EuroIntervention 2023;19:664-675 published online ahead of print August 2023

Clinical outcomes following different stenting techniques for coronary bifurcation lesions: a systematic review and network meta-analysis of randomised controlled trials

Kamil Bujak[1,2], MD; Filippo Maria Verardi[1,3], MD; Victor Arevalos[1], MD; Rami Gabani[1], MD; Francesco Spione[1,4], MD; Pawel Rajwa[5], MD, PhD; Dejan Milasinovic[6,7], MD, PhD; Goran Stankovic[6,7], MD, PhD; Mariusz Gasior[2], MD, PhD; Manel Sabaté[1], MD, PhD; Salvatore Brugaletta[1]*, MD, PhD

1. Hospital Clínic, Cardiovascular Clinic Institute, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain; 2. 3rd Department of Cardiology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland; 3. Cardiology Unit, Azienda Ospedaliera Universitaria di Ferrara, Cona, Italy; 4. Department of Advanced Biomedical Sciences, University of Naples Federico II, Naples, Italy; 5. Department of Urology, Medical University of Vienna, Vienna, Austria; 6. Department of Cardiology, University Clinical Center of Serbia, Belgrade, Serbia; 7. Faculty of Medicine, University of Belgrade, Belgrade, Serbia

This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-23-00013

KEYWORDS

- bifurcation
- drug-eluting stent
- left main
- miscellaneous
- multiple vessel disease

Abstract

Background: Controversy still exists regarding the optimal treatment of coronary bifurcation lesions.

Aims: We aimed to analyse the evidence from randomised controlled trials (RCTs) to compare outcomes following different bifurcation stenting techniques.

Methods: We systematically searched for RCTs comparing different techniques published up to July 2022. We then conducted a pairwise meta-analysis to compare outcomes between provisional stenting (PS) versus upfront 2-stent techniques. Moreover, we performed a network meta-analysis (NMA) to compare all strategies with each other. The primary endpoint was major adverse cardiac events (MACE).

Results: Twenty-four RCTs (6,890 patients) analysed PS, T-stenting, double-kissing (DK)-crush, crush, or culotte stenting. The pairwise meta-analysis did not reveal a significant difference between the PS and 2-stent techniques. However, the prespecified sensitivity analysis, which included RCTs exclusively enrolling patients with true bifurcation lesions, showed a lower rate of MACE following 2-stent techniques, and meta-regression indicated that a longer side branch lesion was associated with a greater benefit from the 2-stent strategy, which was the most apparent in RCTs with a mean lesion length >11 mm. NMA revealed that DK-crush was associated with the lowest MACE rate (odds ratio 0.47, 95% confidence interval: 0.36-0.62; p<0.01; PS as a reference).

Conclusions: Overall, 2-stent techniques were not significantly better than PS in terms of clinical outcomes. However, the results of the sensitivity analysis suggested that there might be a benefit of a 2-stent approach in selected patients with true bifurcation lesions, especially in the case of long side branch lesions. An NMA revealed that DK-crush was associated with the lowest event rates when compared with other techniques.

**Corresponding author: Department of Cardiology, Hospital Clinic, Cardiovascular Clinic Institute, Institut d'Investigacions Biomèdiques August Pi i Sunyer, University of Barcelona, Villarroel 170, Barcelona 08036, Spain. E-mail: sabrugaletta@gmail.com*

SUBMITTED ON 05/01/2023 - REVISION RECEIVED ON 1st 07/04/2023 / 2nd 09/06/2023 - ACCEPTED ON 30/06/2023

DOI: 10.4244/EIJ-D-23-00013

Abbreviations

DES	drug-eluting stents
DK-crush	double-kissing crush
MACE	major adverse cardiac events
MI	myocardial infarction
NMA	network meta-analysis
PCI	percutaneous coronary intervention
POT	proximal optimisation technique
PS	provisional stenting
RCT	randomised controlled trial
TLR	target lesion revascularisation

Introduction

Since the introduction of percutaneous coronary interventions (PCIs), the treatment of lesions located at the coronary bifurcations presents a challenge due to the complexity of these interventions[1]. For that reason, clinical outcomes following PCI for coronary bifurcation lesions are still worse than interventions for other lesions[2].

Multiple approaches have been developed for managing coronary bifurcation lesions, including various bifurcation stenting techniques[3]. The clinical outcomes of these techniques have been evaluated in several randomised controlled trials (RCTs), but the interpretation of individual trials is challenging because of comparisons of different strategies and inconsistent findings[4-6]. In recent years, several network meta-analyses (NMAs) have been performed to synthesise the results of RCTs on different bifurcation stenting strategies, but they did not include the latest trials[7-9]. Moreover, they were limited by comparing bifurcation stenting techniques with dedicated stents[6,10] or analysing aspects of bifurcation treatment other than stenting strategies[6,11].

The latest European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) 2018 Guidelines on myocardial revascularisation recommend provisional stenting (PS) as the first-choice approach for PCI of bifurcation lesions[12]. Nevertheless, the results of a few large RCTs have been published since the publication of these guidelines,[7-9].

We aimed, therefore, to perform a pairwise meta-analysis assessing the outcomes of PS versus all 2-stent techniques considered together and an NMA to compare different stenting strategies to each other, based on the latest available evidence from RCTs.

Editorial, see page 621

Methods

This systematic review was prospectively registered in the PROSPERO (The International Prospective Register of Systematic Reviews) database before completing searches and starting study selection, screening against eligibility criteria, data extraction, risk of bias evaluation, or data analysis (registration number CRD42022340212). Our study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, including the PRISMA extension statement for reporting NMAs. The PRISMA NMA Checklist has been included in **Supplementary Table 1**.

SEARCH STRATEGY, DATA SELECTION, AND EXTRACTION

PubMed and Scopus were searched for original articles, published in English, presenting results of RCTs comparing different PCI techniques of coronary bifurcation lesion treatment. Searches were performed in July 2022, applying the terms "percutaneous coronary intervention," "stenting," "bifurcation," and "randomised." A search strategy is presented in **Supplementary Table 2**. Two co-authors independently performed the initial screening of articles by title and abstract. Then, full texts of reports potentially meeting inclusion criteria were obtained and evaluated for eligibility. Discrepancies between reviewers were resolved by consensus with the co-authors. RCTs were considered eligible for inclusion in the meta-analysis if at least 2 bifurcation lesion-stenting strategies were compared. We excluded reports without at least a 3-month clinical follow-up, RCTs evaluating bifurcation stenting techniques in chronic total occlusion lesions or using dedicated bifurcation stents, and trials assessing aspects of bifurcation treatment other than bifurcation stenting techniques. No restrictions were applied regarding publication year, sample size, or stent generation. In the case of multiple reports from the same trials, papers with the longest follow-up were included in the meta-analysis. Studies' identification, screening, eligibility assessment, and inclusion have been depicted on the PRISMA flowchart **(Figure 1)**.

The following data were extracted from eligible reports: the first author's name/clinical trial name, publication year, number of participating centres, baseline clinical characteristics, angiographic and procedural characteristics, and endpoint definitions. In addition, 2 authors independently extracted outcome data (the number of events, the total number of cases in a given arm, and estimates with corresponding 95% confidence intervals [95% CIs]), and discrepancies were verified and resolved by consensus. Next, the included RCTs were assessed for bias independently by 2 co-authors using the Cochrane risk-of-bias tool for randomised trials version 2 (RoB 2), which encompasses the assessment of the randomisation process, deviations from the intended interventions, missing outcome data, and measurement of the outcome. Using this tool, the included RCTs were then classified as either having a low risk of bias, some concerns, or a high risk of bias. The results of bias evaluation (which represent the authors' consensus) have been depicted on a diagram using a dedicated RoB 2 Excel tool **(Supplementary Figure 1)**.

STUDY ENDPOINTS

The primary outcome of interest was a combined endpoint of major adverse cardiac events (MACE) at the longest available follow-up, defined according to the given study's definition. If the MACE rate was not reported, MACE was considered a composite of cardiac death, myocardial infarction (MI), or target lesion revascularisation (TLR). Secondary analysed outcomes in this meta-analysis were cardiac death, MI, TLR, and stent thrombosis (ST) according to each trial's protocol. The definitions of endpoints in the analysed RCTs are provided in **Supplementary Table 3**.

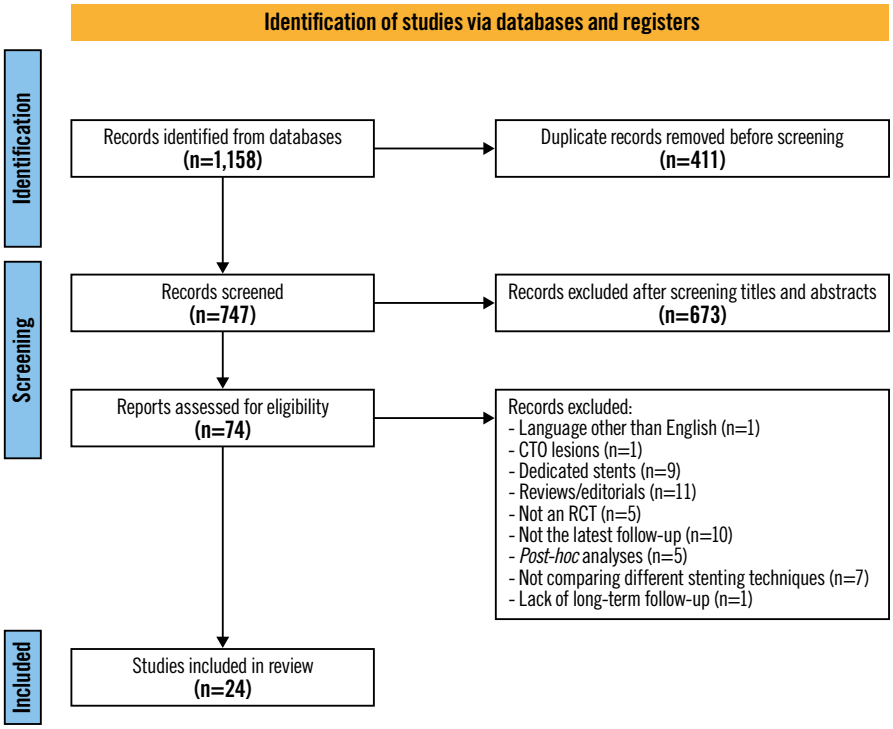


Figure 1. *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of randomised controlled trials included in the systematic review and meta-analysis. CTO: chronic total occlusion; RCT: randomised controlled trial*

STATISTICAL ANALYSIS

All statistical analyses were performed in R version 4.2.0 (The R Foundation for Statistical Computing) using packages "meta", "metafor" and "netmeta." Unless specified otherwise, categorical variables have been shown as the number of patients (percentages), and quantitative variables have been presented as the mean (standard deviation). Odds ratios (ORs) and hazard ratios with corresponding 95% CIs were used as relative treatment effect measures. All meta-analyses were performed according to the intention-to-treat approach. A 2-tailed p-value of less than 0.05 was considered significant.

PAIRWISE META-ANALYSIS

A random-effects pairwise meta-analysis of binary outcomes data was conducted to compare PS versus 2-stent techniques. Heterogeneity in the meta-analysis was tested using Cochrane Q statistics. Moreover, we visually inspected the contour-enhanced funnel plots to assess small-study effects. In the prespecified sensitivity analyses, we included RCTs without a high risk of bias, RCTs that had enrolled only patients with true bifurcations, trials using only second-generation drug-eluting stents (DES), and RCTs in which the proximal optimisation technique (POT) had been required or encouraged by the study's protocol (at least in the PS arm). We also performed a non-prespecified sensitivity analysis by including RCTs enrolling only patients with left main bifurcation lesions. Moreover, to identify the unexplained sources of heterogeneity in the pairwise meta-analysis, we created random-effects meta-regression models using the mean side branch lesion length and publication year as covariates. Owing to the remarkable differences in the follow-up duration between RCTs, we also performed a meta-regression by follow-up duration and sensitivity random-effects meta-analysis of time-to-event outcomes.

NETWORK META-ANALYSIS

A frequentist random-effects NMA was carried out to compare all bifurcation stenting techniques to each other using both direct and indirect evidence on treatment effects. The 2-stent arms of RCTs that allowed more than 1 technique in this group were allocated to the most frequently used strategy in a given arm. To illustrate the network, we generated network plots.

We have presented the network relative effects of treatment using forest plots, where PS was set as a reference. Moreover, we have shown relative treatment effects from the NMA and direct evidence in the league table. The league table's lower triangle contains network treatment estimates from the NMA. The upper triangle incorporates direct treatment estimates from the pairwise comparisons.

The relative ranking of the treatments was estimated using p-scores, which can be interpreted as the mean extent of certainty that one treatment strategy is better than another treatment.

Heterogeneity among the results of included RCTs was assessed using the Q test. In addition, local inconsistency was checked by comparing direct and indirect treatment estimates. To evaluate the small study effects, we drew the "comparison-adjusted" funnel plots, which were assessed for asymmetry visually. Moreover, we performed prespecified sensitivity analyses after excluding RCTs with a high risk of bias and trials with multiple 2-stent techniques in 1 arm.

Results

STUDY SELECTION AND CHARACTERISTICS

After excluding duplicates, 747 records were screened, and after the title and/or abstract evaluation, 74 records were selected for a full-text assessment for eligibility. Finally, 24 RCTs − enrolling a total of 6,890 patients who had undergone bifurcation PCI using one of the following techniques: PS, T-stenting (including all its modifications)[13], double-kissing crush (DK-crush), crush, or culotte stenting − were included in the review[1,7-9,14-33]. A PRISMA flowchart of study inclusion is presented in **Figure 1**, and the details of the included RCTs are shown in **Table 1**. Seven of these trials allowed more than 1 technique in the 2-stent arm. The weighted mean clinical follow-up in all RCTs was 26.2 months. Clinical and angiographic/procedural characteristics are presented in **Supplementary Table 4** and **Supplementary Table 5**, respectively. The results of the risk-of-bias assessment of the analysed RCTs are depicted in **Supplementary Figure 1**.

PAIRWISE META-ANALYSIS COMPARING PS VERSUS 2-STENT TECHNIQUES

This analysis, including 18 RCTs comparing these 2 strategies (5,022 patients), did not show any difference between the 2 groups regarding MACE (OR 1.19, 95% CI: 0.9-1.58; p=0.23) **(Central illustration A)** or any secondary outcomes **(Supplementary Figure 2)**. In this analysis, significant heterogeneity was observed between the RCTs regarding MACE **(Central illustration A)**, MI, and TLR **(Supplementary Figure 2)**. Visual inspection of the contour-enhanced funnel plot for MI revealed asymmetry between the smaller RCTs, but the risk of publication bias was unlikely, since all the trials, except three large-scale trials, were located in the "area of non-significance" **(Supplementary Figure 3)**.

SENSITIVITY ANALYSES AND META-REGRESSION

Four prespecified sensitivity analyses were performed for pairwise meta-analysis. The first of them, including only RCTs enrolling patients with true bifurcations, demonstrated a significant benefit from 2-stent techniques in terms of MACE (OR 1.52, 95% CI: 1.08-2.13; p=0.02) **(Central illustration B)**, mainly driven by a higher risk of TLR following PS (OR 1.64; 95% CI: 1.04-2.56; p=0.03) **(Supplementary Figure 4)**. Other prespecified sensitivity analyses, i.e., after excluding RCTs with a high risk of bias, those using first-generation drug-eluting stents, or those without POT, did not show any significant advantage of the 2-stent technique over PS **(Supplementary Figure 5-Supplementary Figure 7)**. Additionally, the non-prespecified sensitivity analysis, which included only left main bifurcations and a meta-analysis of the time-to-event data, also did not show any difference between the analysed arms **(Supplementary Figure 8, Supplementary Figure 9)**. The statistical heterogeneity regarding the primary endpoint, MI, and TLR remained significant in the above-mentioned sensitivity analyses.

The meta-regression, using the mean side branch lesion length as a continuous covariate, showed lower rates of the primary endpoint of MACE associated with the 2-stent technique in the RCTs that had enrolled patients with longer side branch lesions (estimate of 0.06; 95% CI: 0.02-0.10; p=0.002; residual heterogeneity Q=17.07; p-value for residual heterogeneity of 0.15). This effect was apparent in the RCTs with a mean study-level side branch lesion length of more than 11 mm **(Central illustration C)**. A similar relationship between side branch lesion length and the advantages of 2-stent techniques was also found for myocardial infarction and target lesion revascularisation **(Supplementary Figure 10)**. Another meta-regression demonstrated that the RCTs published in recent years tended to show a lower rate of MI in patients treated with 2-stent techniques; other analysed outcomes were not associated with the publication year **(Supplementary Figure 11)**. Of note, the follow-up duration did not modify the relationship between the 2-stent technique and the primary or secondary outcomes **(Supplementary Figure 12)**.

NETWORK META-ANALYSIS COMPARING ALL TECHNIQUES TO EACH OTHER

In the NMA, 22 RCTs were analysed for the primary endpoint of MACE. Two RCTs were not included in the NMA because of a lack of data on the predominate bifurcation stenting strategy in the 2-stent arm or missing results in the intention-to-treat analysis. The network plots for MACE and secondary endpoints are presented in **Figure 2**, and the number of patients analysed in the NMA, along with event rates according to the bifurcation stenting technique, are shown in **Supplementary Table 6**.

NMA revealed that DK-crush was associated with significantly lower event rates than all other bifurcation stenting strategies regarding the primary endpoint (OR 0.47, 95% CI: 0.36-0.62, as compared to PS, the second-best strategy in terms of MACE) and TLR. Moreover, DK-crush was related to a lower risk of MI and stent thrombosis compared to all other techniques, except for T-stenting. However, the rate of cardiac death in patients treated with DK-crush was similar to patients undergoing bifurcation PCI using other techniques. No other significant differences between bifurcation treatment strategies have been revealed. According to the p-scores, DK-crush ranked highest in terms of all analysed endpoints. The results of the NMA are shown both on the forest plots (using PS as a reference) **(Central illustration D, Figure 3)** and in the league table **(Figure 4)**.

No heterogeneity nor local inconsistency between direct and indirect treatment estimates was revealed in NMA **(Figure 4, Supplementary Table 7)**. Moreover, there was no significant asymmetry in the funnel plots, except for TLR **(Supplementary Figure 13)**.

SENSITIVITY NETWORK META-ANALYSES

The sensitivity analysis, after excluding the RCTs with a high risk of bias, revealed the same findings as the primary analysis **(Supplementary Figure 14, Supplementary Figure 15)**. The second sensitivity analysis, without the RCTs that allowed for multiple techniques in 1 arm, provided similar results to the previous

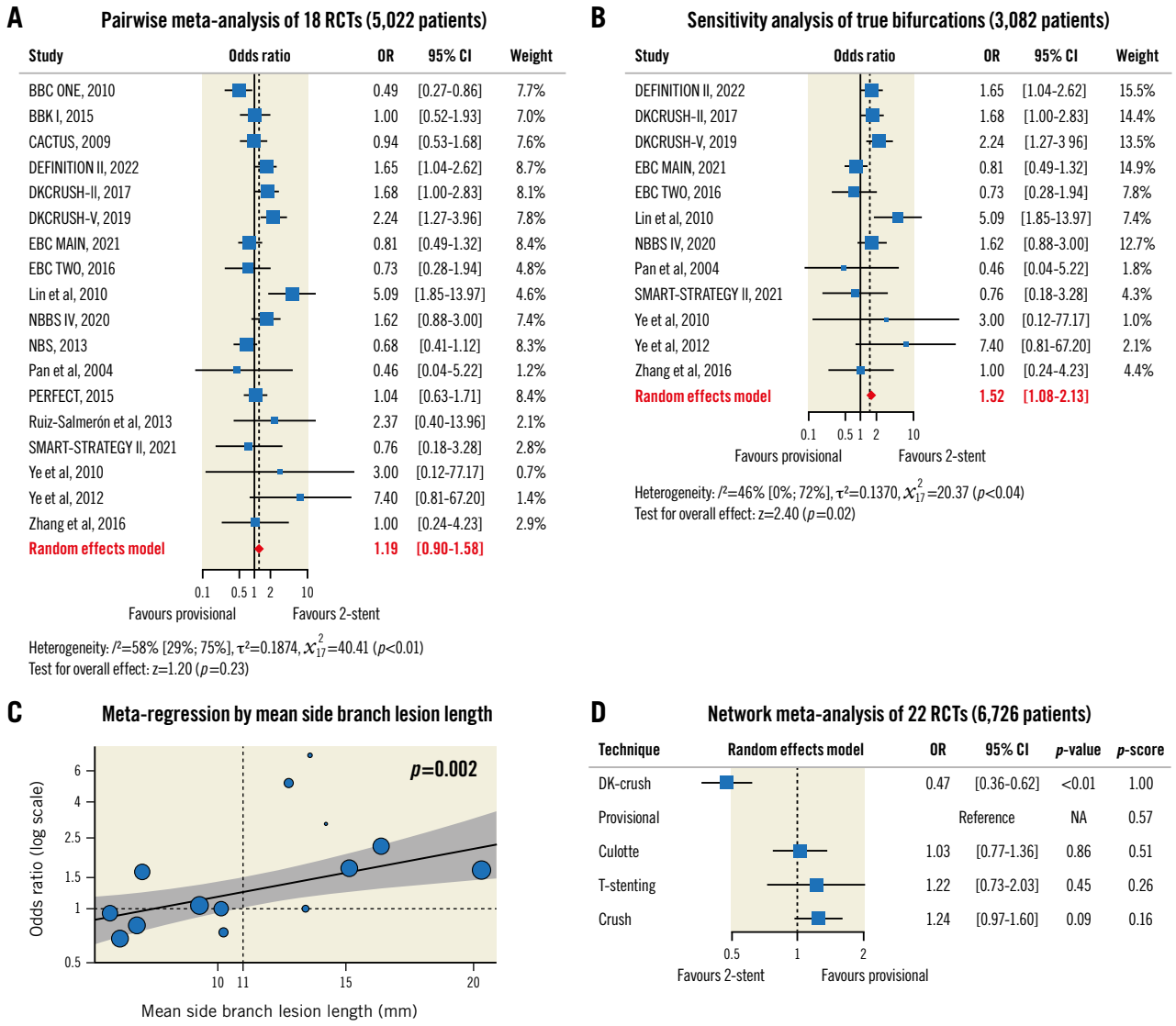
Table 1. Details on included randomised controlled trials.

Study	Publication year	Years of patient enrolment	Multicentre trial	First arm (n)	Second arm (n)	Predominant technique in 2-stent arm	Clinical follow-up (months)	Angiographic follow-up (months; percentage of patients)	DES generation	Routine FKB in the provisional arm (according to protocol)	POT in the provisional arm (according to protocol)
BBC ONE[27]	2010	2004-2007	Yes	Provisional, n=250	2-stent, n=250	Crush, 67.6%	9	NA; NA	First	No	No
BBK I[26]	2015	2005-2006	No	Provisional, n=101	T-stenting, n=101	NA	60	9; 95%	First	Yes	No
BBK II[28]	2016	2010-2015	No	Culotte, n=150	Modified T-stenting, n=150	NA	12	9; 91%	First and second	NA	NA
CACTUS[29]	2009	2004-2007	Yes	Crush, n=177	Provisional, n=173	NA	6	6; 86%	First	Yes	No
Colombo et al[1]	2004	2001-2002	Yes	2-stent, n=63	Provisional, n=22	T-stenting, 93%	6	6; 87.1%	First	Yes	No
DEFINITION II[7]	2022	2015-2018	Yes	2-stent, n=328	Provisional, n=325	DK-crush, 77.8%	36	13; 54.5%	Second	No	Yes
DKCRUSH-I[30]	2009	2005-2006	Yes	Crush, n=156	DK-crush, n=155	NA	24	8; 82%	First	NA	NA
DKCRUSH-II[31]	2017	2007-2009	Yes	DK-crush, n=185	Provisional, n=185	NA	60	8; 91.6%	First	No	No
DKCRUSH-III[32]	2015	2009-2011	Yes	DK-crush, n=210	Culotte, n=209	NA	36	8; 83.5%	Second	NA	NA
DKCRUSH-V[8]	2019	2011-2016	Yes	Provisional, n=242	DK-crush, n=240	NA	36	13; 65.8%	Second	No	Yes
EBC MAIN[9]	2021	2016-2019	Yes	Provisional, n=230	2-stent, n=237	Culotte, 53%	12	NA; NA	Second	Yes	Yes
EBC TWO[33]	2016	2011-2014	Yes	Provisional, n=103	Culotte, n=97	NA	12	NA; NA	Second	No	Encouraged
Lin et al[14]	2010	2007-2009	No	Provisional, n=54	2-stent, n=54	DK-crush, 65%	8	8; ND	First	No	No
NBBS IV[15]	2020	2008-2012	Yes	Provisional, n=221	2-stent, n=229	Culotte, 65.6%	24	8; 68.2%	First and second	No	No
NBS[16]	2013	2004-2005	Yes	Provisional, n=207	2-stent, n=206	Crush, 50%	60	8; 86%	First	No	No
NSTS[17]	2013	2005-2007	Yes	Crush, n=209	Culotte, n=215	NA	36	8; 76.4%	First	NA	NA
Pan et al[18]	2004	2002-2003	Yes	Provisional, n=47	T-stenting, n=44	NA	6	6; 40.7%	First	NA	No
PERFECT[19]	2015	2007-2013	Yes	Crush, n=213	Provisional, n=206	NA	12	8; 71.6%	ND	No	No
Ruiz-Salmerón et al[20]	2013	2009-2011	No	Provisional, n=33	T-stenting, n=36	NA	9	9; 84.1%	Second	No	No
SMART-STRATEGY II[21]	2021	2013-2016	Yes	Provisional, n=23	2-stent, n=23	ND	12	9; ND	Second	No	No
Ye et al[22]	2010	2008-2009	No	DK-crush, n=25	Provisional, n=26	NA	8	8; 21.6%	ND	No	No
Ye et al[25]	2012	2008-2011	No	DK-crush, n=38	Provisional, n=37	NA	12	8; 77%	First and second	No	No
Zhang et al[23]	2016	2010-2013	No	Provisional, n=51	Culotte, n=51	NA	9	9; 100%	First and second	No	No
Zheng et al[24]	2016	2013-2014	No	Crush, n=150	Culotte, n=150	NA	12	12; 84%	ND	NA	NA

BBC ONE: The British Bifurcation Coronary study: Old, New, and Evolving strategies; BBK I: Bifurcations Bad Krozingen I; BBK II: Bifurcations Bad Krozingen II; CACTUS: Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting Stents; DEFINITION II: Two-stent vs Provisional Stenting Techniques for Patients With Complex Coronary Bifurcation Lesions; DES: drug-eluting stent; DKCRUSH-I: Study Comparing the Double Kissing Crush with Classical Crush for the Treatment of Coronary Bifurcation Lesions; DKCRUSH-II: Randomized Study on Double Kissing Crush Technique Versus Provisional Stenting Technique for Coronary Artery Bifurcation Lesions; DKCRUSH-III: DK Crush Versus Culotte Stenting for the Treatment of Unprotected Distal Left Main Bifurcation Lesions; DKCRUSH-V; EBC MAIN: The European Bifurcation Club Left Main Coronary Stent Study; EBC TWO: European Bifurcation Coronary TWO; FKB: final kissing ballon; NA: not applicable; NBBS IV: Nordic Baltic Bifurcation Study IV; NBS: Nordic Bifurcation Study; ND: no data; NSTS: Nordic Stent Technique Study; PERFECT: Optimal Stenting Strategy for True Bifurcation Lesions; POT: proximal optimisation technique; SMART-STRATEGY II: STRATEGY for Left Main Coronary Bifurcation Lesion II

EuroIntervention

CENTRAL ILLUSTRATION Primary endpoints: major adverse cardiac events at the longest follow-up.



A) Forest plot presenting results of the pairwise meta-analysis for MACE. B) Forest plots demonstrating results of the sensitivity analysis of randomised controlled trials enrolling only patients with true bifurcations for MACE. C) Bubble plot showing results of meta-regression testing the influence of the mean side branch lesion length on the benefit from provisional stenting versus 2-stent technique in terms of the primary endpoint of MACE. The "bubbles" represent individual trials, and their size is proportional to the weight given to the trial. The treatment effect for each study is shown on the y-axis, and the study-level covariate (mean side branch length) is on the x-axis. Odds ratio >1 reflects the benefit of the 2-stent technique, and odds ratio <1 indicates the advantage of provisional stenting. The regression line is presented using the solid black line with the grey area indicating a 95% confidence interval. The crossing point of the odds ratio equal to one with the lower limit of the confidence interval corresponds to the mean side branch lesion length of 11 mm, which is a cut-off value over which the benefit of the 2-stent strategy becomes apparent. D) Results of network meta-analysis: forest plots and p-scores for MACE. CI: confidence interval; DK-crush: double-kissing crush; MACE: major adverse cardiac events; OR: odds ratio; RCT: randomised controlled trial

one, but DK-crush was not significantly better than PS regarding MI or stent thrombosis **(Supplementary Figure 16, Supplementary Figure 17)**. In both of these sensitivity analyses, DK-crush was the best single strategy in terms of primary and secondary endpoints according to the treatment rankings.

Discussion

Our systematic review and meta-analysis on the percutaneous treatment of coronary bifurcation lesions have shown the following: 1) overall, there was no significant difference between PS and 2-stent techniques. 2) However, when only the RCTs with

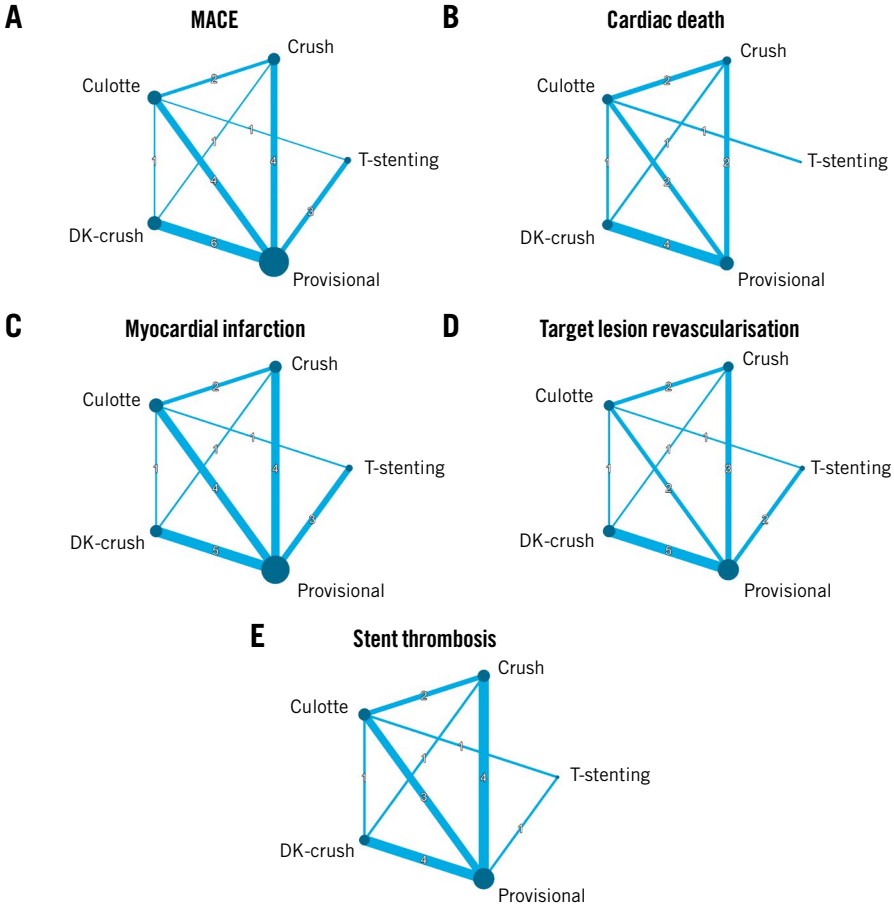


Figure 2. *Network plots for MACE and secondary endpoints. A) MACE, (B) cardiac death, (C) myocardial infarction, (D) target lesion revascularisation, and (E) stent thrombosis. The size of the nodes corresponds to the number of patients randomised to a given strategy, and the thickness of connecting lines correlates with the number of available direct comparisons. DK-crush: double-kissing crush; MACE: major adverse cardiac events*

true bifurcation lesions were included, there was a lower risk of MACE in patients treated with 2-stent techniques. 3) The benefits of the 2-stent strategy were more apparent in patients with longer side branch lesions; this was especially observed in RCTs with a mean lesion length greater than 11 mm. 4) When considering all bifurcation strategies individually, DK-crush was associated with the lowest event rates compared to the observed rates of other techniques within each of the included trials.

Multiple RCTs have provided much of the evidence on different strategies of bifurcation lesion stenting by comparing a simple PS approach with complex upfront 2-stent techniques[1,7-9,14-25,28-33]. However, the results of these RCTs have been somewhat contrasting, posing interpretive challenges. By pooling evidence from all available RCTs, we have shown that PS versus 2-stent techniques do not differ regarding MACE. This is in line with 2 previous meta-analyses[6,34]. Of note, as compared with a previous meta-analysis by Ford et al[35], we did not detect any difference in cardiac death rates between these 2 techniques. Some essential differences should be considered when interpreting this difference. First, Ford et al included trials exclusively with long-term follow-up. Our meta-regression analysis, however, did not show the advantage of any strategy becoming more apparent over a longer follow-up. Second, 2 landmark trials on bifurcation stenting − EBC MAIN (The European Bifurcation Club Left Main Coronary Stent study) and the 3-year outcomes of the DEFINITION II trial (Two-stent vs Provisional Stenting Techniques for Patients With Complex Coronary Bifurcation Lesions) – were not included in the previous meta-analyses, but they were in ours[6,7,9,34,35].

Of note, most of the trials included in this meta-analysis were still using first-generation DES and stenting techniques without POT[1,14-18,23,25,26,28-31]. To make our results more current, sensitivity analyses were performed including only those RCTs using second-generation DES and the POT technique, without any difference from our primary analysis. The lack of improvement may be due to the small number of RCTs included in these sensitivity analyses (6 and 4 trials, respectively). There is still a need for RCTs that include routine POT and final kissing-balloon in the 2-stent techniques, as well as with a greater use of intravascular imaging, which nowadays represents the gold standard for managing bifurcation lesions[5].

Specifically, looking at the RCTs that only included patients with true bifurcation lesions, we showed a lower risk of MACE in

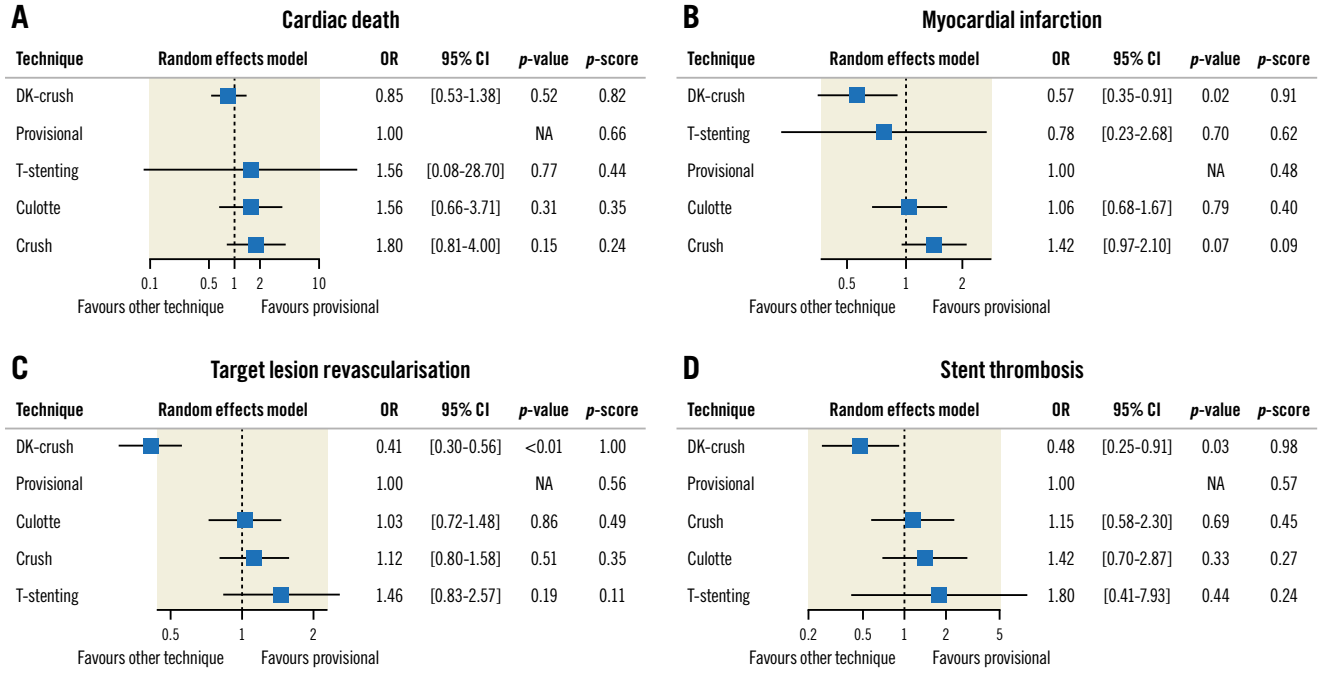


Figure 3. *Forest plots and p-scores presenting the results of network meta-analysis for secondary outcomes. A) Cardiac death, (B) myocardial infarction, (C) target lesion revascularisation, and (D) stent thrombosis. Provisional stenting is shown as a reference. CI: confidence interval; DK-crush: double-kissing crush; NA: not applicable; OR: odds ratio*

the 2-stent versus 1-stent strategy, which, to the best of our knowledge, is a novel finding. However, considering the significant heterogeneity of the included trials, these results suggest improved outcomes in selected patients treated with 2-stent techniques rather than all patients with true bifurcations. For example, subgroup analyses of previous NMAs have shown an advantage of the 2-stent approach only in RCTs where the mean side branch lesion length ≥10 mm[6,36]. Nevertheless, this cut-off in the previous meta-analyses was selected somewhat arbitrarily. Therefore, taking this into account, we performed a meta-regression which demonstrated that the longer the mean study-level side branch lesion was, the greater the advantage of the 2-stent strategy. This was the most apparent in RCTs with a mean length of more than 11 mm. This finding seems to reaffirm the current European Bifurcation Club recommendations to consider an upfront 2-stent strategy if the side branch lesion length is >10 mm[5]. However, bearing in mind the limitations of the meta-regression, it should be interpreted with caution, as this analysis was observational in nature and referred to the study-level rather than patient-level data. Hence, the exact mechanism of the lower incidence of MACE in the 2-stent arms of trials with longer mean side branch lengths remains unclear.

Our NMA, in analysing all the bifurcation techniques individually, demonstrated excellent outcomes with the DK-crush technique, in line with multiple RCTs and previous NMAs[6,11,36]. Contrary to the previous NMA by Di Gioia et al, our meta-analysis demonstrated the benefit of DK-crush, not only in terms of MACE and TLR but also with lower rates of MI and ST. This might be explained by the consideration in our analysis of the 3-year outcomes of the DEFINITION II trial, which included only very complex true bifurcations, where the advantage of DK-crush is the greatest. It is noteworthy to consider, when interpreting the results of RCTs with a limited number of enrolling centres whose operators are highly familiar with DK-crush (e.g., in the DKCRUSH-V trial, the primary operators' previous DK-crush cases were reviewed by the steering committee before starting randomisation to ensure appropriate technique), that the reproducibility of these trials' findings in real life is limited[5]. DK-crush is indeed time- and resource-consuming and requires more experience than the other stenting strategies[5]. In the recent EBC MAIN trial, for example, DK-crush was used only in 5% of cases in the 2-stent arm, demonstrating low utilisation of this technique in European centres. Owing to this, the clinical applicability of findings from the pairwise meta-analysis comparing PS with all 2-stent techniques might be higher than the results of the NMA, especially in the case of centres/operators that are not experienced in performing DK-crush.

A substantial amount of between-trial heterogeneity in the pairwise meta-analysis regarding MACE, MI, and TLR, which remained significant in multiple sensitivity analyses, must be acknowledged. This variation in trial outcomes may result, for example, from differences in study design, endpoint definitions, and patients' clinical and angiographic characteristics. High between-trial heterogeneity might also be explained by differences in the outcomes of techniques included in the 2-stent strategy arm. Of note, we demonstrated a substantial decrease in residual heterogeneity in the meta-regression, indicating the potential effect of study-level side branch lesion length on the benefit of 2-stent techniques. However, as discussed above, this finding should be interpreted as hypothesis-generating rather than confirmatory.

MACE (No. of studies=22; No. of patients=6,726)

Cochran's Q test *p*-value=0.27; I^2=14.7% [0.0%-50.2%]; τ^2=0.02

DK-crush	**0.49 [0.35-0.67]**	**0.29 [0.15-0.55]**	NA	**0.51 [0.28-0.93]**
0.47 [0.36-0.62]	**Provisional**	1.01 [0.69-1.49]	1.06 [0.56-2.01]	0.76 [0.56-1.03]
0.46 [0.33-0.65]	0.97 [0.74-1.29]	**Culotte**	0.57 [0.25-1.26]	0.78 [0.48-1.28]
0.39 [0.22-0.68]	0.82 [0.49-1.37]	0.84 [0.50-1.43]	**T-stenting**	NA
0.38 [0.27-0.53]	0.80 [0.62-1.03]	0.82 [0.60-1.13]	0.98 [0.56-1.71]	**Crush**

Cardiac death (No. of studies=13; No. of patients=4,732)

Cochran's Q test *p*-value=0.98; I^2=0% [0.0%-62.4%]; τ^2=0

DK-crush	0.88 [0.53-1.46]	NA	0.49 [0.12-1.99]	0.33 [0.03-3.22]
0.85 [0.53-1.38]	**Provisional**	NA	0.76 [0.14-4.09]	0.60 [0.21-1.66]
0.55 [0.03-10.15]	0.64 [0.03-11.81]	**T-stenting**	1.00 [0.06-16.14]	NA
0.55 [0.23-1.33]	0.64 [0.27-1.52]	1.00 [0.06-16.14]	**Culotte**	0.87 [0.33-2.31]
0.48 [0.20-1.12]	0.56 [0.25-1.24]	0.87 [0.05-15.69]	0.87 [0.39-1.94]	**Crush**

Myocardial infarction (No. of studies=21; No. of patients=6,675)

Cochran's Q test *p*-value=0.16; I^2=25.1% [0.0%-57.7%]; τ^2=0.09

DK-crush	NA	**0.49 [0.27-0.91]**	0.39 [0.13-1.13]	0.67 [0.27-1.62]
0.73 [0.20-2.70]	**T-stenting**	0.89 [0.22-3.65]	0.50 [0.04-5.92]	NA
0.57 [0.35-0.91]	0.78 [0.23-2.68]	**Provisional**	1.03 [0.58-1.84]	**0.62 [0.39-0.98]**
0.53 [0.30-0.95]	0.73 [0.21-2.63]	0.94 [0.60-1.47]	**Culotte**	0.71 [0.32-1.61]
0.40 [0.23-0.68]	0.55 [0.15-1.98]	0.70 [0.48-1.03]	0.75 [0.45-1.24]	**Crush**

Target lesion revascularisation (No. of studies=17; No. of patients=5,789)

Cochran's Q test *p*-value=0.57; I^2=0% [0.0%-55.0%]; τ^2=0

DK-crush	**0.43 [0.30-0.62]**	**0.25 [0.11-0.55]**	**0.42 [0.23-0.78]**	NA
0.41 [0.30-0.56]	**Provisional**	0.98 [0.60-1.61]	0.84 [0.54-1.32]	0.93 [0.45-1.92]
0.40 [0.26-0.61]	0.97 [0.68-1.39]	**Culotte**	0.88 [0.47-1.67]	0.47 [0.20-1.08]
0.37 [0.25-0.54]	0.89 [0.63-1.25]	0.92 [0.61-1.39]	**Crush**	NA
0.28 [0.15-0.53]	0.69 [0.39-1.21]	0.71 [0.40-1.27]	0.77 [0.41-1.45]	**T-stenting**

Stent thrombosis (No. of studies=17; No. of patients=6,347)

Cochran's Q test *p*-value=0.45; I^2=0% [0.0%-55.0%]; τ^2=0

DK-crush	0.55 [0.26-1.12]	0.39 [0.08-2.07]	**0.12 [0.01-0.97]**	NA
0.48 [0.25-0.91]	**Provisional**	0.83 [0.32-2.12]	1.06 [0.40-2.79]	0.39 [0.07-2.05]
0.41 [0.18-0.97]	0.87 [0.43-1.74]	**Crush**	0.77 [0.32-1.84]	NA
0.34 [0.14-0.80]	0.71 [0.35-1.43]	0.81 [0.40-1.64]	**Culotte**	3.02 [0.12-74.73]
0.27 [0.05-1.33]	0.56 [0.13-2.46]	0.64 [0.13-3.20]	0.79 [0.16-3.82]	**T-stenting**

Figure 4. *The results of the network meta-analysis presented using the league table. The lower triangle (dark blue boxes) contains network treatment estimates (odds ratios and 95% confidence intervals; comparison of treatment in a row versus a column), and the upper triangle (light blue boxes) contains direct treatment estimates from pairwise comparisons (comparison of treatment in a column versus a row). Significant differences in event rates between treatment strategies are in bold. DK-crush: double-kissing crush; NA: not applicable (lack of direct comparisons of 2 techniques in included trials).*

Although some NMAs analysing different bifurcation stenting techniques have been published in recent years[6,10,11,34,36], our paper presents some remarkable novelties. First, our analysis included the recent landmark trials, which provided much new data on the role of particular techniques in the treatment of bifurcation lesions[7,9]. Second, the prespecified sensitivity analysis, which included studies exclusively enrolling patients with true bifurcation lesions, showed a potential benefit of 2-stent techniques in this specific subgroup of patients. Third, the meta-regression showed that the longer the mean side branch lesion was (as a continuous variable), the greater the advantage of the 2-stent strategy. Fourth, we performed the whole spectrum of prespecified sensitivity analyses to assess the evidence on bifurcation techniques in the current bifurcation treatment scenarios by including RCTs utilising second-generation DES or POT.

Limitations

Some limitations should be acknowledged. First, the definitions of endpoints differed across the included RCTs, especially regarding MACE, which was considered in our meta-analysis according to the given study's definition. Moreover, Bifurcation Academic Research Consortium criteria for standardised endpoints in coronary bifurcation studies have been recently published[37]. Owing to this, these standardised definitions were not used in the RCTs included in our meta-analysis. However, the results for secondary endpoints, for which the definitions varied to a lesser degree than those for the primary endpoint, were mainly consistent with the MACE findings.

In addition, RCTs analysed in our paper differed significantly regarding follow-up length. However, meta-regression showed that the follow-up duration did not affect the results. Furthermore, the sensitivity analysis of time-to-event data (available only for 8 of 18 RCTs included in the pairwise meta-analysis) was consistent with the meta-analysis of binary-outcome data.

The trials included were also of mixed quality. Notably, in the older trials the risk of bias was generally higher. In addition, as operators could not be blinded to patient allocation, the included RCTs were not double-blinded, which is a potential source of bias. However, the sensitivity analyses, after excluding the RCTs with the highest risk of bias, demonstrated results consistent with the primary analysis. Moreover, meta-regression by the publication year revealed that the findings of the meta-analysis were consistent across all years except for myocardial infarction (newer RCTs tended to show more benefit from 2-stent techniques in terms of this endpoint).

There was a relatively high crossover rate, especially in the case of RCTs analysing PS versus 2-stent techniques. Unfortunately, our meta-analysis was performed based only on the intention-to-treat principle (23 of 24 RCTs included in the review provided sufficient data for this analysis), as data on per-protocol or as-treated analyses were not routinely reported. However, this high crossover from 1-stent to 2-stent techniques reflects the modern PS approach. Thus, the clinical applicability of the intention-to-treat analysis is the greatest[4].

Additionally, 6 of the RCTs included in NMA allowed for more than 1 technique in the 2-stent strategy arm. In these cases, we allocated these groups to the most frequently used technique in a given arm, which varied from 50% to 93%. Owing to this limitation, we conducted a sensitivity analysis by excluding these RCTs, which provided similar findings as the primary analysis.

Finally, there were considerable differences in terms of devices utilised (i.e., drug-eluting stent generations), interventional techniques (including POT and final kissing-balloon inflation), and bifurcation anatomies (for example, the prevalence of true bifurcations, left main bifurcations, vessel sizes, and lesion lengths), which might explain the heterogeneity of the results. We were able to address some of these issues by performing several sensitivity and meta-regression analyses. However, the others required the use of individual patient data, which were unavailable.

Conclusions

In the treatment of coronary bifurcation lesions, overall, 2-stent techniques were not significantly better than PS. However, there might be some benefit from 2-stent techniques in selected patients with true bifurcation lesions, especially in those with longer side branch lesions. Moreover, when bifurcation stenting techniques are analysed individually at the network level, DK-crush was associated with lower event rates as compared with other techniques.

Impact on daily practice

This meta-analysis demonstrated no advantage of the routine use of 2-stent techniques in patients with coronary bifurcation lesions. However, the results of the sensitivity analysis suggest that there might be a benefit of a 2-stent approach in selected patients with true bifurcation lesions, especially in the case of long side branch lesions. In addition, a network meta-analysis revealed that DK-crush is associated with the lowest event rates compared to all other techniques.

Acknowledgements

The first author (K. Bujak) was supported by the 2021 EAPCI Education and Training Grant. The authors have not received any specific funding for conducting this review.

Conflict of interest statement

D. Milasinovic reports speaker fees from Abbott, Terumo, Boston Scientific, and Biosensors. G. Stankovic reports personal fees from Medtronic, Terumo, Boston Scientific, and Abbott Vascular, outside the submitted work. The other authors have no conflicts of interest to declare.

References

1. Colombo A, Moses JW, Morice MC, Ludwig J, Holmes DR Jr, Spanos V, Louvard Y, Desmedt B, Di Mario C, Leon MB. Randomized Study to Evaluate Sirolimus-Eluting Stents Implanted at Coronary Bifurcation Lesions. *Circulation.* 2004;109:1244-9.

2. Lee JM, Lee SH, Kim J, Choi KH, Park TK, Yang JH, Song YB, Hahn JY, Choi JH, Choi SH, Kim HS, Chun WJ, Nam CW, Hur SH, Han SH, Rha SW, Chae IH, Jeong JO, Heo JH, Yoon J, Lim DS, Park JS, Hong MK, Doh JH, Cha KS, Kim DI, Lee SY, Chang K, Hwang BH, Choi SY, Jeong MH, Hong SJ, Koo BK, Gwon HC. Ten-Year Trends in Coronary Bifurcation Percutaneous Coronary Intervention: Prognostic Effects of Patient and Lesion Characteristics, Devices, and Techniques. *J Am Heart Assoc.* 2021;10:e021632.

3. Sawaya FJ, Lefèvre T, Chevalier B, Garot P, Hovasse T, Morice MC, Rab T, Louvard Y. Contemporary Approach to Coronary Bifurcation Lesion Treatment. *JACC Cardiovasc Interv.* 2016;9:1861-78.

4. Albiero R, Burzotta F, Lassen JF, Lefèvre T, Banning AP, Chatzizisis YS, Johnson TW, Ferenc M, Pan M, Darremont O, Hildick-Smith D, Chieffo A, Louvard Y, Stankovic G. Treatment of coronary bifurcation lesions, part I: implanting the first stent in the provisional pathway. The 16th expert consensus document of the European Bifurcation Club. *EuroIntervention.* 2022;18:E362-76.

5. Lassen JL, Albiero R, Johnson TJ, Burzotta F, Lefèvre T, Iles TL, Pan M, Banning AB, Chatzizisis YC, Ferenc M, Dzavik V, Milasinovic D, Darremont O, Hildick-Smith D, Louvard Y, Stankovic G. Treatment of coronary bifurcation lesions, part II: implanting two stents. The 16th expert consensus document of the European Bifurcation Club. *EuroIntervention.* 2022;18:457-70.

6. Park DY, An S, Jolly N, Attanasio S, Yadav N, Rao S, Vij A. Systematic Review and Network Meta-Analysis Comparing Bifurcation Techniques for Percutaneous Coronary Intervention. *J Am Heart Assoc.* 2022;11:25394.

7. Kan J, Zhang JJ, Sheiban I, Santoso T, Munawar M, Tresukosol D, Xu K, Stone GW, Chen SL; DEFINITION II Investigators. 3-Year Outcomes After 2-Stent With

Provisional Stenting for Complex Bifurcation Lesions Defined by DEFINITION Criteria. *JACC Cardiovasc Interv.* 2022;15:1310-20.

8. Chen X, Li X, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, Santoso T, Paiboon C, Kwan TW, Sheiban I, Leon MB, Stone GW, Chen SL; DKCRUSH-V Investigators. 3-Year Outcomes of the DKCRUSH-V Trial Comparing DK Crush With Provisional Stenting for Left Main Bifurcation Lesions. *JACC Cardiovasc Interv.* 2019;12: 1927-37.

9. Hildick-Smith D, Egred M, Banning A, Brunel P, Ferenc M, Hovasse T, Wlodarczak A, Pan M, Schmitz T, Silvestri M, Erglis A, Kretov E, Lassen JF, Chieffo A, Lefèvre T, Burzotta F, Cockburn J, Darremont O, Stankovic G, Morice MC, Louvard Y. The European bifurcation club Left Main Coronary Stent study: A randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN). *Eur Heart J.* 2021;42:3829-39.

10. Crimi G, Mandurino-Mirizzi A, Gritti V, Scotti V, Strozzi C, de Silvestri A, Montalto C, di Giacomo C, d'Ascenzo F, Repetto A, Ferlini M, Marinoni B, Ferrario M, de Servi S, Visconti LO, Klersy C. Percutaneous Coronary Intervention Techniques for Bifurcation Disease: Network Meta-analysis Reveals Superiority of Double-Kissing Crush. *Can J Cardiol.* 2020;36:906-14.

11. Chiabrando JG, Lombardi M, Vescovo GM, Wohlford GF, Koenig RA, Abbate A, Guzmán LA, Berrocal DH, Biondi-Zoccai G. Stenting techniques for coronary bifurcation lesions: Evidence from a network meta-analysis of randomized clinical trials. *Catheter Cardiovasc Interv.* 2021;97:E306-18.

12. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Jüni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferović PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO. 2018 ESC/EACTS Guidelines on myocardial revascularization. *EuroIntervention.* 2019;14:1435-534.

13. Kjøller-Hansen L, Kelbæk H, Christiansen EH, Hansen PR, Engstrøm T, Junker A, Bligaard N, Jeppesen JL, Galløe AM. Predictors of 10-Year Stent-Related Adverse Outcomes after Coronary Drug-Eluting Stent Implantation: The Importance of Stent Size. *Cardiology.* 2021;146:705-12.

14. Lin QF, Luo YK, Lin CG, Peng YF, Zhen XC, Chen LL. Choice of stenting strategy in true coronary artery bifurcation lesions. *Coron Artery Dis.* 2010;21:345-51.

15. Kumsars I, Holm NR, Niemelä M, Erglis A, Kervinen K, Christiansen EH, Maeng M, Dombrovskis A, Abraitis V, Kibarskis A, Trovik T, Latkovskis G, Sondore D, Narbute I, Terkelsen CJ, Eskola M, Romppanen H, Laine M, Jensen LO, Pietila M, Gunnes P, Hebsgaard L, Frobert O, Calais F, Hartikainen J, Aarøe J, Ravkilde J, Engstrøm T, Steigen TK, Thuesen L, Lassen JF; Nordic Baltic bifurcation study group. Randomised comparison of provisional side branch stenting versus a two-stent strategy for treatment of true coronary bifurcation lesions involving a large side branch: The Nordic-Baltic Bifurcation Study IV. *Open Heart.* 2020;7:e000947.

16. Maeng M, Holm NR, Erglis A, Kumsars I, Niemelä M, Kervinen K, Jensen JS, Galløe A, Steigen TK, Wiseth R, Narbute I, Gunnes P, Mannsverk J, Meyerdierks O, Rotevatn S, Nikus K, Vikman S, Ravkilde J, James S, Aarøe J, Ylitalo A, Helqvist S, Sjögren I, Thayssen P, Virtanen K, Puhakka M, Airaksinen J, Christiansen EH, Lassen JF, Thuesen L; Nordic-Baltic Percutaneous Coronary Intervention Study Group. Long-term results after simple versus complex stenting of coronary artery bifurcation lesions: Nordic Bifurcation Study 5-year follow-up results. *J Am Coll Cardiol.* 2013;62:30-4.

17. Kervinen K, Niemelä M, Romppanen H, Erglis A, Kumsars I, Maeng M, Holm NR, Lassen JF, Gunnes P, Stavnes S, Jensen JS, Galløe A, Narbute I, Sondore D, Christiansen EH, Ravkilde J, Steigen TK, Mannsverk J, Thayssen P, Hansen KN, Helqvist S, Vikman S, Wiseth R, Aarøe J, Jokelainen J, Thuesen L; Nordic PCI Study Group. Clinical outcome after crush versus culotte stenting of coronary artery bifurcation lesions: the Nordic Stent Technique Study 36-month follow-up results. *JACC Cardiovasc Interv.* 2013;6:1160-5.

18. Pan M, de Lezo JS, Medina A, Romero M, Segura J, Pavlovic D, Delgado A, Ojeda S, Melián F, Herrador J, Ureña I, Burgos L. Rapamycin-eluting stents for the treatment of bifurcated coronary lesions: a randomized comparison of a simple versus complex strategy. *Am Heart J.* 2004;148:857-64.

19. Kim YH, Lee JH, Roh JH, Ahn JM, Yoon SH, Park DW, Lee JY, Yun SC, Kang SJ, Lee SW, Lee CW, Seung KB, Shin WY, Lee NH, Lee BK, Lee SG, Nam CW, Yoon J, Yang JY, Hyon MS, Lee K, Jang JS, Kim HS, Park SW, Park SJ. Randomized Comparisons Between Different Stenting Approaches for Bifurcation Coronary Lesions With or Without Side Branch Stenosis. *JACC Cardiovasc Interv.* 2015;8: 550-60.

20. Ruiz-Salmerón RJ, Valenzuela LF, Pérez I, Fuentes M, Rodríguez-Leiras S, Vizcaíno M, Carrascosa C, Marcos F. Approach to coronary bifurcation lesions using the everolimus-eluting stent: comparison between a simple strategy and a complex strategy with T-stenting. *Rev Esp Cardiol (Engl Ed).* 2013;66:636-43.

21. Kim J, Lee JM, Park TK, Yang JH, Hahn JY, Choi JH, Choi SH, Seung KB, Hur SH, Rha SW, Kim JH, Choi RK, Oh JH, Kim HS, Lee SH, Park JS, Lee SY, Jeon DW, Jeong MH, Lee JH, Lee SY, Park WJ, Song Y Bin, Gwon HC. Optimal strategy for side branch treatment in patients with left main coronary bifurcation lesions. *Rev Esp Cardiol (Engl Ed).* 2021;74:691-9.

22. Ye F, Zhang JJ, Tian NL, Lin S, Liu ZZ, Kan J, Xu HM, Zhu Z, Chen SL. The acute changes of fractional flow reserve in DK (Double Kissing), crush, and 1-stent technique for true bifurcation lesions. *J Interv Cardiol.* 2010;23:341-5.

23. Zhang L, Zhong W, Luo Y, Chen L. A Pilot Study on Culottes versus Crossover Single Stenting for True Coronary Bifurcation Lesions. *Acta Cardiol Sin.* 2016;32: 450-9.

24. Zheng XW, Zhao DH, Peng HY, Fan Q, Ma Q, Xu ZY, Fan C, Liu LY, Liu JH. Randomized Comparison of the Crush Versus the Culotte Stenting for Coronary Artery Bifurcation Lesions. *Chin Med J (Engl).* 2016;129:505-10.

25. Ye F, Chen SL, Zhang JJ, Zhu ZS, Kan J, Tian NL, Lin S, Liu ZZ, You W, Xu HM, Xu J. Hemodynamic changes of fractional flow reserve after double kissing crush and provisional stenting technique for true bifurcation lesions. *Chin Med J (Engl).* 2012; 125:2658-62.

26. Ferenc M, Ayoub M, Büttner HJ, Gick M, Comberg T, Rothe J, Valina CM, Hochholzer W, Neumann FJ. Long-term outcomes of routine versus provisional T-stenting for de novo coronary bifurcation lesions: five-year results of the Bifurcations Bad Krozingen I study. *EuroIntervention.* 2015;11:856-9.

27. Hildick-Smith D, de Belder AJ, Cooter N, Curzen NP, Clayton TC, Oldroyd KG, Bennett L, Holmberg S, Cotton JM, Glennon PE, Thomas MR, MacCarthy PA, Baumbach A, Mulvihill NT, Henderson RA, Redwood SR, Starkey IR, Stables RH. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British Bifurcation Coronary Study: old, new, and evolving strategies. *Circulation.* 2010;121:1235-43.

28. Ferenc M, Gick M, Comberg T, Rothe J, Valina C, Toma A, Löffelhardt N, Hochholzer W, Riede F, Kienzle RP, Achtari A, Neumann FJ. Culotte stenting vs. TAP stenting for treatment of de-novo coronary bifurcation lesions with the need for side-branch stenting: The Bifurcations Bad Krozingen (BBK) II angiographic trial. *Eur Heart J.* 2016;37:3399-405.

29. Colombo A, Bramucci E, Saccà S, Violini R, Lettieri C, Zanini R, Sheiban I, Paloscia L, Grube E, Schofer J, Bolognese L, Orlandi M, Niccoli G, Latib A, Airoldi F. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: The CACTUS (Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting stents) Study. *Circulation.* 2009;119: 71-8.

30. Chen SL, Kwan TW. Twenty-four-month update on double-kissing crush stenting of bifurcation lesions. *J Interv Cardiol.* 2009;22:121-7.

31. Chen SL, Santoso T, Zhang JJ, Ye F, Xu YW, Fu Q, Kan J, Zhang FF, Zhou Y, Xie DJ, Kwan TW. Clinical Outcome of Double Kissing Crush Versus Provisional Stenting of Coronary Artery Bifurcation Lesions: The 5-Year Follow-Up Results From a Randomized and Multicenter DKCRUSH-II Study (Randomized Study on Double Kissing Crush Technique Versus Provisional Stenting Technique for Coronary Artery Bifurcation Lesions). *Circ Cardiovasc Interv.* 2017;10:e004497.

32. Chen SL, Xu B, Han YL, Sheiban I, Zhang JJ, Ye F, Kwan TW, Paiboon C, Zhou YJ, Lv SZ, Dangas GD, Xu YW, Wen SY, Hong L, Zhang RY, Wang HC, Jiang TM, Wang Y, Sansoto T, Chen F, Yuan ZY, Li WM, Leon MB. Clinical Outcome After DK Crush Versus Culotte Stenting of Distal Left Main Bifurcation Lesions: The 3-Year Follow-Up Results of the DKCRUSH-III Study. *JACC Cardiovasc Interv.* 2015;8:1335-42.

33. Hildick-Smith D, Behan MW, Lassen JF, Chieffo A, Lefèvre T, Stankovic G, Burzotta F, Pan M, Ferenc M, Bennett L, Hovasse T, Spence MS, Oldroyd K, Brunel P, Carrie D, Baumbach A, Maeng M, Skipper N, Louvard Y. The EBC TWO Study (European Bifurcation Coronary TWO): A Randomized Comparison of Provisional T-Stenting Versus a Systematic 2 Stent Culotte Strategy in Large Caliber True Bifurcations. *Circ Cardiovasc Interv.* 2016;9:e003643.

34. Elbadawi A, Shnoda M, Dang A, Gad M, Abdelazeem M, Saad M, Salama A, Sharma A, Gilani S, Latib A, Rab T, Elgendy IY, Abbott JD. Meta-Analysis Comparing Outcomes With Bifurcation Percutaneous Coronary Intervention Techniques. *Am J Cardiol.* 2022;165:37-45.

35. Ford TJ, McCartney P, Corcoran D, Collison D, Hennigan B, McEntegart M, Hildick-Smith D, Oldroyd KG, Berry C. Single- Versus 2-Stent Strategies for Coronary Bifurcation Lesions: A Systematic Review and Meta-Analysis of Randomized Trials With Long-Term Follow-up. *J Am Heart Assoc.* 2018;7:e008730.

36. Di Gioia G, Sonck J, Ferenc M, Chen SL, Colaiori I, Gallinoro E, Mizukami T, Kodeboina M, Nagumo S, Franco D, Bartunek J, Vanderheyden M, Wyffels E, De Bruyne B, Lassen JF, Bennett J, Vassilev D, Serruys PW, Stankovic G, Louvard Y, Barbato E, Collet C. Clinical Outcomes Following Coronary Bifurcation PCI Techniques: A Systematic Review and Network Meta-Analysis Comprising 5,711 Patients. *JACC Cardiovasc Interv.* 2020;13:1432-44.

37. Lunardi M, Louvard Y, Lefèvre T, Stankovic G, Burzotta F, Kassab GS, Lassen JF, Darremont O, Garg S, Koo B-K, Holm NR, Johnson TW, Pan M, Chatzizisis YS,

Banning AP, Chieffo A, Dudek D, Hildick-Smith D, Garot J, Henry TD, Dangas G, Stone G, Krucoff MW, Cutlip D, Mehran R, Wijns W, Sharif F, Serruys PW, Onuma Y. Definitions and Standardized Endpoints for Treatment of Coronary Bifurcations. *EuroIntervention.* 2022 May 18. [Epub ahead of print].

Supplementary data

Supplementary Table 1. PRISMA NMA Checklist of items to include when reporting a systematic review involving a network meta-analysis.

Supplementary Table 2. Search strategies.

Supplementary Table 3. Definitions of endpoints of included trials.

Supplementary Table 4. Clinical characteristics of patients in included trials, stratified by randomisation arms.

Supplementary Table 5. Angiographic and procedural characteristics of patients in included trials, stratified by randomisation arms.

Supplementary Table 6. The number of patients and event rate according to bifurcation stenting technique in randomised controlled trials included in network meta-analysis.

Supplementary Table 7. Comparison of direct and indirect treatment estimates using "netsplit."

Supplementary Figure 1. Results of risk of bias assessment.

Supplementary Figure 2. Forest plots presenting results of the pairwise meta-analysis for secondary outcomes of interest.

Supplementary Figure 3. Colour-enhanced funnel plots for pairwise meta-analysis.

Supplementary Figure 4. Forest plots presenting results of the sensitivity analysis of trials enrolling only patients with true bifurcations.

Supplementary Figure 5. Forest plots presenting results of the sensitivity analysis after excluding trials with a high risk of bias.

Supplementary Figure 6. Forest plots presenting results of the sensitivity analysis after excluding trials utilising first-generation drug-eluting stents.

Supplementary Figure 7. Forest plots presenting results of the sensitivity analysis after excluding trials without proximal optimisation technique.

Supplementary Figure 8. Forest plots presenting results of the sensitivity analysis, including trials evaluating left main bifurcations.

Supplementary Figure 9. Forest plots presenting results of the sensitivity analysis of time-to-event data.

Supplementary Figure 10. Bubble plots showing the results of meta-regression evaluating the effect of provisional stenting versus 2-stent technique with the mean side branch lesion length as a covariate.

Supplementary Figure 11. Bubble plots showing the results of meta-regression evaluating the effect of provisional stenting versus 2-stent technique with the publication year as a covariate.

Supplementary Figure 12. Bubble plots showing the results of meta-regression evaluating the effect of provisional stenting versus 2-stent technique with the follow-up duration as a covariate.

Supplementary Figure 13. "Comparison-adjusted" funnel plots.

Supplementary Figure 14. League table showing the results of network meta-analysis after excluding trials with a high risk of bias.

Supplementary Figure 15. P-scores in the network meta-analysis after excluding trials with a high risk of bias.

Supplementary Figure 16. League table showing the network meta-analysis results after excluding trials allowing multiple bifurcation stenting techniques in the 2-stent arm.

Supplementary Figure 17. P-scores in the network meta-analysis after excluding trials allowing multiple bifurcation stenting techniques in the 2-stent arm.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-23-00013

Supplementary data

Supplementary Table 1. PRISMA NMA Checklist of items to include when reporting a systematic review involving a network meta-analysis.

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	4

Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary materials
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	27
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	7
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or	7-8

		outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	7
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	7-8
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	7-8
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	7-8
RESULTS†			

Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, 27
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	30-32
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	9-10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	9-10
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	10, 33-39
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	9-10, supplementary materials
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	9-10, supplementary materials
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, *alternative network*	

		geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	15

Abrreviations: PICOS = population, intervention, comparators, outcomes, study design.

Supplementary Table 2. Search strategies.

Database	Queries
Pubmed	Random* AND bifurcation AND (stenting OR PCI OR percutaneous coronary intervention)
Scopus	TITLE-ABS-KEY (random* AND bifurcation AND (stenting OR pci OR (percutaneous AND coronary AND intervention)))

Supplementary Table 3. Definitions of endpoints of included trials.

Study	MACE	Cardiac death	Myocardial infarction	TLR	Stent thrombosis
BBC ONE 2010	All-cause death, MI, TVF	NA	Typical rise and fall of biochemical markers of myocardial necrosis with ischemic symptoms or ECG changes as per European Society of Cardiology/American College of Cardiology guidelines. For patients in the first 24 hours after PCI, CK ≥3 times the upper limit of normal was taken as the cutoff point for the diagnosis of myocardial infarction. For patients who already had a diagnosis of myocardial infarction on the current admission, CK rise to ≥50% of the previous value was used.	ND	ARC criteria (definite ST)
BBK I 2015	All-cause death, MI, TLR	NA	The presence of new Q waves in two or more contiguous electrocardiographic leads or an elevation of creatine kinase or its MB isoenzyme to at least three times the upper limit of normal in two samples during hospitalization. After discharge, the diagnosis of myocardial infarction was made according to the European Society of Cardiology/American College of Cardiology consensus document and based on new rise in troponin T ≥0.03 mg/L associated with either typical symptoms and/or typical ECG changes and/or typical angiographic findings.	Coronary artery bypass surgery or repeat percutaneous angioplasty involving the stented segment and performed for symptoms or signs of ischaemia in the presence of angiographic restenosis.	ARC criteria (definite/probable ST)
BBK II 2016	Cardiac death, TVMI, TLR	ND	The presence of new Q waves in two or more contiguous electrocardiographic leads or an elevation of creatine kinase or its MB isoenzyme to at least three times the upper limit of normal in two samples during hospitalization. After discharge, the diagnosis of myocardial infarction was made according to the European Society of Cardiology/American College of Cardiology consensus document and based on new rise in troponin T ≥0.03 mg/L associated with either typical symptoms and/or typical ECG changes and/or typical angiographic findings.	Coronary artery bypass surgery or repeat PCI involving the stented segment and performed for symptoms or signs of ischemia in the presence of angiographic restenosis or for high grade (>70%) angiographic restenosis irrespective of the clinical presentation.	ARC criteria (definite/probable ST)

CACTUS 2009	Cardiac death, Q-wave or non–Q-wave, MI, TVR	ND	Q-wave MI was defined as the development of new, pathological Q waves in 2 or more contiguous leads with postprocedure CK or CK-MB levels above normal. Non–Q-wave MI was defined as an elevation of postprocedural CK levels 2 times normal levels with elevated CK-MB in the absence of pathological Q waves.	ND	ARC criteria (definite ST)
Colombo et al., 2004	Presence of cardiac death, Q-wave or non–Q-wave MI, or TVR.	NA	ND	Repeat revascularization driven by symptoms or laboratory testing and a stenosis 50% within the treated vessel on follow-up angiography.	Defined as any of the following: angiographic demonstration of stent closure or intrastent thrombus, unexplained sudden death, or MI occurring within 30 days of stent implantation and without concomitant documentation of a patent stent.
DEFINITIO N II 2022	Cardiac death, TVMI, or clinically driven TLR.	Any death without a clear non-cardiac cause.	Peri-procedural MI (within 48 h) was defined as a CK-MB >10 the upper reference limit (URL) of the assay, or >5 URL plus either: (i) new pathological Q waves in >_2 contiguous leads or new left bundle branch abnormality; (ii) angiographically documented graft or coronary artery occlusion or new severe stenosis with thrombosis; (iii) imaging evidence of new loss of viable myocardium; or (iv) new regional wall motion abnormality. Spontaneous MI (after 48 h) was defined as a clinical syndrome consistent with MI with a CK-MB or troponin >1 URL and new ST-segment elevation or depression or other findings as above. All MIs were considered TVMI unless there was clear evidence that they were attributable to a non-target vessel.	Angina or ischaemia (confirmed by symptoms, exercised EKG or nuclear medicine or coronary physiological assessment) referable to the target lesion requiring repeat PCI or coronary artery bypass graft.	ARC criteria (definite/probable ST)
DKCRUSH-1 2009	Cardiac death, MI, TLR by either PCI or CABG.	ND	Creatine kinase-MB (CK-MB) enzyme elevation ≥ 3 times the upper limit of the normal value, either with (Q wave MI) or without (non-Q wave MI), and new Q waves in at least two contiguous leads on electrocardiogram.	Repeat revascularization with a diameter stenosis ≥ 50% within the stent or in the 5 mm distal or proximal	Acute coronary syndrome with angiographic documentation of either vessel occlusion or thrombus within or

				segments adjacent to the stent.	adjacent to a previously successfully implanted stent, or in the absence of angiographic confirmation, either acute MI in the distribution of the treated vessel or death not clearly attributable to other causes.
DKCRUSH-II 2017	Cardiac death, MI, TVR	All deaths were considered as cardiac in origin unless non-cardiac reasons were indicated.	Plasma level of creatine kinase (CK)-MB and troponin I/T increased to >3× the upper normal limit in no fewer than 2 blood samples.	Any repeat revascularization (PCI or CABG) for target lesions in the presence of symptoms or objective signs of ischemia.	ARC criteria (definite/probable ST)
DKCRUSH-III 2015	Cardiac death, MI, TVR	All deaths were considered as cardiac in origin unless non-cardiac reasons were indicated.	Plasma level of creatine kinase (CK)-MB and troponin I/T increased to >3× the upper normal limit in no fewer than 2 blood samples.	Any repeat revascularization (PCI or CABG) for target lesions in the presence of symptoms or objective signs of ischemia.	ARC criteria (definite/probable ST)
DKCRUSH-V 2019	TLF: Cardiac death, TVMI, or clinically driven TLR.	Any death without a clear non-cardiac cause.	Periprocedural MI was defined as creatine kinase-myocardial band >10x the upper reference limit of the assay, or >5× upper reference limit plus: 1) new pathological Q waves in >2 contiguous leads or new left bundle branch block; 2) angiographically documented graft or coronary artery occlusion or new severe stenosis with thrombosis; or 3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. Spontaneous MI (after 72 h) was defined as a clinical syndrome consistent with MI with creatine kinase-myocardial band or troponin >1× upper reference limit and new ST-segment elevation or depression or other findings as previously mentioned.	Angina or ischemia referable to the target lesion requiring repeat PCI or CABG.	ARC criteria (definite/probable ST)
EBC MAIN 2021	All-cause death, MI, TLR	NA	The Universal Definition of Myocardial Infarction (Revision 2013) was used, except for the category of PCI-related myocardial infarction (Type 4a) or	If either main vessel or side vessel requires or undergoes attempted repeat	ARC criteria (definite/probable ST)

			coronary artery bypass graft-related myocardial infarction (Type 5), which were based on the expert consensus definition from Society for Cardiovascular Angiography and Interventions (SCAI). Therefore, in patients who are stable on admission, the peak biomarker measured post-PCI will need to rise to 10x the local laboratory upper limit of normal (ULN) for CK [5× with new persistent left bundle branch block (LBBB) or Q waves] or 70× the local laboratory ULN for troponin (35× with new persistent LBBB or Q waves). In patients with an acute coronary presentation and raised biomarkers on admission, the peak biomarker measured post-PCI will need to rise to an absolute increase of 10x the local laboratory ULN for CK (5× with persistent LBBB or Q waves) or an absolute increase of 70× the local laboratory ULN for troponin (35× with persistent LBBB or Q-waves).	revascularization with either balloon angioplasty, stenting, or coronary artery bypass grafting, within the previous treated vessel area (balloon or stent) or within 5mm adjacent to this area.	
EBC TWO 2016	All-cause death, MI, TVR	NA	Typical rise and fall of biochemical markers of myocardial necrosis with ischemic symptoms or ECG changes as per European Society of Cardiology/ American College of Cardiology guidelines. Periprocedural MI is arbitrarily defined by the elevation of cTn values (>5×99th percentile URL) in patients with normal baseline values (≤99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (1) symptoms suggestive of myocardial ischemia, (2) new ischemic ECG changes, or (3) angiographic findings consistent with a procedural complication or (4) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.	NA	ARC criteria (definite/probable ST)
Lin et al., 2010	Cardiac death, MI, TVR, stent thrombosis	ND	Procedure-related MI was considered if CK-MB or troponin-I increased to more than three times the upper limit of normal (ULN). In the absence of a new Q wave, CK-MB at least 3 × ULN was	Repeat revascularization with stenosis diameter (SD) at least 50% within the stent or in the adjacent segments	ARC criteria (definite/probable ST)

			defined as a non-Q wave MI. Development of a new Q wave in two or more contiguous electrocardiogram leads, with CK-MB at least 3 × ULN, was defined as a new Q wave infarction.	5mm distally or proximally to the stent. If separate stents were placed at either end of a target lesion, this counted as two interventions.	
NBBS IV 2020	Cardiac death, non-procedural M, clinically indicated TLR and definite stent thrombosis.	Death from coronary artery disease including myocardial infarction, sudden death with a possible or definite cardia cause, death from heart failure including cardiogenic shock, and death related to a cardiac procedure within 28 days from the procedure. Cardiac death did not include death due to pulmonary embolism, cerebrovascular attacks or other vascular but non-cardiac events.	Non-procedural myocardial infarction required evidence of myocardial necrosis by at least one of the following criteria: (1) detection of a rise and/ or fall of cardiac biomarkers with at least one value above the 99th percentile of the upper reference limit (URL) and evidence of ischaemia in the myocardium documented by either symptoms of ischaemia, ECG changes indicative of acute ischaemia (new ST-T changes, new left bundle branch block (LBBB), new pathological Q waves in the ECG), evidence of new loss of viable myocardium or new cardiac wall motion abnormality. (2) Sudden and unexpected cardiac death with at least one of the following: cardiac arrest, symptoms suggestive of myocardial ischaemia, presumably new ST-segment elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy. (3) Pathological findings suggestive of acute myocardial infarction.	Target lesion revascularisation was defined as repeat revascularisation by percutaneous coronary intervention (PCI) or coronary artery bypass surgery of the target lesion defined as the stented or balloon-treated segments and their 5 mm margins in all three coronary branches.	ARC criteria (definite/probable ST)
NBS 2013	Cardiac death, non–percutaneous coronary intervention (PCI)-related myocardial	ND	Non–Q-wave myocardial infarction was defined as a CK-MB mass or troponin-T/troponin-I increase to ≥3 times the upper limit of normal combined with clinical signs of myocardial infarction, in the absence of pathological Q waves and not related to an interventional procedure. Q-wave myocardial infarction was defined as development of new	Repeat revascularization by PCI or surgery of the target lesion.	Angiographically documented contrast filling defect of the target lesion in the presence of an acute coronary syndrome.

	infarction (MI), target vessel revascularizatio n (TVR), and stent thrombosis (ST).		pathological Q waves in 2 or more contiguous leads together with clinical signs of myocardial infarction (chest pain or increase in myocardial injury markers).		
NSTS 2013	Cardiac death, MI not related to percutaneous coronary intervention, TVR.	Death was considered cardiac unless other cause documented.	Nonprocedure-related MI, a rise of biochemical markers exceeding the decision limit of myocardial infarction (above the 99th percentile) for a reference population provided an coefficient of variation of <10%) with at least one of the following: (1) ischemic symtomps; (2) ECG changes indicative of ischemia (ST segment elevation or depression; (3) development of pathological Q-wave; and (4) no relation to a PCI procedure.	Repeated revascularization by PCI or surgery of the target lesion.	ARC criteria (definite/probable/possibl e ST)
Pan et al., 2004	Cardiac death, MI, TLR	NA	ND	ND	NA
PERFECT 2015	All-cause death, MI, TVR	Deaths were considered cardiac unless an unequivocal, non-cardiac cause was established.	MI was defined as an increase in creatine kinase-myocardial band concentration to >3× the upper limit of the normal range, with ischemic symptoms or new ischemic electrocardiographic changes.	Repeat revascularization with PCI or coronary artery bypass surgery for restenosis of the entire segment involving the implanted stent and within 5 mm of the distal and proximal margins of the stent.	ND
Ruiz-Salmerón et al., 2013	Cardiac death, MI, TVR	ND	Hospital admission with a diagnosis of acute coronary syndrome with or without ST segment elevation.	NA	ARC criteria (definite/probable ST)
SMART-STRATEGY II 2021	Cardiac death, MI, TLR	All deaths were considered cardiac unless a definite non-cardiac cause could be established.	Elevated cardiac enzymes (troponin or the myocardial band fraction of creatine kinase) greater than the upper limit of normal that occurred with ischemia symptoms or electrocardiogram findings indicative of ischemia that were unrelated to the index procedure. Procedure-related myocardial infarction was defined as an elevated myocardial band fraction of creatine kinase more than 3 times above the upper	Repeat PCI of the lesion within 5 mm of stent deployment	ARC criteria (definite/probable ST)

			limit of normal within 48 hours of the index procedure.		
Ye et al., 2010	Cardiac death, MI, TVR	All deaths were considered to be of cardiac origin unless otherwise documented	A non-Q-wave MI was defined as a rise of creatinine kinase-MB concentration to three times the upper limit of normal in the absence of pathological Q waves.	Repeat revascularization for a stenosis greater than 50% in the target lesion of either theMB or SB.	NA
Ye et al., 2012	Cardiac death, MI, clinical-driven TVR	All deaths were regarded as being of cardiac origin unless otherwise documented.	A non-Q wave myocardial infarction was defined as a creatine kinase (CK)-MB concentration increase three times the upper limit of the normal value in the absence of pathological Q waves.	Repeat revascularization with a stenosis >50% in the target lesion in either the MV or SB.	ND
Zhang et al., 2016	Cardiac death, MI, TVR and ST	ND	Non-Q-wave MI was defined as a CK-MB or cTnT/cTnI that had increased to ≥ 3 times the upper limit of the normal range combined with clinical signs of myocardial infarction (MI), without new onset of pathological Q waves. Q-wave MI was defined as new development of pathological Q waves in two contiguous leads, together with clinical signs of MI (chest pain or increase in myocardial injury markers)	Repeat target lesion therapy either by PCI or by surgery.	ARC criteria
Zheng et al., 2016	Cardiac death, MI, ST, and/or TVR	ARC definition	ARC definition	ND	ARC definition

Abbreviations: ARC = Academic Research Consortium; CABG = coronary artery bypass grafting; NA = not applicable; ND = no data; MI = myocardial infarction; TLR = target lesion revascularization; TVR = target vessel revascularization; ST = stent thrombosis.

Supplementary Table 4. Clinical characteristics of patients in included trials, stratified by randomisation arms.

Study	Comparison	Age, years, mean (SD)	Sex, male, n (%)	Diabetes, n (%)	Smoking, n (%)	Hypertension, n (%)	Previous MI, n (%)	Previous PCI, n (%)	LVEF, %, mean (SD)	ACS, n (%)
BBC ONE 2010	Provisional vs. 2-stent	64 (10); 64 (11)	192 (77); 193 (77)	31 (13); 28 (11)	42 (17); 43 (17)	142 (57); 154 (62)	57 (23); 63 (25)	42 (17); 40 (16)	ND (ND); ND (ND)	79 (31); 89 (35)
BBK I 2015	Provisional vs. T-stenting	66.7 (9.2); 66.9 (10.5)	80 (79.4); 79 (78.2)	26 (25.7); 19 (18.8)	10 (9.9); 14 (13.9)	93 (92.1); 90 (89.1)	19 (18.8); 21 (20.8)	45 (44.6); 52 (51.5)	59 (12); 61 (12)	0 (0); 0 (0)
BBK II 2016	Culotte vs. TAP	66.3 (10.6); 69.1 (10.3)	107 (71.3); 114 (76)	41 (27.3); 42 (28)	17 (11.3); 17 (11.3)	132 (88); 128 (85.3)	24 (16); 32 (21.3)	57 (38); 48 (32)	56 (7.3); 57 (6)	32 (21.3); 29 (19.3)
CACTUS 2009	Crush vs. Provisional	65 (10); 67 (10)	142 (80.2); 132 (76.3)	42 (23.7); 38 (22)	36 (20.3); 29 (16.8)	125 (70.6); 138 (79.8)	79 (44.6); 61 (35.3)	55 (31.1); 46 (26.6)	ND (ND); ND (ND)	78 (44); 63 (47.4)
Colombo et al. 2004	2-stent vs. Provisional	63 (10); 62 (9)	48 (76); 21 (91)	13 (21); 6 (26)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	59 (10); 59 (9)	11 (17); 4 (17)
DEFINITION II 2022	2-stent vs. Provisional	63 (11); 64 (10)	255 (77.7); 250 (76.9)	112 (34.1); 116 (35.7)	93 (28.4); 98 (30.2)	215 (66.2); 230 (70.1)	39 (11.9); 42 (12.9)	65 (19.8); 54 (16.6)	59 (10); 60 (10)	232 (70.8); 237 (73)
DKCRUSH-1 2009	Crush vs. DK-crush	63.9 (8.6); 63.8 (9.2)	ND (70); ND (76.2)	ND (8.4); ND (27)	ND (62.6); ND (63.8)	ND (76.6); ND (76.2)	ND (12.1); ND (8.6)	ND (11.2); ND (11.5)	62.7 (13.2); 61.6 (11.2)	ND (70.1); ND (69.5)

DKCRUSH-II 2017	DK-crush vs. Provisional	63.9 (11.1); 64.6 (9.9)	146 (78.9); 141 (76.2)	36 (19.5); 44 (23.8)	57 (30.8); 44 (23.8)	121 (65.4); 112 (60.5)	32 (17.3); 26 (14.1)	39 (21.1); 38 (20.5)	ND (ND); ND (ND)	153 (82.7); 157 (84.9)
DKCRUSH-III 2015	DK-crush vs. Culotte	64.3 (10.3); 63.3 (9.2)	162 (77.1); 167 (79.9)	67 (31.9); 63 (30.1)	58 (27.6); 54 (25.8)	148 (70.5); 128 (61.2)	32 (15.2); 29 (13.9)	47 (22.4); 31 (14.8)	ND (ND); ND (ND)	165 (78.6); 174 (83.3)
DKCRUSH-V 2019	Provisional vs. DK-crush	64 (10); 65 (9)	188 (77.7); 199 (82.9)	62 (25.6); 69 (28.8)	78 (32.2); 82 (34.2)	156 (64.5); 175 (72.9)	51 (21.1); 52 (21.7)	43 (17.8); 33 (13.8)	60 (9); 59 (9)	206 (85.1); 199 (82.9)
EBC MAIN 2021	Provisional vs. 2-stent	70.8 (10.1); 71.4 (9.8)	182 (79); 177 (74)	66 (29); 62 (27)	36 (16); 30 (13)	180 (79); 190 (82)	60 (26); 62 (27)	93 (41); 99 (43)	ND (ND); ND (ND)	78 (33); 93 (40)
EBC TWO 2016	Provisional vs. Culotte	62.9 (10.8); 63.5 (12.1)	87 (85); 76 (78)	26 (25); 30 (31)	58 (56); 49 (50)	65 (63); 66 (68)	40 (39); 40 (41)	41 (40); 40 (41)	ND (ND); ND (ND)	32 (31); 31 (32)
Lin et al., 2010	Provisional vs. 2-stent	60.6 (7.5); 59.2 (7.2)	45 (83.3); 41 (75.9)	10 (18.5); 7 (13)	16 (29.6); 13 (24.1)	49 (90.7); 45 (83.3)	12 (22.2); 10 (18.5)	13 (24.1); 13 (24.1)	55.63 (6.37); 57.11 (5.87)	23 (42.6); 22 (40.7)
NBBS IV 2020	Provisional vs. 2-stent	64 (12); 63 (11)	ND (ND); ND (ND)	36 (16.5); 35 (15.4)	41 (18.9); 48 (21.1)	152 (70); 149 (65.6)	ND (ND); ND (ND)	77 (35.5); 76 (33.5)	57 (6); 56 (7)	28 (12.9); 38 (16.7)
NBS 2013	Provisional vs. 2-stent	63 (10); 63 (10)	ND (76); ND (78)	ND (13); ND (12)	ND (ND); ND (ND)	ND (54); ND (58)	ND (ND); ND (ND)	ND (25); ND (25)	ND (ND); ND (ND)	ND (32); ND (34)

NSTS 2013	Crush vs. Culotte	65 (10); 65 (11)	149 (71); 154 (71)	28 (13); 31 (15)	42 (20); 58 (27)	130 (62); 129 (60)	ND (ND); ND (ND)	84 (40); 72 (34)	57 (11); 57 (12)	43 (21); 54 (26)
Pan et al., 2004	Provisional vs. T-stenting	61 (10); 58 (11)	34 (72); 38 (86)	20 (42); 17 (39)	18 (38); 23 (52)	28 (59); 25 (57)	9 (19); 17 (39)	ND (ND); ND (ND)	60 (11); 55 (11)	42 (89); 38 (86)
PERFECT 2015	Crush vs. Provisional	60.9 (8.9); 61.8 (8.8)	160 (75.1); 155 (75.2)	55 (25.8); 60 (29.1)	54 (25.4); 67 (32.5)	118 (55.4); 114 (55.4)	9 (4.2); 9 (4.4)	20 (9.4); 11 (5.3)	60.4 (6.8); 59.5 (7.2)	82 (38.7); 78 (38)
Ruiz-Salmerón et al., 2013	Provisional vs. T-stenting	63.4 (13); 63.6 (13.1)	28 (85); 28 (78)	15 (45); 12 (33)	20 (61); 18 (50)	22 (67); 26 (72)	ND (ND); ND (ND)	7 (21); 9 (25)	ND (ND); ND (ND)	0 (0); 0 (0)
SMART-STRATEGY II 2021	Provisional vs. 2-stent	65.5 (8.7); 66.3 (10.6)	15 (65.2); 16 (69.6)	10 (43.5); 11 (47.8)	6 (26.1); 5 (21.7)	18 (78.3); 17 (73.9)	1 (4.3); 2 (8.7)	5 (21.7); 4 (17.4)	59.1 (10.9); 61.5 (9.3)	ND (ND); ND (ND)
Ye et al., 2010	DK-crush vs. Provisional	63.6 (11.5); 63.2 (9.9)	ND (64); ND (73.1)	ND (16); ND (19.2)	ND (ND); ND (ND)	ND (76); ND (73.1)	ND (ND); ND (ND)	ND (ND); ND (ND)	59.2 (9.9); 57.2 (10.1)	ND (96); ND (76.9)
Ye et al., 2012	DK-crush vs. Provisional	63.5 (10.5); 61.7 (9.4)	24 (63.2); 23 (76.7)	7 (18.4); 4 (13.3)	ND (ND); ND (ND)	29 (76.3); 20 (66.7)	4 (10.5); 2 (6.7)	ND (ND); ND (ND)	61.5 (9.8); 64.4 (5.8)	27 (71.1); 19 (63.3)
Zhang et al., 2016	Provisional vs. Culotte	64.5 (10.7); 64.2 (7.3)	48 (92.3); 43 (82.7)	10 (19.2); 11 (21.2)	31 (59.6); 27 (51.9)	35 (67.3); 33 (63.5)	12 (23.1); 10 (19.2)	13 (25); 12 (23.1)	ND (ND); ND (ND)	37 (71.2); 32 (61.5)

Zheng et al., 2016	Crush vs. Culotte	63.8 (8); 64 (9)	109 (72.7); 111 (74)	33 (22); 37 (24.7)	58 (38.7); 67 (44.7)	106 (70.7); 109 (72.7)	ND (ND); ND (ND)	40 (26.7); 34 (22.7)	ND (ND); ND (ND)	124 (82.7); 129 (86)

Abbreviations: ACS = acute coronary syndrome; MI = myocardial infarction; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; other - see Table 1.

Supplementary Table 5. Angiographic and procedural characteristics of patients in included trials, stratified by randomisation arms.

Study	Comparision	Bifurcation LM, n (%)	Bifurcation LAD/D, n (%)	Bifurcation Cx/OM, n (%)	Bifurcation RCA, n (%)	True bifurcation, n (%)	Medina 1.1.1, n (%)	Medina 1.0.1, n (%)	Medina 0.1.1, n (%)	SB lesion lenght, mm, mean (SD)	FKB, n (%)	Imaging-guided PCI, n (%)	Procedural success, n (%)
BBC ONE 2010	Provisional vs. 2-stent	0 (0); 0 (0)	201 (81); 209 (84)	35 (14); 28 (11)	9 (4); 12 (5)	202 (81); 209 (84)	150 (60); 149 (60)	19 (8); 26 (10)	33 (13); 34 (14)	ND (ND); ND (ND)	72 (29); 189 (76)	ND (ND); ND (ND)	235 (94); 234 (94)
BBK I 2015	Provisional vs. T-stenting	0 (0); 0 (0)	76 (75.2); 74 (73.3)	16 (15.8); 21 (20.8)	9 (8.9); 6 (5.9)	69 (68.3); 69 (68.3)	36 (35.6); 31 (30.7)	8 (7.9); 6 (5.9)	25 (24.8); 32 (31.7)	10.4 (4.1); 9.9 (4.2)	101 (100); 101 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)
BBK II 2016	Culotte vs. TAP	28 (18.7); 23 (15.3)	82 (54.7); 83 (55.3)	36 (24); 38 (25.3)	4 (2.7); 6 (4)	147 (98); 143 (95.3)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	13.8 (6.6); 15.5 (6.9)	150 (100); 150 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)
CACTUS 2009	Crush vs. Provisional	0 (0); 0 (0)	131 (74); 121 (70)	34 (19); 43 (25)	12 (7); 9 (5)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	5.9 (4.7); 5.7 (4.2)	163 (92.1); 156 (90.2)	6 (3.4); 7 (4.1)	ND (90.4); ND (91.3)
Colombo et al. 2004	2-stent vs. Provisional	0 (0); 0 (0)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	63 (100); 22 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	5.5 (4.1); 5.1 (4.4)	57 (90.5); 18 (81.8)	22 (100); 63 (100); (after PCI)	58 (92.2); 17 (77.3)
DEFINITION II 2022	2-stent vs. Provisional	94 (28.7); 94 (28.9)	205 (62.5); 197 (60.6)	17 (5.2); 25 (7.7)	12 (3.7); 9 (2.8)	328 (100); 325 (100)	283 (86.3); 268 (82.5)	ND (ND); ND (ND)	41 (12.5); 47 (14.5)	20.7 (10.1); 19.9 (9.3)	287 (99.3); 83 (27.8)	80 (24.4); 101 (31.1)	323 (98.5); 321 (98.8)
DKCRUSH-1 2009	Crush vs. DK-crush	ND (15.9); ND (15.3)	ND (61.7); ND (65.7)	ND (14); ND (11.3)	ND (8.4); ND (7.6)	156 (100); 155 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	10.5 (7.5); 10.3 (6.3)	ND (76); ND (100)	ND (ND); ND (ND)	ND (91.1); ND (96.1)
DKCRUSH-II 2017	DK-crush vs. Provisional	33 (17.8); 29 (15.7)	112 (60.5); 110 (59.5)	23 (12.4); 30 (16.2)	17 (9.2); 16 (8.6)	185 (100); 185 (100)	155 (83.8); 144 (77.8)	0 (0); 0 (0)	30 (16.2); 41 (22.2)	15.4 (11.3); 14.9 (12.5)	185 (100); 147 (79.5)	85 (45.9); 88 (47.6)	179 (96.8); 173 (93.5)
DKCRUSH-III 2015	DK-crush vs. Culotte	210 (100); 209 (100)	0 (0); 0 (0)	0 (0); 0 (0)	0 (0); 0 (0)	210 (100); 209 (100)	207 (98.7); 198 (94.8)	0 (0); 0 (0)	3 (1.3); 11 (5.2)	16.5 (11.1); 17 (13)	209 (99.5); 208 (99.5)	145 (69); 154 (73.7)	203 (96.7); 201 (96.2)
DKCRUSH-V 2019	Provisional vs. DK-crush	242 (100); 240 (100)	0 (0); 0 (0)	0 (0); 0 (0)	0 (0); 0 (0)	242 (100); 240 (100)	190 (78.5); 204 (85)	0 (0); 0 (0)	52 (21.5); 36 (15)	16.6 (11.9); 16.2 (14)	191 (78.9); 239 (99.6)	98 (40.5); 103 (42.9)	ND (ND); ND (ND)
EBC MAIN 2021	Provisional vs. 2-stent	230 (100); 237 (100)	0 (0); 0 (0)	0 (0); 0 (0)	0 (0); 0 (0)	230 (100); 237 (100)	204 (90); 206 (89)	0 (0); 0 (0)	23 (10); 25 (11)	5.8 (4); 7.9 (5.7)	202 (89); 217 (93)	92 (40); 88 (38)	224 (97); 219 (92)
EBC TWO 2016	Provisional vs. Culotte	0 (0); 0 (0)	80 (78); 75 (77)	16 (15); 18 (19)	6 (6); 4 (4)	103 (100); 97 (100)	83 (81); 66 (68)	6 (6); 7 (7)	12 (12); 23 (24)	9.7 (7.1); 10.8 (7.3)	97 (94); 93 (96)	ND (ND); ND (ND)	100 (97); 95 (98)

Lin et al., 2010	Provisional vs. 2-stent	0 (0); 0 (0)	45 (83.3); 43 (79.6)	5 (9.3); 6 (11.1)	4 (7.4); 5 (9.3)	54 (100); 54 (100)	26 (48.1); 23 (42.6)	9 (16.7); 13 (24.1)	19 (35.2); 18 (33.3)	12.91 (3.12); 12.69 (2.75)	51 (94.4); 49 (90.7)	ND (ND); ND (ND)	ND (ND); ND (ND)
NBBS IV 2020	Provisional vs. 2-stent	6 (2.7); 3 (1.3)	161 (74.2); 174 (76.6)	36 (16.6); 40 (17.6)	14 (6.5); 9 (4)	221 (100); 229 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	6.4 (4.1); 7.7 (4.9)	79 (36.1); 208 (91.2)	ND (ND); ND (ND)	ND (ND); ND (ND)
NBS 2013	Provisional vs. 2-stent	ND (2); ND (1)	ND (73); ND (74)	ND (17); ND (18)	ND (7); ND (6)	ND (77); ND (67)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	6.0 (4.8); 6.4 (4.7)	ND (32); ND (74)	ND (ND); ND (ND)	ND (97); ND (94)
NSTS 2013	Crush vs. Culotte	20 (10); 21 (10)	132 (63); 142 (66)	42 (20); 43 (20)	15 (7); 9 (4)	153 (73); 177 (82)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	7.3 (5.8); 7.5 (6)	177 (85); 197 (92)	ND (ND); ND (ND)	205 (98); 210 (98)
Pan et al., 2004	Provisional vs. T-stenting	3 (6); 2 (5)	33 (71); 33 (75)	8 (17); 6 (13)	3 (6); 3 (7)	47 (100); 44 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	28 (60); 34 (77)	ND (ND); ND (ND)	44 (94); 43 (97)
PERFECT 2015	Crush vs. Provisional	0 (0); 0 (0)	200 (93.9); 190 (92.2)	10 (4.7); 15 (7.3)	3 (1.4); 1 (0.5)	194 (93.4); 169 (83.7)	137 (65.9); 126 (62.4)	18 (8.7); 18 (8.9)	39 (18.8); 25 (12.4)	10.3 (8.2); 8.3 (7.3)	204 (95.8); 163 (79.1)	204 (95.8); 197 (95.6)	ND (ND); ND (ND)
Ruiz-Salmerón et al., 2013	Provisional vs. T-stenting	0 (0); 0 (0)	24 (71); 26 (72)	9 (26); 6 (17)	1 (3); 4 (11)	27 (79.4); 33 (91.7)	24 (70.6); 29 (80.6)	3 (8.8); 3 (8.3)	0 (0); 1 (2.8)	ND (ND); ND (ND)	14 (42); 23 (64)	ND (ND); ND (ND)	34 (100); 34 (94)
SMART-STRATEGY II 2021	Provisional vs. 2-stent	23 (100); 23 (100)	0 (0); 0 (0)	0 (0); 0 (0)	0 (0); 0 (0)	23 (100); 23 (100)	16 (69.6); 19 (82.6)	3 (13); 4 (17.4)	4 (17.4); 0 (0)	ND (ND); ND (ND)	16 (69.9); 22 (95.7)	21 (91.3); 23 (100)	ND (ND); ND (ND)
Ye et al., 2010	DK-crush vs. Provisional	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	25 (100); 26 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	17.1 (8); 11.5 (6.9)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)
Ye et al., 2012	DK-crush vs. Provisional	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	38 (100); 35 (100)	ND (ND); ND (ND)	ND (ND); ND (ND)	ND (ND); ND (ND)	16.87 (8.17); 10.24 (8.4)	38 (100); 26 (86.7)	ND (ND); ND (ND)	ND (ND); ND (ND)
Zhang et al., 2016	Provisional vs. Culotte	16 (30.8); 14 (26.9)	33 (63.5); 34 (65.4)	3 (5.8); 2 (3.8)	0 (0); 2 (3.8)	52 (100); 52 (100)	30 (57.7); 34 (65.4)	6 (11.5); 7 (13.5)	16 (30.8); 11 (21.2)	12.8 (4.92); 14.1 (7.12)	43 (82.7); 48 (92.3)	ND (ND); ND (ND)	48 (92.3); 51 (98.1)
Zheng et al., 2016	Crush vs. Culotte	13 (8.7); 19 (12.7)	96 (64); 102 (68)	35 (23.3); 26 (17.3)	6 (4); 3 (2)	150 (100); 150 (100)	109 (72.7); 111 (74)	27 (18); 32 (21.3)	14 (9.3); 7 (4.7)	7.9 (4.1); 7.4 (4.3)	107 (71.3); 129 (86)	ND (ND); ND (ND)	ND (ND); ND (ND)

Abbreviations: Cx = circumflex artery; D = diagonal artery; FKB = final kissing-balloon; LAD = left ascending artery; LM = left main artery; OM = obtuse marginal artery; PCI = percutaneous coronary intervention; SB = side branch; other - see Table 1.

Supplementary Table 6. The number of patients and event rate according to bifurcation stenting technique in randomised controlled trials included in network meta-analysis.

	Crush	Culotte	DK-crush	Provisional	T-stenting
MACE	248/1357 (18.3%)	180/1336 (13.5%)	135/1231 (11.0%)	382/2473 (15.4%)	47/329 (14.3%)
Cardiac death	22/930 (2.4%)	18/1002 (1.8%)	34/1168 (2.9%)	42/1482 (2.8%)	1/150 (0.7%)
Myocardial infarction	137/1357 (10.1%)	76/1336 (5.7%)	47/1206 (3.9%)	157/2447 (6.4%)	5/329 (1.5%)
Target lesion revascularization	106/1107 (9.6%)	93/1187 (7.8%)	72/1193 (6.0%)	192/2007 (9.6%)	36/295 (12.2%)
Stent thrombosis	27/1357 (2.0%)	31/1284 (2.4%)	15/1168 (1.3%)	46/2287 (2.0%)	5/251 (2.0%)

Supplementary Table 7. Comparison of direct and indirect treatment estimates using "netsplit."

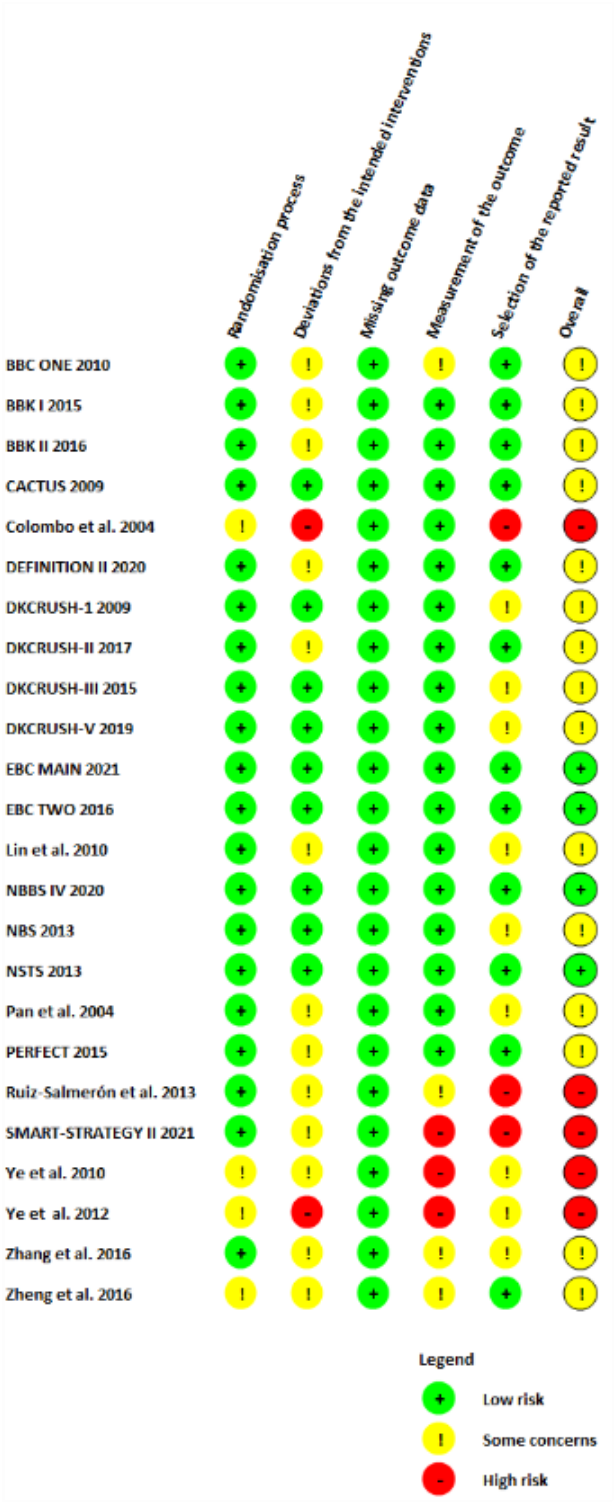
MACE												
Comparison	**k**	**prop**	**nma**	**95%-CI**	**direct**	**95%-CI**	**indir.**	**95%-CI**	**RoR**	**95%-CI**	**z**	**p-value**
Culotte:Crush	2	0.42	0.82	[0.60; 1.13]	0.78	[0.48; 1.28]	0.86	[0.57; 1.30]	0.91	[0.48; 1.73]	-0.29	0.7686
DK-crush:Crush	1	0.29	0.38	[0.27; 0.53]	0.51	[0.28; 0.93]	0.34	[0.23; 0.49]	1.52	[0.74; 3.11]	1.15	0.2508
Provisional:Crush	4	0.69	0.8	[0.62; 1.03]	0.76	[0.56; 1.03]	0.91	[0.58; 1.43]	0.84	[0.49; 1.45]	-0.63	0.5314
T-stenting:Crush	0	0	0.98	[0.56; 1.71]	NA	NA	0.98	[0.56; 1.71]	NA	NA	NA	NA
Culotte:DK-crush	1	0.28	2.17	[1.54; 3.07]	3.48	[1.81; 6.70]	1.81	[1.21; 2.72]	1.92	[0.89; 4.15]	1.67	0.0958
Culotte:Provisional	4	0.53	1.03	[0.77; 1.36]	0.99	[0.67; 1.45]	1.07	[0.71; 1.62]	0.92	[0.52; 1.62]	-0.28	0.7771
Culotte:T-stenting	1	0.43	0.84	[0.50; 1.43]	0.57	[0.25; 1.26]	1.14	[0.57; 2.32]	0.49	[0.17; 1.44]	-1.29	0.1965
DK-crush:Provisional	6	0.71	0.47	[0.36; 0.62]	0.49	[0.35; 0.67]	0.44	[0.27; 0.73]	1.11	[0.61; 2.00]	0.33	0.7407
DK-crush:T-stenting	0	0	0.39	[0.22; 0.68]	NA	NA	0.39	[0.22; 0.68]	NA	NA	NA	NA
Provisional:T-stenting	3	0.64	0.82	[0.49; 1.37]	1.06	[0.56; 2.01]	0.52	[0.22; 1.23]	2.03	[0.69; 5.91]	1.29	0.1965
Cardiac death												
Comparison	**k**	**Prop**	**NMA**	**95%-CI**	**Direct**	**95%-CI**	**Indir.**	**95%-CI**	**RoR**	**95%-CI**	**z**	**p-value**
Culotte:Crush	2	0.69	0.87	[0.39; 1.94]	0.87	[0.33; 2.31]	0.86	[0.20; 3.63]	1.01	[0.18; 5.76]	0.01	0.9884
DK-crush:Crush	1	0.14	0.48	[0.20; 1.12]	0.33	[0.03; 3.22]	0.5	[0.20; 1.27]	0.66	[0.06; 7.64]	-0.34	0.7368

Provisional:Crush	2	0.61	0.56	[0.25; 1.24]	0.6	[0.21; 1.66]	0.5	[0.14; 1.78]	1.19	[0.23; 6.11]	0.21	0.8336
T-stenting:Crush	0	0	0.87	[0.05; 15.69]	NA	NA	0.87	[0.05; 15.69]	NA	NA	NA	NA
Culotte:DK-crush	1	0.4	1.82	[0.75; 4.42]	2.04	[0.50; 8.27]	1.69	[0.54; 5.31]	1.2	[0.20; 7.34]	0.2	0.8397
Culotte:Provisional	2	0.27	1.56	[0.66; 3.71]	1.31	[0.24; 7.04]	1.66	[0.60; 4.56]	0.79	[0.11; 5.61]	-0.24	0.8134
Culotte:T-stenting	1	1	1	[0.06; 16.14]	1	[0.06; 16.14]	NA	NA	NA	NA	NA	NA
DK-crush:Provisional	4	0.9	0.85	[0.53; 1.38]	0.88	[0.53; 1.46]	0.64	[0.14; 2.93]	1.39	[0.28; 6.93]	0.4	0.6891
DK-crush:T-stenting	0	0	0.55	[0.03; 10.15]	NA	NA	0.55	[0.03; 10.15]	NA	NA	NA	NA
Provisional:T-stenting	0	0	0.64	[0.03; 11.81]	NA	NA	0.64	[0.03; 11.81]	NA	NA	NA	NA
Myocardial infarction												
Comparison	**k**	**Prop**	**NMA**	**95%-CI**	**Direct**	**95%-CI**	**Indir.**	**95%-CI**	**RoR**	**95%-CI**	**z**	**p-value**
Culotte:Crush	2	0.39	0.75	[0.45; 1.24]	0.71	[0.32; 1.61]	0.77	[0.40; 1.46]	0.93	[0.33; 2.62]	-0.14	0.8899
DK-crush:Crush	1	0.36	0.4	[0.23; 0.68]	0.67	[0.27; 1.62]	0.3	[0.15; 0.58]	2.22	[0.73; 6.72]	1.41	0.1581
Provisional:Crush	4	0.72	0.7	[0.48; 1.03]	0.62	[0.39; 0.98]	0.96	[0.46; 1.98]	0.65	[0.28; 1.54]	-0.98	0.3268
T-stenting:Crush	0	0	0.55	[0.15; 1.98]	NA	NA	0.55	[0.15; 1.98]	NA	NA	NA	NA
Culotte:DK-crush	1	0.29	1.87	[1.05; 3.33]	2.57	[0.88; 7.48]	1.65	[0.83; 3.26]	1.56	[0.44; 5.54]	0.69	0.4923
Culotte:Provisional	4	0.61	1.06	[0.68; 1.67]	0.97	[0.54; 1.73]	1.22	[0.60; 2.51]	0.79	[0.32; 2.00]	-0.49	0.6232

Culotte:T-stenting	1	0.26	1.36	[0.38; 4.87]	2.01	[0.17; 24.00]	1.18	[0.27; 5.22]	1.7	[0.09; 30.64]	0.36	0.7178
DK-crush:Provisional	5	0.62	0.57	[0.35; 0.91]	0.49	[0.27; 0.91]	0.71	[0.33; 1.53]	0.7	[0.26; 1.86]	-0.72	0.4725
DK-crush:T-stenting	0	0	0.73	[0.20; 2.70]	NA	NA	0.73	[0.20; 2.70]	NA	NA	NA	NA
Provisional:T-stenting	3	0.76	1.28	[0.37; 4.39]	1.13	[0.27; 4.63]	1.92	[0.15; 23.83]	0.59	[0.03; 10.56]	-0.36	0.7178
Target lesion revascularization												
Comparison	**k**	**Prop**	**NMA**	**95%-CI**	**Direct**	**95%-CI**	**Indir.**	**95%-CI**	**RoR**	**95%-CI**	**z**	**p-value**
Culotte:Crush	2	0.41	0.92	[0.61; 1.39]	0.88	[0.47; 1.67]	0.95	[0.55; 1.62]	0.93	[0.40; 2.15]	-0.17	0.8688
DK-crush:Crush	1	0.4	0.37	[0.25; 0.54]	0.42	[0.23; 0.78]	0.33	[0.20; 0.55]	1.26	[0.57; 2.78]	0.58	0.5625
Provisional:Crush	3	0.59	0.89	[0.63; 1.25]	0.84	[0.54; 1.32]	0.96	[0.57; 1.63]	0.88	[0.44; 1.75]	-0.37	0.7123
T-stenting:Crush	0	0	1.3	[0.69; 2.46]	NA	NA	1.3	[0.69; 2.46]	NA	NA	NA	NA
Culotte:DK-crush	1	0.27	2.51	[1.65; 3.80]	4.07	[1.81; 9.14]	2.1	[1.29; 3.42]	1.94	[0.75; 4.97]	1.37	0.1697
Culotte:Provisional	2	0.52	1.03	[0.72; 1.48]	1.02	[0.62; 1.68]	1.05	[0.63; 1.75]	0.98	[0.48; 1.99]	-0.07	0.9458
Culotte:T-stenting	1	0.49	0.71	[0.40; 1.27]	0.47	[0.20; 1.08]	1.05	[0.46; 2.37]	0.45	[0.14; 1.43]	-1.36	0.1751
DK-crush:Provisional	5	0.72	0.41	[0.30; 0.56]	0.43	[0.30; 0.62]	0.36	[0.20; 0.65]	1.19	[0.60; 2.38]	0.5	0.6176
DK-crush:T-stenting	0	0	0.28	[0.15; 0.53]	NA	NA	0.28	[0.15; 0.53]	NA	NA	NA	NA
Provisional:T-stenting	2	0.62	0.69	[0.39; 1.21]	0.93	[0.45; 1.92]	0.42	[0.17; 1.04]	2.24	[0.70; 7.19]	1.36	0.1751
Stent thrombosis												

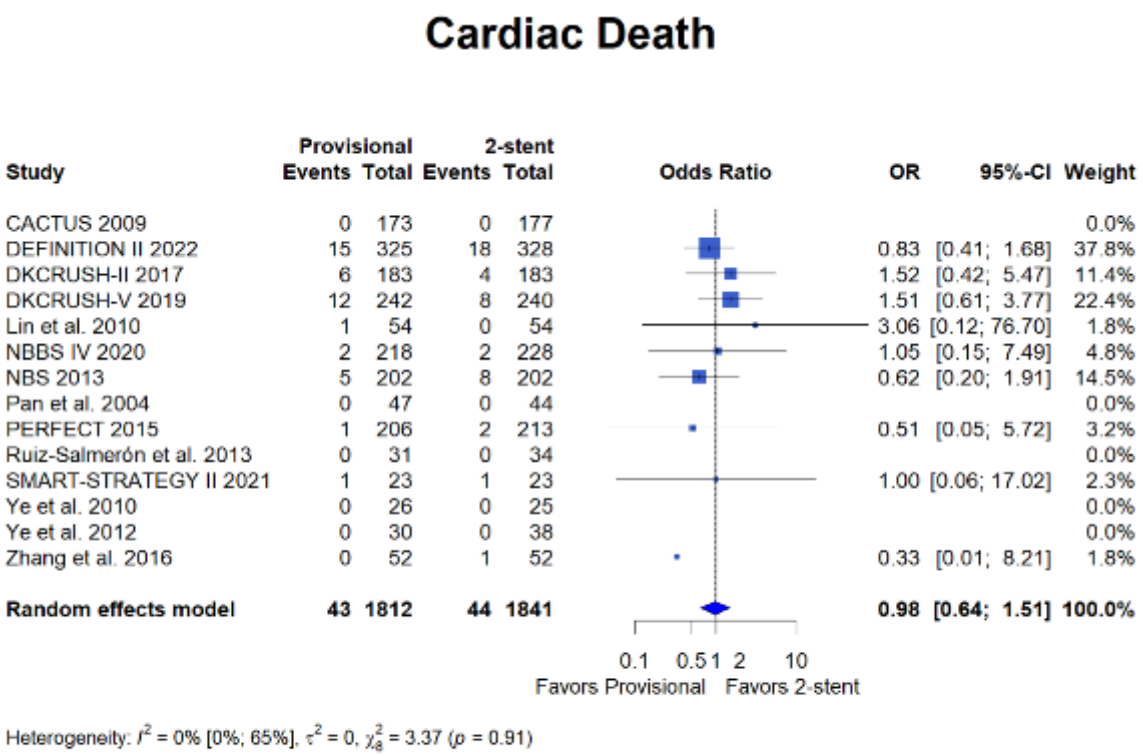
Comparison	k	Prop	NMA	95%-CI	Direct	95%-CI	Indir.	95%-CI	RoR	95%-CI	z	p-value
Culotte:Crush	2	0.65	1.23	[0.61; 2.48]	1.3	[0.54; 3.11]	1.12	[0.34; 3.64]	1.16	[0.27; 5.06]	0.2	0.8386
DK-crush:Crush	1	0.26	0.41	[0.18; 0.97]	0.39	[0.08; 2.07]	0.42	[0.16; 1.13]	0.94	[0.14; 6.42]	-0.07	0.9461
Provisional:Crush	4	0.54	0.87	[0.43; 1.74]	0.83	[0.32; 2.12]	0.92	[0.33; 2.57]	0.9	[0.22; 3.63]	-0.14	0.8853
T-stenting:Crush	0	0	1.56	[0.31; 7.78]	NA	NA	1.56	[0.31; 7.78]	NA	NA	NA	NA
Culotte:DK-crush	1	0.17	2.97	[1.25; 7.08]	8.32	[1.03; 67.14]	2.39	[0.92; 6.22]	3.48	[0.35; 34.54]	1.06	0.2875
Culotte:Provisional	3	0.53	1.42	[0.70; 2.87]	0.94	[0.36; 2.48]	2.26	[0.81; 6.33]	0.42	[0.10; 1.72]	-1.21	0.2257
Culotte:T-stenting	1	0.24	0.79	[0.16; 3.82]	3.02	[0.12; 74.73]	0.51	[0.08; 3.15]	5.87	[0.15; 234.03]	0.94	0.3464
DK-crush:Provisional	4	0.8	0.48	[0.25; 0.91]	0.55	[0.26; 1.12]	0.28	[0.06; 1.20]	1.96	[0.39; 9.99]	0.81	0.4173
DK-crush:T-stenting	0	0	0.27	[0.05; 1.33]	NA	NA	0.27	[0.05; 1.33]	NA	NA	NA	NA
Provisional:T-stenting	1	0.8	0.56	[0.13; 2.46]	0.39	[0.07; 2.05]	2.28	[0.09; 61.04]	0.17	[0.00; 6.78]	-0.94	0.3464

Legend: k = number of studies providing direct evidence; prop = direct evidence proportion; nma = estimated treatment effect (OR) in network meta-analysis; direct = estimated treatment effect (OR) derived from direct evidence; indir. = estimated treatment effect (OR) derived from indirect evidence; RoR = Ratio of Ratios (direct versus indirect); z = z-value of test for disagreement (direct versus indirect); p-value = p-value of test for disagreement (direct versus indirect)



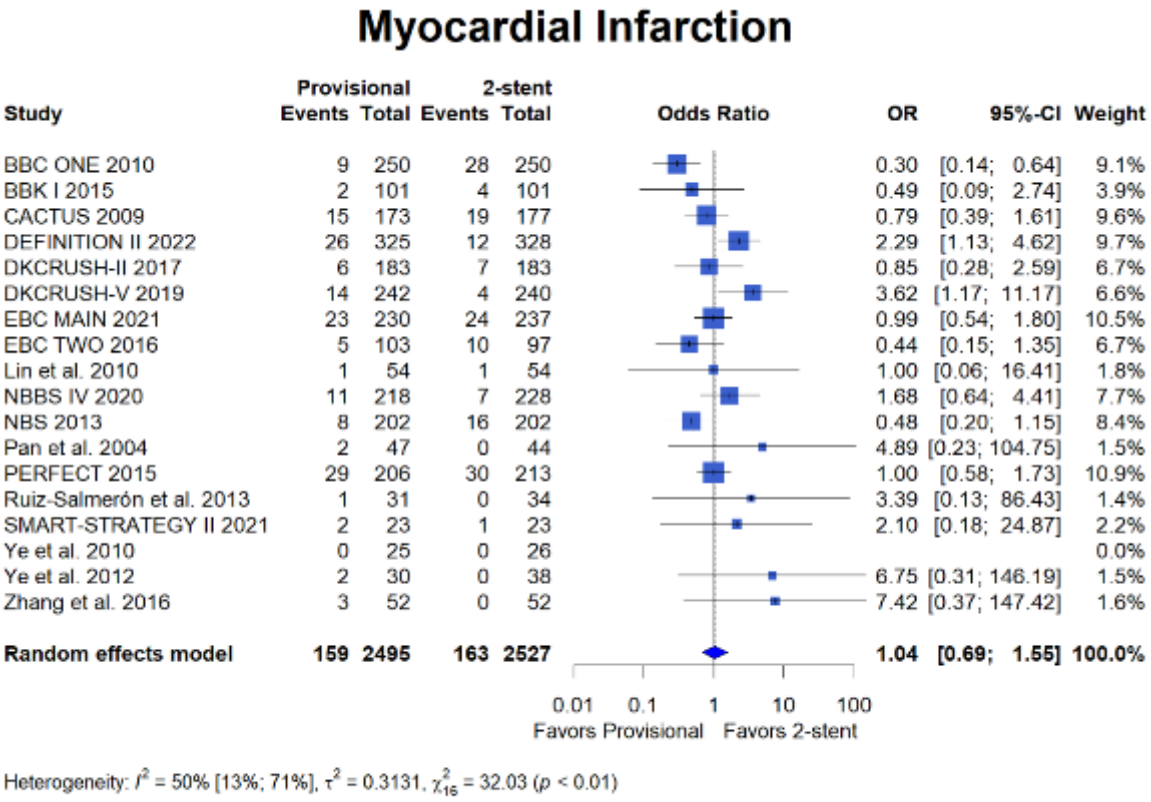
Supplementary Figure 1. Results of risk of bias assessment.

A)



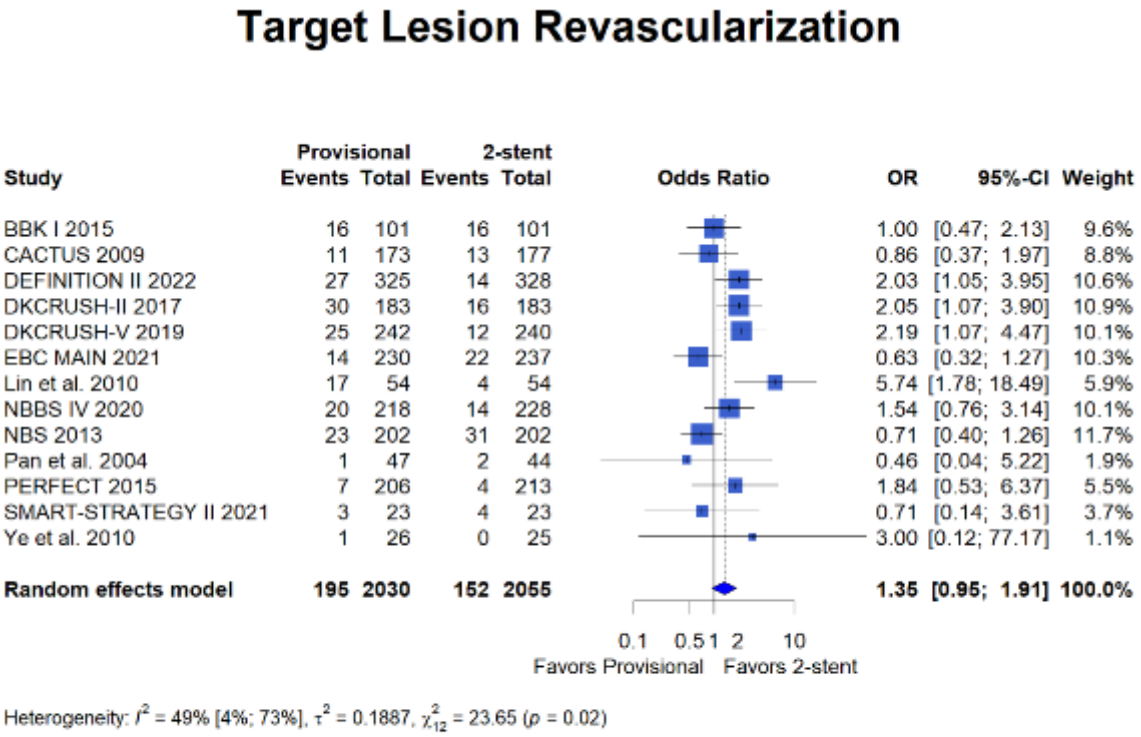
Heterogeneity: I^2 = 0% [0%; 65%], τ^2 = 0, χ^2_8 = 3.37 (p = 0.91)

B)



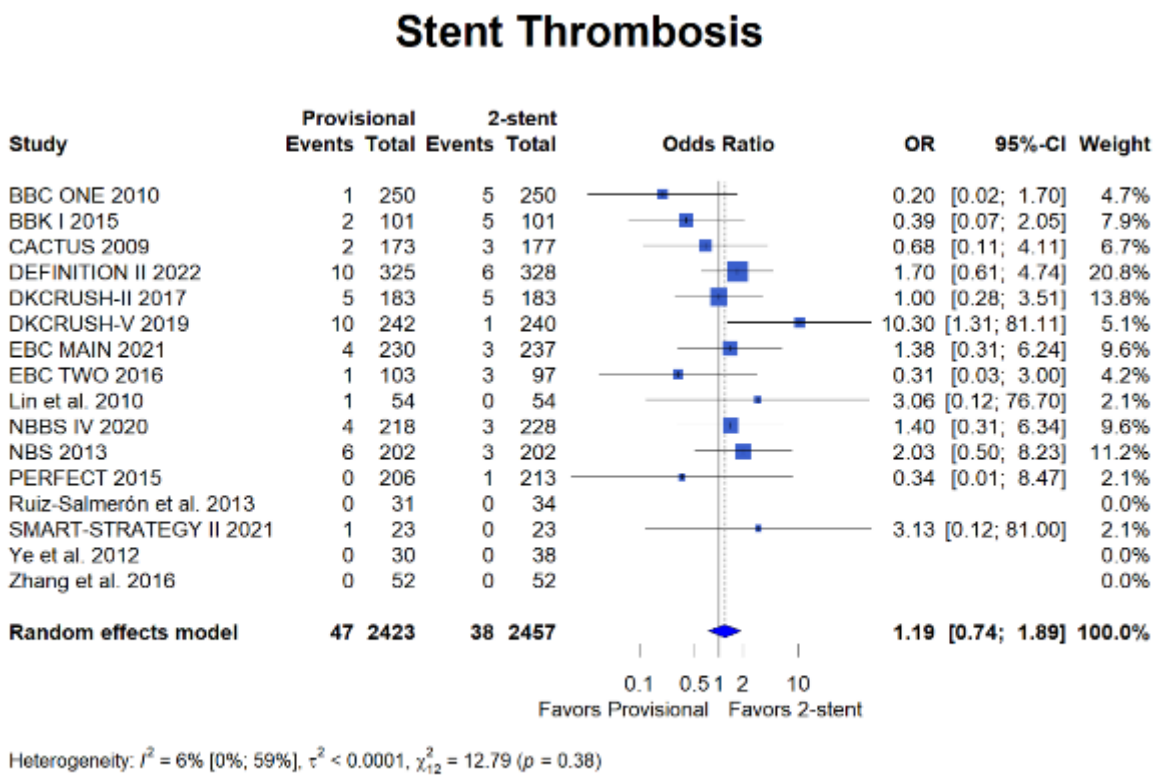
Heterogeneity: I^2 = 50% [13%; 71%], τ^2 = 0.3131, χ^2_{16} = 32.03 (p < 0.01)

C)



Heterogeneity: I^2 = 49% [4%; 73%], τ^2 = 0.1887, χ^2_{12} = 23.65 (p = 0.02)

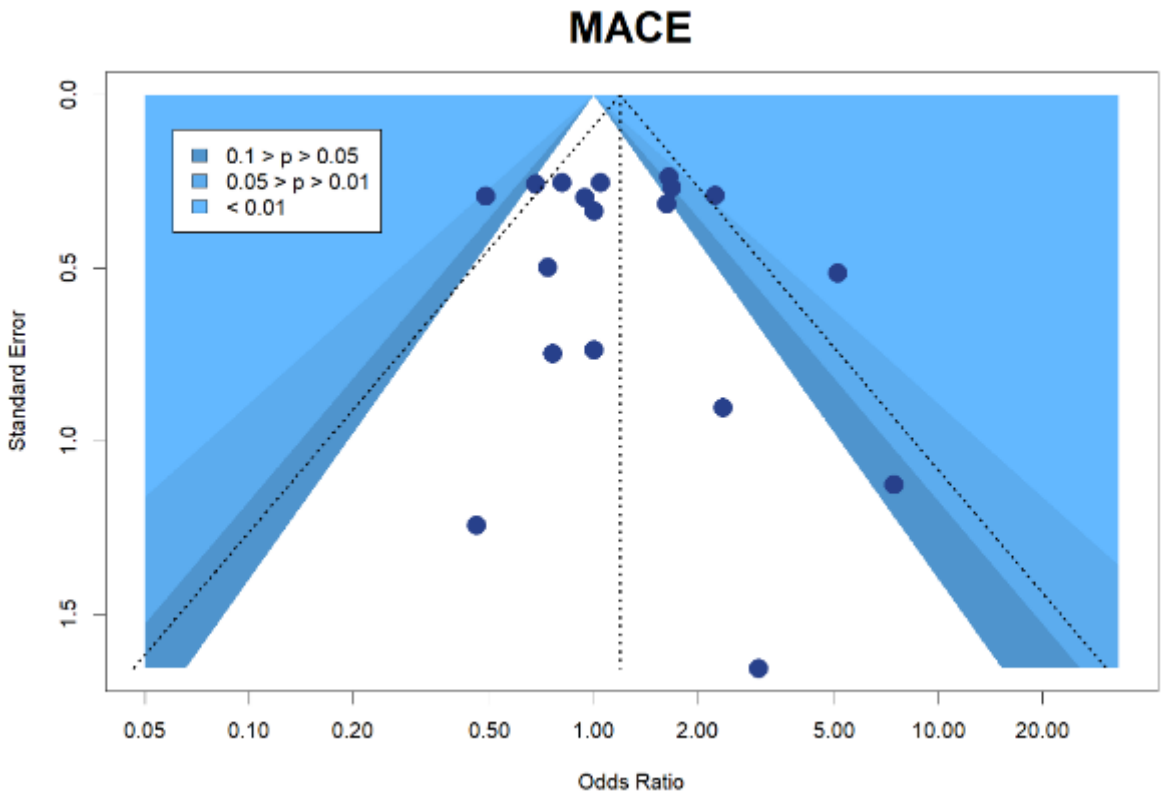
D)



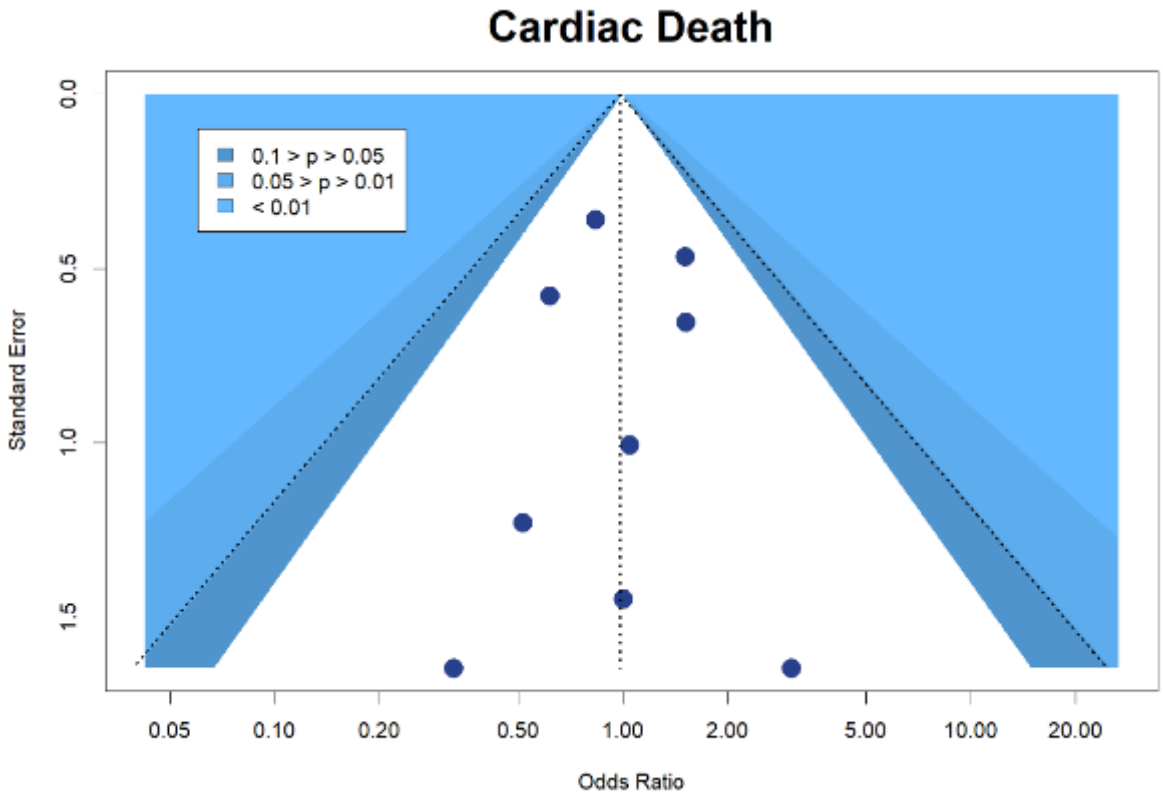
Supplementary Figure 2. Forest plots presenting results of the pairwise meta-analysis for secondary outcomes of interest.

Cardiac death (A), myocardial infarction (B), target lesion revascularization (C), and stent thrombosis (D).

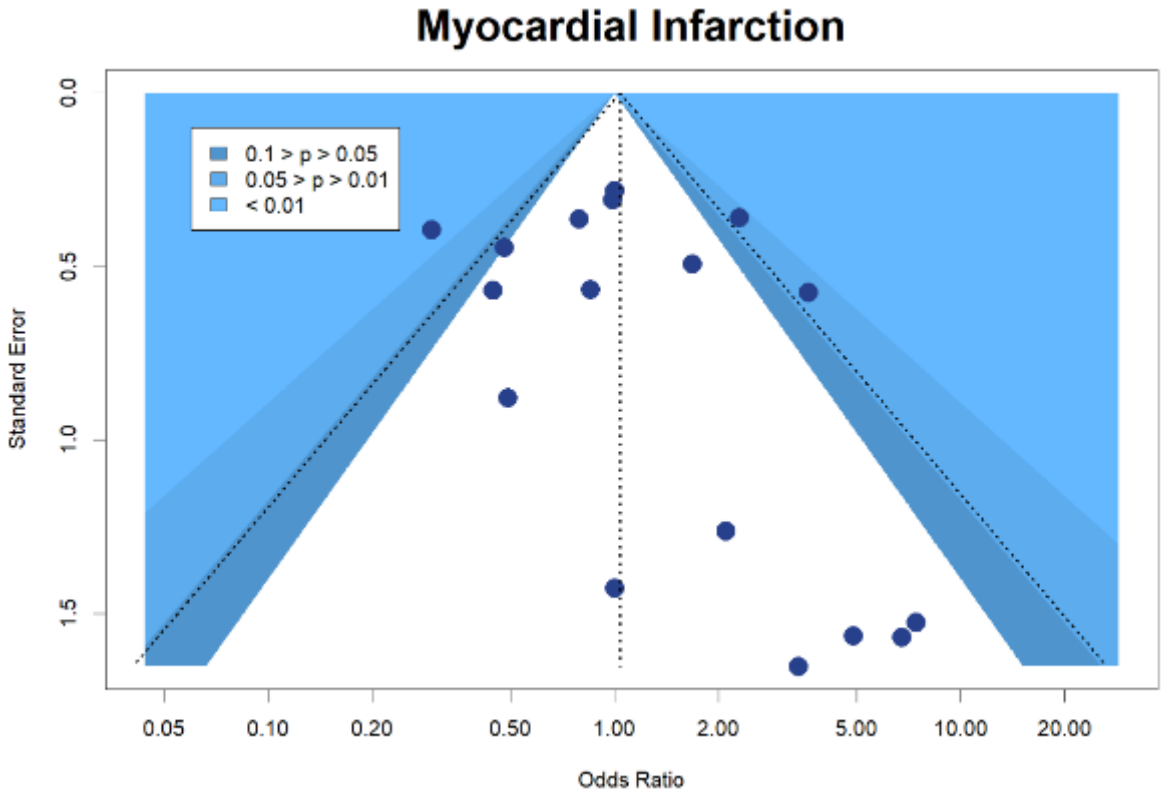
A)


MACE
0.1 > p > 0.05
0.05 > p > 0.01
< 0.01
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio

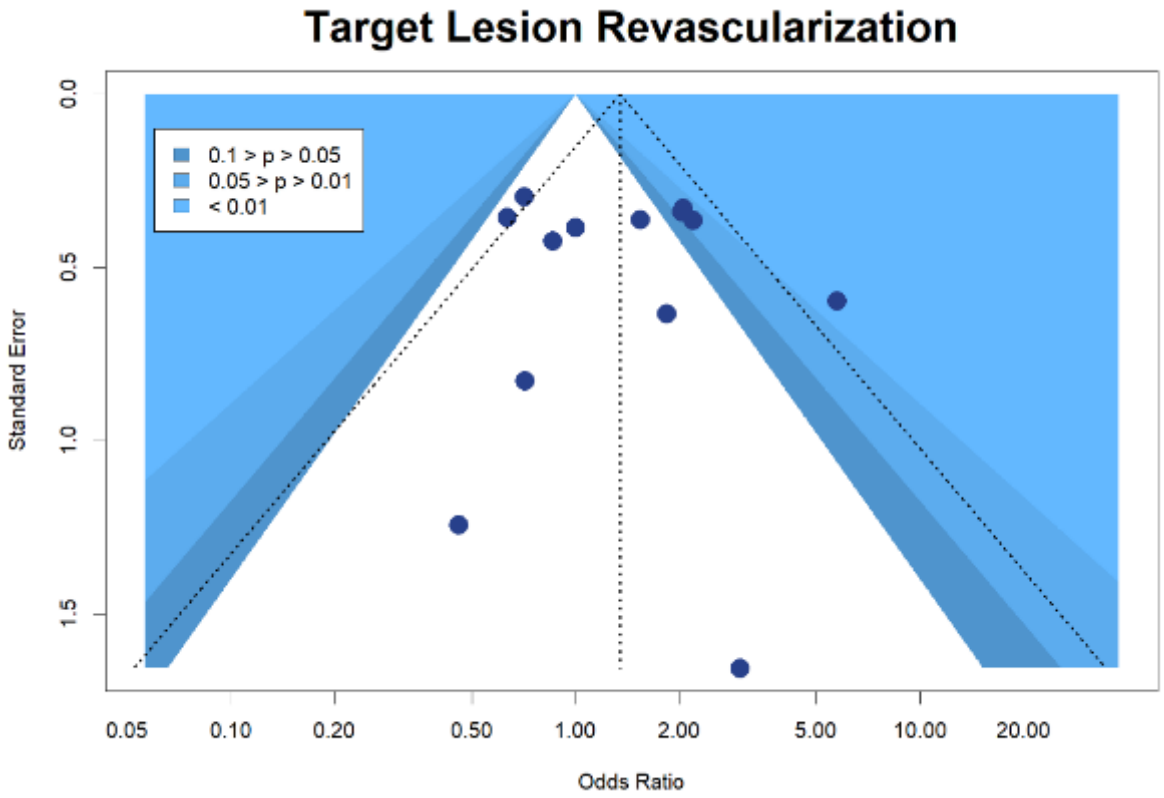
B)


Cardiac Death
0.1 > p > 0.05
0.05 > p > 0.01
< 0.01
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio

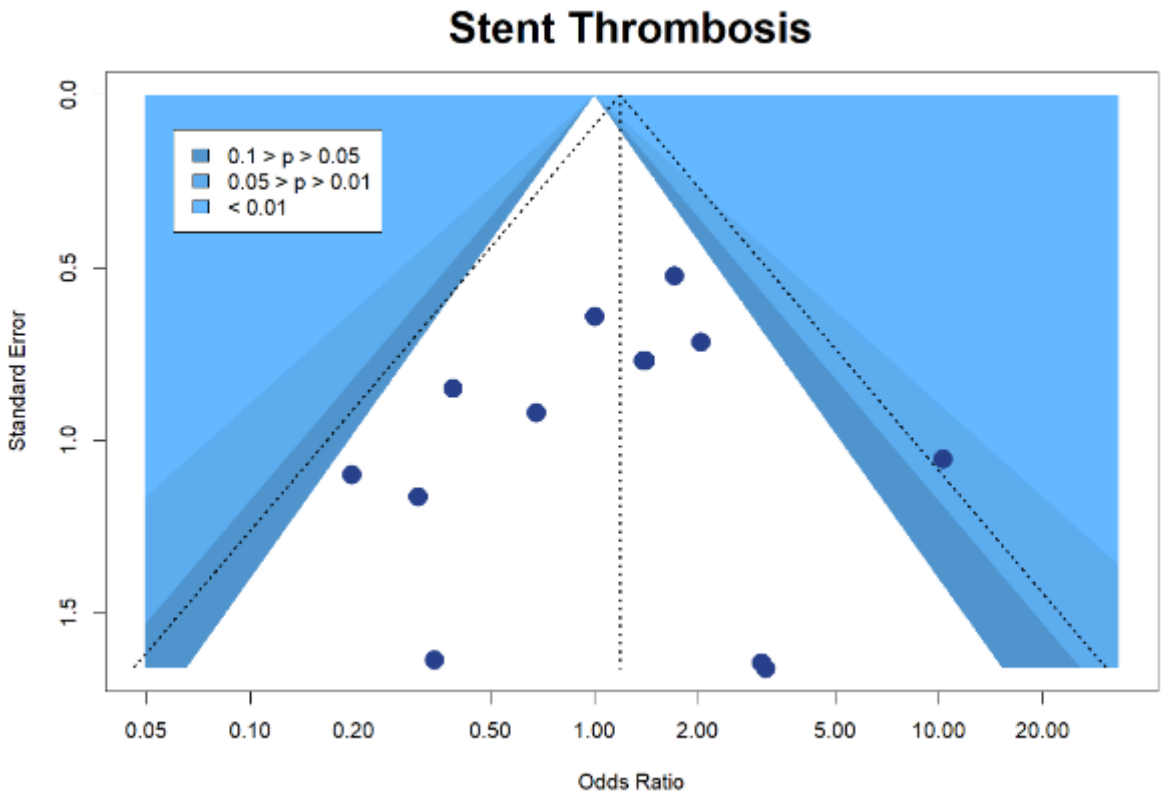
C)


Myocardial Infarction
0.1 > p > 0.05
0.05 > p > 0.01
< 0.01
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio

D)


Target Lesion Revascularization
0.1 > p > 0.05
0.05 > p > 0.01
< 0.01
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio

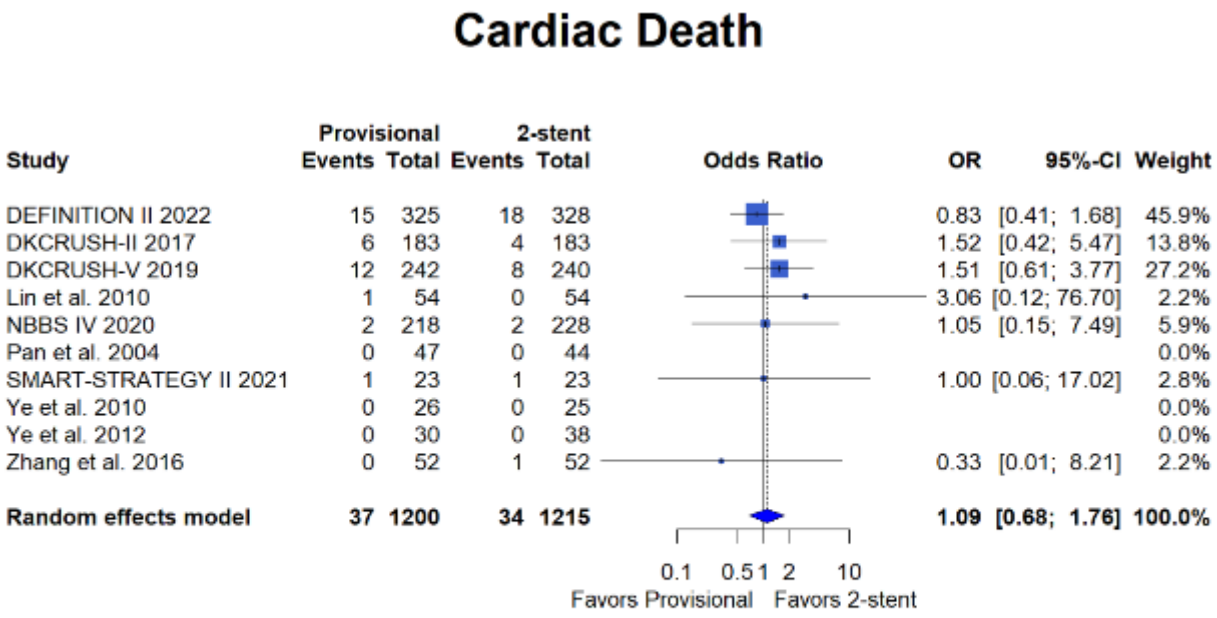
E)



Supplementary Figure 3. Color-enhanced funnel plots for pairwise meta-analysis.

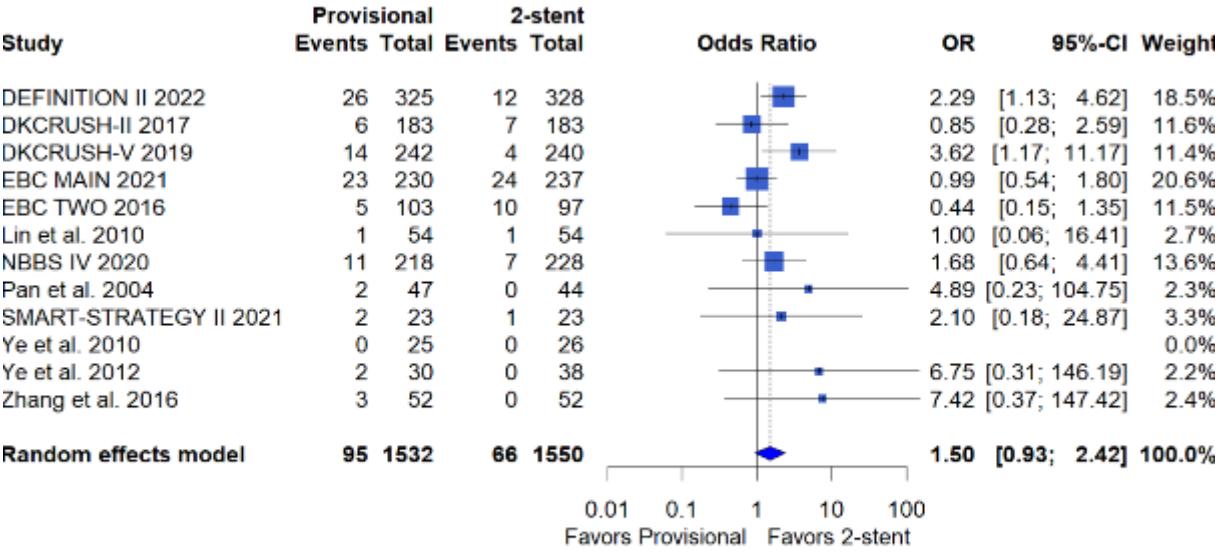
MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularization (D), and stent thrombosis (E).

A)



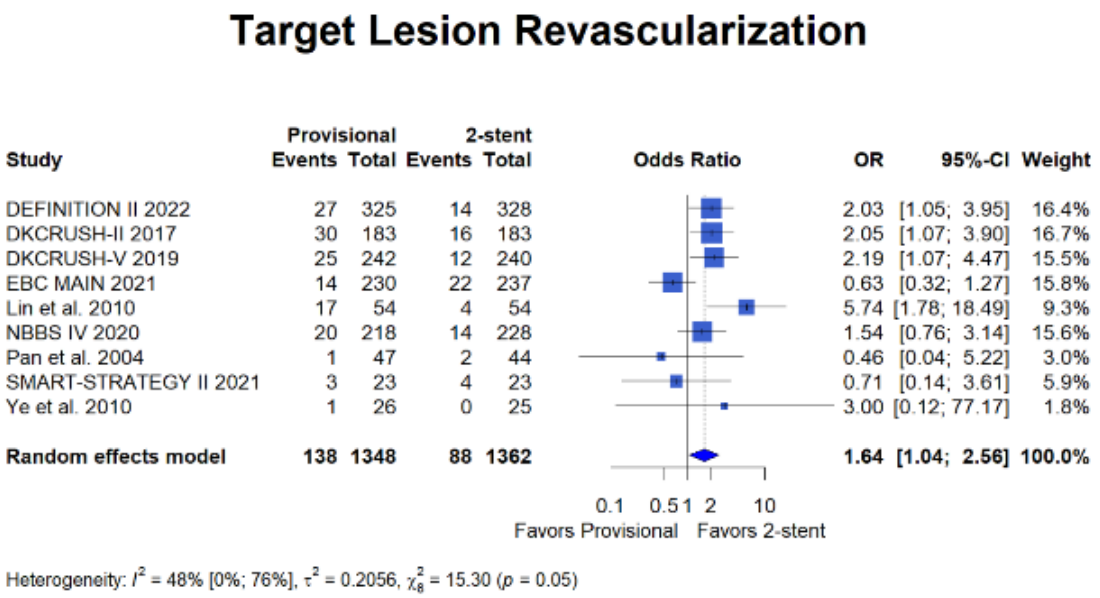
Heterogeneity: I^2 = 0% [0%; 71%], τ^2 = 0, χ^2_6 = 2.25 (p = 0.90)

B)

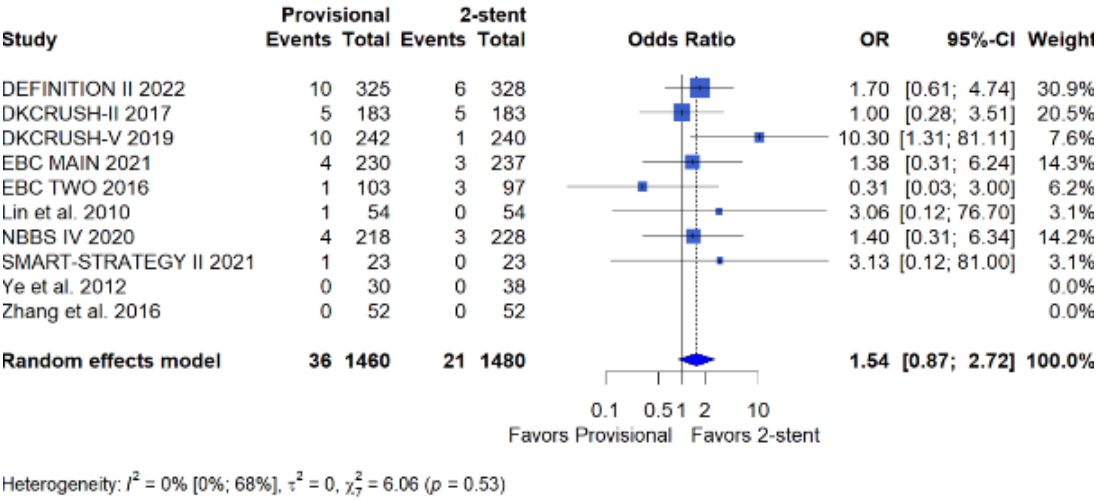


Heterogeneity: I^2 = 28% [0%; 65%], τ^2 = 0.1946, χ^2_{10} = 13.92 (p = 0.18)

C)



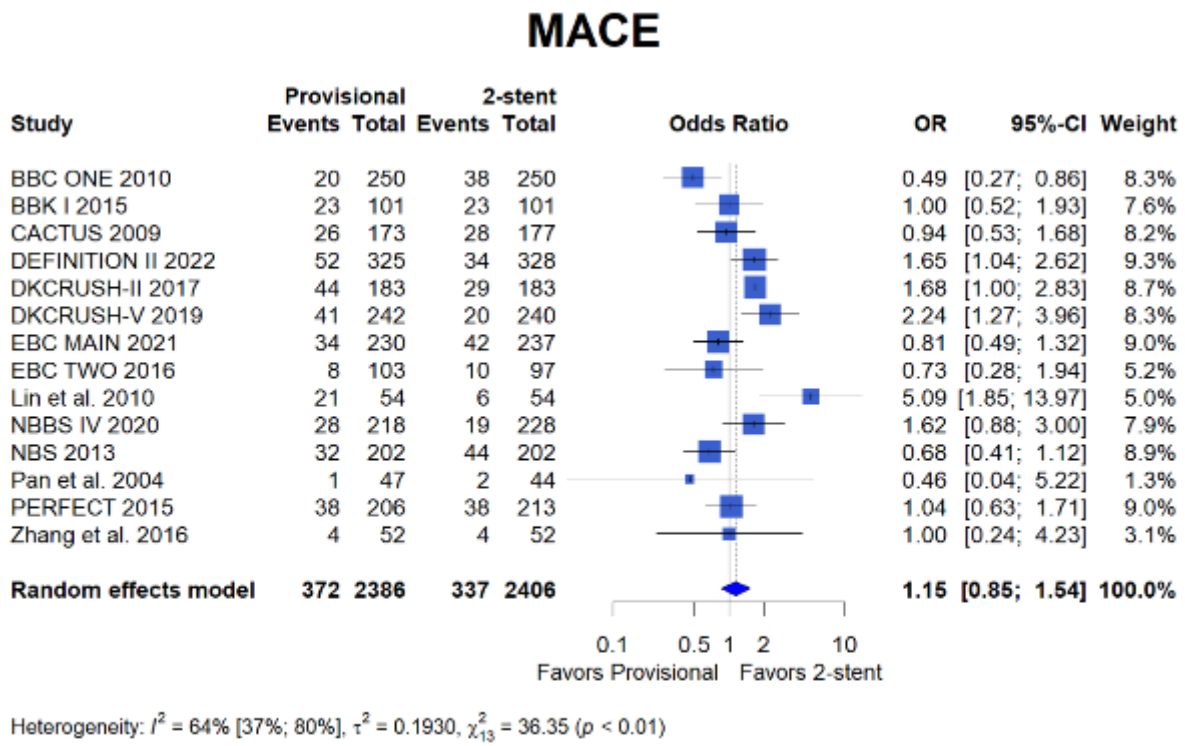
D)



Supplementary Figure 4. Forest plots presenting results of the sensitivity analysis of trials enrolling only patients with true bifurcations.

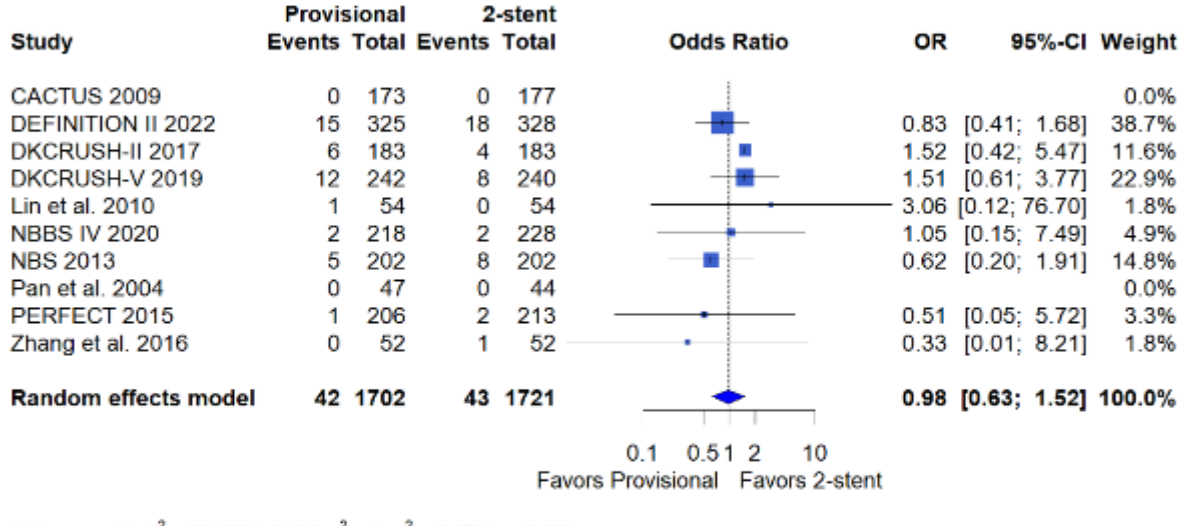
Cardiac death. (A), myocardial infarction (B), target lesion revascularization (C), and stent thrombosis (D).

A)



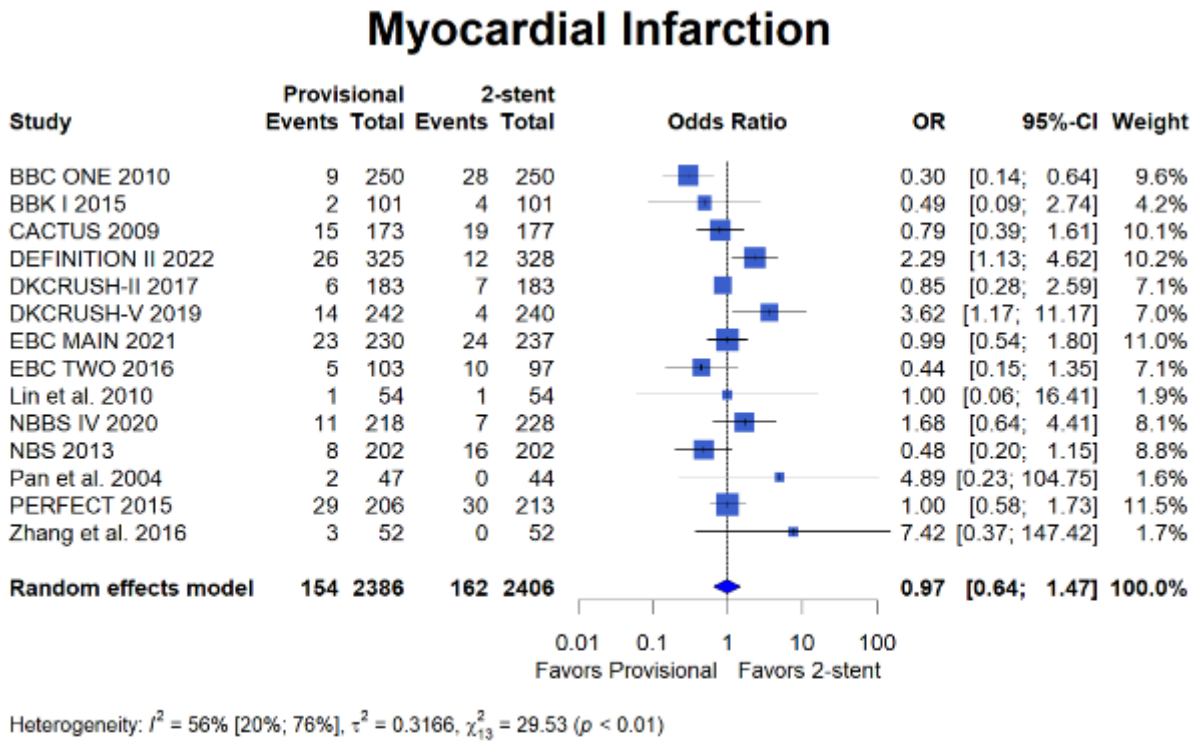
Heterogeneity: I^2 = 64% [37%; 80%], τ^2 = 0.1930, χ^2_{13} = 36.35 (p < 0.01)

B)



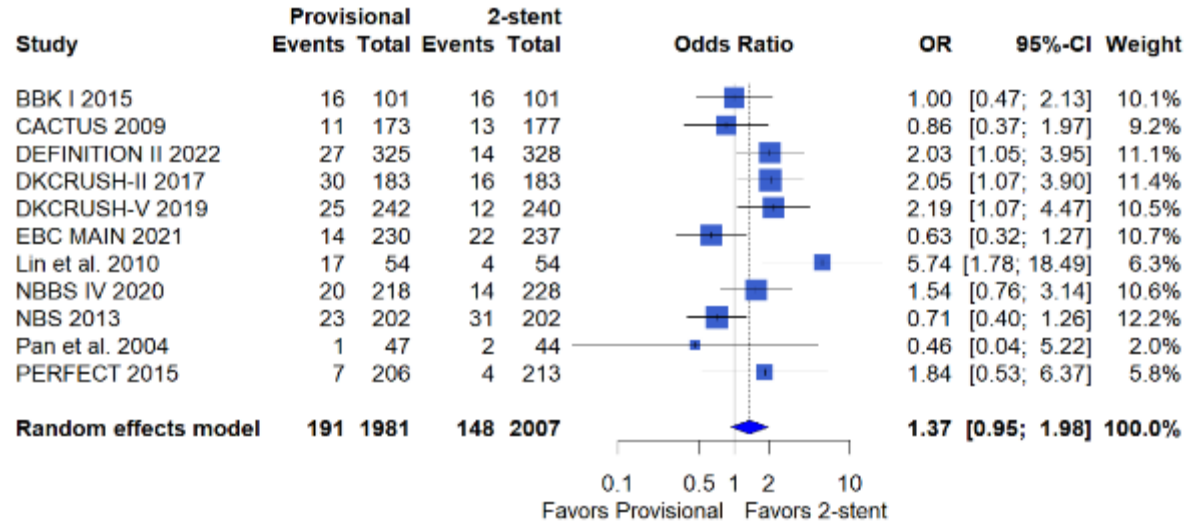
Heterogeneity: I^2 = 0% [0%; 68%], τ^2 = 0, χ^2_7 = 3.37 (p = 0.85)

C)



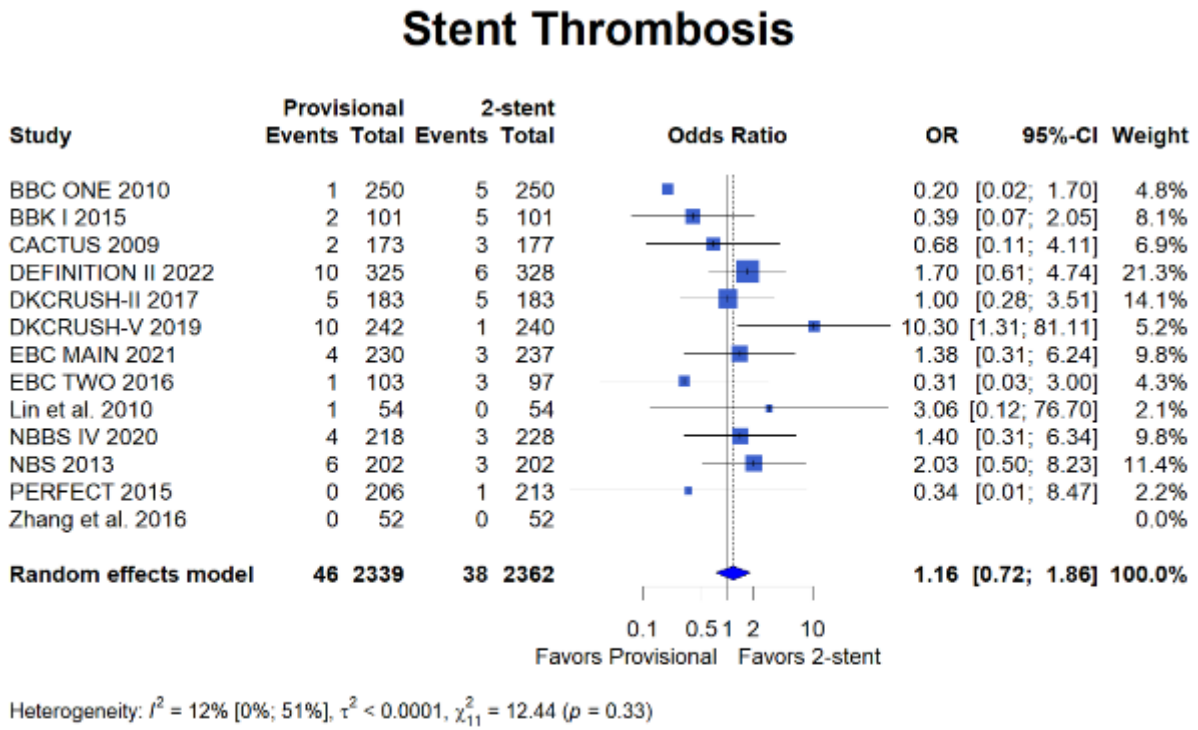
Heterogeneity: I^2 = 56% [20%; 76%], τ^2 = 0.3166, χ^2_{13} = 29.53 (p < 0.01)

D)



Heterogeneity: I^2 = 56% [14%; 78%], τ^2 = 0.2029, χ^2_{10} = 22.86 (p = 0.01)

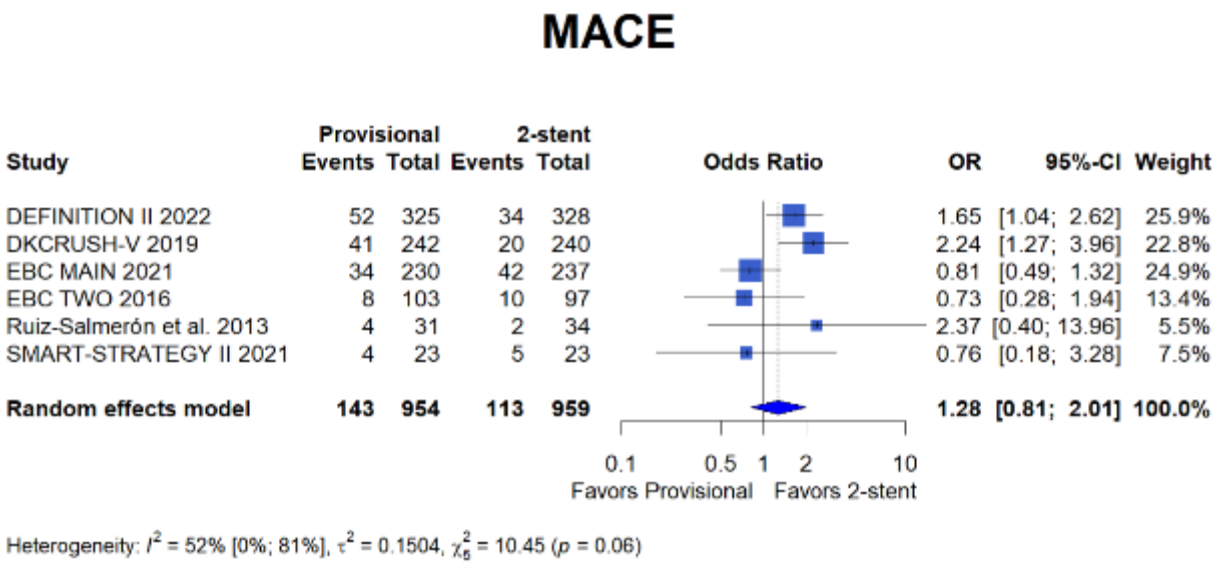
E)



Supplementary Figure 5. Forest plots presenting results of the sensitivity analysis after excluding trials with a high risk of bias.

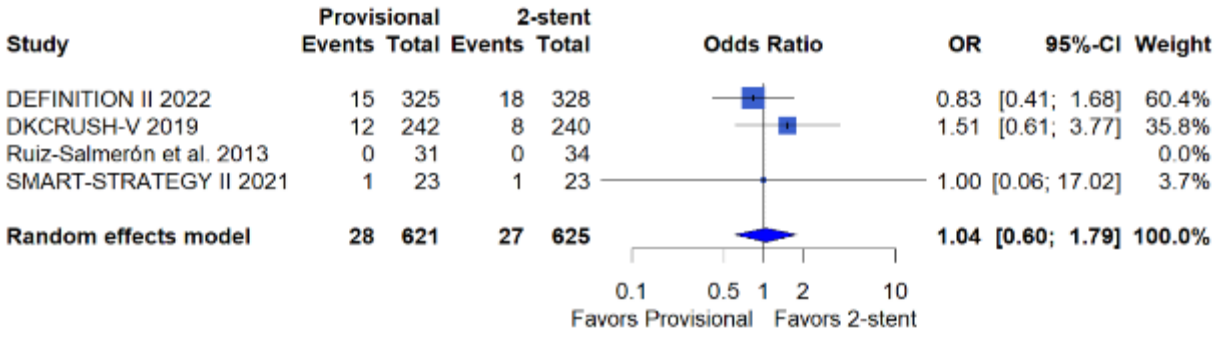
MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularization (D), and stent thrombosis (E)

A)



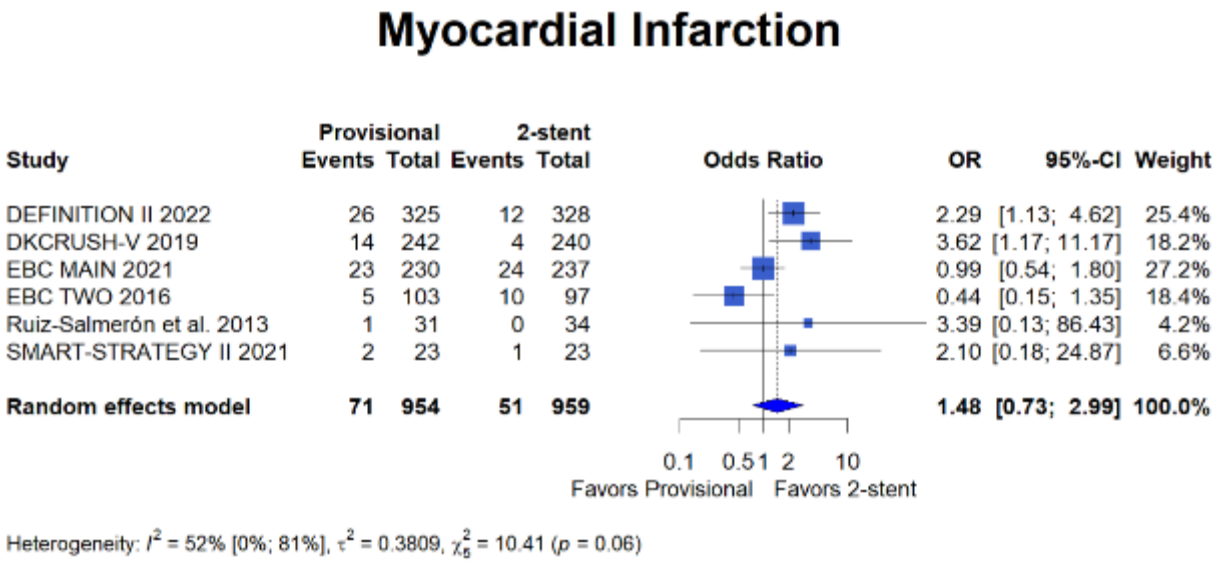
Heterogeneity: I^2 = 52% [0%; 81%], τ^2 = 0.1504, χ^2_5 = 10.45 (p = 0.06)

B)



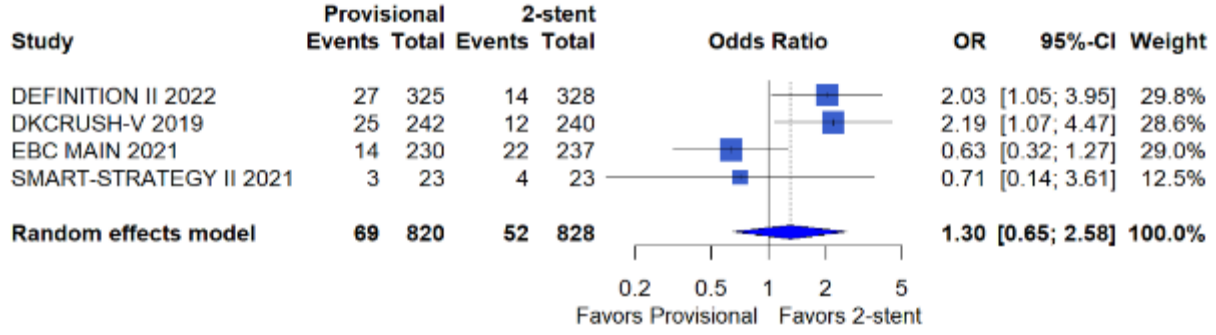
Heterogeneity: I^2 = 0% [0%; 90%], τ^2 = 0, χ^2_2 = 1.03 (p = 0.60)

C)



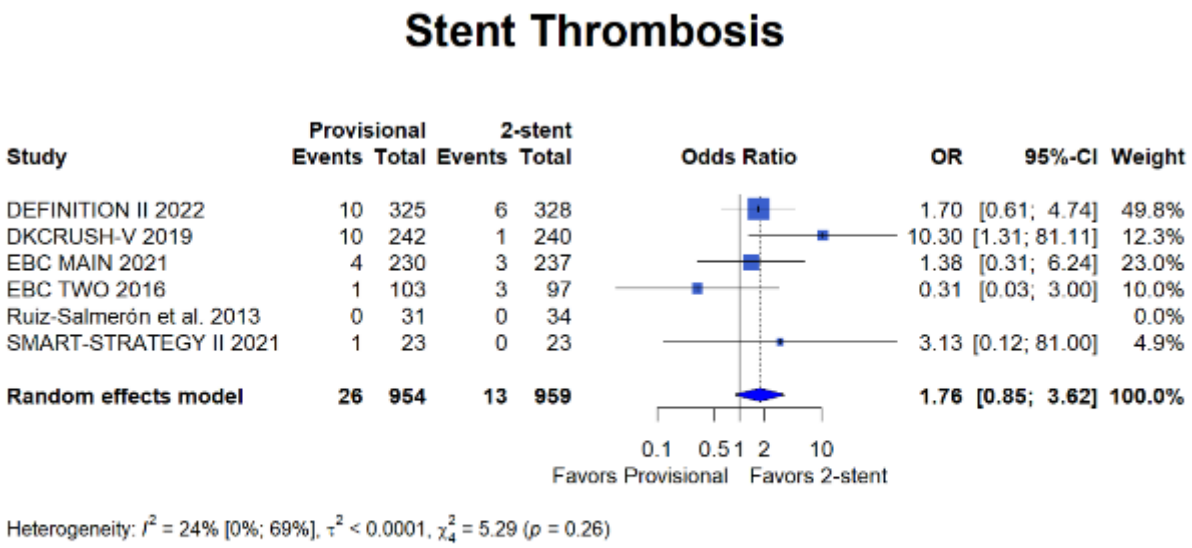
Heterogeneity: I^2 = 52% [0%; 81%], τ^2 = 0.3809, χ^2_5 = 10.41 (p = 0.06)

D)



Heterogeneity: I^2 = 64% [0%; 88%], τ^2 = 0.2956, χ^2_3 = 8.35 (p = 0.04)

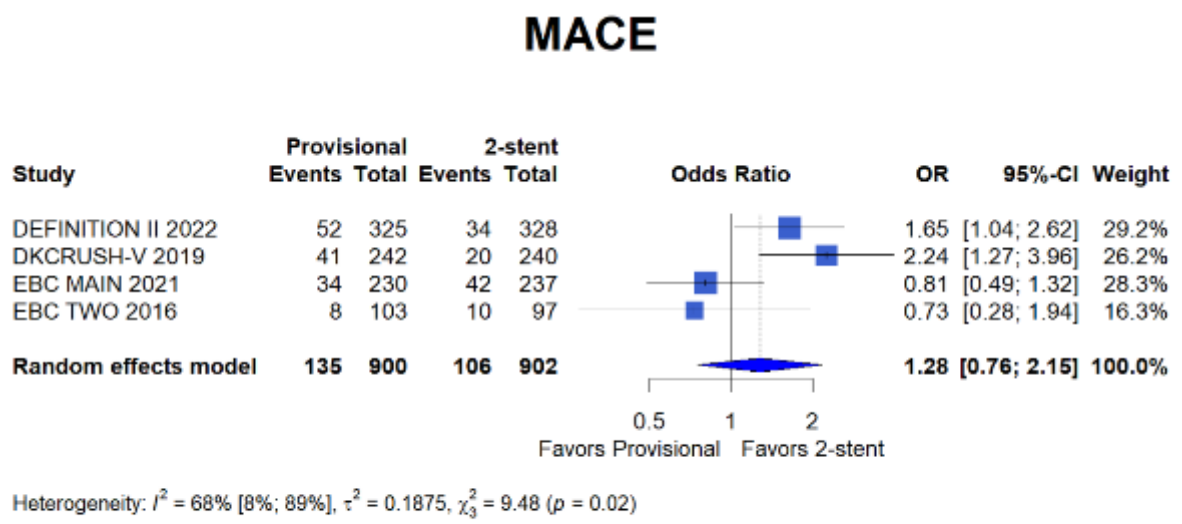
E)



Supplementary Figure 6. Forest plots presenting results of the sensitivity analysis after excluding trials utilising first-generation drug-eluting stents.

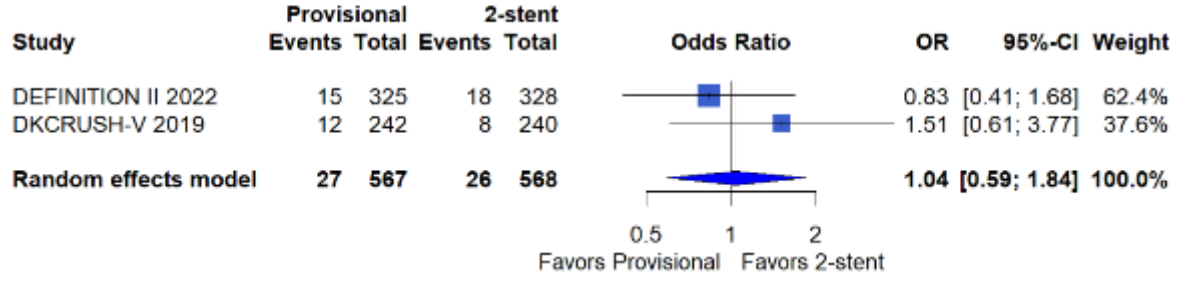
MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularisation (D), and stent thrombosis (E).

A)



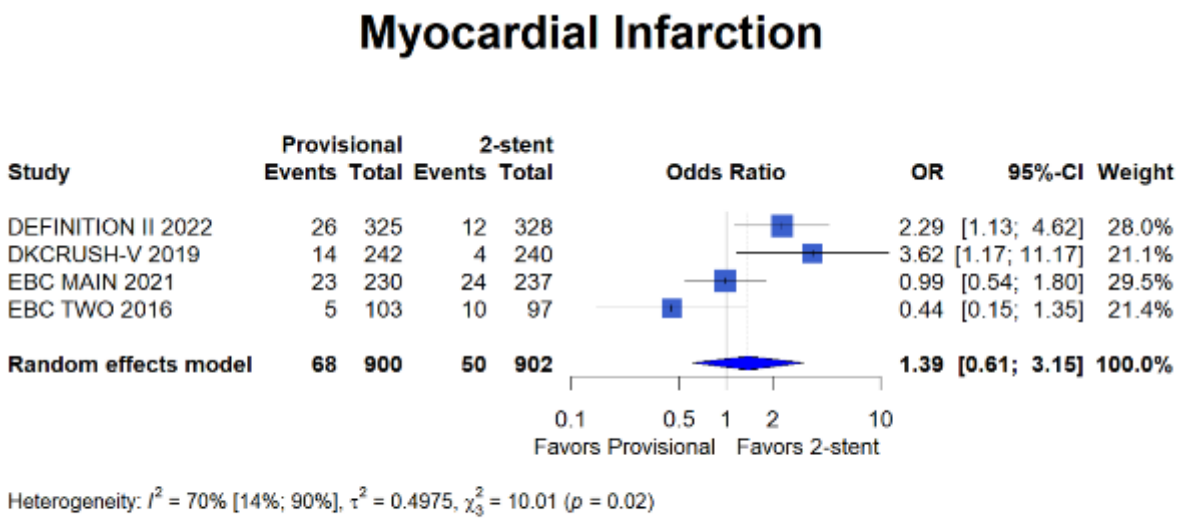
Heterogeneity: I^2 = 68% [8%; 89%], τ^2 = 0.1875, χ^2_3 = 9.48 (p = 0.02)

B)



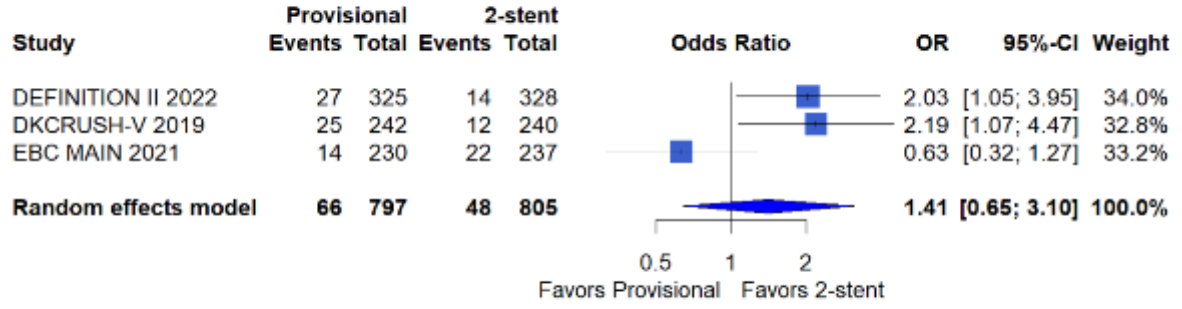
Heterogeneity: I^2 = 3%, τ^2 = 0.0050, χ^2_1 = 1.03 (p = 0.31)

C)



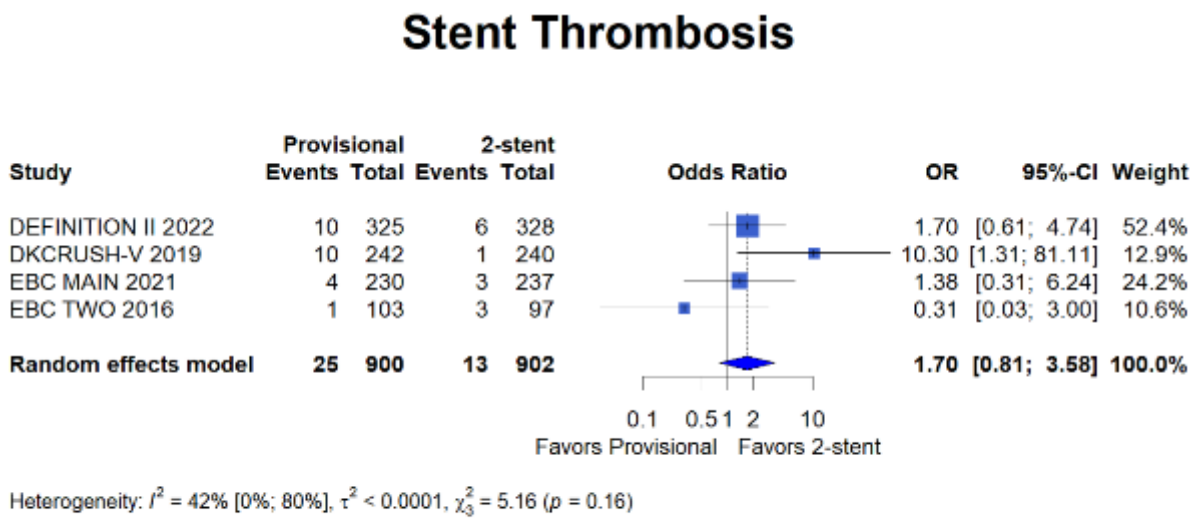
Heterogeneity: I^2 = 70% [14%; 90%], τ^2 = 0.4975, χ^2_3 = 10.01 (p = 0.02)

D)



Heterogeneity: I^2 = 74% [13%; 92%], τ^2 = 0.3566, χ^2_2 = 7.70 (p = 0.02)

E)

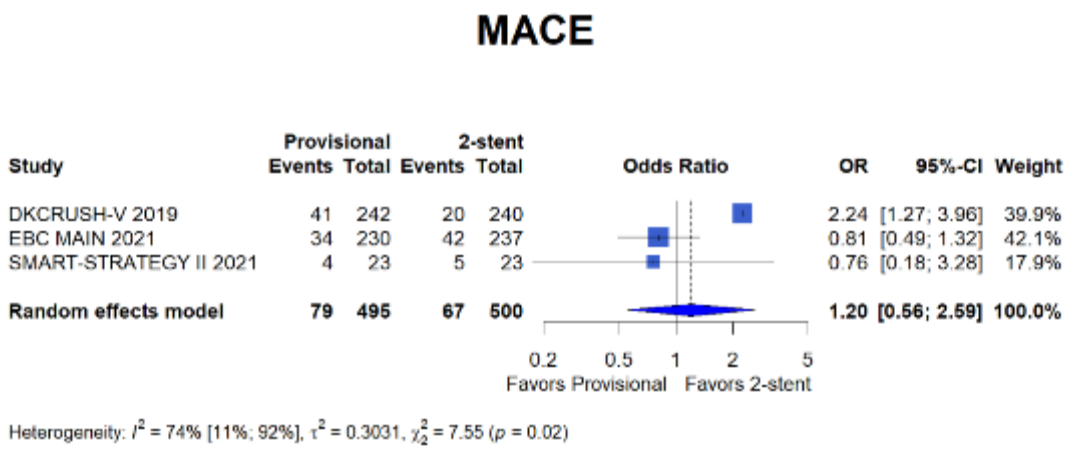


Supplementary Figure 7. Forest plots presenting results of the sensitivity analysis after excluding trials without proximal optimisation technique.

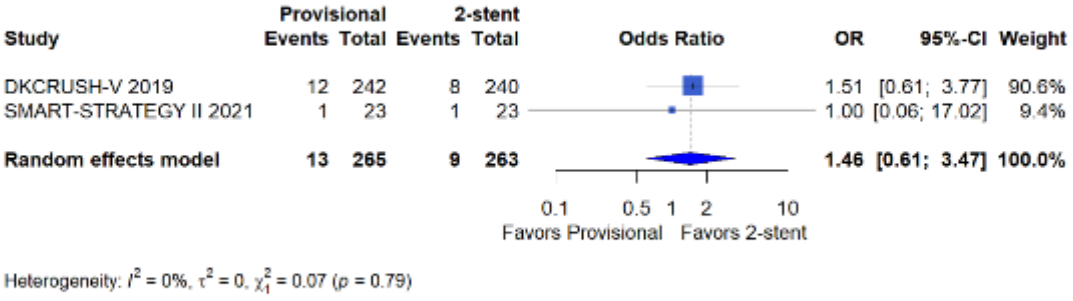
MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularisation (D), and stent thrombosis (E).

.

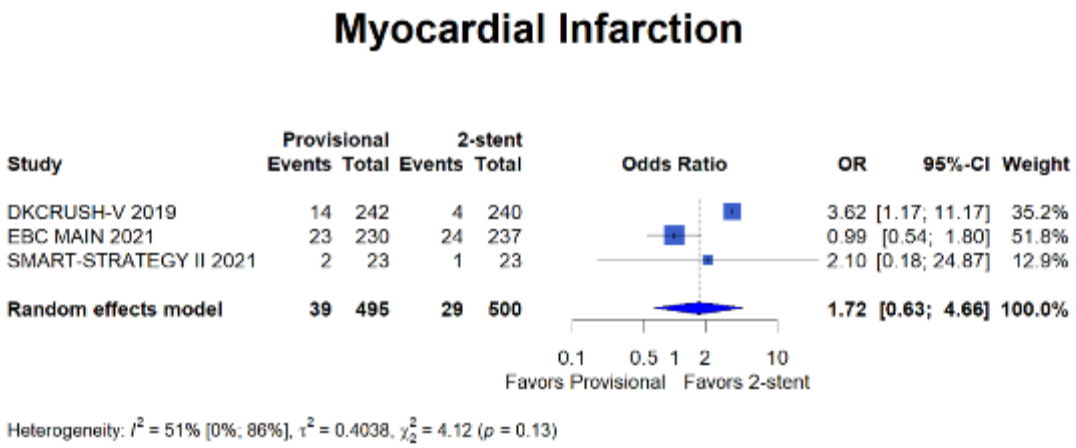
A)


MACE
Study
Provisional Events Total
2-stent Events Total
Odds Ratio
OR 95%-CI Weight
DKCRUSH-V 2019 41 242 20 240 2.24 [1.27; 3.96] 39.9%
EBC MAIN 2021 34 230 42 237 0.81 [0.49; 1.32] 42.1%
SMART-STRATEGY II 2021 4 23 5 23 0.76 [0.18; 3.28] 17.9%
Random effects model 79 495 67 500 1.20 [0.56; 2.59] 100.0%
0.2 0.5 1 2 5
Favors Provisional Favors 2-stent
Heterogeneity: I^2 = 74% [11%; 92%], τ^2 = 0.3031, χ^2_2 = 7.55 (p = 0.02)

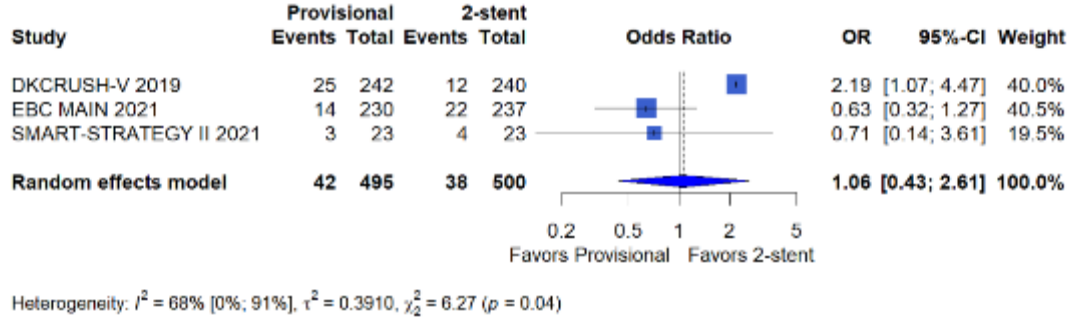
B)


Cardiac Death
Study
Provisional Events Total
2-stent Events Total
Odds Ratio
OR 95%-CI Weight
DKCRUSH-V 2019 12 242 8 240 1.51 [0.61; 3.77] 90.6%
SMART-STRATEGY II 2021 1 23 1 23 1.00 [0.06; 17.02] 9.4%
Random effects model 13 265 9 263 1.46 [0.61; 3.47] 100.0%
0.1 0.5 1 2 10
Favors Provisional Favors 2-stent
Heterogeneity: I^2 = 0%, τ^2 = 0, χ^2_1 = 0.07 (p = 0.79)

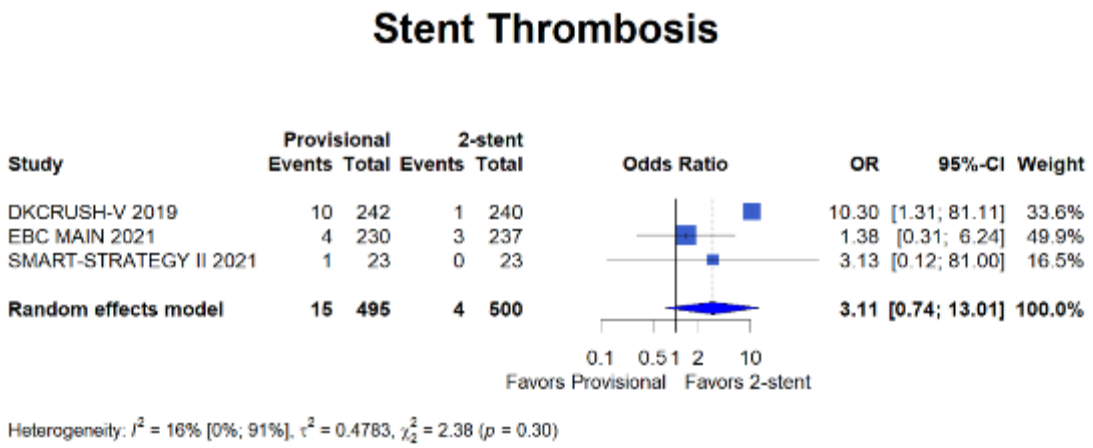
C)


Myocardial Infarction
Study
Provisional Events Total
2-stent Events Total
Odds Ratio
OR 95%-CI Weight
DKCRUSH-V 2019 14 242 4 240 3.62 [1.17; 11.17] 35.2%
EBC MAIN 2021 23 230 24 237 0.99 [0.54; 1.80] 51.8%
SMART-STRATEGY II 2021 2 23 1 23 2.10 [0.18; 24.87] 12.9%
Random effects model 39 495 29 500 1.72 [0.63; 4.66] 100.0%
0.1 0.5 1 2 10
Favors Provisional
Favors 2-stent
Heterogeneity: I^2 = 51% [0%; 86%], τ^2 = 0.4038, χ^2_2 = 4.12 (p = 0.13)

D)


Target Lesion Revascularization
Study
Provisional Events Total
2-stent Events Total
Odds Ratio
OR 95%-CI Weight
DKCRUSH-V 2019 25 242 12 240 2.19 [1.07; 4.47] 40.0%
EBC MAIN 2021 14 230 22 237 0.63 [0.32; 1.27] 40.5%
SMART-STRATEGY II 2021 3 23 4 23 0.71 [0.14; 3.61] 19.5%
Random effects model 42 495 38 500 1.06 [0.43; 2.61] 100.0%
0.2 0.5 1 2 5
Favors Provisional
Favors 2-stent
Heterogeneity: I^2 = 68% [0%; 91%], τ^2 = 0.3910, χ^2_2 = 6.27 (p = 0.04)

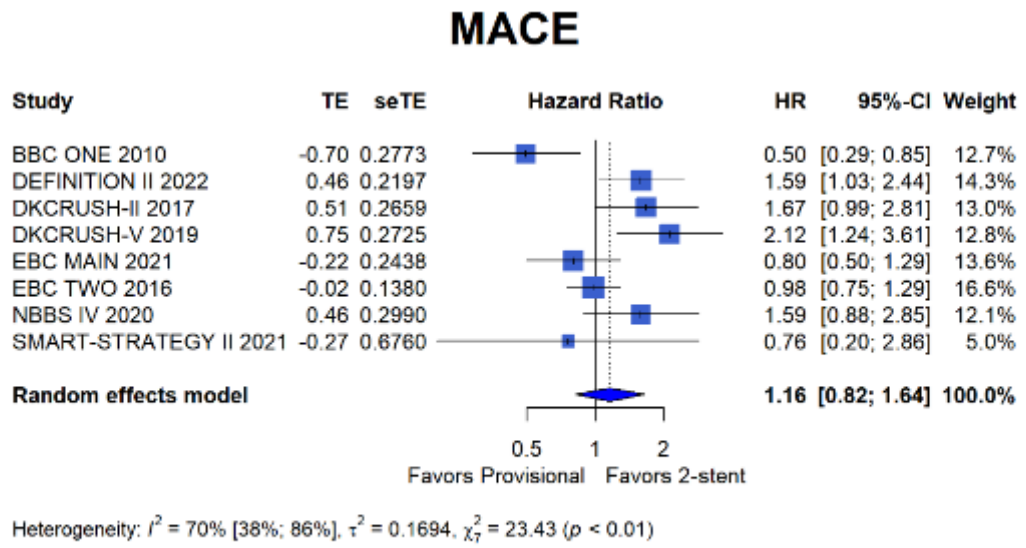
E)



Supplementary Figure 8. Forest plots presenting results of the sensitivity analysis, including trials evaluating left main bifurcations.

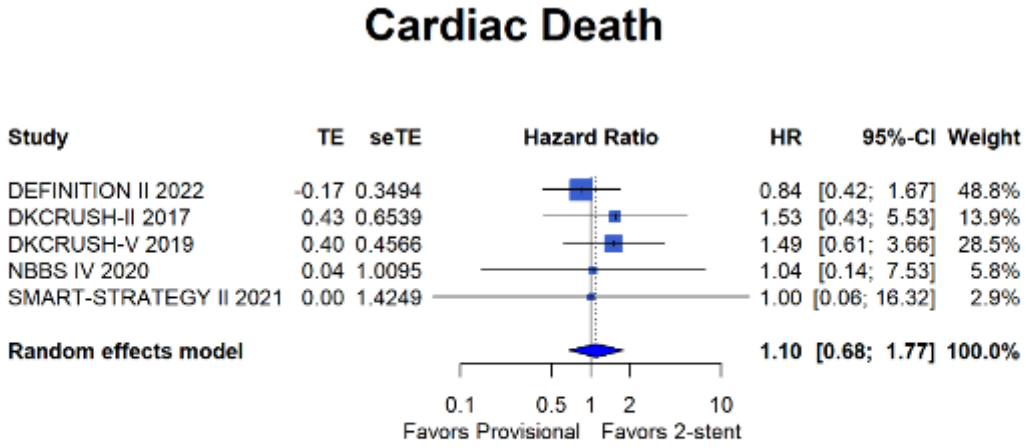
MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularisation (D), and stent thrombosis (E).

A)



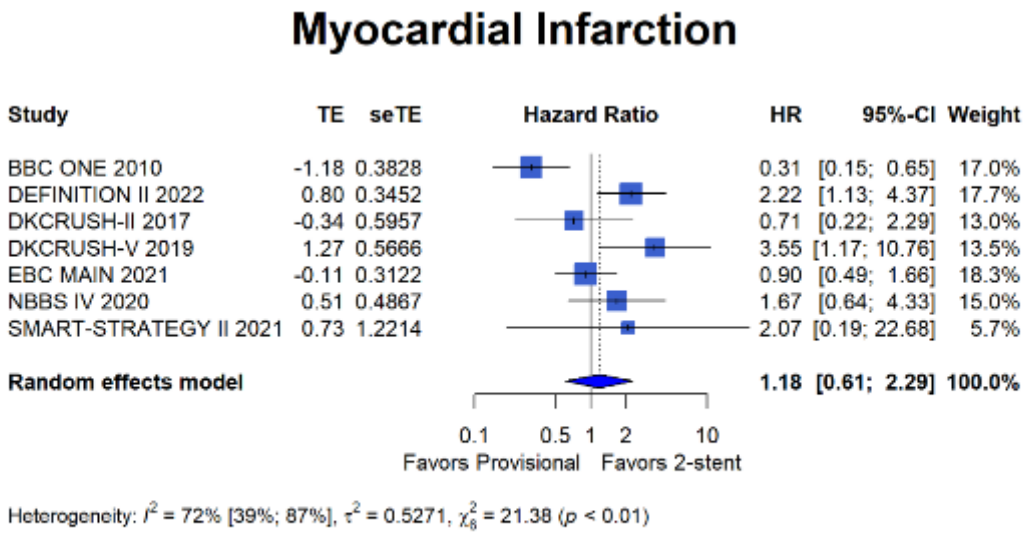
Heterogeneity: I^2 = 70% [38%; 86%], τ^2 = 0.1694, χ^2_7 = 23.43 (p < 0.01)

B)

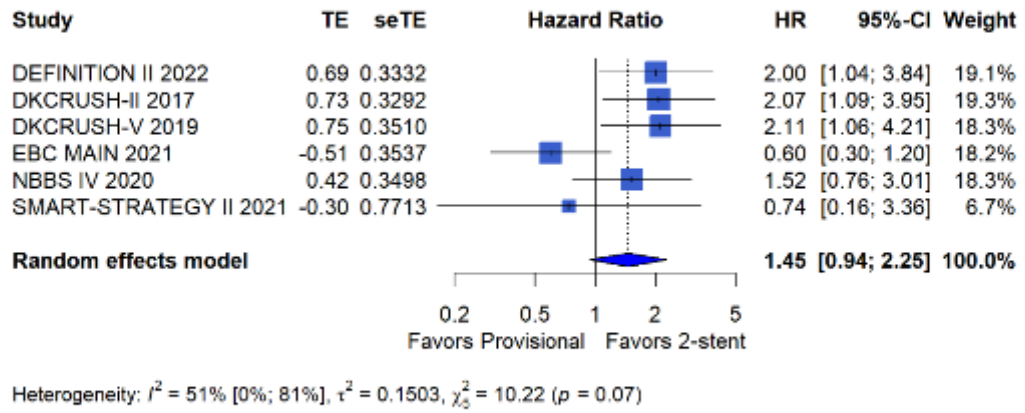


Heterogeneity: I^2 = 0% [0%; 79%], τ^2 = 0, χ^2_4 = 1.31 (p = 0.86)

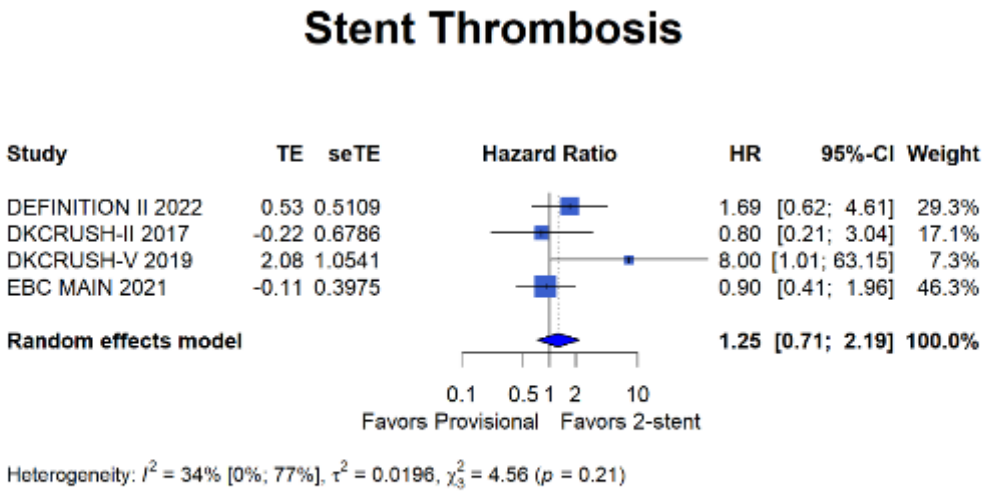
C)


Myocardial Infarction
Study
TE
seTE
Hazard Ratio
HR
95%-CI
Weight
BBC ONE 2010 -1.18 0.3828 0.31 [0.15; 0.65] 17.0%
DEFINITION II 2022 0.80 0.3452 2.22 [1.13; 4.37] 17.7%
DKCRUSH-II 2017 -0.34 0.5957 0.71 [0.22; 2.29] 13.0%
DKCRUSH-V 2019 1.27 0.5666 3.55 [1.17; 10.76] 13.5%
EBC MAIN 2021 -0.11 0.3122 0.90 [0.49; 1.66] 18.3%
NBBS IV 2020 0.51 0.4867 1.67 [0.64; 4.33] 15.0%
SMART-STRATEGY II 2021 0.73 1.2214 2.07 [0.19; 22.68] 5.7%
Random effects model 1.18 [0.61; 2.29] 100.0%
0.1
0.5
1
2
10
Favors Provisional
Favors 2-stent
Heterogeneity: I^2 = 72% [39%; 87%], τ^2 = 0.5271, χ^2_8 = 21.38 (p < 0.01)

D)


Target Lesion Revascularization
Study
TE
seTE
Hazard Ratio
HR
95%-CI
Weight
DEFINITION II 2022 0.69 0.3332 2.00 [1.04; 3.84] 19.1%
DKCRUSH-II 2017 0.73 0.3292 2.07 [1.09; 3.95] 19.3%
DKCRUSH-V 2019 0.75 0.3510 2.11 [1.06; 4.21] 18.3%
EBC MAIN 2021 -0.51 0.3537 0.60 [0.30; 1.20] 18.2%
NBBS IV 2020 0.42 0.3498 1.52 [0.76; 3.01] 18.3%
SMART-STRATEGY II 2021 -0.30 0.7713 0.74 [0.16; 3.36] 6.7%
Random effects model 1.45 [0.94; 2.25] 100.0%
0.2
0.5
1
2
5
Favors Provisional
Favors 2-stent
Heterogeneity: I^2 = 51% [0%; 81%], τ^2 = 0.1503, χ^2_5 = 10.22 (p = 0.07)

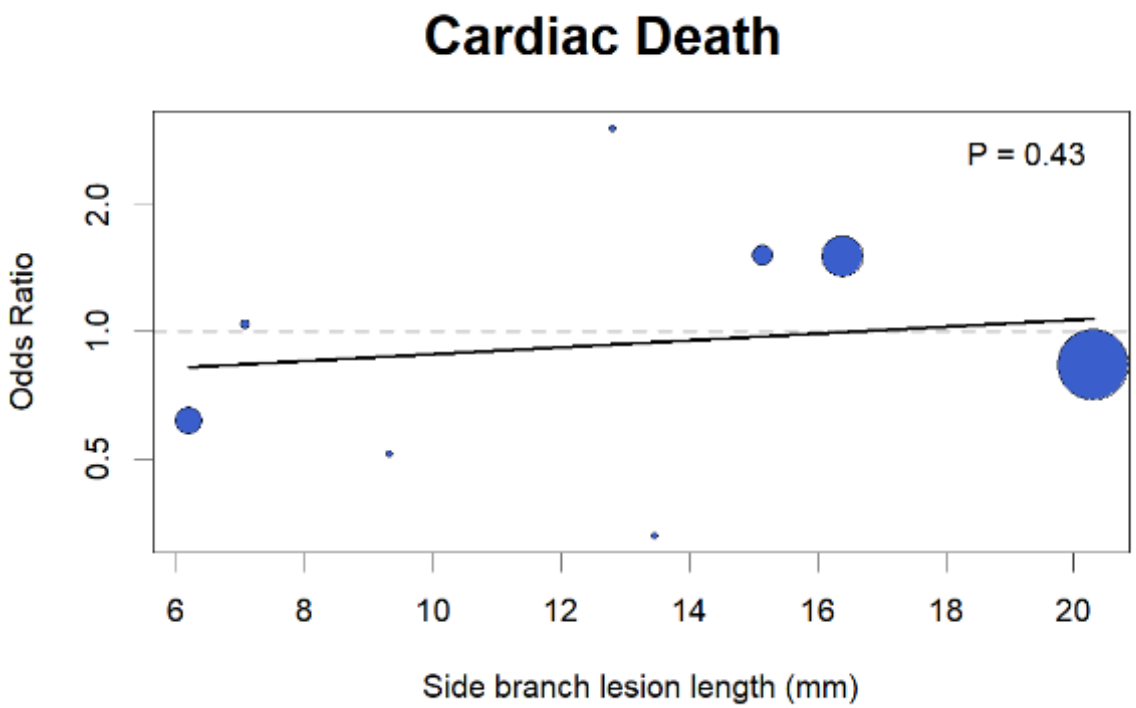
E)



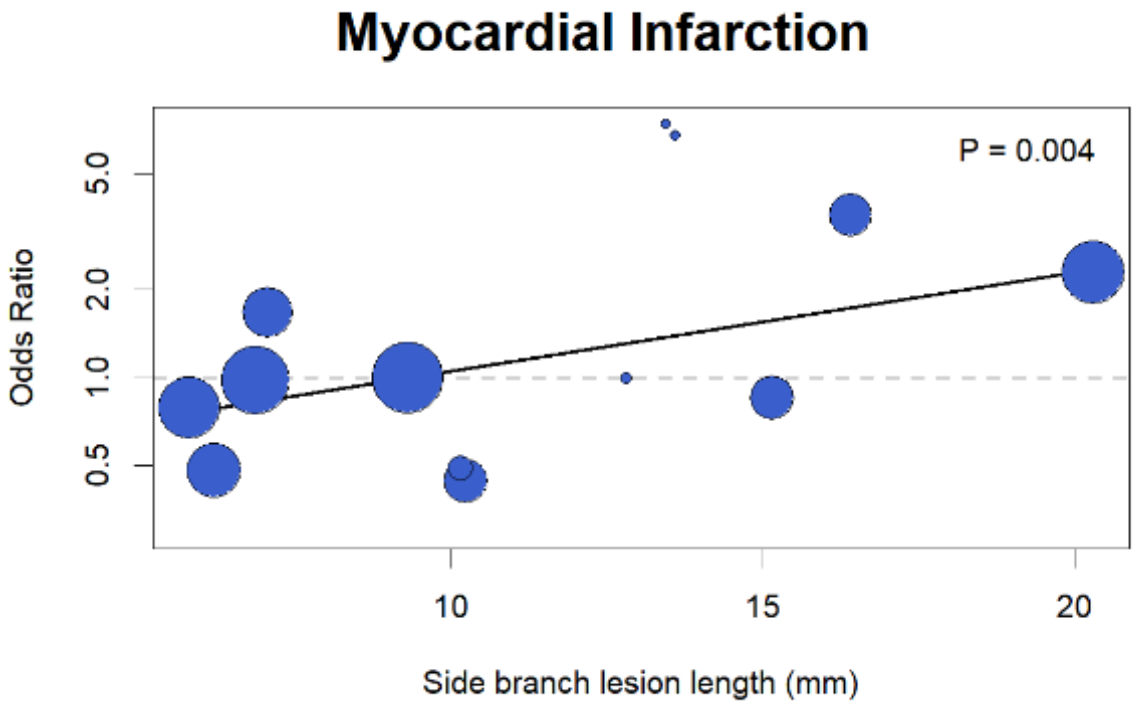
Supplementary Figure 9. Forest plots presenting results of the sensitivity analysis of time-to-event data.

MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularisation (D), and stent thrombosis (E).

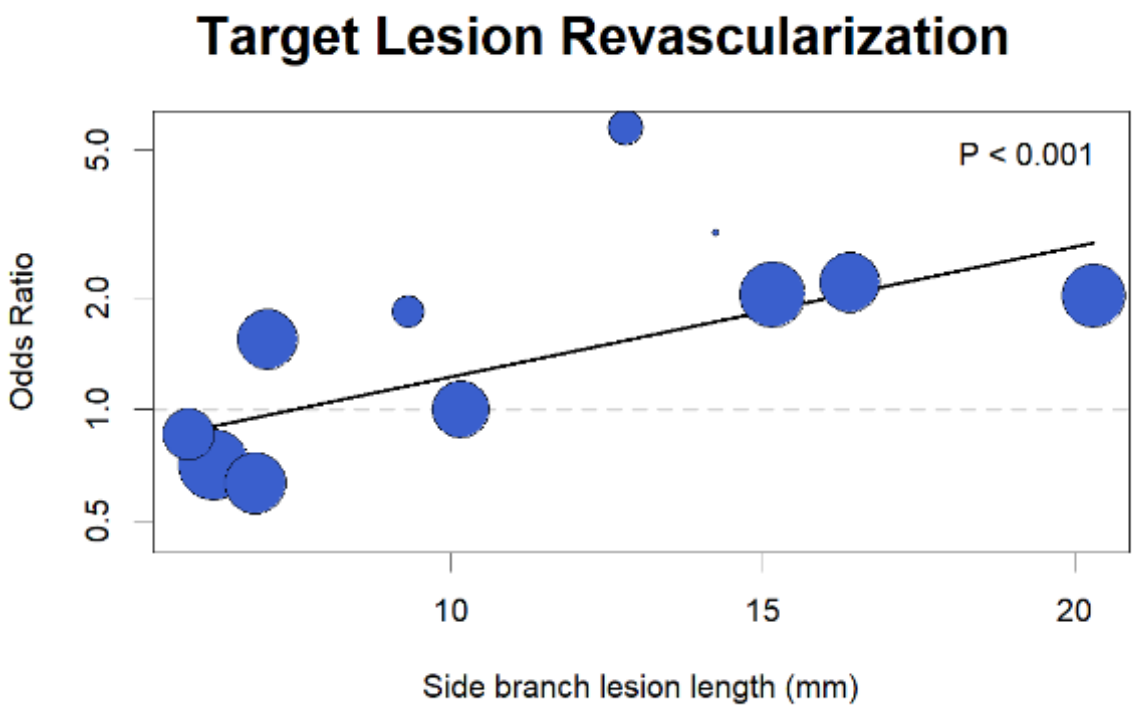
A)


Cardiac Death
P = 0.43
Odds Ratio
0.5
1.0
2.0
6
8
10
12
14
16
18
20
Side branch lesion length (mm)

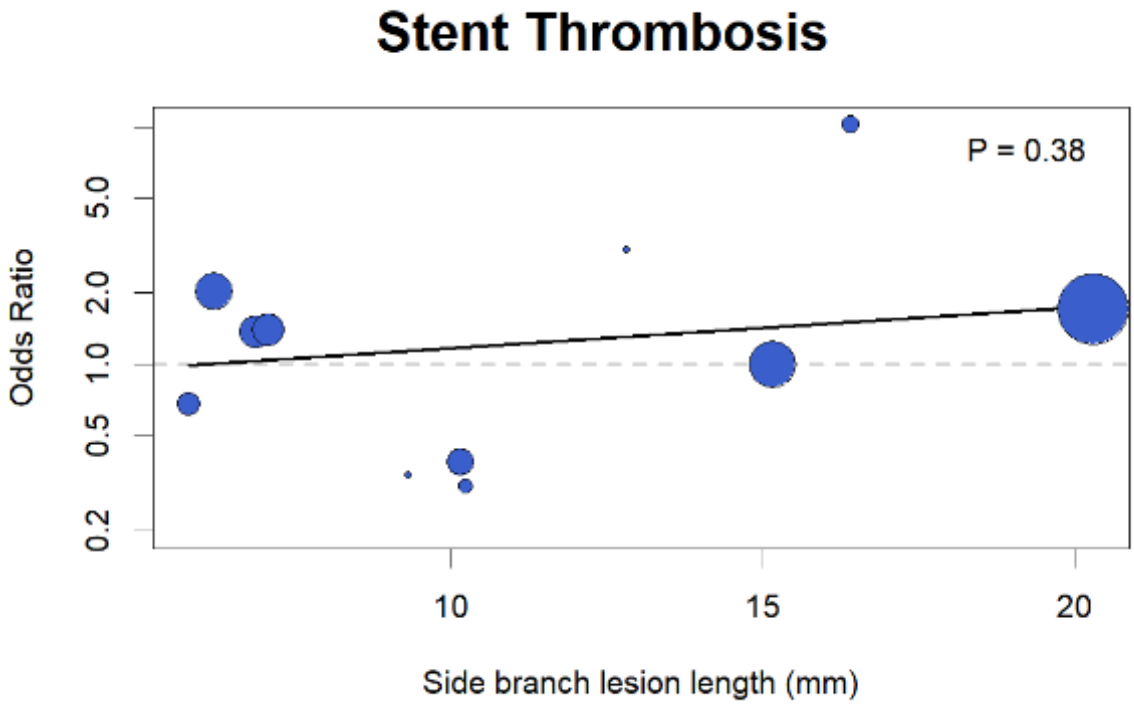
B)


Myocardial Infarction
P = 0.004
Odds Ratio
0.5
1.0
2.0
5.0
10
15
20
Side branch lesion length (mm)

C)



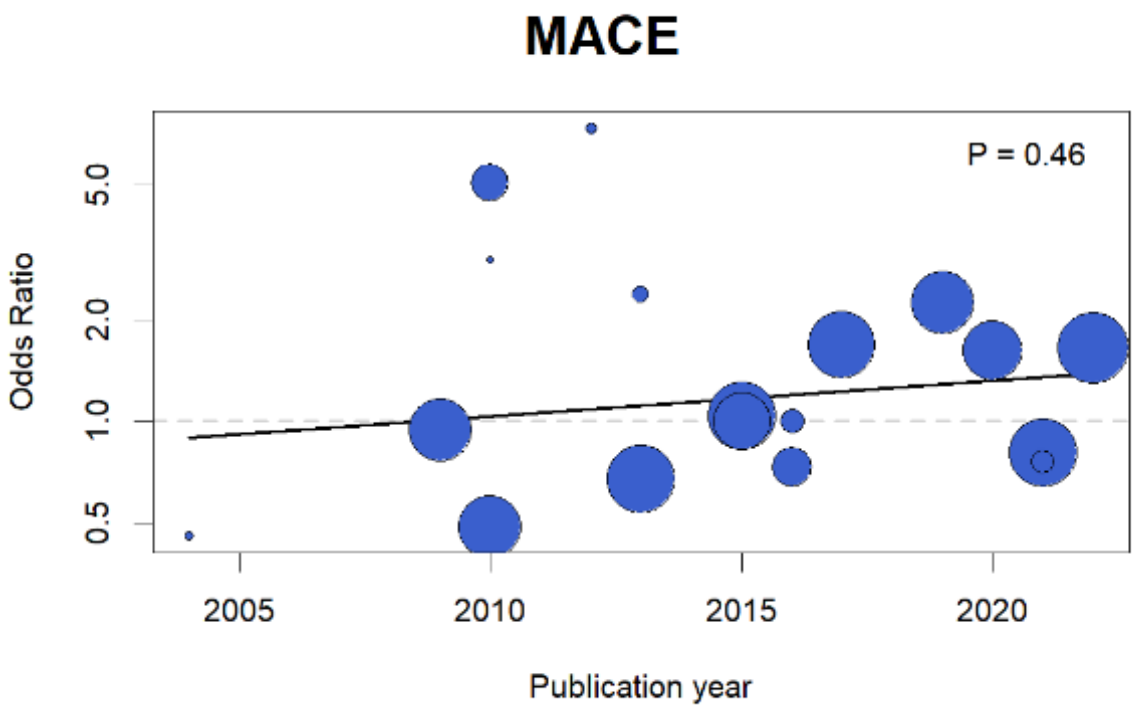
D)



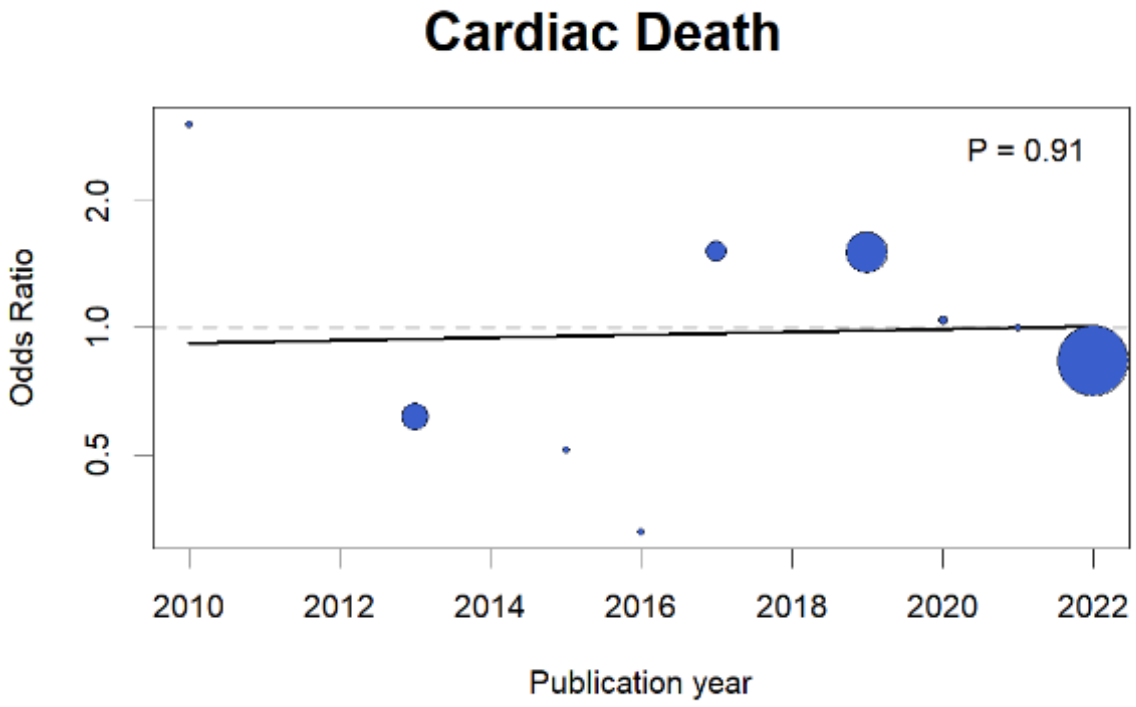
Supplementary Figure 10. Bubble plots showing the results of meta-regression evaluating the effect of provisional stenting vs. 2-stent technique, with the mean side branch lesion length as a covariate.

On cardiac death (A), myocardial infarction (B), target lesion revascularization (C), and stent thrombosis (D).

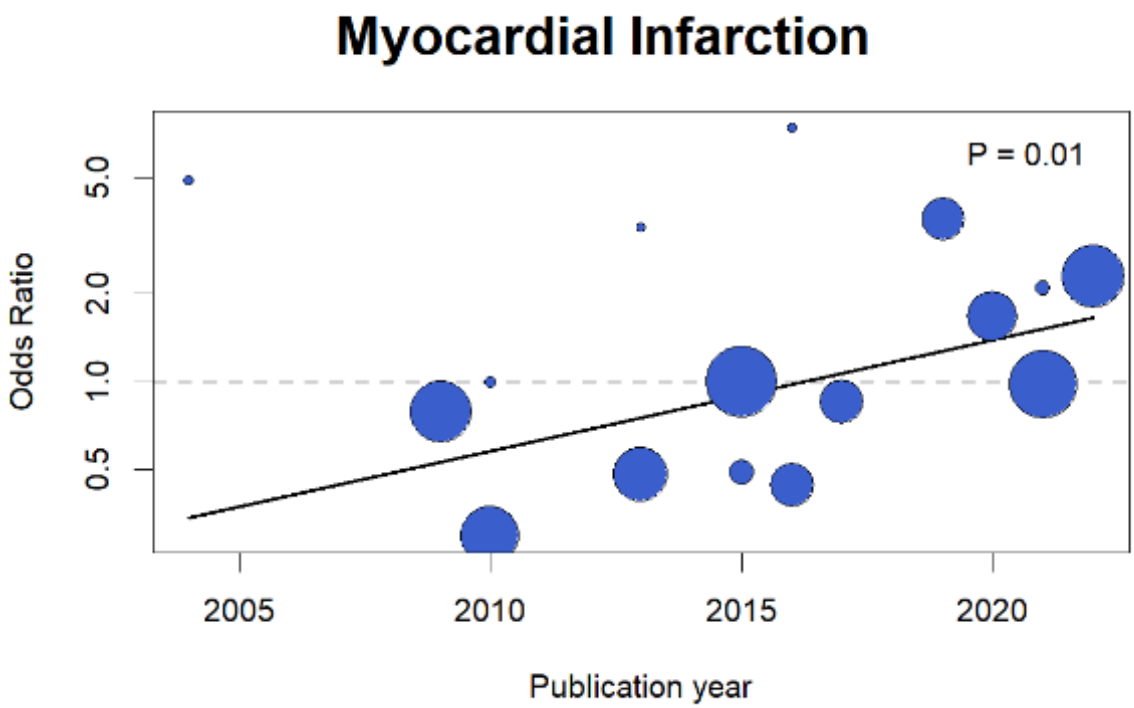
A)


MACE
P = 0.46
Odds Ratio
0.5
1.0
2.0
5.0
2005
2010
2015
2020
Publication year

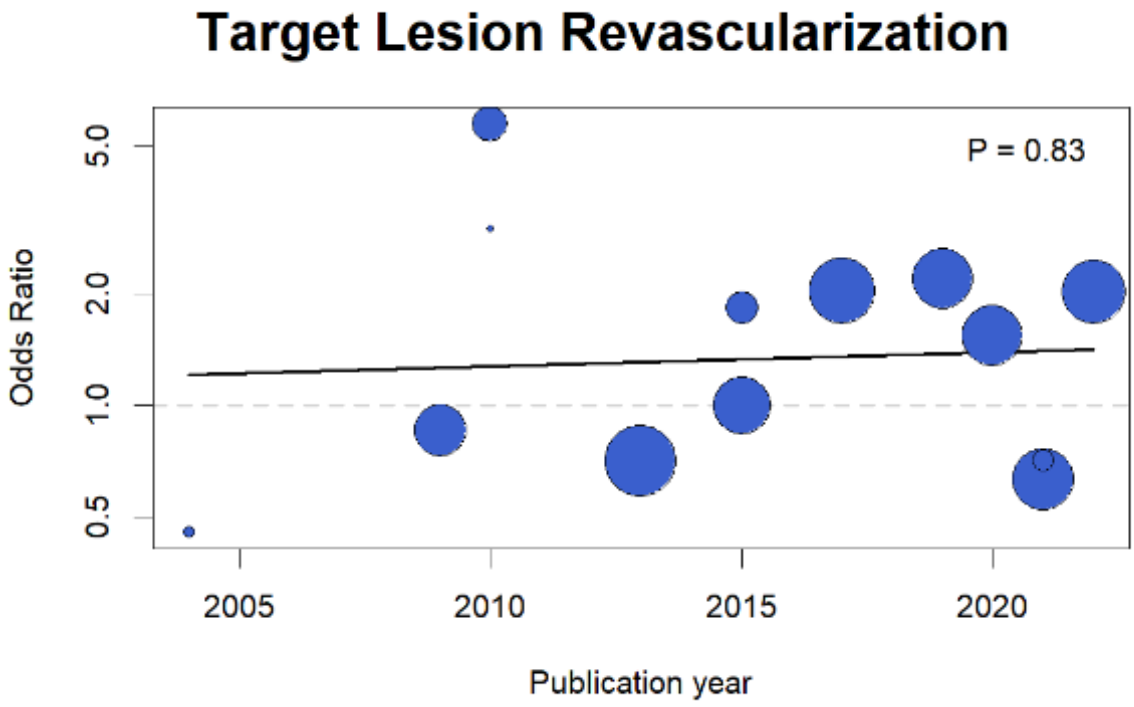
B)


Cardiac Death
P = 0.91
Odds Ratio
0.5
1.0
2.0
2010
2012
2014
2016
2018
2020
2022
Publication year

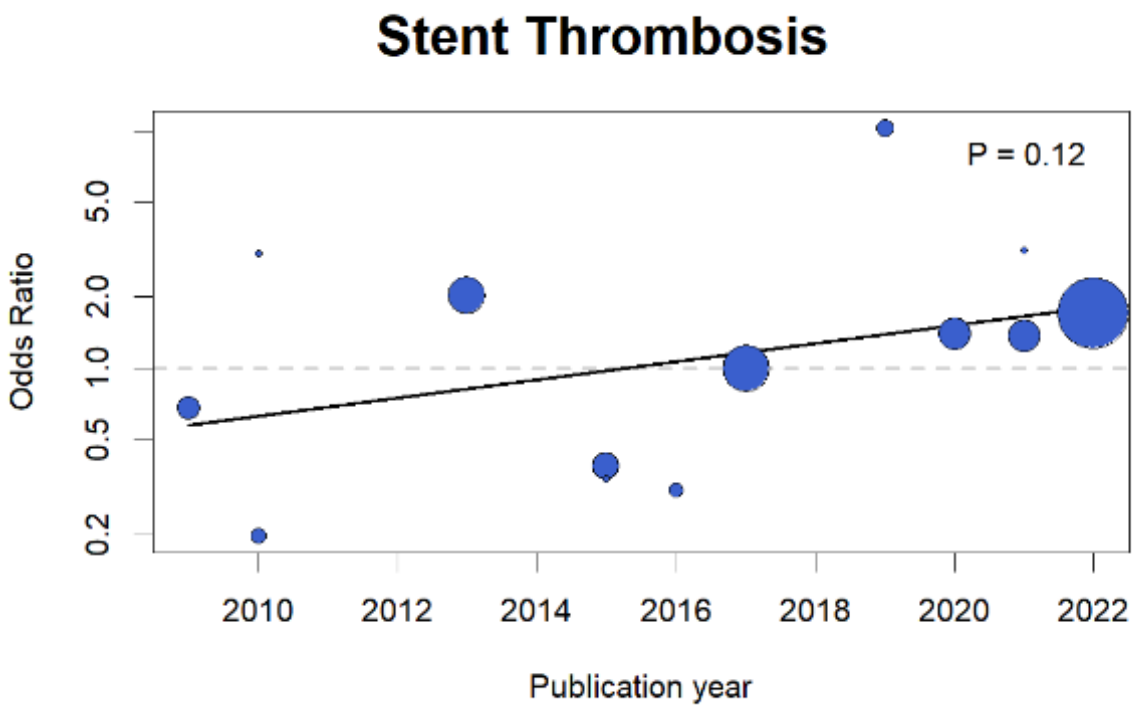
C)


Myocardial Infarction
P = 0.01
Odds Ratio
0.5
1.0
2.0
5.0
2005
2010
2015
2020
Publication year

D)


Target Lesion Revascularization
P = 0.83
Odds Ratio
0.5
1.0
2.0
5.0
2005
2010
2015
2020
Publication year

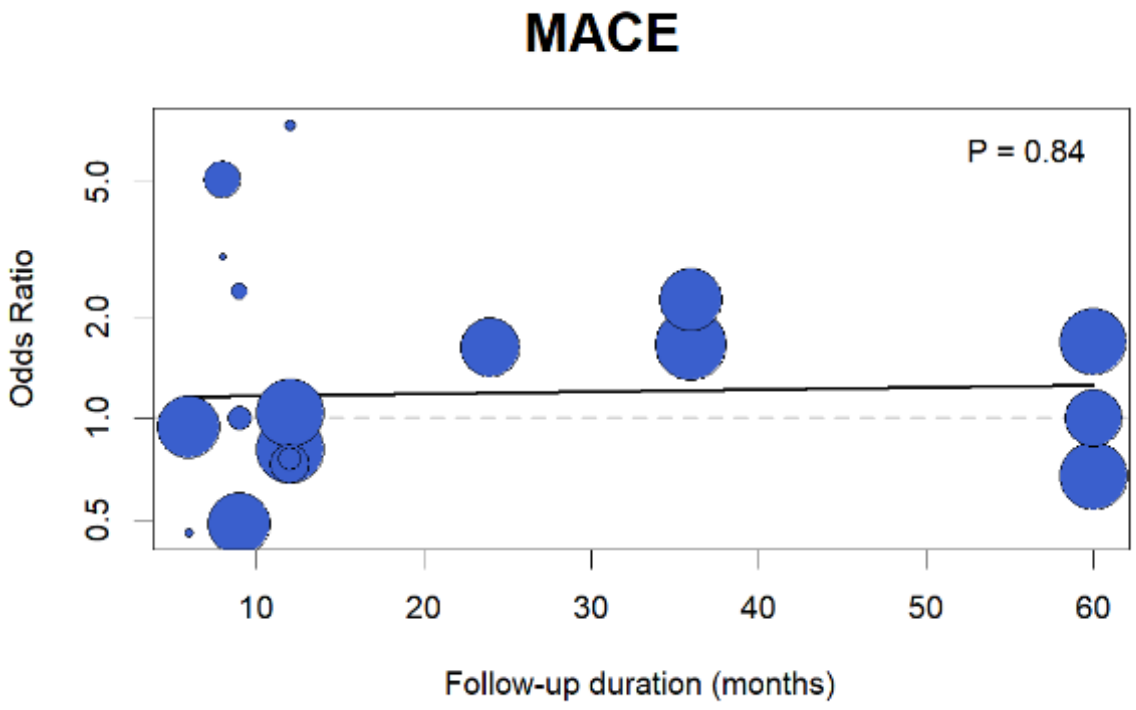
E)



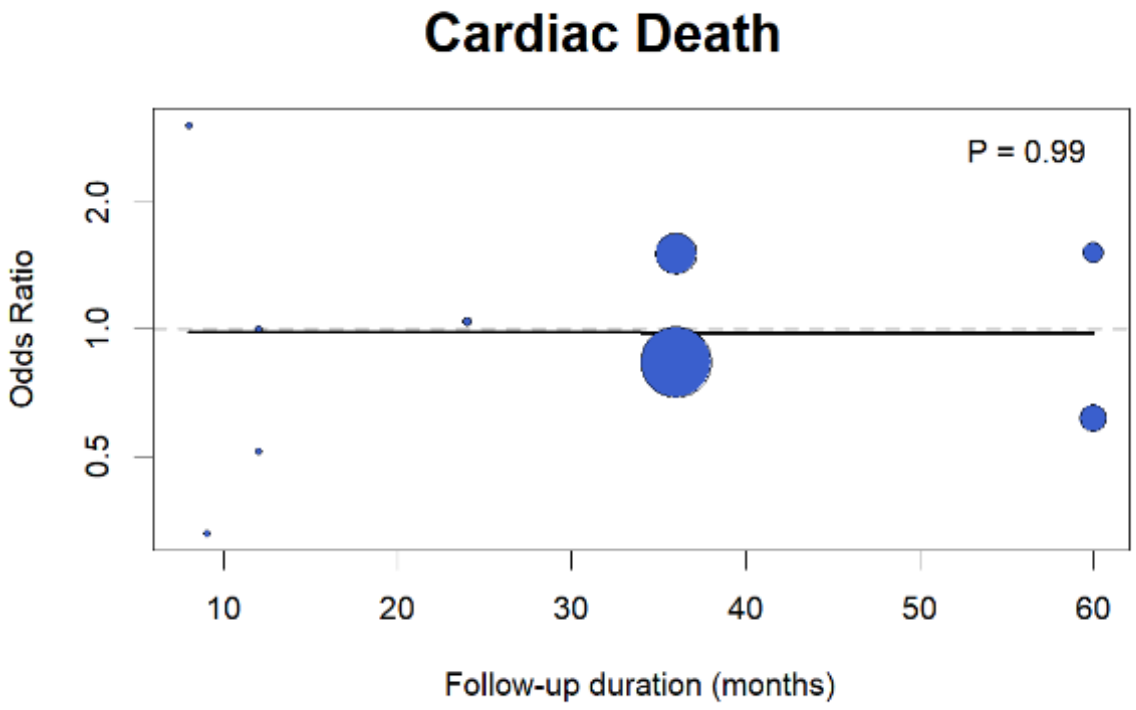
Supplementary Figure 11 Bubble plots showing the results of meta-regression evaluating the effect of provisional stenting versus 2-stent technique with the publication year as a covariate.

MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularization (D), and stent thrombosis (E).

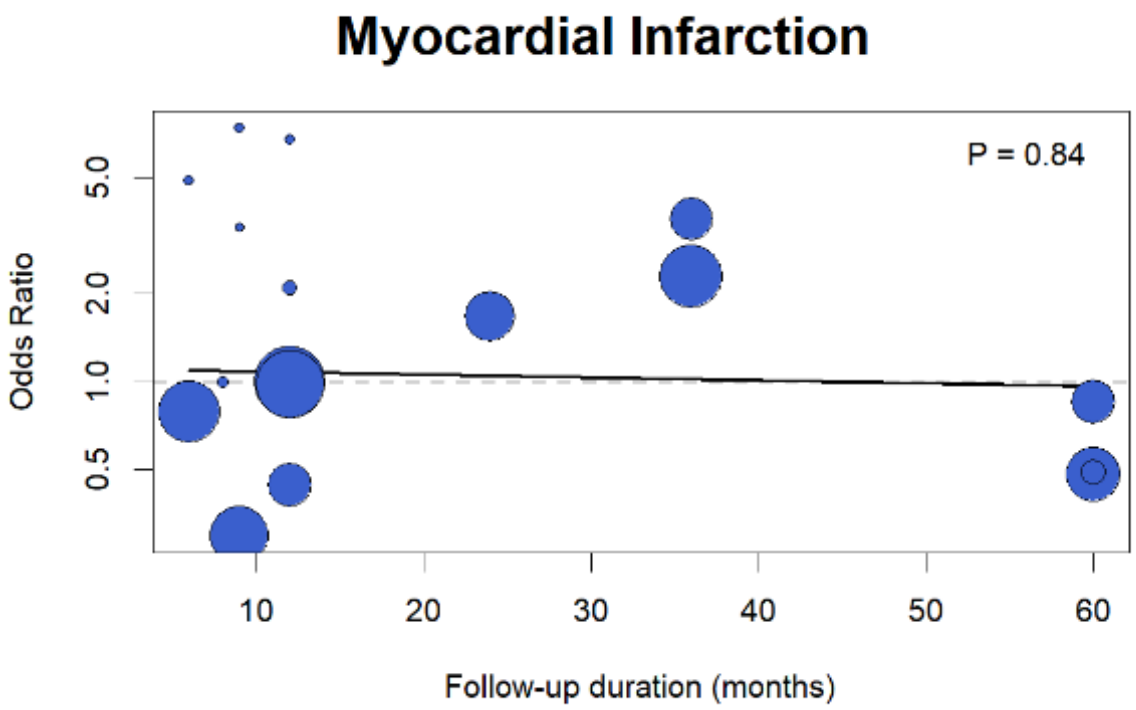
A)


MACE
P = 0.84
Odds Ratio
0.5
1.0
2.0
5.0
10
20
30
40
50
60
Follow-up duration (months)

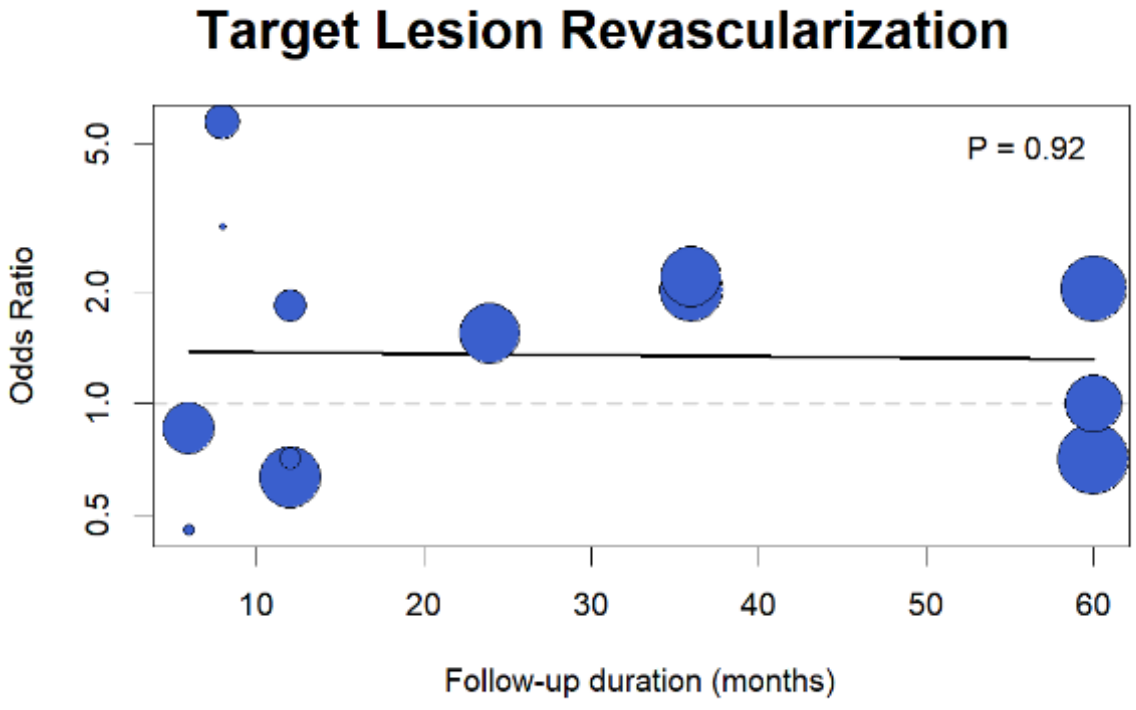
B)


Cardiac Death
P = 0.99
Odds Ratio
0.5
1.0
2.0
10
20
30
40
50
60
Follow-up duration (months)

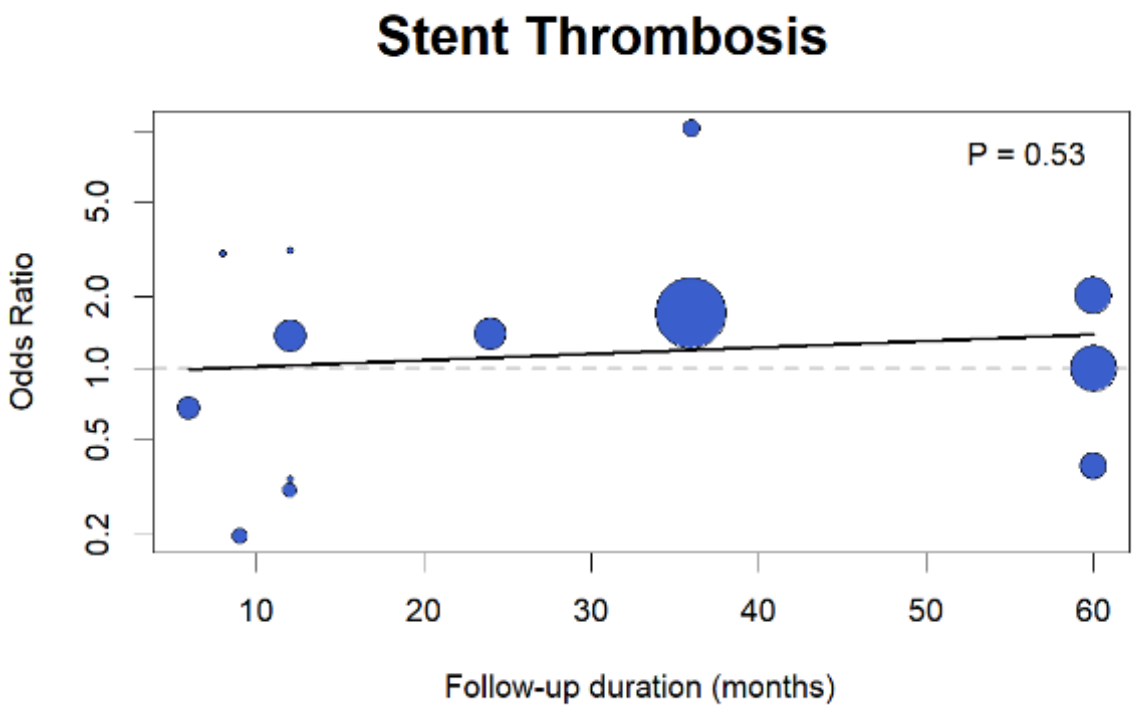
C)


Myocardial Infarction
P = 0.84
Odds Ratio
0.5
1.0
2.0
5.0
10
20
30
40
50
60
Follow-up duration (months)

D)


Target Lesion Revascularization
P = 0.92
Odds Ratio
0.5
1.0
2.0
5.0
10
20
30
40
50
60
Follow-up duration (months)

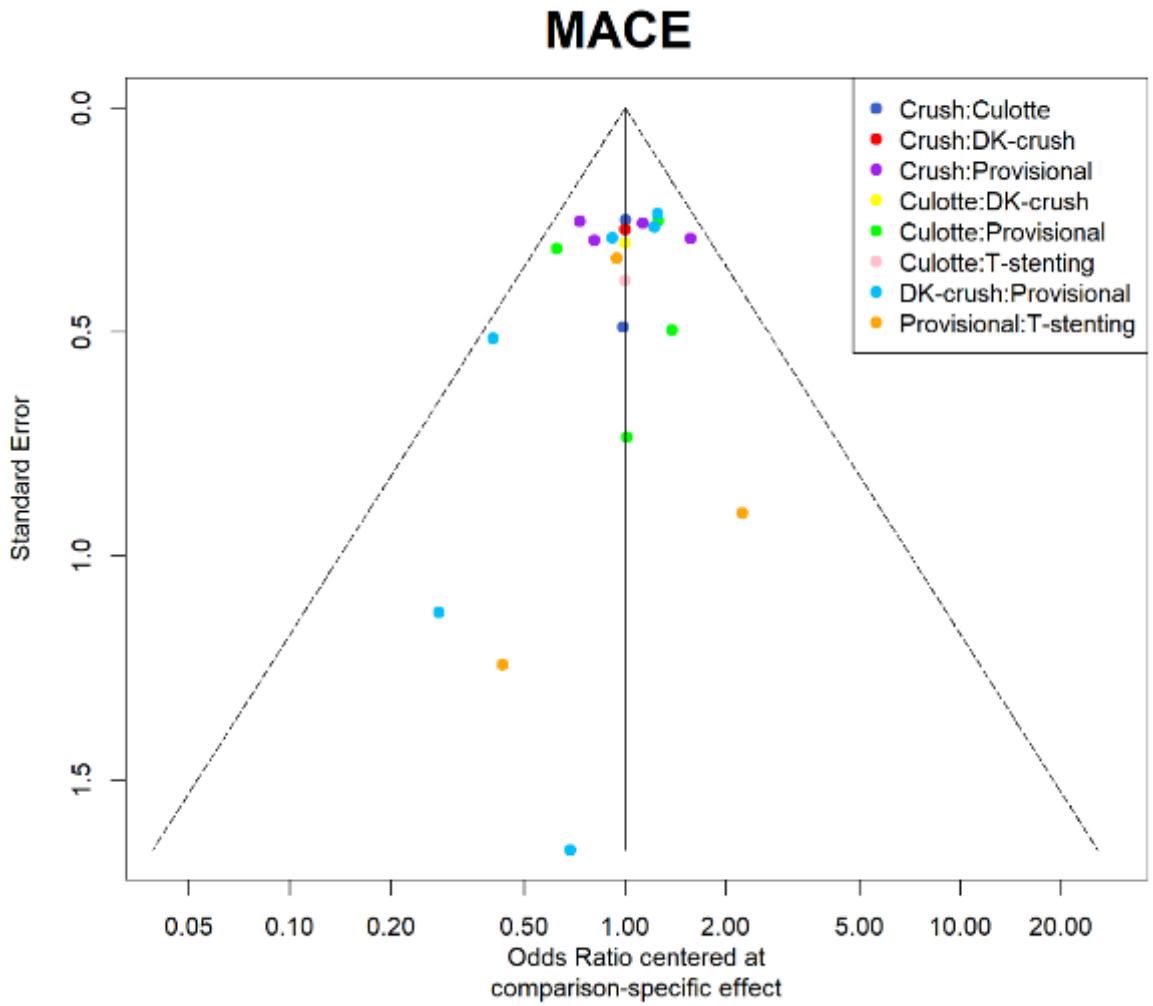
E)



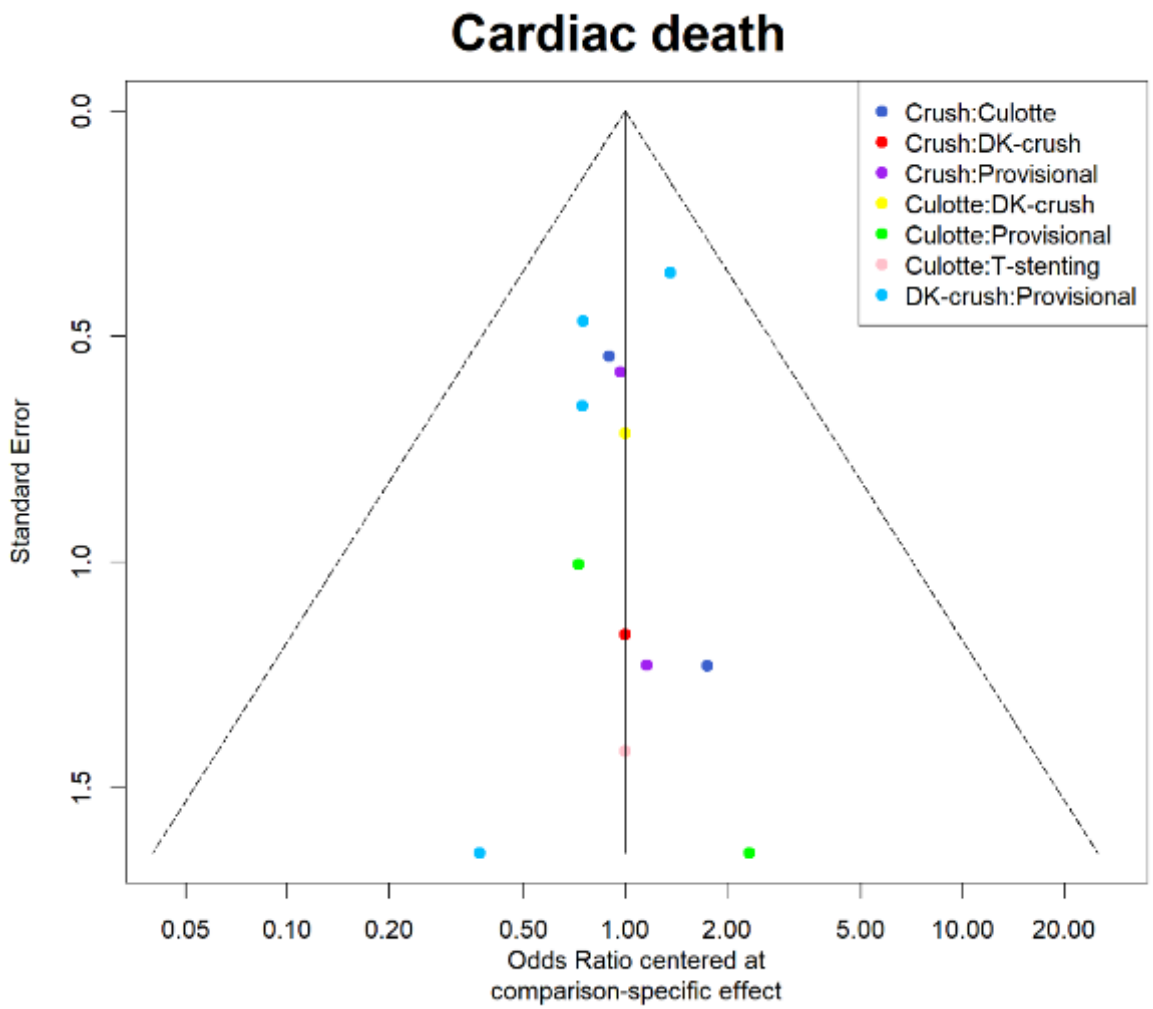
Supplementary Figure 12. Bubble plots showing the results of meta-regression evaluating the effect of provisional stenting versus 2-stent technique with the follow-up duration as a covariate.

MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularisation (D), and stent thrombosis (E).

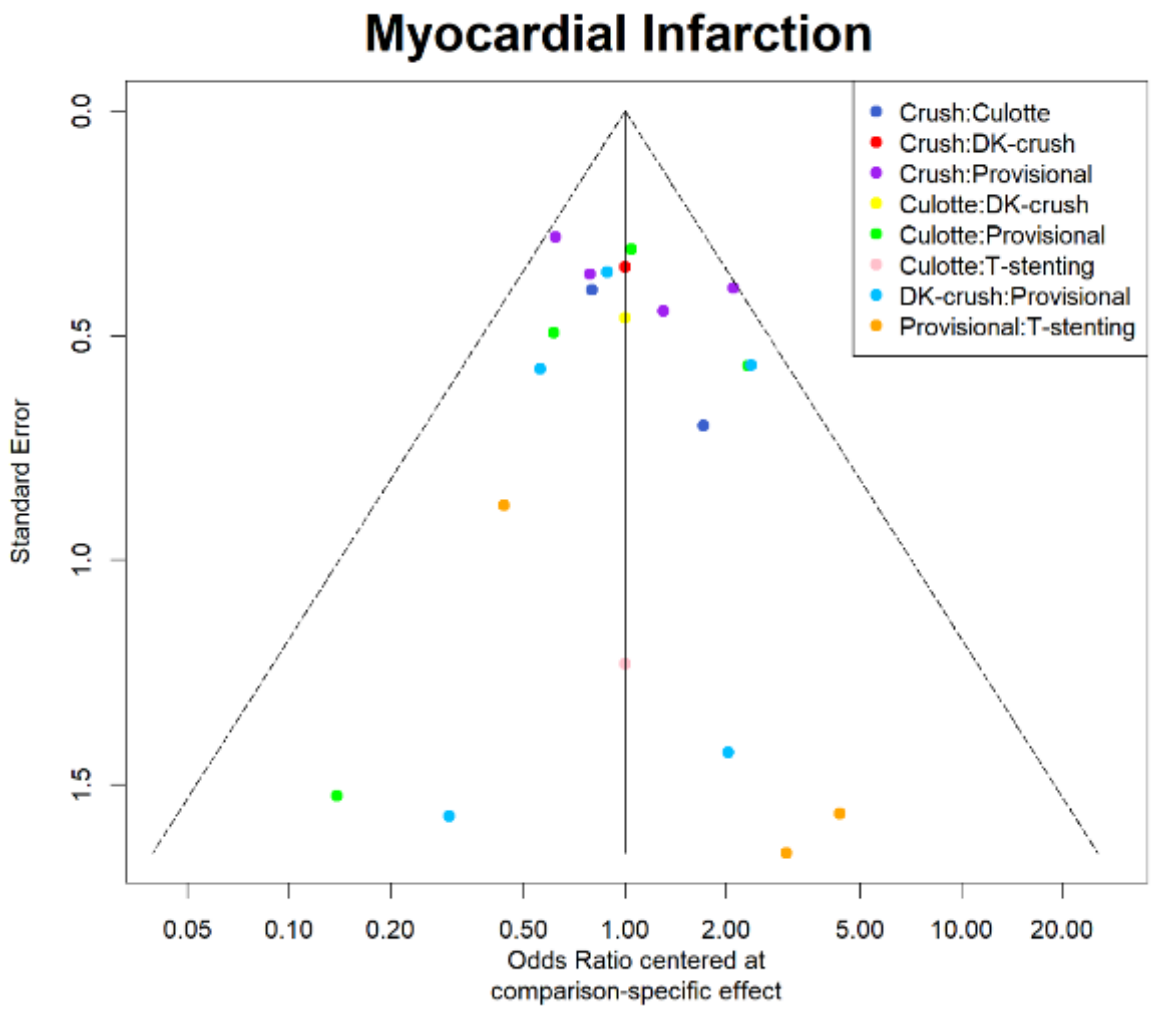
A)


MACE
Crush:Culotte
Crush:DK-crush
Crush:Provisional
Culotte:DK-crush
Culotte:Provisional
Culotte:T-stenting
DK-crush:Provisional
Provisional:T-stenting
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio centered at
comparison-specific effect

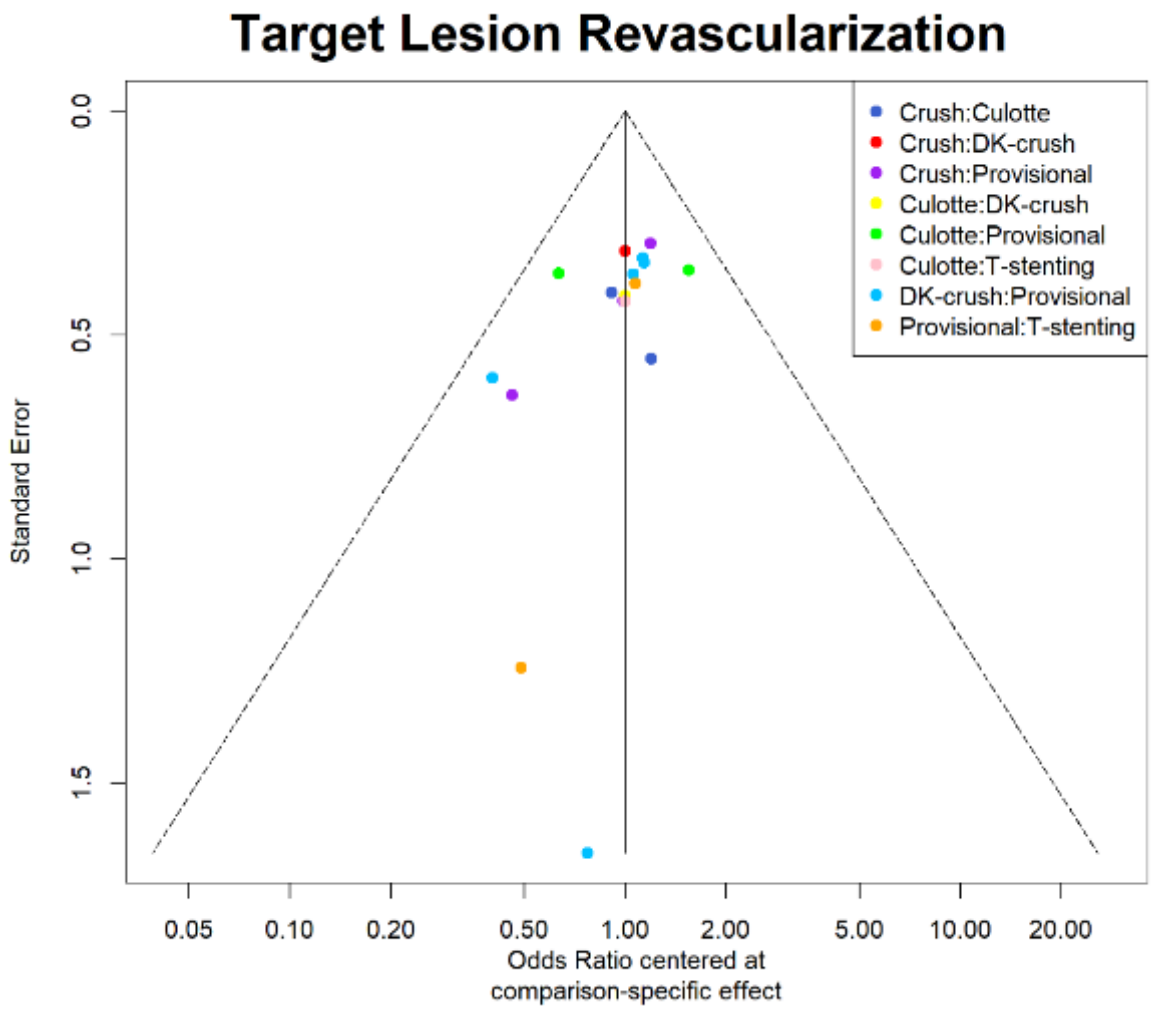
B)


Cardiac death
Crush:Culotte
Crush:DK-crush
Crush:Provisional
Culotte:DK-crush
Culotte:Provisional
Culotte:T-stenting
DK-crush:Provisional
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio centered at
comparison-specific effect

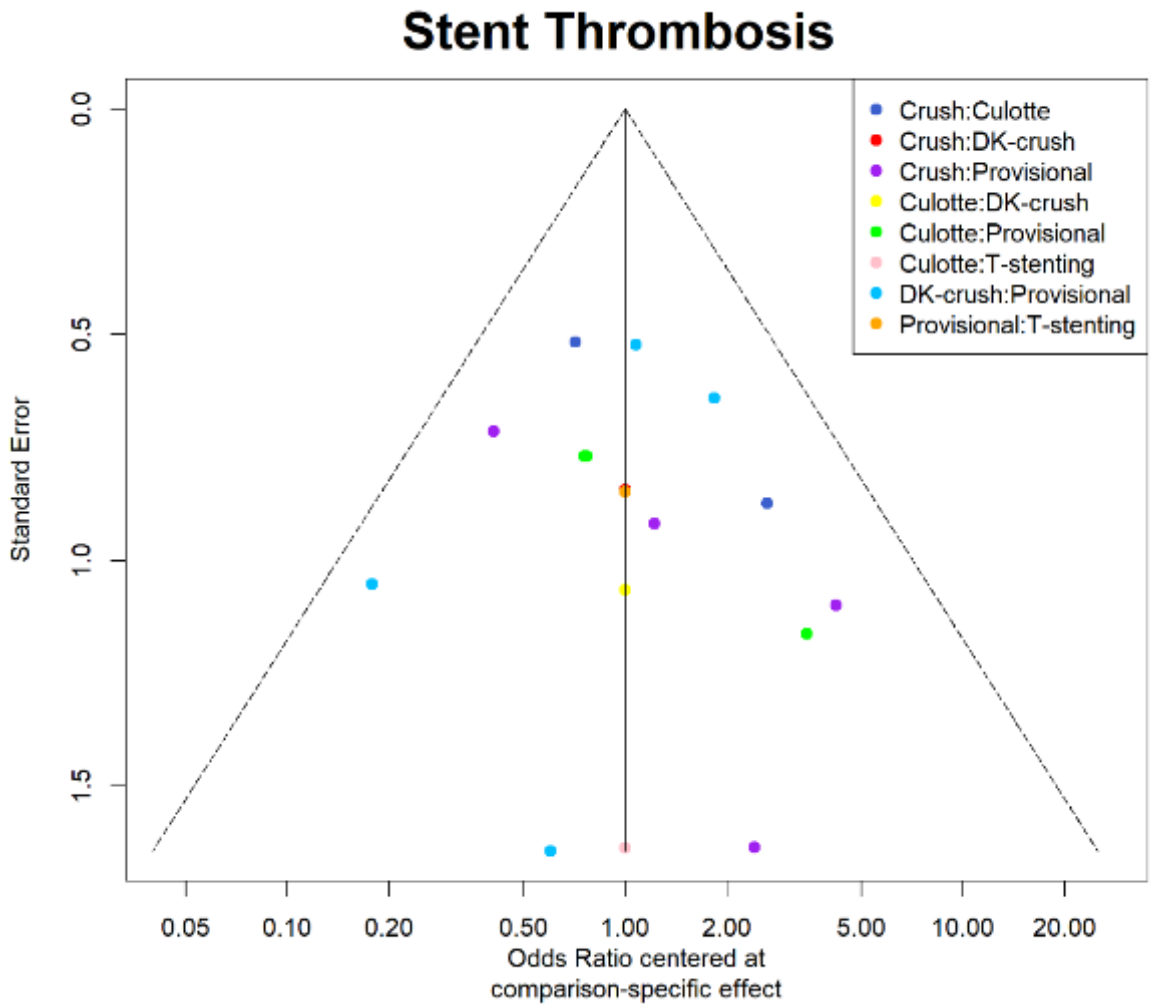
C)


Myocardial Infarction
Crush:Culotte
Crush:DK-crush
Crush:Provisional
Culotte:DK-crush
Culotte:Provisional
Culotte:T-stenting
DK-crush:Provisional
Provisional:T-stenting
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio centered at
comparison-specific effect

D)


Target Lesion Revascularization
Crush:Culotte
Crush:DK-crush
Crush:Provisional
Culotte:DK-crush
Culotte:Provisional
Culotte:T-stenting
DK-crush:Provisional
Provisional:T-stenting
Standard Error
0.0
0.5
1.0
1.5
0.05
0.10
0.20
0.50
1.00
2.00
5.00
10.00
20.00
Odds Ratio centered at
comparison-specific effect

E)



Supplementary Figure 13. "Comparison-adjusted" funnel plots.

MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularization (D), and stent thrombosis (E).

MACE (No. of studies = 19; No. of patients = 6542)

Cochran's Q-test p-value = 0.25; I^2 = 17.9% [0.0%; 54.3%]; τ^2 = 0.02

DK-crush	**0.50 (0.36 to 0.69)**	**0.29 (0.15 to 0.55)**	**0.51 (0.28 to 0.94)**	NA
0.48 (0.37 to 0.63)	**Provisional**	1.01 (0.69 to 1.49)	0.76 (0.56 to 1.03)	0.94 (0.47 to 1.87)
0.46 (0.33 to 0.66)	0.96 (0.72 to 1.28)	**Culotte**	0.78 (0.47 to 1.28)	0.57 (0.25 to 1.27)
0.39 (0.28 to 0.54)	0.80 (0.62 to 1.03)	0.83 (0.60 to 1.15)	**Crush**	NA
0.36 (0.20 to 0.65)	0.75 (0.44 to 1.28)	0.78 (0.45 to 1.35)	0.93 (0.52 to 1.67)	**T-stenting**

Cardiac death (No. of studies = 13; No. of patients = 4732)

Cochran's Q-test p-value = 0.98; I^2 = 0% [0.0%; 62.4%]; τ^2 = 0

DK-crush	0.88 (0.53 to 1.46)	NA	0.49 (0.12 to 1.99)	0.33 (0.03 to 3.22)
0.85 (0.53 to 1.38)	**Provisional**	NA	0.76 (0.14 to 4.09)	0.60 (0.21 to 1.66)
0.55 (0.03 to 10.15)	0.64 (0.03 to 11.81)	**T-stenting**	1.00 (0.06 to 16.14)	NA
0.55 (0.23 to 1.33)	0.64 (0.27 to 1.52)	1.00 (0.06 to 16.14)	**Culotte**	0.87 (0.33 to 2.31)
0.48 (0.20 to 1.12)	0.56 (0.25 to 1.24)	0.87 (0.05 to 15.69)	0.87 (0.39 to 1.94)	**Crush**

Myocardial infarction (No. of studies = 19; No. of patients = 6542)

Cochran's Q-test p-value = 0.12; I^2 = 30.3% [0.0%; 61.8%]; τ^2 = 0.1

DK-crush	NA	**0.52 (0.28 to 0.98)**	0.39 (0.13 to 1.16)	0.67 (0.27 to 1.67)
0.64 (0.16 to 2.64)	**T-stenting**	1.14 (0.23 to 5.50)	0.50 (0.04 to 5.98)	NA
0.59 (0.36 to 0.96)	0.92 (0.24 to 3.49)	**Provisional**	1.03 (0.57 to 1.87)	**0.62 (0.39 to 0.99)**
0.55 (0.30 to 0.99)	0.85 (0.22 to 3.35)	0.93 (0.58 to 1.47)	**Culotte**	0.71 (0.31 to 1.63)
0.41 (0.24 to 0.70)	0.63 (0.16 to 2.54)	0.69 (0.47 to 1.03)	0.75 (0.44 to 1.25)	**Crush**

Target lesion revascularization (No. of studies = 16; No. of patients = 5738)

Cochran's Q-test p-value = 0.49; I^2 = 0% [0.0%; 56.6%]; τ^2 = 0

DK-crush	**0.43 (0.30 to 0.63)**	**0.25 (0.11 to 0.55)**	**0.42 (0.23 to 0.78)**	NA
0.41 (0.30 to 0.56)	**Provisional**	0.98 (0.60 to 1.61)	0.84 (0.54 to 1.32)	0.93 (0.45 to 1.92)
0.40 (0.26 to 0.61)	0.97 (0.68 to 1.38)	**Culotte**	0.88 (0.47 to 1.67)	0.47 (0.20 to 1.08)
0.37 (0.25 to 0.54)	0.89 (0.63 to 1.25)	0.92 (0.61 to 1.39)	**Crush**	NA
0.28 (0.15 to 0.53)	0.69 (0.39 to 1.21)	0.71 (0.40 to 1.27)	0.77 (0.41 to 1.45)	**T-stenting**

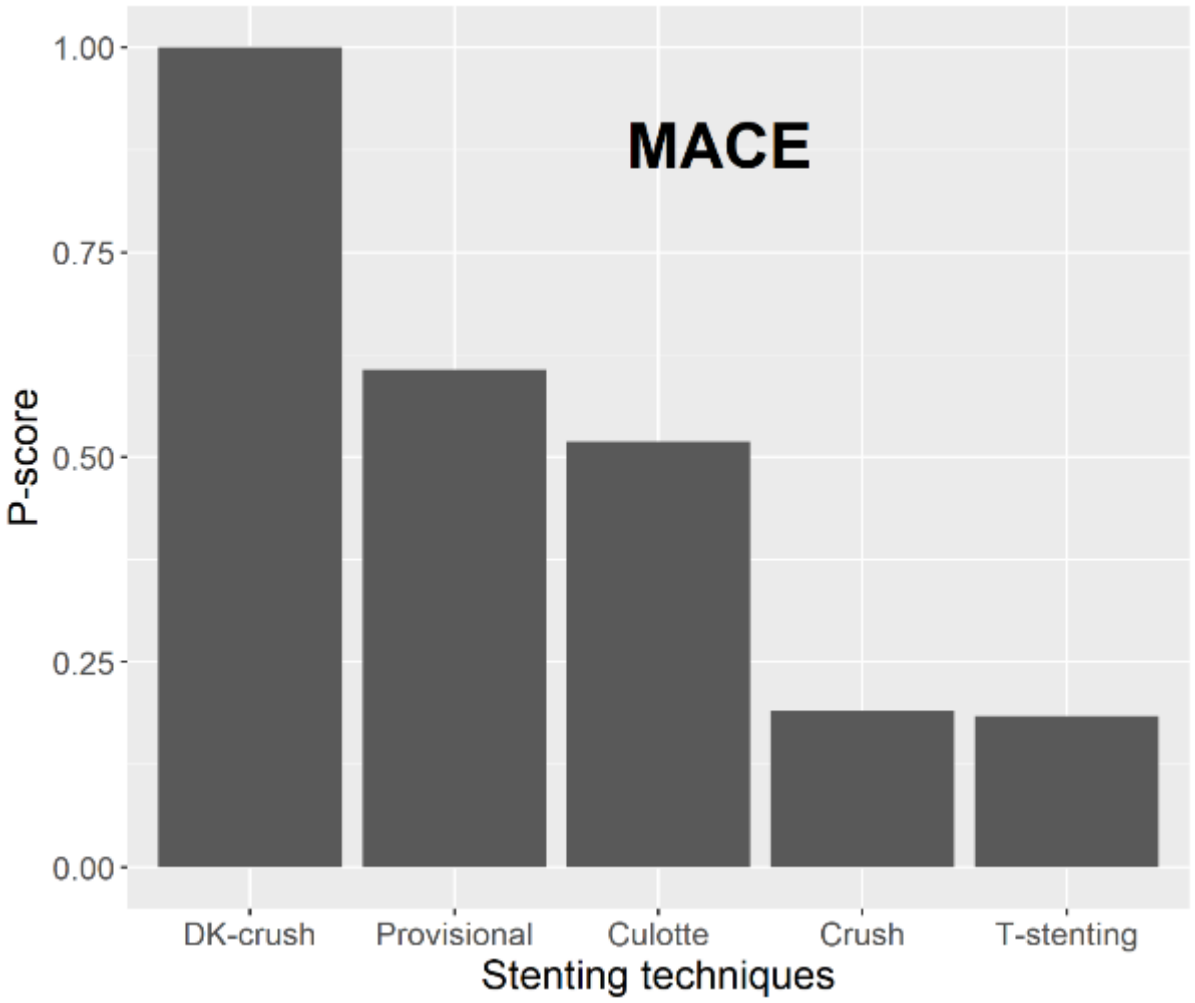
Stent thrombosis (No. of studies = 17; No. of patients = 6347)

Cochran's Q-test p-value = 0.45; I^2 = 0% [0.0%; 55.0%]; τ^2 = 0

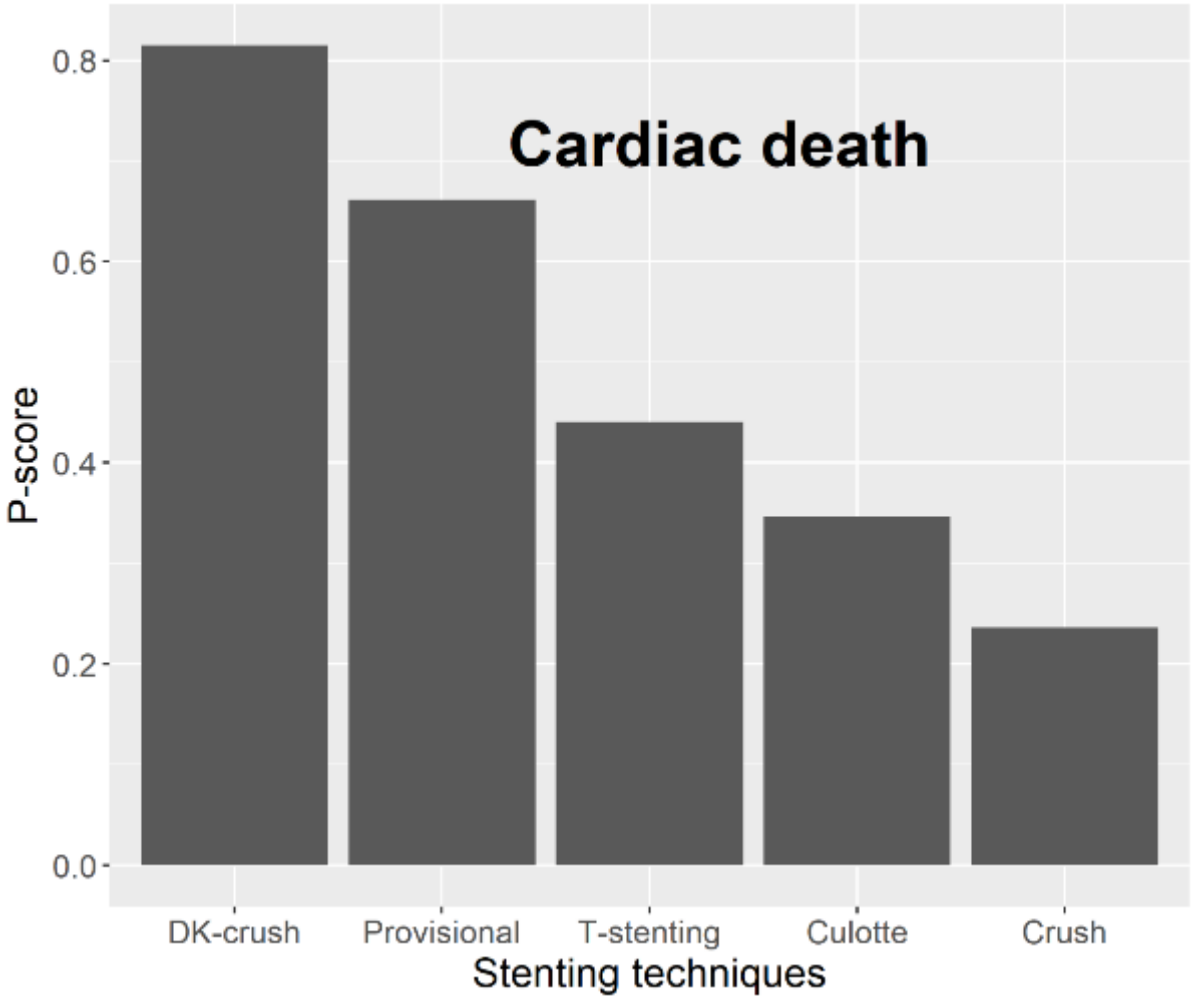
DK-crush	0.55 (0.26 to 1.12)	0.39 (0.08 to 2.07)	**0.12 (0.01 to 0.97)**	NA
0.48 (0.25 to 0.91)	**Provisional**	0.83 (0.32 to 2.12)	1.06 (0.40 to 2.79)	0.39 (0.07 to 2.05)
0.41 (0.18 to 0.97)	0.87 (0.43 to 1.74)	**Crush**	0.77 (0.32 to 1.84)	NA
0.34 (0.14 to 0.80)	0.71 (0.35 to 1.43)	0.81 (0.40 to 1.64)	**Culotte**	3.02 (0.12 to 74.73)
0.27 (0.05 to 1.33)	0.56 (0.13 to 2.46)	0.64 (0.13 to 3.20)	0.79 (0.16 to 3.82)	**T-stenting**

Supplementary Figure 14. League table showing the results of network meta-analysis after excluding trials with a high risk of bias.

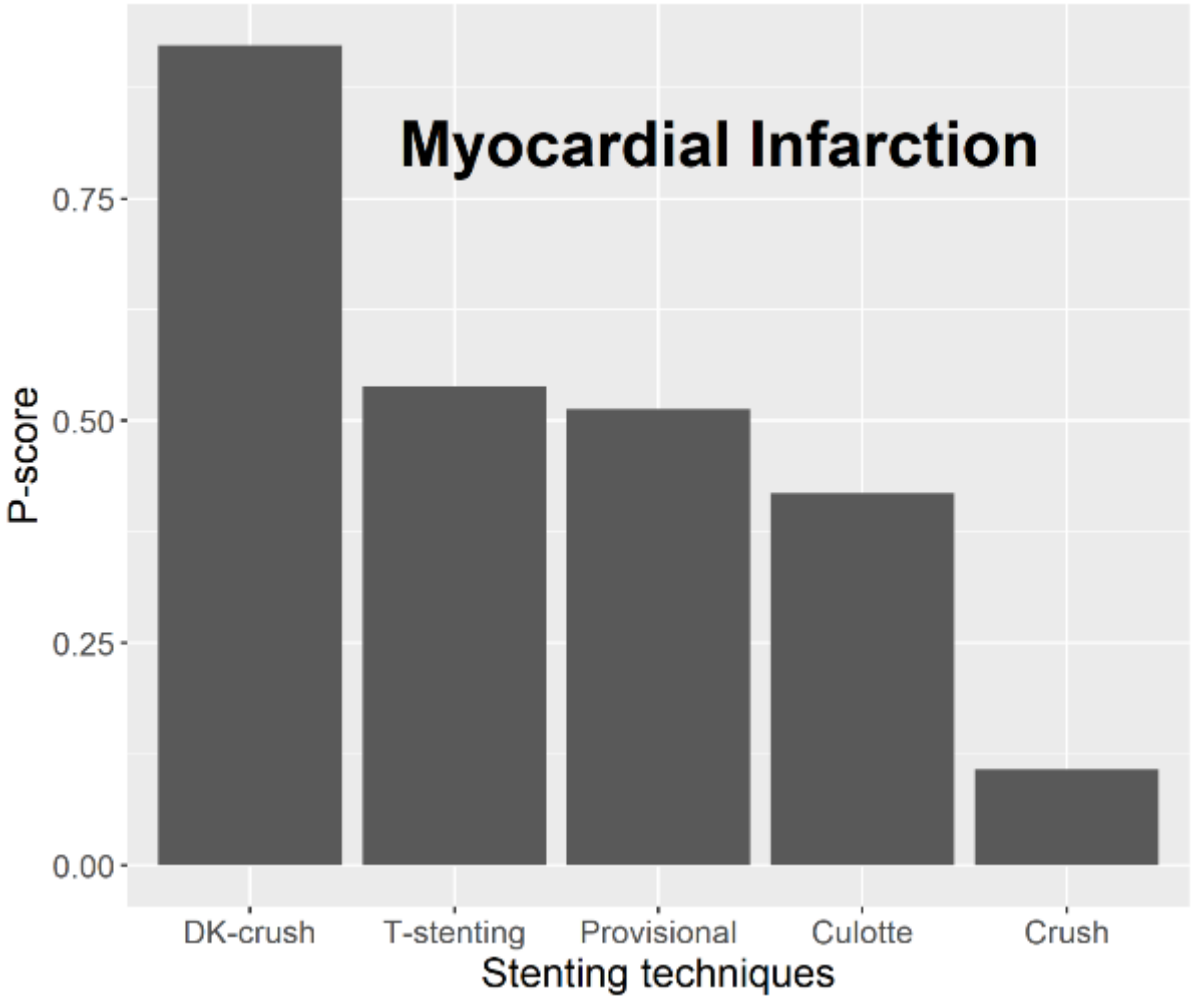
A)


MACE
P-score
1.00
0.75
0.50
0.25
0.00
DK-crush
Provisional
Culotte
Crush
T-stenting
Stenting techniques

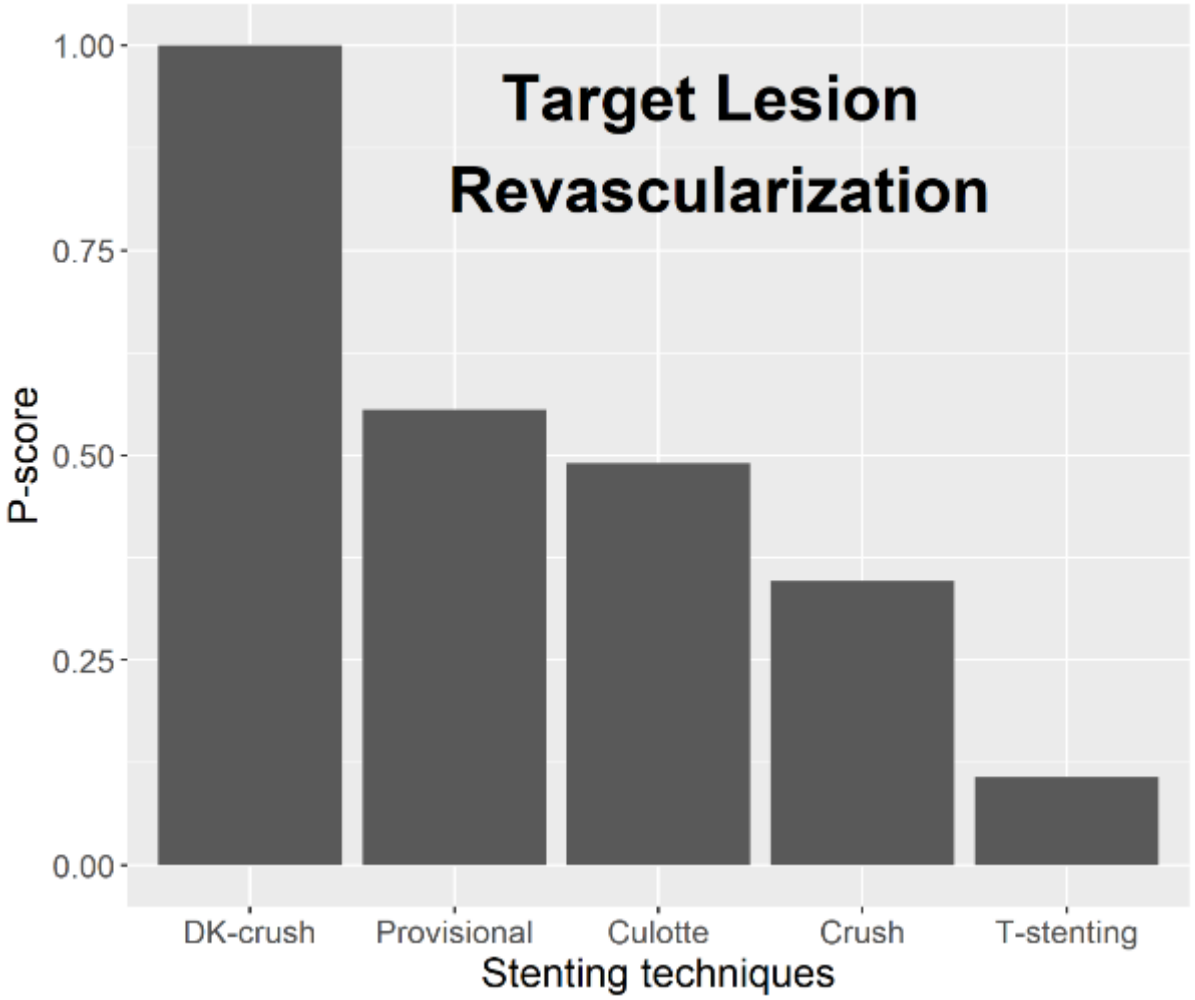
B)


Cardiac death
P-score
0.8
0.6
0.4
0.2
0.0
DK-crush
Provisional
T-stenting
Culotte
Crush
Stenting techniques

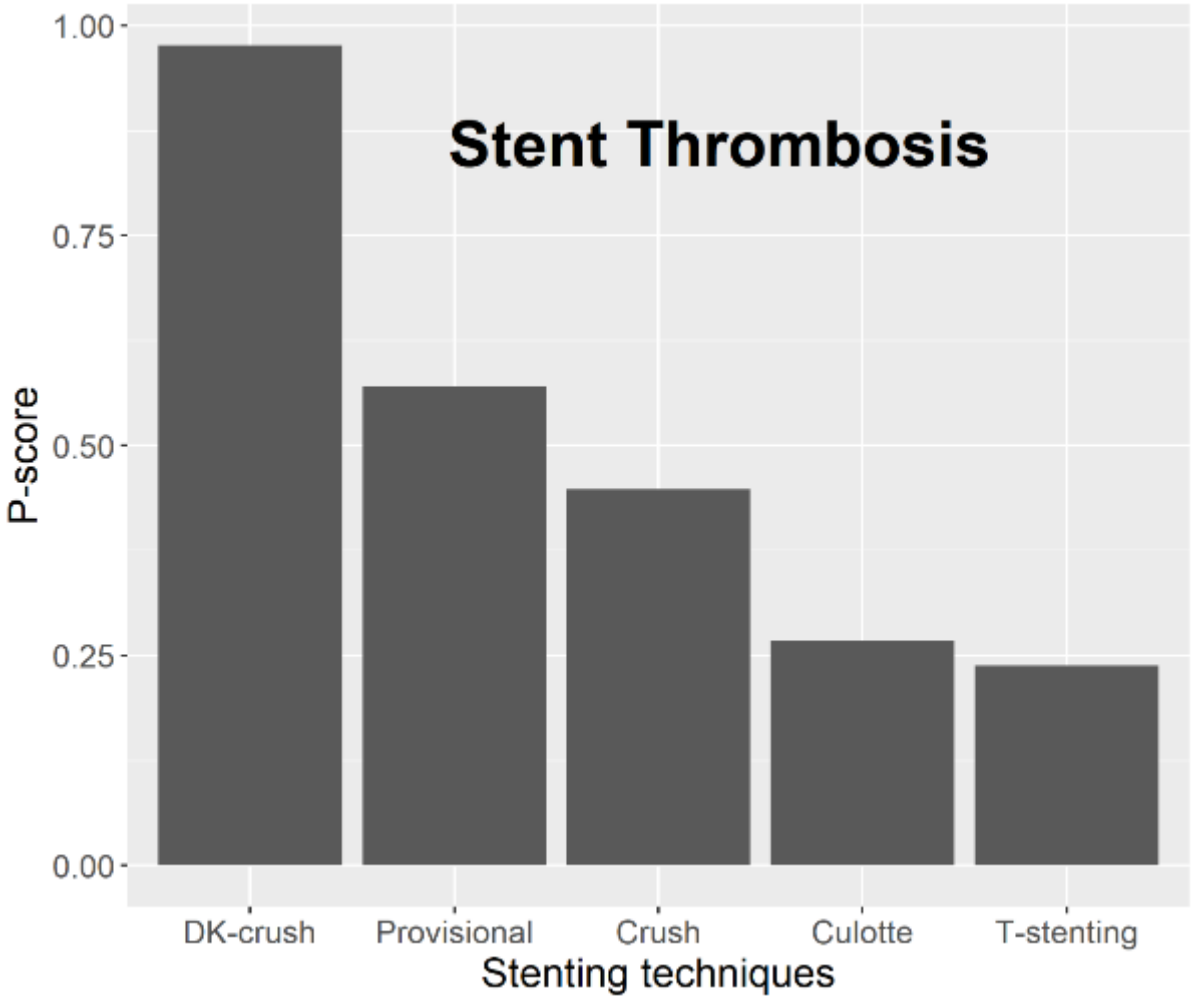
C)


Myocardial Infarction
P-score
0.75
0.50
0.25
0.00
DK-crush
T-stenting
Provisional
Culotte
Crush
Stenting techniques

D)


Target Lesion Revascularization
P-score
1.00
0.75
0.50
0.25
0.00
DK-crush
Provisional
Culotte
Crush
T-stenting
Stenting techniques

E)



Supplementary Figure 15. P-scores in the network meta-analysis after excluding trials with a high risk of bias.

MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularization (D), and stent thrombosis (E).

MACE (No. of studies = 16; No. of patients = 4148)

Cochran's Q-test p-value = 0.69; I^2 = 0% [0.0%; 56.6%]; τ^2 = 0

DK-crush	**0.29 (0.16 to 0.52)**	**0.50 (0.34 to 0.73)**	**0.51 (0.30 to 0.87)**	NA
0.45 (0.31 to 0.66)	**Culotte**	1.24 (0.55 to 2.78)	0.78 (0.50 to 1.21)	0.57 (0.27 to 1.20)
0.45 (0.33 to 0.61)	0.99 (0.69 to 1.42)	**Provisional**	1.00 (0.68 to 1.46)	1.05 (0.58 to 1.91)
0.43 (0.31 to 0.60)	0.94 (0.67 to 1.32)	0.95 (0.70 to 1.28)	**Crush**	NA
0.37 (0.22 to 0.65)	0.82 (0.49 to 1.39)	0.83 (0.51 to 1.35)	0.88 (0.51 to 1.50)	**T-stenting**

Cardiac death (No. of studies = 9; No. of patients = 3121)

Cochran's Q-test p-value = 0.99; I^2 = 0% [0.0%; 74.6%]; τ^2 = 0

DK-crush	0.66 (0.31 to 1.39)	NA	0.49 (0.12 to 1.99)	0.33 (0.03 to 3.22)
0.68 (0.34 to 1.39)	**Provisional**	NA	0.33 (0.01 to 8.21)	0.51 (0.05 to 5.72)
0.42 (0.02 to 8.30)	0.61 (0.03 to 12.63)	**T-stenting**	1.00 (0.06 to 16.14)	NA
0.42 (0.14 to 1.24)	0.61 (0.19 to 2.02)	1.00 (0.06 to 16.14)	**Culotte**	0.87 (0.33 to 2.31)
0.36 (0.11 to 1.16)	0.52 (0.15 to 1.84)	0.85 (0.05 to 15.83)	0.85 (0.35 to 2.07)	**Crush**

Myocardial infarction (No. of studies = 15; No. of patients = 4097)

Cochran's Q-test p-value = 0.32; I^2 = 12.6% [0.0%; 52.4%]; τ^2 = 0.05

DK-crush	NA	0.52 (0.23 to 1.18)	0.39 (0.14 to 1.05)	0.67 (0.30 to 1.48)
0.72 (0.19 to 2.69)	**T-stenting**	0.90 (0.22 to 3.63)	0.50 (0.04 to 5.74)	NA
0.58 (0.33 to 1.03)	0.81 (0.24 to 2.73)	**Provisional**	0.65 (0.21 to 1.96)	0.91 (0.53 to 1.54)
0.51 (0.27 to 0.96)	0.70 (0.19 to 2.56)	0.87 (0.48 to 1.60)	**Culotte**	0.73 (0.34 to 1.54)
0.51 (0.29 to 0.88)	0.70 (0.20 to 2.52)	0.87 (0.56 to 1.37)	1.00 (0.57 to 1.76)	**Crush**

Target lesion revascularization (No. of studies = 12; No. of patients = 3711)

Cochran's Q-test p-value = 0.74; I^2 = 0% [0.0%; 64.8%]; τ^2 = 0

DK-crush	**0.25 (0.11 to 0.55)**	**0.42 (0.23 to 0.78)**	**0.47 (0.29 to 0.76)**	NA
0.41 (0.24 to 0.70)	**Culotte**	0.88 (0.47 to 1.67)	NA	0.47 (0.20 to 1.08)
0.41 (0.26 to 0.63)	0.98 (0.59 to 1.62)	**Crush**	0.92 (0.46 to 1.84)	NA
0.40 (0.27 to 0.60)	0.97 (0.56 to 1.70)	0.99 (0.62 to 1.59)	**Provisional**	0.93 (0.45 to 1.92)
0.28 (0.15 to 0.55)	0.68 (0.36 to 1.29)	0.70 (0.36 to 1.37)	0.70 (0.39 to 1.28)	**T-stenting**

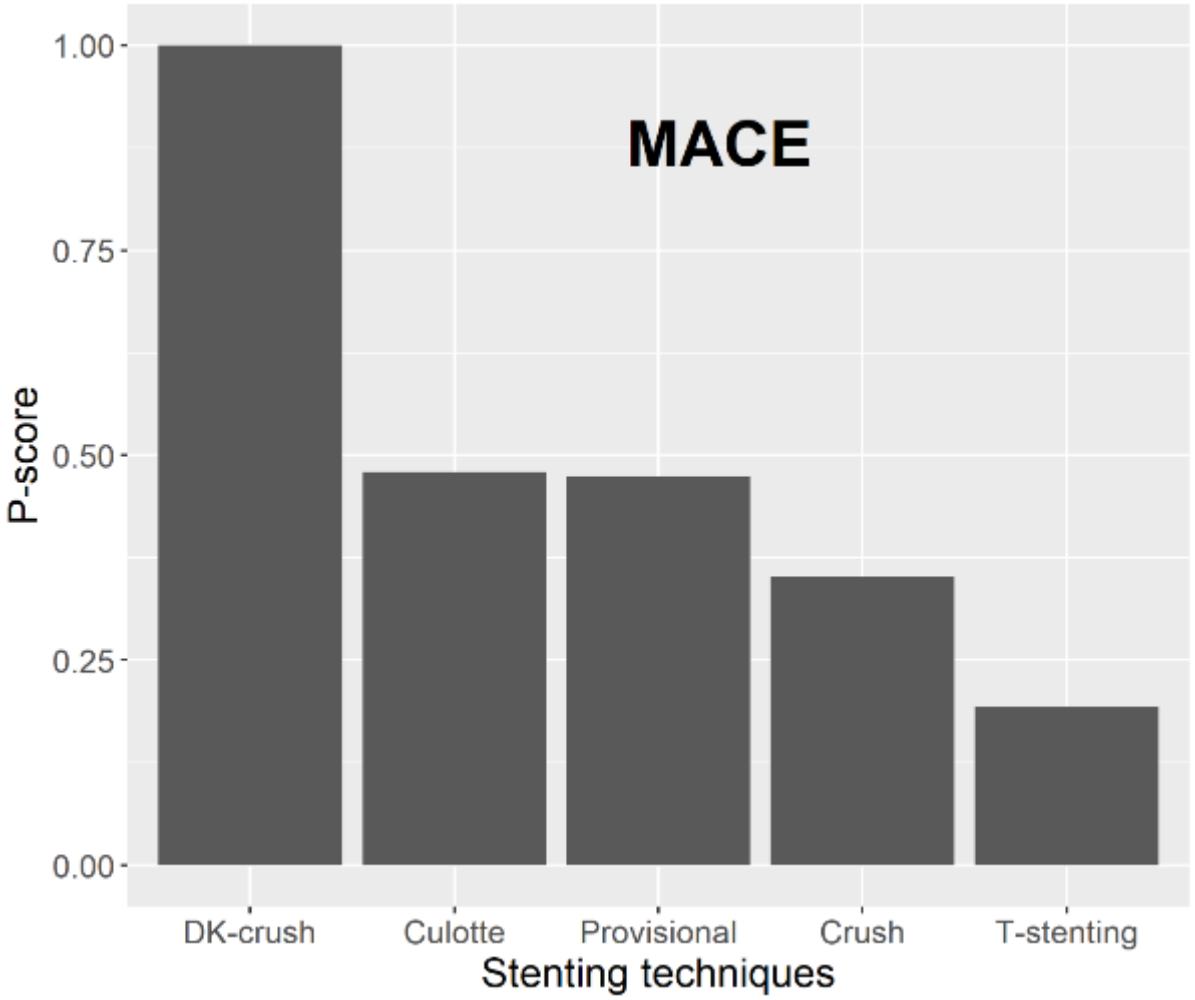
Stent thrombosis (No. of studies = 11; No. of patients = 3769)

Cochran's Q-test p-value = 0.53; I^2 = 0% [0.0%; 67.6%]; τ^2 = 0

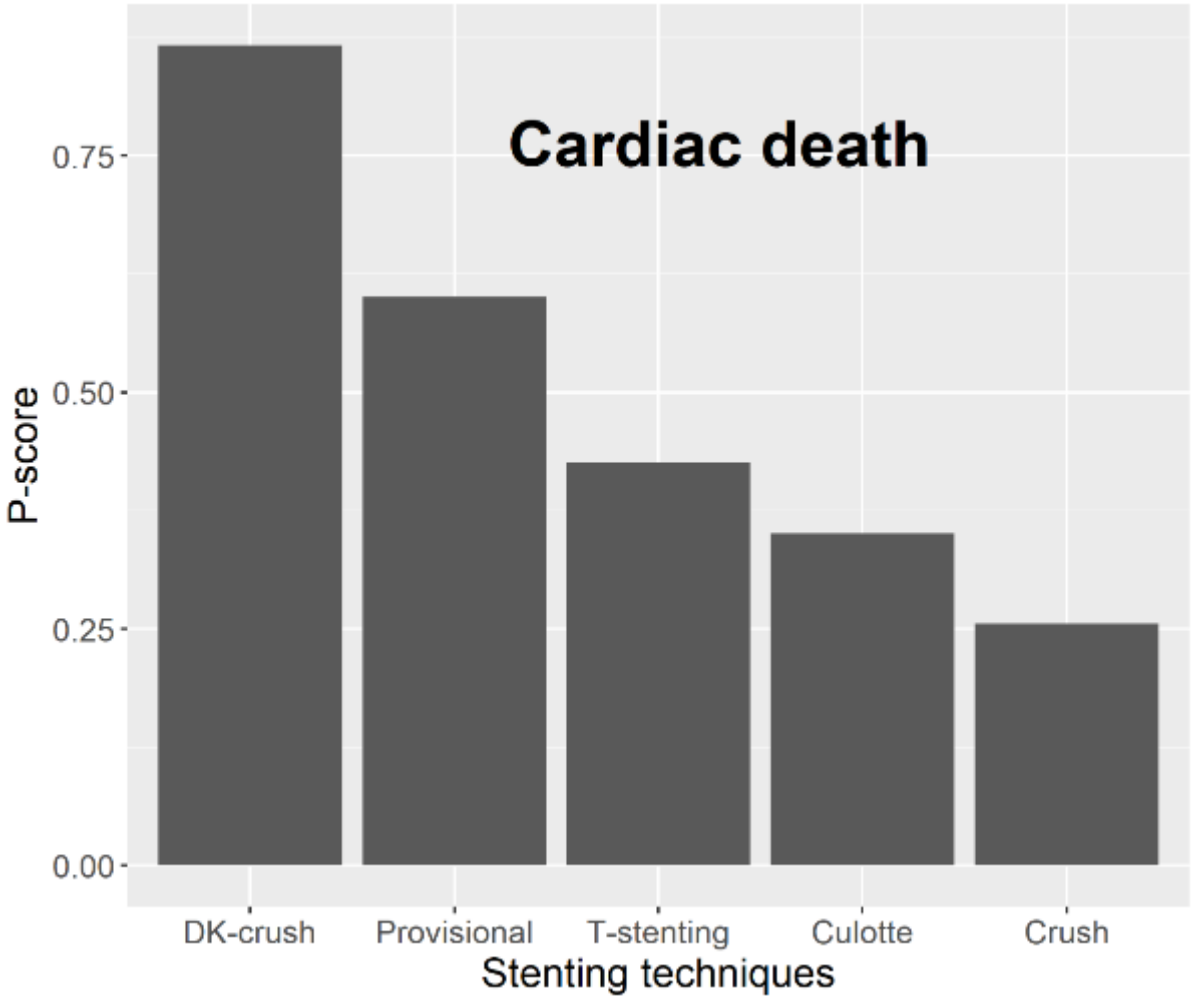
DK-crush	0.53 (0.18 to 1.56)	0.39 (0.08 to 2.07)	NA	0.12 (0.01 to 0.97)
0.55 (0.22 to 1.38)	**Provisional**	0.58 (0.12 to 2.77)	0.39 (0.07 to 2.05)	0.31 (0.03 to 3.00)
0.28 (0.10 to 0.80)	0.50 (0.18 to 1.41)	**Crush**	NA	0.77 (0.32 to 1.84)
0.26 (0.05 to 1.44)	0.47 (0.11 to 2.12)	0.95 (0.17 to 5.30)	**T-stenting**	0.33 (0.01 to 8.19)
0.18 (0.06 to 0.57)	0.33 (0.11 to 1.00)	0.67 (0.30 to 1.47)	0.70 (0.13 to 3.89)	**Culotte**

Supplementary Figure 16. League table showing the network meta-analysis results after excluding trials allowing multiple bifurcation stenting techniques in the 2-stent arm

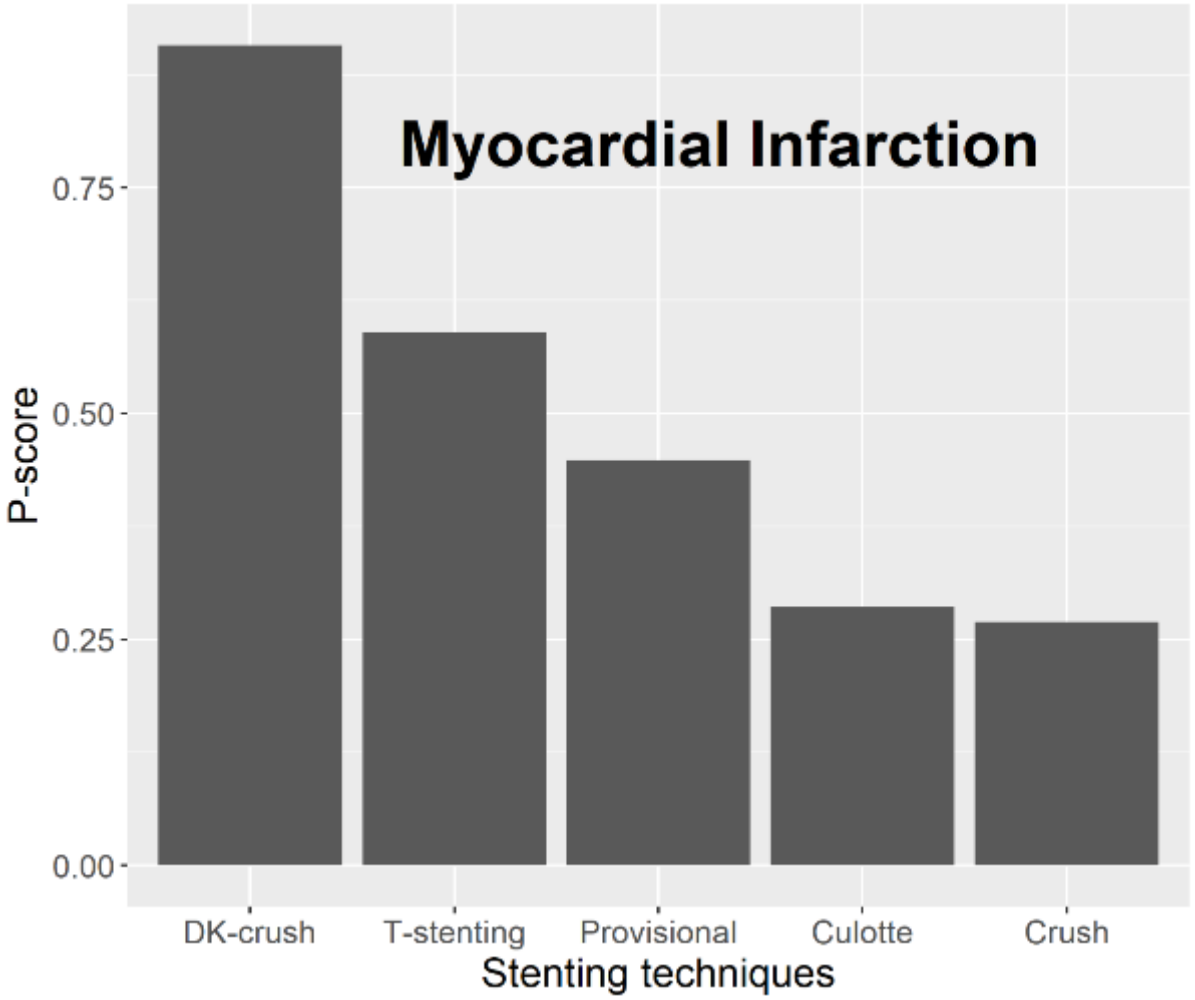
A)


MACE
1.00
0.75
0.50
0.25
0.00
P-score
DK-crush
Culotte
Provisional
Crush
T-stenting
Stenting techniques

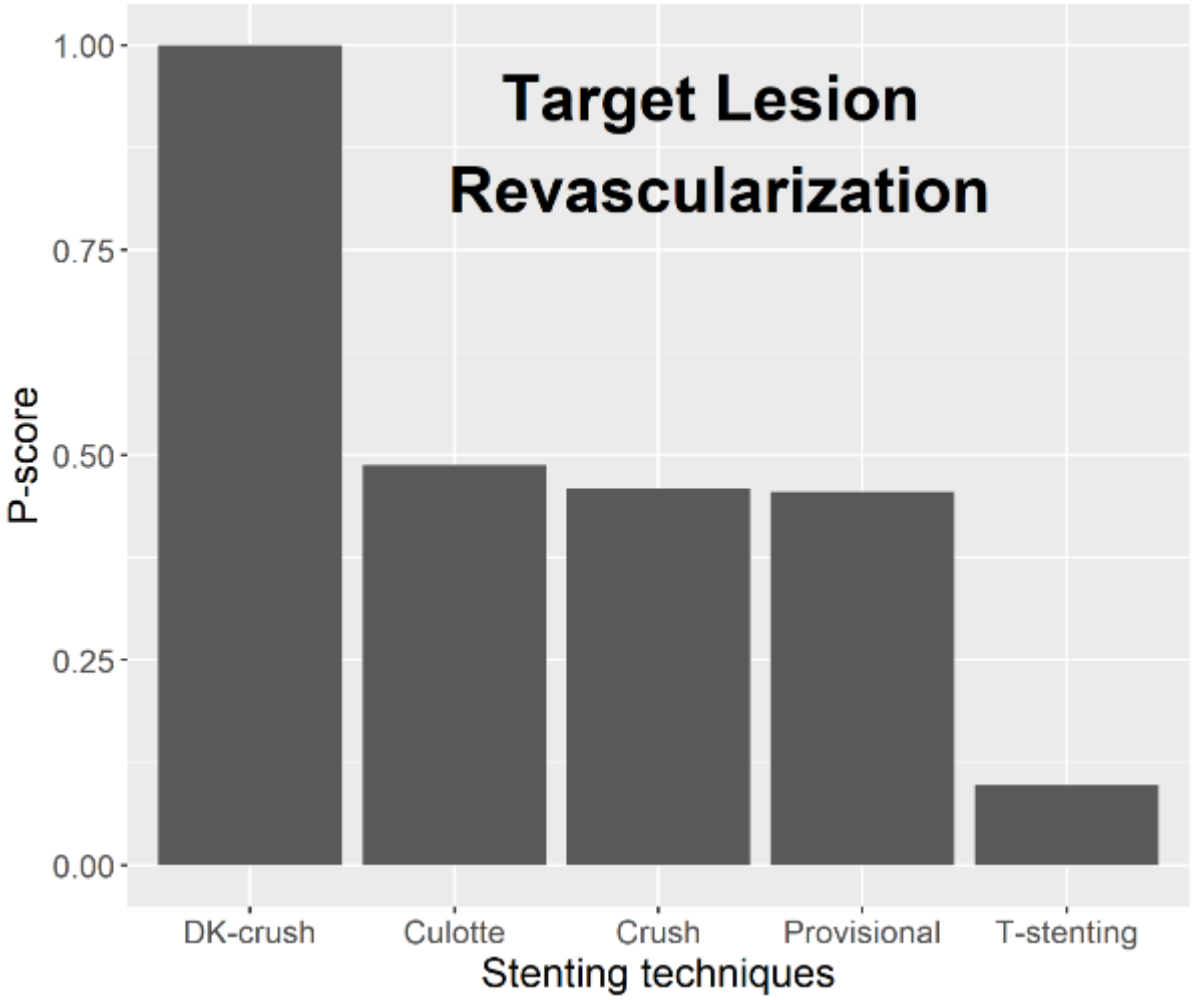
B)


Cardiac death
P-score
0.75
0.50
0.25
0.00
DK-crush
Provisional
T-stenting
Culotte
Crush
Stenting techniques

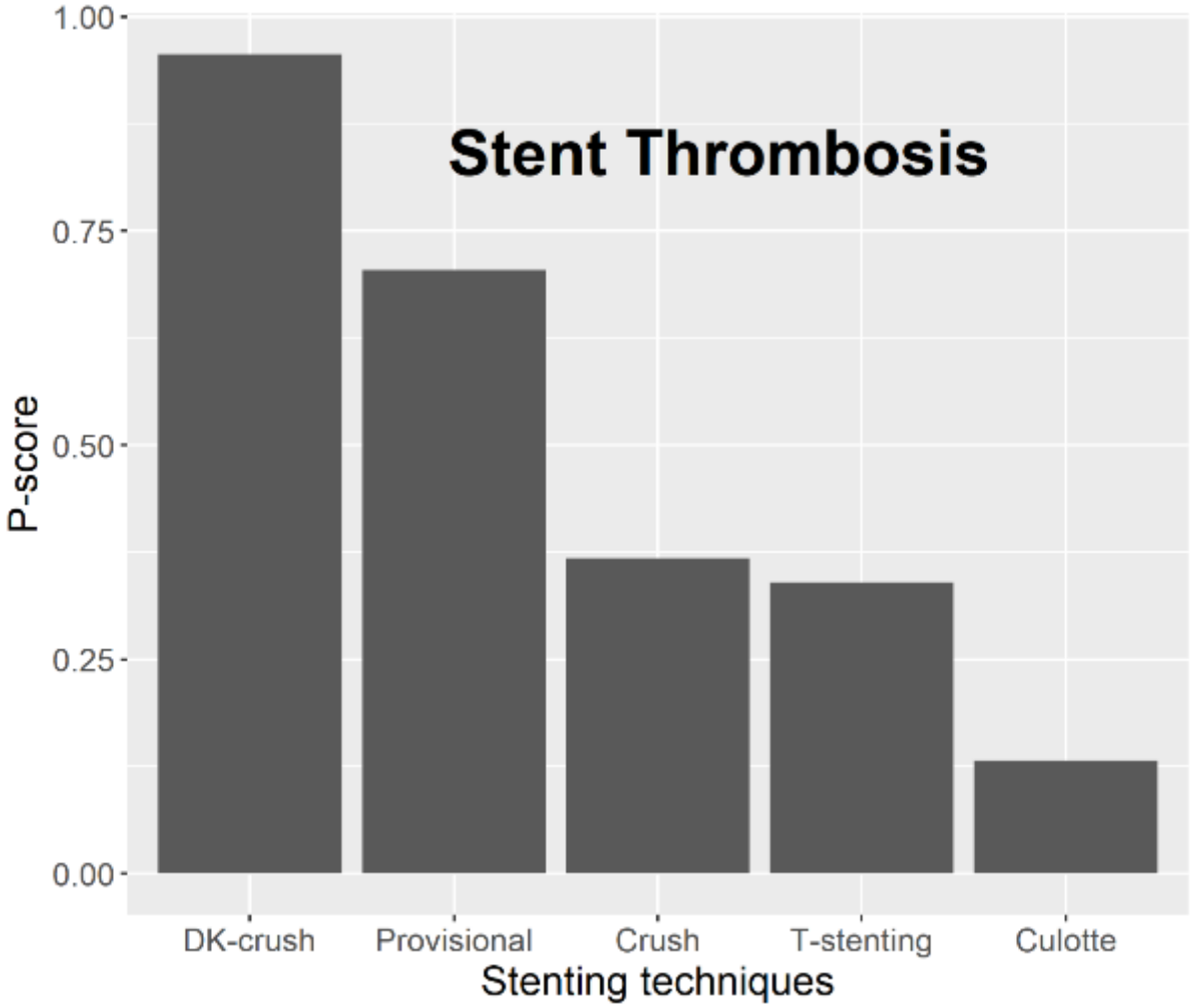
C)


Myocardial Infarction
P-score
0.75
0.50
0.25
0.00
DK-crush
T-stenting
Provisional
Culotte
Crush
Stenting techniques

D)


Target Lesion Revascularization
P-score
1.00
0.75
0.50
0.25
0.00
DK-crush
Culotte
Crush
Provisional
T-stenting
Stenting techniques

E)



Supplementary Figure 17. P-scores in the network meta-analysis after excluding trials allowing multiple bifurcation stenting techniques in the 2-stent arm.

MACE (A), cardiac death (B), myocardial infarction (C), target lesion revascularisation (D), and stent thrombosis (E).