SUPPLEMENTAL MATERIAL

Table S1.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title, Pg 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract, Pg 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Lines 6-14, Pg 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Lines 14-16, Pg 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	"Selection Criteria", Pg 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify thedate when each source was last searched or consulted.	“Methods” Lines 18-23, Pg 3 and Lines 1-10, Pg 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	“Methods” Lines 18-23, Pg 3 and Lines 1-10, Pg 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each recordand each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 12-21, Pg 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in theprocess.	"Data Extraction", Pg 4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in eachstudy were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	"Outcomes", Line 23, Pg4 and Lines 1-4, Pg 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	"Outcomes", Line 23, Pg4 and Lines 1-4, Pg 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	"Assessment of the quality of the included studies", Pg 5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	"Statistical Analysis”, Pg 5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics andcomparing against the planned groups for each synthesis (item #5)).	“Assessment of the quality of the included studies”, Pg 5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or dataconversions.	Not Applicable
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Tables 1,2,3 and Supplemental Tables 2,3,4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe themodel(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	"StatisticalAnalysis", Pg 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Lines 12-18 of "Statistical Analysis" , Pg 5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Lines 19-23 of "Statistical Analysis", Pg 5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	“Assessment of the quality of the included studies”, Pg 5

PRISMA 2020 Checklist

Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	"Assessment of the quality of the included studies", Pg 5

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included inthe review, ideally using a flow diagram.	Lines 4-6, Pg 6 and Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Not Applicable
Study characteristics	17	Cite each included study and present its characteristics.	Line 4-16, Pg 6
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Lines 17-19, Pg 6
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision(e.g. confidence/credible interval), ideally using structured tables or plots.	"Outcomes", Lines 20-22, Pg 6 and Lines 1-19, Pg 7
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Lines 17-19, Pg 6 and Supplemental Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g.confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	"Outcomes", Lines 20-22, Pg 6 and Lines 1-19, Pg 7
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	"Outcomes", Pg 6-7 and Lines 3-5, Pg 12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Lines 3-4,Pg 7 and Lines 5-7, Pg 12
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Lines 17-19, Pg 6 and Supplemental Table 2
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Lines 17-19, Pg 6 and Supplemental Table 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Lines 20-22, Pg 7 and Lines 1-4, Pg 8
	23b	Discuss any limitations of the evidence included in the review.	Lines 1-9, Pg 12
	23c	Discuss any limitations of the review processes used.	Lines 1-3, Pg 12
	23d	Discuss implications of the results for practice, policy, and future research.	"Conclusion" Lines 12-17, Pg 12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Lines 6-10, Pg 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Protocol not prepared. Lines 8-10, Pg 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Not applicable
Competing interests	26	Declare any competing interests of review authors.	Not applicable
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from includedstudies; data used for all analyses; analytic code; any other materials used in the review.	Data is availablewithin manuscript.

PRISMA 2020 Checklist

"

"

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Table S2: Risk of bias among included studies using Newcastle Ottawa score

Study	Selection				Comparability:	Outcome:		Total score
	Representativeness of the sample	Selection of the control group	Ascertainment of the exposure (disease)	Non-respondents	The subjects in different outcome groups are comparable	Assessment of the outcome:	Statistical test:	
Abdelwahab et al.[19]	1	1	2	1	2	2	1	10
Buchanan et al.[18]	1	1	2	1	2	2	1	10
Lee et al.[17]	1	1	2	1	2	2	1	10
Redfors et al.[20]	1	1	2	1	2	2	1	10
Shimonaga et al.[16]	1	1	1	1	1	2	1	8
Takeuchi et al.[21]	1	1	2	1	1	2	1	9
Tamez et al.[15]	1	1	2	1	2	2	1	10
Tang et al.[13]	1	1	2	1	1	2	1	9
Wang et al.[14]	1	1	2	1	1	2	0	8
Richardt et al.[24]	1	1	2	1	1	2	1	9
Gao et al.[23]	1	1	2	1	2	2	1	10
Azzalini et al.[22]	1	1	2	1	2	2	1	10

Table S3: Definition of major adverse cardiac events

Study	MACE definition
Abdelwahab et al.[19]	Composite of all-cause mortality, MI and CVA
Buchanan et al.[18]	Composite of all-cause mortality, MI and ischemia-driven repeat revascularization
Lee et al.[17]	Composite of all-cause mortality, MI and ischemia-driven repeat revascularization
Redfors et al.[20]	Composite of cardiac mortality, MI and stent thrombosis
Shimonaga et al.[16]	NA
Tamez et al.[15]	Composite of all-cause mortality, MI, CVA and ischemia-driven repeat revascularization
Tang et al.[13]	Composite of cardiac mortality, MI and ischemia-driven repeat revascularization
Wang et al.[14]	Composite of all-cause mortality, MI and acute heart failure
Richardt et al.[24]	Composite of all-cause mortality, MI and ischemia-driven repeat revascularization
Gao et al.[23]	Composite of cardiac mortality, MI and ischemia-driven repeat revascularization
Azzalini et al.[22]	Composite of cardiac mortality, MI and ischemia-driven repeat revascularization

Table S4: Risk adjustment in the included studies

Study	Adjusted outcomes?	Variables adjusted for
Abdelwahab et al.[19]	Yes	Age (>75 years), diabetes, hypertension, smoking, hyperlipidaemia, positive family history of coronary artery disease, previous myocardial infarction, atrial fibrillation, STEMI, target vessel: left anterior descending, chronic total occlusion, long lesion (>15 mm), type C lesion, bifurcation lesion and stent type
Buchanan et al.[18]	Yes	Clinical presentation of MI
Lee et al.[17]	Yes	Age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking, chronic renal failure on hemodialysis, history of myocardial infarction, history of coronary artery bypass grafting, history of peripheral artery disease, history of cerebrovascular accident, clinical presentation of index CTO PCI, and ejection fraction (EF).
Redfors et al. [20]	Yes	Age, sex, diabetes, smoking (current), renal insufficiency, clinical presentation, previous MI, previous coronary artery bypass grafting, anemia, PRU, left anterior descending coronary artery (LAD) as culprit vessel, multivessel disease, PCI against a graft vessel, bifurcation lesion, moderate or severe coronary calcification, total stent length, vessel diameter, and DES generation.
Takeuchi et al. [21]	Yes	Age, gender, CKD incidence, hemoglobin level, and hs-CRP level
Tamez et al.[15]	Yes	Age, sex, race, ethnicity, diabetes, chronic kidney disease stage, hypertension, dyslipidaemia, PCI indication, bifurcation lesion, lesion in graft, chronic total occlusion, stent type, total stent length, and minimum stent diameter
Tang et al.[13]	Yes	Adjusted for clinical, angiographic, and procedural variables
Wang et al.[14]	No	
Richardt et al.[24]	No	
Gao et al.[23]	Yes	Sex, age, prior MI, prior percutaneous coronary intervention, previous coronary artery bypass graft, diabetes mellitus, hypertension, unstable angina, left main lesion, number of stents, number of lesions, sirolimus DES treatment, stent diameter, stent length, postdilation angioplasty, use of intravascular ultrasound
Azzalini et al.[22]	Yes	Age, center, prior MI, Diabetes, prior CABG, eGFR, acute coronary syndrome presentation, number of diseased vessels, J-CTO score, PROGRESSCTO score, use of DES, procedural success, major procedural complications, and use of dissection/re-entry techniques.

Table S5: Definitions of Myocardial infarction in included studies

Study	MI definition
Abdelwahab et al.[19]	ST-elevation myocardial infarction (STEMI; ST-elevation at least 1 mm in two or more limb leads, or at least 2 mm in two or more contiguous precordial leads or development of new left bundle branch block on the ECG) or non-ST-elevation myocardial infarction (NSTEMI; pathological increase of cardiac specific enzymes with CK-MB >1.5 times of normal limits, Troponin T or I >99th percentile of normal value)
Buchanan et al.[18]	MI was characterized as either non–ST-segment elevation MI or ST-segment elevation myocardial infarction. Non–ST-segment elevation MI was defined by the presence of typical chest pain or angina-equivalent symptoms in association with elevated troponin cardiac marker. ST-segment elevation myocardial infarction was defined by the presence of typical chest pain or angina-equivalent symptoms in association with ST-segment elevation on presenting electrocardiogram or new left bundle-branch block. MI was further characterized by Q-wave myocardial infarction (QWMI) if new Q waves deeper than 1 mm occurred in the 2 contiguous leads; otherwise, non-QWMI was diagnosed.
Lee et al.[17]	nonfatal MI
Redfors et al.[20]	MI was defined according to the Acute Catheterization and Urgent Intervention Triage Strategy criteria. (A) MI diagnosis before angiography or in medically treated patients: (1) If the peak troponin or creatine kinase (CK)–MB (or CK) levels are elevated but the peak has not yet been reached: Recurrent chest pain or ischemic equivalent symptoms lasting ≥30 minutes, or new ECG changes consistent with MI and the next troponin or CK-MB (or CK) level measured approximately 8 to 12 hours after the event is elevated by at least 50% above the previous level. (2) If the elevated troponin or CK-MB (or CK) levels are falling or have returned to normal: Recurrent chest pain or ischemic equivalent symptoms lasting ≥30 minutes, and a new elevation of troponin or CK-MB (or CK) >upper limits of normal (ULN) if the troponin or CK-MB (or CK) level has returned to <ULN, or a rise above the previous nadir level if the troponin or CK-MB (or CK) level has not returned to <ULN. (B) MI diagnosis after PCI: (1) If the baseline CK-MB (or CK) levels are normal: A new elevation of troponin or CK-MB >3× ULN (or CK >3× ULN) within 24 hours post-PCI. (2) If the baseline CK-MB (or CK) levels are elevated, but documented to be falling: recurrent chest pain or ischemic equivalent symptoms lasting ≥30 minutes, and an absolute rise of CK-MB >3× ULN (or an absolute rise in CK >2× ULN) above the previous nadir level within 24 hours post-PCI. (3) If the peak CK-MB (or CK) has not yet been reached before PCI: Recurrent chest pain or ischemic equivalent symptoms lasting ≥30 minutes, or new electrocardiographic changes consistent with a reinfarction and the next CK-MB (or CK) level measured approximately 8 to 12 hours after the event is elevated by at least 50% above the previous level or >3× ULN, whichever is greater. (C) MI diagnosis after coronary artery bypass surgery: Any CK-MB (or CK) ≥10 × ULN within 24 hours of operation and increased at least 50% over the most recent preoperation levels, or any CK-MB (or CK) ≥5× ULN within 24 hours of operation and increased at least 50% over the most recent preoperation levels and new significant (≥0.04 second) Q waves in ≥2 contiguous electrocardiographic leads. (D) Q-wave versus non–Q-wave MI: All reinfarctions will be adjudicated as being either Q wave (development of new pathologic Q waves in 2 or more contiguous leads) or non–Q wave.
Shimonaga et al.[16]	Periprocedural MI was defined as an increase in the troponin I levels greater than 0.15 ng/mL (3 times the ULN). Major PMI was defined as an increase in the troponin I levels greater than 0.75 ng/mL (15 times the ULN)
Tamez et al.[15]	Not avaialble
Tang et al.[13]	Not avaialble
Wang et al.[14]	Periprocedural MI was defined using the Society for Cardiovascular Angiography and Interventions (SCAI), Academic Research Consortium (ARC)-2, and fourth universal definitions.
Richardt et al.[24]	Myocardial infarction was defined according to an extended historical protocol definition and according to ARC definitions.1-2 A Q-wave myocardial infarction required, in th absence of cardiac enzyme data, a history of chest pain or other acute symptoms consistent with myocardial ischemia together with new pathological Q waves in two or more contiguous ECG leads as assessed by the core lab or clinical events committee. In the presence of elevated cardiac enzymes, new pathological Q waves in two or more contiguous ECG leads as assessed by the core lab or clinical events committee were sufficient to diagnose a Q-wave myocardial infarction. In the absence of an ECG, a Q-wave myocardial infarction could be adjudicated on the basis of the clinical scenario and appropriate cardiac enzyme data.
Gao et al.[23]	MI was diagnosed by electrocardiographic changes and/or a rise and fall of creatine kinase-myocardial band (CK-MB) fraction in the presence of ischemic symptoms. New development of pathological Q waves in 2 contiguous leads was defined as Q-wave MI; and in the absence of pathological Q waves, an elevation in CK-MB level >3 times the upper limit of normal was defined as non– Q-wave MI.
Azzalini et al.[22]	Periprocedural type 4a MI, target vessel MI (Q wave and non-Q wave MI) definition was not explicit

Figure S1: Funnel plot for publication bias

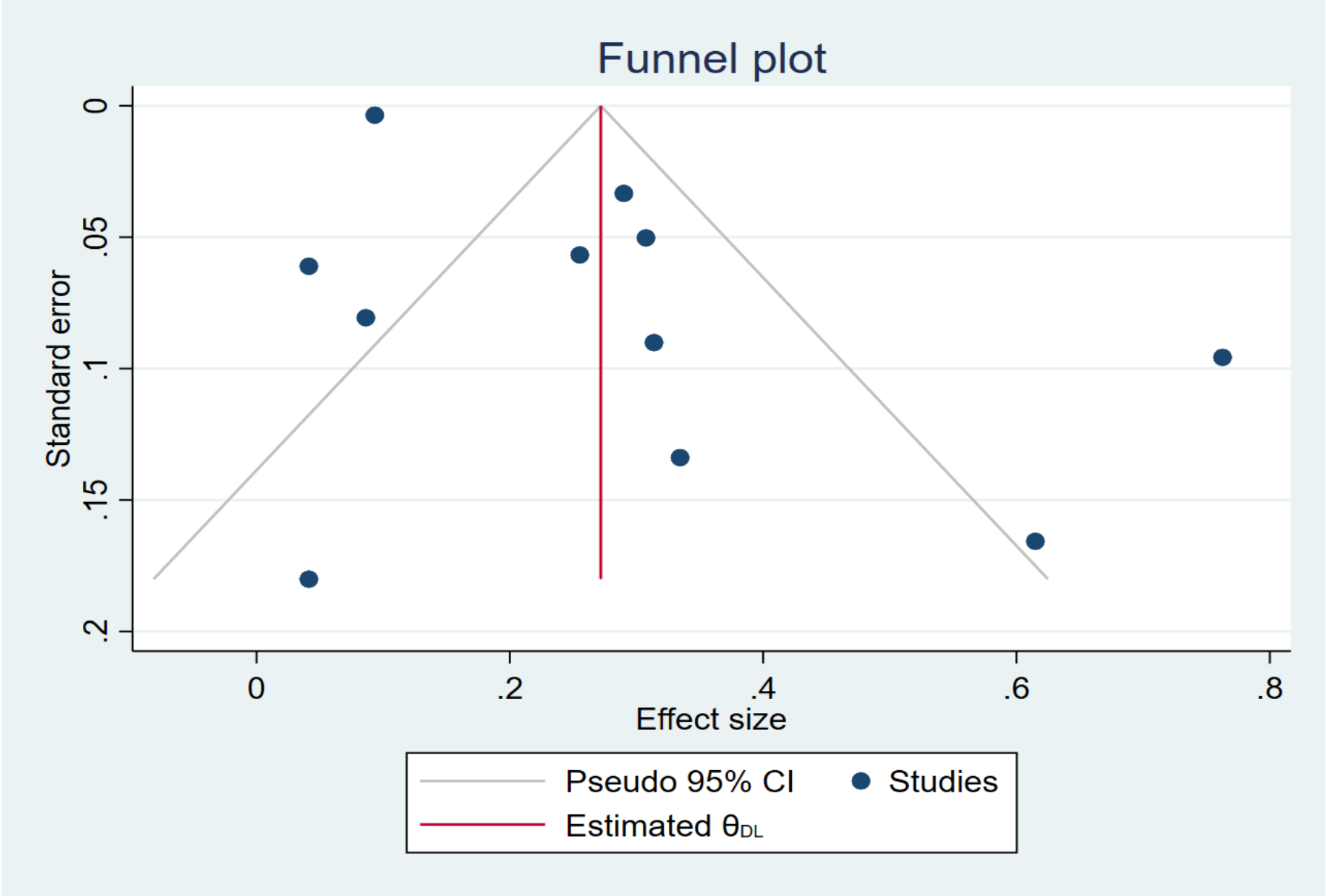

Figure S2: Sensitivity analysis for MACE excluding Richardt et al. and Wang et al.