaneous coronary intervention (PCI), particularly in those with high-risk lesions or diabetes, where the benefits in reducing restenosis are well established. Despite its widespread use, DES is not without its shortcomings. There have been concerns about late and very late stent thrombosis, hypersensitivity reactions to the polymer coating, and incomplete endothelialization of the stented vessel [8–10]. Additionally, prolonged dual antiplatelet therapy (DAPT) is required, posing a bleeding risk [11]. Newer stents, such as bioresorbable vascular scaffolds and polymer-free stents, have emerged as alternatives, addressing some limitations of DES and raising the question of whether these devices may offer superior long-term outcomes [12, 13].

Several recent randomized controlled trials (RCTs) have reported 5-year follow-up data on safety and efficacy outcomes, comparing a range of DES. Thus, the objective of this network meta-analysis is to comprehensively evaluate the 5-year outcomes of currently used second or newer-generation DES, enabling clinicians to make informed decisions regarding long-term management strategies and future innovations in stent technology.

2 | Materials and Methods

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. The study protocol was formally registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the identifier CRD42024578758.

2.1 | Data Source and Search Strategy

We conducted an extensive electronic search on August 12, 2024, across multiple databases, including PubMed, Embase, and Cochrane, from inception to August 2024. The aim was to identify all studies examining the 5-year outcomes of various currently used DES compared with each other or with first-generation DES or BMS. We did not impose any restrictions on the year of publication. Only studies published in English were included to avoid potential translation errors. Our search strategy utilized medical subject headings (MeSH) terms and free text keywords: "drug-eluting stent," "bioabsorbable polymer drug-eluting stent," "thin strut stent," "durable polymer drug-eluting stent," and "bare metal stent," filtered by RCTs. Additionally, we manually reviewed the reference lists of all identified articles to ensure that no relevant studies were overlooked in the initial search. A detailed description of the search strategy is available in Supporting Information S1: Table 1.

2.2 | Eligibility Criteria

We followed the Population, Intervention, Control, Outcomes (PICOS) approach for our systematic review and meta-analysis inclusion criteria, with P representing patients undergoing PCI, I and C referring to different types of currently employed second-generation or newer DES compared with each other (or compared with BMS or first-generation DES to enhance the statistical power of indirect comparisons), and O encompassing several outcomes as discussed below. Data on first-generation DES or BMS are presented in the Supporting Information Material. Eligible studies met the following criteria: (1) RCT design published in any year; (2) enrolled adult patients undergoing PCI; (3) compared currently used second-generation or newer DES with each other or with BMS/first-generation DES; (4) reported 5-year outcomes; and (5) were published in English. Trials that solely compared first-generation DES with each other or with BMS were excluded. To ensure statistical consistency and reduce variability, only currently used DES evaluated in at least three RCTs were included in the main analysis, while data on the rest are reported in the Supporting Information File.

2.3 | Outcomes of Interest

The primary outcome included in our analysis is the definite/probable stent thrombosis, in addition to the secondary outcomes, including all-cause mortality, cardiac death, target vessel revascularization (TVR), target lesion revascularization (TLR), target lesion failure (TLF), target vessel-related myocardial infarction (TV-related MI), and any myocardial infarction (MI).

2.4 | Study Selection and Data Extraction

The studies identified through the literature search were imported into EndNote X9 Software (Clarivate Analytics, USA), and duplicates were removed. Two authors (H.S. and S.H.) independently screened the studies by reviewing titles and abstracts, followed by full-text evaluations. In cases of disagreement, a third author (A.G.) was consulted. Data extraction was performed using a Microsoft Excel sheet, capturing details such as the first author's name, publication year, study design, sample size (for both intervention and control groups), DAPT duration, percentage of patients with comorbidities like ST-elevation myocardial infarction (STEMI), acute coronary syndrome (ACS), and diabetes mellitus (DM) in addition to the reported outcomes.

2.5 | Quality Assessment of the Included Trials

The quality of the included RCTs was assessed using the Cochrane risk of bias tool 2.0 (RoB 2.0) [15]. The tool evaluates potential biases in domains such as selection, performance, detection, attrition, and reporting, with judgments categorized as “Low,” “High,” or “Some concerns.” Two authors (Y.M. and H.S.) independently performed the quality assessment, with any disagreements resolved through consensus.

2.6 | Data Synthesis

A frequentist random-effects model was used in the network meta-analysis to compare the efficacy and safety of various DES currently in use, by two authors (A.G. and H.S.). Dichotomous outcomes were analyzed using odds ratios (ORs) and 95% confidence intervals (CIs) through a frequentist network meta-analysis [16]. Both direct and indirect effect sizes were calculated, and global and local inconsistencies were assessed (with statistical significance for inconsistencies set at < 0.05). Data were extracted from league tables to create new tables containing all direct, indirect, and network comparisons, along with values for global and local inconsistencies. Each stent's probability of being the most effective was ranked based on probability-score values [17]. Meta-regression analyses were conducted to examine the influence of the proportion of DM, STEMI, or ACS using the log OR of stent thrombosis as the dependent variable. Publication bias was evaluated through visual inspection of funnel plots. All analyses were performed using R version 4.4.1 [18], and a p-value of less than 0.05 was considered statistically significant.

3 | Results

3.1 | Study Selection

A total of 10,738 potential articles were initially identified through the electronic database search. Following the removal of duplicate entries ($n = 2628$), a preliminary screening was conducted based on the titles and abstracts, resulting in 294 studies for further evaluation. A full-text assessment was then performed, excluding articles that did not meet the inclusion criteria. Subsequently, additional exclusions were made: 165 studies due to different study designs, 68 due to differing follow-up durations, 20 due to ineligible control groups, and 12 due to inadequate outcomes reported. Ultimately, 29 RCTs met the inclusion criteria and were included in the meta-analysis [19–47]. A detailed overview of the literature search process is presented in the PRISMA flow diagram (Figure 1). These 29 RCTs included a total of 46,502 patients with various indications for undergoing PCI.

3.2 | Study Characteristics

Six second- or newer-generation DES—Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix—were included in the main analysis, while the newer-generation Biofreedom stent was excluded due to data being available from only one study. However, comparisons for Biofreedom, first-generation DES, and BMS are provided in the Supporting Information File. The detailed characteristics of the included studies are shown in Table 1, while the characteristics of different stents compared are given in Supporting Information S1: Table 2.

3.3 | Outcomes

3.3.1 | Primary Outcome

3.3.1.1 | Definite/Probable Stent Thrombosis. The evidence network for stent comparisons in the meta-analysis, assessing the risk of long-term definite/probable stent thrombosis, is shown in Figure 2. The analysis included 29 trials with a total of 46,502 patients [19–47]. After 5 years of follow-up, no statistically significant differences in the risk of definite/probable stent thrombosis were observed among the Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix stents (Table 2). Pooled long-term outcomes for other DES comparisons, including first-generation DES and BMS, along with tests for inconsistency between direct and indirect estimates, are available in Supporting Information S1: Table 3, where no significant global inconsistency was found ($p = 0.32$). Nodal splitting displays comparisons and shows no substantial heterogeneity of direct and indirect effect sizes for definite/probable stent thrombosis (Figure 3, Supporting Information S1: Figure 2A). According to Table 3, Synergy had the highest probability of being the best stent (P-score = 0.85) (Table 3, Figure 4, and Supporting Information S1: Figure 3A).

3.3.2 | Secondary Outcomes

3.3.2.1 | All-Cause Mortality. The evidence network for all-cause mortality (Supporting Information S1: Figure 1A) included 28 trials with a total of 46,202 patients [19–40, 42–47]. After 5 years of follow-up, no statistically significant differences in all-cause mortality were observed among the Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix stents (Table 2). Pooled estimates for other DES comparisons, along with tests for inconsistency, are detailed in Supporting Information S1: Table 4, revealing no significant global ($p = 0.90$) or local inconsistencies, except for the Orsiro versus XIENCE comparison. Synergy had the highest probability of being the best stent (P-score = 0.75) (Table 3, Supporting Information S1: Figure 3B).

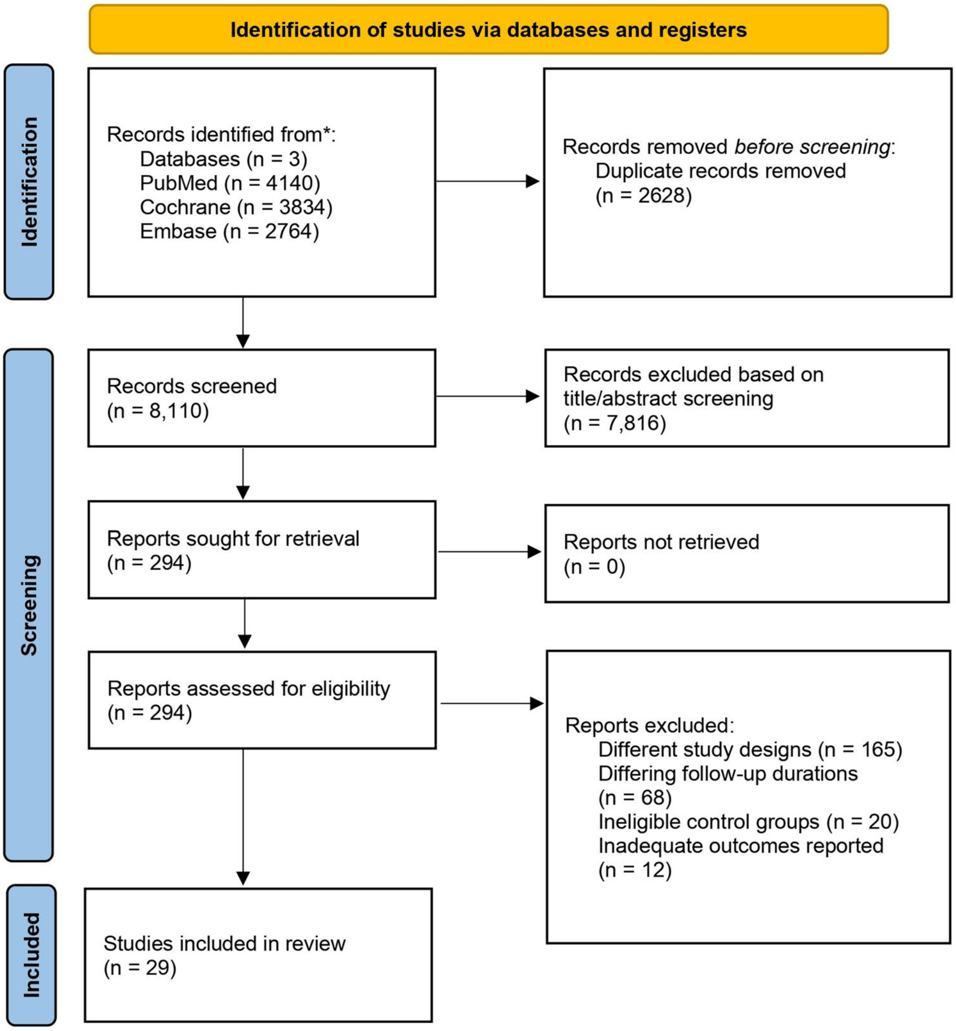

FIGURE 1 | PRISMA flow diagram of study screening and selection. [Color figure can be viewed at wileyonlinelibrary.com]

3.3.2.2 | **Cardiac Death.** The evidence network for cardiac death (Supporting Information S1: Figure 1B) included 29 trials with a total of 46,502 patients [19–47]. After 5 years of follow-up, no statistically significant differences in cardiac death were observed among the Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix stents (Table 2). Pooled estimates for other DES comparisons, along with tests for inconsistency, are detailed in Supporting Information S1: Table 4, showing no significant global ($p = 0.84$) or local inconsistencies. Synergy had the highest probability of being the best stent (P-score = 0.87) (Table 3, Supporting Information S1: Figure 3C).

3.3.2.3 | **Any MI.** The evidence network for any MI (Supporting Information S1: Figure 1C) included 28 trials with a total of 44,691 patients [19–36, 38–47]. After 5 years of follow-up, no statistically significant differences in the risk of any MI were observed among the Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix stents (Table 2). Pooled estimates for other DES comparisons, along with tests for inconsistency, are detailed in Supporting Information S1: Table 4, showing no significant global ($p = 0.25$) or local inconsistencies. Promus had the highest probability of being the best stent (P-score = 0.86) (Table 3, Supporting Information S1: Figure 3D).

3.3.2.4 | **TV-Related MI.** The evidence network for TV-related MI (Supporting Information S1: Figure 1D) included 18 trials with a total of 32,384 patients [20–22, 25–34, 37, 40, 43, 45, 47]. After 5 years of follow-up, no statistically significant differences in TV-related MI were observed among the Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix stents (Table 2). Pooled estimates for other DES comparisons, along with tests for inconsistency, are detailed in Supporting Information S1: Table 4, showing no significant global ($p = 0.65$) or local inconsistencies. Promus had the highest probability of being the best stent (P-score = 0.73) (Table 3, Supporting Information S1: Figure 3E).

3.3.2.5 | **TLF.** The evidence network for TLF (Supporting Information S1: Figure 1E) included 16 trials with 26,392 patients [25–27, 29–33, 35–40, 43, 45]. After 5 years of follow-up, no statistically significant differences were observed among Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix for TLF (Table 2). Pooled estimates for other DES comparisons and tests for inconsistency are detailed in Supporting Information S1: Table 4, showing nonsignificant global ($p = 0.95$) and local inconsistencies. Nobori/BioMatrix had the highest probability of being the best stent (P-score = 0.80) (Table 3, Supporting Information S1: Figure 3F).

TABLE 1 | Baseline characteristics of included trials and participants.

Trial, year	Follow-up, years	Design	Comparators (drug eluted)	Sample size, *n*	Setting	DAPT duration	Mean age, years	Male, %	DM, %	Prior MI, %	ACS, %	STEMI, %	Bifurcations, %	RVD, mm	Lesion length, mm	Quality/risk of bias
Biofreedom 2016	5	Multicenter non-inferiority single blind RCT	Biofreedom (Biolimus A9) Taxus (Paclitaxel)	182	Stable CAD + UA	6–12 months	68	67	27	19	9.2	0	0	2.8	11	Low risk
Examination 2016	5	Multicenter superiority single blind RCT	Xience (Everolimus) BMS	1498	STEMI	≥ 12 months	61	83	17	5	100	100	na	na	23[a]	Low risk
ISAR-TEST 4 2009	5	Double center non-inferiority RCT	Xience (Everolimus) Cypher (Sirolimus) Yukon-BP (Sirolimus)	2603	Stable CAD + NSTE-ACS	≥ 6 months	67	76	29	29	40	11	23	2.8	15	Low risk
ISAR-TEST 5 2016	5	Double center non-inferiority RCT	Yukon-PF (Sirolimus +Probucol) Resolute (Zotarolimus)	3002	Stable CAD + NSTE-ACS	≥ 6 months	68	76	29	29	40	0	28	2.8	16.7	Low risk
Leaders 2013	5	Multicenter non-inferiority single blind RCT	Nobori/Biomatrix (Biolimus A9) Cypher (Sirolimus)	1707	All Comers	≥ 12 months	64	75	24	32	55	16	na	2.6	12.7	Low risk
LIPSIA 2014	5	Three centers non-inferiority RCT	Yukon-PF (Sirolimus) Taxus (Paclitaxel)	236	Stable CAD	12 months	67	69	100	22	0	0	0	2.9	13.6	Low risk
NEXT 2018	5	Multicenter non-inferiority assessor-blind RCT	Nobori/Biomatrix (Biolimus A9) Xience (Everolimus)	3235	Stable CAD + NSTE-ACS	≥ 3 months	69	77	46	28	16	3	44	2.6	19.5	Low risk
NOBORI 2015	5	Multicenter non-inferiority RCT	Nobori/Biomatrix (Biolimus A9) Taxus (Paclitaxel)	363	Stable CAD + UA	≥ 6 months	63	71	22	25	25	0	na	2.7	10	Low risk
Platinum 2017	5	Multicenter single blind	Xience (Everolimus)	1530	Stable CAD + UA	≥ 6months (12months in patients	64	71	23	21	0	0	0	2.6	13	Some concerns

(Continues)

TABLE 1 | (Continued)

Trial, year	Follow-up, years	Design	Comparators (drug eluted)	Sample size, *n*	Setting	DAPT duration	Mean age, years	Male, %	DM, %	Prior MI, %	ACS, %	STEMI, %	Bifurcations, %	RVD, mm	Lesion length, mm	Quality/risk of bias
		non-inferiority RCT	Promus (Everolimus)			at low bleeding risk)										
Sort Out IV 2016	5	Multicenter single blind non-inferiority RCT	Xience (Everolimus) Cypher (Sirolimus)	2774	All Comers	12 months	64	75	14	22	47	10	12	3.2	16.5	Low risk
Spirit III 2013	5	Multicenter single blind non-inferiority RCT	Xience (Everolimus) Taxus (Paclitaxel)	1001	Stable CAD + UA	≥ 6 months	63	69	29	19	0	0	0	2.7	15	Low risk
Bionyx 2024	5	Multicenter non-inferiority single blind assessor blind RCT	Resolute (Zotarolimus) Orsiro (Sirolumus)	2488	All Comers	6–12 months	64	76	21	16	71	25	39	2.8	14.4	Low risk
Bioresort 2022	5	Multicenter non-inferiority single blind assessor blind RCT	Orsiro (Sirolumus) Synergy (Everolimus) Resolute (Zotarolimus)	3514	All Comers	6–12 months	64	72	18	19	31	31	35	2.7	14.6	Low risk
Bioflow IV 2023	5	Multicenter non-inferiority RCT	Orsiro (Sirolumus) Xience (Everolimus)	575	Stable CAD + UA	6–12 months	64	74	31	31	na	0	5	2.7	13	Some concerns
Bioscience 2018	5	Multicenter non-inferiority single blind RCT	Orsiro (Sirolumus) Xience (Everolimus)	2119	All Comers	11 months	66	77	23	20	63	19	17	< 3[b]	55% > 20 mm	Low risk
Comfortable AMI 2019	5	Multicenter superiority single blind assessor blind RCT	Nobori/Biomatrix (Biolimus A9) BMS	1161	STEMI	12 months	60	79	15	5	100	100	9	3	18[a]	Low risk

(Continues)

TABLE 1 | (Continued)

Trial, year	Follow-up, years	Design	Comparators (drug eluted)	Sample size, *n*	Setting	DAPT duration	Mean age, years	Male, %	DM, %	Prior MI, %	ACS, %	STEMI, %	Bifurcations, %	RVD, mm	Lesion length, mm	Quality/risk of bias
Compare 2015	5	Single-center Superiority single blind RCT	Xience (Everolimus) Taxus (Paclitaxel)	1800	All Comers	12 months	63	71	18	17	60	25	18	2.5	16.4	Low risk
Compare II 2017	5	Multicenter Open label non-inferiority RCT	Nobori/Biomatrix (Biolimus A9) Xience (Everolimus)	2707	All Comers	12 months	63	74	22	19	58	21	6.5	2.9	17.2[a]	Low risk
DUTCH Peers Twente II 2019	5	Multicenter non-inferiority single blind RCT	Resolute (Zotarolimus) Promus (Everolimus)	1811	All Comers	12 months	66	73	18	22	58	21	25	2.6	13.5[a]	Low risk
Evolve 2018	5	Multicenter non-inferiority single blind RCT	Synergy (Everolimus) Promus (Everolimus)	192	Stable CAD + UA	6–12 months	63	75	20	33	22	0	0	2.5	13.8	Some concerns
Evolve II 2019	5	Multicenter non-inferiority single blind RCT	Synergy (Everolimus) Promus (Everolimus)	1684	Stable CAD + UA	6–12 months	64	71	31	27	34	0	na	2.6	13.8	Low risk
Biostemi 2023	5	Multicenter Superiority single blind RCT	Orsiro (Sirolumus) Xience (Everolimus)	1300	STEMI	12 months	63	76	12	4	100	100	13	—	71% > 20 mm	Low risk
Spirit II 2013	5	Multicenter single blind RCT	Xience (Everolimus) Taxus (Paclitaxel)	300	Stable CAD + UA	12 months	62	73	31	32	0	0	na	2.8	13	Low risk
Sort Out V 2017	5	Multicenter non-inferiority RCT	Nobori/Biomatrix (Biolimus A9) Cypher (Sirolimus)	2468	All Comers	12 months	65	75	15	17	49	18	15	3.2	18	Low risk
Bioflow II 2018	5	Multicenter non-inferiority assessor-blind RCT	Orsiro (Sirolumus) Xience (Everolimus)	452	Stable CAD + UA	6 months	63	77	28	27	na	0	na	3.1[b]	22[a]	Low risk

(Continues)

TABLE 1 | (Continued)

Trial, year	Follow-up, years	Design	Comparators (drug eluted)	Sample size, *n*	Setting	DAPT duration	Mean age, years	Male, %	DM, %	Prior MI, %	ACS, %	STEMI, %	Bifurcations, %	RVD, mm	Lesion length, mm	Quality/risk of bias
Sort Out III 2014	5	Multicentre, open-label, superiority RCT	Endeavor (Zotarolimus) Cypher (Sirolimus)	2332	Stable CAD	12 months	64	73	14	25	na	7	na	na	na	Low risk
Resolute All-comers 2015	5	Multicenter open label non-inferiority RCT	Xience (Everolimus) Resolute (Zotarolimus)	2292	All Comers	≥ 6 months	64	77	23	30	75	na	17	2.6	12	Low risk
Endeavor III 2011	5	Multicenter single-blind RCT	Endeavor (Zotarolimus) Cypher (Sirolimus)	436	All Comers	60 months	61	69	29	20	na	na	na	2.7	14.9	Low risk
Endeavor IV 2013	5	Multicenter single-blind RCT	Endeavor (Zotarolimus) Taxus (Paclitaxel)	1440	Stable CAD	≥ 6 months	64	68	31	22	na	5	na	2.7	13.6	Low risk

Abbreviations: ACS, acute coronary syndromes; BMS, bare metal stent; BP, bioabsorbable polymer; BP-DES, bioabsorbable polymer drug eluting stent; CAD, coronary artery disease; CTO, chronic total occlusion; DM, diabetes mellitus; DP-DES, durable polymer drug eluting stent; LMD, left main disease; MI, myocardial infarction; MVD, multi-vessel disease; NSTE-ACS, non-ST-elevation acute coronary syndromes; PF, polymer free; RCT, randomized clinical trial; RVD, reference vessel diameter; UA, unstable angina.

[a]Stent length.

[b]Stent diameter

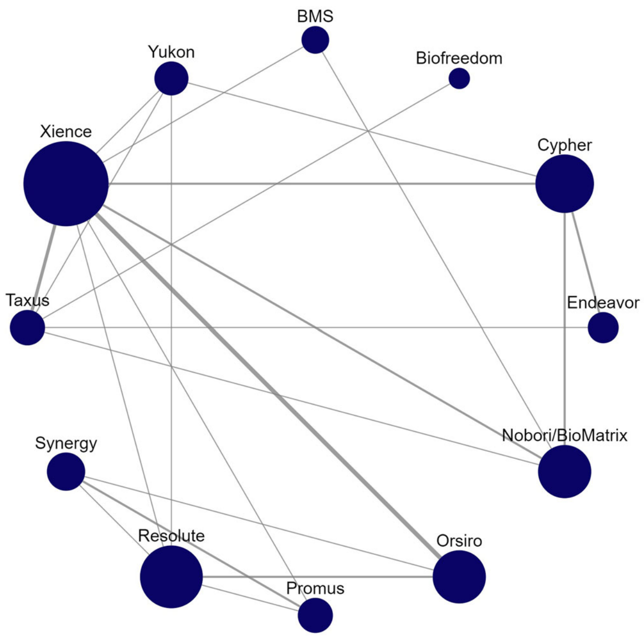

FIGURE 2 | Evidence network for the outcome of definite/probable stent thrombosis. [Color figure can be viewed at wileyonlinelibrary.com]

3.3.2.6 | TLR. The evidence network for TLR (Supporting Information S1: Figure 1F) included 28 trials with 44,691 patients [19–36, 38–47]. After 5 years of follow-up, no statistically significant differences were observed among Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix for TLR (Table 2). Pooled estimates for other DES comparisons and tests for inconsistency are detailed in Supporting Information S1: Table 4, showing nonsignificant global ($p = 0.85$) and local inconsistencies. Promus had the highest probability of being the best stent (P-score = 0.93) (Table 3, Supporting Information S1: Figure 3G).

3.3.2.7 | TVR. The evidence network for TVR (Supporting Information S1: Figure 1G) included 26 trials with 43,236 patient inconsistencies [19, 20, 22, 23, 25–40, 42–47]. After 5 years of follow-up, no statistically significant differences were observed among Orsiro, XIENCE, Resolute, Synergy, Promus, and Nobori/BioMatrix for TVR (Table 2). Pooled estimates for other DES comparisons and tests for inconsistency are detailed in Supporting Information S1: Table 4, showing nonsignificant global ($p = 0.99$) and local inconsistencies. Synergy had the highest probability of being the best stent (P-score = 0.91) (Table 3, Supporting Information S1: Figure 3H).

Overall, Synergy had the highest probability of being the best stent for all-cause mortality (P-score = 0.75), cardiac death (P-score = 0.87), and TVR (P-score = 0.91). Promus ranked highest for any MI (P-score = 0.86), target vessel-related MI (P-score = 0.73), and TLR (P-score = 0.93). Nobori/BioMatrix had the highest probability for TLF (P-score = 0.80) (Table 3, Supporting Information S1: Figures 3B–H).

3.4 | Meta-Regression Analysis

Among the 29 studies included in the meta-analysis, three randomized only ACS patients—all of whom were diagnosed with STEMI (100%)—and one study randomized only DM patients (100%). STEMI rates in the remaining trials ranged from 0% to 31%, ACS rates ranged from 0% to 75%, and DM rates ranged from 12% to 46%. Meta-regression analyses adjusting for these variables found no association between ACS, STEMI, or DM and the treatment effect size for definite/probable stent thrombosis (Supporting Information S1: Figure 4A–C).

3.5 | Quality Assessment

The risk for bias in the included trials was assessed according to the Cochrane Collaboration's tool and is demonstrated in Supporting Information S1: Figure 5A and 5B. Three trials were reported to have some concerns [27, 32, 38], while all others had a low risk of bias. Visual assessment of funnel plots revealed no asymmetry, indicating no to low risk of publication bias for all outcomes (Supporting Information S1: Figure 6A–H).

4 | Discussion

The current study is a thorough network meta-analysis designed to compare the 5-year results of several second-generation or newer DES currently in use. We included data from 29 RCTs with 46,502 patients in our PRISMA-compliant analysis. A substantial data set has been rendered available by these trials to facilitate indirect comparisons between first-generation DES, second-generation DES, newer-generation DES, and BMS. The following are the key conclusions of this meta-analysis: (1) Among second-generation stents (XIENCE, Resolute, Promus) and newer-generation stents (Orsiro, Synergy, Nobori/BioMatrix), there were no statistically significant differences in the probability of definite/probable stent thrombosis at 5 years; (2) Promus showed the highest probability of being the best stent for any MI, even though its efficacy signal was attenuated over time; (3) Synergy ranked as the best stent for stent thrombosis, all-cause mortality, and cardiac death with the highest probability scores, although the differences did not reach statistical significance.

Due to the advancements in stent technology, second-generation or newer DES have significantly improved patient outcomes following PCI over their predecessors. Early DES, which made use of robust polymers, were associated with poor biocompatibility and mechanical problems, including elevated risk of thrombosis and inflammation. To solve these issues, second-generation or newer DES were built with lower-profile components, thinner struts, and thrombus-resistant characteristics, reducing both artery wall inflammation and the possibility of side branch obstruction in bifurcation procedures [23, 48–50]. Additionally, there was less shear stress and turbulence caused by the stent on these thinner-strut platforms. Furthermore, by reducing long-term complications linked to durable polymers, including late and extremely late stent thrombosis, the use of biodegradable polymers in more recent DES has proven advantageous [23, 29]. Even though these developments have led to better patient outcomes, the possibility of late adverse events still exists, which emphasizes the significance of continued advancements in DES technology.

TABLE 2 | Pooled analysis of all outcomes.

Comparisons	Stent thrombosis		Cardiac mortality		TV-related MI		id-TLR		TLF		Any MI		TVR		All-cause mortality	
	Pooled estimate (odds ratio with 95% CI)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate
Xience versus																
Nabori/ biomatrix	1.24 [0.85; 1.82]	0.26	1.11 [0.90; 1.36]	0.34	0.85 [0.59; 1.22]	0.38	1.06 [0.90; 1.24]	0.48	0.77 [0.52; 1.14]	0.20	1.05 [0.87; 1.26]	0.60	1.14 [0.99; 1.32]	0.08	1.04 [0.88; 1.22]	0.66
Orsiro	0.87 [0.64; 1.18]	0.37	1.03 [0.83; 1.28]	0.80	0.92 [0.73; 1.17]	0.50	1.02 [0.85; 1.23]	0.83	0.90 [0.67; 1.23]	0.52	0.94 [0.78; 1.13]	0.52	0.99 [0.84; 1.16]	0.89	1.09 [0.91; 1.31]	0.36
Promus	0.97 [0.51; 1.86]	0.93	0.95 [0.68; 1.35]	0.79	0.83 [0.52; 1.32]	0.44	0.81 [0.57; 1.15]	0.24	0.96 [0.62; 1.49]	0.86	0.82 [0.56; 1.19]	0.30	1.02 [0.81; 1.29]	0.85	0.94 [0.72; 1.22]	0.65
Resolute	1.01 [0.69; 1.47]	0.97	0.97 [0.78; 1.21]	0.81	1.03 [0.82; 1.31]	0.78	1.08 [0.91; 1.29]	0.37	0.96 [0.66; 1.38]	0.81	1.03 [0.84; 1.27]	0.77	1.05 [0.89; 1.24]	0.55	1.05 [0.88; 1.25]	0.61
Synergy	0.73 [0.39; 1.37]	0.33	0.83 [0.56; 1.23]	0.35	0.85 [0.56; 1.29]	0.46	0.91 [0.66; 1.25]	0.57	0.87 [0.53; 1.42]	0.58	0.93 [0.67; 1.28]	0.66	0.91 [0.70; 1.16]	0.44	0.92 [0.69; 1.23]	0.59
Nobori/biomatrix versus																
Orsiro	1.43 [0.88; 2.31]	0.15	1.08 [0.80; 1.45]	0.64	0.92 [0.60; 1.42]	0.71	1.04 [0.82; 1.32]	0.76	0.85 [0.52; 1.40]	0.53	1.12 [0.86; 1.45]	0.40	1.15 [0.93; 1.44]	0.20	0.95 [0.75; 1.21]	0.67
Promus	1.28 [0.61; 2.69]	0.52	1.16 [0.78; 1.73]	0.47	1.02 [0.57; 1.84]	0.94	1.30 [0.89; 1.91]	0.17	0.80 [0.44; 1.45]	0.46	1.28 [0.85; 1.94]	0.24	1.12 [0.85; 1.46]	0.43	1.10 [0.81; 1.50]	0.53
Resolute	1.24 [0.73; 2.08]	0.42	1.14 [0.85; 1.52]	0.39	0.82 [0.53; 1.27]	0.37	0.98 [0.78; 1.23]	0.84	0.81 [0.47; 1.38]	0.44	1.02 [0.78; 1.33]	0.90	1.09 [0.87; 1.35]	0.46	0.99 [0.78; 1.25]	0.93
Synergy	1.69 [0.82; 3.49]	0.15	1.33 [0.86; 2.06]	0.20	1.00 [0.57; 1.73]	0.99	1.16 [0.82; 1.65]	0.40	0.89 [0.47; 1.66]	0.71	1.13 [0.78; 1.63]	0.52	1.26 [0.94; 1.69]	0.12	1.12 [0.81; 1.56]	0.49
Orsiro versus																

(Continues)

TABLE 2 | (Continued)

Comparisons	Stent thrombosis		Cardiac mortality		TV-related MI		id-TLR		TLF		Any MI		TVR		All-cause mortality	
	Pooled estimate (odds ratio with 95% CI)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate	Pooled estimate (odds ratio)	*p* value for the pooled estimate
Promus	0.90 [0.46; 1.73]	0.74	1.08 [0.75; 1.56]	0.69	1.11 [0.68; 1.80]	0.67	1.26 [0.87; 1.81]	0.22	0.94 [0.60; 1.48]	0.79	1.15 [0.79; 1.67]	0.47	0.97 [0.76; 1.23]	0.78	1.16 [0.88; 1.53]	0.30
Resolute	0.87 [0.59; 1.27]	0.46	1.06 [0.83; 1.35]	0.66	0.89 [0.71; 1.12]	0.33	0.94 [0.78; 1.14]	0.54	0.95 [0.67; 1.34]	0.76	0.91 [0.75; 1.11]	0.36	0.94 [0.80; 1.11]	0.47	1.04 [0.87; 1.25]	0.68
Synergy	1.19 [0.65; 2.15]	0.58	1.24 [0.84; 1.81]	0.28	1.08 [0.74; 1.58]	0.69	1.12 [0.82; 1.53]	0.49	1.04 [0.65; 1.66]	0.87	1.01 [0.74; 1.37]	0.95	1.09 [0.86; 1.39]	0.48	1.18 [0.89; 1.55]	0.25
Promus versus																
Resolute	0.97 [0.53; 1.77]	0.91	0.98 [0.71; 1.35]	0.90	0.80 [0.51; 1.26]	0.34	0.75 [0.52; 1.08]	0.12	1.01 [0.66; 1.53]	0.98	0.79 [0.54; 1.16]	0.27	0.97 [0.78; 1.21]	0.81	0.90 [0.70; 1.15]	0.39
Synergy	1.32 [0.66; 2.67]	0.43	1.15 [0.79; 1.67]	0.47	0.97 [0.55; 1.74]	0.93	0.89 [0.64; 1.24]	0.49	1.11 [0.72; 1.70]	0.65	0.88 [0.66; 1.18]	0.40	1.13 [0.90; 1.42]	0.30	1.02 [0.76; 1.35]	0.91
Resolute versus																
Synergy	1.37 [0.76; 2.46]	0.29	1.17 [0.81; 1.68]	0.39	1.21 [0.83; 1.77]	0.32	1.19 [0.87; 1.62]	0.28	1.10 [0.70; 1.72]	0.68	1.11 [0.81; 1.51]	0.51	1.16 [0.92; 1.47]	0.20	1.13 [0.87; 1.47]	0.35

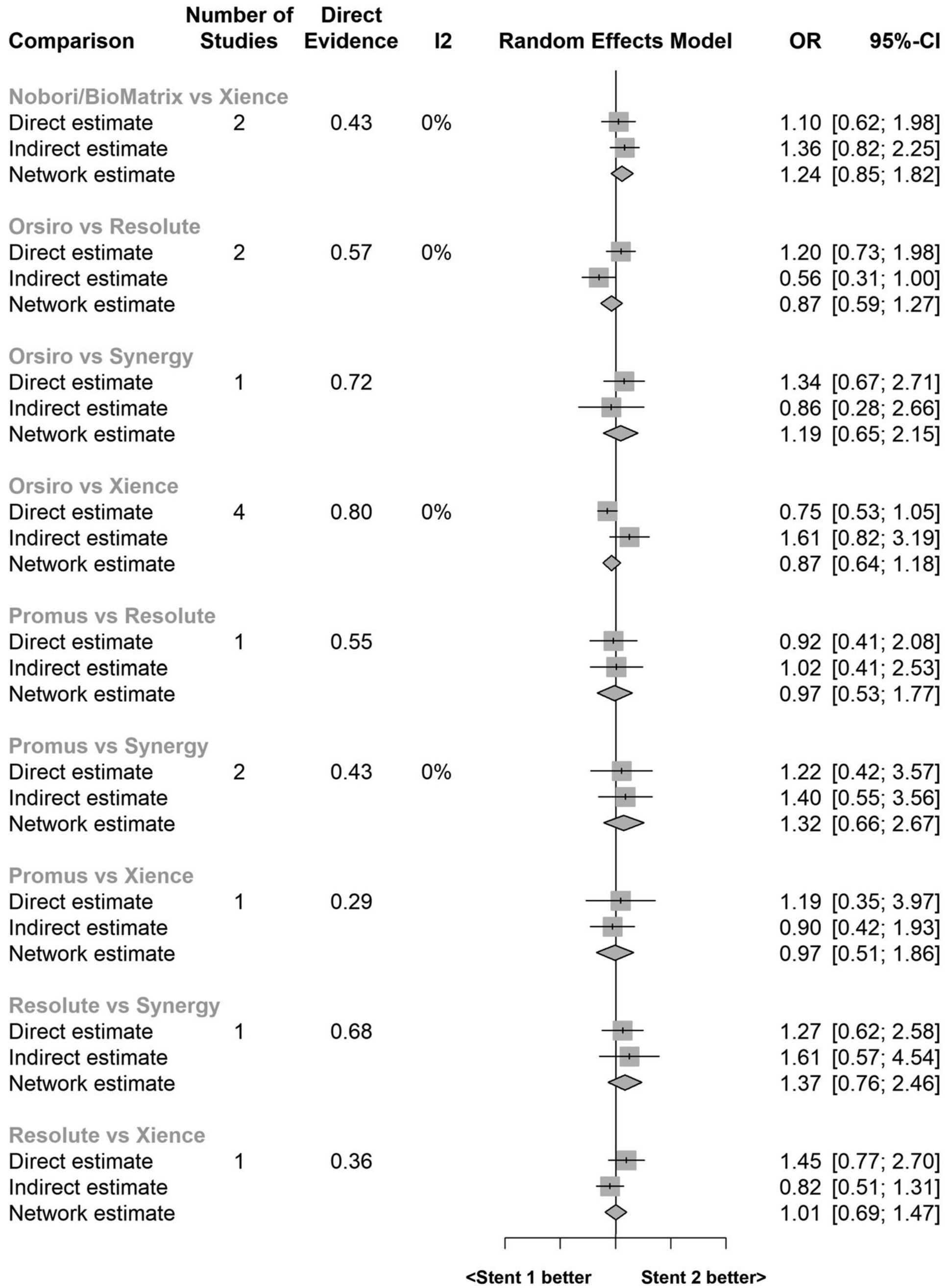

FIGURE 3 | Nodal splitting diagram for the outcome of definite/probable stent thrombosis.

TABLE 3 | P-scores for each intervention and endpoint.

Intervention	Stent thrombosis	All-cause mortality	Any MI	Cardiac death	TLF	TLR	TvMI	TVR
Orsiro	0.7811	0.3825	0.7177	0.5826	0.6020	0.6945	0.6439	0.7911
Synergy	**0.8534**	**0.7565**	0.6896	**0.8714**	0.6482	0.8238	0.7173	**0.9118**
Promus	0.6495	0.7310	**0.8566**	0.6972	0.4825	**0.9293**	**0.7323**	0.7060
Xience	0.6468	0.6332	0.5908	0.6663	0.4040	0.7521	0.5036	0.7783
Resolute	0.6302	0.4795	0.5062	0.6973	0.4925	0.5766	0.4403	0.6511
Nobori/Biomatrix	0.4654	0.5229	0.4820	0.4559	**0.8031**	0.6262	0.7256	0.5117

Note: The interventions with the highest P-score for each endpoint are in bold.
Abbreviations: MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TvMI, target vessel-related myocardial infarction; TVR, target vessel revascularization.

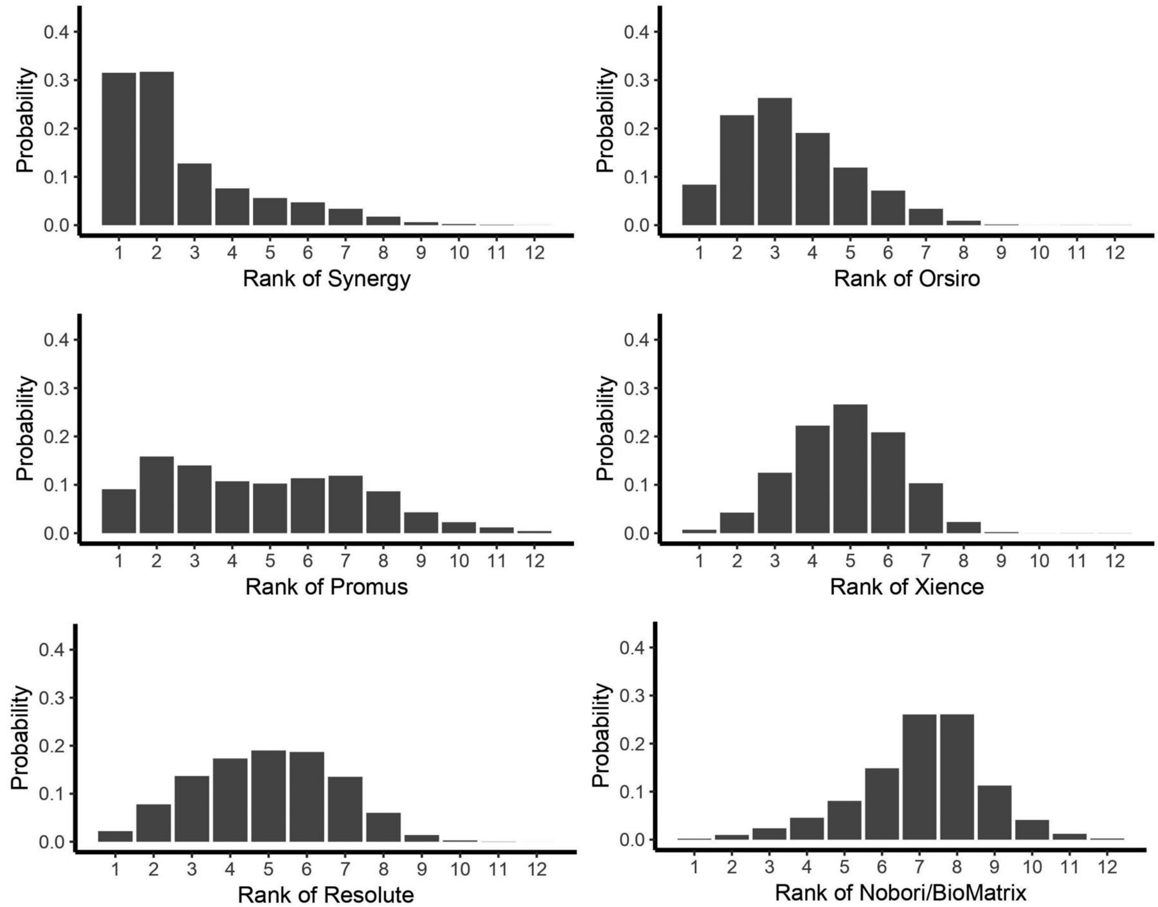

FIGURE 4 | Ranking graphs for the outcome of definite/probable stent thrombosis using P-scores.

The PLATINUM study has made a substantial contribution to our understanding of the long-term consequences of DES, highlighting the need for prolonged follow-up times to assess the safety and effectiveness of these devices [27]. The trial's positive 5-year results, which included low rates of MI, stent thrombosis, and cardiac death for all DES types, demonstrate that, despite possible small differences in function, the overall therapeutic impact of the devices is similar [27]. The results also highlight the significance of stent design parameters, which affect critical clinical outcomes, including flexibility and deliverability. These parameters include metal alloys, radial strength, and polymer kinds. The experiment also highlighted the impact of lesion complexity on event rates, pointing out that patients with lengthy lesions or small vascular disease may have different results [27].

Our results are consistent with recent meta-analyses that emphasize the benefits of currently used DES over BMS and first-generation DES, especially in terms of lowering stent thrombosis and restenosis. SYNERGY emerged as the most likely best-performing stent for several key endpoints. The SYNERGY stent (Boston Scientific Corporation, Marlborough, MA) is a thin-strut platinum–chromium alloy stent that features an ultrathin bioabsorbable polymer, abluminal coated to elute everolimus. The 90-day lifetime of everolimus release is in close agreement with the 120-day resorption period of the polymer [51]. TLF rates at 30 days and 5 years were similar for SYNERGY and durable polymer PROMUS Element EES, respectively, in the EVOLVE First Human Use trial. SYNERGY also exhibited noninferiority for 6-month late lumen loss. Crucially, over the 5-year follow-up period, no stent thrombosis was seen in either therapy group [52]. These results were further supported by the pivotal RCT EVOLVE II, which was designed to evaluate SYNERGY's clinical efficacy and safety for Food and Drug Administration (FDA) approval [53], showing efficacy even in high-risk diabetes patients as demonstrated by the prespecified Diabetes substudy [54].

Our updated study offers a more thorough evaluation by incorporating a broader range of DES, including additional stents like Synergy and Promus, which were not represented in earlier meta-analyses due to the limited number of studies available at that time. This contrasts with the previous network meta-analysis, which found Orsiro to be the best stent at both 1-year and long-term follow-up (where long-term was defined as any follow-up more than 1-year) and also reported XIENCE to have a lower rate of definite stent thrombosis compared with Nobori/BioMatrix [55]. By including data for Synergy and Promus, our network meta-analysis provides a more up-to-date and comprehensive assessment of DES performance, particularly with respect to long-term outcomes such as TLF and stent thrombosis. While Orsiro continues to perform well in our updated analysis, the inclusion of these newer stents allows for a more nuanced understanding of DES efficacy. This expanded analysis enhances our understanding of the long-term safety and performance of DES, building on prior studies by offering a more detailed and current comparison.

However, despite the promising results for SYNERGY, the absence of a statistically significant advantage over other DES raises questions about the clinical relevance of its bioabsorbable design features in long-term follow-up. As observed in our analysis, the advantage of bioabsorbable polymer DES, such as Synergy, in reducing stent thrombosis compared with durable polymer DES (e.g., XIENCE) has not been consistently supported by long-term studies. The nonsignificant variations in cardiac and all-cause mortality among the DES comparators, as reported in our study, demand more discussion. The NOBORI 1 trial provides evidence for the long-term safety of biodegradable polymer stents, showing no stent thrombosis in the Nobori DES arm compared with 3.2% in the TAXUS arm ($p = 0.01$) [56]. Furthermore, in line with other second-generation DES trials, such as SPIRIT III, the low TLR rate of 1.3% at 5 years highlights the effectiveness of the Nobori stent in lowering restenosis [29]. Crucially, the lack of late and extremely late stent thrombosis with Nobori DES implies that advances in patient care, medication, and surgical methods have a greater impact on the safety advantages of more recent-generation stents than just the device itself. These advancements may explain the overall lack of significant differences in long-term outcomes across modern stent platforms despite varying stent designs and technologies.

It is noteworthy that Promus, although having a diminished effectiveness signal, was the best-performing stent for the risk of any MI at 5 years. Numerous reasons, such as variability in the research populations and endpoints, could account for this attenuation. Although its efficacy signal has slightly diminished with time, the Promus platinum–chromium everolimus-eluting stent (PtCr-EES) has become a prominent choice for coronary intervention and is designed to provide greater conformability, radial strength, radiopacity, and fracture resistance [57, 58]. In the large-scale PLATINUM trial, PtCr-EES demonstrated noninferiority to the cobalt–chromium everolimus-eluting stent (CoCr-EES) at 1 year, with a TLF rate of 3.4% compared with 2.9% for CoCr-EES. Long-term follow-up demonstrated comparable 5-year TLF rates of 9.1% for PtCr-EES and 9.3% for CoCr-EES, with no significant differences in adverse events, including cardiac mortality, MI, or stent thrombosis [27]. Furthermore, the PtCr-EES exhibited excellent outcomes in specific patient categories, such as those with tiny arteries and lengthy lesions, where the 5-year TLF rates were 7.0% and 13.6%, respectively [27]. These results highlight the positive safety profile of the PtCr-EES and its potential for successful therapy in a variety of coronary artery lesions [27]. They also call for additional research to fully understand the underlying mechanisms influencing the reported clinical outcomes.

5 | Strengths and Limitations

Our study's strengths lie in its large sample size, the inclusion of only highly qualified RCTs, and the application of network meta-analysis, which allows for indirect comparisons between different stent types, including additional stents like Synergy and Promus that were previously inadequately covered in studies. We especially focused on the 5-year long-term outcomes of DES that are currently in use. Furthermore, the lack of noteworthy discrepancies between direct and indirect comparisons in our network meta-analysis reinforces the resilience and dependability of our conclusions.

Nonetheless, a few limitations must be noted. First, there is always some bias introduced by indirect comparisons, particularly when baseline patient characteristics vary between studies. Second, comorbidities like DM or STEMI may have an impact on the results and long-term outcomes; however, our meta-regression analysis did not reveal any associations. Third, our comparisons' statistical strength is diminished because there is only a limited amount of long-term follow-up data available for some stents. Furthermore, in several secondary endpoints, there was a loss of patients to follow-up in the included RCTs. However, this is a limitation inherent to the included RCTs, and nothing could be done during the meta-analytical stage to circumvent it. Fourth, the results of the trials may have been impacted by the different durations of DAPT, especially concerning stent thrombosis and MI. Fifth is the inclusion of different versions of several stents (e.g., Xience, Resolute), which may introduce variability in outcomes that is difficult to fully account for. Additionally, the Cre8 DES was not included due to an insufficient number of RCTs reporting its 5-year outcomes. Lastly, although we employed a comprehensive search strategy to include a broad spectrum of studies, the exclusion of unpublished studies may have introduced publication bias.

6 | Conclusion

In conclusion, no discernible variations in outcomes between DES presently in use at the 5-year follow-up were discovered by our meta-analysis. However, Synergy and Promus demonstrated superior performance for important outcomes such as MI, mortality, and stent thrombosis, indicating possible benefits for particular outcomes.

Acknowledgments

The authors have nothing to report.

Disclosure

The authors have nothing to report.

Ethics Statement

No ethical approval was required for this study design, as all data were obtained from publicly available de-identified sources.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. M. Koźlik, J. Harpula, P. J. Chuchra, M. Nowak, W. Wojakowski, and P. Gąsior, "Drug-Eluting Stents: Technical and Clinical Progress," *Biomimetics (Basel, Switzerland)* 8, no. 1 (February 2023): 72.

2. S. J. Hong and M. K. Hong, "Drug-Eluting Stents for the Treatment of Coronary Artery Disease: A Review of Recent Advances," *Expert Opinion on Drug Delivery* 19, no. 3 (March 2022): 269–280.

3. K. H. Changal, T. Mir, S. Khan, et al., "Drug-Eluting Stents Versus Bare-Metal Stents in Large Coronary Artery Revascularization: Systematic Review and Meta-Analysis," *Cardiovascular Revascularization Medicine* 23 (February 2021): 42–49.

4. J. Iqbal, J. Gunn, and P. W. Serruys, "Coronary Stents: Historical Development, Current Status and Future Directions," *British Medical Bulletin* 106 (2013): 193–211.

5. S. Hassan, M. N. Ali, and B. Ghafoor, "Evolutionary Perspective of Drug Eluting Stents: From Thick Polymer to Polymer Free Approach," *Journal of Cardiothoracic Surgery* 17, no. 1 (April 2022): 65.

6. S. Silber, B. M. Richartz, and M. Brilmayer, European Society of Cardiology (ESC), "Die ESC-Leitlinien Zur Perkutanen Koronarintervention (PCI): Drei Fallbeispiele," *Herz Kardiovaskuläre Erkrankungen* 31, no. 9 (December 2006): 836–848, 848.

7. L. A. Graham, B. A. Singletary, J. S. Richman, T. M. Maddox, K. M. F. Itani, and M. T. Hawn, "Improved Adverse Postoperative Outcomes With Revised American College of Cardiology/American Heart Association Guidelines for Patients With Cardiac Stents," *JAMA Surgery* 149, no. 11 (November 2014): 1113–1120.

8. J. R. Nebeker, R. Virmani, C. L. Bennett, et al., "Hypersensitivity Cases Associated With Drug-Eluting Coronary Stents," *Journal of the American College of Cardiology* 47, no. 1 (January 2006): 175–181.

9. T. F. Lüscher, J. Steffel, F. R. Eberli, et al., "Drug-Eluting Stent and Coronary Thrombosis: Biological Mechanisms and Clinical Implications," *Circulation* 115, no. 8 (February 2007): 1051–1058.

10. B. L. van der Hoeven, N. M. M. Pires, H. M. Warda, et al., "Drug-Eluting Stents: Results, Promises and Problems," *International Journal of Cardiology* 99, no. 1 (March 2005): 9–17.

11. J. B. Hermiller, M. W. Krucoff, D. J. Kereiakes, et al., "Benefits and Risks of Extended Dual Antiplatelet Therapy After Everolimus-Eluting Stents," *JACC: Cardiovascular Interventions* 9, no. 2 (January 2016): 138–147.

12. Y. Liu, D. Xiao, Y. Wu, et al., "Bioresorbable Scaffolds Vs. Drug-Eluting Stents for Patients With Myocardial Infarction: A Systematic Review and Meta-Analysis of Randomized Clinical Trials," *Frontiers in Cardiovascular Medicine* 9 (2022): 974957.

13. M. Baquet, D. Jochheim, and J. Mehilli, "Polymer-Free Drug-Eluting Stents for Coronary Artery Disease," *Journal of Interventional Cardiology* 31, no. 3 (June 2018): 330–337.

14. M. J. Page, J. E. McKenzie, P. M. Bossuyt, et al., "The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews," *BMJ [Internet]* 372 (March 2021): n71, https://pubmed.ncbi.nlm.nih.gov/33782057/.

15. J. A. C. Sterne, J. Savović, M. J. Page, et al., "RoB 2: A Revised Tool for Assessing Risk of Bias in Randomised Trials," *BMJ [Internet]* 366 (August 2019), https://www.bmj.com/content/366/bmj.l4898.

16. D. M. Caldwell, A. E. Ades, and J. P. T. Higgins, "Simultaneous Comparison of Multiple Treatments: Combining Direct and Indirect Evidence," *BMJ* 331, no. 7521 (October 2005): 897–900.

17. G. Rücker and G. Schwarzer, "Ranking Treatments in Frequentist Network Meta-Analysis Works Without Resampling Methods," *BMC Medical Research Methodology* 15, no. 1 (December 2015): 58.

18. "R: The R Project for Statistical Computing [Internet]," Cited September 29, 2024, https://www.r-project.org/.

19. R. A. Costa, A. Abizaid, R. Mehran, et al., "Polymer-Free Biolimus A9-Coated Stents in the Treatment of De Novo Coronary Lesions," *JACC: Cardiovascular Interventions* 9, no. 1 (January 2016): 51–64.

20. M. Sabaté, S. Brugaletta, A. Cequier, et al., "Clinical Outcomes in Patients With ST-Segment Elevation Myocardial Infarction Treated With Everolimus-Eluting Stents Versus Bare-Metal Stents (EXAMINATION): 5-Year Results of a Randomised Trial," *Lancet* 387, no. 10016 (January 2016): 357–366.

21. S. Kufner, R. A. Byrne, M. Valeskini, et al., "Five-Year Outcomes From a Trial of Three Limus-Eluting Stents With Different Polymer Coatings in Patients With Coronary Artery Disease: Final Results From the ISAR-Test 4 Randomised Trial," *EuroIntervention* 11, no. 12 (March 2016): 1372–1379.

22. S. Kufner, J. Sorges, J. Mehilli, et al., "Randomized Trial of Polymer-Free Sirolimus- and Probucol-Eluting Stents Versus Durable Polymer Zotarolimus-Eluting Stents," *JACC: Cardiovascular Interventions* 9, no. 8 (April 2016): 784–792.

23. P. W. Serruys, V. Farooq, B. Kalesan, et al., "Improved Safety and Reduction in Stent Thrombosis Associated With Biodegradable Polymer-Based Biolimus-Eluting Stents Versus Durable Polymer-Based Sirolimus-Eluting Stents in Patients With Coronary Artery Disease," *JACC: Cardiovascular Interventions* 6, no. 8 (August 2013): 777–789.

24. T. Stiermaier, A. Heinz, D. Schloma, et al., "Five-Year Clinical Follow-Up of a Randomized Comparison of a Polymer-Free Sirolimus-Eluting Stent Versus a Polymer-Based Paclitaxel-Eluting Stent in Patients With Diabetes Mellitus (LIPSIA Yukon Trial)," *Catheterization and Cardiovascular Interventions* 83, no. 3 (February 2014): 418–424.

25. M. Natsuaki, K. Kozuma, T. Morimoto, et al., "Five-Year Outcome of a Randomised Trial Comparing Second-Generation Drug-Eluting Stents Using Either Biodegradable Polymer or Durable Polymer: The NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial (NEXT)," *EuroIntervention* 14, no. 7 (September 2018): 815–818.

26. B. Chevalier, W. Wijns, S. Silber, et al., "Five-Year Clinical Outcome of the Nobori Drug-Eluting Coronary Stent System in the Treatment of Patients With Coronary Artery Disease: Final Results of the NOBORI 1 Trial," *EuroIntervention* 11, no. 5 (September 2015): 549–554.

27. C. R. Kelly, P. S. Teirstein, I. T. Meredith, et al., "Long-Term Safety and Efficacy of Platinum Chromium Everolimus-Eluting Stents in Coronary Artery Disease," *JACC: Cardiovascular Interventions* 10, no. 23 (December 2017): 2392–2400.

28. L. O. Jensen, P. Thayssen, E. H. Christiansen, et al., "Safety and Efficacy of Everolimus- Versus Sirolimus-Eluting Stents," *Journal of the American College of Cardiology* 67, no. 7 (February 2016): 751–762.

29. H. Gada, A. J. Kirtane, W. Newman, et al., "5-Year Results of a Randomized Comparison of XIENCE V Everolimus-Eluting and TAXUS Paclitaxel-Eluting Stents," *JACC: Cardiovascular Interventions* 6, no. 12 (December 2013): 1263–1266.

30. D. van Vliet, E. H. Ploumen, T. H. Pinxterhuis, et al., "Final 5-Year Report of BIONYX Comparing the Thin-Composite Wire-Strut Zotarolimus-Eluting Stent Versus Ultrathin-Strut Sirolimus-Eluting Stent," *Catheterization and Cardiovascular Interventions* 104, no. 1 (July 2024): 1–9.

31. E. H. Ploumen, T. H. Pinxterhuis, R. A. Buiten, et al., "Final 5-Year Report of the Randomized BIO-RESORT Trial Comparing 3 Contemporary Drug-Eluting Stents in All-Comers," *Journal of the American Heart Association* 11, no. 22 (November 2022): e026041.

32. T. Slagboom, R. Toelg, B. Witzenbichler, et al., "Sirolimus-Eluting or Everolimus-Eluting Stents for Coronary Artery Disease: 5-Year Outcomes of the Randomised BIOFLOW-IV Trial," *EuroIntervention* 18, no. 14 (February 2023): 1197–1200.

33. T. Pilgrim, R. Piccolo, D. Heg, et al., "Ultrathin-Strut, Biodegradable-Polymer, Sirolimus-Eluting Stents Versus Thin-Strut, Durable-Polymer, Everolimus-Eluting Stents for Percutaneous Coronary Revascularisation: 5-Year Outcomes of the BIOSCIENCE Randomised Trial," *Lancet* 392, no. 10149 (September 2018): 737–746.

34. L. Räber, K. Yamaji, H. Kelbæk, et al., "Five-Year Clinical Outcomes and Intracoronary Imaging Findings of the COMFORTABLE AMI Trial:

Randomized Comparison of Biodegradable Polymer-Based Biolimus-Eluting Stents With Bare-Metal Stents in Patients With Acute ST-Segment Elevation Myocardial Infarction," *European Heart Journal* 40, no. 24 (June 2019): 1909–1919.

35. P. C. Smits, G. J. Vlachojannis, E. P. McFadden, et al., "Final 5-Year Follow-Up of a Randomized Controlled Trial of Everolimus- and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice," *JACC: Cardiovascular Interventions* 8, no. 9 (August 2015): 1157–1165.

36. G. J. Vlachojannis, P. C. Smits, S. H. Hofma, et al., "Biodegradable Polymer Biolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents in Patients With Coronary Artery Disease," *JACC: Cardiovascular Interventions* 10, no. 12 (June 2017): 1215–1221.

37. P. Zocca, M. M. Kok, K. Tandjung, et al., "5-Year Outcome Following Randomized Treatment of All-Comers With Zotarolimus-Eluting Resolute Integrity and Everolimus-Eluting PROMUS Element Coronary Stents," *JACC: Cardiovascular Interventions* 11, no. 5 (March 2018): 462–469.

38. I. T. Meredith, S. Verheye, C. Dubois, 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, no. 17 (April 2018): 2047–2050.

39. D. J. Kereiakes, S. Windecker, R. L. Jobe, et al., "Clinical Outcomes Following Implantation of Thin-Strut, Bioabsorbable Polymer-Coated, Everolimus-Eluting SYNERGY Stents," *Circulation: Cardiovascular Interventions* 12, no. 9 (September 2019): e008152.

40. J. F. Iglesias, M. Roffi, S. Losdat, et al., "Long-Term Outcomes With Biodegradable Polymer Sirolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents in ST-Segment Elevation Myocardial Infarction: 5-Year Follow-Up of the BIOSTEMI Randomised Superiority Trial," *Lancet* 402, no. 10416 (November 2023): 1979–1990.

41. Y. Onuma, K. Miquel-Hebert, and P. W. Serruys, "Five-Year Long-Term Clinical Follow-Up of the XIENCE V Everolimus-Eluting Coronary Stent System in the Treatment of Patients With De Novo Coronary Artery Disease: The SPIRIT II Trial," *EuroIntervention* 8, no. 9 (January 2013): 1047–1051.

42. L. Jakobsen, E. Christiansen, M. Maeng, et al., "Final Five-Year Outcomes After Implantation of Biodegradable Polymer-Coated Biolimus-Eluting Stents Versus Durable Polymer-Coated Sirolimus-Eluting Stents," *EuroIntervention* 13, no. 11 (December 2017): 1336–1344.

43. T. Lefèvre, M. Haude, F. J. Neumann, et al., "Comparison of a Novel Biodegradable Polymer Sirolimus-Eluting Stent With a Durable Polymer Everolimus-Eluting Stent," *JACC: Cardiovascular Interventions* 11, no. 10 (May 2018): 995–1002.

44. M. Maeng, H. H. Tilsted, L. O. Jensen, et al., "Differential Clinical Outcomes After 1 Year Versus 5 Years in a Randomised Comparison of Zotarolimus-Eluting and Sirolimus-Eluting Coronary Stents (The SORT OUT III Study): A Multicentre, Open-Label, Randomised Superiority Trial," *Lancet* 383, no. 9934 (June 2014): 2047–2056.

45. J. Iqbal, P. W. Serruys, S. Silber, et al., "Comparison of Zotarolimus- and Everolimus-Eluting Coronary Stents," *Circulation: Cardiovascular Interventions* 8, no. 6 (June 2015): e002230.

46. D. E. Kandzari, L. Mauri, J. J. Popma, et al., "Late-Term Clinical Outcomes With Zotarolimus- and Sirolimus-Eluting Stents," *JACC: Cardiovascular Interventions* 4, no. 5 (May 2011): 543–550.

47. A. J. Kirtane, M. B. Leon, M. W. Ball, et al., "The 'Final' 5-Year Follow-Up From the ENDEAVOR IV Trial Comparing a Zotarolimus-Eluting Stent With a Paclitaxel-Eluting Stent," *JACC: Cardiovascular Interventions* 6, no. 4 (April 2013): 325–333.

48. A. Abizaid and J. R. Costa, "New Drug-Eluting Stents," *Circulation: Cardiovascular Interventions* 3, no. 4 (August 2010): 384–393.

49. T. F. Lüscher, J. Steffel, F. R. Eberli, et al., "Drug-Eluting Stent and Coronary Thrombosis," *Circulation* 115, no. 8 (February 2007): 1051–1058.

50. A. Hezi-Yamit, C. Sullivan, J. Wong, et al., "Impact of Polymer Hydrophilicity on Biocompatibility: Implication for DES Polymer Design," *Journal of Biomedical Materials Research. Part A* 90A, no. 1 (June 2009): 133–141.

51. G. J. Wilson, A. Marks, K. J. Berg, et al., "The Synergy Biodegradable Polymer Everolimus Eluting Coronary Stent: Porcine Vascular Compatibility and Polymer Safety Study," *Catheterization and Cardiovascular Interventions* 86, no. 6 (November 2015): 247–257.

52. I. T. Meredith, S. Verheye, C. L. Dubois, et al., "Primary Endpoint Results of the EVOLVE Trial," *Journal of the American College of Cardiology* 59, no. 15 (April 2012): 1362–1370.

53. D. J. Kereiakes, I. T. Meredith, S. Windecker, et al., "Efficacy and Safety of a Novel Bioabsorbable Polymer-Coated, Everolimus-Eluting Coronary Stent," *Circulation: Cardiovascular Interventions* 8, no. 4 (April 2015): e002372.

54. D. Kereiakes, I. Meredith, M. Masotti, et al., "Safety and Efficacy of a Bioabsorbable Polymer-Coated, Everolimus-Eluting Coronary Stent in Patients With Diabetes: The EVOLVE II Diabetes Substudy," *EuroIntervention* 12, no. 16 (March 2017): 1987–1994.

55. N. Taglieri, A. G. Bruno, G. Ghetti, et al., "Target Lesion Failure With Current Drug-Eluting Stents," *JACC: Cardiovascular Interventions* 13, no. 24 (December 2020): 2868–2878.

56. B. Chevalier, P. W. Serruys, S. Silber, et al., "Randomised Comparison of Nobori, Biolimus A9-Eluting Coronary Stent With a Taxus(R), Paclitaxel-Eluting Coronary Stent in Patients With Stenosis in Native Coronary Arteries: The Nobori 1 Trial," *EuroIntervention: Journal of EuroPCR in Collaboration With the Working Group on Interventional Cardiology of the European Society of Cardiology* 2, no. 4 (February 2007): 426–434.

57. B. J. O'Brien, J. S. Stinson, S. R. Larsen, M. J. Eppihimer, and W. M. Carroll, "A Platinum–Chromium Steel for Cardiovascular Stents," *Biomaterials* 31, no. 14 (May 2010): 3755–3761.

58. I. B. A. Menown, R. Noad, E. J. Garcia, and I. Meredith, "The Platinum Chromium Element Stent Platform: From Alloy, to Design, to Clinical Practice," *Advances in Therapy* 27, no. 3 (March 2010): 129–141.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.