

## 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  $\geq 3$  considered high quality)

Author/Study/Year/Ref	Rating Scale List	Response	Jadad Score
<b>Serruys (SYNTAX) 2009 [9]</b>	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	
<b>Makikallio (NOBLE) 2016 [10]</b>	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	
<b>Park (PRECOMBAT) 2011 [6]</b>	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	
<b>Stone (EXCEL) 2019 [1]</b>	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	
<b>Buszman (LE MANS) 2008 [22]</b>	Was the randomization described and appropriate	Yes	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	
<b>Boudriot et al. 2011 [9]</b>	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

Selection Bias					Outcome Bias				
Author/Study/Year	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	Total score
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
Makikikallio 2008	*	*	*	*	**	*	*	*	9
Makikikallio 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 extrac





**S. Table 3****Definition of outcomes used across the randomized controlled trials**

Outcome	Description
<b>Death</b>	<p>The cause of death was adjudicated as being due to cardiovascular or non-cardiovascular causes</p> <ul style="list-style-type: none"> <li>• Cardiovascular death includes sudden cardiac death, death due to acute MI, heart failure or cardiogenic shock, stroke, other cardiovascular causes, or bleeding</li> <li>• Non-cardiovascular death is defined as any death with known cause not of cardiac or vascular causes.</li> </ul>
<b>MI</b>	<p><b>Periprocedural MI:</b> Defined as the occurrence within 48-72 hours after either PCI or CABG</p> <p><b>SCAI Definition:</b></p> <ul style="list-style-type: none"> <li>• CK-MB &gt;10x upper reference limit (URL)*, OR</li> <li>• CK-MB &gt;5x URL*, PLUS</li> <li>- 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</li> </ul> <p><b>Non-procedural MI:</b> SCAI defined non-procedural MI as the occurrence &gt;72 hours after any PCI or CABG.</p> <p><b>SCAI Definition:</b></p> <ul style="list-style-type: none"> <li>• The rise and/or fall of cardiac biomarkers (CK-MB or troponin) &gt;1x URL*</li> </ul> <p>PLUS:</p> <ul style="list-style-type: none"> <li>- ECG changes indicative of new ischemia [ST-segment elevation or depression, or bundle branch block (BBB)], or</li> <li>- Development of pathological Q waves (<math>\geq 0.04</math> seconds in duration and <math>\geq 1</math> mm in depth) in <math>\geq 2</math> contiguous precordial leads or <math>\geq 2</math> adjacent limb leads) of the ECG, or</li> <li>- 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</li> </ul> <p><b>Third Universal Definition of MI:</b> Detection of a rise and/or fall of cardiac biomarker values, with at least one of the values being elevated (i.e., &gt; 99th percentile upper reference limit, URL). The preferred cardiac biomarker of necrosis is highly sensitive and specific cTn.</p>
<b>Stroke</b>	The rapid onset of a new persistent neurologic deficit attributed to an obstruction in cerebral blood flow
<b>Revascularization</b>	A coronary revascularization procedure may be either a CABG or a PCI.
<b>MACCE</b>	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 5

Definitions 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
Makikikallio 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 2008 [42]	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
Wu 2010 [43]	128-128	62-65	72-77	76 (56)-80 (63)	42 (33)-40 (31)	-	-	-	-	MS/D/B	5
Yi Gijong 2012 [44]	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
Yin 2015 [45]	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
Yu 2016 [46]	56-116	-	73-72	32 (57)-60 (52)	56 (100)-116 (100)	44.6-42.4	28 (50)-51 (44)	-	-	DB/total occlusion	2
Zhao 2011 [47]	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
Zheng 2016 [48]											

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-.138, 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)

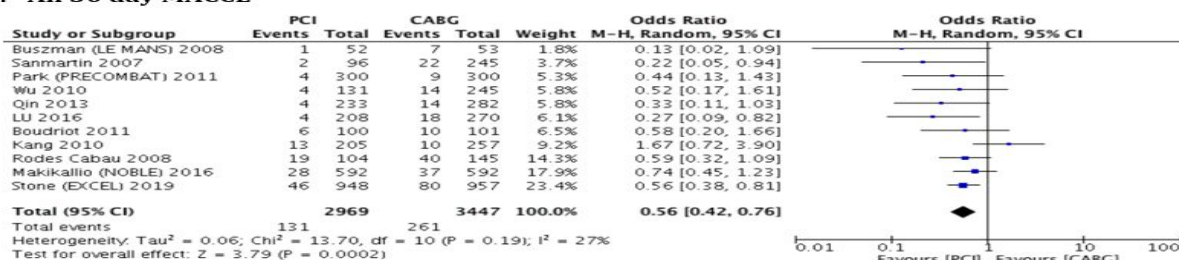


		points across trials, short median follow up (39 months)		
Wang 2019 [85]	19	No subgroup analyses, Variation in the definition of the primary end points,	5 years	1.89 (1.48-2.40)
Ahmad 2020 [86]	5	No comparison of MACCE	5 years	-----

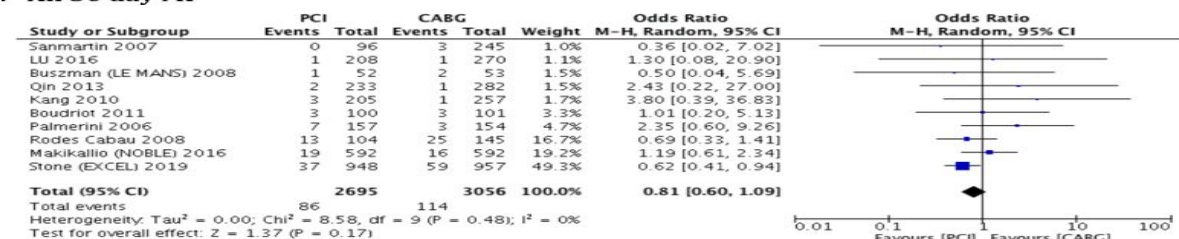
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**D. SUPPLEMENTAL FOREST PLOTS FOR ALL STUDIES:**

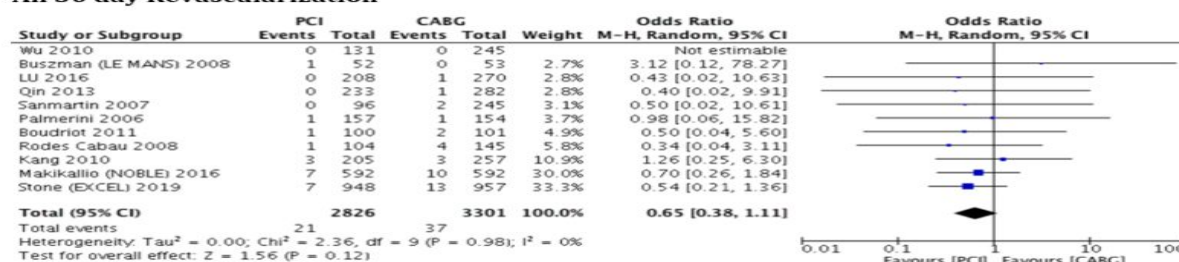
### A. All 30 day MACCE



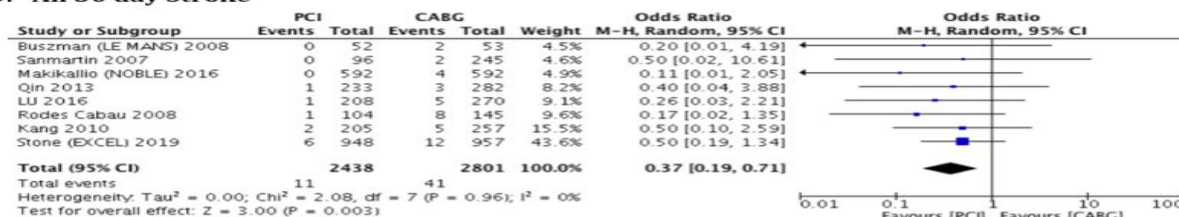
### B. All 30 day MI



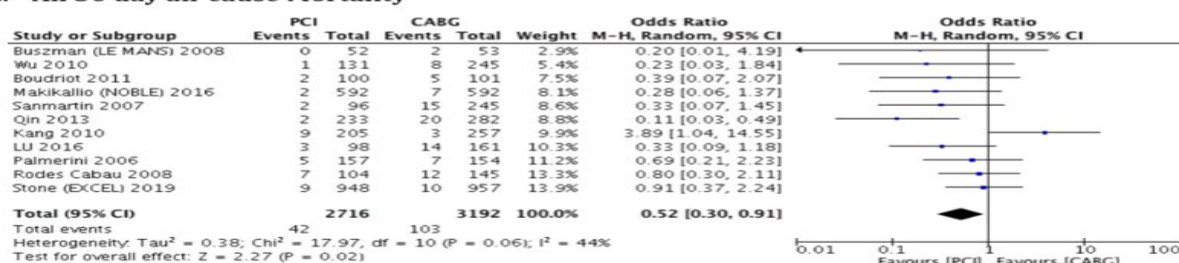
### C. All 30 day Revascularization



### D. All 30 day Stroke

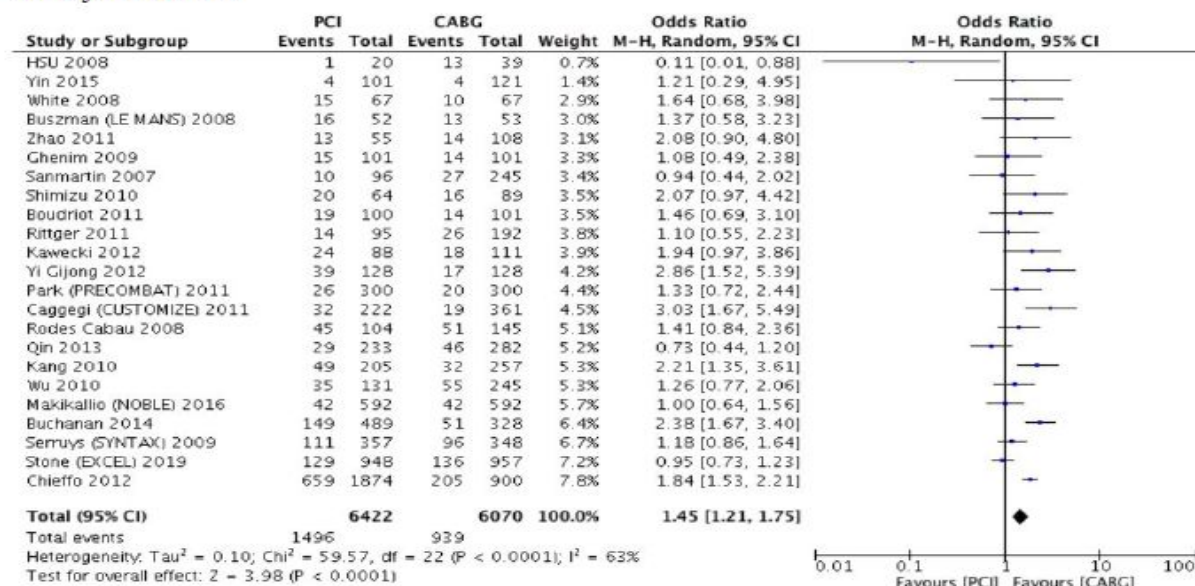


### E. All 30 day all-cause Mortality

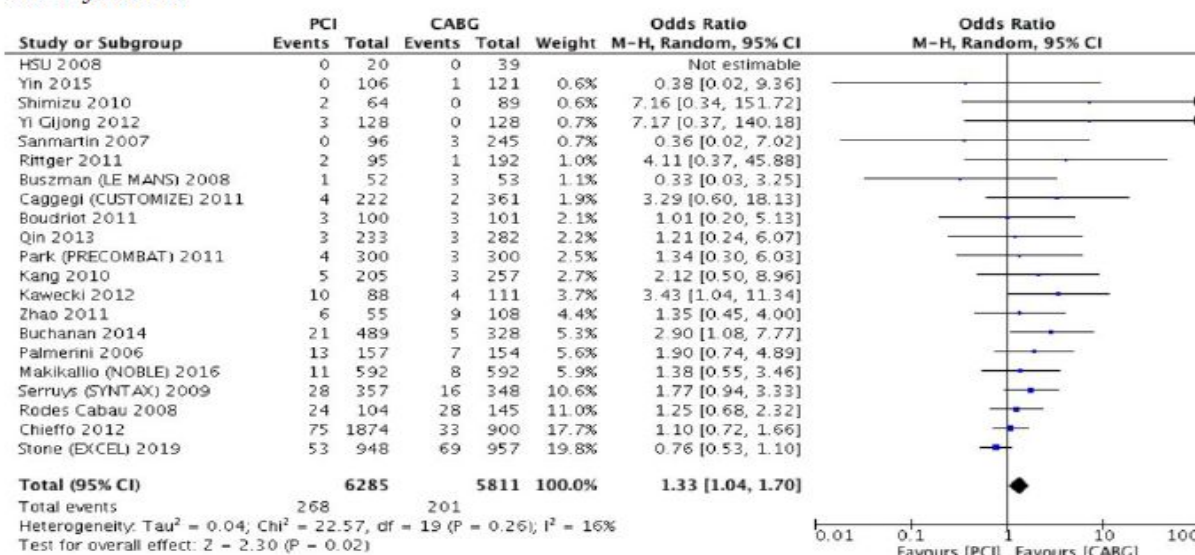


S. Figure 1: Forest Plots showing an individual and pooled OR for all-studies comparing PCI to CABG for LMCAD at 30-days (a. MACCE b. MI c. revascularization d. stroke e. death).

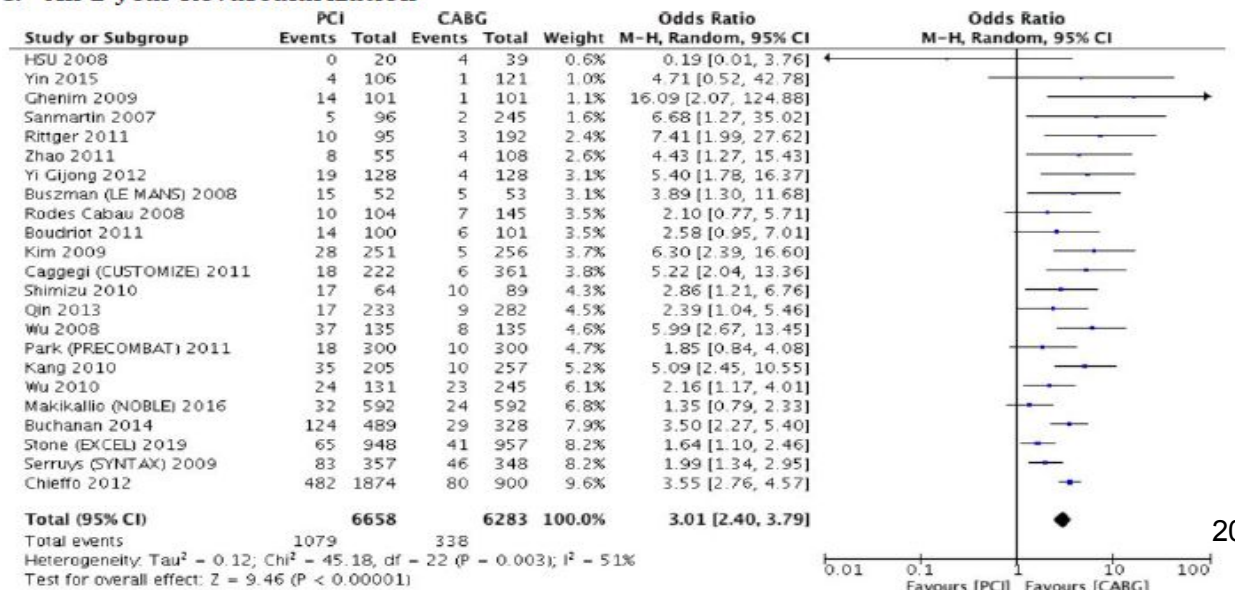
### A. All 1-year MACCE



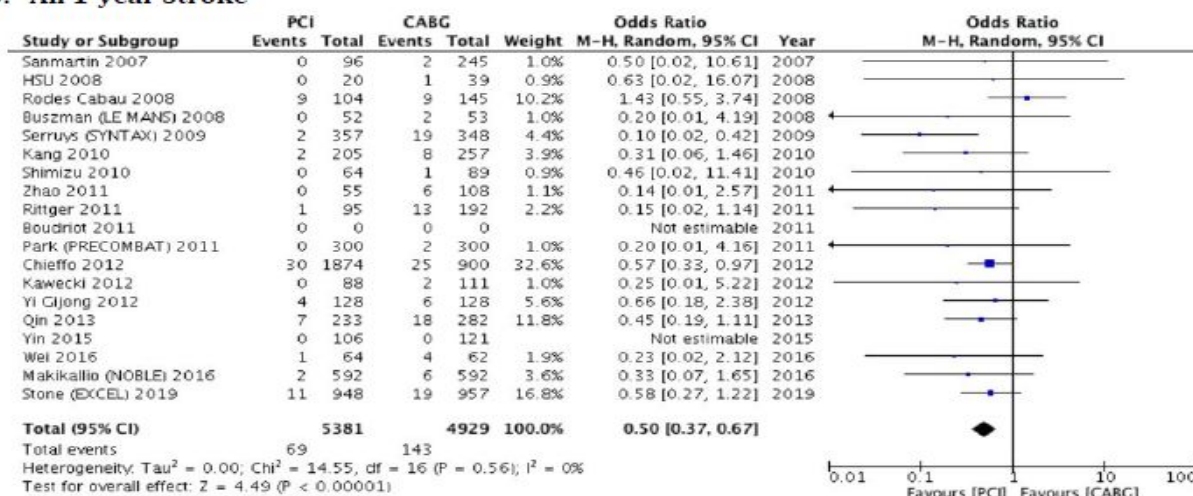
### B. All 1-year MI



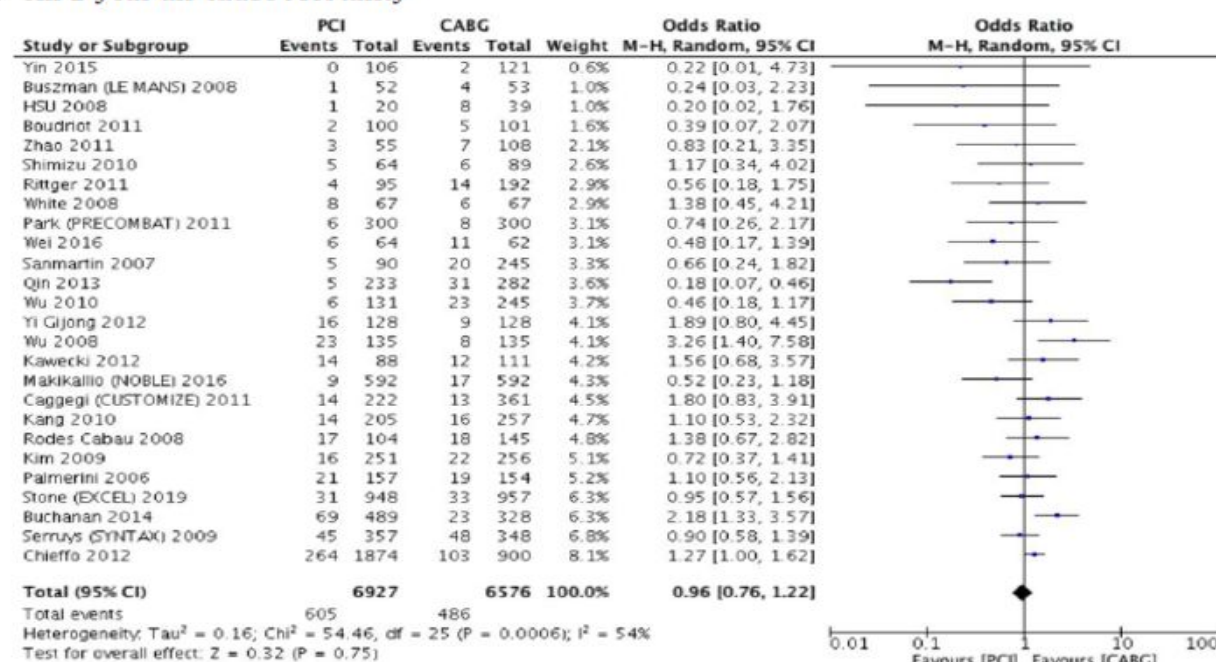
### C. All 1-year Revascularization



#### D. All 1-year Stroke



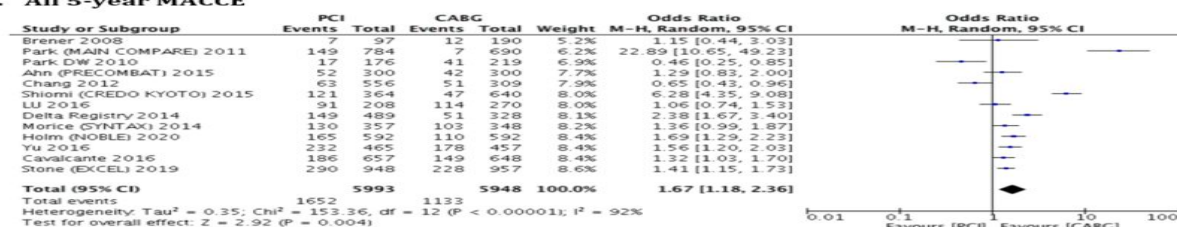
#### E. All 1-year all-cause Mortality



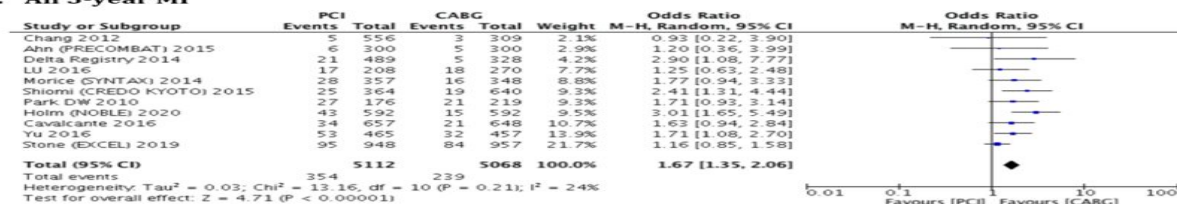
S. Figure 2: Forest Plots showing an individual and pooled OR for all-studies comparing PCI to CABG for LMCAD at 1-year (a. MACCE b. MI c. revascularization d. stroke e. death).



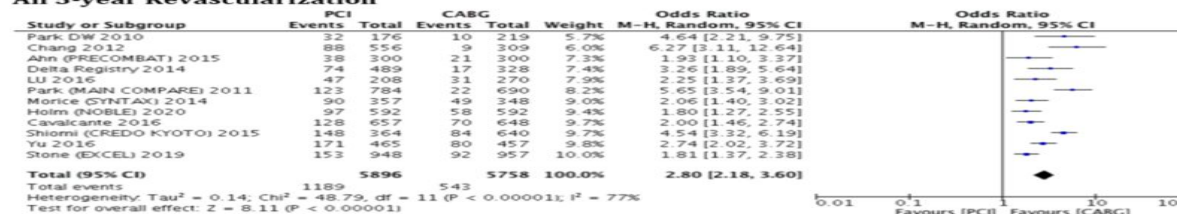
### A. All 5-year MACCE



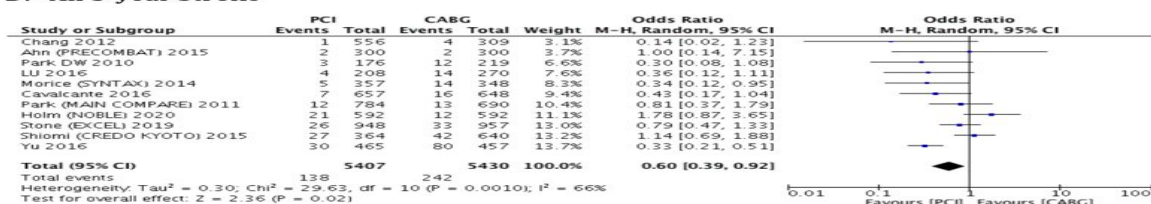
### B. All 5-year MI



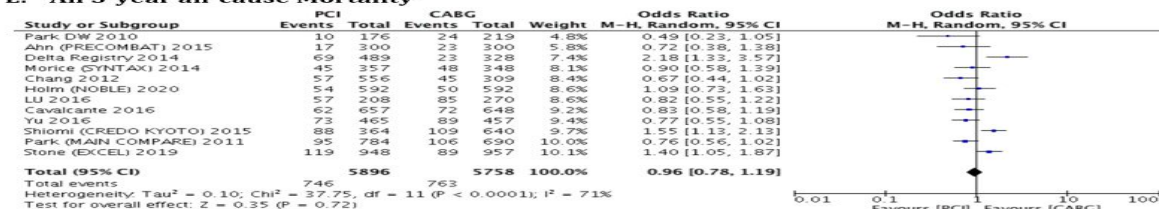
### C. All 5-year Revascularization



### D. All 5-year Stroke

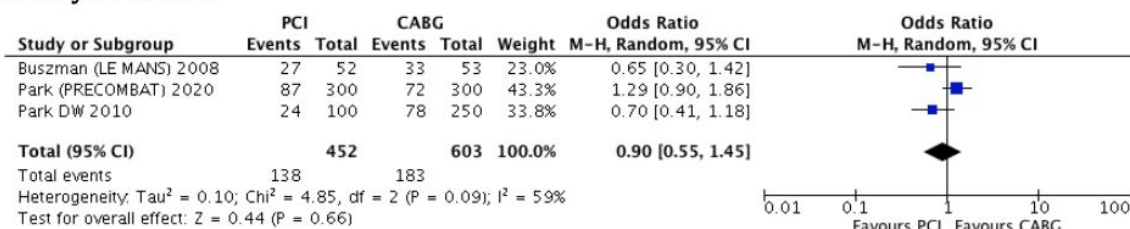


### E. All 5-year all-cause Mortality

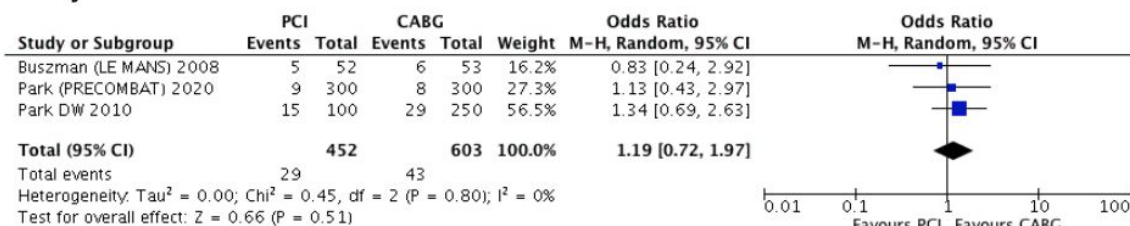


S. Figure 3: Forest Plots showing an individual and pooled OR for all-studies comparing PCI to CABG for LMCAD at 5-Year (a. MACCE b. MI c. revascularization d. stroke e. death)

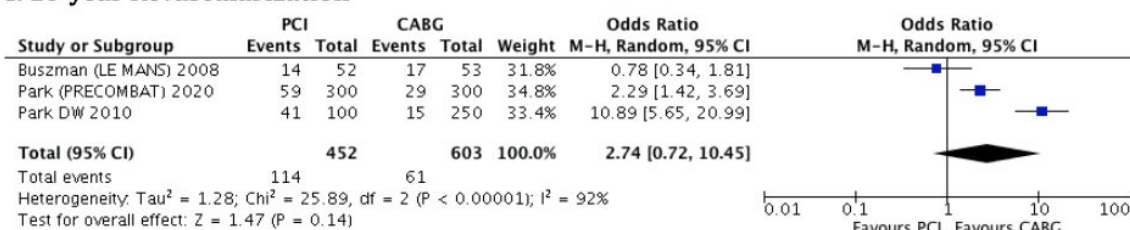
### A. 10-year MACCE



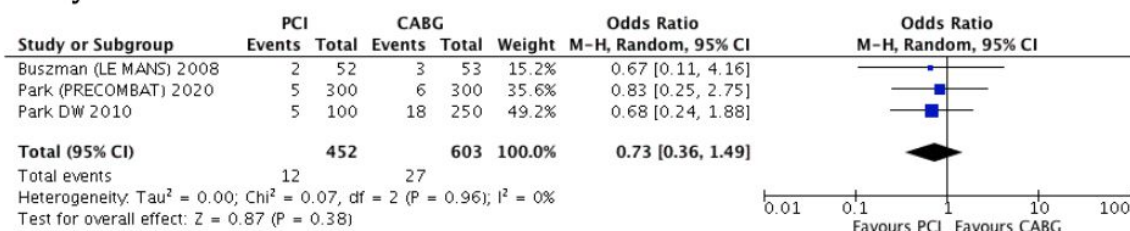
### B. 10-year MI



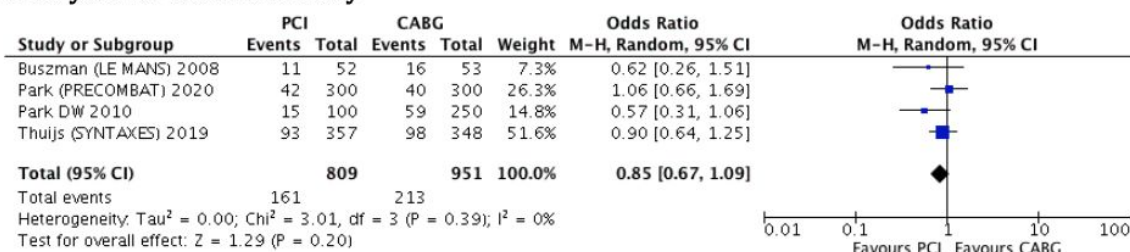
### C. 10-year Revascularization



### D. 10-year Stroke

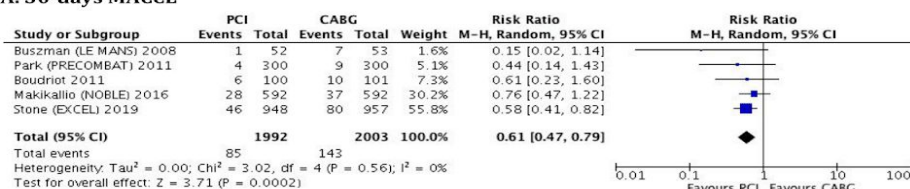


### E. 10-year all-cause Mortality

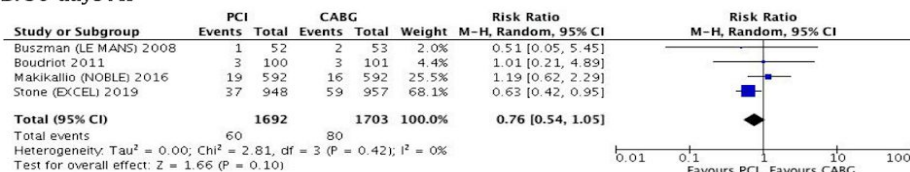


**S. Figure 4: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 10-year (a. MACCE b. MI c. revascularization d. stroke e. death).**

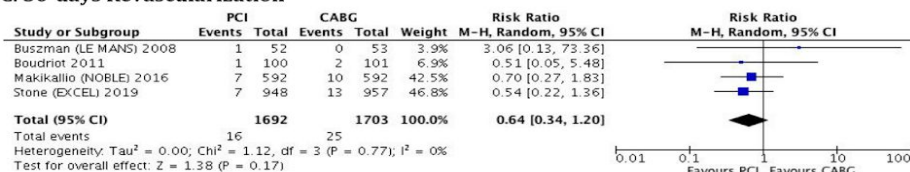
### A. 30-days MACCE



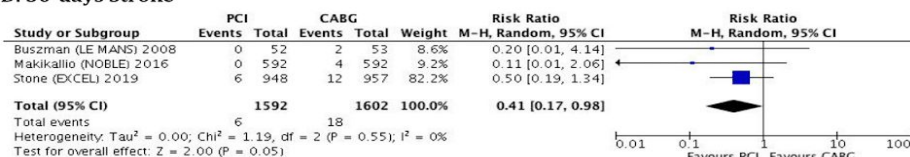
### B. 30-days MI



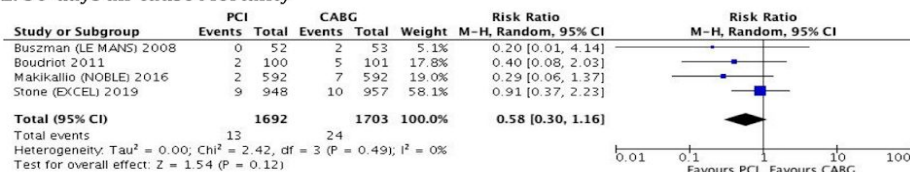
### C. 30-days Revascularization



### D. 30-days Stroke



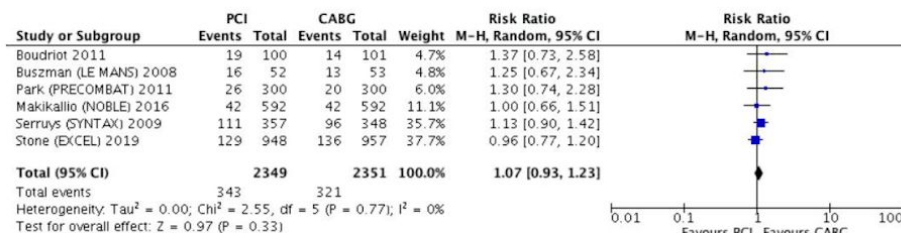
### E. 30-days all-cause Mortality



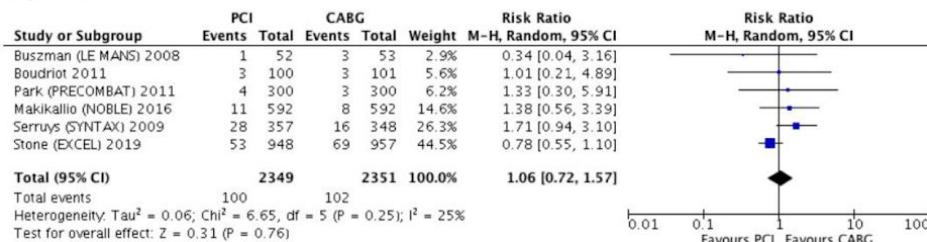


**S. Figure 5: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 30-days (a. MACCE b. MI c. revascularization d. stroke e. death).**

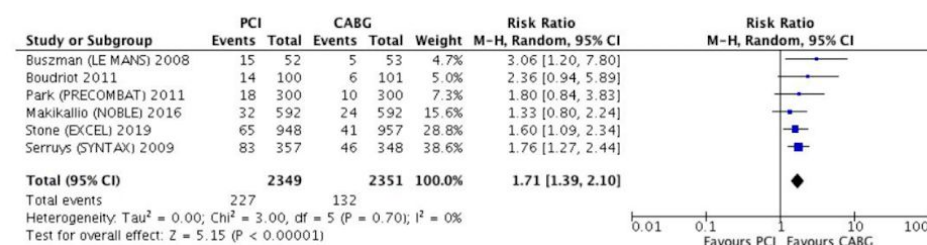
**A. 1-year MAACE**



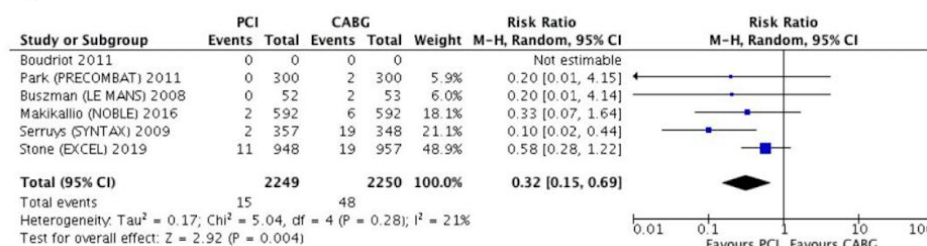
**B. 1-year MI**



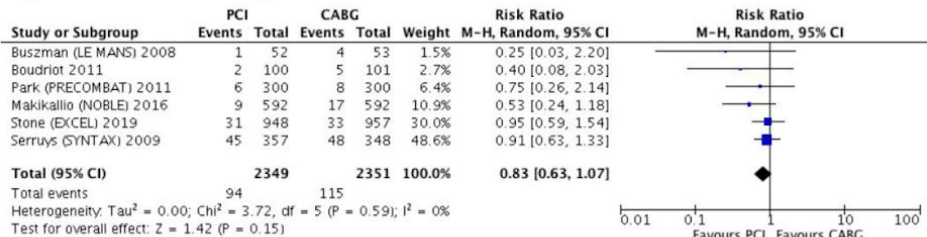
**C. 1-year Revascularization**



**D. 1-year Stroke**

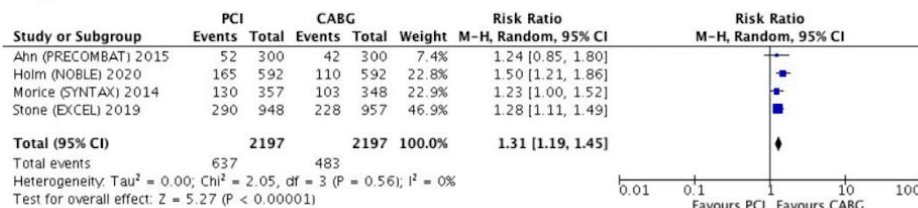


**E. 1-year all-cause Mortality**

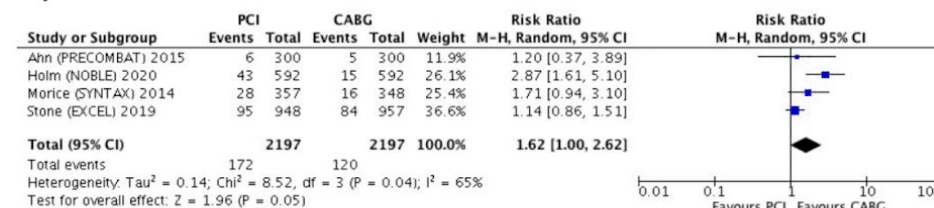


**S. Figure 6: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 1-year (a. MACCE b. MI c. revascularization d. stroke e. death).**

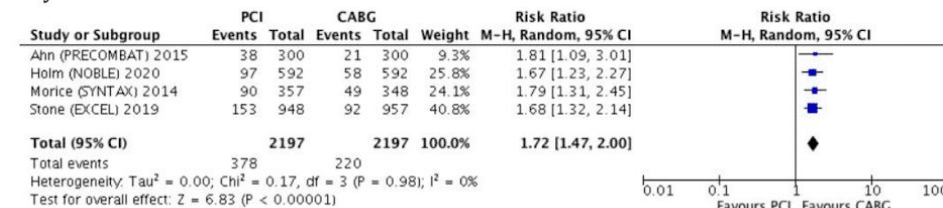
**A. 5-year MAACE**



**B. 5-year MI**



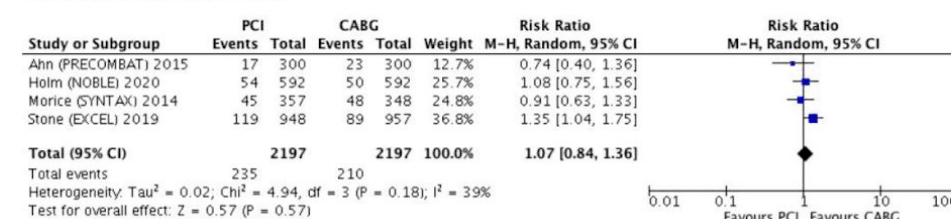
**C. 5-year Revascularization**



**D. 5-year Stroke**

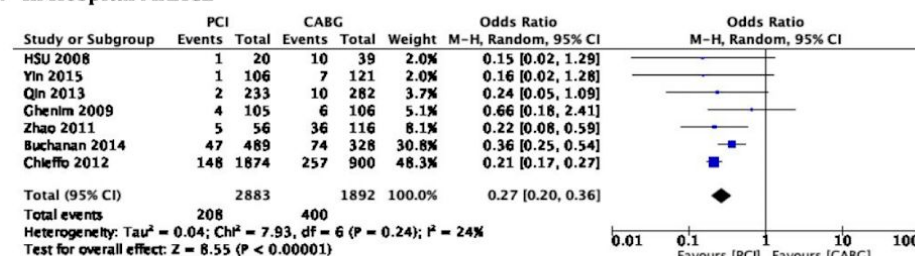


**E. 5-year all-cause Mortality**

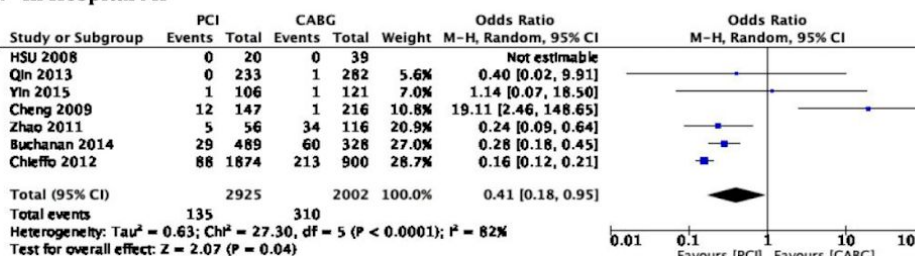


**S. Figure 7: Forest Plots showing an individual and pooled RR for RCTs comparing PCI to CABG for LMCAD at 5-year (a. MACCE b. MI c. revascularization d. stroke e. death).**

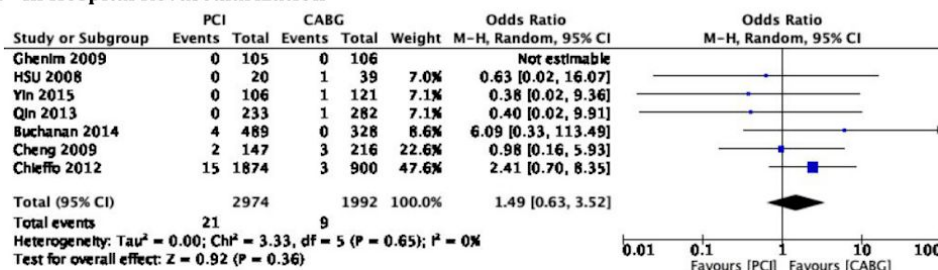
## A. In Hospital MAACE



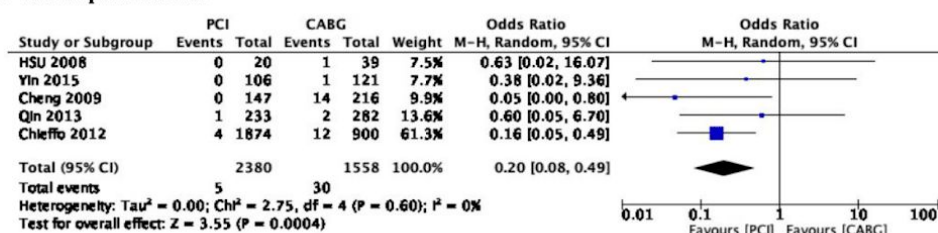
## B. In Hospital MI



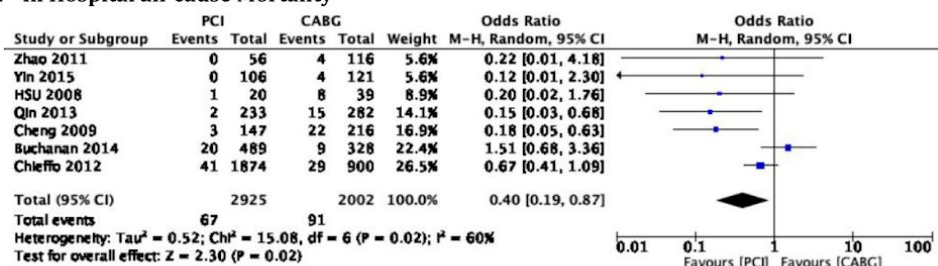
## C. In Hospital Revascularization



## D. In Hospital Stroke

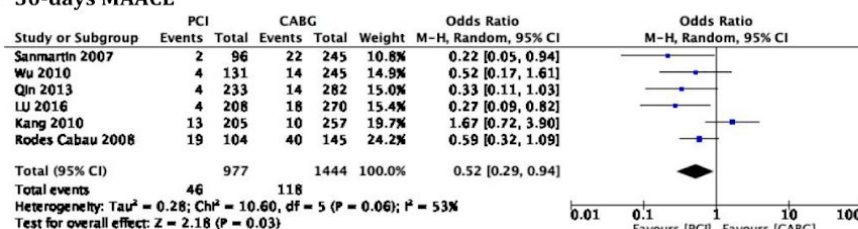


## E. In Hospital all-cause Mortality

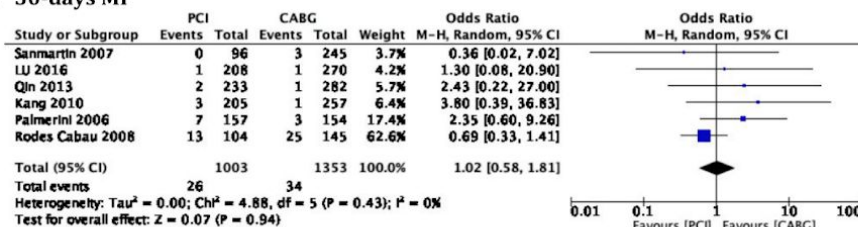


S. Figure 8: In-hospital pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

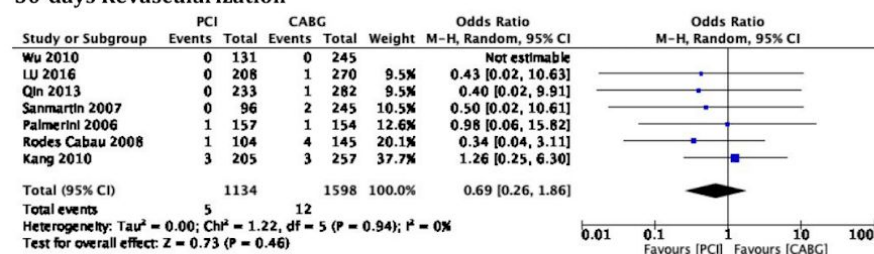
## A. 30-days MAACE



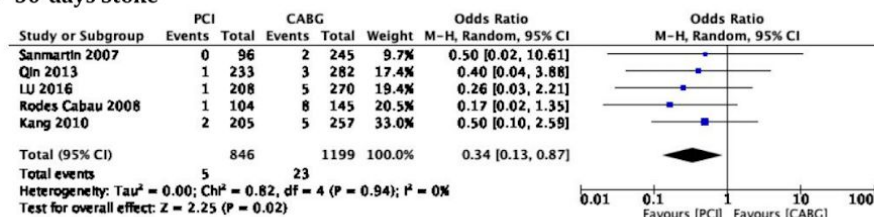
## B. 30-days MI



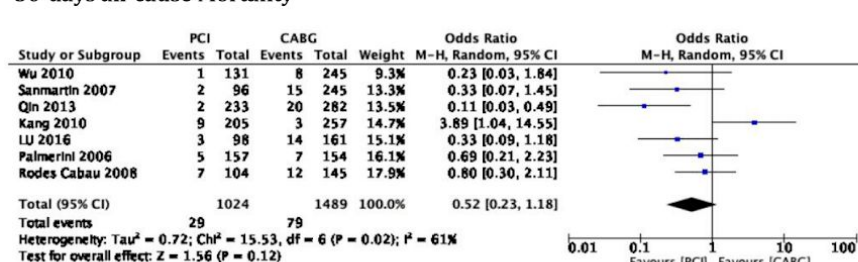
## C. 30-days Revascularization



## D. 30-days Stoke



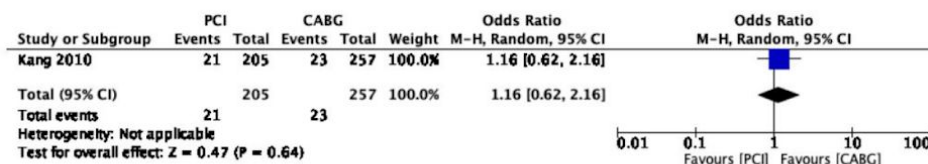
## E. 30-days all-cause Mortality



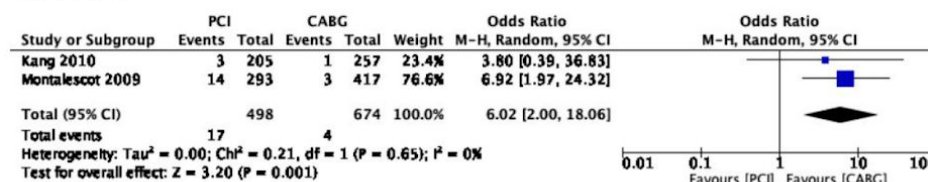
S. Figure 9: 30-days pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.



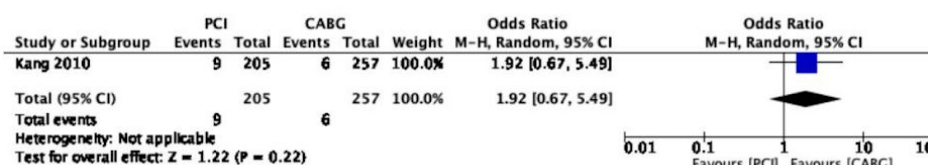
## A. 6-month MAACE



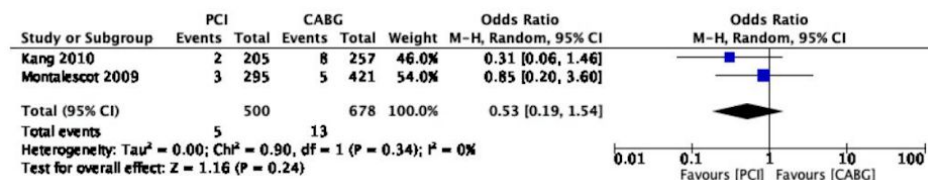
## B. 6-month MI



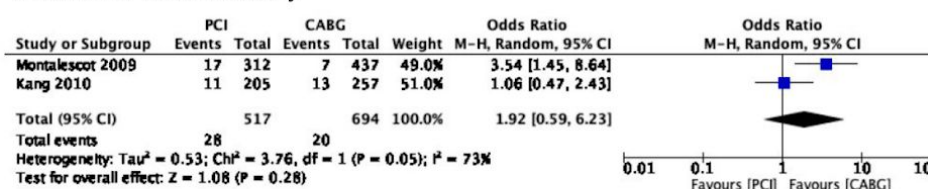
## C. 6-month Revascularization



## D. 6-month Stroke

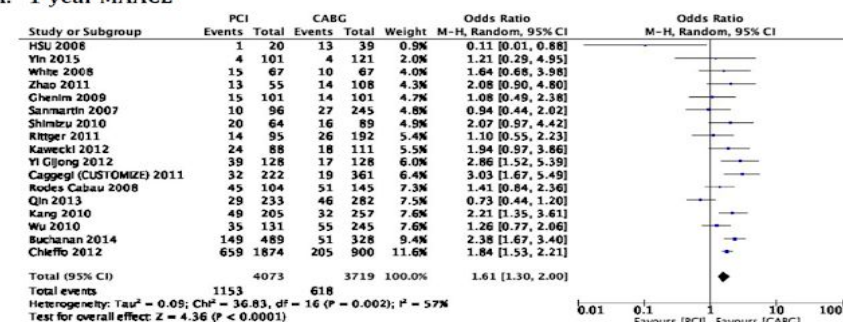


## E. 6-month all-cause Mortality

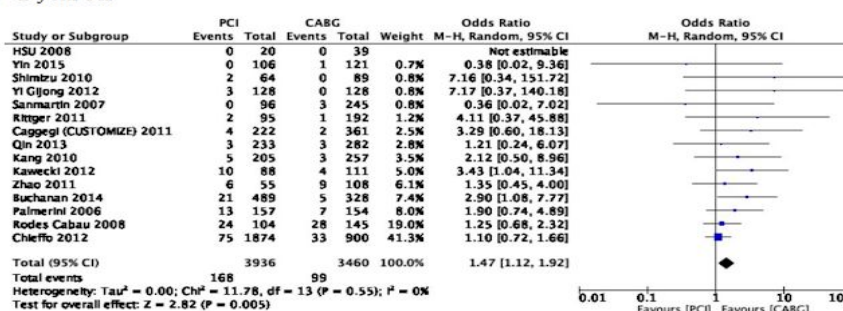


S. Figure 10: 6-months pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

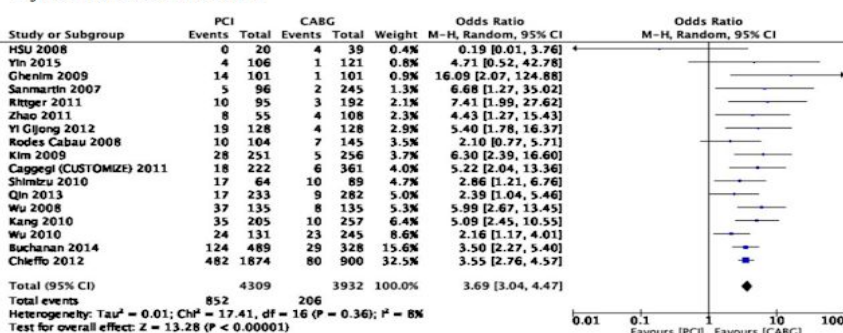
## A. 1-year MAACE



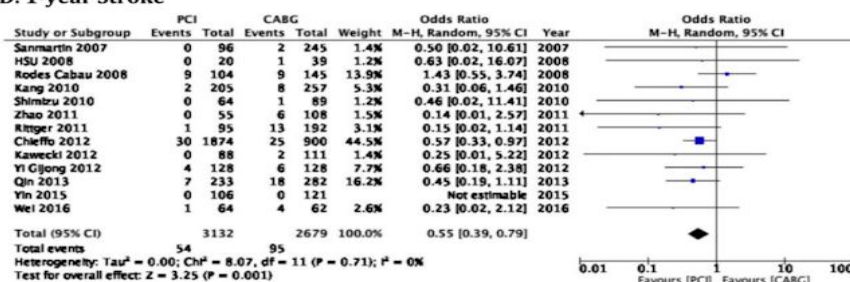
## B. 1-year MI



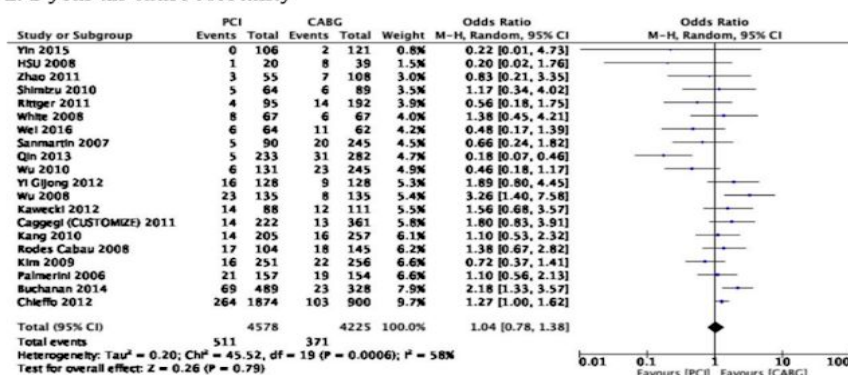
## C. 1-year Revascularization



## D. 1-year Stroke

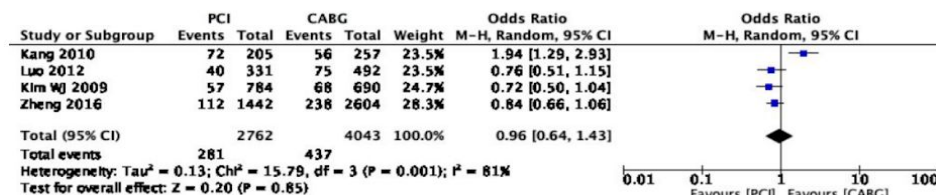


## E. 1-year all-cause Mortality

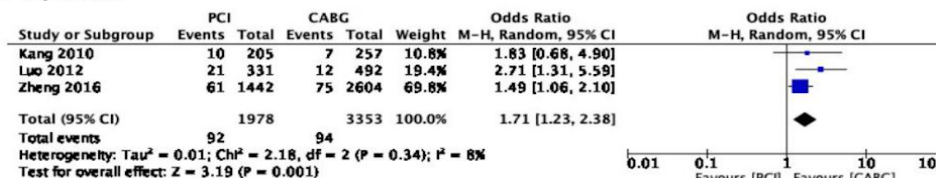


S. Figure 11: 1-year pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

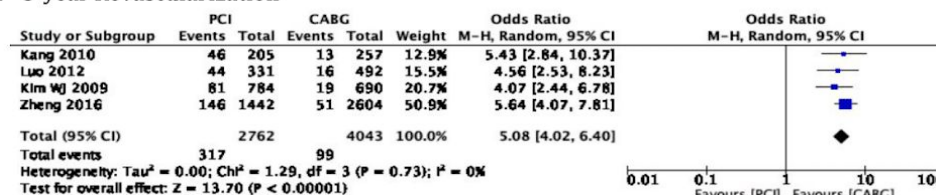
A. 3-year MAACE



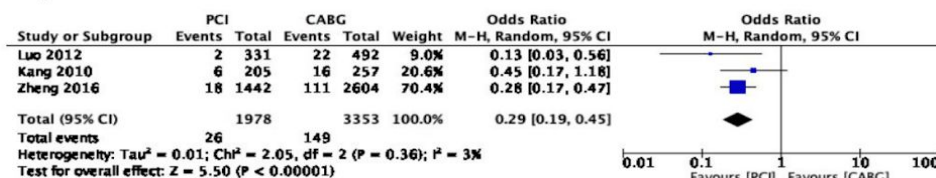
B. 3-year MI



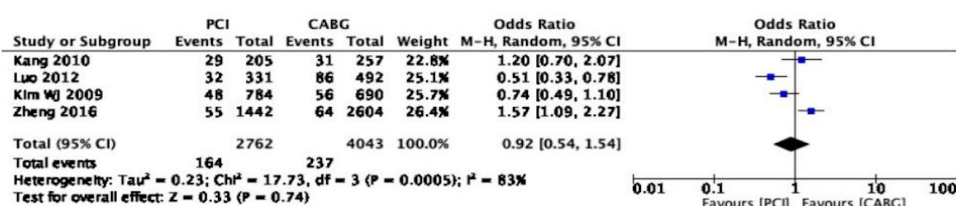
C. 3-year Revascularization



D. 3-year Stroke



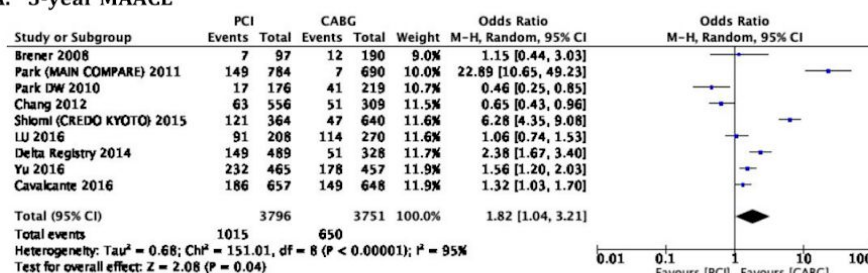
E. 3-year all-cause Mortality



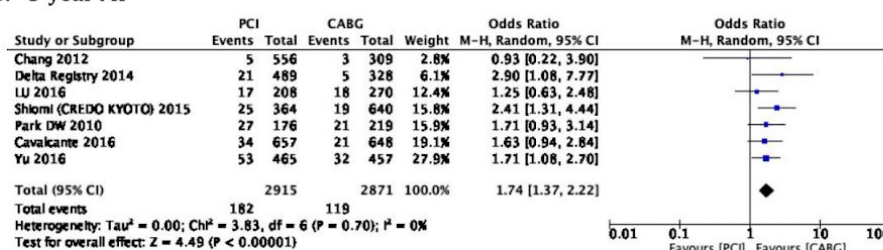
S. Figure 12: 3-year pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.



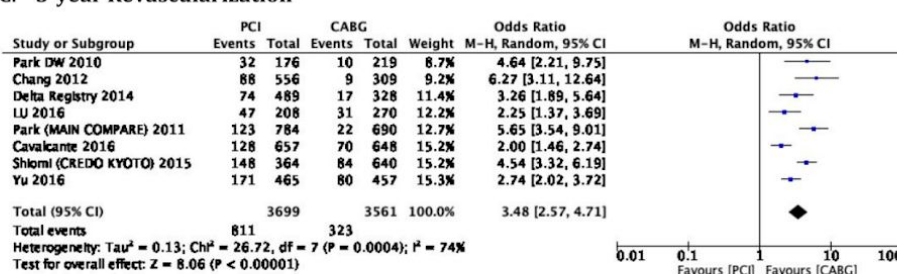
## A. 5-year MAACE



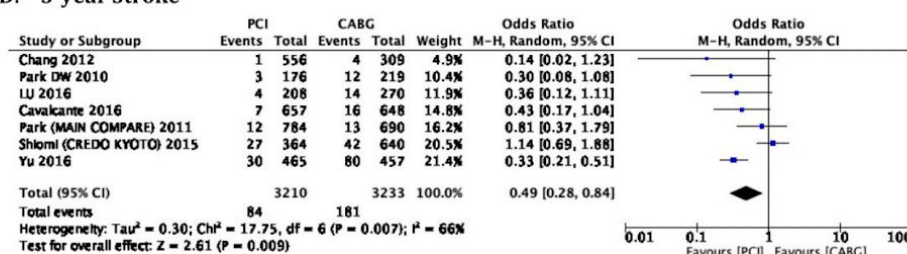
## B. 5-year MI



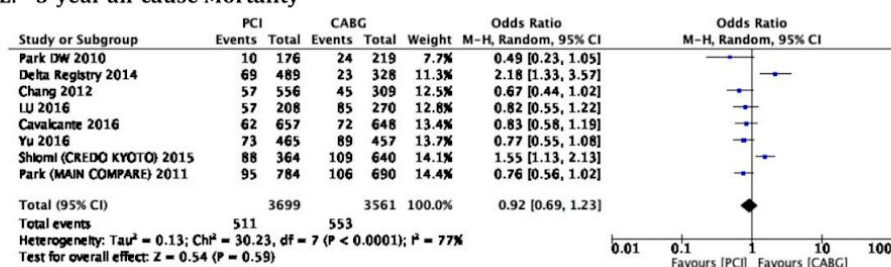
## C. 5-year Revascularization



## D. 5-year Stroke

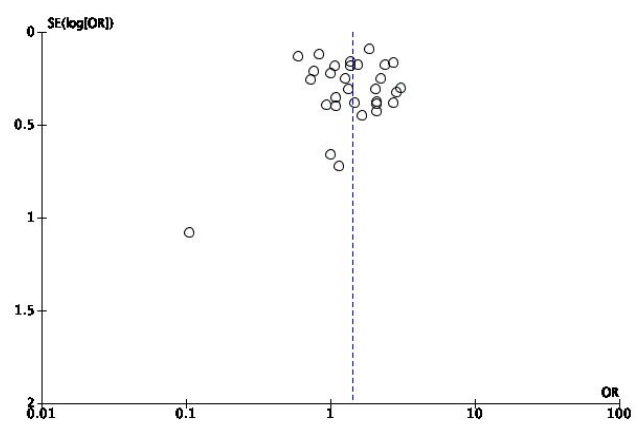


## E. 5-year all-cause Mortality

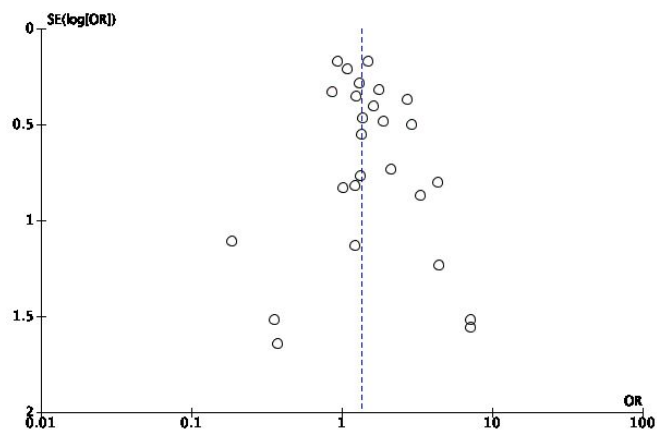


S. Figure 13: 5-year pooled estimates of PCI vs. CABG events for LMCAD across observational cohort studies.

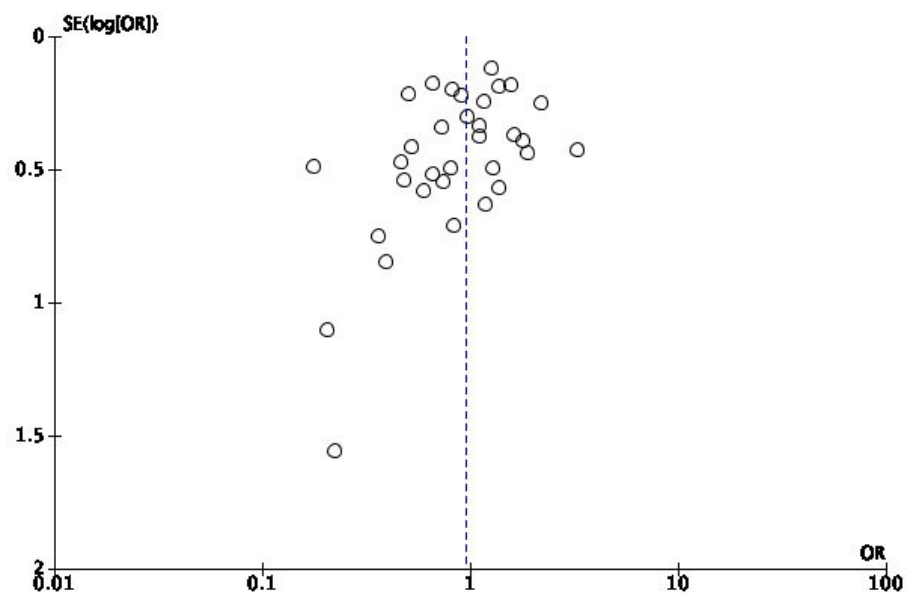
### E. SUPPLEMENTAL FUNNEL PLOTS FOR ALL STUDIES:



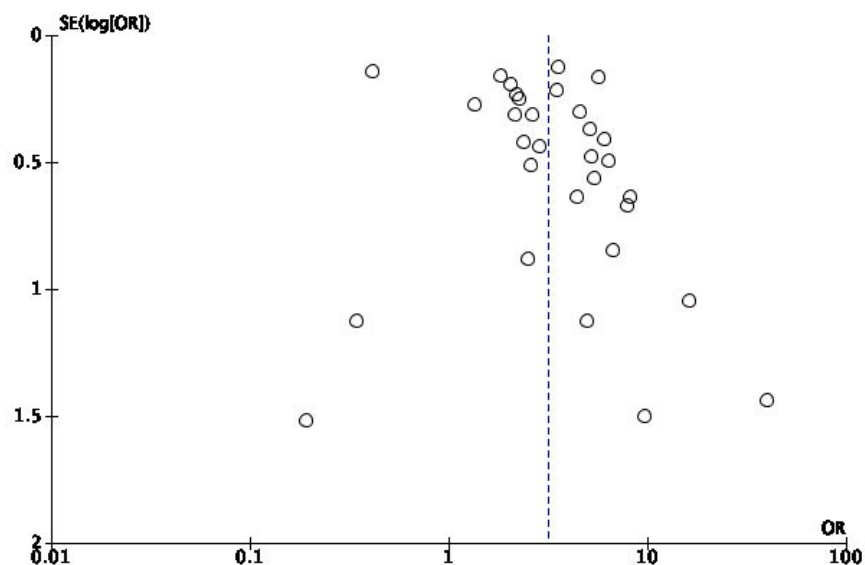
**S. Figure 14: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MACCE at 1-year follow up.**



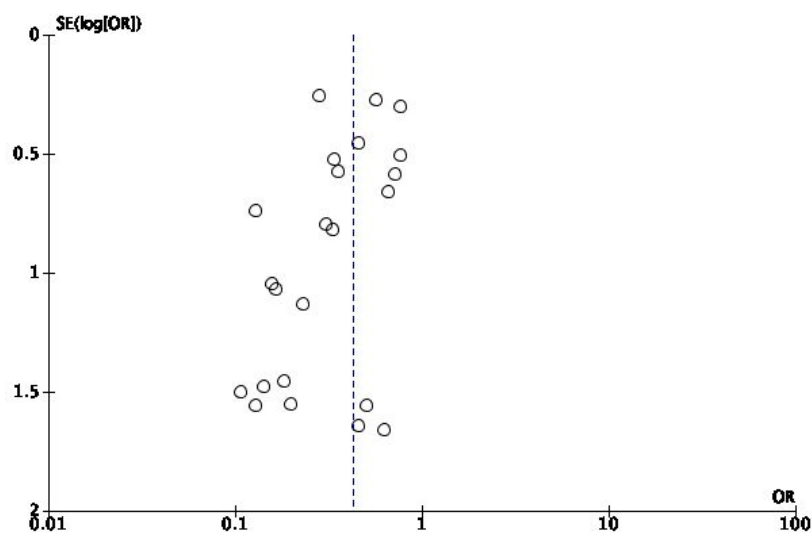
S. Figure 15: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MI at 1-year follow up.



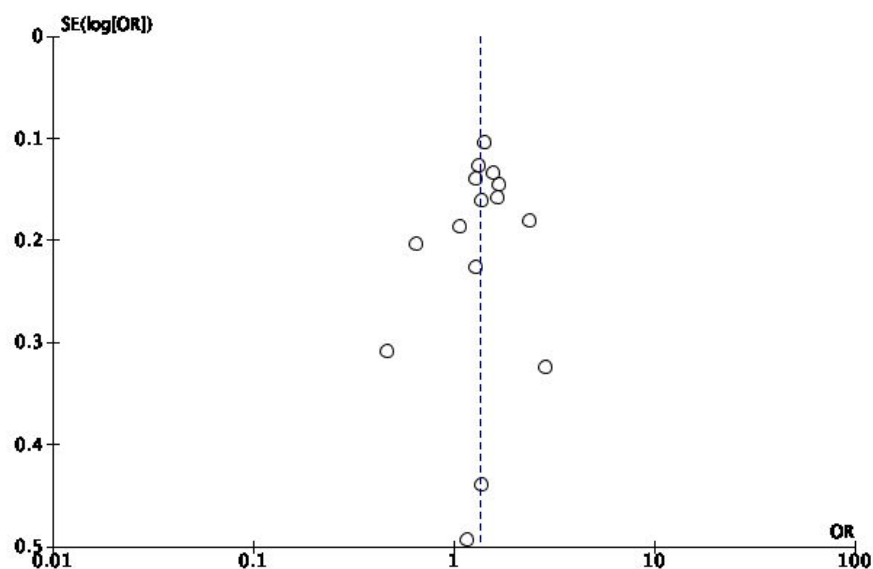
S. Figure 16: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of mortality at 1-year follow up.



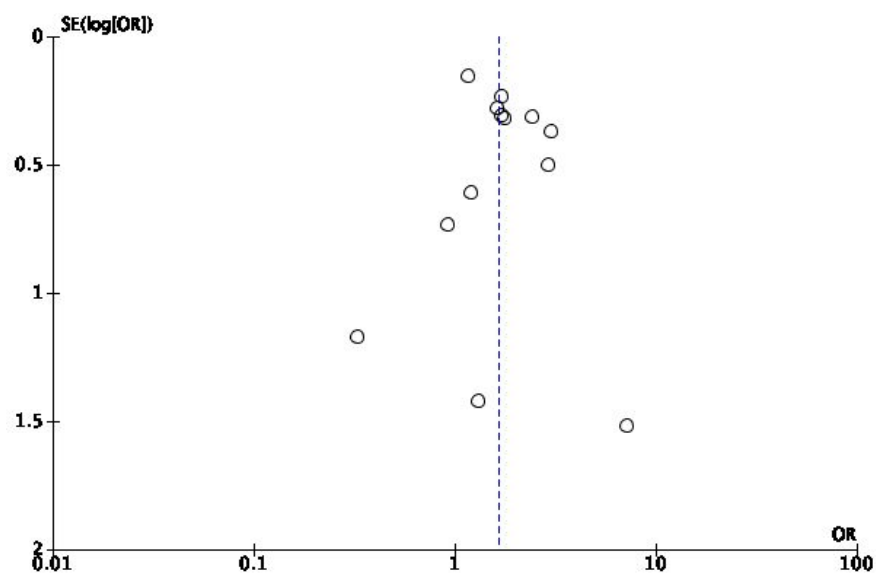
**S. Figure 17: Funnel plot showing minimal to moderate publication bias across studies comparing the pooled estimate of revascularization at 1-year follow up.**



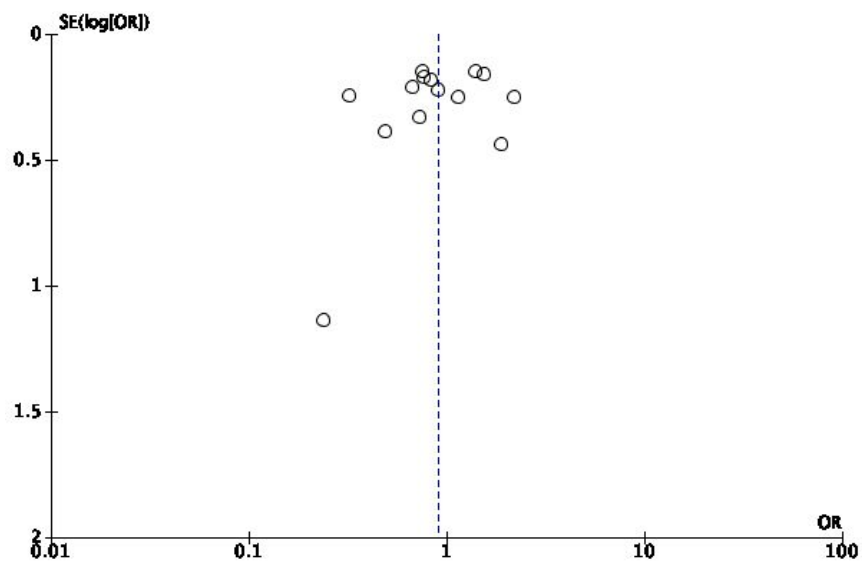
**S. Figure 18: Funnel plot showing minimal to moderate publication bias across studies comparing the pooled estimate of a stroke at 1-year follow up.**



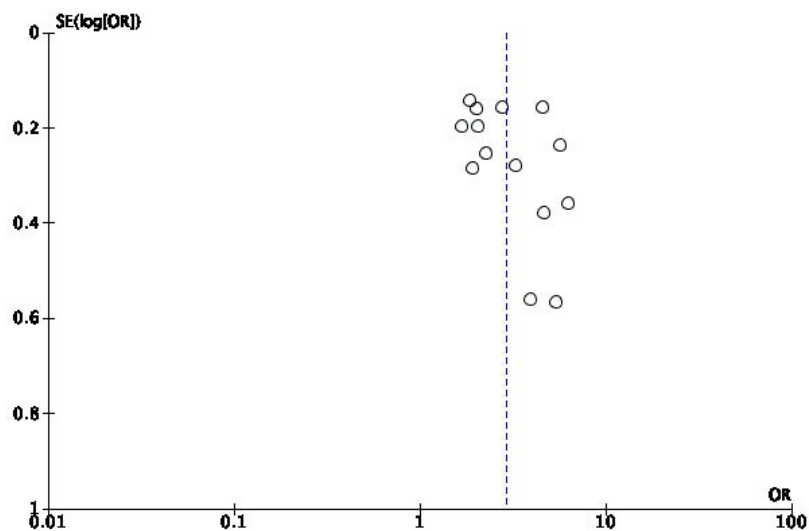
S. Figure 19: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MACCE at 5-year follow up.



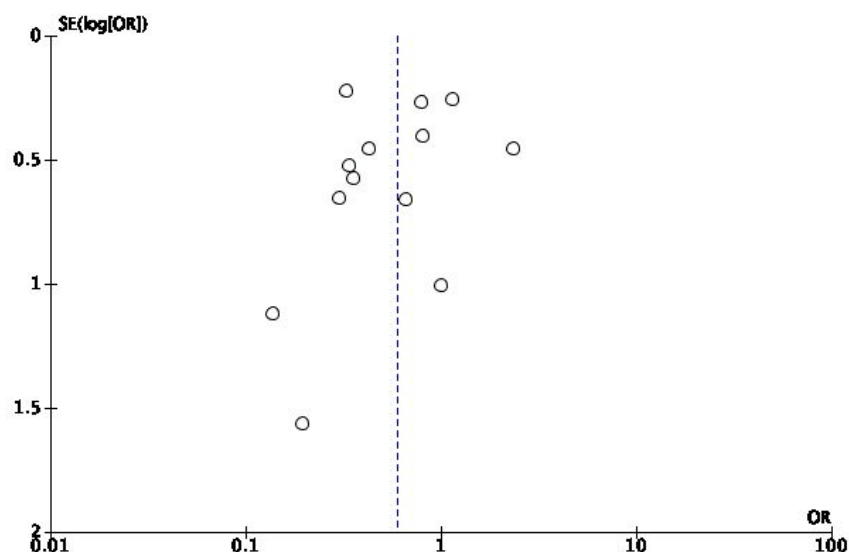
S. Figure 20: Funnel plot showing minimal publication bias across studies comparing the pooled estimate of MI at 5-year follow up.



**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.**

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