

Supplementary Appendix

TITLE:

Percutaneous Intervention or Coronary Artery Bypass Graft for Left Main Stem Coronary Artery Disease? A Systematic Review and Meta-Analysis

Abbreviations:

PRECOMBAT: Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery

EXCEL: Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization

NOBLE: Nordic-Baltic-British Left Main Revascularization Study

LEMANS: Left Main Stenting Versus Bypass Surgery

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A. ADDITIONAL RESULTS:

On a stratified analysis of RCTs only, PCI was favored due to a lower risk of MACCE (RR 0.61, 95% CI, 0.47-0.79, $p=0.0002$) and stroke (RR 0.41, 95% CI 0.17-0.98, $p=0.05$) and no significant difference in the risk of MI (RR 0.76, 95% CI 0.54-1.05, $p=0.10$), revascularization (RR 0.64, 95% CI 0.34-1.20, $p=0.17$) and all-cause mortality (RR 0.58, 95% CI 0.30-1.16, $p=0.12$) at 30-days. At 1 year, CABG showed significant benefits in terms of the lower need for revascularization (RR 1.71, 95% CI 1.39-2.10, $p<0.00001$), while PCI was favored due to a lower rate of stroke (RR 0.32, 95% CI 0.15-0.69, $p=0.004$). While CABG did show a numerical advantage of a lower rate of MACCE and MI over PCI, this difference did not reach the statistical significance; (RR 1.07, 95% CI 0.93-1.23, $p=0.33$ and RR 1.06, 95% CI 0.72-1.57, $p=0.76$), respectively. Similarly, there was no significant difference in the risk of all-cause mortality (RR 0.83, 95% CI 0.63-1.07, $p=0.15$). A trend favoring CABG for MACCE (RR 1.31, 95% CI 1.19-1.45, $p<0.00001$) and revascularization (RR 1.72, 95% CI 0.47-2.00, $p<0.00001$) was observed at follow-up duration of 5-years. Nonetheless, the risk of all-cause mortality (RR 1.07, 95% CI 0.84-1.36, $p=0.57$) and MI (RR 1.62, 95% CI 1.0-2.62, $p=0.05$) was consistently identical between the two groups. In contrast to 1-year results, no significant difference was observed in the risk of stroke (RR 0.86, 95% CI 0.44-1.68, $p=0.66$). (S. Figure 5-7, S. Table 8)

B. SEARCH STRATEGY and MAP:

The MEDLINE (PubMed, Ovid), Embase, Clinicaltrials.org and Cochrane databases were queried with various combinations of medical subject headings (MeSH) to identify relevant articles. There were no language or time restrictions placed. Backward snowballing was performed to retrieve unidentified studies that were missed on the initial search. The MeSH used included two subsets: one for PCI using the terms like "PCI," "angiography," "percutaneous intervention," "coronary stenting," "drug-eluting stents," "cardiac catheterization," "left heart cath," and the other for CABG using "left main coronary artery bypass graft," "coronary graft," "LMCAD graft," and "CABG." The two subsets of MeSH were combined in a 1:1 combination using Boolean operators. Results from all possible combinations were downloaded into an EndNote library. All randomized control trials (RCT) and observational cohort studies (OCS) until February 20, 2020, were evaluated. Studies comparing the safety and efficacy of PCI with CABG in LMCAD stenosis were included. The primary endpoint was a composite of major adverse cardiovascular and cerebrovascular events (MACCE). Secondary outcomes included individual components of MACCE [all-cause death, revascularization, stroke, and myocardial infarction (MI)]. Review articles, case reports, conference papers, and studies with no control arm or insufficient data were excluded. Patients with acute coronary syndrome were excluded.

(((((((((((PCI AND left main left main coronary artery bypass graft)) OR (angiography AND left main left main coronary artery bypass graft)) OR (percutaneous intervention AND left main left main coronary artery bypass graft)) OR (coronary stenting AND left main left main coronary artery bypass graft)) OR (drug-eluting stents AND left main left main coronary artery bypass graft)) OR (cardiac catheterization AND left main left main coronary artery bypass graft)) OR (left heart cath AND left main left main coronary artery bypass graft)))) OR (((((((((((PCI AND CABG)) OR (angiography AND CABG)) OR (percutaneous intervention AND CABG)) OR (coronary stenting AND CABG)) OR (drug-eluting stents AND CABG)) OR (cardiac catheterization AND CABG)) OR (left heart cath AND CABG)))) OR (((((((((((PCI AND LMCAD graft)) OR (angiography AND LMCAD graft)) OR (percutaneous intervention AND LMCAD graft)) OR (coronary stenting AND LMCAD graft)) OR (drug-eluting stents AND LMCAD graft)) OR (cardiac catheterization AND LMCAD graft)) OR (left heart cath AND LMCAD graft)))

C. SUPPLEMENTAL TABLES:

S. Table 1

Randomized studies quality assessment using the Oxford Quality Scoring System.
(Jadad score ≥ 3 considered high quality)

Author/Study/Year/Ref	Rating Scale List	Response	Jadad Score
Serruys (SYNTAX) 2009 [9]	Was the study described as random	Yes	3
	Was the randomization described and appropriate	Yes	
	Was the study described as double-blind	No	
	Was the method of double-blinding appropriate	No	
Makikallio (NOBLE) 2016 [10]	Was there a description of dropouts and withdrawals	Yes	3
	Was the study described as random	Yes	
	Was the randomization described and appropriate	Yes	
	Was the study described as double-blind	No	
Park (PRECOMBAT) 2011 [6]	Was the method of double-blinding appropriate	No	3
	Was there a description of dropouts and withdrawals	Yes	
	Was the study described as random	Yes	
	Was the randomization described and appropriate	Yes	
Stone (EXCEL) 2019 [1]	Was the study described as double-blind	No	3
	Was the method of double blinding appropriate	No	
	Was there a description of dropouts and withdrawals	Yes	
	Was the study described as random	Yes	
Buszman (LE MANS) 2008 [22]	Was the randomization described and appropriate	No	2
	Was the study described as double-blind	No	
	Was the method of double blinding appropriate	No	
	Was there a description of dropouts and withdrawals	Yes	
Boudriot et al. 2011 [9]	Was the study described as random	Yes	3
	Was the randomization described and appropriate	Yes	
	Was the study described as double-blind	No	
	Was the method of double blinding appropriate	No	
	Was there a description of dropouts and withdrawals	Yes	

S. Table 2

NewCastle-Ottawa scale (NOS) for assessing quality of observational studies

Author/Study/Year	Selection Bias				Outcome Bias				Total score
	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Outcome not present at baseline	Comparability of the cohort	Assessment of outcome	Enough follow-up duration	Adequate follow-up	
Brener 2008	*	*	*	*	**	*	*	-	8
Buchanan (Delta Registry) 2014	*	*	*	*	**	*	*	-	8
Caggegi (CUSTOMIZE) 2011	*	*	*	*	**	*	*	-	8
Cavalcante 2016	*	*	-	*	*	*	*	-	6
Chang 2012	*	*	*	*	*	*	*	-	7
Chieffo 2012	*	*	*	*	*	*	*	-	7
Cheng 2009	*	*	*	*	*	*	*	-	7
Ghenim 2009	*	*	*	*	*	*	*	-	7
Hong 2005	*	*	*	*	**	*	*	-	8
Kang 2010	*	*	*	*	*	*	*	-	7
Kawecki 2012	*	*	*	*	*	*	*	*	8
Kim 2009	*	*	*	*	*	-	*	*	7
Lee 2006	*	*	*	*	**	*	*	-	8
Luo 2012	*	*	*	*	**	*	*	-	7
Lu 2016	*	*	-	*	*	*	-	-	5
Makikallio 2008	*	*	*	*	**	*	*	*	9
Makikallio 2016	*	*	*	*	**	*	*	*	9
Montalescot 2009	*	*	*	*	*	*	*	*	8
Naganuma 2014	*	*	*	*	*	*	*	-	7
Palmerini 2006	*	*	*	*	**	*	*	*	9
Park DW 2010	*	*	*	*	**	*	*	*	9
Park (MAIN COMPARE) 2011	*	*	-	*	*	-	*	-	4
Park SJ 2011	*	*	*	*	*	-	-	-	5
Qin 2013	*	*	*	*	*	*	*	*	7
Rittger 2011	*	*	*	*	*	*	*	*	8
Rodes- Cabau 2008	*	*	*	*	**	*	*	-	8
Sanmartin 2007	*	*	*	*	**	*	*	-	8
Shimizu 2010	*	*	*	*	*	*	*	*	8
Shiomi (CREDO KYOTO 2 2015)	*	*	-	*	*	*	*	-	6
Stone EXCEL 2019	*	*	*	*	**	*	*	*	9
Stone EXCEL 2016	*	*	-	*	*	*	-	-	5
Thiele 2009	*	*	*	*	*	*	*	-	7
Te Hsu 2008	*	*	*	*	**	*	*	-	8
Wei 2016	*	*	*	*	*	*	-	-	6
White 2008	*	*	*	*	**	*	*	*	9
Wu 2008	*	*	*	*	**	*	*	*	9
Wu 2010	*	*	*	*	**	*	*	-	8
Yi Gijong 2012	*	*	*	*	*	*	*	-	7
Yin 2015	*	*	-	*	-	-	-	-	3
Yu 2016	*	*	-	*	-	-	*	-	4
Zhao 2011	*	*	-	*	*	*	*	-	6
Zheng 2016	*	*	-	*	-	-	*	*	5

The methodological quality of retrospective or prospective observational studies was done using Newcastle-Ottawa scale (NOS) quality scale. Each asterisk/star in the Newcastle-Ottawa Scaling System (NOS) represents responses of the biases questionnaire. Each bias assessment part gets one star except comparability that gets a maximum of 2 stars. Each star counts towards the total score. Score <5 represents poor quality, 5-6 represents moderate quality and 7 to 9 are considered as high quality. Total of 30 studies had a NOS score >7 representing a high quality. Rest of the studies had moderate to poor quality owing to the ascertainment bias, comparability, and follow up limitations.

- Not Available or unable to extract

S. Table 3

Definition of outcomes used across the randomized controlled trials

Outcome	Description
Death	<p>The cause of death was adjudicated as being due to cardiovascular or non-cardiovascular causes</p> <ul style="list-style-type: none"> • Cardiovascular death includes sudden cardiac death, death due to acute MI, heart failure or cardiogenic shock, stroke, other cardiovascular causes, or bleeding • Non-cardiovascular death is defined as any death with known cause not of cardiac or vascular causes.
MI	<p>Periprocedural MI: Defined as the occurrence within 48-72 hours after either PCI or CABG</p> <p>SCAI Definition:</p> <ul style="list-style-type: none"> • CK-MB >10x upper reference limit (URL)*, OR • CK-MB >5x URL*, PLUS - new pathological Q waves in at least 2 contiguous leads or new persistent non-rate related LBBB, or angiographically documented graft or native coronary artery occlusion or new severe stenosis with thrombosis and/or diminished epicardial flow, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality <p>Non-procedural MI: SCAI defined non-procedural MI as the occurrence >72 hours after any PCI or CABG.</p> <p>SCAI Definition:</p> <ul style="list-style-type: none"> • The rise and/or fall of cardiac biomarkers (CK-MB or troponin) >1x URL* <p>PLUS:</p> <ul style="list-style-type: none"> - ECG changes indicative of new ischemia [ST-segment elevation or depression, or bundle branch block (BBB)], or - Development of pathological Q waves (≥ 0.04 seconds in duration and ≥ 1 mm in depth) in ≥ 2 contiguous precordial leads or ≥ 2 adjacent limb leads) of the ECG, or - Angiographically documented graft or native coronary artery occlusion or new severe stenosis with thrombosis and/or diminished epicardial flow, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality <p>Third Universal Definition of MI: Detection of a rise and/or fall of cardiac biomarker values, with at least one of the values being elevated (i.e., > 99th percentile upper reference limit, URL). The preferred cardiac biomarker of necrosis is highly sensitive and specific cTn.</p>
Stroke	The rapid onset of a new persistent neurologic deficit attributed to an obstruction in cerebral blood flow
Revascularization	A coronary revascularization procedure may be either a CABG or a PCI.
MACCE	Major adverse cardiovascular or cerebrovascular events were defined as all-cause mortality, stroke or transient ischemic attack, nonfatal MI, acute coronary syndrome (including unstable angina), and left ventricular failure requiring hospital admission.

S. Table 4

Inclusion Criteria of RCTs.

Trials	Inclusion Criteria	MACCE Components
LE MANS	Stable LMCAD >50% stenosis, symptomatic, documented myocardial ischemia	MI, death, stroke, and revascularization
EXCEL	Stable LMCAD 50-70% stenosis, symptomatic	MI, death, and stroke
NOBLE	Stable, unstable angina, ACS, LMCAD >50% stenosis, FFR <0.80, symptomatic, documented myocardial ischemia	MI, death, stroke, and revascularization
PRECOMBAT	Stable, unstable angina, NSTEMI, LMCAD >50% stenosis, symptomatic, documented myocardial ischemia	MI, death, stroke, and revascularization
SYNTAX	Stable LMCAD or multivessel >50% stenosis, symptomatic, documented myocardial ischemia	MI, death, stroke, and revascularization
Boudriot et al.	Stable LMCAD >50% stenosis, symptomatic, documented myocardial ischemia	MI, death, and revascularization

S. Table 5Definitions and Descriptions of Terminologies/Scores

Terminology	Definition
SYNTAX Score	The SYNTAX score is a grading system that evaluates the complexity and prognosis of patients undergoing percutaneous coronary intervention (PCI). The SYNTAX score is the sum of the points assigned to each individual lesion identified in the coronary tree with greater than 50% diameter narrowing in vessels of greater than 1.5 mm diameter. The coronary tree is divided into 16 segments according to the AHA classification.
Ascertainment bias	Ascertainment bias is a systematic distortion in measuring the true frequency of a phenomenon due to the way in which the data are collected

S. Table 6

Selected baseline characteristics of randomized trials.

Author/Study/ Year	PCI-CA BG	Mean Age	Male %	HTN	DM	HLD	Smokers	Mean Syntax Score	EuroScore	Site of Lesion	FU
Ahn-PRECOMBAT 2015 [1]	300-300	62-63	76-77	-	102 (34)-90 (30)	-	-	-	-	D	5
Boudriot et al. 2011 [2]	100-101	66-69	72-77	82 (82)-83 (82)	40 (40)-33 (33)	68 (68)-65 (64)	35 (35)-28 (28)	24-23	2.4-2.6	Ost/D	1
Buszman-LE MANS 2016 [3]	52-53	60-61	60-73	39 (75)-37 (70)	10 (19)-9 (17)	34 (65)-32 (60)	-	25.2-24.7	3.3-3.5	-	10
Holm-NOBLE 2020 [4]	592-592	66-66	80-76	386 (66)-389 (66)	94 (16)-90 (15)	482 (81)-464 (78)	108 (18)-127 (21)	22-22	2-2	Ost/MS/B	5
Mäkikallio-NOBLE 2016 [5]	592-592	66-66	80-76	386 (66)-389 (66)	86 (15)-90 (15)	482 (81)-464 (78)	108 (18)-127 (21)	22-22	2-2	Ost/MS/B	3
Morice-SYNTAX 2014 [6]	357-348	NA-66	74-76	250 (70)-215 (62)	85 (24)-89 (26)	289 (81)-261 (75)	64 (18)-83 (24)	29-30	3.9-3.9	Ost/MS/B	5
Park-PRECOMBAT 2015 [7]	300-300	62-63	76-74	-	102 (34)-90 (30)	-	-	-	-	D	1
Stone-EXCEL 2019 [8]	948-957	66-66	21-19	703 (74)-701 (73)	72 (8)-62 (7)	668 (70)-652 (68)	222 (23)-193 (20)	20-20	-	-	5
Stone-EXCEL 2016 [9]	948-957	66-66	76-77	703 (74)-701 (73)	286 (30)-268 (28)	668 (70)-652 (68)	222 (23)-193 (20)	20-20	-	B	3
Serruys-SYNTAX 2009 [10]	357-348	65-65	74-76	250 (70)-215 (62)	87 (25)-89 (26)	289 (81)-261 (75)	64 (18)-83 (24)	29-30	-	Ost/MS/B	1
Thuijs-SYNTAX 2019 [11]	357-348	65-65	76-79	246 (69) - 257(74)	87 (25)-89 (26)	289 (81)-261 (75)	64 (18)-83 (24)	29-30	-	Ost/MS/B	10

All data is presented in the format of PCI/ CABG if applicable.

PCI: Percutaneous Coronary Intervention, CABG: Coronary Artery Bypass Graft HTN= Hypertension, DM= Diabetes Mellitus, HL= Hyperlipidemia, SYNTAX: Synergy between percutaneous coronary intervention (PCI) with taxus and cardiac surgery, EuroScore: European System for Cardiac Operative Risk Evaluation, Ost: Ostial, MS: Midshaft, D: Distal Bifurcation, B: Bifurcation, PRECOMBAT: Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease, Le MANS: Left Main Coronary Artery Stenting, EXCEL: Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization.

-Not available or unable to extract, * Age presented as - mean PCI - mean CABG (%) = Percentages

S. Table 7

Selected baseline characteristics of observational studies.

Author/Study/ Year	PCI-CAB G	Mea n Age	Male %	HTN	DM	HLD	Smokers	Syntax Score	EuroSco re	Site of Lesion	FU
Brener 2008 [12]	97-190	68-68	72-74	82 (85)-144 (76)	42 (43)-25 (13)	-	11 (11)-101 (53)	-	4.6-4.5	-	3
Buchanan Delta 2014 [13]	489-328	67-68	-	359 (73)-240 (73)	161 (33)-101 (31)	323 (66)-232 (71)	122 (25)-55 (17)	26.8-37.1	5.6-5.4	-	3
Caggegi CUSTOMIZE 2011 [14]	222-361	67-66	76-78	159 (72)-266 (74)	79 (36)-146	123 (55)-191	97 (44)-162 (49)	26-33.6	6.3-5.6	Ost-MS-DB	1
Cavalcante 2016 [15]	657-648	64-64	74-76	-	187 (28) -179 (28)	416 (63)-380 (59)	153 (23)-165 (25)	27-28	3.3-3.4	-	5
Chang 2012 [16]	558-309	64-65	73-72	330 (59)-171 (55)	184 (33)-121 (39)	177 (32)-102 (33)	135 (24)-80 (26)	25-34	3.8-4.2	-	5
Cheng 2009 [17]	94-216	68-67	74-76	68 (72)-155 (72)	32 (34)-108 (50)	67 (71)-97 (45)	18 (19)-64 (30)	-	6.9-6.4	Ost/MS/B	1
Chieffo 2012 [18]	1874-900	66-66	74-64	1200 (64)-609 (68)	520 (28) -306 (34)	1159 (62)-582 (65)	847 (45)-384 (43)	28-38	4.9-5.1	Ost/MS/B	4
Ghenim 2009 [19]	105-106	81-79	64-72	69 (66)-77 (73)	25 (24)-32 (30)	44 (42)-67 (63)	26 (25)-21 (20)	-	7-8	D	1
Kang 2010 [20]	205-257	64-66	70-74	130 (63)-173 (67)	77 (38)-112 (44)	112 (55)-153 (60)	89 (43)-127 (49)	-	4.2-5.6	Ost/shaft/B	3
Kawecki 2012 [21]	34-111	67-66	68-73	25 (74)-80 (72)	6 (18)-34 (30)	16 (47)-45 (41)	4 (12)-19 (17)	-	4.7-4.8	Ost/MS/B	1
Kim 2009 [22]	251-256	64-66	71-72	418-343	251 (100)-256 (100)	241 (96)-254 (99)	166 (66)-22 (9)	-	4-5	Ost/MS/DB	3
Lee 2007 [23]	50-123	72-70	50-76	44 (88)-99 (81)	18 (36)-38 (31)	37 (74)-88 (72)	6 (12)-23 (19)	-	-	Ost/MS	1
Lu 2016 [24]	208-270	70-69	84-86	163 (78)-223 (83)	98 (47)-124 (46)	112 (54)-135 (50)	104 (50)-180 (67)	-	7.1-6.4	D/B	5
Luo 2012 [25]	331-492	61-63	79-80	194 (59)-294 (60)	99 (30)-127 (26)	55 (17)-102 (21)	150 (45) -199 (40)	-	5-5	Ost/MS/DB	2
Makikallio 2008 [26]	49-238	72-70	59-80	23 (47)-108 (45)	10 (20)-40(17)	-	10 (20)-43 (18)	-	7.7-5.2	Ost/D	1
Montalescot 2009 [27]	514-612	-	73-74	321 (62)-430 (70)	140 (27)-169 (28)	233 (45)-351 (57)	271 (53)-370 (60)	-	-	-	6
Naganuma 2014 [28]	482-374	64-67	73-62	307 (64)-264 (71)	127 (26)-138 (37)	284 (59)-240 (64)	231 (48)-169 (45)	26-35	4.5-5.2	Ost/MS	3.5
Palmerini 2006 [29]	157-154	73-69	70-76	109 (69)-112 (72)	41 (26)-39 (25)	98 (62)-111 (72)	76 (48)-74 (48)	-	6-5	Ost/MS/B	≥1
Park DW 2010 [30]	176-219	61-62	71-74	83 (47)-121 (55)	52 (30)-81 (37)	62 (35)-121 (55)	31 (18)-43 (20)	-	3.3-4.5	Ost/MS/DB	5
Park DW 2010 [30]	100-250	55-61	60-74	23 (23)-125 (50)	21 (21)-82 (33)	34 (34)-115 (46)	36 (36)-68 (27)	-	3.3-4.4	Ost/MS/DB	10
Park MAIN COMPARE 2011 [31]	784-690	62-64	70-72	418 (53)-343 (50)	251 (32)-256 (37)	240 (31)-253 (37)	193 (25)-178 (26)	-	-	Ost/MS/DB	5
Park SJ 2011 [32]	300-300	62-68	76-77	163 (54)-154 (51)	102 (34)-90 (30)	127 (42)-120 (40)	89-83	-	2.6-2.8	B involved	2
Qin 2013 [33]	233-282	65-67	84-87	132 (57)-195 (69)	57 (24)-77 (27)	82 (35)-113 (40)	112 (48)-113 (40)	24-34	3.7-4.5	B: 155/213	≥2
Rittger 2011 [34]	95-192	73-73	76-72	84 (88)-124 (65)	35 (37)-68 (35)	54 (57)-194 (100)	-	-	-	Ost/MS/DB	1
Rodes-Cabau 2008 [35]	104-145	85-82	54-63	78 (75)-105 (72)	28 (27)-38 (26)	63 (61)-119 (82)	3 (3)-9 (6)	-	9.5-8.4	Ost/MS/DB	2
Sanmartin 2007 [36]	96-245	66-66	81-87	42 (44)-148 (60)	18 (19)-78 (32)	40 (42)-112 (46)	37 (39)-112 (46)	-	25% >6	Ost/MS/D	≥1
Shimizu 2010 [37]	64-89	71-70	81-85	54 (84)-70 (79)	31 (48)-41 (46)	29 (45)-52 (58)	42 (66)-58 (65)	-	-	-	2
Shiomi CREDO-KYOTO-2 2015 [38]	364-640	71-69	71-77	312 (86)-542 (85)	154 (42)-291 (45)	117 (32)-112 (18)	78 (21)-157 (25)	26-30	-	-	5
Te Hsu 2008 [39]	20-39	66-66	60-69	8 (40)-20 (51)	9 (45)-14 (36)	5 (25)-12 (31)	4 (20)-11 (28)	-	6.3-5.5	Ost/MS/DB	1
Wei 2016 [40]	64-62	74-71	75-79	39 (61)-45 (73)	28 (44)-21 (34)	11 (17)-13 (21)	25 (39)-36 (58)	27-35	6.8-6	Ost/MS/B	1
White 2008 [41]	120-223	71-69	58-77	90 (76)-170 (76)	42 (36)-60 (27)	89 (75)-171 (77)	21 (18)-37 (17)	-	-	Ost/MS/DB	3
Wu 2008 [42]	135-135	71-68	64-71	-	29 (21)-29 (21)	-	-	-	-	-	1
Wu 2010 [43]	131-245	61-NA	75-82	85 (65)-153 (62)	35 (27)-71 (29)	42 (32)-75 (31)	51 (39)-96 (39)	-	4.3-4.2	Ost/MS/D	3
Yi Gijong 2012 [44]	128-128	62-65	72-77	76 (56)-80 (63)	42 (33)-40 (31)	-	-	-	-	MS/D/B	5
Yin 2015 [45]	106-121	62-61	68-56	71 (67)-79 (65)	23 (22)-26 (21)	47 (44)-66 (55)	34 (32)-37 (31)	26-32	-	Ost/MS/B	1
Yu 2016 [46]	465-457	62-64	79-82	286 (62)-269 (59)	143 (31)-131 (29)	231 (50)-158 (35)	230 (49)-205 (45)	-	5-5	Ost/MS/B	7
Zhao 2011 [47]	56-116	-	73-72	32 (57)-60 (52)	56 (100)-116 (100)	44.6-42.4	28 (50)-51 (44)	-	-	DB/total occlusion	2
Zheng 2016 [48]	1442-2604	60-62	82-79	782 (54)-1674 (64)	348 (24)-806 (31)	722 (50)-1539 (59)	671 (47)-1395 (54)	23-33	1.8-2.8	Ost/MS/B	3

All data is presented in the format of PCI/ CABG if applicable.

PCI: Percutaneous Coronary Intervention, CABG: Coronary Artery Bypass Graft HTN= Hypertension, DM= Diabetes Mellitus, HL= Hyperlipidemia, MAIN COMPARE: Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization. DELTA: Drug-eluting stent for left main coronary artery disease. CUSTOMIZE: The Appraise a Customized Strategy for Left Main Revascularization. Credo-KYOTO: Coronary REvascularization Demonstrating Outcome Study in Kyoto

-Not available or unable to extract, * Age presented as - mean PCI - mean CABG (%) = Percentages, FU: Follow up period

S. Table 8

Pooled outcomes of PCI vs. CABG, based on follow up durations across RCTs.

Event	30 days	1 year	5 year	10 year
MACCE	0.61 (0.47-0.79, p=0.0002)	1.07 (1.93-1.23, p= 0.33)	1.31(1.19-1.45, p<0.00001)	0.68 (0.44-1.06, p=0.09)
MI	0.76 (0.54-1.05, P=0.10)	1.06 (0.72-1.57, P=0.76)	1.62 (1.00-2.62, P=0.05)	1.21 (0.67-2.18, P=0.53)
Revascularization	0.64 (0.34-1.20, P=0.17)	1.71 (1.39-2.10, P=<0.00001)	1.72 (1.47-2.00, P=<0.00001)	2.95 (0.22-39.28, P=0.41)
Stroke	0.41 (0.17-0.98, P=0.05)	0.32 (0.15-0.69, P= 0.004)	0.86 (0.44-1.68, P=0.66)	0.68 (0.28-1.65, P=0.39)
Mortality	0.58(0.30-1.16, P=0.12)	0.83(0.63-1.07, P=0.15)	1.07 (0.84-1.36, P=0.57)	0.79 (0.60-1.05, P=0.10)

MI: Myocardial Infarction, MACCE: Major Adverse Cardiovascular and Cerebrovascular events.

S. Table 9

Pooled results of PCI vs. CABG; based on follow up durations across observational studies.

Follow Up	MACCE	MI	Revascularization	Stroke	Mortality
IH	0.27 (0.20-0.36, p <0.00001)	0.41 (0.12-0.95, p= 0.04)	1.49 (0.63-3.52, p= 0.36)	0.20 (0.08-0.49, p= 0.0004)	0.40 (0.19-0.87, p= 0.02)
30 days	0.52 (0.29-0.94, p= 0.03)	1.02 (0.58-1.81, p= 0.94)	0.69 (0.26-1.86, p=0.46)	0.34 (0.13-0.87, p= 0.02)	0.52 (0.23-1.18, p=0.12)
6 months	1.16 (0.62-2.16, p= 0.64)	6.02 (2.00-18.06, p= 0.001)	1.92 (0.67-5.49, p= 0.22)	0.53 (0.19-1.54, p= 0.24)	1.92 (0.59-6.23, p= 0.28)
1 year	1.61 (1.30-2.00, p <0.0001)	1.47 (1.12-1.92, p=0.005)	1.69 (1.04-4.47, p <0.00001)	0.55 (0.19-0.79, p= 0.001)	1.04 (0.78-1.38, p= 0.79)
3 year	0.96 (0.64-1.43, p= 0.85)	1.71 (1.23-2.38, p= 0.001)	5.08 (4.02-6.40, p <0.00001)	0.29 (0.19-0.45, p <0.00001)	0.92 (0.54-1.54, p= 0.74)
5 year	1.82 (1.04-3.21, p=0.04)	1.74 (1.37-2.22, p <0.00001)	1.48 (2.57-4.71, p <0.00001)	0.49 (0.28-0.84, p= 0.009)	0.92 (0.69-1.23, p=0.59)
10 year	0.68 (0.44-1.06, p= 0.09)	1.21 (0.67-2.18, p= 0.53)	2.95 (0.22-39.28, p= 0.41)	0.68 (0.28-1.65, p= 0.39)	0.79 (0.60-1.05, p= 0.10)

Abbreviations: IH: In-hospital, MI: Myocardial Infarction, MACCE: Major Adverse Cardiovascular and Cerebrovascular events

S. Table 10

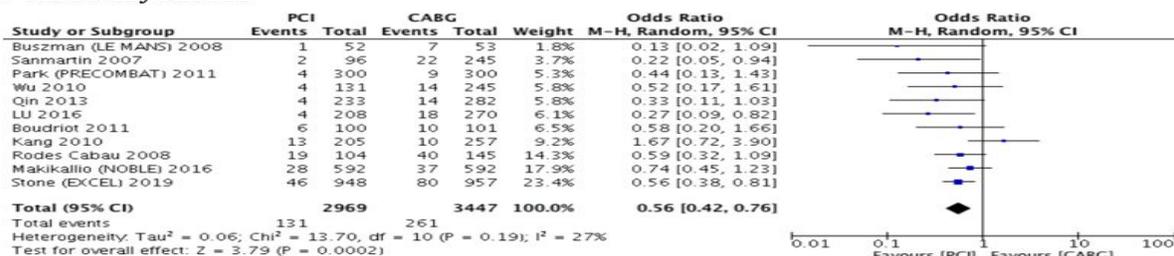
Results and Limitations of previous meta-analyses on PCI vs. CABG for LMCAD.

Author/Year/Reference	Studies	Limitations	Follow-up	MACCE
De Rosa 2018 [49]	5	No subgroup analyses, Variation in the definition of the primary end points	5 years	1.33 (1.12-1.58)
Kodumuri 2018 [50]	12	No subgroup analyses, Variation in the definition of the primary end points,	5 years	1.23 (1.01-1.51)
Bittl 2018 [51]	12	No subgroup analyses, Variation in the definition of the primary end points,	1 year	1.00 (0.72-1.40)
Bajaj 2018 [52]	6	No subgroup analyses, Variation in the definition of the primary end points,	1 year	1.21 (1.05-1.40)
Upadhaya 2018 [53]	5	Variation in the definition of the primary end points, follow-up data for only 1-3 years. Less population	1 year	1.36 (1.18-1.58)
Khan 2017 [54]	6	Unexplored heterogeneities with regards to study design, patient characteristics, methods employed, types of stents used	5 years	1.32 (1.13-1.53)
Zhang 2017 [55]	28	Selective outcome reporting was observed in a number of observational studies, and publication bias	1 year	1.42 (1.14-1.77)
Kajimoto 2017 [56]	3	Follow-up period was limited to one year, Less population	1 year	0.40 (0.29 to 0.55)
Jang 2017 [57]	12	No subgroup analyses, Variation in the definition of the primary end points,	1 year	0.70 (0.49 to 1.00)
Tamburino 2017 [58]		Lower population and confounding variables.	2 years	
Alam 2017 [59]	10	Limited data on the medical therapies, no long-term follow-up	1 year	0.82 (0.47-1.41)
Capodanno 2017 [60]	4	Variation in study design, endpoint definitions, and possible publication bias	1 year	1.276 (0.950-1.715)
Biondi-Zoccai 2017 [61]	17	No subgroup analyses, Variation in the definition of the primary end points,	1 year	2.5 (1.2-3.8)
Palmerini 2017 [62]	19	No subgroup analysis on Syntax data, shorter duration, less patients	30 days	2.94 (1.69 to 5.09)
Ye 2017 [63]	6	Variation in revascularization and myocardial infarction were not resolved	1 year	1.21 (1.05-1.40)
Ali 2017 [64]	29	Lack of bias assessment, High selection bias	5 years	1.22 (0.95-1.56)
Naik 2016 [65]	10	Short duration of follow up. Variable study designs and publication bias	1 year	0.82 (0.62-1.09)
Lee 2015 [66]	8	Short length of follow up duration; non-availability of clinical event rates on anatomical basis	1 year	1.25 (0.86-1.82)
Alam 2014 [67]	27	Lack of longer length of follow up; not all studies reported rates of stent thrombosis or cardiac death	5 years	1.30 (1.10-1.55)
Athappan 2013 [68]	24	Variable definitions of endpoints by primary studies	5 years	0.64 (0.51-0.803)
Sa 2013 [69]	16	Short length of follow ups in studies	1 year	1.607
Ali 2013 [70]	29	Short follow-up; Risk of selection bias, variable definition of MI	5 years	1.22 (0.95-1.56)
Lee CW 2012 [71]	3	Definition of clinical outcome was different across trials; Imbalance drug use	5 years	0.46 (0.33-0.64)
Khan 2012 [72]	9	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	1.19 (0.93-1.54)
Testa 2012 [73]	6	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	1.02 (0.76-1.38)
Putzu 2012 [74]	5	Variability in nature of the two treatments; individual patient data could not be explored	5 years	0.55 (0.45-0.67)
Sharma 2012 [75]	6	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	1.79 (1.22-2.64)
Spinthakis 2012 [76]	5	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	2.04 (1.30-3.19)
Moore 2011 [77]	4	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	1.37 (1.18-1.58)
Garg 2011 [78]	5	No subgroups on SYNTAX score	5 years	1.45 (0.87-2.40)
Shah 2010 [79]	8	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	1.20 (1.03-1.40)
Mahmoud 2010 [80]	6	No subgroup analyses based on DES, Variation in the definition of the primary end points and follow ups	5 years	1.19 (1.01-1.41)
Khan AR 2009 [81]	8	No subgroup analyses, Variation in the definition of the primary end points,	5 years	1.16 (0.95-1.43)
Nerlekar 2008 [82]	5	No long-term data; variable definition of repeat revascularization, No subgroup analyses on DES	5 years	1.46 (0.88-2.45)
Giacoppo 2017 [83]	4	No subgroup analyses, Variation in the definition of the primary end points,	5 years	1.06 (0.85-1.32)
Palmerini 2012 [84]	6	Differences in baseline characteristics, variation in definition of clinical end	5 years	1.33 (0.84-2.11)

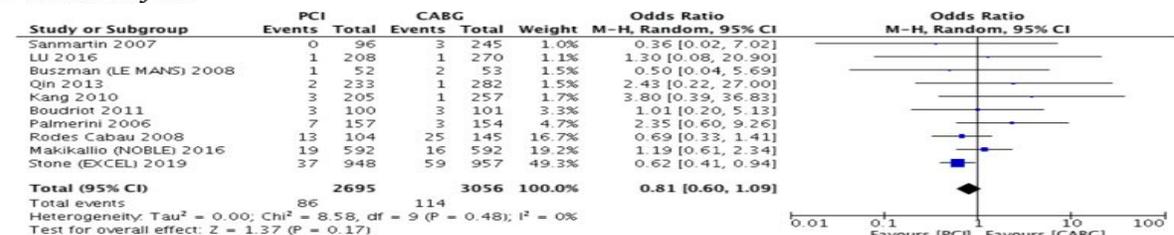
		points across trials, short median follow up (39 months)		
Wang 2019 [85]	19	No subgroup analyses, Variation in the definition of the primary end points,	5 years	1.89 (1.48-2.40)
Ahmad 2020 [86]	5	No comparison of MACCE	5 years	-----

D. SUPPLEMENTAL FOREST PLOTS FOR ALL STUDIES:

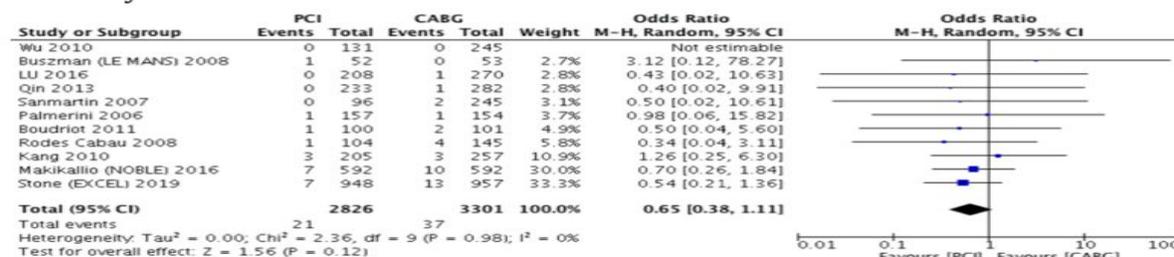
A. All 30 day MACCE



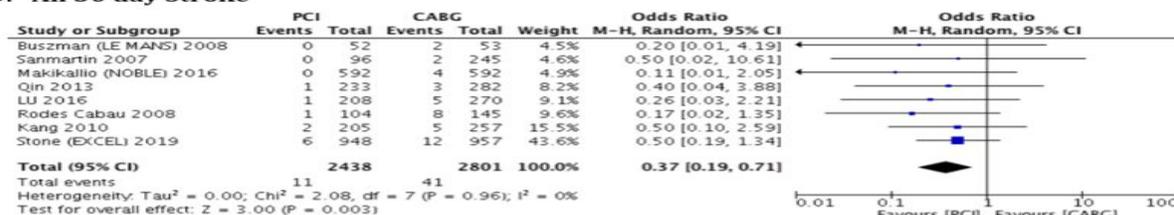
B. All 30 day MI



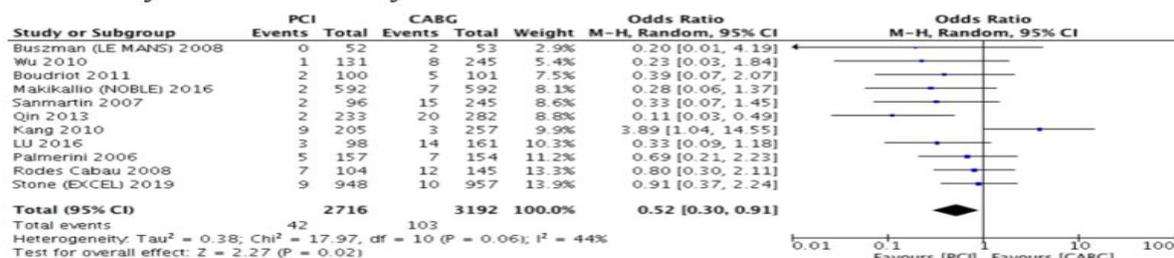
C. All 30 day Revascularization



D. All 30 day Stroke

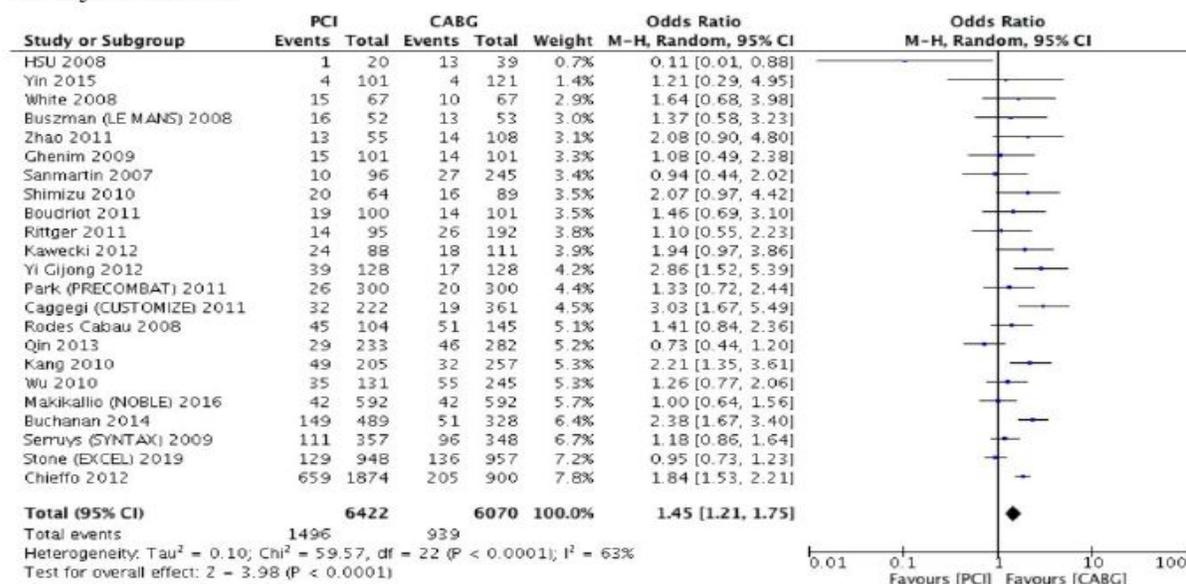


E. All 30 day all-cause Mortality

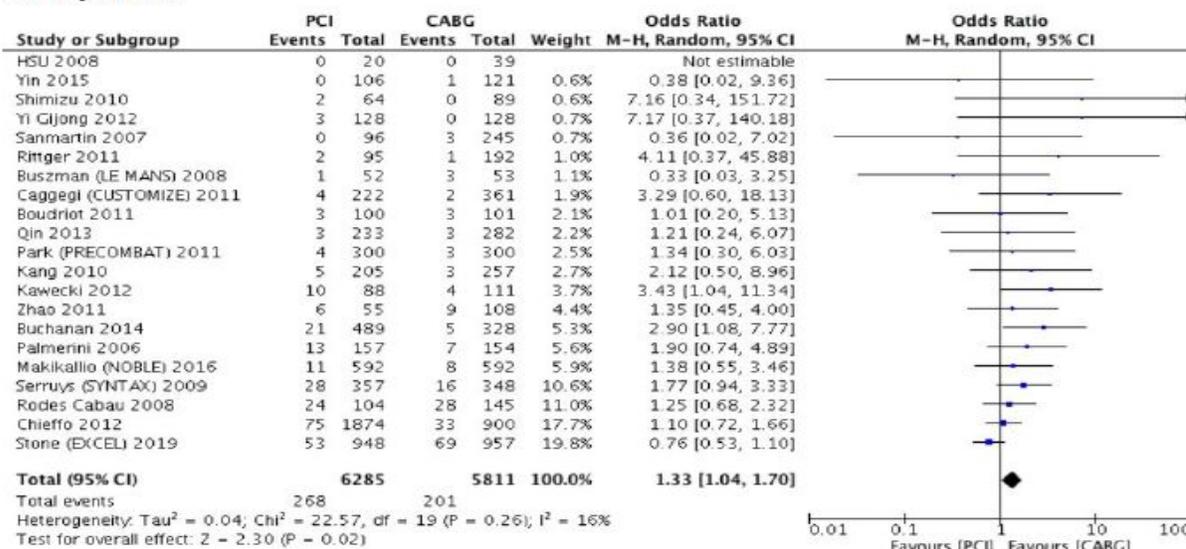


S. Figure 1: Forest Plots showing an individual and pooled OR for all-studies comparing PCI to CABG for LMCAD at 30-days (a. MACCE b. MI c. revascularization d. stroke e. death).

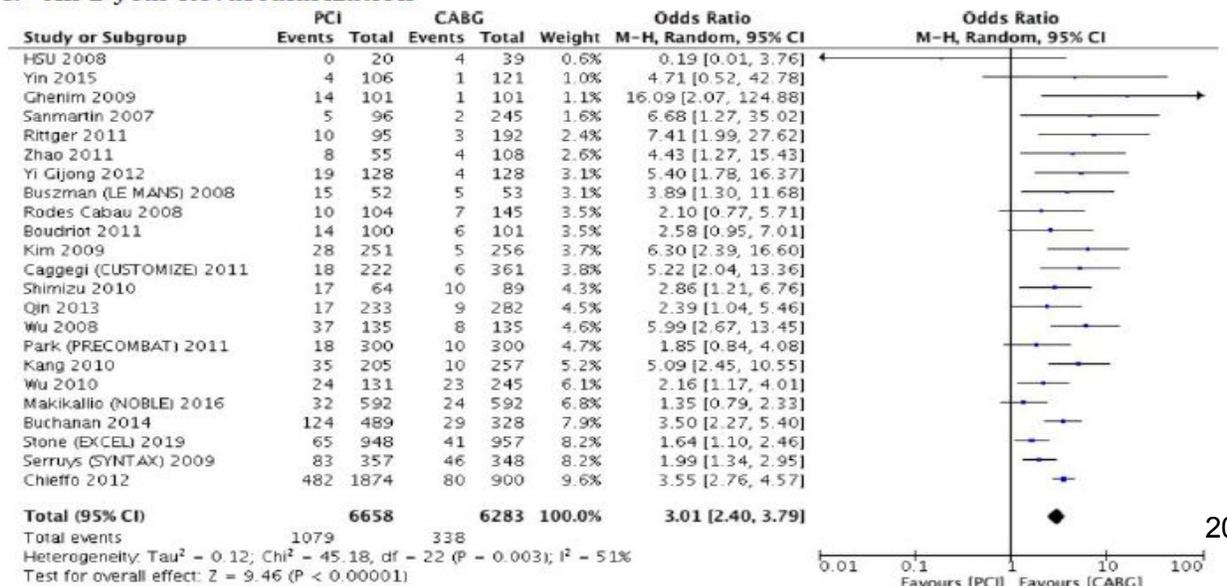
A. All 1-year MACCE



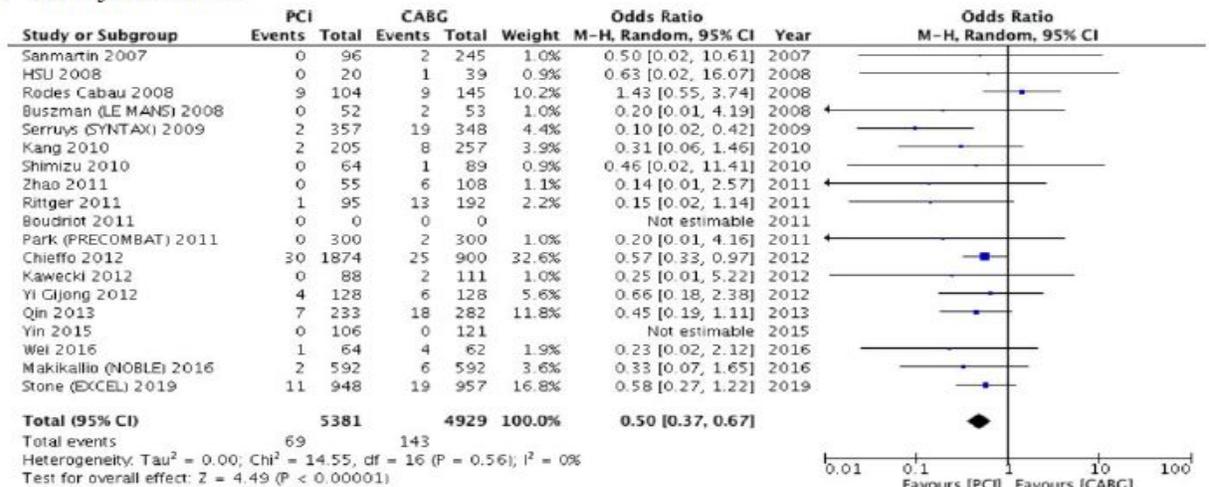
B. All 1-year MI



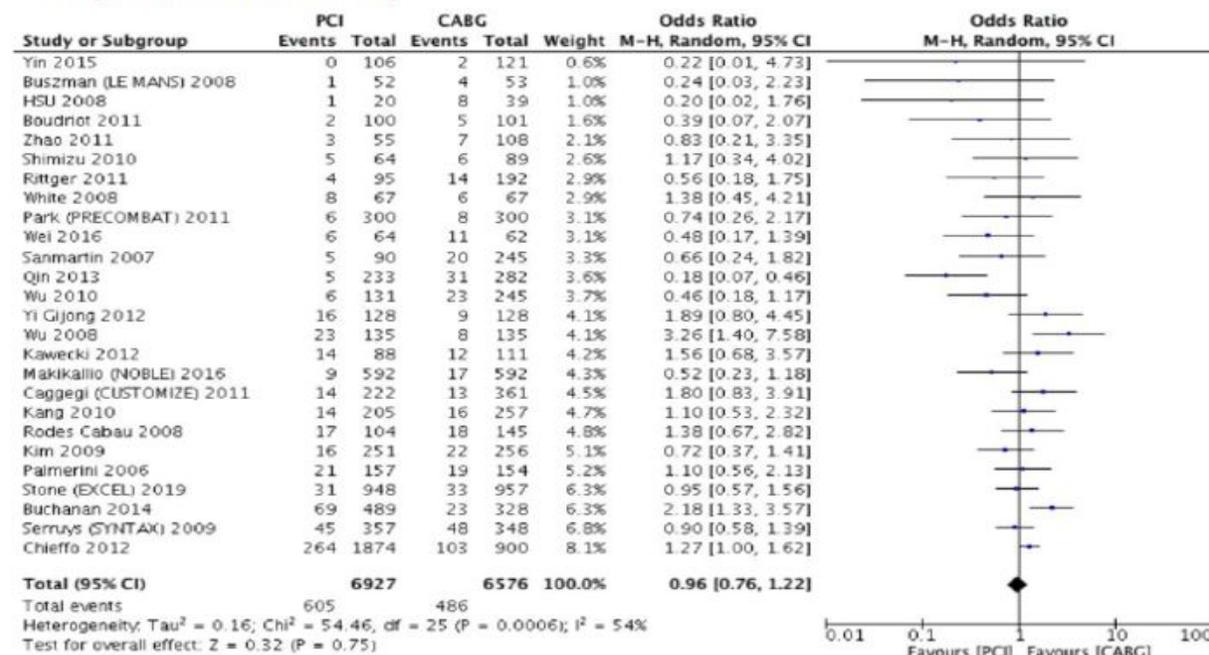
C. All 1-year Revascularization



D. All 1-year Stroke

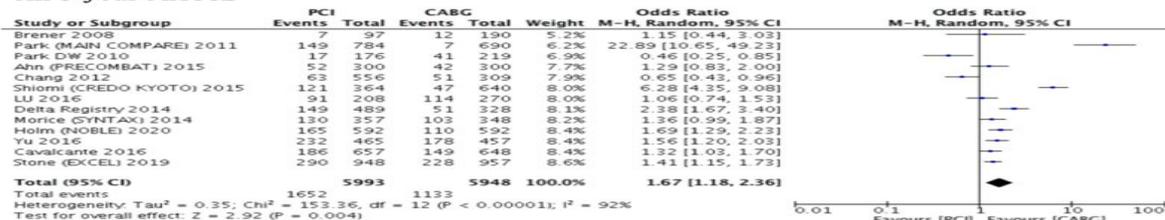


E. All 1-year all-cause Mortality

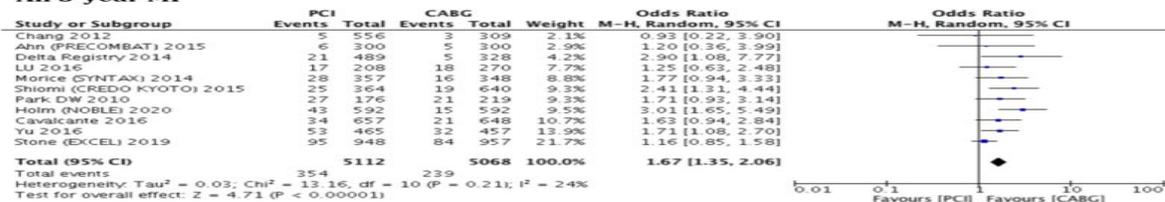


S. Figure 2: Forest Plots showing an individual and pooled OR for all-studies comparing PCI to CABG for LMCAD at 1-year (a. MACCE b. MI c. revascularization d. stroke e. death).

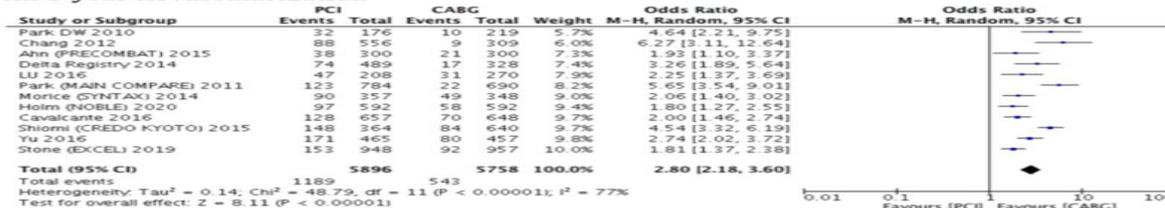
A. All 5-year MACCE



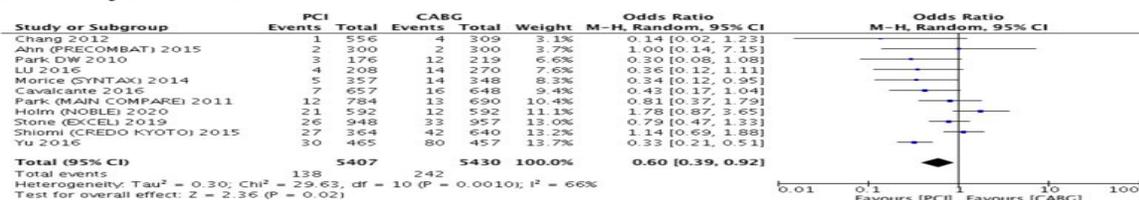
B. All 5-year MI



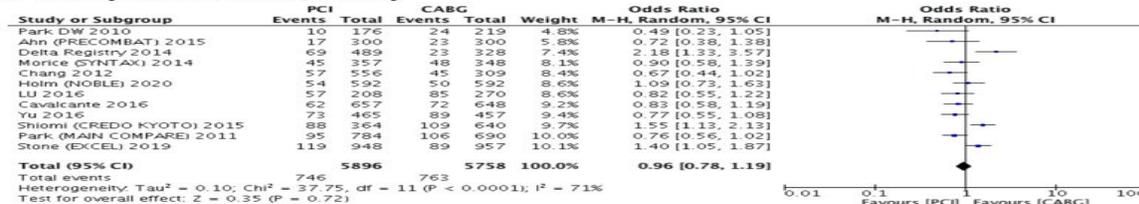
C. All 5-year Revascularization



D. All 5-year Stroke

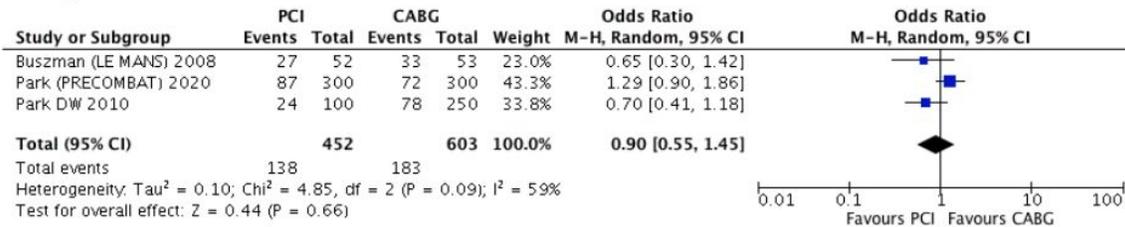


E. All 5-year all-cause Mortality

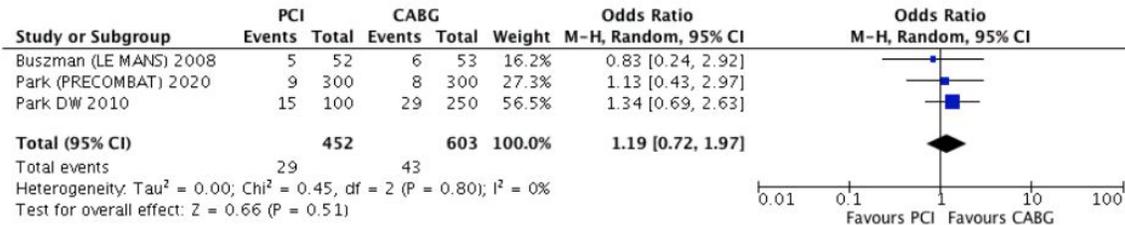


S. Figure 3: Forest Plots showing an individual and pooled OR for all-studies comparing PCI to CABG for LMCAD at 5-Year (a. MACCE b. MI c. revascularization d. stroke e. death)

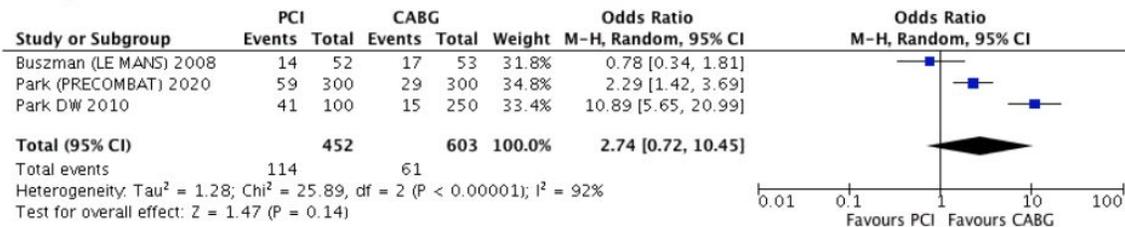
A. 10-year MACCE



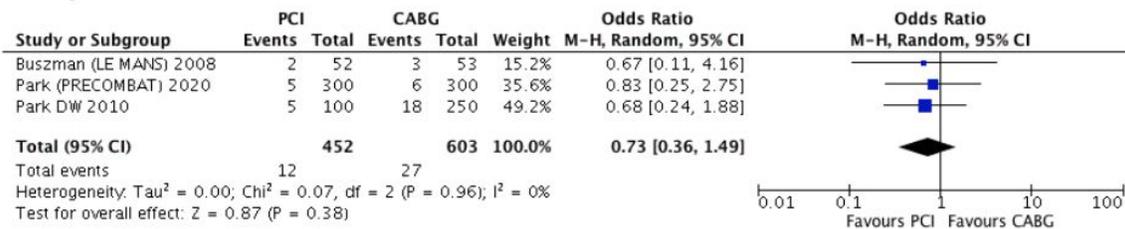
B. 10-year MI



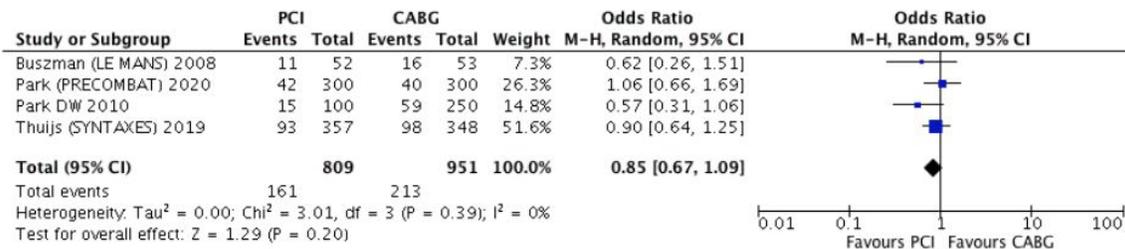
C. 10-year Revascularization



D. 10-year Stroke

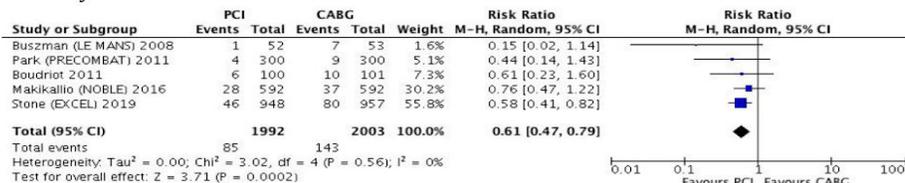


E. 10-year all-cause Mortality

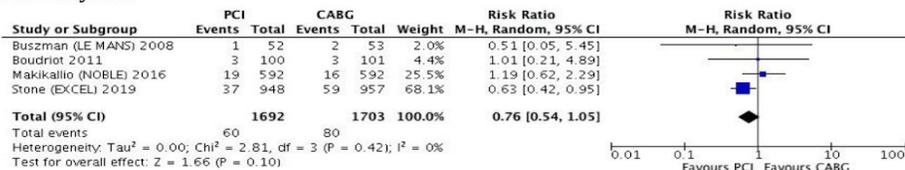


S. Figure 4: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 10-year (a. MACCE b. MI c. revascularization d. stroke e. death).

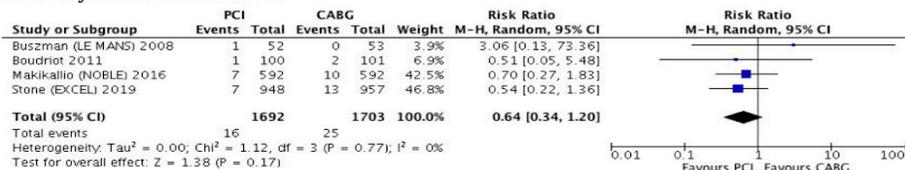
A. 30-days MACCE



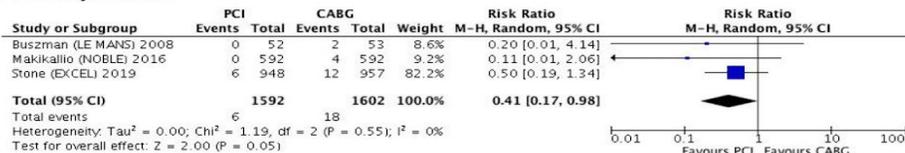
B. 30-days MI



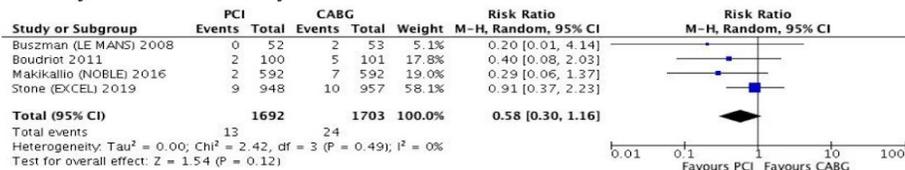
C. 30-days Revascularization



D. 30-days Stroke



E. 30-days all-cause Mortality

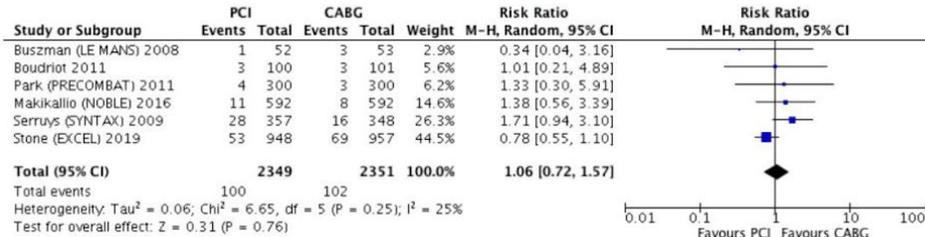


S. Figure 5: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD (a. MACCE b. MI c. revascularization d. stroke e. death).

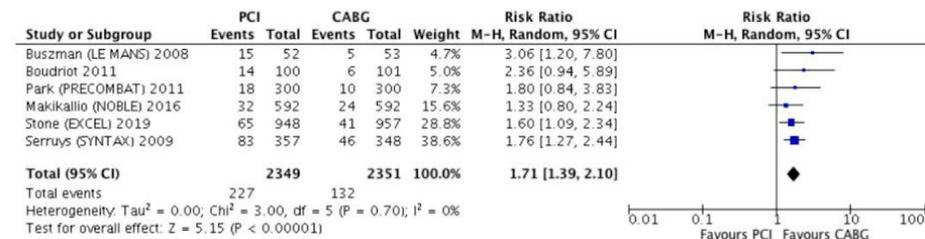
A. 1-year MAACE



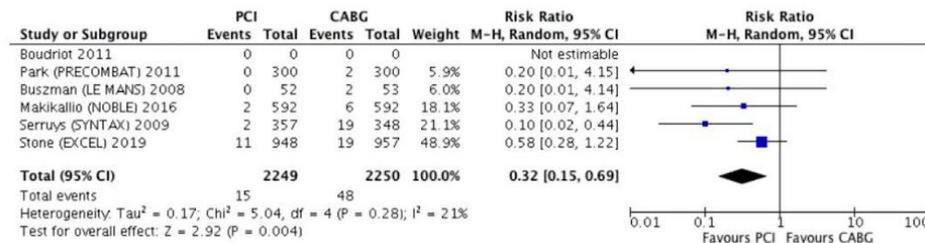
B. 1-year MI



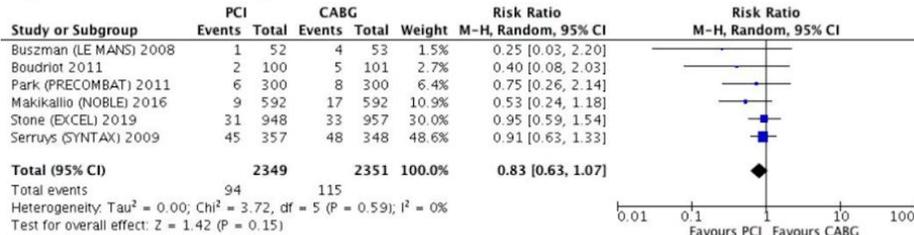
C. 1-year Revascularization



D. 1-year Stroke

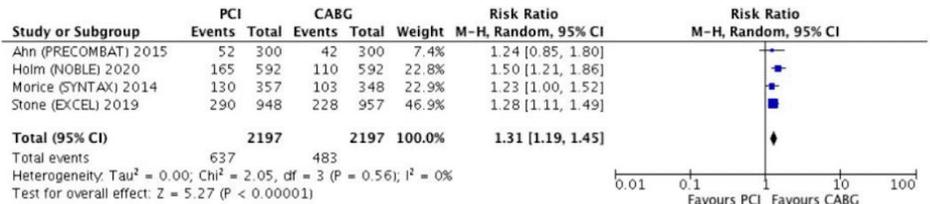


E. 1-year all-cause Mortality

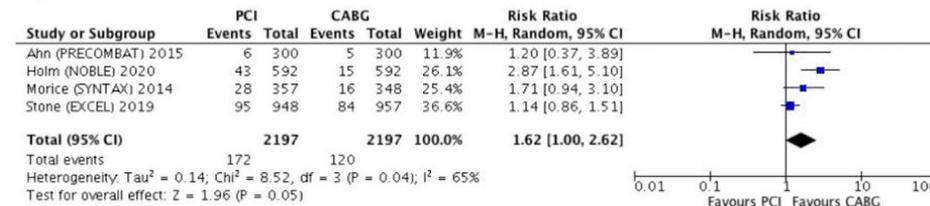


S. Figure 6: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 1-year (a. MACCE b. MI c. revascularization d. stroke e. death).

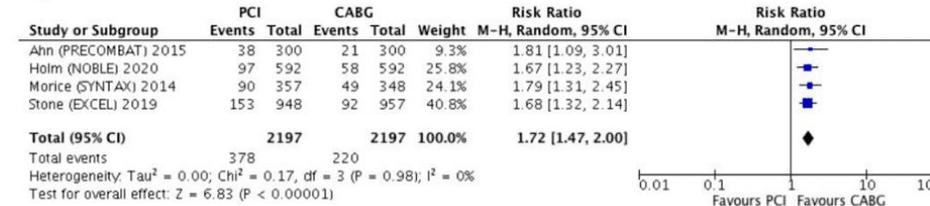
A. 5-year MAACE



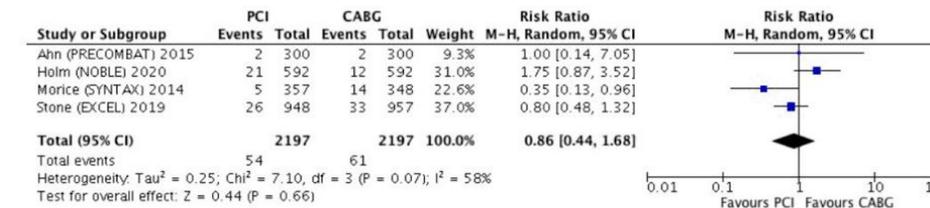
B. 5-year MI



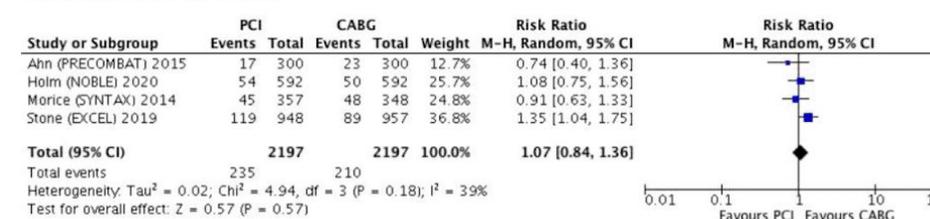
C. 5-year Revascularization



D. 5-year Stroke

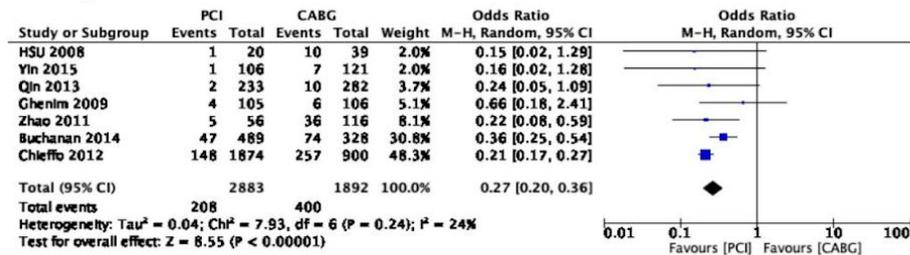


E. 5-year all-cause Mortality

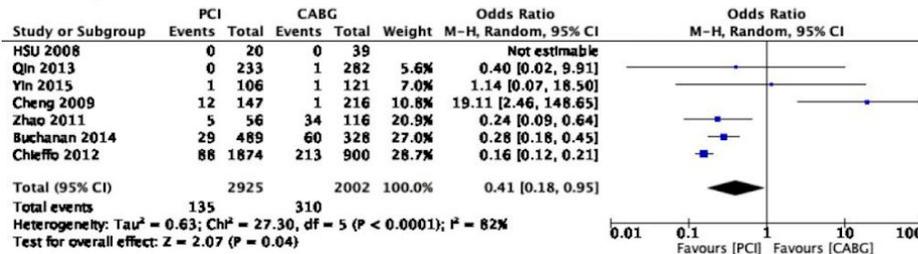


S. Figure 7: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 5-year (a. MACCE b. MI c. revascularization d. stroke e. death).

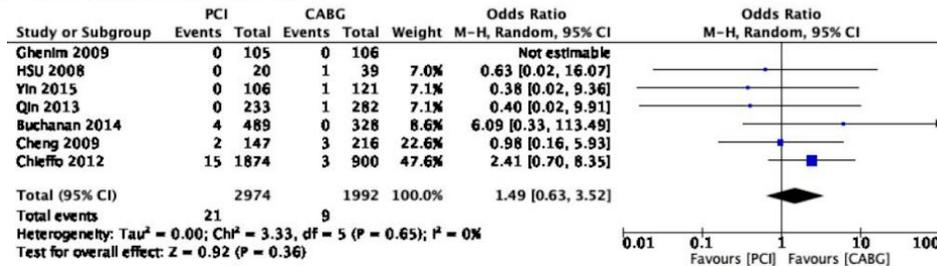
A. In Hospital MAACE



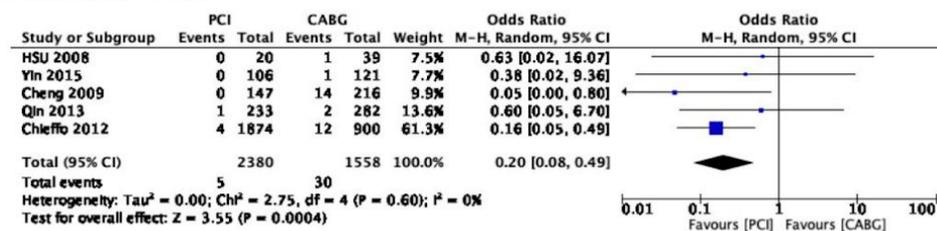
B. In Hospital MI



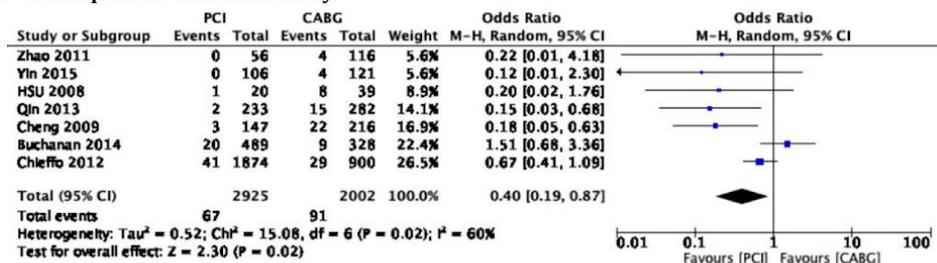
C. In Hospital Revascularization



D. In Hospital Stroke

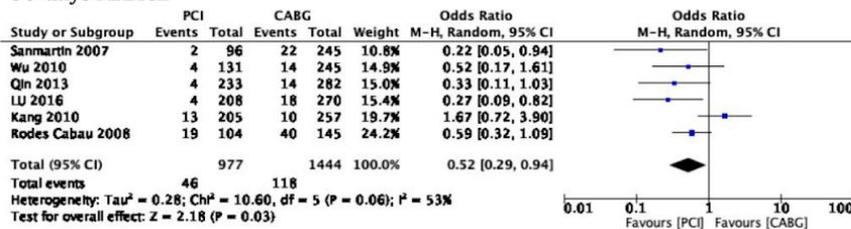


E. In Hospital all-cause Mortality

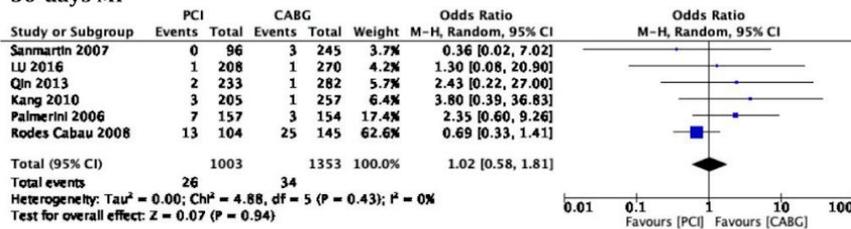


S. Figure 8: In-hospital pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

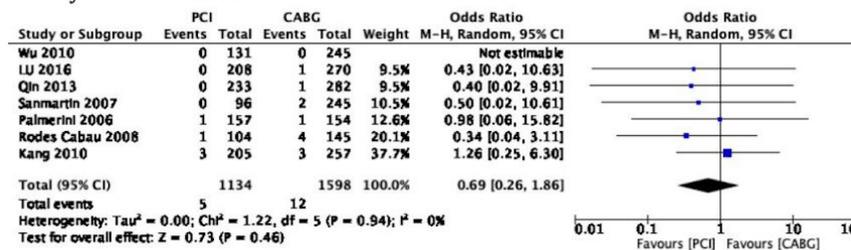
A. 30-days MAACE



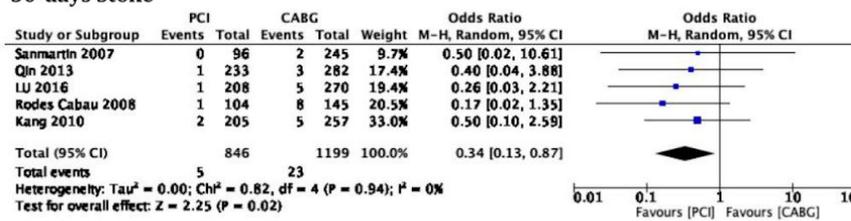
B. 30-days MI



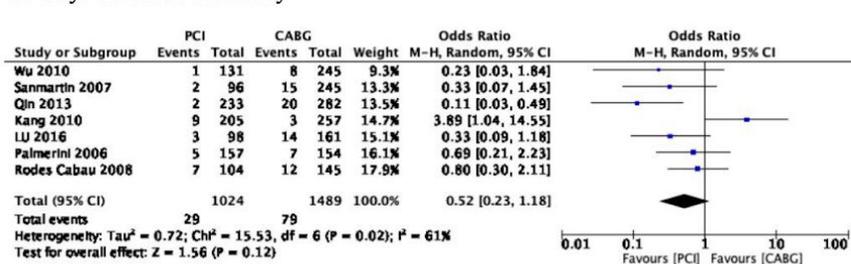
C. 30-days Revascularization



D. 30-days Stoke

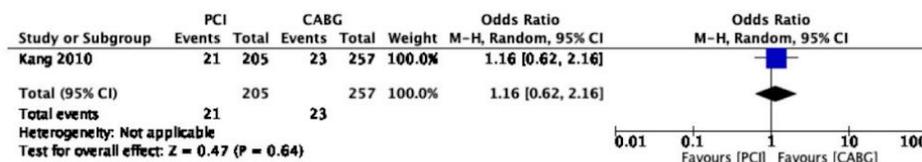


E. 30-days all-cause Mortality

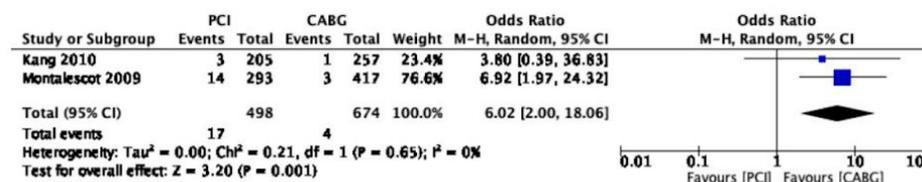


S. Figure 9: 30-days pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

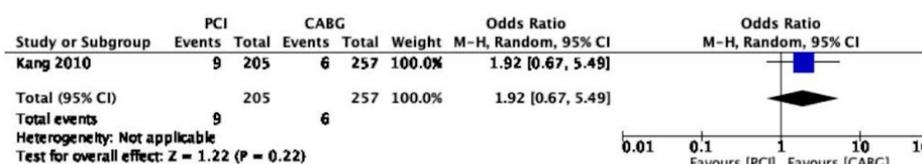
A. 6-month MAACE



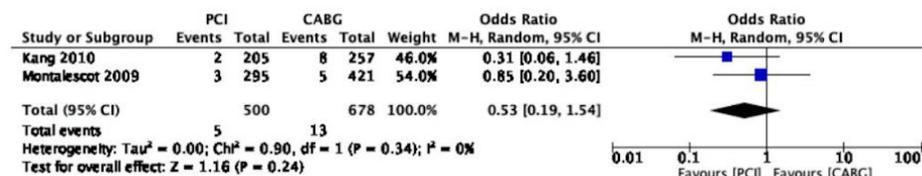
B. 6-month MI



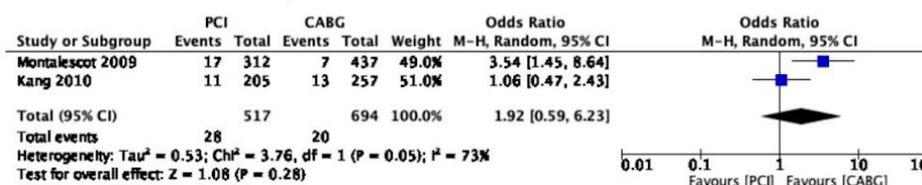
C. 6-month Revascularization



D. 6-month Stroke

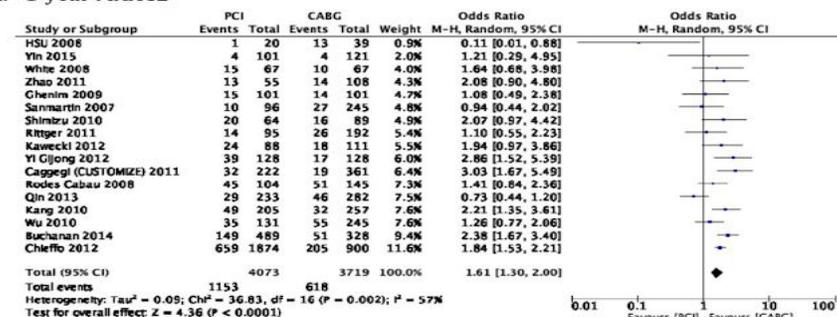


E. 6-month all-cause Mortality

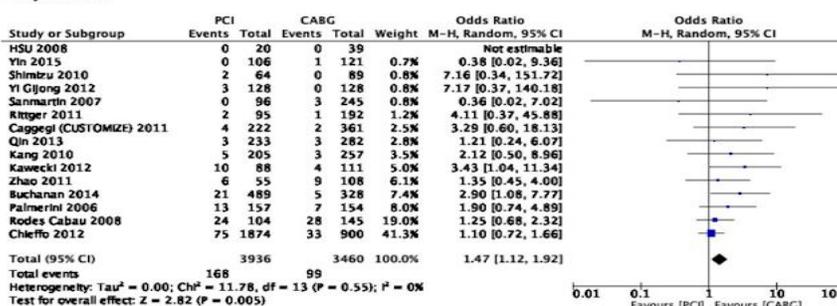


S. Figure 10: 6-months pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

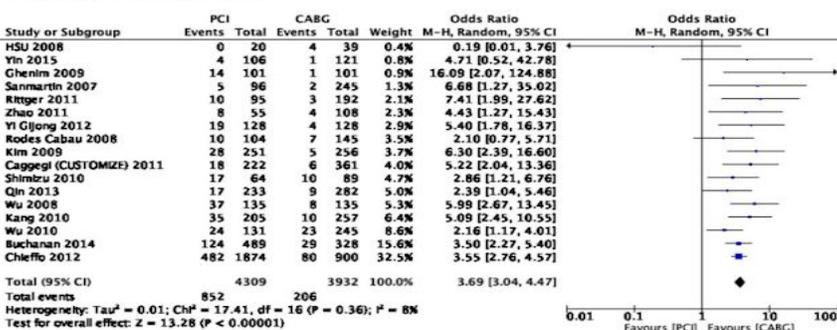
A. 1-year MAACE



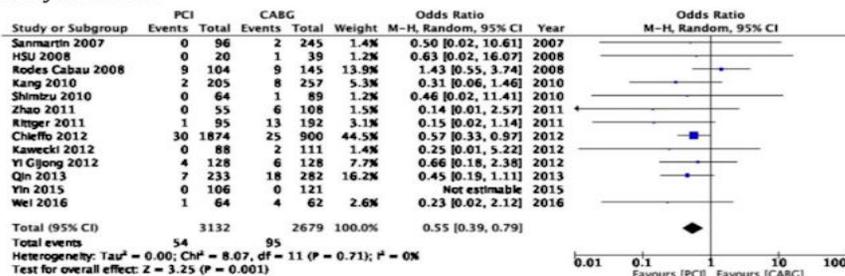
B. 1-year MI



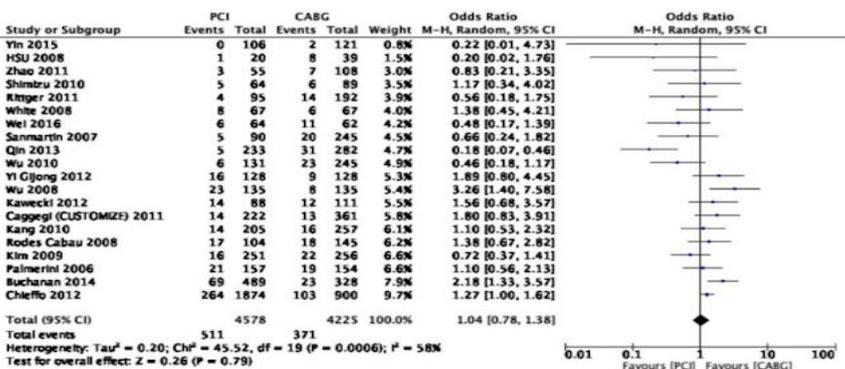
C. 1-year Revascularization



D. 1-year Stroke

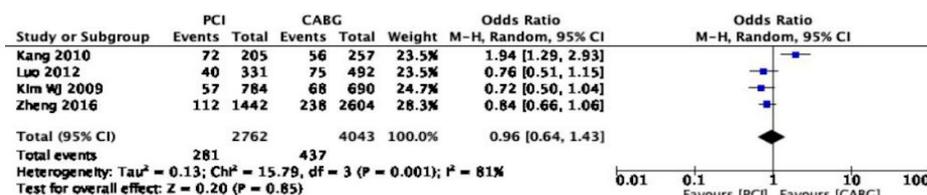


E. 1-year all-cause Mortality

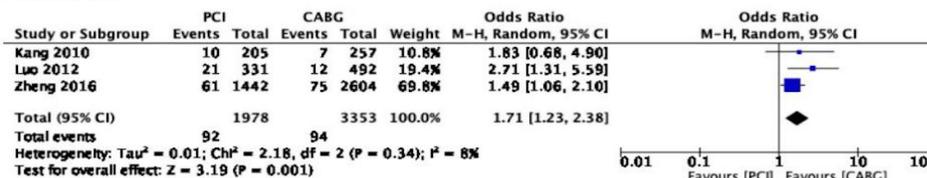


S. Figure 11: 1-year pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

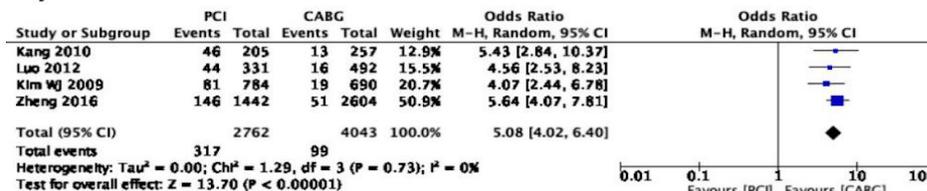
A. 3-year MAACE



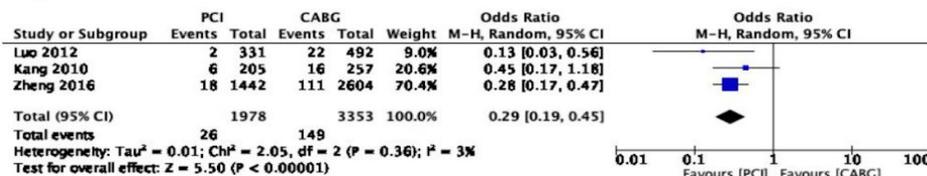
B. 3-year MI



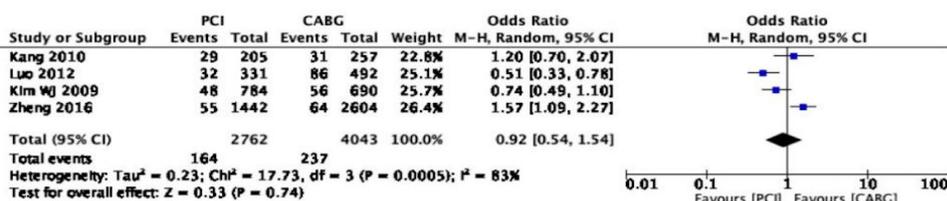
C. 3-year Revascularization



D. 3-year Stroke

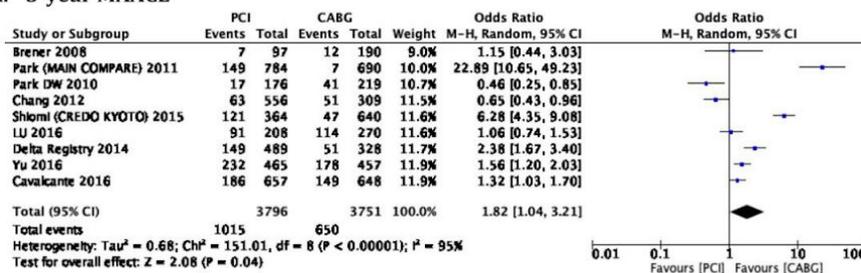


E. 3-year all-cause Mortality

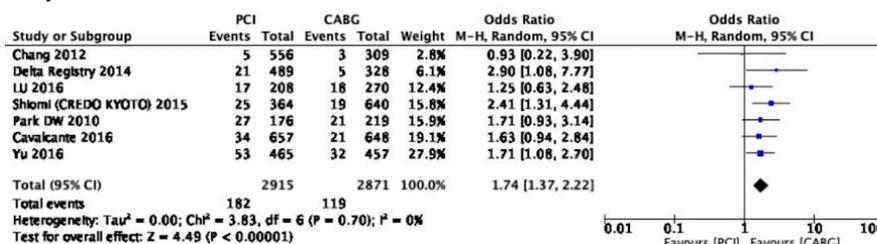


S. Figure 12: 3-year pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

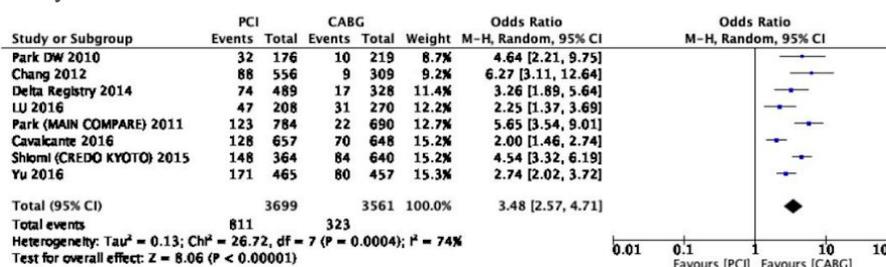
A. 5-year MAACE



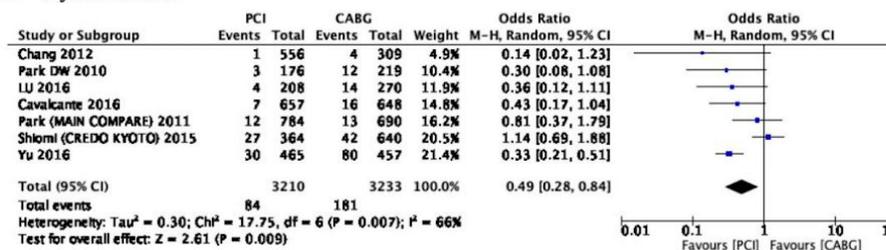
B. 5-year MI



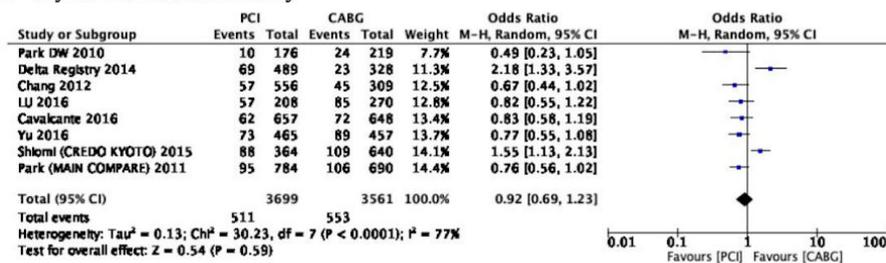
C. 5-year Revascularization



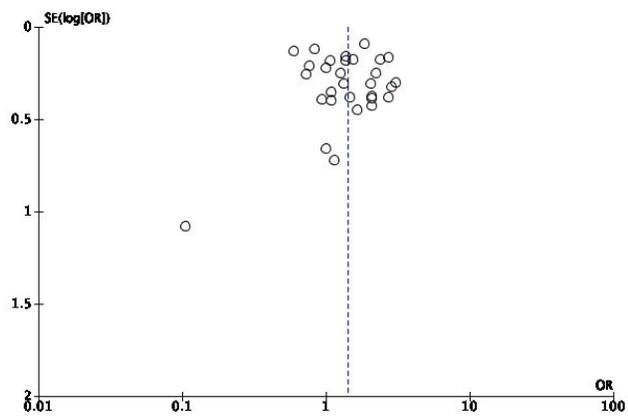
D. 5-year Stroke



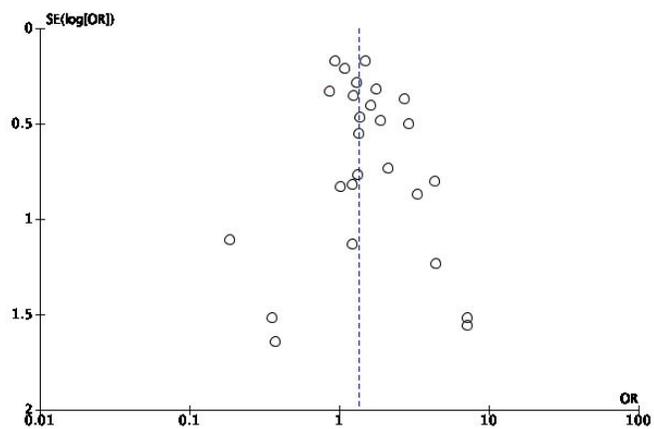
E. 5-year all-cause Mortality



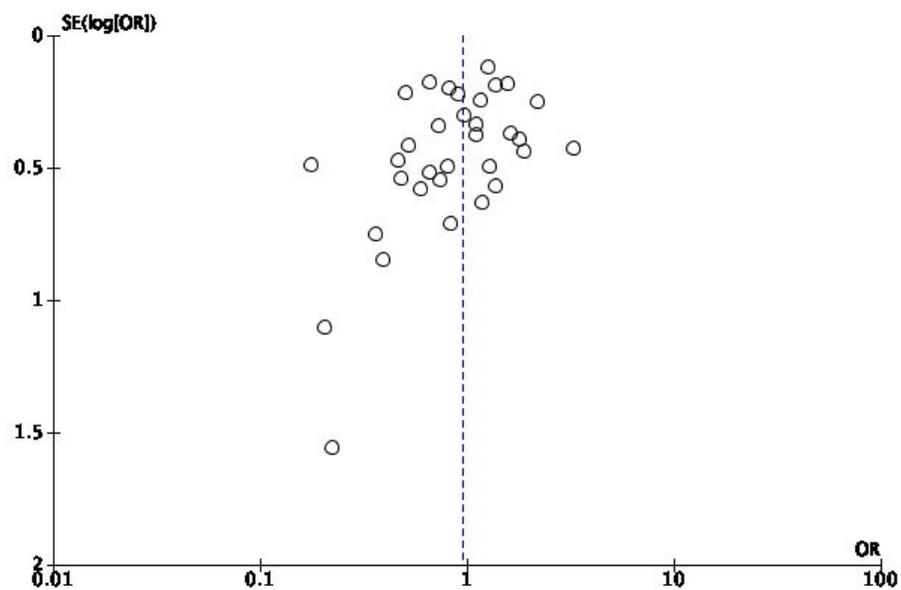
S. Figure 13: 5-year pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

E. SUPPLEMENTAL FUNNEL PLOTS FOR ALL STUDIES:

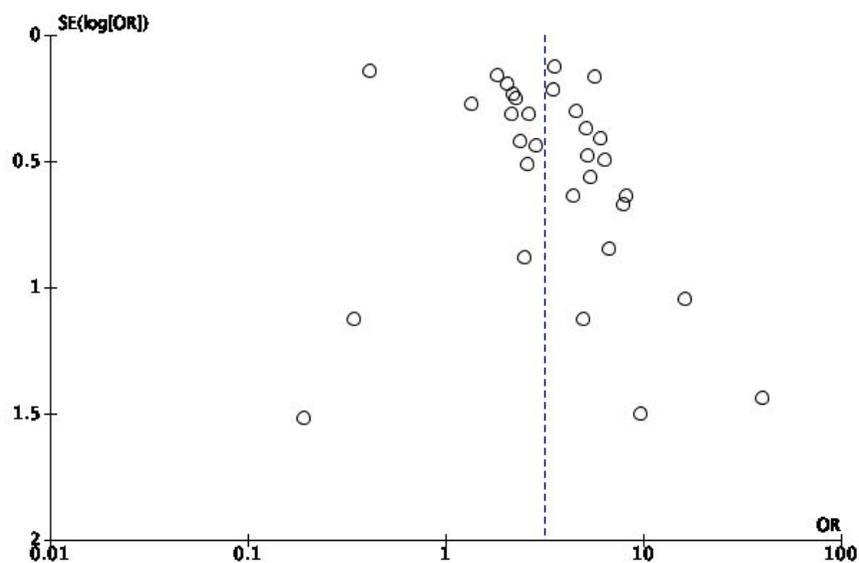
S. Figure 14: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MACCE at 1-year follow up.



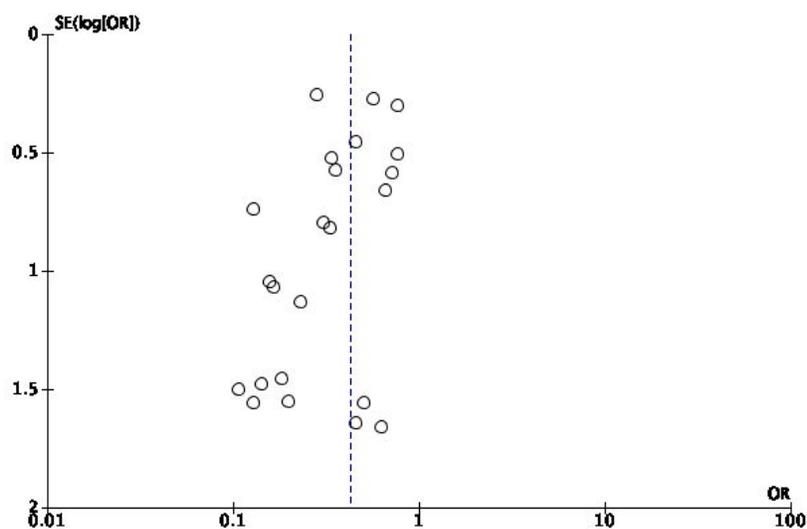
S. Figure 15: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MI at 1-year follow up.



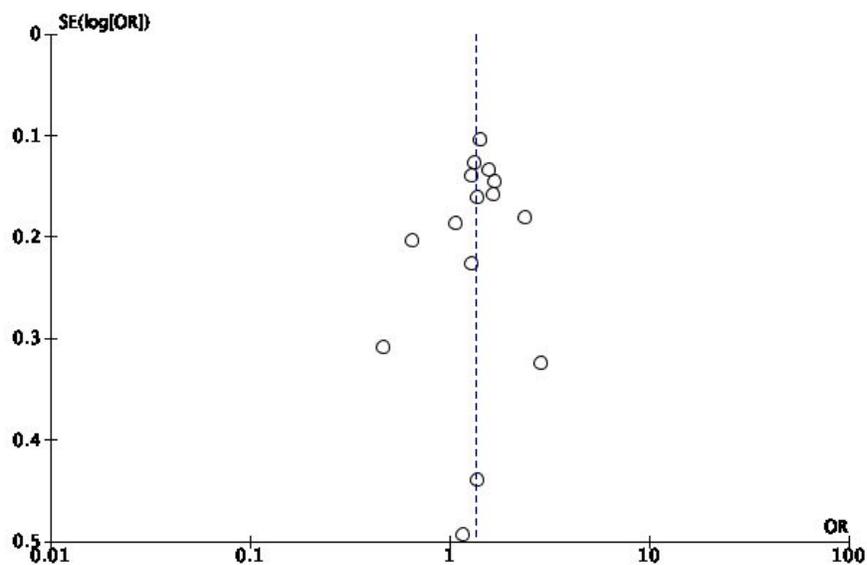
S. Figure 16: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of mortality at 1-year follow up.



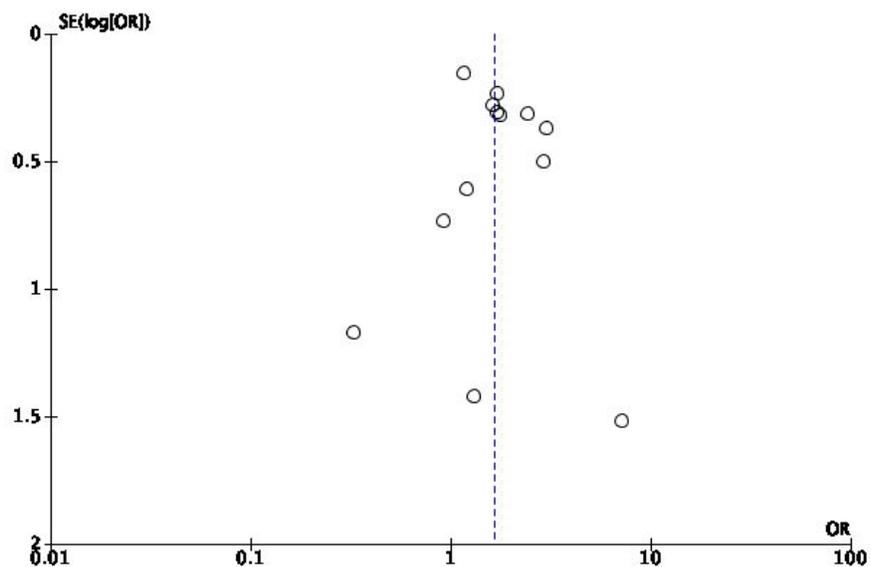
S. Figure 17: Funnel plot showing minimal to moderate publication bias across studies comparing the pooled estimate of revascularization at 1-year follow up.



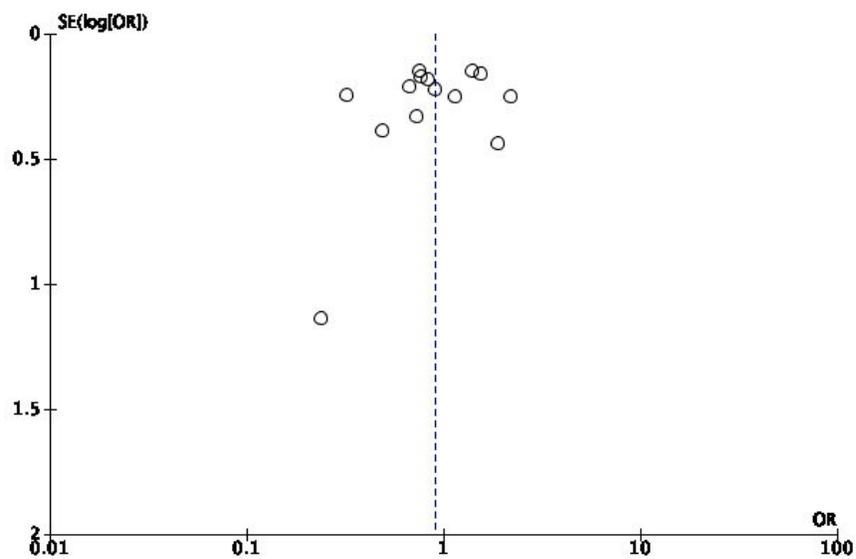
S. Figure 18: Funnel plot showing minimal to moderate publication bias across studies comparing the pooled estimate of a stroke at 1-year follow up.



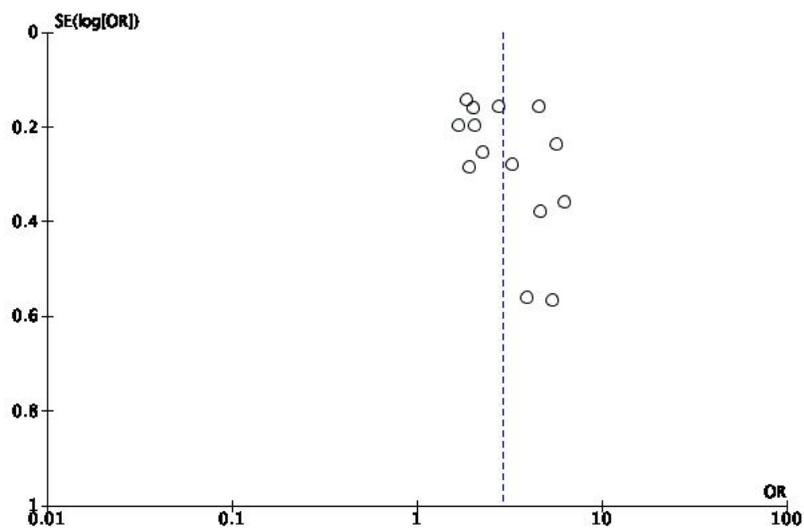
S. Figure 19: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MACCE at 5-year follow up.



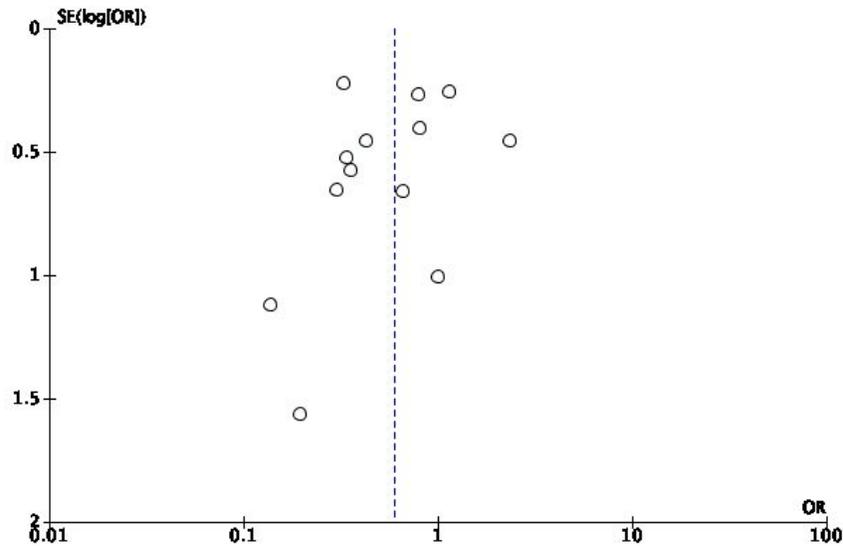
S. Figure 20: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MI at 5-year follow up.



S. Figure 21: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of mortality at a 5-year follow up.



S. Figure 22: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of revascularization at 5-year follow up.



S. Figure 23: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of a stroke at 5-year follow up.

E. REFERENCES:

1. Ahn JM, Roh JH, Kim YH, Park DW, Yun SC, Lee PH, Chang M, Park HW, Lee SW, Lee CW, Park SW, Choo SJ, Chung C, Lee J, Lim DS, Rha SW, Lee SG, Gwon HC, Kim HS, Chae IH, Jang Y, Jeong MH, Tahk SJ, Seung KB, Park SJ. Randomized trial of stents versus bypass surgery for left main coronary artery disease: 5-year outcomes of the PRECOMBAT study. *J Am Coll Cardiol* 2015;65:2198–2206.
2. Boudriot E, Thiele H, Walther T, Liebetrau C, Boeckstegers P, Pohl T, Reichart B, Mudra H, Beier F, Gansera B, Neumann FJ. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. *Journal of the American College of Cardiology*. 2011 Feb 1;57(5):538-45.
3. Buszman PE, Buszman PP, Banasiewicz-Szkróbka I, et al. Left main stenting in comparison with surgical revascularization: 10-year outcomes of the (Left Main Coronary Artery Stenting) LE MANS trial. *JACC: Cardiovascular Interventions*. 2016 Feb 22;9(4):318-27.
4. Holm NR, Mäkikallio T, Lindsay MM, Spence MS, Erglis A, Menown IB, Trovik T, Kellerth T, Kalinauskas G, Mogensen LJ, Nielsen PH. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. *The Lancet*. 2020 Jan 18;395(10219):191-9.
5. Makikallio T, Holm NR, Lindsay M et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis (NOBLE): a prospective,

- randomised, open-label, non-inferiority trial. *Lancet* 2016;388:2743-2752.
6. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Ståhle E, Colombo A, Mack MJ, Holmes DR, Choi JW, Ruzyllo W, Religa G. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. *Circulation*. 2014 Jun 10;129(23):2388-94.
 7. Park SJ, Kim YH, Park DW, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. *N Eng J Med*. 2011 May 5;364(18):1718-27.
 8. Stone GW, Kappetein AP, Sabik JF, et al. Five-year outcomes after PCI or CABG for left main coronary disease. *New England Journal of Medicine*. 2019 Nov 7;381(19):1820-30
 9. Stone GW, Sabik JF, Serruys PW, et al. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. *N Eng J Med* 2016;375:2223-35.
 10. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, Ståhle E, Feldman TE, Van Den Brand M, Bass EJ, Van Dyck N. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *New England Journal of Medicine*. 2009 Mar 5;360(10):961-72.
 11. Thuijs DJ, Kappetein AP, Serruys PW, Mohr FW, Morice MC, Mack MJ, Holmes Jr DR, Curzen N, Davierwala P, Noack T, Milojevic M. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *The Lancet*. 2019 Oct 12;394(10206):1325-34.
 12. Brener SJ, Galla JM, Bryant III R, Sabik III JF, Ellis SG. Comparison of percutaneous versus surgical revascularization of severe unprotected left main coronary stenosis in matched patients. *The American journal of cardiology*. 2008 Jan 15;101(2):169-72.
 13. Buchanan GL, Chieffo A, Meliga E, Mehran R, Park SJ, Onuma Y, Capranzano P, Valgimigli M, Narbutė I, Makkar RR, Palacios IF, Kim YH, Buszman PP, Chakravarty T, Sheiban I, Naber C, Margey R, Agnihotri A, Marra S, Capodanno D, Allgar V, Leon MB, Moses JW, Fajadet J, Lefevre T, Morice MC, Erglis A, Tamburino C, Alfieri O, Serruys PW, Colombo A. Comparison of percutaneous coronary intervention (with drug-eluting stents) versus coronary artery bypass grafting in women with severe narrowing of the left main coronary artery (from the Women-Drug-Eluting stent for Left main coronary Artery disease Registry). *Am J Cardiol* 2014;113:1348-1355
 14. Caggegi A, Capodanno D, Capranzano P, Chisari A, Ministeri M, Mangiameli A, Ronsivalle G, Ricca G, Barrano G, Monaco S, Di Salvo ME. Comparison of one-year outcomes of percutaneous coronary intervention versus coronary artery bypass grafting in patients with unprotected left main coronary artery disease and acute coronary syndromes (from the CUSTOMIZE Registry). *The American journal of cardiology*. 2011 Aug 1;108(3):355-9.
 15. Cavalcante R, Sotomi Y, Lee CW, et al. Outcomes after percutaneous coronary intervention or bypass surgery in patients with unprotected left main disease. *J Am Coll Cardiol* 2016;68:999-1009.
 16. Chang K, Koh YS, Jeong SH, et al. Long-term outcomes of percutaneous coronary intervention versus coronary artery bypass grafting for unprotected left main coronary bifurcation disease in the drug-eluting stent era. *Heart* 2012;98:799-805.
 17. Cheng CI, Lee FY, Chang JP, et al. Long-term outcomes of intervention for unprotected left main coronary artery stenosis: coronary stenting vs coronary artery bypass grafting. *Circ J* 2009;73:705-12.
 18. Chieffo A, Meliga E, Latib A, et al. Drug-eluting stent for left main coronary artery disease. The DELTA registry: a multicenter registry evaluating percutaneous coronary intervention versus coronary artery bypass grafting for left main treatment. *JACC Cardiovasc Interv* 2012;5:718-27.
 19. Ghenim R, Roncalli J, Tidjane AM, et al. One-year follow-up of nonrandomized comparison between coronary artery bypass grafting surgery and drug-eluting stent for the treatment of unprotected left main coronary artery disease in elderly patients (aged > or=75 years). *J Interv Cardiol*

- 2009;22:520–6
20. Kang SH, Park KH, Choi DJ, et al. Coronary artery bypass grafting versus drug-eluting stent implantation for left main coronary artery disease (from a two-center registry). *Am J Cardiol* 2010;105:343–51.
 21. Kawecki D, Morawiec B, Fudal M, et al. Comparison of coronary artery bypass grafting with percutaneous coronary intervention for unprotected left main coronary artery disease. *Yonsei Med J* 2012;53:58–67.
 22. Kim WJ, Park DW, Yun SC, Lee JY, Lee SW, Kim YH, Lee CW, Park SW, Park SJ. Impact of diabetes mellitus on the treatment effect of percutaneous or surgical revascularization for patients with unprotected left main coronary artery disease: a subgroup analysis of the MAIN-COMPARE study. *JACC: Cardiovascular Interventions*. 2009 Oct 1;2(10):956–63.
 23. Lee MS, Jamal F, Kedia G et al (2007) Comparison of bypass surgery with drug-eluting stents for diabetic patients with multivessel disease. *Int J Cardiol* 123:34–42
 24. Lu TM, Lee WL, Hsu PF, et al. Long-term results of stenting versus coronary artery bypass surgery for left main coronary artery disease—a single-center experience. *J Chin Med Assoc* 2016;79:356–62.
 25. Luo Y, Yu X, Chen F, Du X, He J, Gao Y, Zhang X, Zhang Y, Ren X, Lv S, Ma C. Impact of diabetes mellitus on patients with unprotected left main coronary artery lesion disease treated with either percutaneous coronary intervention or coronary-artery bypass grafting. *Coronary artery disease*. 2012 Aug 1;23(5):322–9.
 26. Mäkikallio TH, Niemelä M, Kervinen K, et al. Coronary angioplasty in drug eluting stent era for the treatment of unprotected left main stenosis compared to coronary artery bypass grafting. *Ann Med* 2008;40: 437–43.
 27. Montalescot G, Brieger D, Eagle KA, Anderson Jr FA, FitzGerald G, Lee MS, Steg PG, Avezum A, Goodman SG, Gore JM, GRACE Investigators. Unprotected left main revascularization in patients with acute coronary syndromes. *European heart journal*. 2009 Aug 30;30(19):2308–17.
 28. Naganuma T, Chieffo A, Meliga E, et al. Long-term clinical outcomes after percutaneous coronary intervention versus coronary artery bypass grafting for ostial/midshaft lesions in unprotected left main coronary artery from the DELTA registry: a multicenter registry evaluating percutaneous coronary intervention versus coronary artery bypass grafting for left main treatment. *JACC Cardiovasc Interv* 2014;7: 354–61.
 29. Palmerini T, Marzocchi A, Marrozzini C. Comparison between coronary angioplasty and coronary artery bypass surgery for the treatment of unprotected left main coronary artery stenosis (the Bologna Registry). *Am J Cardiol* 2006;98:54–9.
 30. Park DW, Kim YH, Yun SC, et al. Long-term outcomes after stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: 10-year results of bare-metal stents and 5-year results of drug-eluting stents from the ASAN-MAIN (ASAN Medical Center-Left MAIN Revascularization) Registry. *J Am Coll Cardiol* 2010;56:1366–75
 31. Park DW, Seung KB, Kim YH, Lee JY, Kim WJ, Kang SJ, Lee SW, Lee CW, Park SW, Yun SC, Gwon HC. Long-term safety and efficacy of stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: 5-year results from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry. *Journal of the American College of Cardiology*. 2010 Jul 6;56(2):117–24.
 32. Park SJ, Kim YH, Park DW, Yun SC, Ahn JM, Song HG, Lee JY, Kim WJ, Kang SJ, Lee SW, Lee CW. Randomized trial of stents versus bypass surgery for left main coronary artery disease. *New England Journal of Medicine*. 2011 May 5;364(18):1718–27.
 33. Qin Q, Qian J, Wu X, et al. A comparison between coronary artery bypass grafting surgery and percutaneous coronary intervention for the treatment of unprotected left main coronary artery

- disease. *Clin Cardiol* 2013;36:54–60.
34. Rittger H, Rieber J, Kögler K, Sinha A, Schmidt M, Breithardt OA, et al. Clinical outcome and quality of life after interventional treatment of left main disease with drug-eluting-stents in comparison to CABG in elderly and younger patients. *Clin Res Cardiol* 2011; 100: 439–446.
 35. Rodés-Cabau J, Deblois J, Bertrand OF, Mohammadi S, Courtis J, Larose E, Dagenais F, Déry JP, Mathieu P, Rousseau M, Barbeau G, Baillot R, Gleeton O, Perron J, Nguyen CM, Roy L, Doyle D, De Larochellière R, Bogaty P, Voisine P. Nonrandomized comparison of coronary artery bypass surgery and percutaneous coronary intervention for the treatment of unprotected left main coronary artery disease in octogenarians. *Circulation* 2008;118:2374e2381.
 36. Sanmartin M, Baz JA, Claro R, et al. Comparison of drug-eluting stents versus surgery for unprotected left main coronary artery disease. *Am J Cardiol* 2007;100:970–3.
 37. Shimizu T, Ohno T, Ando J, et al. Mid-term results and costs of coronary artery bypass vs drug-eluting stents for unprotected left main coronary artery disease. *Circ J* 2010;74:449–55.
 38. Shiomi H, Morimoto T, Furukawa Y, et al. Comparison of percutaneous coronar intervention with coronary artery bypass grafting in unprotected left main coronary artery disease—5-year outcome from CREDO-Kyoto PCI/CABG Registry Cohort-2. *Circ J* 2015;79:1282–9.
 39. Te Hsu J, Chu CM, Chang ST, Kao CL, Chung CM. Percutaneous coronary intervention versus coronary artery bypass graft surgery for the treatment of unprotected left main coronary artery stenosis. *International heart journal*. 2008;49(3):355-70.
 40. Wei Z, Xie J, Wang K, et al. Comparison of percutaneous coronary intervention versus coronary artery bypass graft in aged patients with unprotected left main artery lesions. *Int Heart J* 2016;57:682–8.
 41. White AJ, Kedia G, Mirocha JM, Lee MS, Forrester JS, Morales WC, Dohad S, Kar S, Czer LS, Fontana GP, Trento A. Comparison of coronary artery bypass surgery and percutaneous drug-eluting stent implantation for treatment of left main coronary artery stenosis. *JACC: Cardiovascular Interventions*. 2008 Jun 1;1(3):236-45.
 42. Wu C, Hannan EL, Walford G, et al. Utilization and outcomes of unprotected left main coronary artery stenting and coronary artery bypass graft surgery. *Ann Thorac Surg* 2008;86:1153–9.
 43. Wu X, Chen Y, Kubo T, et al. Long-term (4-year) outcomes and predictors of adverse cardiac events after sirolimus-eluting stent implantation in unprotected left main coronary artery. *Int Heart J* 2010;51:377–82.
 44. Yi G, Youn YN, Hong S, et al. Midterm outcome of off-pump bypass procedures versus drug-eluting stent for unprotected left main coronary artery disease. *Ann Thorac Surg* 2012;94:15–22.
 45. Yin Y, Xin X, Geng T, et al. Clinical comparison of percutaneous coronary intervention with domestic drug-eluting stents versus off pump coronary artery bypass grafting in unprotected left main coronary artery disease. *Int J Clin Exp Med* 2015;8:14376–82.
 46. Yu XP, Wu CY, Ren XJ, et al. Very long-term outcomes and predictors of percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting for patients with unprotected left main coronary artery disease. *Chin Med J (Engl)* 2016;129:763–70.
 47. Zhao X, Zhou Y, Song H, Guan L, Zheng G, Jin Z, Shi D, Li Y, Guo Y, Shi GP, Cheng XW. Comparison of bypass surgery with drug-eluting stents in diabetic patients with left main coronary stenosis. *Yonsei medical journal*. 2011 Nov 1;52(6):923-32.
 48. Zheng Z, Xu B, Zhang H, et al. Coronary artery bypass graft surgery and percutaneous coronary interventions in patients with unprotected left main coronary artery disease. *JACC Cardiovasc Interv* 2016;9:1102–11.
 49. De Rosa S, Polimeni A, Sabatino J, Indolfi C. Long-term outcomes of coronary artery bypass grafting versus stent-PCI for unprotected left main disease: a meta-analysis. *BMC cardiovascular disorders*. 2017 Dec;17(1):240.

50. Kodumuri V, Balasubramanian S, Vij A, Siddamsetti S, Sethi A, Khalafallah R, Khosla S. A meta-analysis comparing percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in unprotected left main disease. *The American journal of cardiology*. 2018 Apr 15;121(8):924-33.
51. Bittl JA, He Y, Jacobs AK, Yancy CW, Normand SL. Bayesian methods affirm the use of percutaneous coronary intervention to improve survival in patients with unprotected left main coronary artery disease. *Circulation*. 2013 Jun 4;127(22):2177-85.
52. Bajaj NS, Patel N, Kalra R, Marogil P, Bhardwaj A, Arora G, Arora P. Percutaneous coronary intervention vs. coronary artery bypass grafting for left main revascularization: an updated meta-analysis. *European Heart Journal-Quality of Care and Clinical Outcomes*. 2017 Jul 1;3(3):173-82.
53. Upadhaya S, Baniya R, Madala S, Subedi SK, Khan J, Velagapudi RK, Bachuwa G. Drug-eluting stent placement versus coronary artery bypass surgery for unprotected left main coronary artery disease: A meta-analysis of randomized controlled trials. *Journal of cardiac surgery*. 2017 Feb;32(2):70-9
54. Khan SU, Rahman H, Arshad A, Khan MU, Lekkala M, Yang T, Mishra A, Kaluski E. Percutaneous Coronary Intervention Versus Surgery in Left Main Stenosis—A Meta-Analysis and Systematic Review of Randomised Controlled Trials. *Heart, Lung and Circulation*. 2018 Feb 1;27(2):138-46.
55. Zhang XL, Zhu QQ, Yang JJ, Chen YH, Li Y, Zhu SH, Xie J, Wang L, Kang LN, Xu B. Percutaneous intervention versus coronary artery bypass graft surgery in left main coronary artery stenosis: a systematic review and meta-analysis. *BMC medicine*. 2017 Dec;15(1):84.
56. Kajimoto K, Miyauchi K, Yamamoto T, Daida H, Amano A. Meta-analysis of Randomized Controlled Trials on the Treatment of Unprotected Left Main Coronary Artery Disease: One-Year Outcomes with Coronary Artery Bypass Grafting Versus Percutaneous Coronary Artery Intervention with Drug-Eluting Stent. *Journal of cardiac surgery*. 2012 Mar;27(2):152-7.
57. Jang JS, Choi KN, Jin HY, Seo JS, Yang TH, Kim DK, Kim DS, Urm SH, Chun JH, Kang SJ, Park DW. Meta-analysis of three randomized trials and nine observational studies comparing drug-eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery disease. *The American journal of cardiology*. 2012 Nov 15;110(10):1411-8.
58. Tamburino C, Capodanno D, Di Salvo ME, Caggegi A, Tomasello D, Cincotta G, Miano M, Petralia A, Varone E, Patanè M, Tamburino C. Routine versus selective coronary artery bypass for left main coronary artery revascularization: The appraise a customized strategy for left main revascularization (CUSTOMIZE) study. *International journal of cardiology*. 2011 Aug 4;150(3):307-14.
59. Alam M, Huang HD, Shahzad SA, Kar B, Virani SS, Rogers PA, Paniagua D, Bozkurt B, Palacios I, Kleiman NS, Jneid H. Percutaneous coronary intervention vs. coronary artery bypass graft surgery for unprotected left main coronary artery disease in the drug-eluting stents era. *Circulation journal*. 2012:CJ-12.
60. Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. *Journal of the American College of Cardiology*. 2011 Sep 27;58(14):1426-32.
61. Biondi-Zoccai GG, Lotrionte M, Moretti C, Meliga E, Agostoni P, Valgimigli M, Migliorini A, Antoniucci D, Carrié D, Sangiorgi G, Chieffo A. A collaborative systematic review and meta-analysis on 1278 patients undergoing percutaneous drug-eluting stenting for unprotected left main coronary artery disease. *American heart journal*. 2008 Feb 1;155(2):274-83.
62. Palmerini T, Serruys P, Kappetein AP, Genereux P, Della Riva D, Reggiani LB, Christiansen EH, Holm NR, Thuesen L, Makikallio T, Morice MC. Clinical outcomes with percutaneous coronary revascularization vs coronary artery bypass grafting surgery in patients with unprotected left main

- coronary artery disease: a meta-analysis of 6 randomized trials and 4,686 patients. *American heart journal*. 2017 Aug 1;190:54-63.
63. Ye Y, Yang M, Zhang fS, Zeng Y. Percutaneous coronary intervention versus cardiac bypass surgery for left main coronary artery disease: A trial sequential analysis. *Medicine*. 2017 Oct;96(41).
 64. Ali WE, Vaidya SR, Ejeh SU, Okoroafor KU. Meta-analysis study comparing percutaneous coronary intervention/drug eluting stent versus coronary artery bypass surgery of unprotected left main coronary artery disease: clinical outcomes during short-term versus long-term (> 1 year) follow-up. *Medicine*. 2018 Feb;97(7).
 65. Naik H, White AJ, Chakravarty T, Forrester J, Fontana G, Kar S, Shah PK, Weiss RE, Makkar R. A meta-analysis of 3,773 patients treated with percutaneous coronary intervention or surgery for unprotected left main coronary artery stenosis. *JACC: Cardiovascular Interventions*. 2009 Aug 1;2(8):739-47.
 66. Lee MS, Yang T, Dhoot J, Liao H. Meta-analysis of clinical studies comparing coronary artery bypass grafting with percutaneous coronary intervention and drug-eluting stents in patients with unprotected left main coronary artery narrowings. *The American journal of cardiology*. 2010 Apr 15;105(8):1070-5.
 67. Alam M, Virani SS, Shahzad SA, Siddiqui S, Siddiqui KH, Mumtaz SA, Kleiman NS, Coselli JS, Lakkis NM, Jneid H. Comparison by meta-analysis of percutaneous coronary intervention versus coronary artery bypass grafting in patients with a mean age of ≥ 70 years. *The American journal of cardiology*. 2013 Sep 1;112(5):615-22.
 68. Athappan G, Patvardhan E, Tuzcu ME, Ellis S, Whitlow P, Kapadia SR. Left main coronary artery stenosis: a meta-analysis of drug-eluting stents versus coronary artery bypass grafting. *JACC: Cardiovascular Interventions*. 2013 Dec 1;6(12):1219-30.
 69. Sá MP, Soares AM, Lustosa PC, Martins WN, Browne F, Ferraz PE, Vasconcelos FP, Lima RC. Meta-analysis of 5674 patients treated with percutaneous coronary intervention and drug-eluting stents or coronary artery bypass graft surgery for unprotected left main coronary artery stenosis. *European Journal of Cardio-Thoracic Surgery*. 2012 Apr 19;43(1):73-80.
 70. Al Ali J, Franck C, Filion KB, Eisenberg MJ. Coronary artery bypass graft surgery versus percutaneous coronary intervention with first-generation drug-eluting stents: a meta-analysis of randomized controlled trials. *JACC: Cardiovascular Interventions*. 2014 May 1;7(5):497-506.
 71. Lee CW, Ahn JM, Cavalcante R, Sotomi Y, Onuma Y, Suwannasom P, Tenekecioglu E, Yun SC, Park DW, Kang SJ, Lee SW. Coronary artery bypass surgery versus drug-eluting stent implantation for left main or multivessel coronary artery disease: a meta-analysis of individual patient data. *JACC: Cardiovascular Interventions*. 2016 Dec 19;9(24):2481-9.
 72. Khan MR, Kayani WT, Ahmad W, Hira RS, Virani SS, Hamzeh I, Jneid H, Lakkis N, Alam M. Meta-analysis of comparison of 5-year outcomes of percutaneous coronary intervention versus coronary artery bypass grafting in patients with unprotected left main coronary artery in the era of drug-eluting stents. *The American journal of cardiology*. 2017 Nov 1;120(9):1514-20.
 73. Testa L, Latib A, Bollati M, Montone RA, Colombo A, Crea F, Bedogni F. Unprotected left main revascularization: Percutaneous coronary intervention versus coronary artery bypass. An updated systematic review and meta-analysis of randomised controlled trials. *PloS one*. 2017 Jun 28;12(6):e0179060.
 74. Putzu A, Gallo M, Martino EA, Ferrari E, Pedrazzini G, Moccetti T, Cassina T. Coronary artery bypass graft surgery versus percutaneous coronary intervention with drug-eluting stents for left main coronary artery disease: a meta-analysis of randomized trials. *International journal of cardiology*. 2017 Aug 15;241:142-8.

75. Sharma SP, Dahal K, Khatra J, Rosenfeld A, Lee J. Percutaneous coronary intervention vs coronary artery bypass grafting for left main coronary artery disease? A systematic review and meta-analysis of randomized controlled trials. *Cardiovascular therapeutics*. 2017 Jun;35(3):e12260.
76. Spinthakis N, Farag M, Gorog DA, Prasad A, Mahmood H, Gue Y, Wellsted D, Nabhan A, Srinivasan M. Percutaneous coronary intervention with drug-eluting stent versus coronary artery bypass grafting: A meta-analysis of patients with left main coronary artery disease. *International journal of cardiology*. 2017 Dec 15;249:101-6.
77. Moore P, Burrage M, Garrahy P, Lim R, McCann A, Camuglia A. Drug-Eluting Stents Versus Coronary Artery Bypass Grafts for Left Main Coronary Disease: A Meta-Analysis and Review of Randomised Controlled Trials. *Heart, Lung and Circulation*. 2018 Dec 1;27(12):1437-45.
78. Garg A, Rao SV, Agrawal S, Theodoropoulos K, Mennuni M, Sharma A, Garg L, Ferrante G, Meelu OA, Sargsyan D, Reimers B. Meta-analysis of randomized controlled trials of percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease. *The American journal of cardiology*. 2017 Jun 15;119(12):1942-8.
79. Shah R, Morsy MS, Weiman DS, Vetrovec GW. Meta-analysis comparing coronary artery bypass grafting to drug-eluting stents and to medical therapy alone for left main coronary artery disease. *The American journal of cardiology*. 2017 Jul 1;120(1):63-8.
80. Mahmoud AN, Elgendy IY, Mentias A, Saad M, Ibrahim W, Mojadidi MK, Nairooz R, Eshtehardi P, David Anderson R, Samady H. Percutaneous coronary intervention or coronary artery bypass grafting for unprotected left main coronary artery disease. *Catheterization and Cardiovascular Interventions*. 2017 Oct 1;90(4):541-52.
81. Khan A. R., Golwala H., Tripathi A., et al. Meta-analysis of percutaneous coronary intervention versus coronary artery bypass grafting in left main coronary artery disease. *American Journal of Cardiology*. 2017;119(12):1949–1956. doi: 10.1016/j.amjcard.2017.03.022
82. Nerlekar N, Ha FJ, Verma KP, Bennett MR, Cameron JD, Meredith IT, Brown AJ. Percutaneous coronary intervention using drug-eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery stenosis: a meta-analysis of randomized trials. *Circulation: Cardiovascular Interventions*. 2016 Dec;9(12):e004729.
83. Giacoppo D, Colleran R, Cassese S, Frangieh AH, Wiebe J, Joner M, Schunkert H, Kastrati A, Byrne RA. Percutaneous coronary intervention vs coronary artery bypass grafting in patients with left main coronary artery stenosis: a systematic review and meta-analysis. *JAMA cardiology*. 2017 Oct 1;2(10):1079-88.
84. Palmerini T, Biondi-Zoccai G, Reggiani LB, Sangiorgi D, Alessi L, De Servi S, Branzi A, Stone GW. Risk of stroke with coronary artery bypass graft surgery compared with percutaneous coronary intervention. *Journal of the American College of Cardiology*. 2012 Aug 28;60(9):798-805.
85. Wang Z, Zhan B, Bao H, Huang X, Wu Y, Liang Q, Zhang W, Jiang L, Cheng X. Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Unprotected Left Main Coronary Artery Stenosis. *The American journal of the medical sciences*. 2019 Mar 1;357(3):230-41.
86. Ahmad Y, Howard JP, Arnold AD, et al. Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials *Eur Heart J*. 2020, doi: 10.1093/eurheartj/ehaa135

