

SYSTEMATIC REVIEW AND META-ANALYSIS

Systematic Review and Network Meta-Analysis Comparing Bifurcation Techniques for Percutaneous Coronary Intervention

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BACKGROUND: Bifurcation lesions account for 20% of all percutaneous coronary interventions and represent a complex subset which are associated with lower procedural success and higher rates of restenosis. The ideal bifurcation technique, however, remains elusive.

METHODS AND RESULTS: Extensive search of the literature was performed to pull data from randomized clinical trials that met predetermined inclusion criteria. Conventional meta-analysis produced pooled relative risk (RR) and 95% CI of 2-stent technique versus provisional stent on prespecified outcomes. Both frequentist and Bayesian network meta-analyses were performed to compare bifurcation techniques. A total of 8318 patients were included from 29 randomized clinical trials. Conventional meta-analysis showed no significant differences in all-cause mortality, cardiac death, major adverse cardiac events, myocardial infarction, stent thrombosis, target lesion revascularization, and target vessel revascularization between 2-stent techniques and provisional stenting. Frequentist network meta-analysis revealed that double kissing crush was associated with lower cardiac death (RR, 0.57; 95% CI, 0.38–0.84), major adverse cardiac events (RR, 0.50; 95% CI, 0.39–0.64), myocardial infarction (RR, 0.60; 95% CI, 0.39–0.90), stent thrombosis (RR, 0.50; 95% CI, 0.28–0.88), target lesion revascularization, and target vessel revascularization when compared with provisional stenting. Double kissing crush was also superior to other 2-stent techniques, including T-stent or T and protrusion, dedicated bifurcation stent, and culotte.

CONCLUSIONS: Double kissing crush was associated with lower risk of cardiac death, major adverse cardiac events, myocardial infarction, stent thrombosis, target lesion revascularization, and target vessel revascularization compared with provisional stenting and was superior to other 2-stent techniques. Superiority of 2-stent strategy over provisional stenting was observed in subgroup meta-analysis stratified to side branch lesion length ≥ 10 mm.

Key Words: bifurcation technique ■ coronary ■ DK crush ■ percutaneous coronary intervention ■ provisional ■ stent ■ two-stent

See Editorial by Alasnag and Mamas

Bifurcation lesions account for up to 20% of all percutaneous coronary interventions (PCI) and have been associated with worse clinical outcomes when compared with non-bifurcation lesions.^{1,2} Over the years, several bifurcation techniques have

been developed to improve procedural and clinical outcomes, but the ideal technique remains elusive.³ The European Bifurcation Club published its 14th consensus statement in 2019 and advocated for provisional stenting strategy as the standard technique

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Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.122.025394>

For Sources of Funding and Disclosures, see page 13.

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CLINICAL PERSPECTIVE

What Is New?

- We used both frequentist and Bayesian approaches of network meta-analysis in comparing different bifurcation techniques.
- We included the findings of newer trials, performed multiple sensitivity analyses, and incorporated results from trials on dedicated bifurcation stents to produce more robust indirect evidence.

What Are the Clinical Implications?

- Results of our conventional analysis demonstrated no benefit of 2-stent strategies over provisional stenting.
- Two-stent strategy should be favored over provisional stenting when lesion length of the side branch is >10 mm.
- Double kissing crush technique of bifurcation had more favorable clinical outcomes when compared with provisional stenting, crush, culotte, or T-stenting or T and protrusion.

Nonstandard Abbreviations and Acronyms

DBS	dedicated bifurcation stent
DK	double kissing
FKBI	final kissing balloon inflation
LM	left main
MACE	major adverse cardiac events
POT	proximal optimization technique
SB	side branch
T/TAP	T-stent or T and protrusion
TLR	target lesion revascularization
TVR	target vessel revascularization

for majority of bifurcation lesions.⁴ Upfront 2-stent approach should be reserved for select cases with appropriate lesion preparation, proximal optimization technique (POT) and final kissing balloon inflation (FKBI).⁴ Double kissing (DK) crush received a class IIB recommendation as the choice or upfront 2-stent technique.⁵

Two previous Bayesian network meta-analysis have compared the outcomes between different bifurcation techniques but were limited by misclassification and lack of contemporary intervention practices in older trials.^{6,7} Additional trials comparing bifurcation techniques have since been published, therefore, we performed an updated network meta-analysis using both frequentist and Bayesian models to compare the various bifurcation techniques.

METHODS

Search Strategy and Inclusion Criteria

The authors declare that all supporting data are available within the article. An extensive literature search was conducted by 2 authors (D.P. and S.A.) using the online libraries, PubMed, Medline, Embase, and Cochrane Library from inception to November 24, 2021. The search terms applied were “bifurcation,” “coronary,” and “randomized trial.” The inclusion criteria were as follows: (1) randomized controlled trials (RCTs) with 1 bifurcation technique in case group and another bifurcation technique in the control group; (2) pre-specified end points which included all-cause mortality, cardiac death, major adverse cardiac events (MACE), myocardial infarction (MI), stent thrombosis, target lesion revascularization (TLR), and target vessel revascularization (TVR). Multiple bifurcation techniques could be included in 1 arm if the percentage of each technique was specified. If an RCT had multiple publications, the latest data were collected. For 6 RCTs that included >1 bifurcation technique in 1 arm,^{8–13} outcomes were attributed to the predominantly used technique.

Data Extraction and Quality Assessment

Two authors (D.P. and S.A.) collaboratively reviewed full text articles to assess for predetermined eligibility. All the articles were perused for reference citations which were also included if eligible. For each selected RCT, author, published year, follow-up period, bifurcation techniques, duration of antiplatelet therapy, dual antiplatelet agent, and stent types were arranged into tables (Table 1 and Table S1). Inclusion and exclusion criteria of the RCTs were also summarized in Tables S2 and S3. Anatomical characteristics of bifurcation lesions, demographics, clinical presentation, procedural characteristics, definition of outcomes, and quantitative coronary angiography at baseline were extracted and further organized in Table 2 and Tables S3 through S6. The present meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.¹⁴ Risk of biases were assessed using Cochrane Collaboration's tool (Table S7).¹⁵ Only data from published papers that are publicly available were used, so the study was not under the purview of the institutional review board.

Statistical Analysis

For conventional meta-analysis, random effects model based on DerSimonian and Laird method was used to produce pooled relative risk (RR) and 95% CI of 2-stent technique versus provisional stent on prespecified outcomes. Haldane-Ascombe corrections were made for zero-cell corrections. Egger and Begg-Mazumdar tests

Table 1. Characteristics of Selected Trials

Trial	Author	Y	Follow-up	DAPT	Left main	Total	Predominant bifurcation		Control	
							Technique	n	Technique	n
EBC MAIN ⁹	Hildick-Smith et al	2021	1 y	6 mo	Yes	467	Culotte (53%), T/TAP (32%), DK crush (5%), missing (7%)	237	PS	230
NBBS IV ¹⁰	Kumsars et al	2020	2 y	12 mo	Yes	446	Culotte (66%), crush (22%), T-stent (7%), others (6%)	228	PS	218
DEFINITION II ¹³	Zhang et al	2020	1 y	12 mo	Yes	653	DK crush (78%), culotte (18%), TAP (3%), others (1%)	328	PS	325
DKCRUSH-V ¹⁶	Chen et al	2019	3 y	12 mo	Yes	482	DK crush	240	PS	242
COBRA ¹⁷	Bennett et al	2018	5 y	12 mo	No	40	DBS	20	Culotte	20
DKCRUSH-II ¹⁸	Chen et al	2017	5 y	12 mo	Yes	366	DK crush	183	PS	183
BBK II ¹⁹	Ferenc et al	2016	1 y	6 mo	Yes	300	Culotte	150	TAP	150
POLBOS II ²⁰	Gil et al	2016	1 y	12 mo	Yes	202	DBS	102	PS	100
EBC TWO ²¹	Hildick-Smith et al	2016	1 y	12 mo	No	200	Culotte	97	PS	103
SMART-STRATEGY ²²	Song et al	2016	3 y		Yes	258	TAP	130	PS	128
Zhang et al (2016) ²³	Zhang et al	2016	9 mo	12 mo	Yes	104	Culotte	52	PS	52
Zheng et al (2016) ²⁴	Zheng et al	2016	1 y	12 mo	Yes	300	Crush	150	Culotte	150
DKCRUSH-III ²⁵	Chen et al	2015	3 y	12 mo	Yes	415	DK crush	208	Culotte	207
BBK I ²⁶	Ferenc et al	2015	5 y	6 mo	No	202	T-stent	101	PS	101
TRYTON ²⁷	Genereux et al	2015	9 mo	6–12 mo	No	704	DBS	355	PS	349
POLBOS I ²⁸	Gil et al	2015	1 y	12 mo	Yes	243	DBS	120	PS	123
PERFECT ²⁹	Kim et al	2015	1 y	12 mo	No	419	Crush	213	PS	206
NSTS ³⁰	Kervinen et al	2013	3 y	6–12 mo	Yes	424	Crush	209	Culotte	215
NBS ¹²	Maeng et al	2013	5 y	6–12 mo	Yes	404	Crush (50%), culotte (21%), others (29%)	202	PS	202
Ruiz-Salmeron et al (2013) ³¹	Ruiz-Salmeron et al	2013	9 mo	12 mo	No	65	T-stent	34	PS	31
Ye et al (2012) ³²	Ye et al	2012	1 y	12 mo	No	68	DK crush	38	PS	30
BBC ONE ⁸	Hildick-Smith et al	2010	9 mo	9 mo	No	500	Crush (68.1%), culotte (30.2%), others (1.6%)	250	PS	250
Lin et al (2010) ¹¹	Lin et al	2010	8 mo	12 mo	No	108	DK crush (65%), culotte (25%), others (10%)	54	PS	54
Ye et al (2010) ³³	Ye et al	2010	8 mo	12 mo	No	51	DK crush	25	PS	26
CACTUS ³⁴	Colombo et al	2009	6 mo	6 mo	No	350	Crush	177	PS	173
Cervinka et al (2008) ³⁵	Cervinka et al	2008	1 y	1 mo	No	60	DBS	30	PS	30

(Continued)

Table 1. Continued

Trial	Author	Y	Follow-up	DAPT	Left main	Total	Predominant bifurcation		Control	
							Technique	n	Technique	n
DKCRUSH-I ³⁶	Chen et al	2008	8 mo	12 mo	Yes	311	DK crush	155	Crush	156
Colombo et al (2004) ³⁷	Colombo et al	2004	6 mo	3 mo	No	85	T-stent	63	PS	22
Pan et al (2004) ³⁸	Pan et al	2004	6 mo	12 mo	Yes	91	T-stent	44	PS	47

BBC ONE indicates British Bifurcation Coronary Study; BBK I, Bifurcations Bad Krozingen I; BBK II, Bifurcations Bad Krozingen II; CACTUS, Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting Stents; COBRA, Complex Coronary Bifurcation Lesions: Randomized Comparison of a Strategy Using a Dedicated Self-Expanding Bifurcating Stent Versus a Culotte Strategy Using Everolimus-Eluting Stents; DBS, dedicated bifurcation stent; DEFINITION II, Definitions and Impact of Complex Bifurcation Lesions on Clinical Outcomes After Percutaneous Coronary Intervention Using Drug-Eluting Stents; DKCRUSH-I, Study Comparing the Double Kissing Crush With Classical Crush for the Treatment of Coronary Bifurcation Lesions; DKCRUSH-II, Double Kissing Crush Versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions; DKCRUSH-III, Double Kissing Crush Versus Culotte Stenting for the Treatment of Unprotected Distal Left Main Bifurcation Lesions; DKCRUSH-V, Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions; DK crush, double kissing crush; EBC MAIN, European Bifurcation Club Left Main Coronary Stent Study; EBC TWO, European Bifurcation Coronary TWO; NBBS IV, Nordic-Baltic Bifurcation Study IV; NBS, Nordic Bifurcation Study; NSTS, Nordic Stent Technique Study; PERFECT, Optimal Stenting Strategy for True Bifurcation Lesions; POLBOS I, Polish Bifurcation Optimal Stenting I; POLBOS II, Polish Bifurcation Optimal Stenting II; PS, provisional stent; SMART-STRATEGY, Smart Angioplasty Research Team-Optimal STRATEGY for Provisional Side Branch Intervention in Coronary Bifurcation Lesions; T/TAP, T-stenting or T and protrusion; and TRYTON, Prospective, Single Blind, Randomized Controlled Study to Evaluate the Safety & Effectiveness of the Tryton Side Branch Stent Used With DES in Treatment of de Novo Bifurcation Lesions in the Main Branch & Side Branch in Native Coronaries.

were applied after visualization of funnel plots to evaluate for publication biases (Table S8). Both Cochran's Q and Higgins and Thompson's I^2 statistic were generated to describe the heterogeneities among the trials. P value <0.05 or 95% CI not including 1 was statistically significant.

Network meta-analysis based on frequentist framework was first performed to produce network estimates from direct and indirect estimates. To evaluate for inconsistencies, node-splitting analysis was conducted to compare direct and indirect evidence for each outcome. P value <0.05 signified the presence of inconsistency. Tau-squared and I^2 were used to assess the heterogeneities in the network models, which was then broken down into heterogeneities within designs and between designs, each evaluated with Cochran's Q (Table S9). P-scores of each bifurcation technique were also calculated for all outcomes (Table S10). P-scores were interpreted only for outcomes in which the network meta-analysis showed significant difference among the bifurcation techniques. Bayesian network meta-analysis was additionally performed whereby estimates of the bifurcation techniques were calculated through a generalized linear model fitted under a hierarchic Bayesian random-effect framework. Models were computed by Markov-chain Monte Carlo simulations using 4 chains, 5000 adaptations, and 100 000 iterations. Convergence was observed by visual inspection of time-series and density plots. Surface under the cumulative ranking scores were calculated from the Bayesian model to validate the P-scores from the frequentist model (Table S11). Hierarchy of bifurcation techniques were then displayed using rankograms (Table S12). Frequentist network meta-analysis was performed with *meta* and *netmeta* packages, and Bayesian network meta-analysis with *gemtc* and *rjags* packages, all with the use of R version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Bibliographic Search and Trial Characteristics

After a comprehensive search of the literature, 29 RCTs, published from 2004 to 2021, were included in the study (Figure 1). A total of 8318 patients were included consisting of 3225 provisional stenting, 1357 crush, 1356 culotte, 1231 DK crush, 627 dedicated bifurcation stent (DBS), and 522 T-stent or T and protrusion (T/TAP) (Table 1). The follow-up period ranged from 6 months to 5 years. Left main (LM) bifurcations were included in 16 trials¹ while solely non-LM bifurcations were included in 13 trials.² Most of the trials prescribed clopidogrel as the dual antiplatelet agent, with some older studies also

[†]References 4, 9, 10, 12, 13, 16, 18–20, 22–25, 28, 30, 36, 38.

[‡]References 8, 11, 17, 21, 26, 27, 29, 31–35, 37.

Table 2. Demographics, Clinical Presentation, and Characteristics of Lesion

Case/control, %	EBC MAIN ⁹	NBBS IV ¹⁰	DEFINITION II ¹³	DKCRUSH-V ¹⁶	COBRA ¹⁷	DKCRUSH-II ¹⁸	BBK II ¹⁹	POLBOS II ²⁰	EBC TWO ²¹
Age, y	71.4/70.8	63.0/64.0	63.0/64.0	65.0/64.0	66.0/64.0	63.9/64.7	66.3/69.1	67.2/66.6	63.5/62.9
Male	74/79	...	77.7/76.9	82.9/77.7	14.0/15.0	78.8/75.8	71.3/76.0	76.9/75.0	78.0/85.0
BMI, mean	28.4/28.6	...	24.8/24.7	...	...	...	...	...	...
Diabetes	27.0/29.0	15.4/16.5	34.1/35.7	28.8/25.6	25.0/20.0	19.6/23.1	27.3/28.0	44.1/32.0	31.0/25.0
Hypertension	82.0/79.0	65.6/70.0	66.2/70.1	72.9/64.5	75.0/70.0	65.2/60.9	88.0/85.3	84.3/81.0	68.0/63.0
Dyslipidemia	72.0/70.0	81.1/82.0	69.2/68.6	47.5/47.5	95.0/95.0	33.7/29.1	...	83.3/81.0	70.0/70.0
Smoking	13.0/16.0	21.1/18.9	28.4/30.2	...	25.0/20.0	...	11.3/11.3	20.6/26.0	50.0/56.0
PVD	16.0/14.0	...	5.8/4.6	...	...	...	...	3.9/9.0	8.0/6.0
Renal failure	4.0/5.0	...	...	...	...	...	...	10.8/7.0	...
Family history	33.0/33.0	47.4/50.0	...	...	...	...	40.7/39.3	...	...
Previous MI	28.0/26.0	...	11.9/12.9	21.7/21.1	30.0/10.0	17.4/14.2	16.0/21.3	43.1/48.0	41.0/39.0
Previous PCI	43.0/41.0	33.5/35.5	19.8/16.6	...	40.0/20.0	21.2/20.9	38.0/32.0	52.0/57.0	41.0/40.0
Previous stroke	7.0/7.0	...	...	...	...	...	...	...	...
LVEF, mean	...	56.0/57.0	59.0/60.0	...	67.0/68.0	...	56.0/57.0	...	...
Stable CAD	60.0/66.0	...	...	...	80.0/80.0	...	...	...	68.0/69.0
Stable angina	...	82.4/86.6	24.1/21.8	...	...	15.3/11.0	...	...	...
Silent ischemia	...	1.3/0.5	5.2/5.2	...	...	1.6/3.8	...	...	...
ACS	40.0/33.0	...	...	...	...	...	21.3/19.3	...	32.0/31.0
Unstable angina	...	16.7/12.9	48.8/50.5	...	20.0/20.0	66.8/68.7	...	...	...
Acute MI	...	...	22.0/22.5	...	...	16.3/16.3	...	...	...
SYNTAX, mean	23.2/22.6	...	24.7/24.2	...	...	...	...	17.5/18.2	...
0-22	26.0/30.0	...	44.8/48.6	...	...	...	...	...	...
22-32	57.0/56.0	...	33.8/32.6	...	...	...	...	...	...
>32	...	...	21.3/18.8	37.9/36.4	...	...	...	...	...
Medina class	...	...	...	...	...	...	...	...	...
1,0,0	0/0	...	...	...	...	...	...	...	...
0,1,0	0/0	...	...	...	...	...	...	...	...
1,1,0	0/0	...	...	...	0/5.0	...	...	...	...
1,1,1	89.0/90.0	...	86.3/82.5	...	50.0/70.0	84.2/78.7	...	...	68.0/81.0
0,0,1	0/0	...	...	...	...	...	...	...	...
1,0,1	0/0	...	...	...	15.0/10.0	...	...	...	7.0/6.0
0,1,1	11.0/10.0	...	12.5/14.5	...	35.0/15.0	15.8/21.3	...	...	24.0/12.0
Complex features	...	...	...	...	...	...	...	...	...
Trifurcation	4.0/5.0	...	9.5/6.8	...	...	...	...	...	...

(Continued)

Table 2. Continued

Case/control, %	EBC MAIN ⁹	NBBS IV ¹⁰	DEFINITION II ¹³	DKCRUSH-V ¹⁶	COBRA ¹⁷	DKCRUSH-II ¹⁸	BBK II ¹⁹	POLBOS II ²⁰	EBC TWO ²¹	
Calcification	54.0/44.0	43.6/48.4	38.7/40.3	37.1/39.7	...	...	...	...	17.0/19.0	
Tortuosity	24.0/19.0	7.0/2.8	...	...	...	...	...	...	15.0/10.0	
Lesion location										
Left main	100/100	1.3/2.77	28.7/28.9	100/100	...	17.8/15.7	18.7/15.3	35.3/38	...	
LAD	...	76.7/74.2	62.5/60.6	...	≥95/≥95	60.5/59.5	54.7/55.3	44.1/43	77/78	
LCx	...	17.6/16.6	5.2/7.7	...	...	12.4/16.2	24.0/25.3	15.7/15.0	19/15	
RCA	...	4.0/6.5	3.7/2.8	...	...	9.2/8.6	2.7/4.0	4.9/4.0	4/6	
Case/control, %	SMART-STRATEGY ²²	Zhang et al (2016) ²³	Zheng et al (2016) ²⁴	DKCRUSH-III ²⁵	BBK I ²⁶	TRYTON ²⁷	POLBOS I ²⁸	PERFECT ²⁹	NSTS ³⁰	NBS ³²
Age, y	61.5/61.8	64.2/64.5	63.0/64.0	64.3/63.3	66.9/66.7	64.5/64.6	65.9/66.2	60.9/61.1	65.0/65.0	63.0/63.0
Male	83.1/82.0	0.83/0.92	72.7/74.0	77.1/79.9	78.2/79.4	71.8/73.4	68.8/68.3	75.1/75.2	71.0/71.0	78.0/76.0
BMI, mean	...	...	...	...	...	...	...	24.9/24.9	...	...
Diabetes	25.4/28.9	21.2/19.2	22.0/24.7	31.9/30.1	18.8/25.7	23.9/28.1	37.5/25.2	25.8/29.1	13.0/15.0	12.0/13.0
Hypertension	57.7/54.7	63.5/67.3	70.7/72.7	70.5/61.2	89.1/92.1	73.2/73.6	78.3/73.2	55.4/55.3	62.0/60.0	58.0/54.0
Dyslipidemia	13.1/12.5	11.5/11.5	76.0/70.0	41.4/42.1	...	74.1/77.3	62.5/56.9	62.0/57.3	84.0/74.0	72.0/78.0
Smoking	17.7/25.8	51.9/59.6	38.7/44.7	...	13.9	...	21.7/25.2	25.4/32.5	20.0/27.0	...
PVD	...	...	...	...	...	...	9.2/5.7	...	...	...
Renal failure	3.1/1.6	...	...	...	23.7/20.8	...	10.0/9.8	0.5/0.5	...	...
Family history	14.6/13.3	...	30.0/34.7	...	...	36.9/32.5	...	14.1/12.6	57.0/62.0	54.0/58.0
Previous MI	3.8/5.5	19.2/23.1	...	...	20.8/18.8	30.0/37.8	45.8/35.0	4.2/4.4	...	...
Previous PCI	6.9/10.9	23.1/25.0	26.7/22.7	...	51.5/44.6	38.0/41.8	49.2/48.0	...	40.0/34.0	25.0/25.0
Previous stroke	7.7/3.9	...	...	...	...	2.3/3.8	...	...	...	...
LVEF, mean	59.3/60.5	...	...	...	61.0/59.0	57.7/5.75	...	60.4/59.5	57.0/57.0	...
Stable CAD	...	...	...	...	...	...	91.8/94.3	...	...	...
Stable angina	63.1/62.5	38.5/28.8	9.3/8.0	...	...	73.8/74.8	...	...	78.0/72.0	...
Silent ischemia	5.4/10.2	...	8.0/6.0	...	...	5.6/5.2	...	...	2.0/3.0	...
ACS	...	...	...	...	...	...	9.2/5.7	...	...	...
Unstable angina	23.8/20.3	53.8/48.1	82.7/86.0	...	...	20.0/19.8	...	...	21.0/26.0	...
Acute MI	7.7/7.0	...	...	...	...	...	...	...	...	...
SYNTAX, mean	...	...	21.6/22.4	...	...	...	...	...	...	...
0–22	...	...	...	...	...	...	...	...	...	...
22–32	...	...	...	...	...	...	...	...	...	...
>32	...	...	...	...	...	...	...	...	...	...

(Continued)

Table 2. Continued

Case/control, %	SMART-STRATEGY ²²	Zhang et al (2016) ²³	Zheng et al (2016) ²⁴	DKCRUSH-III ²⁵	BBK ²⁶	TRYTON ²⁷	POLBOS ²⁸	PERFECT ²⁹	NSTS ³⁰	NBS ¹²
Medina class										
1,0,0	1.5/1.6	...	...	...	2.0/3.0	...	4.2/4.9	1.0/2.0	...	...
0,1,0	14.6/20.3	...	...	...	13.9/11.9	...	2.5/4.1	1.9/2.5	...	...
1,1,0	14.6/13.3	...	...	...	9.9/11.9	...	16.7/15.4	2.4/10.9	...	...
1,1,1	58.5/53.1	65.4/57.7	72.7/74.0	98.7/94.8	30.7/35.6	73.2/68.7	42.5/45.5	65.9/62.4	...	...
0,0,1	0.8/0.8	...	...	...	5.9/5.0	...	...	1.4/1.0	...	...
1,0,1	3.1/6.3	13.5/11.5	18.0/21.3	...	5.9/7.9	11.5/12.4	10.8/7.3	8.7/8.9	...	...
0,1,1	6.9/4.7	21.2/30.8	9.3/4.7	1.3/5.2	31.7/24.8	14.6/18.7	23.3/22.8	18.8/12.4	...	...
Complex features										
Trifurcation	...	...	...	...	...	...	...	...	...	...
Calcification	...	5.8/9.6	...	...	...	16.4/22.3	...	...	...	...
Tortuosity	...	17.3/21.2	...	...	...	0.0/2.0	...	...	...	8.0/4.0
Lesion location										
Left main	43.8/44.5	26.9/30.8	8.7/12.7	100/100	...	...	22.5/14.6	...	10/10	1/2
LAD	50.8/40.6	65.4/63.5	64.0/68.0	...	73.3/75.2	75.8	52.5/69.9	93.9/92.2	63/66	74/73
LCx	2.3/7.8	3.8/5.8	23.3/17.3	...	20.8/15.8	18.2	17.5/13.0	4.7/7.3	20/20	18/17
RCA	3.1/7.0	3.8/0	4.0/2.0	...	5.9/8.9	6.0	7.5/2.4	1.4/0.5	7/4	6/7
Case/control, %	Ruiz-Salmeron et al (2013) ³¹	Ye et al (2012) ³²	BBC One ³	Lin et al (2010) ¹¹	Ye et al (2010) ³³	CACTUS ³⁴	Cervinka et al (2008) ³⁵	DKCRUSH-I ³⁶	Colombo et al (2004) ³⁷	Pan et al (2004) ³⁸
Age, y	63.6/63.4	63.5/61.7	64.0/64.0	59.2/60.6	63.6/63.2	65.0/67.0	65.3/61.5	63.8/63.9	63.0/62.0	58.0/61.0
Male	78.0/85.0	63.2/76.7	77.0/77.0	75.9/83.3	64.0/73.1	80.2/76.3	85.0/83.0	76.2/70.0	76.0/91.0	86.0/72.0
BMI, mean	...	...	28.0/28.0	...	...	...	...	...	21.0/26.0	...
Diabetes	33.0/45.0	18.4/13.3	11.0/13.0	13.0/18.5	16.0/19.2	23.7/22.0	30.0/27.0	27.0/8.4	...	39.0/42.0
Hypertension	72.0/67.0	76.3/66.7	62.0/57.0	83.3/90.7	76.0/73.1	70.6/79.8	...	76.2/76.6	...	57.0/59.0
Dyslipidemia	64.0/51.0	18.4/20.0	76.0/76.0	...	16.0/11.5	63.8/70.5	67.0/70.0	68.6/62.6	...	41.0/53.0
Smoking	50.0/61.0	...	17.0/17.0	24.1/29.6	...	...	73.0/80.0	63.8/62.6	...	52.0/38.0
PVD	...	...	5.0/5.0	...	...	...	...	...	...	...
Renal failure	...	...	...	...	...	...	...	...	...	...
Family history	...	...	41.0/42.0	...	...	46.9/35.8	23.0/27.0	...	...	...
Previous MI	...	10.5/6.7	25.0/23.0	18.5/22.2	...	44.6/35.3	...	8.6/12.1	...	39.0/19.0
Previous PCI	25.0/21.0	...	16.0/17.0	24.1/24.1	...	31.1/26.6	...	11.5/11.2	...	...
Previous stroke	...	...	...	...	...	...	...	...	...	...
LVEF, mean	...	61.5/64.4	...	57.1/55.6	59.2/57.2	55.0/57.0	...	61.6/62.7	59.0/59.0	55.0/60.0
Stable CAD	...	...	...	...	...	...	...	...	...	...

(Continued)

Table 2. Continued

Case/control, %	Ruiz-Salmeron et al (2013) ³¹	Ye et al (2012) ³²	BBC One ⁸	Lin et al (2010) ¹¹	Ye et al (2010) ³³	CACTUS ³⁴	Cervinka et al (2008) ³⁵	DKCRUSH-I ³⁶	Colombo et al (2004) ³⁷	Pan et al (2004) ³⁸
Stable angina	...	...	...	...	...	31.1/36.4	55.0/50.0	...	...	...
Silent ischemia	...	...	...	...	...	17.5/13.3	...	...	...	...
ACS	...	...	29.0/27.0	...	...	...	...	...	...	86.0/89.0
Unstable angina	...	71.1/63.3	...	40.7/42.6	96.0/76.9	44.0/47.4	...	69.5/70.1	17.0/17.0	...
Acute MI	...	...	...	...	...	...	...	15.2/16.8	...	...
SYNTAX, mean	...	...	...	...	...	...	...	...	...	...
0-22	...	...	...	...	...	...	...	...	...	...
22-32	...	...	...	...	...	...	...	...	...	...
>32	...	...	...	...	...	...	...	...	...	...
Medina class										
1,0,0	2.8/2.9	...	5.0/4.0	...	...	...	43.0/50.0	...	...	...
0,1,0	0/5.9	...	2.0/4.0	...	...	...	20.0/20.0	...	...	...
1,1,0	5.6/11.8	...	8.0/10.0	...	...	...	...	...	...	...
1,1,1	80.6/70.6	...	60.0/60.0	42.6/48.1	...	...	37.0/30.0	...	...	...
0,0,1	...	...	1.0/0	...	...	...	...	...	...	...
1,0,1	8.3/8.8	...	10.0/8.0	24.1/16.7	...	...	...	...	...	...
0,1,1	2.8/0	...	14.0/13.0	33.3/35/2	...	...	...	...	...	...
Complex features										
Trifurcation	...	...	84.0/81.0	...	...	...	...	...	...	...
Calcification	...	...	...	27.8/25.9	...	...	...	...	...	...
Tortuosity	...	...	...	...	...	...	...	...	...	...
Lesion location										
Left main	...	...	...	...	...	...	...	15.3/15.9	...	5/6
LAD	72/71	78	84/81	79.6/83.3	...	74/70	80/77	65.7/61.7	75.3	75/71
LCx	17/26	15	11/14	11.1/9.3	...	19/25	17/23	11.3/14.0	17.6	13/17
RCA	11/3	7	5/4	9.3/7.4	...	7/5	3/0	7.6/8.4	8.2	7/6

ACS indicates acute coronary syndrome; BBC ONE, British Bifurcation Coronary Study; BBK I, Bifurcations Bad Krozingen I; BBK II, Bifurcations Bad Krozingen II; CACTUS, Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-eluting stents; CAD, coronary artery disease; COBRA, Complex Coronary Bifurcation Lesions: Randomized Comparison of a Strategy Using a Dedicated Self-Expanding Biolimus-Eluting Stent Versus a Culotte Strategy Using Everolimus-Eluting Stents; DEFINITION II, Definitions and Impact of Complex Bifurcation Lesions on Clinical Outcomes After Percutaneous Coronary Intervention Using Drug-Eluting Stents; DKCRUSH-I, Study Comparing the Double Kissing Crush with Classical Crush for the Treatment of Coronary Bifurcation Lesions; DKCRUSH-II, Double Kissing Crush Versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions; DKCRUSH-III, Double Kissing Crush Versus Culotte Stenting for the Treatment of Unprotected Distal Left Main Bifurcation Lesions; DKCRUSH-V, Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions; EBC MAIN, European Bifurcation Club Left Main Coronary Stent Study; EBC TWO, European Bifurcation Coronary TWO; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; MI, myocardial infarction; NBBS IV, Nordic-Baltic Bifurcation Study IV; NBS, Nordic Bifurcation Study; NSTS, Nordic Stent Technique Study; PERFECT, Optimal Stenting Strategy for True Bifurcation Lesions; POLBOS I, Polish Bifurcation Optimal Stenting I; POLBOS II, Polish Bifurcation Optimal Stenting II; SMART-STRATEGY, Smart Angioplasty Research Team-Optimal STRATEGY for Provisional Side Branch Intervention in Coronary Bifurcation Lesions; PVD, peripheral vascular disease; RCA, right coronary artery; and TRYTON, Prospective, Single Blind, Randomized Controlled Study to Evaluate the Safety & Effectiveness of the Tryton Side Branch Stent Used With DES in Treatment of de Novo Bifurcation Lesions in the Main Branch & Side Branch in Native Coronaries.

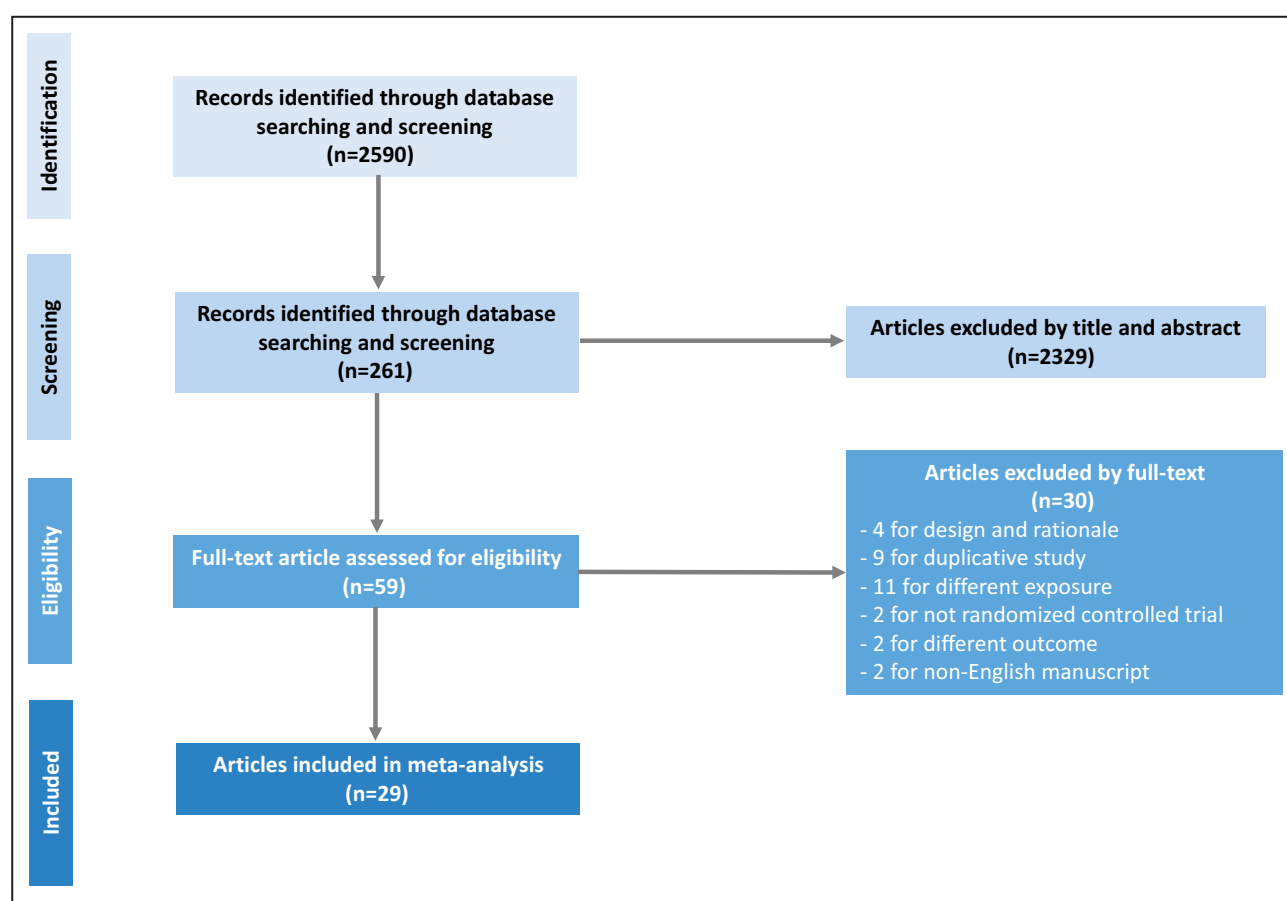


Figure 1. Flow diagram of the search for relevant trials.

The flow diagram illustrates the process of searching and screening the databases to identify trials that meet the prespecified inclusion criteria.

administering ticlopidine (Table S1). The types of stents used varied widely across the studies. Demographics, clinical presentation, and characteristics of bifurcation lesions in each of the trials were also heterogeneous (Table 2). Clinical and anatomical inclusion criteria are summarized in Tables S2 and S3. Details of quantitative angiography and PCI procedural information were inconsistent across all trials (Tables S4 and S6). Angiographic follow-ups were provided for most trials and ranged between 6 and 13 months after index procedure (Table S13).

Comparison of Bifurcation Techniques

Conventional meta-analysis was initially performed to compare clinical outcomes between 2-stent and provisional stent strategies. There were no significant differences in all-cause mortality, cardiac death, MACE, MI, stent thrombosis, TLR, and TVR (Figures S1 through S7). However, in subgroup analysis stratified to the length of side branch (SB) lesion, 2-stent strategies performed better than provisional stents at reducing cardiac death (RR, 0.60; 95% CI, 0.40–0.90), MACE (RR, 0.68; 95% CI, 0.50–0.93), TLR (RR, 0.55; 95%

CI, 0.39–0.78), and TVR (RR, 0.58; 95% CI, 0.36–0.95) when the lesion in the SB was ≥ 10 mm (Figures S8 through S14). On the other hand, the risk of MACE (RR, 1.20; 95% CI, 1.00–1.44) was marginally greater in 2-stent strategy than provisional stenting when the length of the SB lesion was < 10 mm (Figure S10).

Frequentist network meta-analysis (Figure 2) revealed that DK crush was associated with lower cardiac death (RR, 0.57; 95% CI, 0.38–0.84), MACE (RR, 0.50; 95% CI, 0.39–0.64), MI (RR, 0.60; 95% CI, 0.39–0.90), stent thrombosis (RR, 0.50; 95% CI, 0.28–0.88), TLR (RR, 0.44; 95% CI, 0.33–0.59), and TVR (RR, 0.48; 95% CI, 0.34–0.66) when compared with provisional stenting (Figure 3). T/TAP performed worse than provisional stenting and was associated with increased risk of stent thrombosis (RR, 2.37; 95% CI, 1.02–5.51). Node-splitting analysis showed no inconsistencies between direct and indirect evidence for all outcomes (Table S14).

DK crush was associated with lower risk of cardiac death, MACE, MI, stent thrombosis, TLR, and TVR compared with crush. It was also associated with lower risk of MACE, MI, stent thrombosis, TLR, and TVR compared

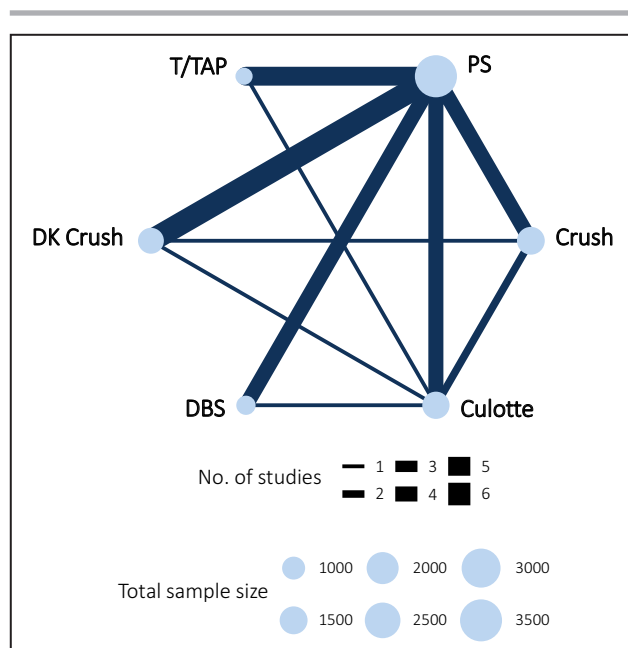


Figure 2. Network plot of selected trials.

The network plot demonstrates the number of studies and patients included among trials that compared double kissing crush, dedicated bifurcation stent, culotte, crush, provisional stenting, and T-stent or T and protrusion. The size of the blue circles and blue lines are proportional to the total sample size and number of relevant studies, respectively. DBS indicates dedicated bifurcation stent; DK, double kissing; PS, provisional stenting; and T/TAP, T-stent or T and protrusion.

with culotte. Similarly, DK crush was associated with better outcomes compared with DBS, T/TAP, and provisional stent (Table S15). The superiority of DK crush was consistently observed in sensitivity analysis of trials that only included true bifurcations (Table S16) or those that excluded LM bifurcations (Table S17). Similar outcomes were found on sensitivity analysis excluding trials without LM bifurcations (Table S18). After excluding trials allowing multiple bifurcation techniques in 1 arm, outcomes still favored DK crush (Table S19).

P-scores calculated by the frequentist model demonstrated that DK crush ranked the highest for MACE, MI, stent thrombosis, TLR, and TVR, most often followed by provisional strategy (Figure 4). Culotte, crush, and T/TAP were associated with lower ranks. Surface under the cumulative ranking scores from Bayesian model produced identical results (Figures S15 and S16). Rankograms redemonstrated the superiority of DK crush and the inferiority of culotte, crush, and T/TAP (Figure 5).

DISCUSSION

The results from our present comprehensive meta-analysis show that DK crush was superior to other bifurcation techniques in reducing the risk of not only stent thrombosis, TLR, TVR, but also the hard

end points including cardiac death, MACE, and MI. Subgroup analysis within conventional meta-analysis demonstrated upfront 2-stent strategy was superior to provisional stenting when the SB lesion length was ≥ 10 mm.

Two previous network meta-analyses have been reported comparing different bifurcation techniques.^{6,7} Crimi et al compiled 26 RCTs and showed that DK crush was associated with the lowest device-oriented clinical event consisting of cardiac death, target-vessel MI, stent thrombosis, TLR, and TVR.⁶ This was in line with the findings of the present network meta-analysis, which also presented highest P-scores as well as surface under the cumulative ranking scores for DK crush. However, Crimi et al mislabeled THUEBIS (Thueringer bifurcation Study) trial as a trial on DBS versus provisional stent and did not account for case groups in which >1 bifurcation techniques were used. Di Gioia et al performed a similar meticulous network meta-analysis on the same subject that included 21 RCTs and 3 sensitivity analyses. They showed that DK crush was associated with lower MACE which was driven by lower rates of TLR and TVR.⁷ However, they did not include trials with DBS, and their sensitivity analysis on trials with only non-LM bifurcations included a significant number of trials with LM bifurcations.

Several theories have been proposed to explain the superiority of DK crush over more conventional and less complex bifurcation techniques. DK crush is advantageous in that it is not affected by the bifurcation angle and maintains wire access in the MV.^{3,39} However, it is a complex multi-step process that requires crossing stent struts twice and results in greater radiation and contrast exposures.³⁹ FKBI, an important step in the DK crush technique, may also be contributing to favorable outcomes. Summary of procedural characteristics in our analysis also showed that FKBI was performed more frequently in the DK crush arms (Table S4). Bench modeling demonstrated greater occurrence of stent malapposition in single kissing compared with DK with FKBI.⁴⁰ Chen et al claimed that DK crush reduced the strut layer in the SB ostium, thereby increasing the success of the final kissing balloon inflation.¹⁶ Ye et al also explained the superiority of DK crush with the higher rate of FKBI, which potentially leads to improved stent apposition, optimized stent geometry, and reduced flow disturbance.^{33,41} However, FKBI after PCI of distal LM bifurcation lesions was not associated with improved outcomes within the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial.⁴² Similarly, in DEFINITION II (Definitions and Impact of Complex Bifurcation Lesions on Clinical Outcomes After Percutaneous Coronary Intervention Using Drug-Eluting Stents) trial, despite having similar percentages

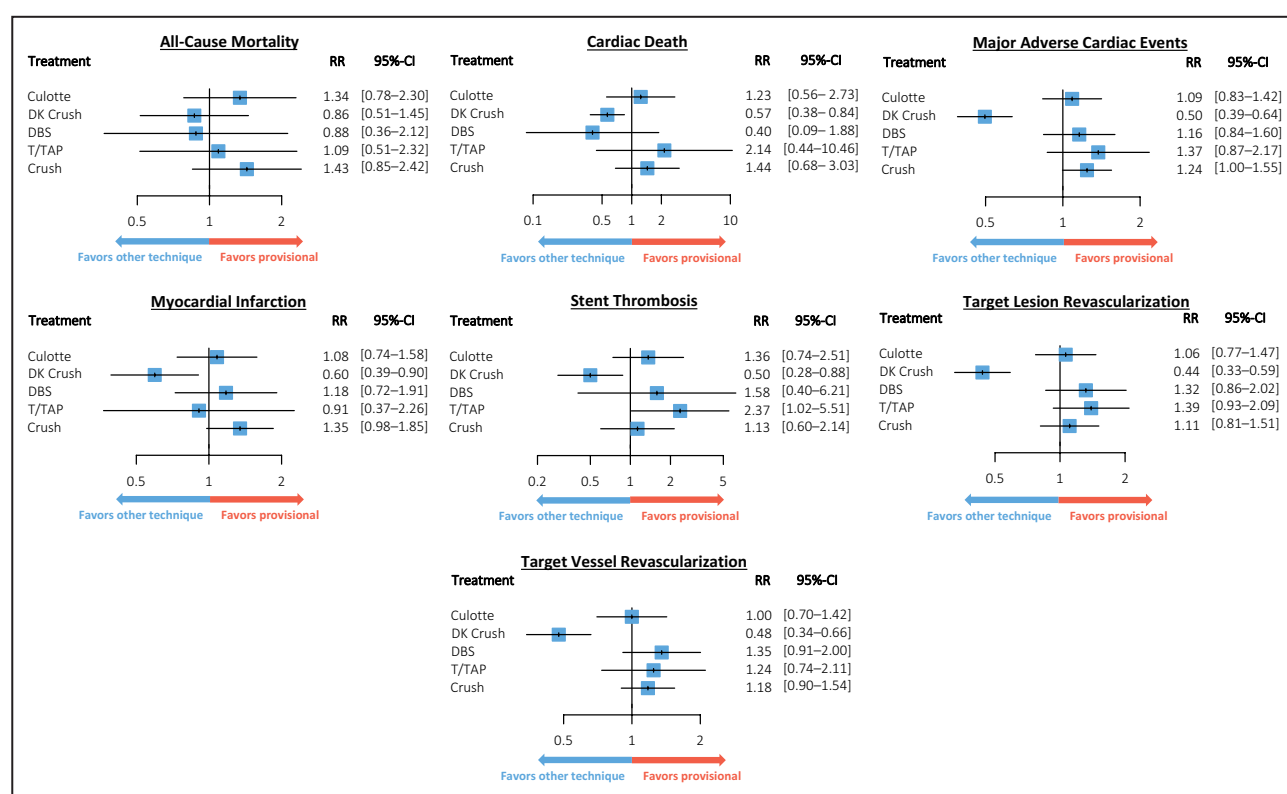


Figure 3. Network meta-analysis of bifurcation techniques with provisional stenting as reference.

The figures show the relative risk of each bifurcation technique compared to provisional stenting for 7 different outcomes. The vertical line inside the blue box represents the relative risk and the perpendicular horizontal line represents the 95% CI. Relative risk above 1 favors provisional stenting (red arrow) whereas that below 1 favors the compared bifurcation technique (blue arrow). DBS indicates dedicated bifurcation stent; DK, double kissing; RR, relative risk; and T/TAP, T-stent or T and protrusion.

of FKBIs in both arms, outcomes still favored the 2-stent strategy (78% of which was DK crush).¹³

Dedicated bifurcation stents, despite their initial promise to address the limitations of standard 2-stent strategies, did not show any benefit over conventional stenting techniques. Although the results of our analysis gave high ranking to DBS for all-cause mortality and cardiac death, these results are not statistically significant and hence this finding is unfounded (Table S15). The accuracy of P-scores and surface under the cumulative ranking scores are compromised with non-significant results and the higher ranks of DBS likely occurred because of the relatively smaller sample and low number of events.

Crush technique has been a historic favorite and has continued to evolve over time with smaller and smaller protrusion of the side branch stent: classic, mini, and nano. The included trials have predominantly used the classic crush technique, except for the PERFECT (Optimal Stenting Strategy for True Bifurcation Lesions) trial, which used the mini-crush technique.²⁹ Results could be anticipated to be different if more trials had used mini-crush or nano-crush techniques and will need future trials to evaluate further.⁴³

Coronary intravascular imaging has shifted the paradigm of coronary interventions from “guessing” based on quantitative angiography to “knowing” accurate vessel and lesion characteristics. Recent meta-analysis demonstrated that the use of intravascular ultrasound during bifurcation PCI was associated with lower risk of MACE compared with angiography-guided PCI.⁴⁴ Only 9 out of the 29 RCTs included in our present study reported the use of intravascular ultrasound,[§] which was not significantly different between the 2 arms except in the PERFECT trial (Table S4). Similarly, only European Bifurcation Club MAIN reported the percentage of optical coherence tomography in both its arms. Perhaps a more standardized and uniform use and reporting of imaging would improve our understanding of bifurcation lesion preparation and optimization.

Proximal optimization technique, which was introduced in 2010, has been proposed to reconstruct the natural and fractal geometry of coronary bifurcations and achieve optimal stent expansion and apposition in the proximal segment. POT was strongly

[§]References 9, 13, 16, 18, 22, 25, 29, 34, 37, 42.

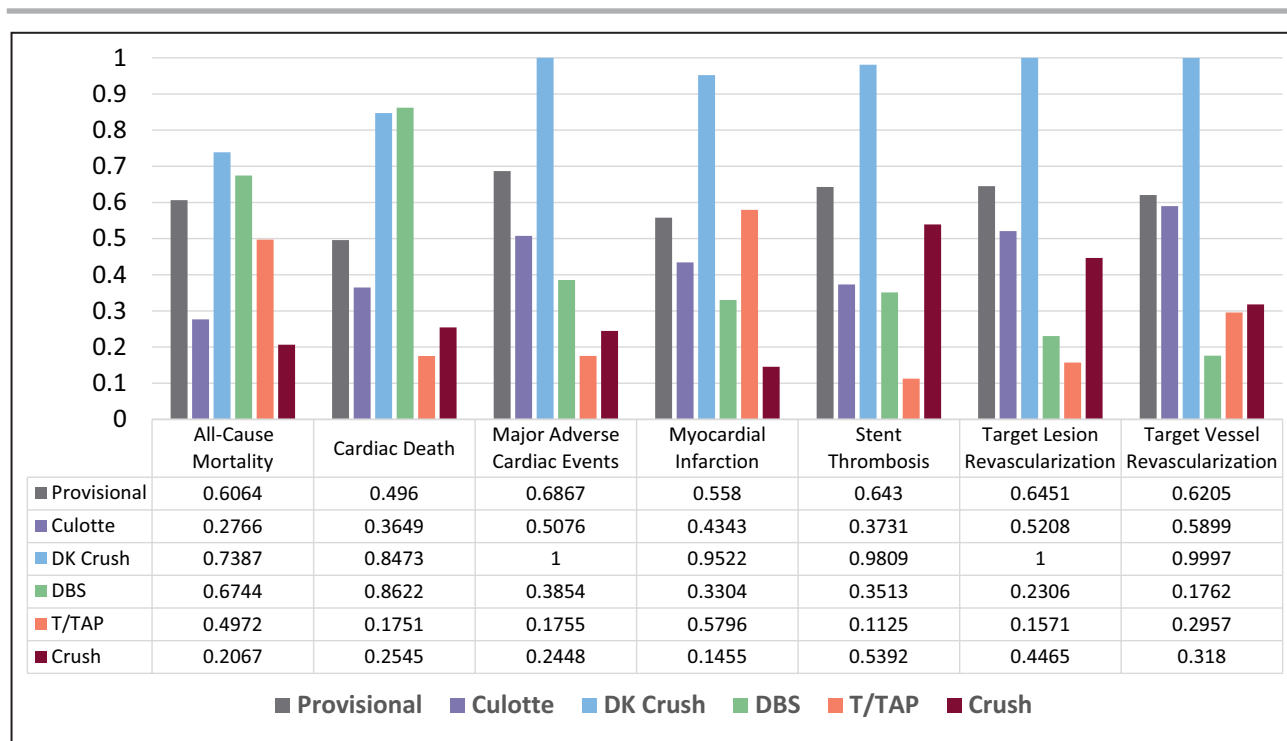


Figure 4. Bar graph showing P-scores of each bifurcation technique for every outcome.

The bar graphs show the P-scores of provisional stenting (gray), culotte (lavender), DK crush (blue), dedicated bifurcation stent (green), T-stent or T and protrusion (orange), and crush (red) from the frequentist network meta-analysis for each outcome. P-scores measure the extent of certainty that the bifurcation technique is better than competing techniques. DBS indicates dedicated bifurcation stent; DK, double kissing; and T/TAP, T-stent or T and protrusion.

recommended by European Bifurcation Club across all 2 stent strategies.⁴ However, it was reported in only 5 RCTs.^{9,13,16,20,28} The difference in POT percentage was not significant between the 2 arms in the European Bifurcation Club MAIN (European Bifurcation Club Left Main Coronary Stent Study [EBC MAIN]) and DKCRUSH-V (Double Kissing Crush versus Provisional Stenting for Left Main Distal Bifurcation Lesions) trials, but was significantly different in DEFINITION II and POLBOS I and II (Polish Bifurcation Optimal Stenting Polish Bifurcation Optimal Stenting) trials (Table S4). Analysis of e-ULTIMASTER (Prospective, Single-Arm, Multi Centre Observations Ultimaster Des) multinational registry⁴⁵ showed that POT was associated with reduction in target lesion failure and stent thrombosis regardless of bifurcation anatomy and technique, so the potential differences in the use of POT could have also affected the studied outcomes.

Other potential confounding variables such as the site of access (radial versus femoral) were only reported in 10 RCTs.^{8,9,13,19–21,25,27–29} However, the difference was not significant between any of the 2 arms (Table S4), and a propensity-matched analysis of Coronary Bifurcation Stenting Registry in Korea also did not observe any differences in cardiac death, MI, TLR, and MACE between transradial and transfemoral approaches.⁴⁶ Antiplatelet

use after bifurcation stenting varied across trials. More recent trials^{9,19} included ticagrelor and prasugrel as their choice of antiplatelet, while most other studies used clopidogrel and some older studies^{11,34,37,42} used ticlopidine (Table S1). A recent network meta-analysis suggested that ticagrelor and prasugrel performed better than clopidogrel in reducing cardiovascular outcomes, so choice of dual antiplatelet agent also need dedicated analysis in bifurcation lesions.⁴⁷ Furthermore, the heterogeneities in the anatomical characteristics of the bifurcation lesions in each of the RCTs were greatly variable, with some trials including more complex cases as those described in the DEFINITION criteria,⁴⁸ limiting our results to be applied across all patient population (Tables S4 and S7).

Limitations

The present network meta-analysis is subject to several limitations. Individual patient level data were unavailable. The time RCTs were conducted spanned from the year 2004 to 2021, and there have been significant improvements in secondary prevention, stent design, choice of anti-proliferative agent in stents, and functional testing of lesions. Events were attributed to the most performed bifurcation technique in 6 RCTs^{8–13} where >1 technique was performed. Sensitivity analyses accounting for heterogeneities

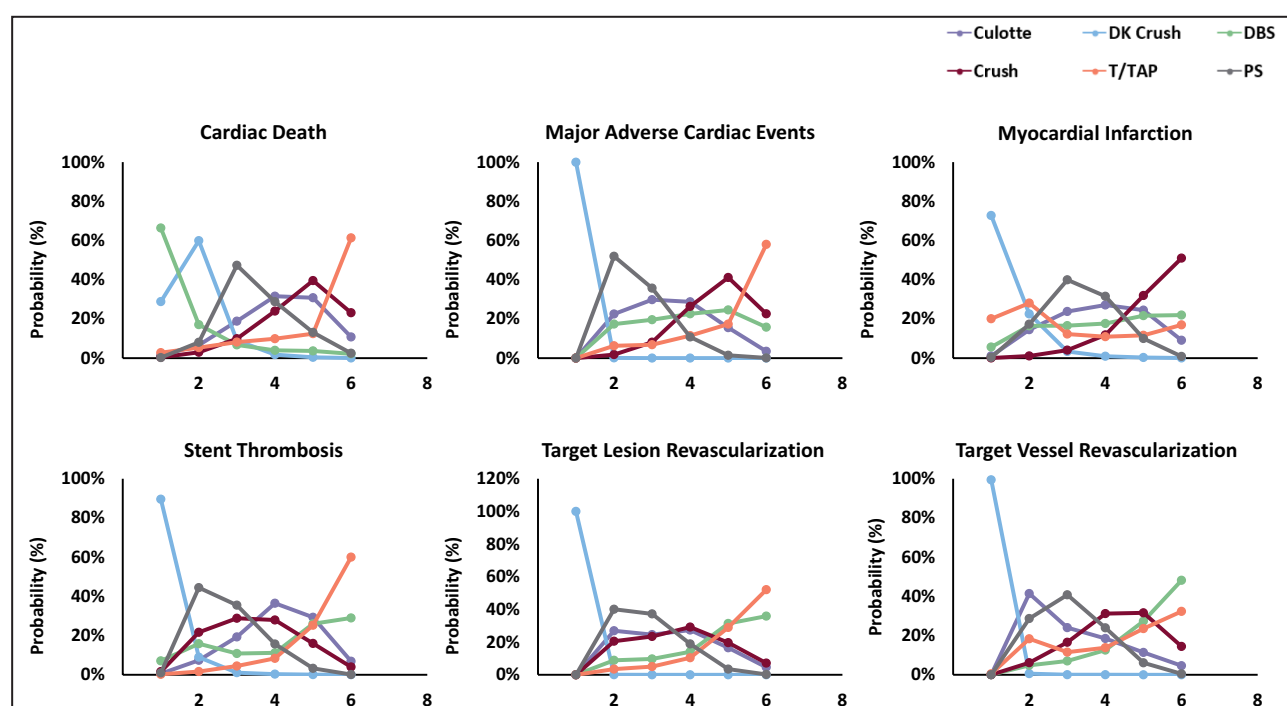


Figure 5. Rank probability analysis for outcomes of interest.

Displayed as rankograms, results of rank probability analysis show the probability of culotte (lavendar), double kissing crush (blue), dedicated bifurcation stent (green), crush (red), T-stent or T and protrusion (orange), and provisional stenting (gray) being the best, second, third, fourth, fifth, and sixth for each of the outcomes. The x-axis and y-axis represent the rank and probability, respectively. DBS indicates dedicated bifurcation stent; DK, double kissing; PS, provisional stenting; and T/TAP, T-stent or T and protrusion.

among the trials were conducted, which yielded similar results (Tables S15 through S19). Several RCTs were subject to high risk of bias primarily attributable to the lack of blinding and conducting open-label studies. Operators could not be masked because of the nature of the study. Significant crossovers occurred in many of the provisional stent arms, and many of the RCTs were conducted by the same group of experts at high-volume centers who would be more proficient in performing complex interventions. Outcomes after DK crush may vary depending on the level of expertise of operators, so further studies reproducing similar safety and efficacy will be required to validate the superiority of the DK crush technique.

CONCLUSIONS

The findings of the present network meta-analysis of bifurcation techniques showed that DK crush was associated with lower risk of cardiac death, MACE, MI, stent thrombosis, TLR, and TVR compared with provisional stenting. Superiority of 2-stent strategy over provisional stenting was observed in subgroup meta-analysis stratified to SB lesion length ≥ 10 mm. Given the findings from successive network meta-analysis, including our present study, and those from

DEFINITION II and DKCRUSH-V trials, DK crush can be considered over other 2-stent strategies in patients with complex bifurcation lesions. Further studies will be required to reproduce and validate these findings.

ARTICLE INFORMATION

Received March 10, 2022; accepted April 7, 2022.

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Acknowledgments

Author contributions: Conceptualization: A.V.; Methodology: D.P., S.An, and A.V.; Software: D.P. and S.An; Validation: D.P., S.R., and A.V.; Formal analysis: D.P. and S.An; Investigation: D.P. and S.An; Resources: D.P. and S.An; Data curation: D.P. and S.An; Original draft preparation: D.P. and S.An; Review and revision: D.P., S.An, N.J., S.A, N.Y., S.R., and A.V.; Visualization: D.P. and S.An; Supervision: S.R. and A.V.; Project administration: A.V.; Funding acquisition: N/A.

Sources of Funding

None.

Disclosures

None.

Supplemental Material

Tables S1–S19

Figures S1–S16

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SUPPLEMENTAL MATERIAL

Table S1. Type of dual antiplatelet agents and stents used in the trials.

Trials	Case		Control	
	Dual Antiplatelet Agent	Stent	Dual Antiplatelet Agent	Stent
EBC MAIN	Clopidogrel (67%) Ticagrelor (20%) Prasugrel (6%)	Onyx ZES	Clopidogrel (66%) Ticagrelor (22%) Prasugrel (5%)	Onyx ZES
NBBS IV	Clopidogrel (100%)	Cypher SES	Clopidogrel (99.5%)	Cypher SES
DEFINITION II	Clopidogrel (100%)	Firebird-2 SES, Excel SES, BuMA SES, Partner SES, Xience EES, Endeavor ZES	Clopidogrel (100%)	Firebird-2 SES, Excel SES, BuMA SES, Partner SES, Xience EES, Endeavor ZES
DKCRUSH-V	Clopidogrel (100%)	Xience Prime EES, Resolute ZES	Clopidogrel (100%)	Xience Prime EES, Resolute ZES
COBRA	Clopidogrel (100%)	Axxess BES, Biomatrix BES	Clopidogrel (100%)	Xience EES
DKCRUSH-II	Clopidogrel (100%)	Excel SES	Clopidogrel (100%)	Excel SES
BBK II	Clopidogrel, ticagrelor, or prasugrel	Cypher SES (8%), Xience pro EES (8.7%), Promus EES (28.7%), Resolute ZES (36.0%), Orsiro SES (11.3%), Synergy SES (7.3%)	Clopidogrel, ticagrelor, or prasugrel	Cypher SES (10.0%), Xience pro EES (10.0%), Promus EES (32.7%), Resolute ZES (30.7%), Orsiro SES (14.0%), Synergy SES (3.3%)
POLBOS II	-	BiOSS LIM SES	-	EES (46%), SES (24%), EES (22%), BES (6%), ZES (2%)
EBC TWO	Clopidogrel (100%)	Nobori BES	Clopidogrel (100%)	Nobori BES
SMART-STRATEGY	-	SES (48%), EES (27%), others (25%)	-	SES (47%), EES (31%), others (22%)
Zhang et al. (2016)	Clopidogrel (100%)	SES (79%), ZES (12%), EES (10%)	Clopidogrel (100%)	SES (62%), EES (19%), ZES (15%), PES (4%)
Zheng et al. (2016)	Clopidogrel (100%)	SES	Clopidogrel (100%)	SES
DKCRUSH-III	Clopidogrel (100%)	Firebird-2 SES, Xience V EES	Clopidogrel (100%)	Firebird-2 SES, Xience V EES
BBK I	Clopidogrel (100%)	Cypher SES	Clopidogrel (100%)	Cypher SES
TRYTON	Clopidogrel (100%)	Tryton side branch stent (100%), Xience EES (59.0%), Promus EES (27.5%), Resolute Integrity ZES (6.0%), Endeavor ZES (4.3%), SES (3.2%)	Clopidogrel (100%)	Xience EES (59.2%), Promus EES (30.6%), Resolute Integrity (5.2%), Endeavor EES (2.6%), SES (2.3%), others (0.3%)
POLBOS I	Clopidogrel (100%)	BiOSS Expert PES	Clopidogrel (100%)	EES (41.5%), PES (38.2%), BES (9.8%), SES (8.9%), ZES (0.8%), TES (0.8%)
PERFECT	Clopidogrel (100%)	SES (60%), EES (28%), ZES (9%), PES (1%), others (3%)	Clopidogrel (100%)	SES (57%), EES (29%), ZES (9%), PES (2%), others (3%)
NSTS	Clopidogrel (100%)	Cypher SES	Clopidogrel (100%)	Cypher SES
NBS	Clopidogrel (99.5%)	Cypher SES	Clopidogrel (100%)	Cypher SES
Ruiz et al. (2013)	-	Xience Prime EES	-	Xience Prime EES
Ye et al. (2012)	Clopidogrel (100%)	Cypher SES, Firebird-2 SES	Clopidogrel (100%)	Cypher SES, Firebird-2 SES
BBC ONE	Clopidogrel (100%)	Taxus PES	Clopidogrel (100%)	Taxus PES
Lin et al. (2010)	Clopidogrel or ticlopidine	SES (57%), PES (43%)	Clopidogrel or ticlopidine	SES (65%), PES (35%)
Ye et al. (2010)	Clopidogrel (100%)	SES (57.4%)	Clopidogrel (100%)	SES (64.8%)
CACTUS	Clopidogrel or ticlopidine	Cypher SES	Clopidogrel or ticlopidine	Cypher SES
Cervinka et al. (2008)	Clopidogrel (100%)	Twin-Rail BMS	Clopidogrel (100%)	Liberte BMS
DKCRUSH-I	Clopidogrel (100%)	PES or SES	Clopidogrel (100%)	PES or SES
Colombo et al. (2004)	Clopidogrel or ticlopidine	Cypher SES	Clopidogrel or ticlopidine	Cypher SES
Pan et al. (2004)	Clopidogrel (100%)	SES	Clopidogrel (100%)	SES

Abbreviations: BES = biolimus-eluting stent; BMS = bare metal stent; EES = everolimus-eluting stent; PES = paclitaxel-eluting stent; SES = sirolimus-eluting stent; TES = tacrolimus-eluting stent; ZES = ziroimus-eluting stent

Table S2. Inclusion and exclusion criteria.

Case/Control	Inclusion Criteria	Exclusion Criteria
EBC MAIN	Age ≥ 18 years Medina type 1,1,1 or 0,1,1 Both MV and SB $>50\%$ narrowed Both MV and SB RVD ≥ 2.75 mm Ischemic symptoms, positive non-invasive imaging, positive fractional flow reserve, or LM stem IVUS-derived minimum luminal area <6 mm ²	Acute STEMI Cardiogenic shock Chronic total occlusion of either vessel LM trifurcation with all three vessels ≥ 2.75 mm diameter LM stem diameter >5.75 mm Life expectancy <12 months Known relevant allergies
NBBS IV	Stable angina pectoris, unstable angina, or silent ischemia Medina 1,1,1, 1,0,1, or 0,1,1 MV diameter ≥ 3.0 mm SB diameter ≥ 2.75 mm	STEMI within 24 hours SB lesion length >15 mm Life expectancy <1 year Serum creatinine $>200\mu\text{mol/L}$ Allergy to aspirin, clopidogrel, ticlopidine, sirolimus, or everolimus
DEFINITION II	Age ≥ 18 years Medina 1,1,1 or 0,1,1 SB RVD ≥ 2.5 mm Native coronary lesion Complex bifurcation lesions based on DEFINITION study	STEMI within 24 hours Pregnancy or breastfeeding Life expectancy $<50\%$ at 12 months Scheduled major surgery in 12 months Allergy to aspirin, clopidogrel, or ticagrelor History of major hemorrhage Chronic total occlusion in either LAD, LCx, or RAD Severe calcification needing rotational atherectomy
DKCRUSH-V	Ages 18 to 80 years Stable angina, unstable angina, or myocardial infarction Medina 1,1,1 or 0,1,1 De novo unprotected LM lesion Unprotected LM lesion with chronic total occlusion in LAD, LCx, or RCA after recanalization Diameter stenosis in LAD/LM and LCx $\geq 50\%$ by visual estimation	Acute myocardial infarction within 24 hours Severe calcification needing rotational atherectomy Restenotic lesion Allergies to study or protocol-required medications Intolerance to dual anti-platelet therapy Life expectancy <12 months Pregnancy or breastfeeding Distal LM coronary restenosis
COBRA	Age >18 years Stable angina, unstable angina, or positive functional study De novo true native coronary bifurcation lesion Medina 1,1,1, 1,0,1, or 0,1,1 Proximal MV RVD 2.75-3.75mm SB RVD >2.25 mm	LVEF $<30\%$ Serum creatinine >2.0 mg/dL Previous or planned brachytherapy of target vessel Unprotected lesion of the LM trunk 50% Intraluminal thrombus in the target vessel Moderate to severe calcification or tortuosity Allergies to protocol stent or medications Pregnancy or breastfeeding Life expectancy <12 months
DKCRUSH-II	Age ≥ 18 years Silent ischemia, angina, or acute myocardial infarction Chronic total occlusion in MV or SB immediately after successful recanalization Unprotected distal LM bifurcation lesions involving both ostia of LAD and LCx without chronic total occlusion in the RCA	Liver dysfunction Life expectancy <12 months Heavy calcification requiring rotational atherectomy Pregnancy Contraindication to one of the study drugs

BBK II	Only one coronary bifurcation lesion Medina 1,1,1 and 0,1,1 Diameter stenosis >50% in both vessels with RVD between 2.5 and 4.0mm De novo bifurcation lesion MV RVD 2.5 to 4.0mm SB RVD ≥ 2.25 mm and ≤ 1.0 mm smaller than that of RV	Acute STEMI Hemodynamic instability History of bleeding diathesis or coagulopathy Intraluminal thrombus Heavy calcification Severe tortuosity Contraindication to study drugs
POLBOS II	Age ≥ 18 years Stable coronary artery disease or non-STEMI De novo coronary bifurcation lesion MV RVD ≥ 2.5 mm SB RVD ≥ 2.0 mm	STEMI LVEF $\leq 30\%$ Medina 0,0,1 Serum creatinine ≥ 2.0 mg/dL Inability to take dual antiplatelet therapy for 12 months
EBC TWO	Age ≥ 18 years Both MV and SV >50% narrowed Both MV and SV RVD ≥ 2.5 mm SB ostial disease ≥ 5 mm SB lesion causing angina and a potential target for intervention	Acute STEMI Cardiogenic shock Unprotected LM stem narrowing $\geq 50\%$ Chronic total occlusion of either vessel Additional type C lesion requiring PCI LVEF $\leq 20\%$ Platelet count $\leq 50,000/\mu\text{L}$ Life expectancy < 12 months Known relevant allergies
SMART-STRATEGY	Stable coronary artery disease or non-STEMI De novo coronary bifurcation lesion, including unprotected LM MV RVD ≥ 2.5 mm SB RVD ≥ 2.3 mm	Hemodynamic instability LVEF <25% Undergoing primary PCI
Zhang et al. (2016)	Age ≥ 18 years De novo true coronary bifurcation lesion Medina 1,1,1, 0,1,1, and 1,0,1 Located either in LM stem, LAD, and LCx MV RVD ≥ 2.5 mm SB RVD ≥ 2.0 mm	Acute STEMI within 24 hours Life expectancy <12 months Allergies to any drugs used in the study
Zheng et al. (2016)	De novo coronary true bifurcation lesion SB RVD ≥ 2.25 mm	Acute STEMI within 24 hours Liver or renal dysfunction LVEF $\leq 30\%$ Life expectancy <1 year Platelet count $\leq 10,000/\mu\text{L}$ Suspected intolerance to any of the drugs used
DKCRUSH-III	Age ≥ 18 years Ischemic symptoms or myocardial ischemia LMV RVD ≤ 5 mm Difference in RVD between LAC and LCX ≤ 1 mm Medina 1,1,1 or 0,1,1 De novo LM distal branch lesion Chronic total occlusion after successful recanalization	Acute myocardial infarction within 2 weeks Liver dysfunction Lung cancer LVEF <30% eGFR <40mL/min/1.73m ² Trifurcation lesions or heavy calcification Pregnancy

BBK I	Stable angina or positive stress test De novo bifurcation lesion Native coronary artery >50% diameter stenosis MV RVD 2.5-4mm SB RVD $\geq$ 2.25mm	Platelet count $\leq$ 10,000/ μ L Suspected intolerance to any of the study drugs LM stenosis Intraluminal thrombus Heavy calcification Severe tortuosity Contraindication to drug or stent used in the study History of bleeding diathesis or coagulopathy
TRYTON	Symptoms or objective evidence of ischemia True bifurcation lesion $\geq$ 50% narrowing Medina 1,1,1, 1,0,1, and 0,1,1 MV RVD 2.5-4mm SB RVD 2.5-3.5mm Lesion length in MV $\leq$ 28mm Lesion length in SB $\leq$ 5mm	STEMI within 72 hours Non-STEMI within 7 days LVEF <30% Serum creatinine >2.5mg/dL LM disease Trifurcation lesion Total occlusion of target vessel Severe calcification Excessive tortuosity Angiographic evidence of thrombus
POLBOS I	Age $\geq$ 18 years Stable coronary artery disease or non-STEMI De novo coronary bifurcation lesion MV RVD $\geq$ 2.5mm SB RVD $\geq$ 2.0mm	STEMI Medina 0,0,1 Serum creatinine $\geq$ 2.0mg/dL Inability to receive dual antiplatelet therapy for 12 months LVEF $\leq$ 30%
PERFECT	Age 18-75 years Angina with bifurcation coronary disease requiring protection MV RVD $\geq$ 2.5mm MV lesion length $\leq$ 50mm SB RVD $\geq$ 2.0mm	LM disease In-stent restenosis Graft lesions Chronic total occlusion STEMI within 2 weeks Decreased SB flow Renal failure LVEF $\leq$ 35% Life expectancy <12 months
NSTS	Age $\geq$ 18 years Stable angina, unstable angina, or silent ischemia De novo coronary bifurcation lesion MV RVD $\geq$ 3.0mm SB RVD $\geq$ 2.5mm	STEMI within 24 hours Life expectancy <12 months Serum creatinine $\geq$ 200 μ mol/L Allergy to any of the drugs used
NBS	Age $\geq$ 18 years Stable angina, unstable angina, or silent ischemia MV RVD $\geq$ 2.5mm SB RVD $\geq$ 2.0mm	STEMI within 24 hours Life expectancy <12 months Serum creatinine $\geq$ 200 μ mol/L Allergy of any of the drugs used LM bifurcation in a left dominant system
Ruiz et al. (2013)	True bifurcation lesions MV RVD 2.5-4mm SB RVD >2mm	LM disease Thrombotic lesions Acute coronary syndrome within 48 hours LVEF <30% Serum creatinine >3mg/dL

<i>Ye et al. (2012)</i>	Age 18-75 years Medina 1,1,1, 1,0,1, or 0,1,1 SB RVD ≥ 2.25 mm	LVEF $\leq 30\%$ Life expectancy <12 months Pregnancy Severe diffuse or calcified MV or SB lesions Platelet count $\leq 10,000/\mu\text{L}$ Serum creatinine $>3\text{mg/dL}$ Cerebrovascular events within 6 months STEMI or other condition with refractory hypotension Intolerance to injection of adenosine
BBC ONE	Age ≥ 18 years MV RVD ≥ 2.5 mm SB RVD ≥ 2.25 mm	STEMI Cardiogenic shock Chronic total occlusion of either vessel LM stem narrowing $\geq 50\%$ Additional type C or bifurcation lesion that required PCI LVEF $\leq 20\%$ Platelet count $\leq 50,000/\mu\text{L}$ Life expectancy <12 months Known relevant allergies
<i>Lin et al. (2010)</i>	Age ≥ 18 years Stable angina, unstable angina, or silent ischemia De novo coronary true bifurcation Bifurcation angle ≤ 60 degrees MV RVD ≥ 2.5 mm SB RVD ≥ 2.22 mm	Myocardial infarction within 24 hours Life expectancy <12 months Serum creatinine $>3.0\text{mg/dL}$ Allergy to any of the drugs used LM bifurcation in a left dominant system
<i>Ye et al. (2010)</i>	Age 18-75 years Single vessel disease with de novo bifurcation lesion Medina 1,1,1, 1,0,1, or 0,1,1 MV RVD ≥ 2.0 mm SB RVD ≥ 2.0 mm	STEMI LVEF $\leq 30\%$ Life expectancy <1 year Pregnancy Severely diffuse or calcified lesions Platelet count $\leq 100,000/\mu\text{L}$ Cerebrovascular events within 6 months Allergy to aspirin, clopidogrel, or sirolimus
CACTUS	Age ≥ 18 years Stable angina, unstable angina, or silent ischemia De novo true coronary bifurcation lesion Stenosis in both MB and ostium of the SB $>50\%$ Both branches with TIMI flow ≥ 1 Treatable lesion length ≤ 28 mm MV RVD 2.5-3.5mm SB RVD 2.25-3.5mm	Myocardial infarction within 24 hours LM trunk unprotected by a graft Visible thrombus within target lesion Chronic total occlusion LVEF $<35\%$ Serum creatinine $\geq 2.65\mu\text{mol/L}$ Contraindication to one of the study drugs
<i>Cervinka et al. (2008)</i>	Symptoms or signs of angina All types but Medina 0,1,0 Lesion length <15 mm MV RVD 2.7-4.0mm SB RVD >2.2 mm	Not reported
DKCRUSH-I	MV RVD ≥ 2.5 mm SB RVD ≥ 2.0 mm	Life expectancy <12 months Liver dysfunction

Two or more bifurcation lesions if there was one bifurcation lesion per vessel
Another single lesion in a different target vessel that could be covered by a single DES were also included

Plasma creatinine $\geq 200 \mu\text{mol/L}$
Cerebrovascular within 6 months
History of coronary artery bypass grafting
Allergy to aspirin, clopidogrel, and stent
Myocardial infarction within 24 hours
Stenosis of LM unprotected by graft
Thrombus within the target lesion
LVEF $\leq 35\%$
Serum creatinine $\geq 3.0 \text{mg/dL}$
Suspected intolerance to one of the study drugs

Colombo et al. (2004)

Age ≥ 18 years
Stable angina, unstable angina, or silent ischemia
De novo true coronary bifurcation lesion
Stenosis in both MB and ostium of the SB $> 50\%$
Both branches with TIMI flow ≥ 1
Treatable lesion length $\leq 24 \text{mm}$
Both MV and SB RVD 2.5-3.5mm

Pan et al. (2004)

Lesion located in major bifurcation regardless of morphology and angulation
MV RVD $\geq 2.5 \text{mm}$
SB RVD $\geq 2.25 \text{mm}$
Significant stenosis in both main vessel and SB origin

Diffuse SB lesions

Abbreviations: IVUS = intravascular ultrasound; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LM = left main coronary artery; LVEF = left ventricular ejection fraction; MV = main vessel; RCA = right coronary artery; RVD = reference vessel diameter; SB = side branch (vessel); STEMI = ST elevation myocardial infarction

Table S3. Anatomical characteristics of bifurcation lesions included in each trial.

Trial	Left Main Included	True Bifurcation	Medina Classification	Main Vessel		Side Branch		Lesion Length, mm
				Diameter, mm	Stenosis, %	Diameter, mm	Stenosis, %	
EBC MAIN	Yes	Yes	1,1,1 0,1,1	≥2.75	>50%	≥2.75	>50%	-
NBBS IV	Yes	Yes	1,1,1 1,0,1 0,1,1	≥3.0	≥50%	≥2.75	≥50%	SB ≤15
DEFINITION II	Yes	Yes	1,1,1 0,1,1	<2.5*	-	≥2.5	Distal LM ≥70%* Non-LM ≥90%*	MV ≥25* SB ≥10*
DKCRUSH-V	Yes	Yes	1,1,1 0,1,1	-	≥50%	-	≥50%	-
COBRA	No	Yes	1,1,1 1,0,1 0,1,1	2.75-3.75	-	2.25	-	-
DKCRUSH-II	Yes	Yes	1,1,1 0,1,1	2.5-4.0	>50%	2.5-4.0	>50%	≤2 stents
BBK II	Yes	No	1,0,0 0,1,0 1,1,0	2.5-4.0	-	2.25	-	-
			1,1,1 0,0,1					
			1,0,1 0,1,1					
			1,0,0 0,1,0					
			1,1,0 1,1,1 1,0,1 0,1,1					
POLBOS II	Yes	No	1,1,0 1,1,1 1,0,1 0,1,1	≥2.5	-	≥2.0	-	-
EBC TWO	No	Yes	1,1,1 1,0,1 0,1,1	≥2.5	>50%	≥2.5	>50%	-
SMART-STRATEGY	Yes	No	1,0,0 0,1,0 1,1,0	≥2.5	-	≥2.3	-	-
			1,1,1 0,0,1					
			1,0,1 0,1,1					
			1,1,1					
			1,0,1 0,1,1					
Zhang et al. (2016)	Yes	Yes	1,1,1 1,0,1 0,1,1	≥2.5	-	≥2.0	-	-

Zheng et al. (2016)	Yes	Yes	1,1,1 1,0,1 0,1,1	-	-	≥ 2.25	-	-
DKCRUSH-III	Yes	Yes	1,1,1 0,1,1	≤ 5	-	-	-	-
BBK I	No	No	1,0,0 0,1,0 1,1,0 1,1,1 0,0,1 1,0,1 0,1,1	2.5-4	>50%	≥ 2.25	>50%	-
TRYTON	No	Yes	1,1,1 1,0,1 0,1,1	2.5-4	$\geq 50\%$	2.5-3.5	$\geq 50\%$	MV ≤ 28 SB ≤ 5
POLBOS I	Yes	No	1,0,0 0,1,0 1,1,0 1,1,1 1,0,1 0,1,1	≥ 2.5	-	≥ 2.0	-	-
PERFECT	No	No	1,0,0 0,1,0 1,1,0 1,1,1 0,0,1 1,0,1 0,1,1	≥ 2.5	-	≥ 2.0	$\geq 50\%$	MV ≤ 50
NSTS	Yes	No	-	≥ 3.0	-	≥ 2.5	-	-
NBS	Yes	No	-	≥ 2.5	-	≥ 2.0	-	-
Ruiz et al. (2013)	No	No	1,0,0 0,1,0 1,1,0 1,1,1 1,0,1 0,1,1	2.5-4	-	>2	-	-
Ye et al. (2012)	No	Yes	1,1,1 1,0,1 0,1,1	-	-	≥ 2.25	-	≤ 2 stents
BBC ONE	No	No	1,0,0 0,1,0 1,1,0 1,1,1 0,0,1	≥ 2.5	-	≥ 2.25	-	-

			1,0,1 0,1,1 1,1,1					
Lin et al. (2010)	No	Yes	1,0,1 0,1,1	≥ 2.5	-	≥ 2.2	-	-
Ye et al. (2010)	No	Yes	1,1,1 1,0,1 0,1,1	≥ 2.0	-	≥ 2.0	-	-
CACTUS	No	Yes	1,1,1 1,0,1 0,1,1	2.5-3.5	>50%	2.25-3.5	>50%	≤ 28
Cervinka et al. (2008)	No	No	1,1,1 1,0,0 0,1,0	2.7-4.0	-	>2.2	-	<15
DKCRUSH-I	Yes	Yes	-	≥ 2.5	-	≥ 2.0	-	≤ 2 stents
Colombo et al. (2004)	No	Yes	-	2.5-3.5	>50%	2.5-3.5	>50%	≤ 24
Pan et al. (2004)	Yes	Yes	1,1,1 0,1,1	≥ 2.5	Significant	≥ 2.25	Significant	-

*One of the criteria of complex bifurcation lesions included in the trial

Abbreviations: LM = left main coronary artery; MV = main vessel; SB = side branch

Table S4. Procedural characteristics.

Trial Case/Control	Radial Approach, %	Intravascular Ultrasound, %	Main Vessel		Side Branch		POT, %	FKBI, %
			Stent Diameter, mm ± SD	Stent Length, mm ± SD	Stent Diameter, mm ± SD	Stent Length, mm ± SD		
EBC MAIN	70/71	31/36	3.6±0.6/3.8±0.5	21.8±7.0/22.1±7.0	3.6±0.6/3.5±0.6	19.3±6.7/17.6±6.9	87/85	93/22
NBBS IV	-	-	-	24.3±9.6/25.0±9.5	-	9(6:13)/13([8:15])*	-	91.2/36.1
DEFINITION II	80.6/78.7	24.4/31.1	3.1±0.3/3.0±0.3	46.3±19.3/46.5±19.7	2.6±0.3/2.8±0.4	25.6±11.3/26.5±12.3	64.6/100	99.3/95.9
DKCRUSH-V	-	42.9/40.5	-	-	-	-	99.2/98.8	99.6/78.9
COBRA	-	-	3.4±0.2/3.0±0.3	49.2±14.1/49.1±17.8**	2.7±0.2/2.7±0.3	-	-	100/100
DKCRUSH-II	-	46.2/47.8	-	28.6±12.4/28.8±13.5	-	16.2±9.1/16.7±8.6	-	100/79.2
BBK II	35.3/37.3	-	3.3±0.4/3.3±0.4	26.7±9.4/26.4±11.7	2.9±0.4/2.8±0.4	21.6±7.7/18.5±8.9	-	100/100
POLBOS II	63.7/81	-	3.7±0.5/3.35±0.5	17.8±2.7/19.9±6.3	-	-	37.3/68	32.7/49.0
EBC TWO	57/63	-	3.0±0.3/3.1±0.3	22.9±5.1/23.4±4.8	2.7±0.3/2.6±0.3	20.7±5.5/19.9±6.8	-	96/94
SMART-STRATEGY	-	98.5/96.9	3.3±0.4/3.3±0.4	25.1±5.3/24.9±5.6	2.9±0.4/2.8±0.2	17.7±5.6/18.4±7.8	-	68.5/25.8
Zhang et al. (2016)	-	-	-	-	-	-	-	92.3/82.7
Zheng et al. (2016)	-	-	-	22.8±7.5/24.6±6.7	-	10.4±5.6/10.2±5.8	-	71.3±86.0
DKCRUSH-III	58.1/58.9	69.0/73.7	3.4±0.3/3.3±0.4	33.5±14.0/35.7±16.0	3.0±0.4/3.0±0.4	25.9±13.8/26.7±11.9	-	99.5/99.5
BBK I	-	-	-	-	-	-	-	100/100
TRYTON	34.6/35.5	-	3.1±0.4/3.1±0.4	14.8±4.0/14.4±3.5	2.6±0.4/2.4±0.4	13.4±3.3/13.8±3.5	-	89.3/88.8
POLBOS I	80.8/82.1	-	3.7±0.3/3.2±0.5	17.4±2.5/20.7±6.8	-	-	37.5/69.1	30.8/49.6
PERFECT	11.7/12.1	91.5/79.6	3.3±0.3/3.3±0.3	37.3±14.7/36.9±15.3	2.7±0.2/2.7±0.2	21.4±6.7/21.5±6.9	-	95.8/79.1
NSTS	-	-	-	23.5±9.3/23.6±9.1	-	10.6±5.6/10.6±5.8	-	85/92
NBS	-	-	-	23.2±8.6/23.4±8.6	-	10.3±5.0/2.8±6.1	-	74/32
Ruiz et al. (2013)	-	-	-	22±11/25±11	-	-	-	64/42
Ye et al. (2012)	-	-	3.1±0.4/3.2±0.4	33.5±12.4/30.7±16.3	2.7±0.3/2.8±0.3	20.7±7.4/18.0±8.2	-	100/86.7
BBC ONE	29/34	-	3.2±0.3/3.0±0.3	22±6/21±6	2.6±0.3/NR	16±5/NR	-	90/31
Lin et al. (2010)	-	-	3.5±0.1/3.6±0.2	23.6±2.1/23.8±2.6	2.9±0.1/2.9±0.2	12.7±2.8/12.9±3.1	-	90.7/94.4
Ye et al. (2010)	-	-	-	-	-	-	-	-
CACTUS	-	3.4/4.1	-	23.8±5.9/22.2±5.7	-	17.9±5.0/18.1±6.2	-	92.1/90.2
Cervinka et al. (2008)	-	-	-	-	-	-	-	97/97
DKCRUSH-I	-	-	3.4±0.4/3.4±0.5	22.2±12.5/25.0±12.7	2.7±0.4/2.8±0.4	17.4±5.6/17.9±7.0	-	100/76.1
Colombo et al. (2004)	-	100/100	3.1±0.3/3.2±0.3	-	2.7±0.3/2.6±0.4	-	-	90.5/81.8
Pan et al. (2004)	-	-	2.9±0.3/2.9±0.3	26±9/25±12	-	-	-	77/60

*Median with interquartile range

**Includes stent length in the side branch

Abbreviation: FKBI = final kissing balloon inflation; NR = not reported; POT = proximal optimization technique; SD = standard deviation

Table S5. Definition of outcomes.

Trial	Cardiac Death	Myocardial Infarction	Target Lesion Revascularization	Target Vessel Revascularization	Stent Thrombosis	Major Adverse Cardiac Events
EBC MAIN	Not specified	Third Universal Definition of Myocardial Infarction except for PCI- and CABG-related MI, for which Society for Cardiovascular Angiography and Interventions (SCAI) consensus definition was used	Repeat revascularization of MV or SB within treated vessel or 5mm adjacent area	Not specified	ARC definition	All-cause death, MI, TLR
NBBS IV	Death from coronary artery disease, heart failure, or cardiac procedure within 28 days	Rise or fall of cardiac biomarkers with at least one value above the 99 th percentile of ULN and evidence of ischemia in the myocardium documented by either ischemic symptoms, ECG changes, evidence of new loss of viable myocardium, or new RMWA Sudden and unexpected cardiac death Pathological findings suggestive of acute MI Post-procedure (within 48 hours after PCI): CK-MB ≥ 10 times ULN or ≥ 5 times with new pathologic Q waves in at least 2 contiguous leads or new LBBB, rise in CK-MB to aforementioned increment from the most recent pre-procedure level Spontaneous MI (48 hours after PCI): rise of CK-MB or troponin >1 times ULN with evidence of prolonged ischemia, ischemic ST segment changes, new pathological Q waves, angiographic evidence of flow-limiting complication, imaging evidence of new loss of viable myocardium, or new RWMA	Repeat revascularization by PCI or CABG of the target lesion in stented segments or their 5mm margins	Not specified	ARC definition	Cardiac death, non-procedural MI, clinically indicated TLR, definite stent thrombosis within 6 months
DEFINITION II	Death from sudden cardiac death, acute MI, arrhythmia, heart failure, stroke, other cardiovascular causes, or bleeding	Spontaneous MI (48 hours after PCI): rise of CK-MB or troponin >1 times ULN with evidence of prolonged ischemia, ischemic ST segment changes, new pathological Q waves, angiographic evidence of flow-limiting complication, imaging evidence of new loss of viable myocardium, or new RWMA Peri-procedural MI: CK-MB >10 times ULN or >5 times ULN with either new pathological Q waves in 2 contiguous leads; angiographically documented graft or coronary artery occlusion or new severe stenosis with thrombosis; or imaging evidence of new loss of viable myocardium or new RWMA Spontaneous MI 72 hours after PCI: clinical syndrome consistent with MI with CK-MB or troponin >1 times ULN and new ST segment elevation or depression or equivalent	Repeat revascularization for target lesions in the presence of symptoms or objective signs of ischemia	Repeat revascularization for target vessels in the presence of symptoms or objective signs of ischemia	ARC definition	Cardiac death, target-vessel MI, clinically driven TLR
DKCRUSH-V	Any death without a clear non-cardiac cause	Peri-procedural MI: CK-MB >10 times ULN or >5 times ULN with either new pathological Q waves in 2 contiguous leads; angiographically documented graft or coronary artery occlusion or new severe stenosis with thrombosis; or imaging evidence of new loss of viable myocardium or new RWMA Spontaneous MI 72 hours after PCI: clinical syndrome consistent with MI with CK-MB or troponin >1 times ULN and new ST segment elevation or depression or equivalent	Angina or ischemic referable to the target lesion requiring clinically driven PCI or CABG	Not specified	ARC definition	Cardiac death, target-vessel MI (all MI unless clearly attributable to non-target vessel), TLR
COBRA	All deaths considered cardiac unless unequivocal non-cardiac cause demonstrated	Evidence of myocardial necrosis consistent with myocardial ischemia, typically including detection of cardiac biomarkers with at least one value above the 99 th percentile of ULN together with ischemic symptoms, pathognomonic ECG, or imaging evidence of ischemia By convention, increase of cardiac biomarkers above 3 times ULN was used to defined PCI-related MI	Revascularization of significant angiographic restenosis $\geq 70\%$ anywhere in the target lesion in combination with angina or FFR <0.80 in MV or SB subtending a large myocardial territory	Not specified	Not specified	Cardiac death, MI (CK-MB based), TVR
DKCRUSH-II	All deaths considered cardiac	Rise of biochemical markers above 99 th percentile with at least one of the following ischemic symptoms:	Repeat revascularization by	Repeat revascularization by	ARC definition	Cardiac death, MI, TVR

	unless other cause documented	ECG changes indicative of ischemia, development of pathological Q waves, and no relation to PCI procedure	PCI or surgery of the target lesion	PCI or surgery of the target vessel		
BBK II	Not specified	During hospitalization: presence of new Q waves in 2 or more contiguous ECG leads or an elevation of CK or CK-MB to at least 3 times of ULN in 2 samples After discharge: ESC/ACC guidelines (2000) and based on new rise in troponin T associated with typical symptoms, ECG changes, and/or angiographic findings	CABG or repeat PCI involving the stented segment and performed for symptoms or signs of ischemia in the presence of angiographic restenosis	Not specified	ARC definition	All-cause death, MI, TLR
POLBOS II	All deaths deemed cardiac unless proven otherwise	Third Universal Definition of Myocardial Infarction	Re-intervention of target lesion because of symptomatic stenosis $\geq 50\%$ of diameter	Revascularization of any segment of the index coronary artery	Not specified	Cardiac death, MI TLR
EBC TWO	Not specified	Typical rise and fall of biochemical markers of myocardial necrosis with ischemic symptoms or ECG changes as per ESC/ACC 2000 Peri-procedural MI: elevation of troponin >5 times the 99 th percentile in patients with normal baseline values or rise $>20\%$ if the baseline values are elevated and are stable or falling In addition, either symptoms suggestive of myocardial ischemia, new ischemic ECG changes, angiographic findings consistent with procedural complication, or imaging demonstrating of new loss of viable myocardium or new RWMA	Not specified	PCI or CABG of either the MV or SB and/or TIMI flow <3 in either the MV or SB after vasodilators	ARC definition	All-cause death, MI, TVR during index admission
SMART-STRATEGY	All deaths considered cardiac unless definite non-cardiac cause established	Elevated troponin or CK-MB greater than ULN with ischemic symptoms or ECG findings indicative of ischemia unrelated to the index procedure	Repeat PCI of lesion within 5 mm of stent or CABG of the target vessel	Repeat revascularization of target vessel by PCI or CABG	ARC definition	Target-vessel failure, target bifurcation revascularization, TVL, TVR
Zhang et al. (2016)	Not specified	NQWMI: CK-MB or troponin-T/I increase ≥ 3 times ULN with clinical signs of MI but without Q waves and not related to intervention QWMI: New pathological Q waves in 2 or more contiguous leads with clinical signs of MI	Repeat target lesion therapy either by PCI or surgery	Repeat target vessel therapy either by PCI or surgery	ARC definition	Cardiac death, MI, TLR, TVR, stent thrombosis
Zheng et al. (2016)	ARC definition	ARC definition	ARC definition	ARC definition	ARC definition	Cardiac death, MI, TVR, stent thrombosis
DKCRUSH-III	ARC definition	ARC definition	Any repeat PCI of the stented segment, including 5mm proximal and distal margins	Not specified	ARC definition	Cardiac death, MI, TVR
BBK I	Not specified	During hospitalization: presence of new Q waves in 2 or more contiguous ECG leads or an elevation of CK or CK-MB to at least 3 times of ULN in 2 samples	CABG or repeat PCI involving the stented segment and	Not specified	ARC definition	All-cause death, MI, TLR

		After discharge: ESC/ACC guidelines (2000) and based on new rise in troponin T associated with typical symptoms, ECG changes, and/or angiographic findings	performed for symptoms or signs of ischemia in the presence of angiographic restenosis			
TRYTON	Not specified	CK-MB >3 times ULN	Clinically or ischemia-driven revascularization of target lesion	Clinically or ischemia-driven revascularization of target vessel	ARC definition	All-cause death, MI, CABG, TLR
POLBOS I	All deaths deemed cardiac unless proven otherwise	Third Universal Definition of Myocardial Infarction	Re-intervention of target lesion because of symptomatic stenosis $\geq 50\%$ of diameter	Revascularization of any segment of the index coronary artery	Not specified	Cardiac death, MI TLR
PERFECT	All deaths considered cardiac unless unequivocal non-cardiac cause established	Increase in CK-MB >3 times ULN with ischemic symptoms or new ischemic ECG changes	Repeat revascularization with PCI or CABG within the stent or adjacent 5mm margins	Repeat revascularization in treated vessel with $\geq 50\%$ stenosis and ischemic signs or symptoms	Not specified	All-cause death, MI, TVR
NSTS	All deaths considered cardiac unless other cause documented	Rise of biochemical markers above the 99 th percentile of ULN with ischemic symptoms, ischemic ECG changes, pathological Q waves, or no relation to PCI procedure	Repeat revascularization by PCI or surgery of the target lesion	Repeat revascularization by PCI or surgery of the target vessel	ARC definition	All-cause death, MI, TVR, stent thrombosis
NBS	All deaths considered cardiac unless other cause documented	NQWMI: CK-MB or troponin-T/I increase ≥ 3 times ULN with clinical signs of MI and not related to intervention QWMI: New pathological Q waves in 2 or more contiguous leads with clinical signs of MI	Repeat revascularization by PCI or surgery of the target lesion	Repeat revascularization by PCI or surgery of the target vessel	Angiographically verified	Cardiac death, MI, TVR, stent thrombosis
Ruiz et al. (2013)	Not specified	Hospital admission with diagnosis of acute coronary syndrome with or without ST segment elevation	Not specified	Repeat revascularization of target vessel	ARC definition	Cardiac death, MI, TVR
Ye et al. (2012)	All deaths considered cardiac unless otherwise documented	Rise of CK-MB 3 times ULN	Repeat revascularization for a stenosis $>50\%$ in target lesion	Clinically driven revascularization of target vessel	ARC definition	Cardiac death, MI, TLR, TVR
BBC ONE	Not specified	First 24 hours after PCI: CK 3 times ULN, CK rise to 50% of the previous value for patient who already had a diagnosis of MI After 24 hours from PCI: ESC/ACC guidelines (2000)	Not specified	PCI or CABG of either the MV or SB and/or TIMI flow <3 in either the MV or SB after vasodilators	ARC definition	All-cause death, MI, target-vessel failure
Lin et al. (2010)	Not specified	Not specified	Repeat revascularization with stenosis diameter $\geq 50\%$ within the stent or adjacent 5mm margins	Repeat revascularization within the treated vessel	ARC definition	Cardiac death, MI, TVR, stent thrombosis
Ye et al. (2010)	All deaths considered cardiac	Rise of CK-MB 3 times ULN	Repeat revascularization for a	Repeat revascularization	ARC definition	Cardiac death, MI, TLR, TVR

	unless otherwise documented		stenosis >50% in target lesion	within the treated vessel		
CACTUS	Not specified	QWMI: New Q waves in 2 or more contiguous leads with post-procedure CK or CK-MB above ULN NQWMI: Postprocedural CK levels 2 times ULN with elevated CK-MB in the absence of pathological Q waves	Not specified	Not specified	ARC definition	Cardiac death, MI, TVR
Cervinka et al. (2008)	Not specified	QWMI: New Q waves in 2 or more ECG leads with post-procedural elevation of CK 3 times ULN and CK-MB >10% of CK level NQWMI: Post-procedural elevation of CK 3 times ULN and CK-MB above normal	Revascularization within 5mm of the stent edges	Revascularization in the treated vessel	ARC definition	All-cause death, MI, CABG, PCI
DKCRUSH-I	Not specified	CK-MB enzyme elevation 3 times ULN either with or without Q waves in at least two contiguous leads on ECG	Repeat revascularization with a diameter stenosis $\geq 50\%$ within the stent or in the 5mm distal or proximal margins	Repeat revascularization within the treated vessel	ARC definition	Cardiac death, MI, TLR
Colombo et al. (2004)	Not specified	Not specified	Not specified	Not specified	In-stent occlusion or thrombus, or death or MI within 30 days	Cardiac death, MI, TVR
Pan et al. (2004)	Not specified	Increase in CK level 3 times ULN	Not specified	Not specified	Not specified	Cardiac death, MI, TVR

Abbreviations: CABG = coronary artery bypass graft; CK = creatine kinase; ECG = electrocardiogram; FFR = fractional flow reserve; MI = myocardial infarction; MV = main vessel; NQWMI = non-Q-wave myocardial infarction; PCI = percutaneous coronary intervention; QWMI = Q-wave myocardial infarction; RWMA = regional wall motion abnormality; SB = side branch; TLR = target lesion revascularization; TVR = target vessel revascularization; ULN = upper limit of normal

Table S6. Quantitative coronary angiography at baseline.

Trial	Proximal Main Vessel				Distal Main Vessel				Side Branch			
Case/Control	RVD (mm)	MLD (mm)	DS (%)	Length (mm)	RVD (mm)	MLD (mm)	DS (%)	Length (mm)	RVD (mm)	MLD (mm)	DS (%)	Length (mm)
EBC MAIN	3.8 ± 0.7	1.6 ± 0.8	56 ± 21	6.3 ± 2.8	2.9 ± 0.6	1.3 ± 0.5	56 ± 17	8.0 ± 5.1	2.7 ± 0.5	1.19 ± 0.5	55 ± 16	7.9 ± 5.7
	3.8 ± 0.8	1.8 ± 0.9	53 ± 21	6.4 ± 3.2	2.8 ± 0.4	1.1 ± 0.4	59 ± 14	8.4 ± 6.1	2.7 ± 0.6	1.29 ± 0.6	52 ± 19	5.8 ± 4.0
NBBS IV	3.2 ± 0.6	1.41 ± 0.6	57 ± 17	19.5 ± 8.9	2.61 ± 0.5	1.43 ± 0.6	43 ± 22	-	2.40 ± 0.5	1.21 ± 0.5	49 ± 17	7.7 ± 4.9
	3.1 ± 0.5	1.29 ± 0.6	59 ± 16	20.8 ± 9.9	2.57 ± 0.5	1.43 ± 0.6	40 ± 20	-	2.33 ± 0.5	1.43 ± 0.7	43 ± 18	6.4 ± 4.1
DEFINITION II	3.5 ± 0.5	2.0 ± 1.0	43 ± 26	41 ± 13*	2.7 ± 0.4	1.12 ± 0.5	58 ± 19	-	2.38 ± 0.4	0.91 ± 0.4	62 ± 16	20.7 ± 10
	3.4 ± 0.5	2.0 ± 1.0	43 ± 25	42 ± 15*	2.7 ± 0.4	1.15 ± 0.5	57 ± 18	-	2.37 ± 0.5	0.91 ± 0.4	62 ± 15	19.9 ± 9
DKCRUSH-V	3.1 ± 0.5	1.2 ± 0.6	61 ± 7	22.4 ± 13	-	-	-	-	2.7 ± 0.4	1.03 ± 0.5	66 ± 7	16.2 ± 14
	3.1 ± 0.5	1.2 ± 0.5	62 ± 8	23.5 ± 13	-	-	-	-	2.7 ± 0.4	1.02 ± 0.4	65 ± 8	16.6 ± 12
COBRA	3.4 ± 0.5	1.86 ± 0.7	57 ± 13	7.35 ± 3.7	2.56 ± 0.5	1.32 ± 0.5	48 ± 16	10.6 ± 8.0	2.33 ± 0.3	0.94 ± 0.4	59 ± 18	9.2 ± 5.9
	3.4 ± 0.5	1.46 ± 0.7	62 ± 14	10.1 ± 3.7	2.49 ± 0.6	1.51 ± 0.6	39 ± 17	7.6 ± 5.8	2.21 ± 0.4	1.19 ± 0.6	46 ± 23	7.1 ± 5.3
DKCRUSH-II	2.9 ± 0.3	0.94 ± 0.4	67 ± 14	28.4 ± 13	-	-	-	-	2.38 ± 0.3	0.89 ± 0.3	63 ± 15	15.4 ± 11
	2.8 ± 0.4	0.86 ± 0.4	69 ± 17	28.7 ± 16	-	-	-	-	2.29 ± 0.4	0.84 ± 0.3	63 ± 14	14.9 ± 13
BBK II	3.1 ± 0.5	1.28 ± 0.8	59 ± 23	23.9 ± 7.6	2.9 ± 0.5	1.24 ± 0.8	58 ± 23	-	2.68 ± 0.5	0.85 ± 0.5	68 ± 19	13.8 ± 6.6
	3.2 ± 0.5	1.29 ± 0.8	59 ± 24	22.7 ± 7.3	3.0 ± 0.5	1.19 ± 0.7	60 ± 23	-	2.62 ± 0.5	0.82 ± 0.6	69 ± 19	15.5 ± 6.9
POLBOS II	3.6 ± 0.2	1.40 ± 0.2	61 ± 14	9.3 ± 3.4	3.01 ± 0.1	1.56 ± 0.2	48 ± 16	8.3 ± 2.9	2.45 ± 0.4	1.13 ± 0.2	54 ± 24	4.2 ± 2.1
	3.5 ± 0.3	1.43 ± 0.3	59 ± 16	9.7 ± 3.7	3.07 ± 0.2	1.57 ± 0.2	49 ± 16	9.8 ± 3.4	2.34 ± 0.3	1.29 ± 0.2	45 ± 18	3.9 ± 2.8
EBC TWO	-	1.1 ± 0.5	48 ± 21	18 ± 8.8	-	-	-	-	-	0.93 ± 0.3	55 ± 14	10.8 ± 7.3
	-	1.1 ± 0.5	51 ± 21	18 ± 6.7	-	-	-	-	-	0.96 ± 0.4	54 ± 16	9.7 ± 7.1
SMART-STRATEGY	3.1 ± 0.6	0.82 ± 0.5	73 ± 15	13.7 ± 8.1	-	-	-	-	2.49 ± 0.5	1.27 ± 0.7	50 ± 23	4.9 ± 4.0
	3.0 ± 0.5	0.77 ± 0.5	75 ± 15	13.2 ± 6.9	-	-	-	-	2.46 ± 0.6	1.29 ± 0.7	49 ± 22	4.4 ± 4.5
Zhang et al. (2016)	3.3 ± 0.5	1.16 ± 0.8	65 ± 24	8.1 ± 4.5	3.0 ± 0.4	0.85 ± 0.6	72 ± 20	15.8 ± 8.6	2.56 ± 0.3	0.56 ± 0.3	78 ± 13	14.1 ± 7.1
	3.4 ± 0.6	1.29 ± 0.9	61 ± 27	7.6 ± 4.9	3.1 ± 0.5	0.76 ± 0.6	75 ± 21	14.7 ± 7.7	2.44 ± 0.4	0.59 ± 0.3	76 ± 11	12.8 ± 4.9
Zheng et al. (2016)	3.4 ± 0.4	1.85 ± 0.5	56 ± 9	16.1 ± 6.3	-	1.42 ± 0.5	64 ± 8	-	2.6 ± 0.3	1.23 ± 0.3	56 ± 10	7.9 ± 4.1
	3.3 ± 0.5	1.87 ± 0.5	57 ± 10	18.5 ± 7.6	-	1.47 ± 0.4	66 ± 9	-	2.7 ± 0.4	1.32 ± 0.3	56 ± 12	7.4 ± 4.3
DKCRUSH-III	-	1.47 ± 0.4	60 ± 9	6.36 ± 3.7	-	1.09 ± 0.4	65 ± 6	16.7 ± 9	-	1.01 ± 0.4	65 ± 7	16.5 ± 11
	-	1.49 ± 0.4	59 ± 8	6.97 ± 3.9	-	1.07 ± 0.4	66 ± 6	18.7 ± 12	-	1.07 ± 0.5	63 ± 8	17.0 ± 13
BBK I	3.1 ± 0.4	1.63 ± 0.9	47 ± 26	20.9 ± 8.2	-	1.20 ± 0.7	55 ± 24	-	2.38 ± 0.3	2.30 ± 0.4	54 ± 22	9.9 ± 4.2
	3.1 ± 0.4	1.53 ± 0.8	50 ± 27	21.7 ± 7.5	-	1.28 ± 0.7	53 ± 24	-	2.39 ± 0.3	1.97 ± 0.5	53 ± 23	10.4 ± 4.1
TRYTON	2.9 ± 0.4	0.99 ± 0.4	66 ± 12	16.8 ± 7.3	-	-	-	-	2.25 ± 0.3	0.95 ± 0.3	58 ± 14	4.8 ± 1.6
	2.9 ± 0.4	1.01 ± 0.4	65 ± 11	16.0 ± 6.8	-	-	-	-	2.21 ± 0.3	1.02 ± 0.3	54 ± 14	4.4 ± 1.1
POLBOS I	3.7 ± 0.2	-	56 ± 16	8.5 ± 2.4	3.1 ± 0.4	-	69 ± 13	5.8 ± 1.9	2.65 ± 0.3	-	61 ± 17	3.7 ± 1.3
	3.6 ± 0.3	-	62 ± 17	8.9 ± 2.7	3.2 ± 0.3	-	64 ± 11	7.5 ± 3.4	2.43 ± 0.4	-	54 ± 21	2.9 ± 1.8
PERFECT	3.6 ± 0.4	1.1 ± 0.4	64 ± 12	28.9 ± 15	2.6 ± 0.4	-	-	-	2.2 ± 0.4	1.1 ± 0.4	57 ± 14	10.3 ± 8.2
	3.7 ± 0.5	1.1 ± 0.4	66 ± 12	27.8 ± 13	2.6 ± 0.4	-	-	-	2.2 ± 0.4	1.1 ± 0.4	53 ± 17	8.3 ± 7.3
NSTS	3.0 ± 0.7	1.9 ± 0.8	36 ± 22	17.4 ± 10	2.59 ± 0.6	1.53 ± 0.7	40 ± 23;41	-	2.39 ± 0.6	1.45 ± 0.6	39 ± 23	7.3 ± 5.8
	3.0 ± 0.7	1.8 ± 0.8	40 ± 23	17.4 ± 10	2.49 ± 0.6	1.48 ± 0.7	± 24	-	2.38 ± 0.6	1.39 ± 0.7	42 ± 23	7.5 ± 6.0
NBS	3.0 ± 0.7	1.62 ± 0.9	46 ± 27	23.2 ± 8.6	2.63 ± 0.6	1.32 ± 0.7	50 ± 25	-	2.28 ± 0.5	1.22 ± 0.6	47 ± 26	6.4 ± 4.7
	2.9 ± 0.7	1.43 ± 0.8	40 ± 27	23.4 ± 8.6	2.41 ± 0.6	1.18 ± 0.7	52 ± 24	-	2.24 ± 0.5	1.21 ± 0.6	46 ± 26	6.0 ± 4.8
Ruiz et al. (2013)	-	1.10 ± 0.7	62 ± 22	-	-	1.35 ± 0.6	45 ± 24	-	-	1.23 ± 0.6	42 ± 24	-
	-	1.15 ± 0.8	62 ± 23	-	-	1.26 ± 0.7	47 ± 21	-	-	1.10 ± 0.4	45 ± 20	-
Ye et al. (2012)	2.9 ± 0.5	0.97 ± 0.3	64 ± 7	28.9 ± 11	-	-	-	-	2.27 ± 0.3	0.97 ± 0.3	70 ± 7	16.9 ± 8.2
	2.8 ± 0.5	0.95 ± 0.4	65 ± 9	25.5 ± 10	-	-	-	-	2.39 ± 0.5	1.01 ± 0.3	61 ± 8	10.2 ± 8.4
BBC ONE	-	-	85 ± 11	-	-	-	-	-	-	-	68 ± 29	-

			87 ± 10								63 ± 31	
<i>Lin et al. (2010)</i>	3.9 ± 0.4	1.6 ± 0.4	60 ± 8	23.6 ± 2.1	3.82 ± 0.5	1.43 ± 0.2	62 ± 5	-	2.79 ± 0.2	0.84 ± 0.1	70 ± 5	12.7 ± 2.8
	4.0 ± 0.4	1.7 ± 0.4	60 ± 8	23.8 ± 2.6	3.91 ± 0.6	1.45 ± 0.3	63 ± 4	-	2.82 ± 0.3	0.85 ± 0.2	70 ± 5	12.9 ± 3.1
<i>Ye et al. (2010)</i>	3.1 ± 0.6	2.0 ± 0.7	-	12.6 ± 7.2	2.4 ± 0.5	1.4 ± 0.6	-	29.3 ± 8.3	2.2 ± 0.4	1.2 ± 0.4	-	17.1 ± 8.0
	3.3 ± 0.7	2.1 ± 0.7	-	12.3 ± 5.1	2.8 ± 0.7	1.6 ± 0.6	-	25.3 ± 7.7	2.4 ± 0.7	1.3 ± 0.5	-	11.5 ± 6.9
CACTUS	2.9 ± 0.3	0.90 ± 0.4	68 ± 12	15.8 ± 8.7	-	-	-	-	2.30 ± 0.3	0.84 ± 0.3	63 ± 12	5.9 ± 4.7
	2.7 ± 0.4	0.83 ± 0.3	69 ± 12	14.7 ± 8.2	-	-	-	-	2.16 ± 0.3	0.83 ± 0.3	61 ± 13	5.7 ± 4.2
<i>Cervinka et al. (2008)</i>	3.4 ± 0.4	-	-	-	-	-	-	-	2.59 ± 0.4	-	-	-
	3.5 ± 0.4	-	-	-	-	-	-	-	2.53 ± 0.4	-	-	-
DKCRUSH-I	2.85 ± 0.5	0.93 ± 0.5	65 ± 13	21.3 ± 11	2.53 ± 0.4	0.65 ± 0.3	66 ± 20	-	2.46 ± 0.5	0.84 ± 0.6	65 ± 20	10.3 ± 6.3
	2.86 ± 0.6	0.94 ± 0.6	64 ± 14	20.0 ± 10	2.56 ± 0.5	0.62 ± 0.3	62 ± 12	-	2.45 ± 0.5	0.84 ± 0.5	66 ± 19	10.5 ± 7.5
<i>Colombo et al. (2004)</i>	2.6 ± 0.4	0.99 ± 0.4	62 ± 12	10.8 ± 4.8	-	-	-	-	2.1 ± 0.3	0.88 ± 0.4	57 ± 17	5.5 ± 4.1
	2.6 ± 0.5	0.92 ± 0.3	65 ± 11	12.2 ± 5.6	-	-	-	-	2.1 ± 0.3	1.14 ± 0.5	46 ± 22	5.1 ± 4.4
<i>Pan et al. (2004)</i>	-	0.76 ± 0.4	74 ± 11	-	-	-	-	-	-	0.85 ± 0.4	65 ± 14	-
	-	0.74 ± 0.5	77 ± 14	-	-	-	-	-	-	0.93 ± 0.4	64 ± 13	-

*Lesion length including both proximal and distal main vessel

Abbreviations: DS = diameter stenosis; MLD = minimum lumen diameter; RVD = reference vessel diameter

Table S7. Risk of bias in the selected trials using the Cochrane Risk Assessment Tool.

Trial	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants and Personnel* (Performance Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Other Bias
EBC MAIN	Low	Low	Low	Low	Low	Low	Low
NBBS IV	High	High	High	High	Low	Low	Low
DEFINITION II	Low	Low	Low	Low	Low	Low	Low
DKCRUSH-V	Low	Low	Unclear	Low	Low	Low	Low
COBRA	Low	Low	Unclear	Low	Low	Low	Low
DKCRUSH-II	Unclear	Low	Unclear	Low	Low	Low	Low
BBK II	Unclear	Low	High	Low	Low	Low	Low
POLBOS II	Low	Low	High	Unclear	Low	Low	Low
EBC TWO	Low	Low	Unclear	Unclear	Low	Low	Low
SMART-STRATEGY	Unclear	Low	High	Low	Low	Low	Low
Zhang et al. (2016)	Low	Low	Unclear	Unclear	Low	Low	Low
Zheng et al. (2016)	Unclear	Low	Unclear	Unclear	Low	Low	Low
DKCRUSH-III	Unclear	Low	Unclear	Unclear	Low	Low	Low
BBK I	Low	Low	High	Unclear	Low	Unclear	Low
TRYTON	Low	Low	Low	Low	High	Low	Low
POLBOS I	Low	Low	High	Low	Low	Low	High
PERFECT	Low	Low	High	Unclear	Low	Low	Low
NSTS	Low	Low	High	Low	Low	Low	Low
NBS	Low	Low	High	Unclear	Low	Low	Low
Ruiz et al. (2013)	Unclear	Low	Unclear	High	Unclear	Low	High
Ye et al. (2012)	High	High	Unclear	Unclear	Low	Unclear	Low
BBC ONE	Low	Low	Unclear	Unclear	Low	Low	Low
Lin et al. (2010)	Low	Low	Unclear	Unclear	Low	Unclear	Low
Ye et al. (2010)	High	High	Unclear	Unclear	Low	Unclear	Low
CACTUS	Unclear	Low	Unclear	Low	Low	Low	Low
Cervinka et al. (2008)	Low	Low	Unclear	Low	Low	Low	Low
DKCRUSH-I	Low	Low	Unclear	Low	Low	Unclear	Low
Colombo et al. (2004)	Unclear	Low	Unclear	Low	Low	Unclear	High
Pan et al. (2004)	High	High	Unclear	Unclear	Low	Unclear	High

*Single-blinded trials were assessed to have low risk of bias as operators could not be completely blinded due to the nature of the study

Table S8. Assessment of publication bias for each outcome in conventional meta-analysis.

	Begg and Mazumdar' Test, <i>P</i> -value	Egger's Test, <i>P</i> -value
All-cause mortality	0.93	0.44
Cardiac Death	0.09	0.40
Major Adverse Cardiac Events	0.32	0.39
Myocardial Infarction	0.43	0.29
Stent Thrombosis	0.37	0.02
Target Lesion Revascularization	0.71	0.93
Target Vessel Revascularization	0.09	0.40

Table S9. Assessment of heterogeneities in the network model.

Outcome	τ^2	I^2	Total			Within Designs			Between Designs		
			Q	DF	P -value	Q	DF	P -value	Q	DF	P -value
All-cause mortality	0	0%	4.80	14	0.9884	2.59	11	0.9951	2.21	3	0.5292
Cardiac Death	0	0%	4.92	18	0.9990	4.27	13	0.9880	0.65	5	0.9856
Major Adverse Cardiac Events	0.0172	14.8%	24.64	21	0.2632	20.02	16	0.2195	4.62	5	0.4637
Myocardial Infarction	0.0366	11.4%	27.10	24	0.2997	22.79	19	0.2469	4.32	5	0.5048
Stent Thrombosis	0	0%	11.54	23	0.9770	8.48	18	0.9705	3.06	5	0.6915
Target Lesion Revascularization	0	0%	14.27	21	0.8578	10.29	16	0.8510	3.98	5	0.5526
Target Vessel Revascularization	0	0%	14.38	18	0.7042	9.38	14	0.8058	5.00	4	0.2877

Abbreviations: DF = degrees of freedom

Table S10. P-scores of each bifurcation technique for every outcome.

	Provisional	Culotte	DK Crush	DBS	T/TAP	Crush
All-cause mortality	0.6064	0.2766	0.7387	0.6744	0.4972	0.2067
Cardiac Death	0.4960	0.3649	0.8473	0.8622	0.1751	0.2545
Major Adverse Cardiac Events	0.6867	0.5076	1.0000	0.3854	0.1755	0.2448
Myocardial Infarction	0.5580	0.4343	0.9522	0.3304	0.5796	0.1455
Stent Thrombosis	0.6430	0.3731	0.9809	0.3513	0.1125	0.5392
Target Lesion Revascularization	0.6451	0.5208	1.0000	0.2306	0.1571	0.4465
Target Vessel Revascularization	0.6205	0.5899	0.9997	0.1762	0.2957	0.3180

Abbreviation: DBS = dedicated bifurcation stent; DK crush = double kissing crush; T/TAP = T-stenting or T and protrusion

Table S11. SUCRA scores of each bifurcation technique for every outcome.

	Provisional	Culotte	DK Crush	DBS	T/TAP	Crush
All-cause mortality	0.5826	0.3111	0.7048	0.6655	0.5119	0.2242
Cardiac Death	0.4923	0.3676	0.8292	0.8639	0.1853	0.2627
Major Adverse Cardiac Events	0.6759	0.5046	0.9998	0.3968	0.1721	0.2508
Myocardial Infarction	0.5278	0.4266	0.9324	0.41019	0.5663	0.1450
Stent Thrombosis	0.6474	0.3854	0.9750	0.3596	0.1264	0.5061
Target Lesion Revascularization	0.6271	0.5055	0.9999	0.2486	0.1576	0.4613
Target Vessel Revascularization	0.5822	0.5730	0.9987	0.1864	0.3228	0.3369

Abbreviation: DBS = dedicated bifurcation stent; DK crush = double kissing crush; T/TAP = T-stenting or T and protrusion

Table S12. Best rank analyses with hierarchical Bayesian model for each outcome.

		1st	2nd	3rd	4th	5th	6th
All-cause Mortality	Culotte	0.03300	0.07775	0.11763	0.20628	0.32578	0.23958
	DK Crush	0.33365	0.26843	0.15513	0.11625	0.07445	0.05210
	DBS	0.37618	0.18980	0.12650	0.11200	0.09328	0.10225
	Crush	0.01923	0.04540	0.07813	0.15545	0.28853	0.41328
	T/TAP	0.18905	0.17388	0.14315	0.17163	0.14450	0.17780
	PS	0.04890	0.24475	0.37948	0.23840	0.07348	0.01500
		1st	2nd	3rd	4th	5th	6th
Cardiac Death	Culotte	0.01343	0.06648	0.18848	0.31595	0.30783	0.10785
	DK Crush	0.28798	0.59903	0.09003	0.01778	0.00440	0.00080
	DBS	0.66385	0.17045	0.06743	0.03983	0.03675	0.02170
	Crush	0.00420	0.02993	0.09915	0.23995	0.39528	0.23150
	T/TAP	0.02810	0.05340	0.08155	0.09883	0.12485	0.61328
	PS	0.00245	0.08073	0.47338	0.28768	0.13090	0.02488
		1st	2nd	3rd	4th	5th	6th
Major Adverse Cardiac Events	Culotte	0.00003	0.22493	0.29793	0.28718	0.15508	0.03488
	DK Crush	0.99903	0.00098	0.00000	0.00000	0.00000	0.00000
	DBS	0.00088	0.17345	0.19593	0.22605	0.24593	0.15778
	Crush	0.00000	0.01795	0.08110	0.26393	0.41103	0.22600
	T/TAP	0.00008	0.06313	0.06823	0.11473	0.17348	0.58038
	PS	0.00000	0.51958	0.35683	0.10813	0.01450	0.00098
		1st	2nd	3rd	4th	5th	6th
Myocardial Infarction	Culotte	0.01085	0.14490	0.23765	0.27080	0.24463	0.09118
	DK Crush	0.72735	0.22533	0.03380	0.00978	0.00315	0.00060
	DBS	0.05663	0.16495	0.16580	0.17635	0.21653	0.21975
	Crush	0.00060	0.01100	0.04065	0.11825	0.31935	0.51015
	T/TAP	0.20100	0.28068	0.12290	0.10935	0.11648	0.16960
	PS	0.00358	0.17315	0.39920	0.31548	0.09988	0.00873

		1st	2nd	3rd	4th	5th	6th
Stent Thrombosis	Culotte	0.00573	0.07410	0.19285	0.36505	0.29340	0.06888
	DK Crush	0.89528	0.08993	0.01055	0.00333	0.00085	0.00008
	DBS	0.07113	0.15840	0.10823	0.11203	0.26023	0.29000
	Crush	0.01613	0.21670	0.28818	0.27925	0.15993	0.03983
	T/TAP	0.00220	0.01653	0.04500	0.08358	0.25273	0.59998
	PS	0.00955	0.44435	0.35520	0.15678	0.03288	0.00125
		1st	2nd	3rd	4th	5th	6th
Target Lesion Revascularization	Culotte	0.00003	0.26973	0.24548	0.27343	0.16533	0.04603
	DK Crush	0.99973	0.00028	0.00000	0.00000	0.00000	0.00000
	DBS	0.00023	0.08858	0.09708	0.14105	0.31400	0.35908
	Crush	0.00000	0.20553	0.23448	0.29223	0.19633	0.07145
	T/TAP	0.00003	0.03478	0.05028	0.10430	0.28953	0.52110
	PS	0.00000	0.40113	0.37270	0.18900	0.03483	0.00235
		1st	2nd	3rd	4th	5th	6th
Target Vessel Revascularization	Culotte	0.00090	0.41400	0.24023	0.18490	0.11398	0.04600
	DK Crush	0.99393	0.00580	0.00023	0.00005	0.00000	0.00000
	DBS	0.00053	0.04838	0.07040	0.12575	0.27323	0.48173
	Crush	0.00008	0.06155	0.16600	0.31193	0.31615	0.14430
	T/TAP	0.00450	0.18350	0.11535	0.13800	0.23550	0.32315
	PS	0.00008	0.28678	0.40780	0.23938	0.06115	0.00483

Table S13. Follow up coronary angiography and time at outcome assessment.

Trial	Angiographic Follow Up	Clinical Follow Up
EBC MAIN	N/A	1 year
NBBS IV	8 months	2 years
DEFINITION II	13 months	1 year
DKCRUSH-V	13 months	3 years
COBRA	9 months	5 years
DKCRUSH-II	8 months	5 years
BBK II	9 months	1 year
POLBOS II	12 months	1 year
EBC TWO	N/A	1 year
SMART-STRATEGY	9 months	3 years
Zhang et al. (2016)	9 months	9 months
Zheng et al. (2016)	12 months	1 year
DKCRUSH-III	8 months	3 years
BBK I	9 months	5 years
TRYTON	9 months	9 months
POLBOS I	12 months	1 year
PERFECT	8 months	1 year
NSTS	8 months	3 years
NBS	8 months	5 years
Ruiz et al. (2013)	9 months	9 months
Ye et al. (2012)	8 months	1 year
BBC ONE	N/A	9 months
Lin et al. (2010)	8 months	8 months
Ye et al. (2010)	8 months	8 months
CACTUS	6 months	6 months
Cervinka et al. (2008)	12 months	1 year
DKCRUSH-I	8 months	8 months
Colombo et al. (2004)	6 months	6 months
Pan et al. (2004)	6 months	6 months

Table S14. Node-splitting analysis for each outcome.

Outcome	Comparison	K	Prop	NMA	Direct	Indirect	Difference	Z-value	P-value
All-cause Mortality	Culotte vs Crush	2	0.59	-0.0670	0.2098	-0.4617	0.6714	1.13	0.2593
	Culotte vs DBS	1	0.18	0.4225	-0.6931	0.6727	-1.3658	-1.04	0.2968
	Culotte vs PS	3	0.57	0.2922	0.1136	0.5272	-0.4136	-0.74	0.4566
	Culotte vs T/TAP	1	0.24	0.2070	0.4055	0.1443	0.2612	0.25	0.8015
	DBS vs PS	4	0.86	-0.1303	-0.3172	1.0486	-1.3658	-1.04	0.2968
	PS vs Crush	3	0.72	-0.3592	-0.5460	0.1254	-0.6714	-1.13	0.2593
	PS vs T/TAP	3	0.84	-0.0852	-0.1281	0.1331	-0.2612	-0.25	0.8015
Cardiac Death	Culotte vs Crush	2	0.66	-0.1545	-0.1324	-0.1977	0.0652	0.08	0.9374
	Culotte vs DBS	1	0.19	1.1243	0.0000	1.3844	-1.3844	-0.63	0.5278
	Culotte vs DK Crush	1	0.36	0.7791	0.6980	0.8242	-0.1262	-0.14	0.8851
	Culotte vs PS	2	0.23	0.2097	0.2682	0.1923	0.0759	0.08	0.9374
	Culotte vs T/TAP	1	0.36	-0.5517	0.0000	-0.8612	0.8612	0.49	0.6248
	DBS vs PS	4	0.85	-0.9146	-1.1254	0.2589	-1.3844	-0.63	0.5278
	DK Crush vs Crush	1	0.12	-0.9337	-1.0922	-0.9111	-0.1811	-0.15	0.8828
	DK Crush vs PS	6	0.92	-0.5694	-0.5715	-0.5445	-0.0270	-0.04	0.9721
	PS vs Crush	3	0.61	-0.3642	-0.3582	-0.3737	0.0155	0.02	0.9841
	PS vs T/TAP	2	0.70	-0.7614	1.0224	-0.1612	-0.8612	-0.49	0.6248
Major Adverse Cardiac Events	Culotte vs Crush	2	0.45	-0.1336	-0.2095	-0.0707	-0.1388	-0.47	0.6350
	Culotte vs DBS	1	0.02	-0.0641	1.6094	-0.0967	1.7062	1.11	0.2675
	Culotte vs DK Crush	1	0.30	0.7825	1.0634	0.6611	0.4023	1.14	0.2539
	Culotte vs PS	4	0.46	0.0832	0.0785	0.0872	-0.0086	-0.03	0.9745
	Culotte vs T/TAP	1	0.38	-0.2345	-0.5878	-0.0169	-0.5709	-1.12	0.2607
	DBS vs PS	4	0.99	0.1472	0.1667	-1.5395	1.7062	1.11	0.2675
	DK Crush vs Crush	1	0.26	-0.9161	-0.7408	-0.9779	0.2371	0.69	0.4875
	DK Crush vs PS	6	0.72	-0.6993	-0.6729	-0.7658	0.0928	0.33	0.7382
	PS vs Crush	4	0.72	-0.2168	-0.2239	-0.1982	-0.0258	-0.10	0.9181
	PS vs T/TAP	2	0.70	-0.3177	-0.1438	-0.7147	0.5709	1.12	0.2607
Myocardial Infarction	Culotte vs Crush	2	0.36	-0.2197	-0.2961	-0.1758	-0.1203	-0.27	0.7902
	Culotte vs DBS	1	0.04	-0.0859	1.0986	-0.1319	1.2305	0.75	0.4547
	Culotte vs DK Crush	1	0.28	0.5944	0.8921	0.4775	0.4146	0.73	0.4625
	Culotte vs PS	4	0.61	0.0767	-0.0161	0.2245	-0.2406	-0.60	0.5467
	Culotte vs T/TAP	1	0.16	0.1723	0.6931	0.0736	0.6196	0.46	0.6453
	DBS vs PS	4	0.98	0.1627	0.1912	-1.0393	1.2305	0.75	0.4547

	DK Crush vs Crush	1	0.40	-0.8141	-0.3565	-1.1225	0.7660	1.64	0.1002
	DK Crush vs PS	6	0.57	-0.5176	-0.6955	-0.2840	-0.4114	-0.96	0.3386
	PS vs Crush	4	0.73	-0.2964	-0.4020	-0.0056	-0.3965	-1.08	0.2804
	PS vs T/TAP	5	0.86	0.0956	0.0100	0.6296	-0.6196	-0.46	0.6453
Stent Thrombosis	Culotte vs Crush	2	0.73	0.1854	0.2310	0.0647	0.1663	0.25	0.7998
	Culotte vs DBS	1	0.14	-0.1501	0.0000	-0.1752	0.1752	0.08	0.9346
	Culotte vs DK Crush	1	0.14	1.0032	2.0843	0.8325	1.2518	1.10	0.2707
	Culotte vs PS	4	0.54	0.3083	-0.0551	0.7361	-0.7912	-1.26	0.2065
	Culotte vs T/TAP	1	0.10	-0.5529	1.0986	-0.7400	1.8386	1.07	0.2847
	DBS vs PS	4	0.88	0.4584	0.4797	0.3045	0.1752	0.08	0.9346
	DK Crush vs Crush	1	0.23	-0.8178	-0.9099	-0.7910	-0.1189	-0.13	0.8996
	DK Crush vs PS	5	0.84	-0.6949	-0.5874	-1.2717	0.6843	0.87	0.3849
	PS vs Crush	4	0.47	-0.1229	-0.1794	-0.0723	-0.1071	-0.16	0.8694
	PS vs T/TAP	5	0.93	-0.8612	-0.9855	0.8530	-1.8386	-1.07	0.2847
Target Lesion Revascularization	Culotte vs Crush	2	0.39	-0.0418	-0.1169	0.0066	-0.1236	-0.31	0.7547
	Culotte vs DBS	1	0.03	-0.2152	1.0986	-0.2540	1.3526	0.83	0.4058
	Culotte vs DK Crush	1	0.26	0.8872	1.2927	0.7442	0.5485	1.22	0.2231
	Culotte vs PS	3	0.51	0.0604	0.0776	0.0425	0.0351	0.11	0.9150
	Culotte vs T/TAP	1	0.36	-0.2713	-0.6931	-0.0343	-0.6589	-1.35	0.1782
	DBS vs PS	4	0.98	0.2756	0.3005	-1.0521	1.3526	0.83	0.4058
	DK Crush vs Crush	1	0.37	-0.9290	-0.7218	-1.0531	0.3313	0.86	0.3904
	DK Crush vs PS	6	0.71	-0.8268	-0.8113	-0.8645	0.0531	0.16	0.8731
	PS vs Crush	3	0.61	-0.1022	-0.1616	-0.0085	-0.1531	-0.47	0.6391
	PS vs T/TAP	4	0.77	-0.3317	-0.1800	0.8389	0.6589	1.35	0.1782
Target Vessel Revascularization	Culotte vs Crush	2	0.53	-0.1634	-0.2146	-0.1060	-0.1086	-0.31	0.7588
	Culotte vs DBS	1	0.05	-0.3027	0.6931	-0.3560	1.0491	0.86	0.3877
	Culotte vs DK Crush	1	0.40	0.7409	1.1835	0.4510	0.7325	1.81	0.0708
	Culotte vs PS	3	0.37	-0.0014	-0.3762	0.2234	-0.5995	-1.61	0.1084
	DBS vs PS	4	0.97	0.3013	0.3308	-0.7183	1.0491	0.86	0.3877
	DK Crush vs Crush	1	0.39	-0.9042	-0.7473	-1.0052	0.2578	0.72	0.4744
	DK Crush vs PS	3	0.58	-0.7422	-0.6233	-0.9040	0.2807	0.83	0.4049
	PS vs Crush	4	0.71	-0.1620	-0.1919	-0.0885	-0.1034	-0.34	0.7340

Table S15. Pooled estimates of network meta-analysis for each outcome.

All-cause Mortality (19 trials)	Culotte	0.65 (0.31-1.37)	0.66 (0.24-1.77)	0.81 (0.34-1.94)	1.07 (0.60-1.90)	0.75 (0.44-1.28)
	1.55 (0.73-3.28)	DK Crush	1.02 (0.36-2.83)	1.26 (0.50-3.15)	1.66 (0.79-3.46)	1.16 (0.69-1.95)
	1.53 (0.57-4.12)	0.98 (0.35-2.74)	DBS	1.24 (0.39-3.93)	1.63 (0.59-4.47)	1.14 (0.47-2.75)
	1.23 (0.52-2.94)	0.79 (0.32-1.98)	0.81 (0.25-2.56)	T/TAP	1.32 (0.54-3.22)	0.92 (0.43-1.95)
	0.94 (0.53-1.66)	0.60 (0.29-1.26)	0.61 (0.22-1.68)	0.76 (0.31-1.86)	Crush	0.70 (0.41-1.18)
	1.34 (0.78-2.30)	0.86 (0.51-1.45)	0.88 (0.36-2.12)	1.09 (0.51-2.32)	1.43 (0.85-2.42)	Provisional
Cardiac Death (23 trials)	Culotte	0.46 (0.20-1.04)	0.32 (0.06-1.74)	1.74 (0.33-9.10)	1.17 (0.54-2.52)	0.81 (0.37-1.80)
	2.18 (0.96-4.95)	DK Crush	0.71 (0.14-3.47)	3.78 (0.75-19.20)	2.54 (1.15-5.64)	1.77 (1.19-2.63)
	3.08 (0.57-16.50)	1.41 (0.29-6.92)	DBS	5.34 (0.59-48.20)	3.59 (0.66-19.41)	2.50 (0.53-11.69)
	0.58 (0.11-3.02)	0.26 (0.05-1.34)	0.19 (0.02-1.69)	T/TAP	0.67 (0.12-3.67)	0.47 (0.10-2.28)
	0.86 (0.40-1.85)	0.39 (0.18-0.87)	0.28 (0.05-1.50)	1.49 (0.27-8.12)	Crush	0.69 (0.33-1.46)
	1.23 (0.56-2.73)	0.57 (0.38-0.84)	0.40 (0.09-1.88)	2.14 (0.44-10.46)	1.44 (0.68-3.03)	Provisional
Major Adverse Cardiac Events (26 trials)	Culotte	0.46 (0.33-0.63)	1.07 (0.71-1.61)	1.26 (0.78-2.05)	1.14 (0.86-1.52)	0.92 (0.71-1.20)
	2.19 (1.59-3.00)	DK Crush	2.33 (1.56-3.49)	2.76 (1.66-3.49)	2.50 (1.86-3.35)	2.01 (1.57-2.57)
	0.94 (0.62-1.42)	0.43 (0.29-0.64)	DBS	1.19 (0.68-2.07)	1.07 (0.73-1.58)	0.86 (0.63-1.19)
	0.79 (0.49-1.28)	0.36 (0.22-0.60)	0.84 (0.48-1.47)	T/TAP	0.90 (0.55-1.48)	0.73 (0.46-1.15)
	0.87 (0.66-1.16)	0.40 (0.30-0.54)	0.93 (0.63-1.38)	1.11 (0.67-1.82)	Crush	0.81 (0.65-1.00)
	1.09 (0.83-1.42)	0.50 (0.39-0.64)	1.16 (0.84-1.60)	1.37 (0.87-2.17)	1.24 (1.00-1.55)	Provisional
Myocardial Infarction (29 trials)	Culotte	0.55 (0.39-0.91)	1.09 (0.59-2.01)	0.84 (0.32-2.21)	1.25 (0.81-1.91)	0.93 (0.63-1.36)
	1.81 (1.10-2.98)	DK Crush	1.97 (1.04-3.74)	1.53 (0.56-4.13)	2.26 (1.44-3.53)	1.68 (1.11-2.55)
	0.92 (0.50-1.69)	0.51 (0.27-0.96)	DBS	0.77 (0.28-2.17)	1.14 (0.64-2.04)	0.85 (0.52-1.38)
	1.19 (0.45-3.12)	0.66 (0.24-1.78)	1.29 (0.46-3.63)	T/TAP	1.48 (0.57-3.86)	1.10 (0.44-2.73)
	0.80 (0.52-1.23)	0.44 (0.28-0.69)	0.87 (0.49-1.56)	0.68 (0.26-1.76)	Crush	0.74 (0.54-1.02)
	1.08 (0.74-1.58)	0.60 (0.39-0.90)	1.18 (0.72-1.91)	0.91 (0.37-2.26)	1.35 (0.98-1.85)	Provisional
Stent Thrombosis (28 trials)	Culotte	0.37 (0.17-0.79)	1.16 (0.27-5.04)	1.74 (0.63-4.81)	0.83 (0.47-1.47)	0.73 (0.40-1.35)
	2.73 (1.27-5.86)	DK Crush	3.17 (0.73-13.3)	4.74 (1.72-13.04)	2.27 (1.05-4.90)	2.00 (1.14-3.51)
	0.86 (0.20-3.73)	0.32 (0.07-1.38)	DBS	1.50 (0.30-7.45)	0.71 (0.16-3.17)	0.63 (0.16-2.48)
	0.58 (0.21-1.59)	0.21 (0.08-0.58)	0.67 (0.13-3.33)	T/TAP	0.48 (0.17-1.36)	0.42 (0.18-0.98)
	1.20 (0.68-2.14)	0.44 (0.20-0.95)	1.40 (0.32-6.20)	2.09 (0.74-5.94)	Crush	0.88 (0.47-1.67)
	1.36 (0.74-2.51)	0.50 (0.28-0.88)	1.58 (0.40-6.21)	2.37 (1.02-5.51)	1.13 (0.60-2.14)	Provisional
Target Lesion Revascularization (26 trials)	Culotte	0.41 (0.28-0.61)	1.24 (0.73-2.11)	1.31 (0.83-2.08)	1.04 (0.71-1.52)	0.94 (0.68-1.30)
	2.43 (1.65-3.58)	DK Crush	3.01 (1.79-5.07)	3.19 (1.95-5.20)	2.53 (1.76-3.65)	2.29 (1.70-3.07)
	0.81 (0.47-1.37)	0.33 (0.20-0.56)	DBS	1.06 (0.59-1.90)	0.84 (0.50-1.43)	0.76 (0.49-1.17)

	0.76 (0.48-1.21)	0.31 (0.19-0.51)	0.95 (0.53-1.70)	T/TAP	0.79 (0.48-1.30)	0.72 (0.48-1.07)
	0.96 (0.66-1.40)	0.39 (0.27-0.57)	1.19 (0.70-2.02)	1.26 (0.77-2.06)	Crush	0.90 (0.66-1.23)
	1.06 (0.77-1.47)	0.44 (0.33-0.59)	1.32 (0.86-2.02)	1.39 (0.93-2.09)	1.11 (0.81-1.51)	Provisional
Target Vessel Revascularization (23 trials)	Culotte	0.48 (0.32-0.70)	1.35 (0.80-2.28)	1.25 (0.66-2.35)	1.18 (0.83-1.66)	1.00 (0.70-1.43)
	2.10 (1.42-3.09)	DK Crush	2.84 (1.71-4.72)	2.61 (1.41-4.86)	2.47 (1.75-3.49)	2.10 (1.52-2.91)
	0.74 (0.44-1.25)	0.35 (0.21-0.59)	DBS	0.92 (0.48-1.78)	0.87 (0.54-1.40)	0.74 (0.50-1.10)
	0.80 (0.43-1.51)	0.38 (0.21-0.71)	1.09 (0.56-2.09)	T/TAP	0.94 (0.52-1.71)	0.80 (0.47-1.36)
	0.85 (0.60-1.20)	0.40 (0.29-0.57)	1.15 (0.71-1.85)	1.06 (0.59-1.91)	Crush	0.85 (0.65-1.11)
	1.00 (0.70-1.42)	0.48 (0.34-0.66)	1.35 (0.91-2.00)	1.24 (0.74-2.11)	1.18 (0.90-1.54)	Provisional

Table S16. Sensitivity analysis of trials that only included true bifurcations.

All-cause Mortality (10 trials)	Culotte	0.77 (0.32-1.87)	0.88 (0.20-3.87)	0.55 (0.05-5.82)	2.00 (0.18-21.82)	0.89 (0.44-1.83)
	1.30 (0.54-3.14)	DK Crush	1.14 (0.28-4.62)	0.72 (0.07-7.16)	2.59 (0.20-33.13)	1.16 (0.69-1.95)
	1.14 (0.26-5.01)	0.88 (0.22-3.56)	DBS	0.63 (0.05-8.40)	2.27 (0.14-37.88)	1.02 (0.28-3.72)
	1.81 (0.17-18.99)	1.39 (0.14-13.92)	1.59 (0.12-21.18)	T/TAP	3.61 (0.13-103.4)	1.61 (0.17-15.17)
	0.50 (0.05-5.46)	0.41 (0.03-5.18)	0.56 (0.04-8.28)	0.29 (0.01-8.33)	Crush	0.47 (0.04-5.68)
	1.12 (0.55-2.29)	0.86 (0.51-1.45)	0.98 (0.27-3.61)	0.62 (0.07-5.83)	2.24 (0.18-27.15)	Provisional
Cardiac Death (12 trials)	Culotte	0.52 (0.19-1.40)	0.95 (0.09-9.87)	N/A	1.21 (0.25-5.89)	0.93 (0.34-2.54)
	1.93 (0.72-5.21)	DK Crush	1.83 (0.18-18.13)	N/A	2.34 (0.52-10.58)	1.79 (1.20-2.69)
	1.06 (0.10-11.01)	0.55 (0.06-5.43)	DBS	N/A	1.28 (0.09-18.75)	0.98 (0.10-9.52)
	N/A	N/A	N/A	T/TAP	N/A	N/A
	0.83 (0.17-4.02)	0.43 (0.09-1.94)	0.78 (0.05-11.47)	N/A	Crush	0.77 (0.17-3.52)
	1.08 (0.39-2.94)	0.56 (0.37-0.84)	1.02 (0.11-9.90)	N/A	1.30 (0.28-5.99)	Provisional
Major Adverse Cardiac Events (14 trials)	Culotte	0.72 (0.33-1.57)	1.29 (0.47-3.56)	N/A	1.13 (0.47-2.70)	1.00 (0.55-1.81)
	1.40 (0.64-3.05)	DK Crush	1.80 (0.68-4.74)	N/A	1.57 (0.59-4.17)	1.40 (0.84-2.33)
	0.77 (0.28-2.14)	0.56 (0.21-1.46)	DBS	N/A	0.87 (0.27-2.81)	0.78 (0.34-1.76)
	N/A	N/A	N/A	T/TAP	N/A	N/A
	1.07 (0.71-1.61)	0.46 (0.32-0.65)	1.23 (0.76-2.00)	N/A	Crush	0.91 (0.64-1.29)
	1.00 (0.55-1.81)	0.72 (0.43-1.19)	1.29 (0.57-2.94)	N/A	1.13 (0.49-2.59)	Provisional
Myocardial Infarction (16 trials)	Culotte	0.55 (0.34-0.89)	1.35 (0.80-2.30)	1.19 (0.28-5.06)	1.05 (0.61-1.81)	0.99 (0.68-1.44)
	1.82 (1.13-2.94)	DK Crush	2.46 (1.42-4.28)	2.17 (0.51-9.27)	1.92 (1.21-3.04)	1.81 (1.21-2.69)
	0.74 (0.43-1.26)	0.41 (0.23-0.70)	DBS	0.88 (0.21-3.75)	0.78 (0.43-1.42)	0.73 (0.50-1.08)
	0.39 (0.10-1.54)	0.18 (0.05-0.67)	0.54 (0.06-4.60)	T/TAP	0.57 (0.12-2.70)	0.36 (0.11-1.14)
	0.95 (0.55-1.63)	0.52 (0.33-0.83)	1.29 (0.71-2.35)	1.13 (0.26-4.93)	Crush	0.94 (0.59-1.50)
	1.01 (0.69-1.46)	0.55 (0.37-0.82)	1.36 (0.93-2.00)	1.20 (0.30-4.85)	1.06 (0.67-1.69)	Provisional
Stent Thrombosis (15 trials)	Culotte	0.47 (0.20-1.09)	1.36 (0.21-9.03)	2.54 (0.65-9.95)	1.45 (0.49-4.33)	0.91 (0.44-1.87)
	2.15 (0.92-5.03)	DK Crush	2.93 (0.44-19.43)	5.46 (1.50-19.86)	3.12 (1.08-8.98)	1.95 (1.11-3.46)
	0.73 (0.11-4.86)	0.34 (0.05-2.27)	DBS	1.86 (0.22-16.01)	1.07 (0.14-8.40)	0.67 (0.11-4.09)
	0.39 (0.10-1.54)	0.18 (0.05-0.67)	0.54 (0.06-4.60)	T/TAP	0.57 (0.12-2.70)	0.36 (0.11-1.14)
	0.69 (0.23-2.06)	0.32 (0.11-0.92)	0.94 (0.12-7.40)	1.75 (0.37-8.27)	Crush	0.63 (0.22-1.76)
	1.10 (0.53-2.26)	0.51 (0.29-0.90)	1.50 (0.24-9.17)	2.79 (0.88-8.90)	1.60 (0.57-4.49)	Provisional
Target Lesion Revascularization (15 trials)	Culotte	0.42 (0.24-0.73)	1.30 (0.60-2.81)	2.00 (0.40-10.03)	1.18 (0.60-2.31)	0.95 (0.62-1.45)
	2.37 (1.37-4.12)	DK Crush	3.08 (1.48-6.42)	4.76 (0.97-23.39)	2.79 (1.35-5.79)	2.25 (1.58-3.20)
	0.77 (0.36-1.67)	0.32 (0.16-0.68)	DBS	1.54 (0.29-8.30)	0.91 (0.37-2.24)	0.73 (0.38-1.39)

	0.50 (0.10-2.50)	0.21 (0.04-1.03)	0.65 (0.12-3.48)	T/TAP	0.59 (0.11-3.15)	0.47 (0.10-2.24)
	1.08 (0.64-1.84)	0.41 (0.26-0.65)	1.22 (0.55-2.66)	1.97 (0.38-10.01)	Crush	0.93 (0.58-1.49)
	1.06 (0.69-1.61)	0.44 (0.31-0.63)	1.37 (0.72-2.61)	2.11 (0.45-9.99)	1.24 (0.65-2.35)	Provisional
Target Vessel Revascularization (12 trials)	Culotte	0.76 (0.38-1.49)	2.00 (0.85-4.72)	1.64 (0.45-5.94)	1.41 (0.72-2.75)	1.41 (0.84-2.37)
	1.32 (0.67-2.60)	DK Crush	2.65 (1.19-5.92)	2.17 (0.62-7.60)	1.86 (0.88-3.93)	1.87 (1.21-2.87)
	0.50 (0.21-1.18)	0.38 (0.17-0.84)	DBS	0.82 (0.21-3.19)	0.70 (0.28-1.75)	0.70 (0.36-1.39)
	0.61 (0.17-2.22)	0.46 (0.13-1.62)	1.22 (0.31-4.77)	T/TAP	0.86 (0.23-3.24)	0.86 (0.26-2.80)
	0.95 (0.54-1.66)	0.43 (0.27-0.70)	1.25 (0.53-2.97)	1.13 (0.31-4.16)	Crush	0.97 (0.59-1.62)
	0.71 (0.42-1.20)	0.54 (0.35-0.82)	1.42 (0.72-2.80)	1.16 (0.36-3.77)	1.00 (0.54-1.84)	Provisional

Table S17. Sensitivity analysis excluding trials that did not include left main bifurcations.

All-cause Mortality (11 trials)	Culotte	0.60 (0.27-1.32)	0.36 (0.08-1.62)	0.53 (0.11-2.49)	1.01 (0.55-1.84)	0.69 (0.38-1.26)
	1.67 (0.76-3.68)	DK Crush	0.60 (0.13-2.63)	0.88 (0.16-4.78)	1.69 (0.78-3.65)	1.16 (0.69-1.95)
	2.80 (0.62-12.71)	1.68 (0.38-7.41)	DBS	1.47 (0.17-12.41)	2.83 (0.63-12.74)	1.94 (0.48-7.80)
	1.90 (0.40-9.01)	1.14 (0.21-6.21)	0.68 (0.08-5.72)	T/TAP	1.92 (0.37-9.90)	1.32 (0.26-6.62)
	0.99 (0.54-1.80)	0.59 (0.27-1.28)	0.35 (0.08-1.59)	0.52 (0.10-2.68)	Crush	0.69 (0.39-1.22)
	1.44 (0.80-2.61)	0.86 (0.51-1.45)	0.51 (0.13-2.07)	0.76 (0.15-3.81)	1.46 (0.82-2.58)	Provisional
Cardiac Death (14 trials)	Culotte	0.42 (0.18-0.98)	0.12 (0.01-1.20)	1.92 (0.32-11.47)	1.16 (0.53-2.56)	0.73 (0.32-1.69)
	2.39 (1.02-5.57)	DK Crush	0.30 (0.03-2.54)	4.59 (0.78-27.00)	2.78 (1.18-6.51)	1.75 (1.16-2.63)
	8.09 (0.84-78.34)	3.39 (0.39-29.14)	DBS	15.56 (1.0-240.1)	9.41 (0.98-90.55)	5.93 (0.72-49.04)
	0.52 (0.09-3.10)	0.22 (0.04-1.28)	0.60 (0.00-0.99)	T/TAP	0.60 (0.10-3.83)	0.38 (0.07-2.17)
	0.86 (0.39-1.89)	0.36 (0.15-0.84)	0.11 (0.01-1.02)	1.65 (0.26-10.47)	Crush	0.63 (0.28-1.42)
	1.36 (0.59-3.14)	0.57 (0.38-0.86)	0.17 (0.02-1.39)	2.62 (0.46-14.94)	1.59 (0.70-3.58)	Provisional
Major Adverse Cardiac Events (15 trials)	Culotte	0.46 (0.34-0.62)	0.79 (0.45-1.37)	2.09 (1.04-4.19)	1.14 (0.861.51)	0.84 (0.64-1.10)
	2.16 (1.61-2.91)	DK Crush	1.70 (1.00-2.91)	4.51 (2.13-9.55)	2.47 (1.82-3.35)	1.82 (1.44-2.30)
	1.27 (0.73-2.20)	0.59 (0.34-1.00)	DBS	2.65 (1.10-6.38)	1.45 (0.83-2.53)	1.07 (0.66-1.73)
	0.48 (0.24-0.96)	0.22 (0.10-0.47)	0.38 (0.16-0.91)	T/TAP	0.55 (0.26-1.15)	0.40 (0.19-0.84)
	0.87 (0.66-1.16)	0.40 (0.30-0.55)	0.69 (0.39-1.20)	1.83 (0.87-3.85)	Crush	0.73 (0.56-0.97)
	1.19 (0.91-1.56)	0.55 (0.43-0.70)	0.94 (0.58-1.52)	2.48 (1.19-5.18)	1.36 (1.03-1.80)	Provisional
Myocardial Infarction (16 trials)	Culotte	0.60 (0.35-1.03)	0.61 (0.16-2.35)	1.54 (0.28-8.51)	1.27 (0.74-2.19)	1.07 (0.67-1.70)
	1.67 (0.97-2.88)	DK Crush	1.02 (0.26-3.95)	2.57 (0.44-14.84)	2.13 (1.23-3.69)	1.78 (1.10-2.88)
	1.63 (0.42-6.27)	0.98 (0.25-3.77)	DBS	2.51 (0.30-20.99)	2.08 (0.52-8.24)	1.74 (0.49-6.14)
	0.65 (0.12-3.61)	0.39 (0.07-2.25)	0.40 (0.05-3.34)	T/TAP	0.83 (0.14-4.85)	0.69 (0.13-3.83)
	0.78 (0.46-1.35)	0.47 (0.27-0.82)	0.48 (0.12-1.91)	1.21 (0.21-7.04)	Crush	0.84 (0.48-1.45)
	0.94 (0.59-1.50)	0.56 (0.35-0.91)	0.58 (0.16-2.03)	1.44 (0.26-7.97)	1.20 (0.69-2.07)	Provisional
Stent Thrombosis (16 trials)	Culotte	0.45 (0.20-1.00)	1.51 (0.17-13.58)	2.26 (0.65-7.90)	0.76 (0.42-1.38)	0.95 (0.48-1.88)
	2.25 (1.00-5.04)	DK Crush	3.39 (0.39-29.60)	5.08 (1.48-17.46)	1.70 (0.73-3.97)	2.12 (1.19-3.80)
	0.66 (0.07-5.95)	0.29 (0.03-2.57)	DBS	1.50 (0.14-15.82)	0.50 (0.05-4.61)	0.63 (0.08-5.04)
	0.44 (0.13-1.54)	0.20 (0.06-0.68)	0.67 (0.06-7.05)	T/TAP	0.33 (0.09-1.23)	0.42 (0.14-1.25)
	1.32 (0.73-2.41)	0.59 (0.25-1.38)	2.00 (0.22-18.39)	2.99 (0.81-11.01)	Crush	1.25 (0.59-2.67)
	1.06 (0.53-2.10)	0.47 (0.26-0.84)	1.60 (0.20-12.88)	2.39 (0.80-7.17)	0.80 (0.38-1.71)	Provisional
Target Lesion Revascularization (16 trials)	Culotte	0.43 (0.29-0.64)	1.19 (0.61-2.33)	1.55 (0.89-2.68)	1.07 (0.72-1.60)	0.89 (0.64-1.24)
	2.34 (1.57-3.49)	DK Crush	2.78 (1.43-5.41)	3.62 (1.97-6.65)	2.51 (1.70-3.72)	2.08 (1.51-2.86)
	0.84 (0.43-1.65)	0.36 (0.18-0.70)	DBS	1.30 (0.59-2.89)	0.90 (0.46-1.79)	0.74 (0.42-1.34)

	0.65 (0.37-1.12)	0.28 (0.15-0.51)	0.77 (0.35-1.70)	T/TAP	0.69 (0.37-1.29)	0.57 (0.33-0.99)
	0.93 (0.63-1.39)	0.40 (0.27-0.59)	1.11 (0.56-2.19)	1.44 (0.77-2.68)	Crush	0.83 (0.58-1.18)
	1.13 (0.81-1.57)	0.48 (0.35-0.66)	1.34 (0.47-2.40)	1.74 (1.01-2.99)	1.21 (0.84-1.73)	Provisional
Target Vessel Revascularization (12 trials)	Culotte	0.49 (0.31-0.77)	1.27 (0.64-2.55)	1.32 (0.60-2.90)	1.19 (0.79-1.79)	0.93 (0.60-1.43)
	2.03 (1.30-3.19)	DK Crush	2.59 (1.31-5.13)	2.68 (1.23-5.86)	2.42 (1.58-3.72)	1.88 (1.23-2.87)
	0.78 (0.39-1.57)	0.39 (0.19-0.77)	DBS	1.04 (0.44-2.42)	0.94 (0.48-1.83)	0.73 (0.42-1.25)
	0.76 (0.34-1.67)	0.37 (0.17-0.82)	0.97 (0.41-2.26)	T/TAP	0.90 (0.42-1.96)	0.70 (0.36-1.36)
	0.84 (0.56-1.26)	0.41 (0.27-0.63)	1.07 (0.55-2.09)	1.11 (0.51-2.39)	Crush	0.78 (0.52-1.16)
	1.08 (0.70-1.67)	0.53 (.035-0.81)	1.37 (0.80-2.35)	1.42 (0.74-2.75)	1.29 (0.86-1.93)	Provisional

Table S18. Sensitivity analysis of trials that included only non-left main bifurcations.

All-cause Mortality (7 trials)	Culotte	N/A	1.86 (0.12-28.03)	2.33 (0.18-29.33)	3.06 (0.19-49.33)	1.88 (0.17-20.44)
	N/A	DK Crush	N/A	N/A	N/A	N/A
	0.54 (0.04-8.14)	N/A	DBS	1.26 (0.27-5.94)	1.65 (0.24-11.38)	1.02 (0.28-3.72)
	0.43 (0.03-5.41)	N/A	0.80 (0.17-3.77)	T/TAP	1.32 (0.25-6.95)	0.81 (0.34-1.90)
	0.33 (0.02-5.26)	N/A	0.61 (0.09-4.17)	0.76 (0.14-4.02)	Crush	0.61 (0.15-2.56)
	0.53 (0.05-5.76)	N/A	0.98 (0.27-3.61)	1.24 (0.53-2.91)	1.63 (0.39-6.78)	Provisional
Cardiac Death (8 trials)	Culotte	N/A	N/A	N/A	N/A	N/A
	N/A	DK Crush	1.68 (0.05-53.06)	1.55 (0.02-127.3)	1.72 (0.10-29.10)	1.69 (0.21-13.52)
	N/A	0.60 (0.02-18.89)	DBS	0.92 (0.01-108.7)	1.03 (0.04-29.57)	1.01 (0.06-15.93)
	N/A	0.65 (0.01-53.31)	1.08 (0.01-127.9)	T/TAP	1.12 (0.01-85.22)	1.09 (0.02-53.52)
	N/A	0.58 (0.03-9.80)	0.97 (0.03-27.97)	0.90 (0.01-68.53)	Crush	0.98 (0.14-6.66)
	N/A	0.59 (0.07-4.73)	0.99 (0.06-15.66)	0.91 (0.02-44.74)	1.02 (0.15-6.92)	Provisional
Major Adverse Cardiac Events (10 trials)	Culotte	0.20 (0.06-0.64)	1.04 (0.40-2.70)	0.75 (0.27-2.09)	0.90 (0.36-2.27)	0.75 (0.31-1.83)
	4.96 (1.55-15.80)	DK Crush	5.18 (2.28-11.74)	3.73 (1.51-9.21)	4.45 (2.01-9.83)	3.73 (1.77-7.87)
	0.96 (0.37-2.47)	0.19 (0.09-0.44)	DBS	0.72 (0.39-1.33)	0.86 (0.56-1.32)	0.72 (0.51-1.01)
	1.33 (0.48-3.69)	0.27 (0.11-0.66)	1.39 (0.75-2.55)	T/TAP	1.19 (0.67-2.12)	1.00 (0.60-1.66)
	1.11 (0.44-2.81)	0.22 (0.10-0.50)	1.16 (0.76-1.79)	0.84 (0.47-1.49)	Crush	0.84 (0.64-1.10)
	1.33 (0.55-3.22)	0.27 (0.13-0.56)	1.39 (0.99-1.94)	1.00 (0.60-1.66)	1.19 (0.91-1.56)	Provisional
Myocardial Infarction (12 trials)	Culotte	0.21 (0.02-2.15)	0.65 (0.18-2.37)	0.34 (0.07-1.67)	0.67 (0.20-2.29)	0.47 (0.15-1.47)
	4.85 (0.47-50.54)	DK Crush	3.16 (0.37-26.77)	1.67 (0.16-16.98)	3.27 (0.40-26.55)	2.28 (0.29-17.70)
	1.53 (0.42-5.58)	0.32 (0.04-2.67)	DBS	0.53 (0.15-1.84)	1.03 (0.49-2.19)	0.72 (0.39-1.32)
	2.91 (0.60-14.15)	0.60 (0.06-6.12)	1.90 (0.54-6.64)	T/TAP	1.96 (0.60-6.39)	1.37 (0.46-4.10)
	1.48 (0.44-5.04)	0.31 (0.04-2.49)	0.97 (0.46-2.05)	0.51 (0.16-1.66)	Crush	0.70 (0.45-1.09)
	2.12 (0.68-6.64)	0.44 (0.06-3.39)	1.39 (0.76-2.54)	0.73 (0.24-2.18)	1.43 (0.92-2.23)	Provisional
Stent Thrombosis (11 trials)	Culotte	0.15 (0.01-4.15)	0.51 (0.02-10.65)	0.70 (0.05-9.50)	0.78 (0.06-10.24)	0.31 (0.03-2.97)
	6.75 (0.24-189.0)	DK Crush	3.46 (0.14-84.60)	4.72 (0.29-77.39)	5.27 (0.33-83.63)	2.12 (0.18-24.84)
	1.94 (0.09-40.56)	0.29 (0.01-7.07)	DBS	1.36 (0.12-15.56)	1.52 (0.14-16.73)	0.61 (0.08-4.71)
	1.43 (0.11-19.47)	0.21 (0.01-3.48)	0.73 (0.06-8.37)	T/TAP	0.73 (0.06-8.37)	1.12 (0.18-6.97)
	1.28 (0.10-16.79)	0.19 (0.01-3.01)	0.66 (0.06-7.20)	0.89 (0.14-5.57)	Crush	0.40 (0.11-1.41)
	3.19 (0.34-30.11)	0.47 (0.04-5.53)	1.63 (0.21-12.55)	2.23 (0.59-8.41)	2.49 (0.71-8.74)	Provisional
Target Lesion Revascularization (9 trials)	Culotte	N/A	N/A	N/A	N/A	N/A
	N/A	DK Crush	5.54 (1.85-16.62)	4.32 (1.47-12.68)	3.78 (1.25-11.39)	4.05 (1.66-9.86)
	N/A	0.18 (0.06-0.54)	DBS	0.78 (0.32-1.89)	0.68 (0.27-1.71)	0.73 (0.38-1.39)

	N/A	0.23 (0.08-0.68)	1.28 (0.53-3.11)	T/TAP	0.87 (0.36-2.13)	0.94 (0.51-1.72)
	N/A	0.26 (0.09-0.80)	1.47 (0.59-3.67)	1.14 (0.47-2.79)	Crush	1.07 (0.56-2.06)
	N/A	0.25 (0.10-0.60)	1.37 (0.72-2.61)	1.07 (0.58-1.96)	0.93 (0.49-1.79)	Provisional
Target Vessel Revascularization (10 trials)	Culotte	0.71 (0.06-8.11)	4.01 (0.38-41.95)	2.20 (0.18-26.81)	3.03 (0.31-29.99)	2.83 (0.30-26.70)
	1.40 (0.12-15.97)	DK Crush	5.63 (1.78-17.86)	3.08 (0.73-13.05)	4.26 (1.51-12.00)	3.96 (1.56-10.07)
	0.25 (0.02-2.60)	0.18 (0.06-0.56)	DBS	0.55 (0.15-2.00)	0.76 (0.33-1.71)	0.70 (0.36-1.39)
	0.45 (0.04-5.55)	0.32 (0.08-1.37)	1.83 (0.50-6.66)	T/TAP	1.38 (0.42-4.53)	1.29 (0.43-3.86)
	0.33 (0.03-3.26)	0.23 (0.08-0.66)	1.32 (0.59-2.99)	0.72 (0.22-2.38)	Crush	0.93 (0.59-1.46)
	0.35 (0.04-3.35)	0.25 (0.10-0.64)	1.42 (0.72-2.80)	0.78 (0.26-2.34)	1.07 (0.68-1.69)	Provisional

Table S19. Sensitivity analysis excluding trials with multiple bifurcation techniques in either arm.

All-cause Mortality (14 trials)	Culotte	0.87 (0.25-3.06)	0.82 (0.23-2.94)	1.01 (0.32-3.22)	0.88 (0.43-1.79)	0.97 (0.33-2.85)
	1.15 (0.33-4.03)	DK Crush	0.94 (0.31-2.83)	1.16 (0.42-3.18)	1.01 (0.27-3.77)	1.12 (0.58-2.14)
	1.22 (0.34-4.34)	1.06 (0.35-3.20)	DBS	1.23 (0.39-3.90)	1.07 (0.28-4.14)	1.18 (0.48-2.89)
	0.99 (0.31-3.15)	0.86 (0.31-2.37)	0.81 (0.26-2.58)	T/TAP	0.87 (0.25-3.04)	0.96 (0.44-2.08)
	1.13 (0.56-2.31)	0.99 (0.27-3.69)	0.93 (0.24-3.60)	1.15 (0.33-4.00)	Crush	1.10 (0.35-3.47)
	1.03 (0.35-3.01)	0.90 (0.47-1.72)	0.85 (0.35-2.06)	1.04 (0.48-2.25)	0.91 (0.29-2.85)	Provisional
Cardiac Death (19 trials)	Culotte	0.44 (0.17-1.17)	0.34 (0.06-1.94)	1.79 (0.33-9.81)	1.11 (0.48-2.57)	0.84 (0.31-2.27)
	2.26 (0.86-5.94)	DK Crush	0.76 (0.15-3.75)	4.03 (0.79-20.67)	2.50 (0.87-7.20)	1.91 (1.22-2.98)
	2.97 (0.52-17.11)	1.32 (0.27-6.52)	DBS	5.31 (0.59-47.98)	3.29 (0.53-20.31)	2.51 (0.53-11.80)
	0.56 (0.10-3.08)	0.25 (0.05-1.27)	0.19 (0.02-1.70)	T/TAP	0.62 (0.10-3.75)	0.47 (0.10-2.34)
	0.90 (0.39-2.10)	0.40 (0.14-1.15)	0.30 (0.05-1.87)	1.61 (0.27-9.75)	Crush	0.76 (0.26-2.22)
	1.18 (0.44-3.18)	0.52 (0.34-0.82)	0.40 (0.08-1.87)	2.11 (0.43-10.44)	1.31 (0.45-3.81)	Provisional
Major Adverse Cardiac Events (20 trials)	Culotte	0.48 (0.34-0.66)	1.12 (0.74-1.71)	1.25 (0.78-1.99)	1.04 (0.78-1.40)	0.94 (0.68-1.29)
	2.10 (1.51-2.92)	DK Crush	2.36 (1.61-3.46)	2.62 (1.62-4.23)	2.19 (1.63-2.95)	1.97 (1.51-2.57)
	0.89 (0.59-1.35)	0.42 (0.29-0.62)	DBS	1.11 (0.67-1.84)	0.93 (0.64-1.35)	0.83 (0.63-1.10)
	0.80 (0.50-1.28)	0.38 (0.24-0.62)	0.90 (0.54-1.50)	T/TAP	0.84 (0.52-1.34)	0.75 (0.49-1.15)
	0.96 (0.72-1.28)	0.46 (0.34-0.61)	1.08 (0.74-1.57)	1.19 (0.75-1.91)	Crush	0.90 (0.70-1.16)
	1.07 (0.78-1.46)	0.51 (0.39-0.66)	1.20 (0.91-1.58)	1.33 (0.87-2.03)	1.11 (0.86-1.44)	Provisional
Myocardial Infarction (23 trials)	Culotte	0.53 (0.31-0.91)	1.06 (0.57-1.96)	0.77 (0.29-2.08)	0.94 (0.58-1.50)	0.84 (0.51-1.39)
	1.89 (1.10-3.24)	DK Crush	2.00 (1.11-3.61)	1.45 (0.54-3.93)	1.76 (0.54-2.74)	1.58 (0.99-2.52)
	0.94 (0.51-1.75)	0.50 (0.28-0.90)	DBS	0.73 (0.28-1.91)	0.88 (0.54-1.45)	0.79 (0.55-1.14)
	1.30 (0.48-3.49)	0.69 (0.25-1.86)	1.37 (0.52-3.60)	T/TAP	1.21 (0.47-3.12)	1.09 (0.44-2.65)
	1.07 (0.67-1.72)	0.57 (0.36-0.88)	1.13 (0.69-1.86)	0.82 (0.32-2.12)	Crush	0.90 (0.64-1.25)
	1.19 (0.72-1.98)	0.63 (0.40-1.01)	1.26 (0.88-1.82)	0.92 (0.38-2.25)	1.12 (0.80-1.56)	Provisional
Stent Thrombosis (22 trials)	Culotte	0.22 (0.08-0.59)	0.64 (0.13-3.15)	0.92 (0.27-3.12)	0.73 (0.39-1.37)	0.37 (0.14-0.95)
	4.56 (1.71-12.19)	DK Crush	2.92 (0.64-13.20)	4.20 (1.44-12.24)	3.35 (1.29-8.73)	1.69 (0.87-3.31)
	1.56 (0.32-7.71)	0.34 (0.08-1.55)	DBS	1.44 (0.29-7.18)	1.15 (0.23-5.70)	0.58 (0.15-2.29)
	1.08 (0.32-3.67)	0.24 (0.08-0.69)	0.69 (0.14-3.46)	T/TAP	0.80 (0.24-2.69)	0.40 (0.17-0.94)
	1.36 (0.73-2.54)	0.30 (0.11-0.78)	0.87 (0.18-4.32)	1.25 (0.37-4.24)	Crush	0.51 (0.20-1.28)
	2.69 (1.05-6.92)	0.59 (0.30-1.16)	1.72 (0.44-6.77)	2.48 (1.06-5.79)	1.98 (0.78-4.99)	Provisional
Target Lesion Revascularization (21 trials)	Culotte	0.42 (0.26-0.68)	1.23 (0.65-2.34)	1.31 (0.77-2.22)	0.95 (0.60-1.51)	0.94 (0.58-1.52)
	2.36 (1.47-3.79)	DK Crush	2.91 (1.67-5.08)	3.08 (1.84-5.15)	2.25 (1.47-3.43)	2.21 (1.54-3.16)
	0.81 (0.43-1.54)	0.34 (0.20-0.60)	DBS	1.06 (0.58-1.92)	0.77 (0.42-1.42)	0.76 (0.49-1.17)

	0.77 (0.45-1.30)	0.32 (0.19-0.54)	0.94 (0.52-1.71)	T/TAP	0.73 (0.42-1.27)	0.72 (0.47-1.09)
	1.05 (0.66-1.66)	0.45 (0.29-0.68)	1.29 (0.71-2.37)	1.37 (0.97-2.38)	Crush	0.98 (0.64-1.52)
	1.07 (0.66-1.73)	0.45 (0.32-0.65)	1.32 (0.86-2.02)	1.40 (0.92-2.11)	1.02 (0.66-1.57)	Provisional
Target Vessel Revascularization (19 trials)	Culotte	0.43 (0.38-0.66)	1.06 (0.57-1.97)	0.97 (0.47-2.00)	0.99 (0.67-1.46)	0.78 (0.47-1.28)
	2.33 (1.51-3.60)	DK Crush	2.47 (1.43-4.28)	2.26 (1.17-4.35)	2.30 (1.56-3.39)	1.81 (1.23-2.68)
	0.94 (0.51-1.76)	0.40 (0.23-0.70)	DBS	0.91 (0.47-1.76)	0.93 (0.52-1.65)	0.73 (0.50-1.09)
	1.03 (0.50-2.13)	0.44 (0.23-0.85)	1.09 (0.57-2.11)	T/TAP	1.02 (0.52-2.01)	0.80 (0.47-1.36)
	1.01 (0.68-1.50)	0.43 (0.30-0.64)	1.07 (0.60-1.91)	0.98 (0.50-1.93)	Crush	0.79 (0.51-1.21)
	1.29 (0.78-2.11)	0.55 (0.37-0.81)	1.36 (0.92-2.02)	1.24 (0.74-1.94)	1.27 (0.83-1.94)	Provisional

Figure S1. Forest plot of two-stent versus provisional stent on all-cause mortality.

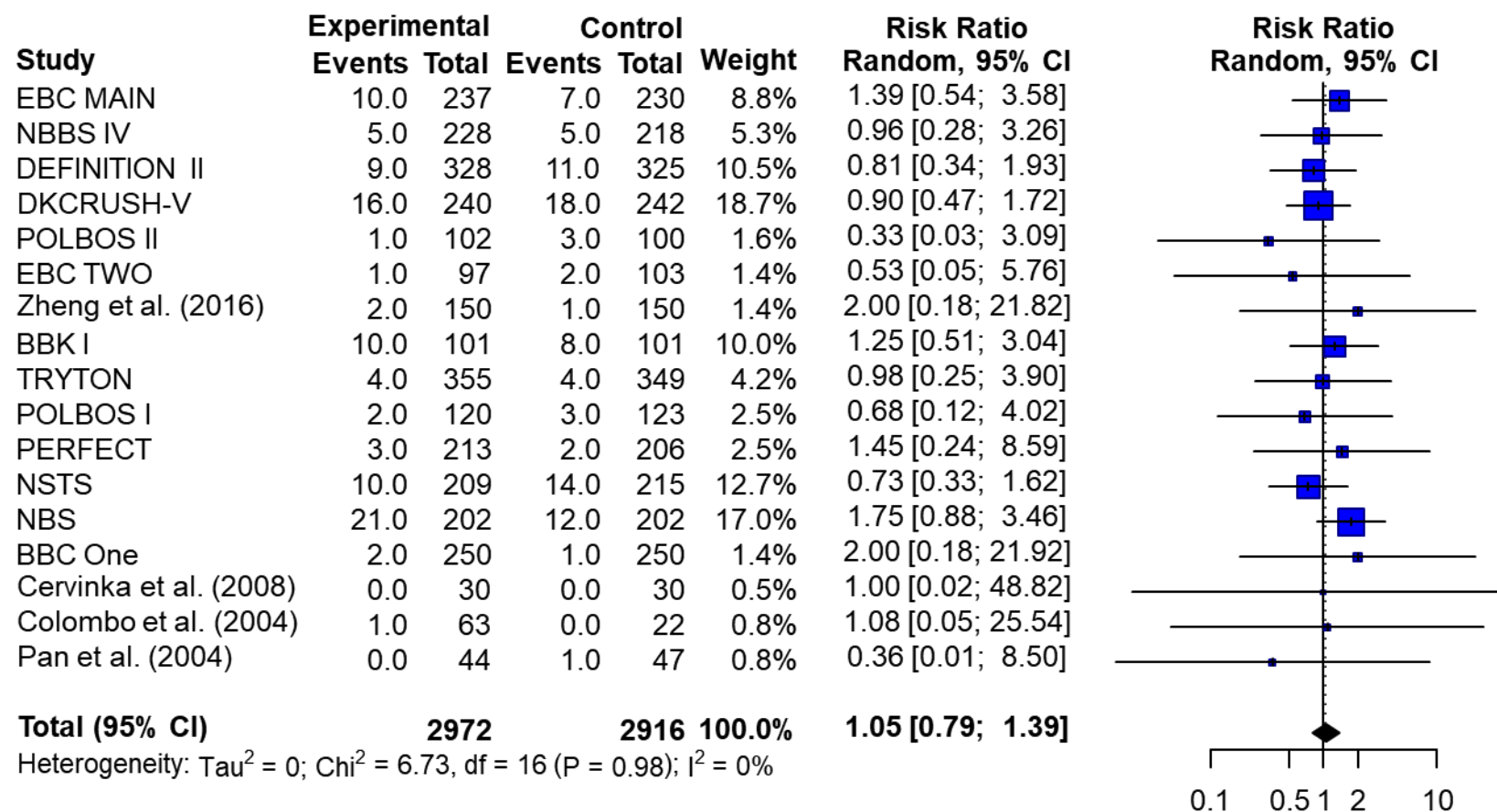


Figure S2. Forest plot of two-stent versus provisional stent on cardiac death.

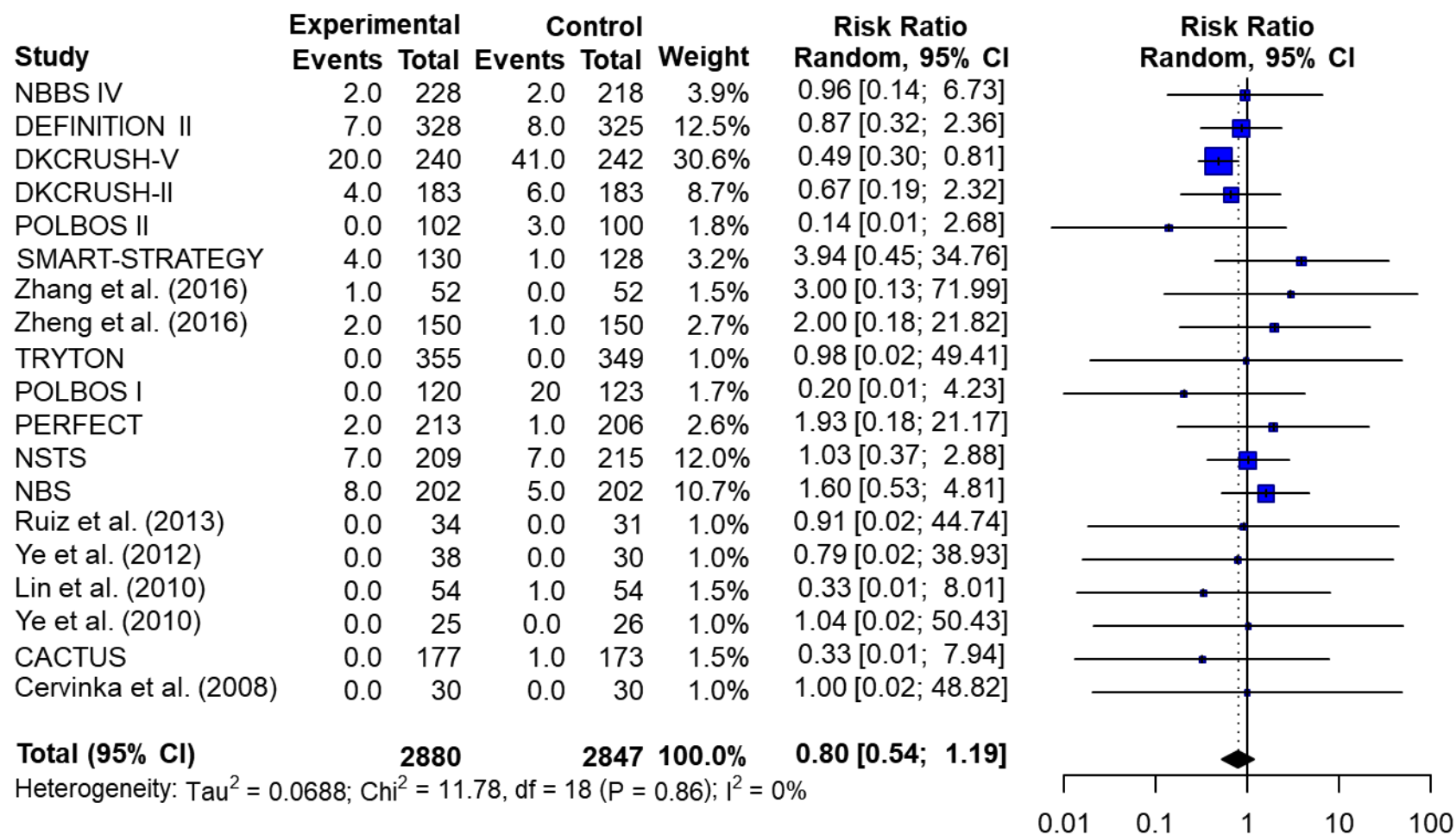


Figure S3. Forest plot of two-stent versus provisional stent on major adverse cardiac events.

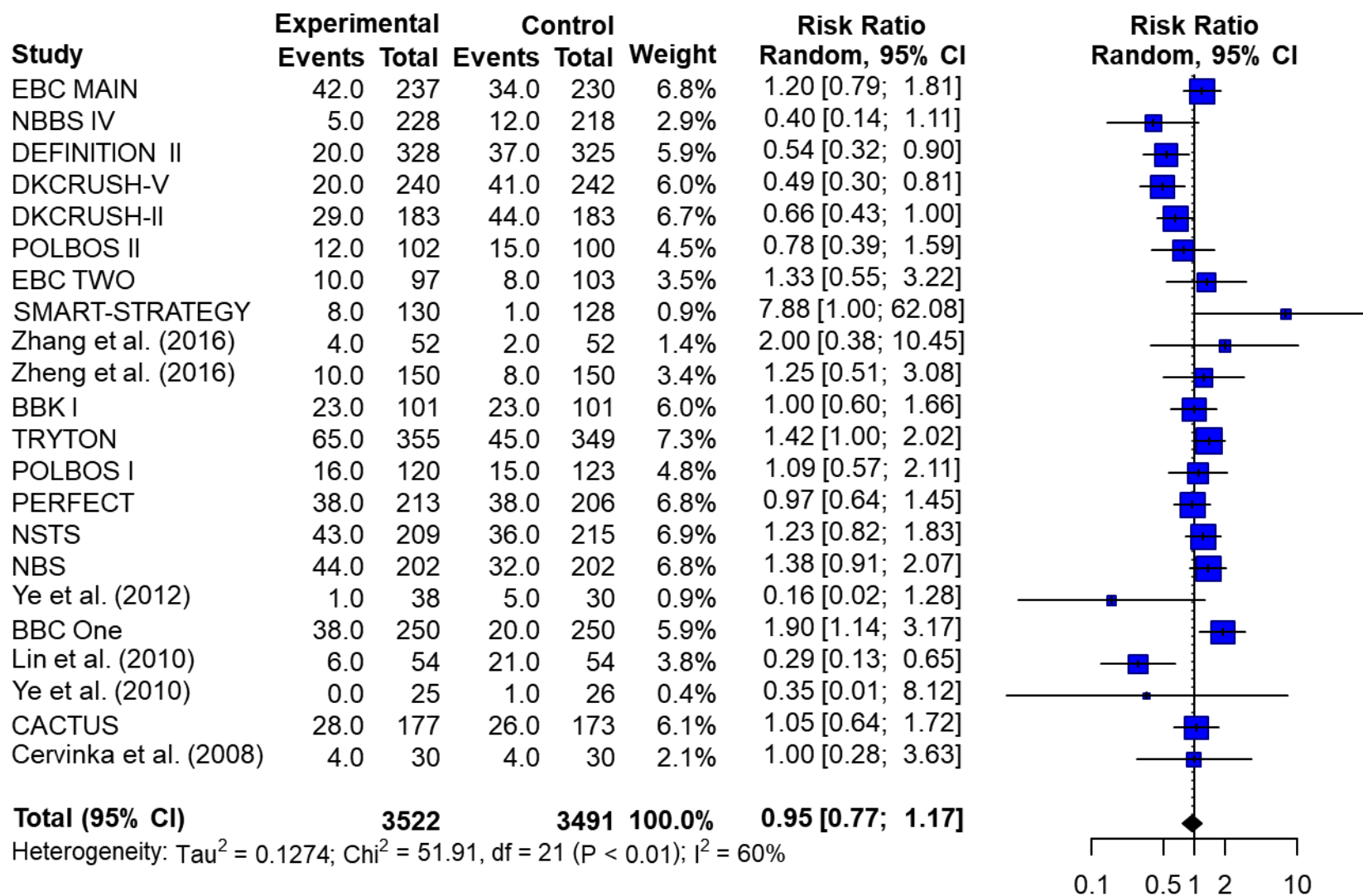


Figure S4. Forest plot of two-stent versus provisional stent on myocardial infarction.

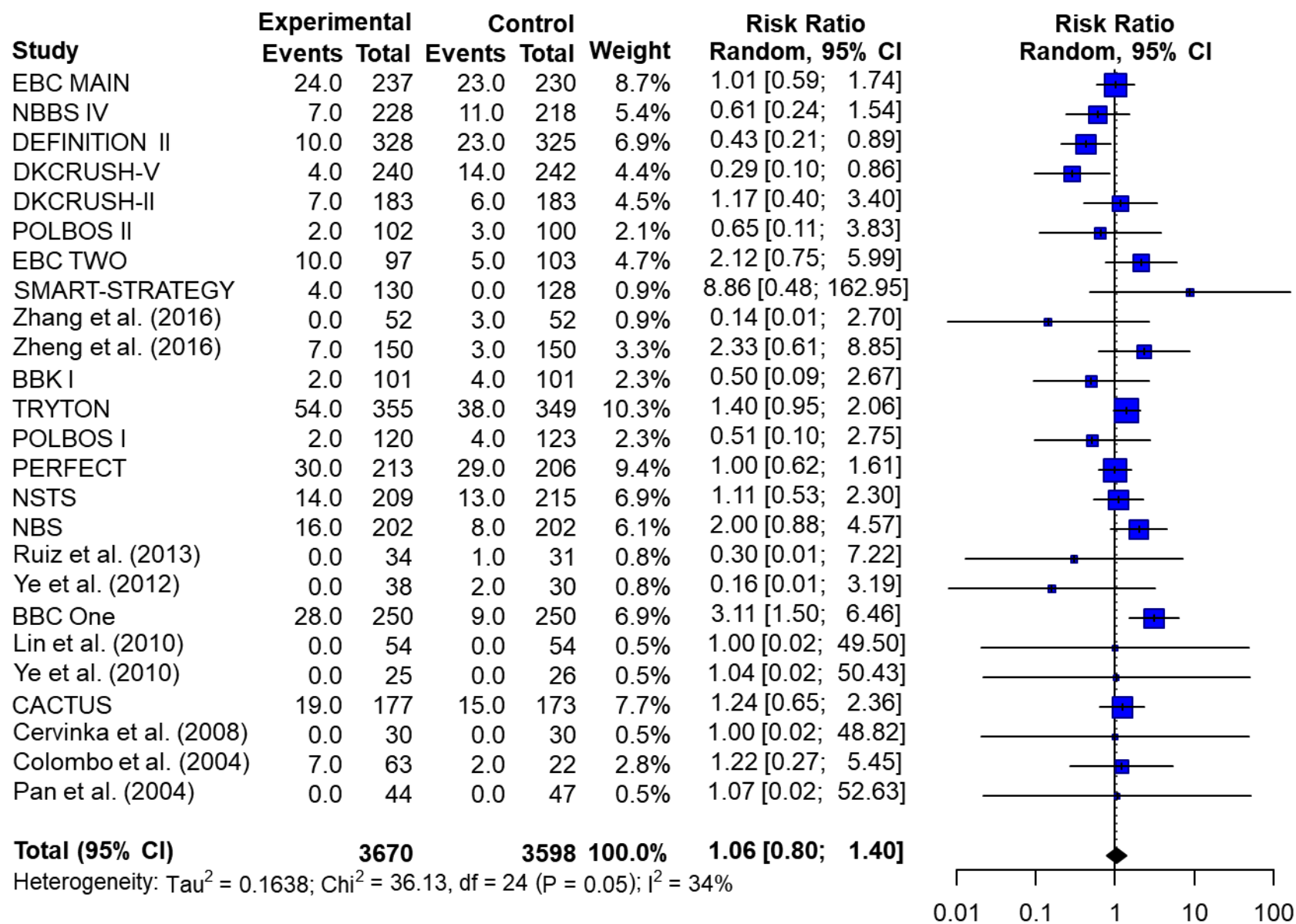


Figure S5. Forest plot of two-stent versus provisional stent on stent thrombosis.

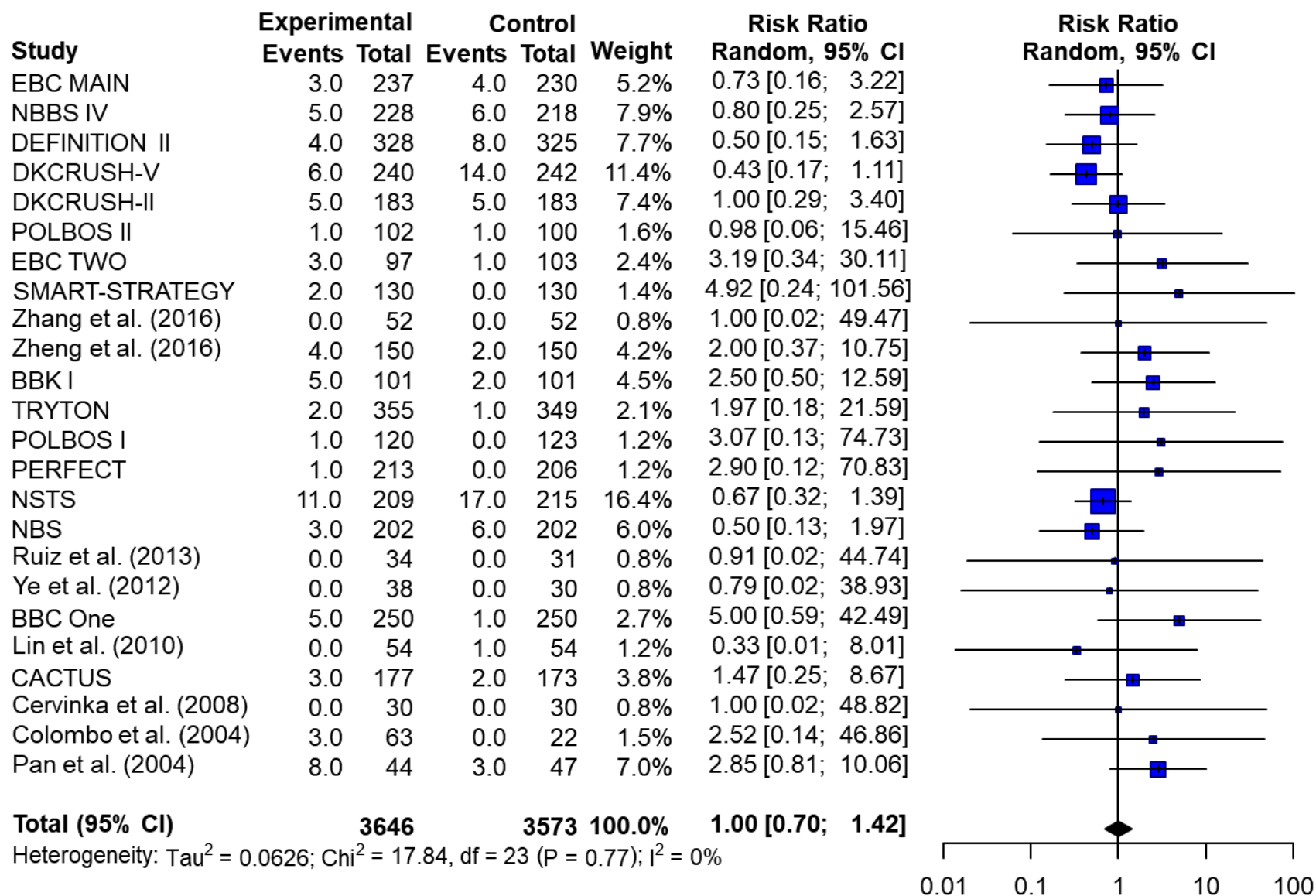


Figure S6. Forest plot of two-stent versus provisional stent on target lesion revascularization.

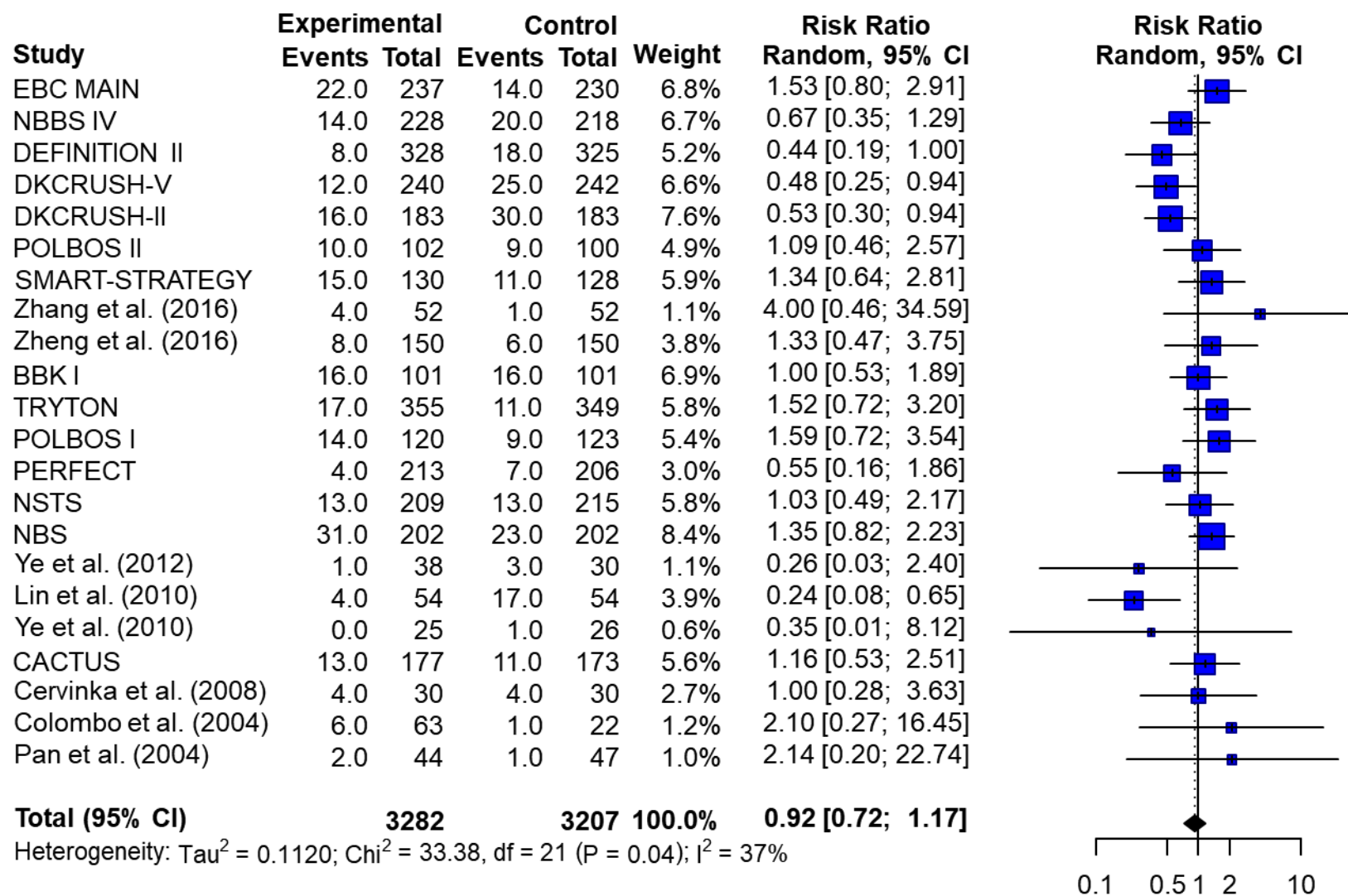


Figure S7. Forest plot of two-stent versus provisional stent on target vessel revascularization.

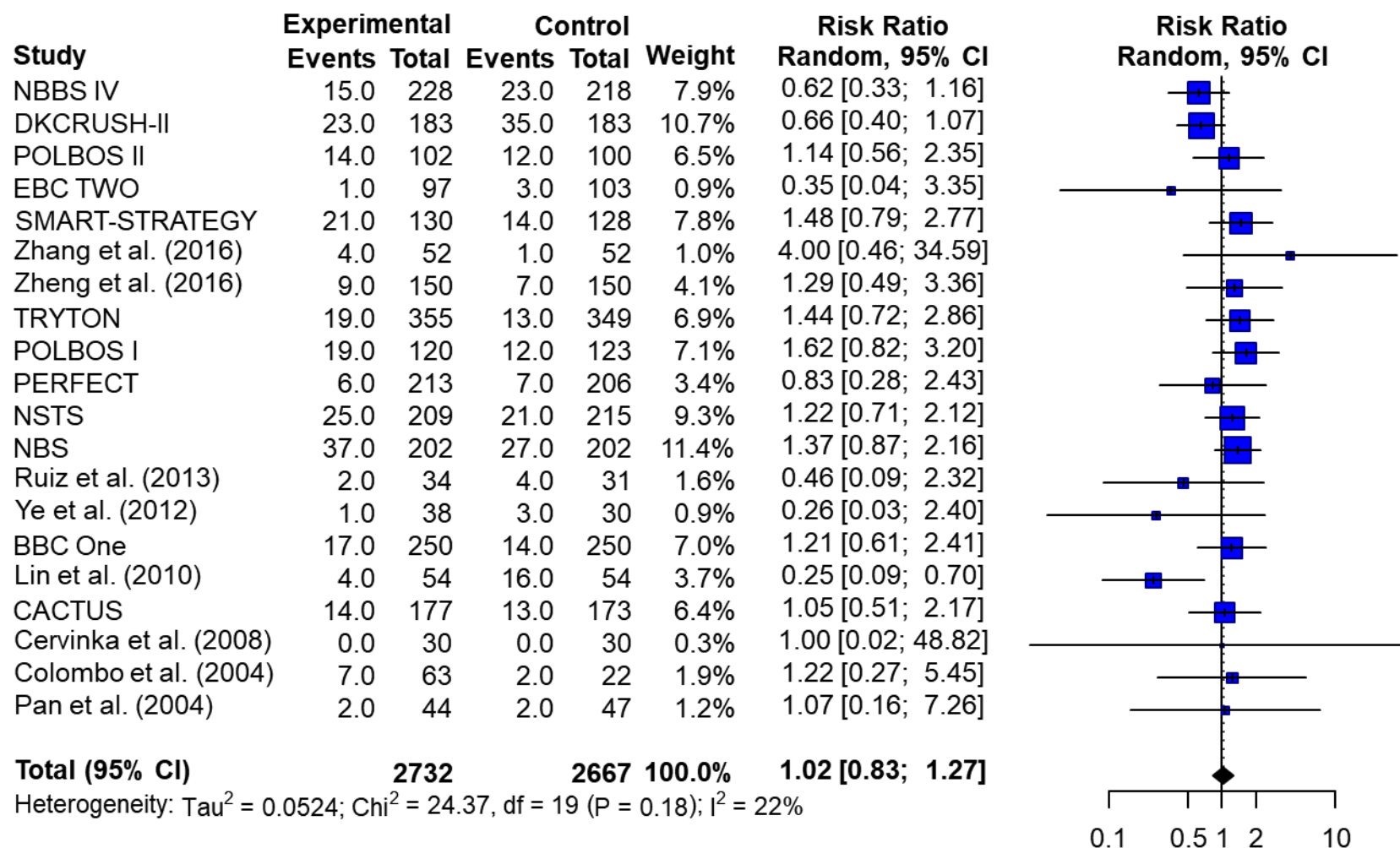


Figure S8. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on all-cause mortality.

Study or Subgroup	Experimental		Control		Risk Ratio Random, 95% CI
	Events	Total	Events	Total	
Group = SB <10mm					
EBC MAIN	10.0	237	7.0	230	1.39 [0.54; 3.58]
NBBS IV	5.0	228	5.0	218	0.96 [0.28; 3.26]
POLBOS II	1.0	102	3.0	100	0.33 [0.03; 3.09]
TRYTON	4.0	355	4.0	349	0.98 [0.25; 3.90]
POLBOS I	2.0	120	3.0	123	0.68 [0.12; 4.02]
NBS	21.0	202	12.0	202	1.75 [0.88; 3.46]
Colombo et al. (2004)	1.0	63	0.0	22	1.08 [0.05; 25.54]
Total (95% CI)		1308		1245	1.27 [0.81; 1.97]

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 3.1$, $df = 6$ ($P = 0.80$); $I^2 = 0\%$

Group = SB ≥ 10 mm					
DEFINITION II	9.0	328	11.0	325	0.81 [0.34; 1.93]
DKCRUSH-V	16.0	240	18.0	242	0.90 [0.47; 1.72]
EBC TWO	1.0	97	2.0	103	0.53 [0.05; 5.76]
BBK I	10.0	101	8.0	101	1.25 [0.51; 3.04]
PERFECT	3.0	213	2.0	206	1.45 [0.24; 8.59]
Total (95% CI)	979		977		0.96 [0.62; 1.47]

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 0.97$, $df = 4$ ($P = 0.91$); $I^2 = 0\%$

Test for subgroup differences: $\chi^2 = 0.80$, $df = 1$ ($P = 0.37$)

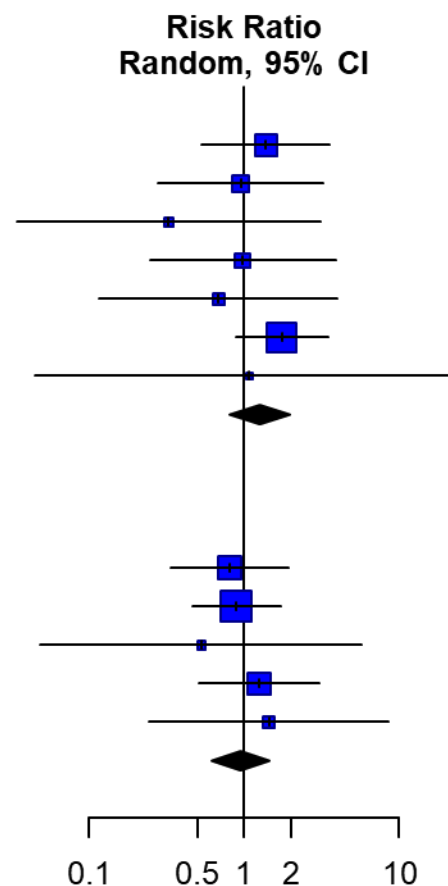


Figure S9. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on cardiac death.

Study or Subgroup	Experimental		Control		Risk Ratio
	Events	Total	Events	Total	Random, 95% CI
Group = SB <10mm					
NBBS IV	2.0	228	2.0	218	0.96 [0.14; 6.73]
POLBOS II	0.0	102	3.0	100	0.14 [0.01; 2.68]
SMART-STRATEGY	4.0	130	1.0	128	3.94 [0.45; 34.76]
TRYTON	0.0	355	0.0	349	0.98 [0.02; 49.41]
POLBOS I	0.0	120	2.0	123	0.20 [0.01; 4.23]
NBS	8.0	202	5.0	202	1.60 [0.53; 4.81]
CACTUS	0.0	177	1.0	173	0.33 [0.01; 7.94]
Total (95% CI)		1318		1297	1.10 [0.51; 2.37]

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 5.4$, $df = 6$ ($P = 0.49$); $I^2 = 0\%$

Group = SB ≥ 10 mm					
DEFINITION II	7.0	328	8.0	325	0.87 [0.32; 2.36]
DKCRUSH-V	20.0	240	41.0	242	0.49 [0.30; 0.81]
DKCRUSH-II	4.0	183	6.0	183	0.67 [0.19; 2.32]
Zhang et al. (2016)	1.0	52	0.0	52	3.00 [0.13; 71.99]
PERFECT	2.0	213	1.0	206	1.93 [0.18; 21.17]
Ye et al. (2012)	0.0	38	0.9	38	0.79 [0.02; 38.93]
Lin et al. (2010)	0.0	54	1.0	54	0.33 [0.01; 8.01]
Ye et al. (2010)	0.0	25	0.0	26	1.04 [0.02; 50.43]
Total (95% CI)		1137		1122	0.60 [0.40; 0.90]

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 3.28$, $df = 7$ ($P = 0.86$); $I^2 = 0\%$

Test for subgroup differences: $\chi^2 = 1.83$, $df = 1$ ($P = 0.18$)

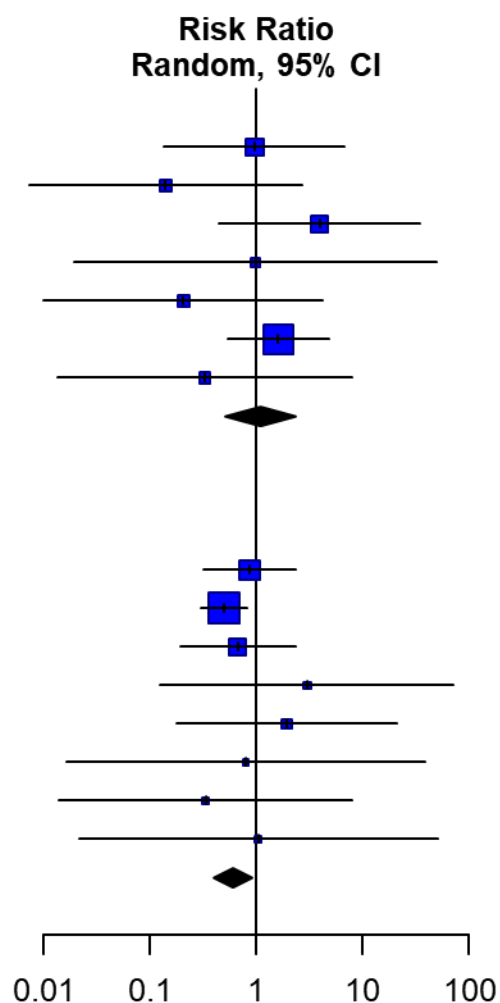


Figure S10. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on major adverse cardiac events.

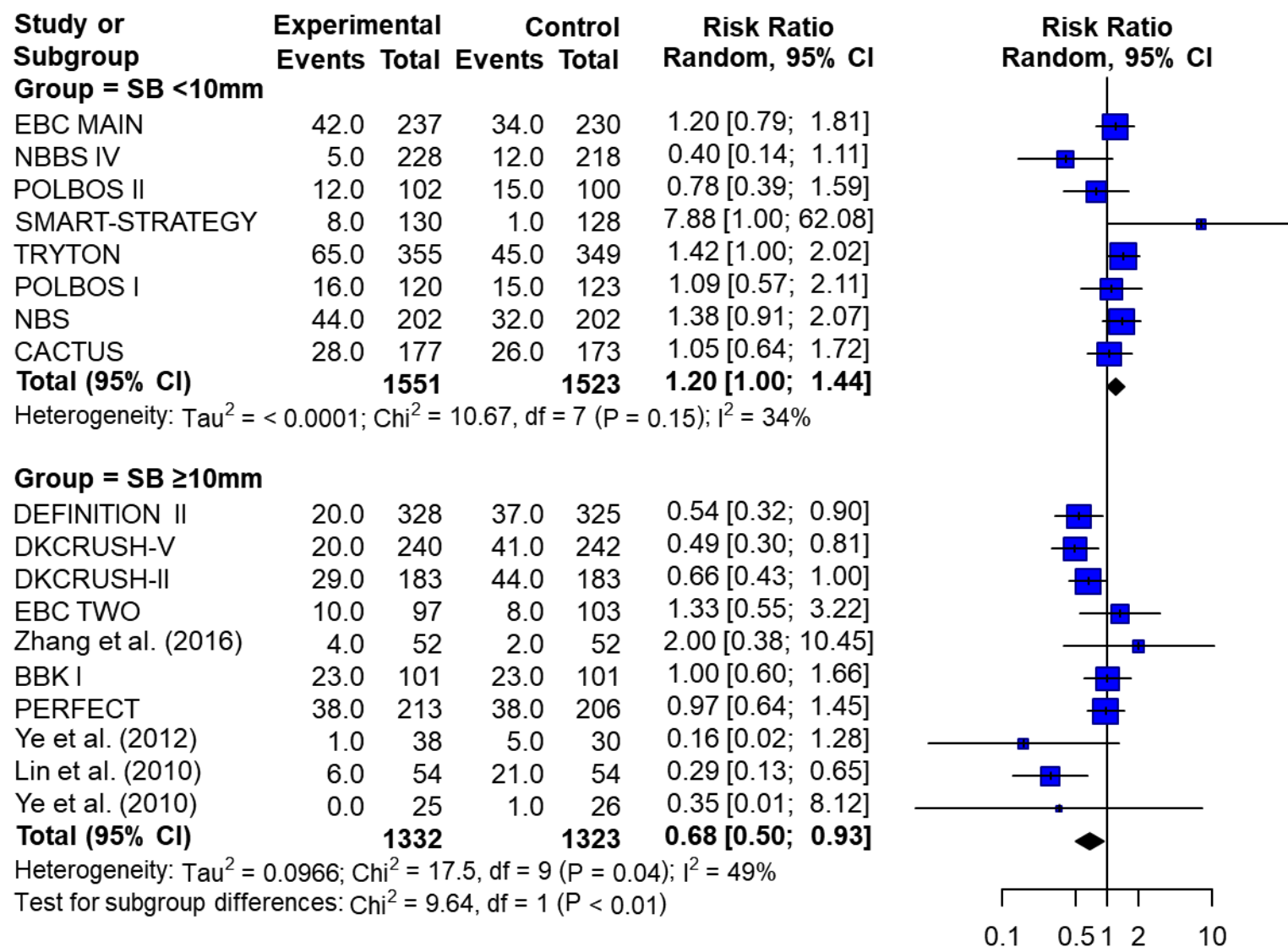


Figure S11. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on myocardial infarction.

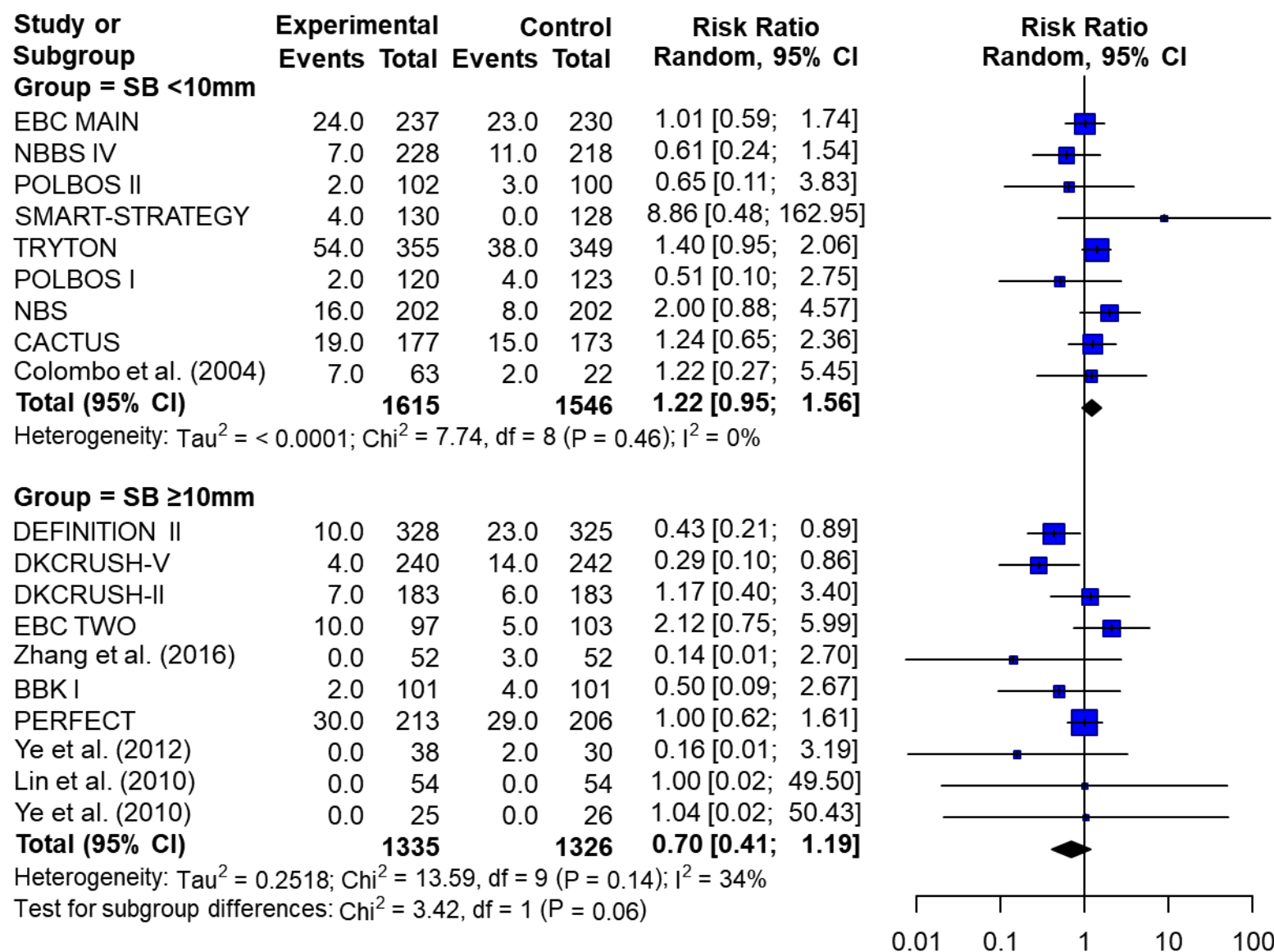


Figure S12. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on stent thrombosis.

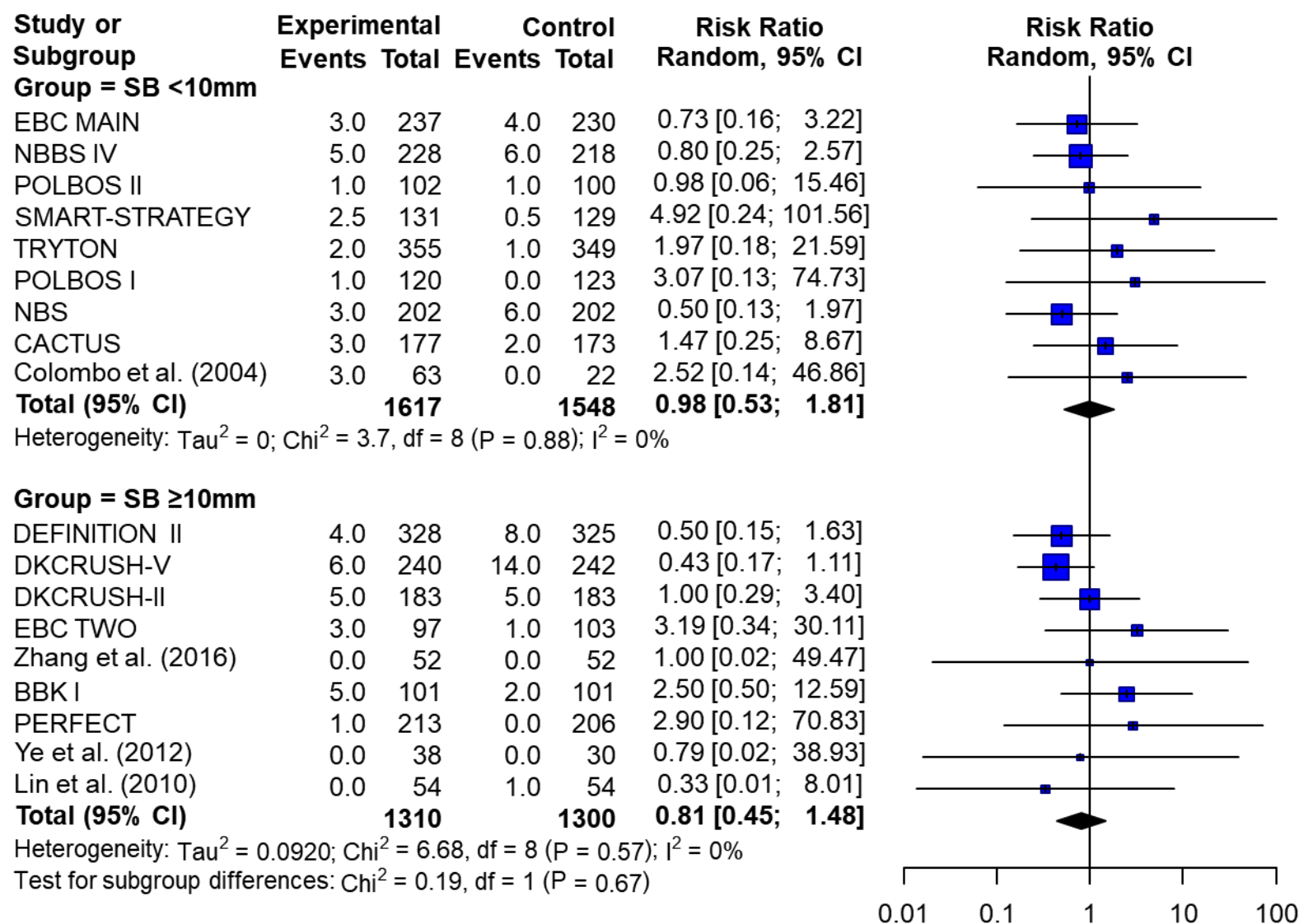


Figure S13. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on target lesion revascularization.

Study or Subgroup	Experimental		Control		Risk Ratio
	Events	Total	Events	Total	Random, 95% CI
Group = SB <10mm					
EBC MAIN	22.0	237	14.0	230	1.53 [0.80; 2.91]
NBBS IV	14.0	228	20.0	218	0.67 [0.35; 1.29]
POLBOS II	10.0	102	9.0	100	1.09 [0.46; 2.57]
SMART-STRATEGY	15.0	130	11.0	128	1.34 [0.64; 2.81]
TRYTON	17.0	355	11.0	349	1.52 [0.72; 3.20]
POLBOS I	14.0	120	9.0	123	1.59 [0.72; 3.54]
NBS	31.0	202	23.0	202	1.35 [0.82; 2.23]
CACTUS	13.0	177	11.0	173	1.16 [0.53; 2.51]
Colombo et al. (2004)	6.0	63	1.0	22	2.10 [0.27; 16.45]
Total (95% CI)		1614		1545	1.25 [0.98; 1.59]

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 4.96$, $df = 8$ ($P = 0.76$); $I^2 = 0\%$

Group = SB ≥ 10 mm					
DEFINITION II	8.0	328	18.0	325	0.44 [0.19; 1.00]
DKCRUSH-V	12.0	240	25.0	242	0.48 [0.25; 0.94]
DKCRUSH-II	16.0	183	30.0	183	0.53 [0.30; 0.94]
Zhang et al. (2016)	4.0	52	1.0	52	4.00 [0.46; 34.59]
BBK I	16.0	101	16.0	101	1.00 [0.53; 1.89]
PERFECT	4.0	213	7.0	206	0.55 [0.16; 1.86]
Ye et al. (2012)	1.0	38	3.0	30	0.26 [0.03; 2.40]
Lin et al. (2010)	4.0	54	17.0	54	0.24 [0.08; 0.65]
Ye et al. (2010)	0.0	25	1.0	26	0.35 [0.01; 8.12]
Total (95% CI)	1235		1220		0.55 [0.39; 0.78]

Heterogeneity: $\tau^2 = 0.0487$; $\chi^2 = 10.23$, $df = 8$ ($P = 0.25$); $I^2 = 22\%$

Test for subgroup differences: $\chi^2 = 14.40$, $df = 1$ ($P < 0.01$)

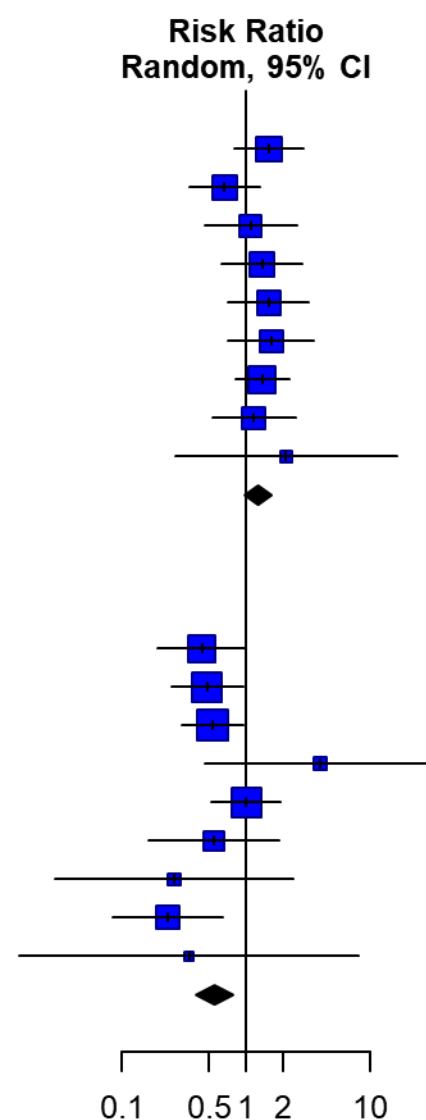


Figure S14. Comparison of two-stent versus provisional stent stratified to lesion length of side branch on target vessel revascularization.

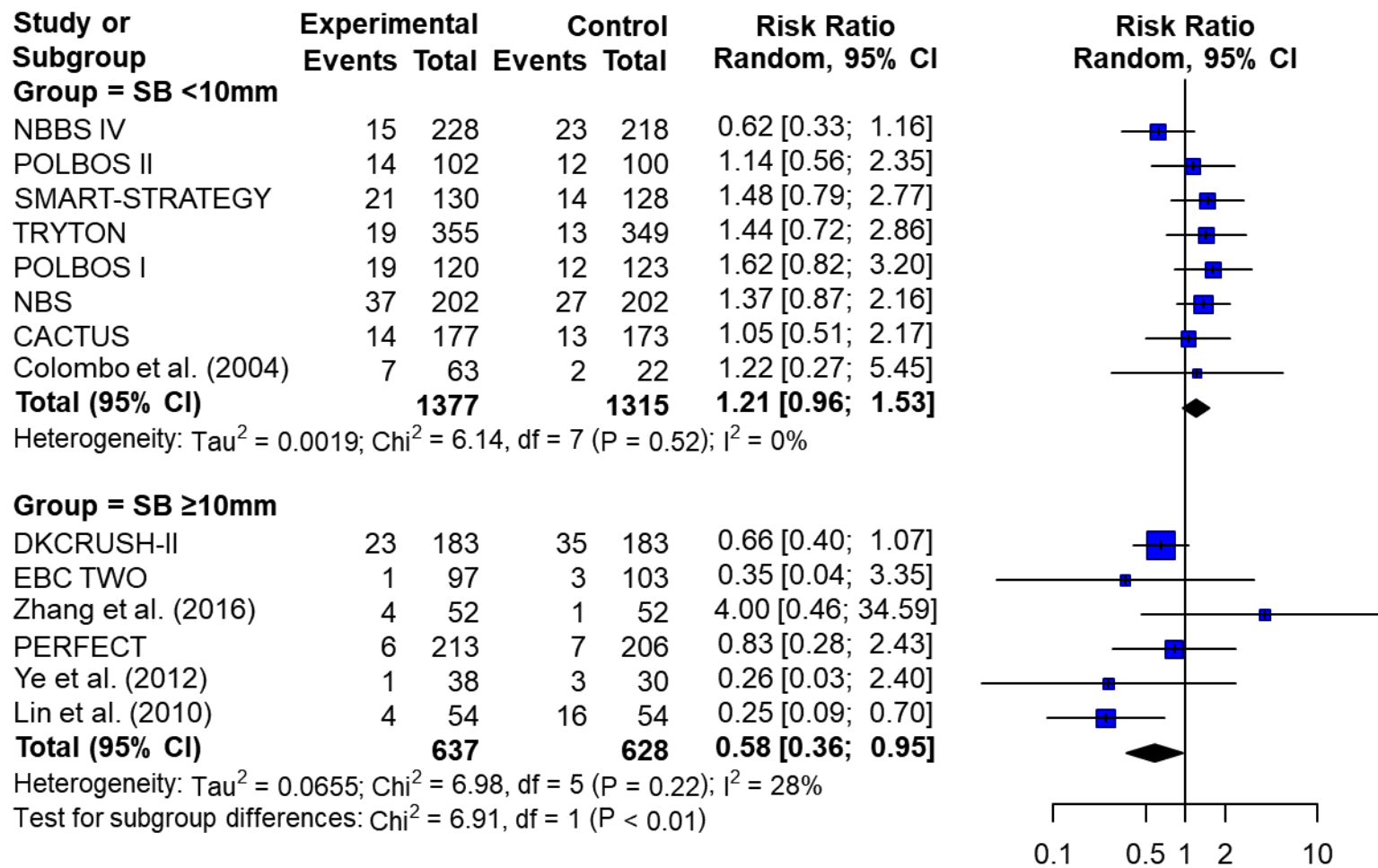


Figure S15. Bar graph showing SUCRA scores of each bifurcation technique for every outcome.

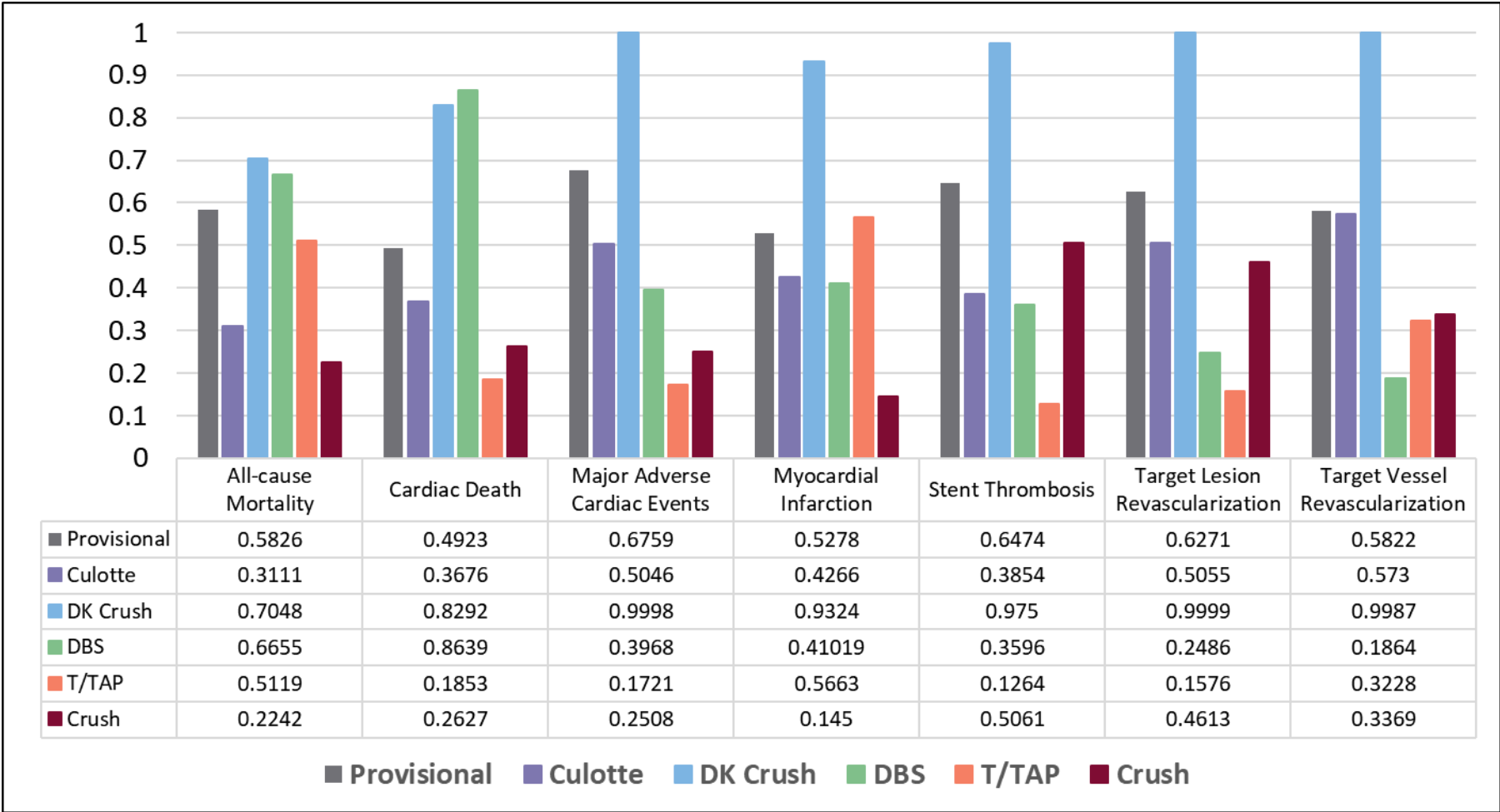


Figure S16. Bayesian network meta-analysis.

