Intravascular Imaging-Guided Versus Coronary Angiography-Guided Complex PCI: A Meta-Analysis of Randomized Controlled Trials

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Supplemental Table 1

PRISMA 2020 CHECKLIST

Section and Topic	Item#	Checklist item	Pages where item is reported
TITLE			
Title	1	Identify the report as a systematic review .	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Overview	3	Overview on the recent data and current evidence	3
Rationale	4	Describe the rationale for the review in the context of existing know ledge.	3
Objectives	5	Provide a clear statement of the objectives of the review	3
METHODS			
Data sources and Search strategy	6	Provide the full search strategies that includes all databases, w ebsites and prior meta-analyses including search terms used.	3-4
Eligibility criteria	7	Specify the inclusion and exclusion criteria for the review and how studies w ere grouped for the syntheses.	4
Data extraction	8	Specify the number of investigators and how the data w as extracted, w hether they w ork independently, and the process of confirming data from study investigators	4
Outcomes	9	Identify the primary and secondary outcomes including definition of endpoints	4
Study risk of bias assessment	10	Provides how risk of bias w as evaluated in the included studies and the criteria used in the evaluation	4-5
Statistical analysis	11	Describe methods used to synthesize results, assess the presence and degree of heterogenicity and the software package used in the analysis	5
Certainty assessment	12	Describe methods used to assess certainty for outcomes	5
RESULTS			
Study selection	13	Describe the study selection process from the number of identified from the search to the number of studies included in the review using a flow diagram	Page 5, Figure 1
Study characteristics	14	Cite each included study and present its characteristics	5-6
Risk of bias in included studies	15	Provides assessments of risk of bias for each included study	6
outcomes	16	Provides primary and secondary outcomes using appropriate structured tables or plots.	6-7

PRISMA 2020 CHECKLIST

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	17a	Provide a general interpretation of the results	7
	17b	Compare the review to previously published review s and their limitations. It also provides an explanation on the importance of this review in overcoming those limitations.	7
	17c	Provide possible reasons of the review outcomes by providing previous evidence.	8
	17d	Discuss implications of the review results in current practice and future research.	8
LIMITATIONS			
Limitations	18	Discuss certain limitations of this review and w ays to overcome those limitations	8-9
CONCLUSION			
Conclusion	19	Summarize review outcome by draw ing conclusions	9
OTHER INFORMATION			
Registration and protocol	19	Provided registration information of the review and how to assess review protocol	4

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

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

Supplemental Table 2: Complex artery lesion classification

Studies	Complex artery lesions
HOME DES IVUS	Defined as lesion type B2 and C according to the American Heart Association, proximal left anterior descending artery, left main disease, reference vessel diameter <2.5 mm, lesion length >20 mm and in-stent restenosis
Kim et al.	**Long lesion requiring a stent ≥28 mm in length**
AVIO	Complex lesions which were defined as one of the following: long lesions (>28 mm); chronic total occlusion, ie, a total occlusion of duration more than 3-**months; lesions involving a bifurcation; small vessels (≤2.5mm) and patients requiring 4 or more stents.**
AIR-CTO	Patients with at least one CTO lesion (defined as TIMI grade 0 and occlusion duration >3 months) that had been successfully recanalized (defined as a wire-crossed CTO lesion and at the distal true lumen according to angiograms)
Tan et al.	Unprotected left main coronary artery lesion
CTO-IVUS	Complex lesions were defined as chronic total occlusion
Liu et al.	Defined as unprotected left main coronary artery lesions (defined as at least 50% stenosis in the left main coronary artery from visual assessment)
IVUS-XPL	Complex coronary lesions were defined as long coronary lesion **(implanted stent ≥28 mm in length)**
ULTIMATE	Unprotected left main disease, long lesions, chronic total occlusion, and complex bifurcation lesions
RENOVATE-COMPLEX- PCI	Complex coronary-artery lesions were defined as true bifurcation lesions according to the Medina classification system with a side-branch diameter of at least 2.5 mm; a chronic total occlusion; unprotected left main coronary artery disease; long coronary-artery lesions that would involve an expected stent length of at least 38 mm; multivessel PCI involving at least two major epicardial coronary arteries being treated at the same time; a lesion that would necessitate the use of multiple stents (at least three planned stents); a lesion involving in-stent restenosis; a severely calcified lesion; or ostial lesions of a major epicardial coronary artery.

Supplemental Table 3: Major adverse cardiac events (MACE) per each study

Studies	MACE
HOME DES IVUS	Not defined
Kim et al.	Composite of cardiac death, MI, stent thrombosis, or ischemia driven repeat revascularization
AVIO	Composite of any cardiac death, MI or ischemia driven repeat revascularization.
AIR-CTO	Composite of cardiac death, MI, or ischemia driven repeat revascularization
Tan et al.	Composite of death, non-fatal MI, and ischemia driven repeat revascularization
CTO-IVUS	Composite of death, MI, or ischemia driven repeat revascularization
Liu et al.	Composite of cardiac death, MI, or ischemia driven repeat revascularization
IVUS-XPL	Composite of cardiac death, target lesion–related MI, or ischemia driven repeat revascularization
ULTIMATE	Composite of cardiac death, target-vessel related MI or ischemia driven repeat revascularization
RENOVATE-COMPLEX-PCI	Composite of cardiac death, target-vessel MI, or ischemia driven repeat revascularization

MI: myocardial infarction

Supplemental Table 4: Myocardial infarction (MI) definition per each study

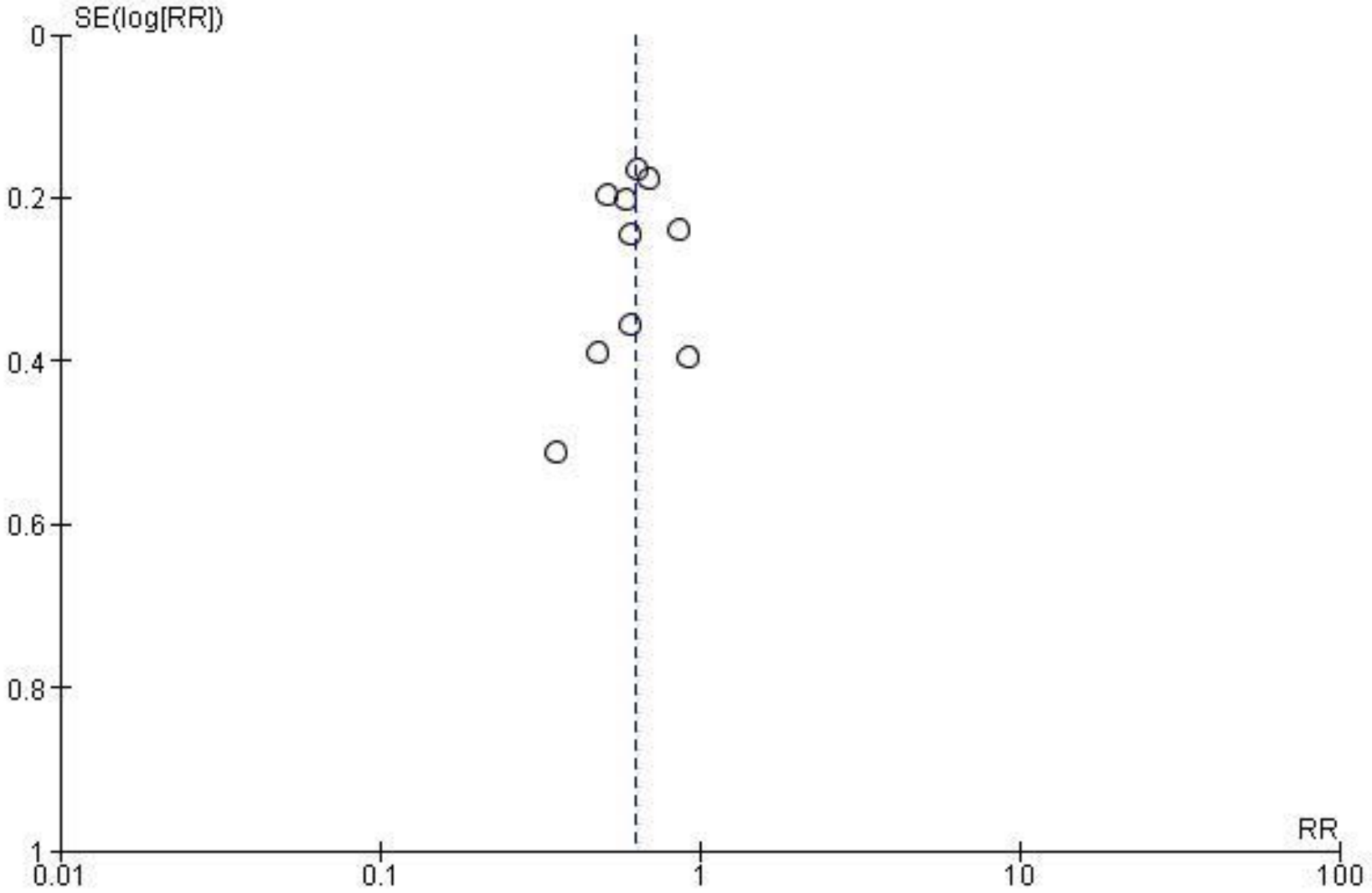
HOME DES IVUS	Not defined
Kim et al.	Myocardial infarction was defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal imaging findings of myocardial infarction combined with an increase in creatine kinase myocardial band fraction to greater than 3X the upper limit of the normal range or an increase in troponin T/troponin I to more than the 99th percentile of the upper normal limit, unrelated to an interventional procedure
AVIO Trial	Not defined
AIR-CTO	Periprocedural MI (PMI) was diagnosed when the plasma level of troponin I/T increased to >3 times the upper reference limit (URL) in no fewer than two blood samples. Subsequent MI was defined as CK-MB >threefold the URL
Tan et al.	non-fatal myocardial infarction
CTO-IVUS	MI was defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal imaging findings associated with MI combined with an increase in creatine kinase-MB above the upper normal limit or troponin T/I greater than the 99th percentile of the upper normal limit, unrelated to an interventional procedure
Liu et al.	Periprocedural MI was confirmed if creatine kinase–myocardial band (CK-MB) increased >10× the upper reference limit (URL) or presenting with any of the following symptoms: **(1) newly appeared pathological Q waves in ≥2 contiguous leads or left bundle** branch block (2) imaging evidence indicating new loss of viable myocardium, or (3) CK-MB increased >5× the URL only but presented with new occlusion or severe stenosis proven by angiography.
IVUS-XPL	MI was defined as presence of clinical symptoms, electrocardiographic changes, or abnormal imaging findings of MI, combined with an increase in the creatine kinase-MB fraction above the upper normal limits or an increase in troponin T or troponin I to a level greater than the 99th percentile of the upper normal limit
ULTIMATE	Protocol-defined peri-procedural MI was defined as a peak creatine kinase-MB **≥10 times the upper limit of normal measured within 72 h after the procedure or ≥5 times the upper limit of normal plus:** 1) new pathological Q waves in 2 or more contiguous leads or new left bundle branch block; 2) angiographically documented coronary artery or graft occlusion or new severe stenosis with thrombosis; or 3) imaging evidence of new regional wall motion abnormality or new loss of viable myocardium. Spontaneous MI (after 72 h) was defined as a clinical syndrome consistent with MI with CK-MB or troponin >1 time the URL and new ST-segment elevation or depression, or other findings as mentioned earlier in the text. All MIs were considered to be target-vessel MI unless there was clear evidence that they were attributable to a nontarget vessel
RENOVATE COMPLEXPCI	Target-vessel–related MI, spontaneous myocardial infarction, Procedure-related myocardial infarction and non–target-vessel–related myocardial infarction

Supplemental Table 5: Risk of bias of the individual studies by Cochrane risk assessment tool

	HOME DES IVUS 2010	KIM ET AL. 2013	AVIO 2013	AIR-CTO 2015	TAN ET AL. 2015	CTO-IVUS 2015	LIU ET AL. 2019	IVUS-XPL 2020	ULTIMATE 2021	RENOVATE-COMPLEX-PCI 2023
Random sequence generation *(Selection bias)*	+	+	+	+	+	+	+	+	+	+
Allocation concealment *(Selection bias)*	+	+	+	+	?	+	+	+	+	+
Blinding of participants and personnel *(Performance bias)*	-	-	-	-	-	-	-	-	-	-
Blinding of outcome assessment *(Detection bias)*	?	+	+	+	?	+	+	+	+	+
Incomplete outcome data *(Attrition bias)*	+	+	+	+	+	+	+	+	+	+
Selective reporting *(Reporting bias)*	+	+	+	+	+	+	+	+	+	+
Other sources of bias	+	+	+	+	+	+	+	+	+	+

+ = Low risk of bias - = Risk of bias ? = Unclear

Supplemental Figure 1: Funnel plot for MACE

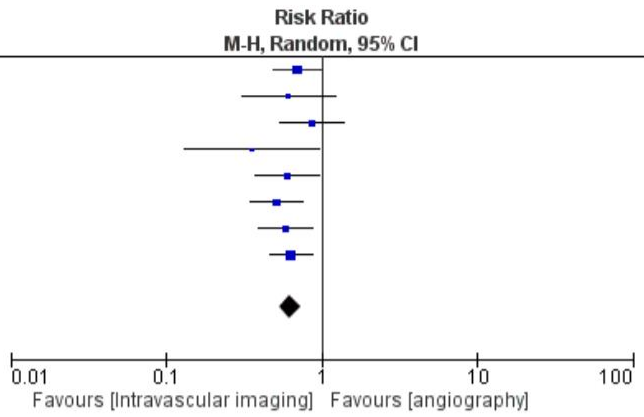


Supplemental Figure 2

Major adverse cardiac events (MACE) excluding studies with high risk of bias

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
AVIO 2013	37	142	53	142	19.2%	0.70 [0.49, 0.99]	2013
Kim et al. 2013	12	269	20	274	4.8%	0.61 [0.30, 1.23]	2013
AIR-CTO 2015	25	115	29	115	10.7%	0.86 [0.54, 1.38]	2015
CTO-IVUS 2015	5	201	14	201	2.3%	0.36 [0.13, 0.97]	2015
Liu et al. 2019	22	167	37	169	10.1%	0.60 [0.37, 0.97]	2019
IVUS-XPL 2020	36	700	70	700	15.6%	0.51 [0.35, 0.76]	2020
ULTIMATE 2021	35	479	60	482	14.8%	0.59 [0.39, 0.87]	2021
RENOVATE-COMPLEX-PCI 2023	76	1092	60	547	22.5%	0.63 [0.46, 0.88]	2023
Total (95% CI)		**3165**		**2630**	**100.0%**	**0.63 [0.54, 0.73]**	
Total events	248		343				

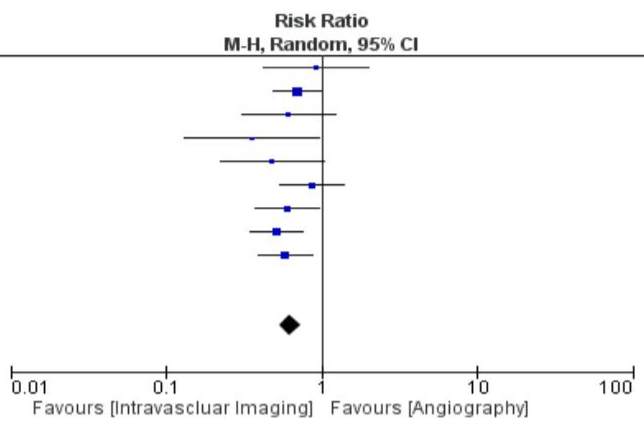
Heterogeneity: Tau² = 0.00; Chi² = 4.54, df = 7 (P = 0.72); I² = 0%
Test for overall effect: Z = 6.00 (P < 0.00001)



MACE excluding studies using OCT

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
HOME DES IVUS 2009	11	105	12	105	4.6%	0.92 [0.42, 1.98]	2009
AVIO 2013	37	142	53	142	22.4%	0.70 [0.49, 0.99]	2013
RESET 2013	12	269	20	274	5.7%	0.61 [0.30, 1.23]	2013
CTO-IVUS 2015	5	201	14	201	2.7%	0.36 [0.13, 0.97]	2015
Tan et al. 2015	8	61	17	62	4.7%	0.48 [0.22, 1.03]	2015
AIR-CTO 2015	25	115	29	115	12.5%	0.86 [0.54, 1.38]	2015
Liu et al. 2019	22	167	37	169	11.8%	0.60 [0.37, 0.97]	2019
IVUS-XPL 2020	36	700	70	700	18.2%	0.51 [0.35, 0.76]	2020
ULTIMATE 2021	35	479	60	482	17.4%	0.59 [0.39, 0.87]	2021
RENOVATE-COMPLEX-PCI 2023	76	1092	60	547	0.0%	0.63 [0.46, 0.88]	2023
Total (95% CI)		**2239**		**2250**	**100.0%**	**0.63 [0.53, 0.74]**	
Total events	191		312				

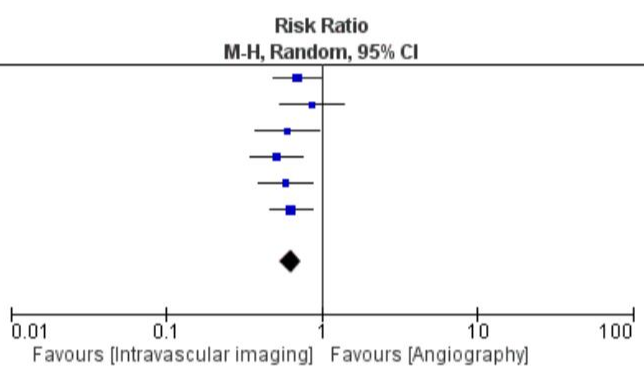
Heterogeneity: Tau² = 0.00; Chi² = 5.95, df = 8 (P = 0.65); I² = 0%
Test for overall effect: Z = 5.53 (P < 0.00001)



MACE including studies with consistent MACE definitions

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
AVIO 2013	37	142	53	142	20.6%	0.70 [0.49, 0.99]	2013
AIR-CTO 2015	25	115	29	115	11.5%	0.86 [0.54, 1.38]	2015
Liu et al. 2019	22	167	37	169	10.8%	0.60 [0.37, 0.97]	2019
IVUS-XPL 2020	36	700	70	700	16.8%	0.51 [0.35, 0.76]	2020
ULTIMATE 2021	35	479	60	482	16.0%	0.59 [0.39, 0.87]	2021
RENOVATE-COMPLEX-PCI 2023	76	1092	60	547	24.3%	0.63 [0.46, 0.88]	2023
Total (95% CI)		**2695**		**2155**	**100.0%**	**0.64 [0.54, 0.74]**	
Total events	231		309				

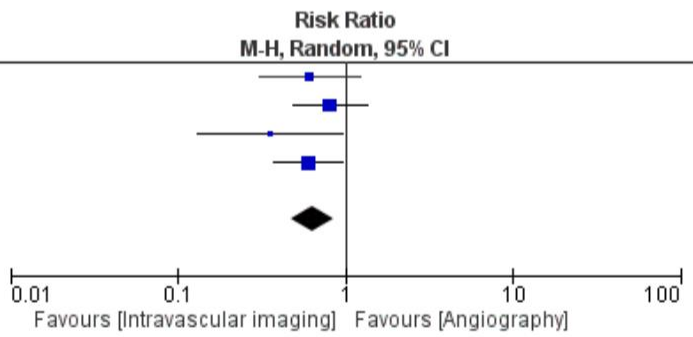
Heterogeneity: Tau² = 0.00; Chi² = 3.28, df = 5 (P = 0.66); I² = 0%
Test for overall effect: Z = 5.59 (P < 0.00001)



MACE at 1 year follow-up

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kim et al. 2013	12	269	20	274	18.5%	0.61 [0.30, 1.23]	2013
AIR-CTO 2015	21	115	26	115	34.0%	0.81 [0.48, 1.35]	2015
CTO-IVUS 2015	5	201	14	201	8.9%	0.36 [0.13, 0.97]	2015
Liu et al. 2019	22	167	37	169	38.5%	0.60 [0.37, 0.97]	2019
Total (95% CI)		**752**		**759**	**100.0%**	**0.64 [0.47, 0.86]**	
Total events	60		97				

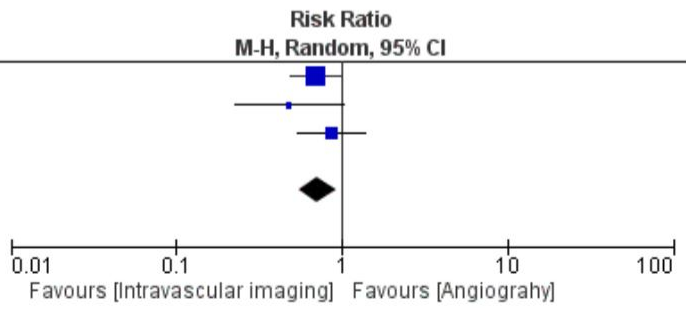
Heterogeneity: Tau² = 0.00; Chi² = 2.19, df = 3 (P = 0.53); I² = 0%
Test for overall effect: Z = 2.96 (P = 0.003)



MACE at 2 years follow-up

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
AVIO 2013	37	142	53	142	56.6%	0.70 [0.49, 0.99]	2013
Tan et al. 2015	8	61	17	62	11.9%	0.48 [0.22, 1.03]	2015
AIR-CTO 2015	25	115	29	115	31.5%	0.86 [0.54, 1.38]	2015
Total (95% CI)		**318**		**319**	**100.0%**	**0.71 [0.55, 0.93]**	
Total events	70		99				

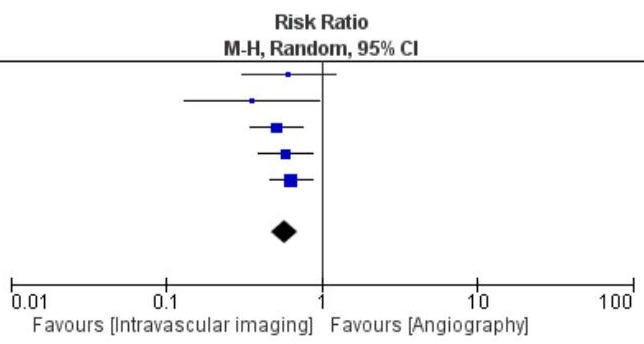
Heterogeneity: Tau² = 0.00; Chi² = 1.70, df = 2 (P = 0.43); I² = 0%
Test for overall effect: Z = 2.52 (P = 0.01)



MACE including studies exclusively using second generation DES

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kim et al. 2013	12	269	20	274	8.1%	0.61 [0.30, 1.23]	2013
CTO-IVUS 2015	5	201	14	201	3.9%	0.36 [0.13, 0.97]	2015
IVUS-XPL 2020	36	700	70	700	25.9%	0.51 [0.35, 0.76]	2020
ULTIMATE 2021	35	479	60	482	24.7%	0.59 [0.39, 0.87]	2021
RENOVATE-COMPLEX-PCI 2023	76	1092	60	547	37.5%	0.63 [0.46, 0.88]	2023
Total (95% CI)		**2741**		**2204**	**100.0%**	**0.57 [0.47, 0.70]**	
Total events	164		224				

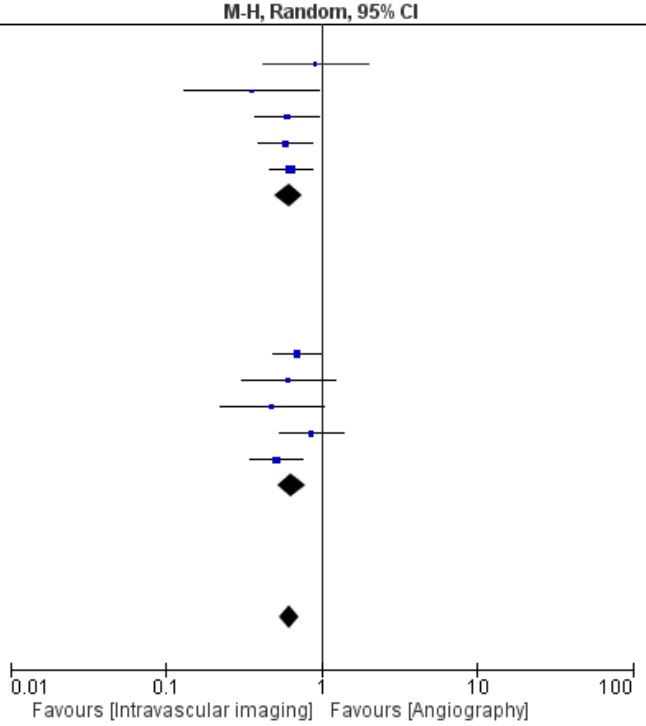
Heterogeneity: Tau² = 0.00; Chi² = 1.59, df = 4 (P = 0.81); I² = 0%
Test for overall effect: Z = 5.50 (P < 0.00001)



Supplemental Figure 3

Major adverse cardiac events (MACE) including studies reporting left main coronary artery (LMCA) PCI

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.1.1 Studies reporting LMCA PCI							
HOME DES IVUS 2009	11	105	12	105	3.6%	0.92 [0.42, 1.98]	2009
Tan et al. 2015	5	201	14	201	2.2%	0.36 [0.13, 0.97]	2015
Liu et al. 2019	22	167	37	169	9.3%	0.60 [0.37, 0.97]	2019
ULTIMATE 2021	35	479	60	482	13.8%	0.59 [0.39, 0.87]	2021
RENOVATE-COMPLEX-PCI 2023	76	1092	60	547	20.9%	0.63 [0.46, 0.88]	2023
Subtotal (95% CI)		**2044**		**1504**	**49.7%**	**0.62 [0.50, 0.76]**	
Total events	149		183				
Heterogeneity: Tau² = 0.00; Chi² = 2.26, df = 4 (P = 0.69); I² = 0%							
Test for overall effect: Z = 4.55 (P < 0.00001)							
1.1.2 Studies not reporting LMCA PCI							
AVIO 2013	37	142	53	142	17.8%	0.70 [0.49, 0.99]	2013
Kim et al. 2013	12	269	20	274	4.5%	0.61 [0.30, 1.23]	2013
AIR-CTO 2015	8	61	17	62	3.7%	0.48 [0.22, 1.03]	2015
CTO-IVUS 2015	25	115	29	115	9.9%	0.86 [0.54, 1.38]	2015
IVUS-XPL 2020	36	700	70	700	14.4%	0.51 [0.35, 0.76]	2020
Subtotal (95% CI)		**1287**		**1293**	**50.3%**	**0.64 [0.52, 0.79]**	
Total events	118		189				
Heterogeneity: Tau² = 0.00; Chi² = 3.63, df = 4 (P = 0.46); I² = 0%							
Test for overall effect: Z = 4.20 (P < 0.0001)							
Total (95% CI)		**3331**		**2797**	**100.0%**	**0.63 [0.54, 0.73]**	
Total events	267		372				
Heterogeneity: Tau² = 0.00; Chi² = 5.95, df = 9 (P = 0.75); I² = 0%							
Test for overall effect: Z = 6.18 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.80), I² = 0%							



MACE including studies reporting chronic total occlusion (CTO) PCI

Study or Subgroup	Intravascular imaging Events	Total	Angiography Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.2.1 Studies including CTO PCI							
AVIO 2013	37	142	53	142	18.0%	0.70 [0.49, 0.99]	2013
AIR-CTO 2015	25	115	29	115	10.1%	0.86 [0.54, 1.38]	2015
CTO-IVUS 2015	5	201	14	201	2.2%	0.36 [0.13, 0.97]	2015
ULTIMATE 2021	35	479	60	482	14.0%	0.59 [0.39, 0.87]	2021
RENOVATE-COMPLEX-PCI 2023	76	1092	60	547	21.2%	0.63 [0.46, 0.88]	2023
Subtotal (95% CI)		**2029**		**1487**	**65.4%**	**0.66 [0.55, 0.79]**	
Total events	178		216				
Heterogeneity: Tau² = 0.00; Chi² = 3.21, df = 4 (P = 0.52); I² = 0%							
Test for overall effect: Z = 4.46 (P < 0.00001)							
1.2.2 Studies not including CTO PCI							
HOME DES IVUS 2009	11	105	12	105	3.7%	0.92 [0.42, 1.98]	2009
Kim et al. 2013	12	269	20	274	4.6%	0.61 [0.30, 1.23]	2013
Tan et al. 2015	5	201	14	201	2.2%	0.36 [0.13, 0.97]	2015
Liu et al. 2019	22	167	37	169	9.5%	0.60 [0.37, 0.97]	2019
IVUS-XPL 2020	36	700	70	700	14.6%	0.51 [0.35, 0.76]	2020
Subtotal (95% CI)		**1442**		**1449**	**34.6%**	**0.57 [0.44, 0.73]**	
Total events	86		153				
Heterogeneity: Tau² = 0.00; Chi² = 2.65, df = 4 (P = 0.62); I² = 0%							
Test for overall effect: Z = 4.35 (P < 0.0001)							
Total (95% CI)		**3471**		**2936**	**100.0%**	**0.63 [0.54, 0.73]**	
Total events	264		369				
Heterogeneity: Tau² = 0.00; Chi² = 6.69, df = 9 (P = 0.67); I² = 0%							
Test for overall effect: Z = 6.16 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.81, df = 1 (P = 0.37), I² = 0%