SUPPLEMENTARY DATA

RESEARCH ALGORITHMS

PubMed/MEDLINE search algorithm: ((Fractional Flow Reserve) OR (Instantaneous wave-free ratio) OR (non-hyperaemic coronary pressure) OR (resting full cycle ratio) OR (diastolic pressure ratio) OR (distal coronary aortic pressure ratio)) AND ((coronary artery disease) OR (percutaneous coronary intervention) OR (coronary revascularization))

Cochrane/Central search algorithm: "Fractional flow reserve"

FURTHER SENSITIVITY ANALYSES

Secondary analysis for the three coprimary endpoints after excluding prospective non-PSWM adjusted studies.

Endpoint	**HR and 95%CI**
All-cause death	0.76 (0.62-0.93)
MI	0.80 (0.68-0.94)
MACE	0.87 (0.78-0.96)

95% CI, 95% confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction; PSWM, propensity score weighted matching.

Table 1 of the supplementary data. MACE definitions across included studies

Study and year	MACE definition
NRSI	
Wrongpraparut et al. 2005 [23]	Death, MI, TLR
Koo 2008 [24]	Cardiac death, MI, TVR
Puymirat 2012 [25]	Cardiac death, MI, TVR
Di Serafino 2013 [26]	Death, MI, TVF, CVA
Li 2013 [27]	Death, MI, any revascularization
Toth 2013 [28]	Death, MI, TVR
Di Gioia 2016 [35]	Death, MI, any revascularization
De Backer 2016 [36]	Death, MI, any revascularization
Sawant 2018 [13]	Death, MI, stroke, any revascularization
Fournier 2018 [37]	Death, MI, TVR
Lunardi 2019 [11]	Cardiac death, MI, any revascularization, disabling stroke
Di Gioia 2020 [14]	Death, MI, any revascularization, stroke
Parikh 2020 [38]	Death, MI, any revascularization
Adjedj 2022 [41]	Death, MI, unplanned revascularization, TLR, stroke, BARC bleeding 3-5
Gerhardt 2023 [44]	Death, MI, any revascularization,
RCT	
Layland 2015 (FAMOUS-NSTEMI) [30]	Cardiac death, MI, unplanned hospitalization for HF
Chen 2015 (DK-CRUSH VI) [31]	Cardiac death, MI, ischemia-driven TVR
Park 2015 (DEFER-DES) [32]	Cardiac death, MI, TLR
Van Nunen 2015 (FAME) [33]	Death, MI, any revascularization
Zhang 2016 [45]	Cardiac death, MI, unplanned hospitalization for HF
Theusen 2018 (FARGO) [12]	Death, MI, any revascularization, stroke
Toth 2019 (GRAFFITI) [10]	Death, MI, any revascularization, stroke
Puymirat 2021 (FLOWER-MI) [5]	Death, MI, unplanned hospitalization leading to urgent revascularization
Rioufol 2021 (FUTURE) [15]	Death, MI, stroke, unplanned revascularization
Stables 2022 (RIPCORD-2) [16]	Death, MI, stroke, unplanned revascularization
Lee 2022 (FRAME-AMI) [43]	Death, MI, any revascularization

CVA, cerebrovascular accident; HF, heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; TLR, target lesion revascularization; TVR, target vessel revascularization).

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Table 2 of the supplementary data. Patients' baseline characteristics in the included studies

Study and year	Age, years (median)	Male (%)	HBP (%)	DM (%)	Dyslipidemia (%)	Smoking (%)	Family History (%)	Prior MI (%)	Prior PCI (%)	Prior CABG (%)	ACS (%)	LVEF (median)
NRSI												
Wrongpraparut et al. 2005 [23]	60	78	74	39	62	48	N/A	N/A	N/A	N/A	0	51
Koo 2008 [24]	62	63	N/A	26	N/A	N/A	N/A	N/A	N/A	N/A	63	N/A
Puymirat 2012 [25]	72	65	63	31	65	43	31	N/A	39	12	18	67
Di Serafino 2013 [26]	70	77	57	27	63	43	N/A	35	42	100	24	63
Li 2013 [27]	67	69	78	29	78	13	N/A	29	33	N/A	11	N/A
Toth 2013 [28]	68	75	79	27	66	42	24	16	32	N/A	0	71
Frohlich 2014 [29]	65	74	52	22	49	16	N/A	31	25	12	40	N/A
Di Gioia 2016 [35]	73	70	57	24	54	34	27	N/A	N/A	5	8	69
De Backer 2016 [36]	65	73	68	25	74	25	48	34	46	15	0	N/A
Sawant 2018 [13]	63	76	83	33	93	17	38	32	44	20	N/A	57
Fournier 2018 [37]	66	80	76	21	65	45	26	17	N/A	N/A	0	70
Lunardi 2019 [11]	84	48	92	31	N/A	N/A	N/A	19	N/A	14	N/A	N/A
Di Gioia 2020 [14]	67	80	49	28	56	55	25	N/A	18	10	0	39
Parikh 2020 [38]	69	97	89	45	86	N/A	15	22	24	N/A	0	52
Völz 2020 [39]	66	76	75	22	77	11	N/A	28	32	N/A	0	N/A
Omran 2020 [42]	65	65	78	43	70	N/A	N/A	N/A	N/A	N/A	100	N/A
Wong 2021 [40]	67	73	N/A	26	N/A	42	N/A	5	N/A	N/A	49	N/A
Adjedj 2022 [41]	68	76	62	24	52	16	22	17	41	2	0	N/A
Gerhardt 2023 [44]	69	68	80	37	65	N/A	N/A	N/A	N/A	N/A	100	N/A
Layland 2015 (FAMOUS-NSTEMI) [30]	62	74	45	15	36	41	N/A	13	11	N/A	100	N/A
Chen 2015 (DK-CRUSH VI) [31]	65	74	69	28	18	41	N/A	10	14	<1	17	61
Park 2015 (DEFER-DES) [32]	62	73	64	26	70	26	N/A	19	19	N/A	51	62
Van Nunen 2015 (FAME) [33]	64	75	62	24	72	28	39	36	27	N/A	N/A	57
Zhang 2016 [45]	70	69	74	34	83	27	N/A	24	N/A	N/A	100	N/A
Theusen 2018 (FARGO) [12]	66	91	67	23	80	22	55	25	21	N/A	23	N/A
Toth 2019 (GRAFFITI) [10]	67	81	74	37	79	49	N/A	12	18	N/A	11	N/A
Puymirat	62	83	44	15	42	38	28	6	9	N/A	100	50

2021 (FLOWER-MI) [5]												
Rioufol 2021 (FUTURE) [15]	66	83	59	31	60	24	N/A	20	26	N/A	46	55
Stables 2022 (RIPCORD-2) [16]	64	75	55	19	57	N/A	N/A	22	26	N/A	52	N/A
Lee 2022 (FRAME-AMI) [43]	63	84	53	33	41	33	7	3	6	0	100	53

ACS, acute coronary syndromes; CABG, coronary artery bypass grafting; DM, diabetes mellitus; HBP, high blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NRS, and non-randomized studies; PCI, percutaneous coronary intervention; RCT, randomized controlled trials.

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Table 3 of the supplementary data. CABG anastomoses per patient

Study and year	FFR (+/- SD)	Angio (+/- SD)	P value
NRSI			
Toth 2013 [28]	Arterial: 2 (1-2) Venous: 1 (0-1)	Arterial: 2 (1-2) Venous: 1 (1-2)	.068 <.001
Di Gioia 2016 [35]	Arterial: 0.84 +/- 0.73 Venous: 0.61 +/- 0.85	Arterial: 0.86 +/- 0.72 Venous: 0.94 +/- 1.00	.87 .032
Fournier 2018 [37]	Arterial: 2 (1-2) Venous: 0 (1-2)	Arterial: 2 (1-2) Venous: 0 (1-2)	.717 .047
Di Gioia 2020 [14]	Arterial: 1.53 +/- 0.68 Venous: 1.16 +/- 0.89	Arterial: 1.43 +/- 0.79 Venous: 1.54 +/- 0.97	.34 .007
RCT			
Theusen 2018 [12]	Total: 2.6 +/- 0.9	Total: 3.0 +/- 0.9	.005
Toth 2019 [10]	Arterial: 1 (1-2) Venous: 1 (0-2)	Arterial: 1 (1-2) Venous: 1 (1-2)	.218 .031
Rioufol 2021 [15]	Total: 2.9 +/- 0.9	Total: 2.9 +/- 0.9	.81

CABG, coronary artery bypass grafting; FFR, fractional-flow reserve; NRSI, non randomized studies of intervention; RCT, randomized clinical trials; SD, standard deviation.

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Table 4 of the supplementary data. PCI revascularizations according to the reported variables

Study and year	Reported variable	FFR (+/- SD or %)	Angio (+/- SD or %)	P value
NRSI				
Wongpaparut 2005 [23]	PCI vessels per pt	1.12 +/- 0.30	2.75 +/- 0.54	<.001[a]
Koo 2008 [24]	SB intervention	33/110 (30%)	49/110 (45%)	.03 [a]
Puymirat 2012 [25]	PCI vessels per pt	1.10 +/- 1.01	1.17 +/- 0.03	.044 [a]
Di Serafino 2012 [26]	PCI performed	23/65 (35%)	90/158 (57%)	<.01 [a]
Li 2013 [27]	Stents per pt	0.6 +/- 0.9	1.5 +/- 1.0	<.001 [a]
Frolich 2014 [29]	Lesions attempted per pt	1.3 +/- 0.8	1.5 +/- 0.8	<.0001 [a]
Di Gioia 2016 [35]	PCI performed	25/106 (24%)	28/212 (13%)	.019[b]
De Backer 2016 [36]	PCI lesions Total stent number	485/947 (51.2%) 486	957/957 (100%) 951	.001 [a] <.001°
Lunardi 2019 [11]	PCI performed Lesions treated	24/94 (25.5%) 31/142 (21.8%)	43/122 (35.2%) 54/184 (29.3%)	.19 .13
Di Gioia 2020 [14]	PCI performed Stents per pt	155/433 (36%) 1.55 +/- 0.81	261/866 (30%) 1.47 +/- 0.47	.039 [b] .35
Parikh 2020 [38]	PCI performed	487/2967 (16.4%)	331/15 022 (2.2%)	N/A
Volz 2020 [39]	Stents per pt	0.84 +/- 0.62	1.07 +/- 0.79	.009 [a]
Wong 2020 [40]	More than 1 stent per single vessel	74/542 (14%)	1855/9762 (19%)	.002 [a]
Omran 2020 [42]	Total number of stents used	55	54.5	.34
Adjedj 2022 [41]	Number of stents implanted	1.48 ± 0.81	1.47 ± 0.85	.208
Gerhardt 2023 [44]	Number of stents	1.48	1.60	.175
RCT				
Layland 2015 [30]	PCI performed	125/176 (71%)	139/174 (79.9%)	.057
Chen 2015 [31]	SB intervention	30/160 (25.9)	61/160 (38.1)	.01 [a]
Park 2015 [32]	Total stent number	53/114	187/115	N/A
Van Nunen 2015 [33]	DES per pt Lesions stented	1.9 +/- 1.3 819 (94%)	2.7 +/- 1.2 1237 (92%)	<.001 [a] .07
Zhang 2016 [45]	PCI performed	95/110 (86.4%)	104/110 (94.5%)	N/A
Puymirat 2021 [5]	Non-culprit PCI performed Stents per pt	388/586 (66.2%) 1.01 +/- 0.99	560/577 (97.1%) 1.50 +/- 0.86	N/A N/A
Rioufol 2021 [15]	Stents per pt	2.2 +/- 1.2	2.1 +/- 1.2	.54
Stables 2022 [16]	PCI/CABG performed	373/548 (68.0%)	387/552 (70.1%)	.2
Lee 2022 [43]	PCI of NCL	64.1	97.1	°<.001

CABG, coronary artery bypass grafting; FFR, fractional-flow reserve; NCL, non-culprit lesion; NRSI, non-randomized studies of intervention; PCI, percutaneous coronary intervention; RCT, SB, side branch; SD, standard deviation.

[a] Favours FFR.

[b] Favours angio.

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Table 5 of the supplementary data. Studies including periprocedural events in MI definition

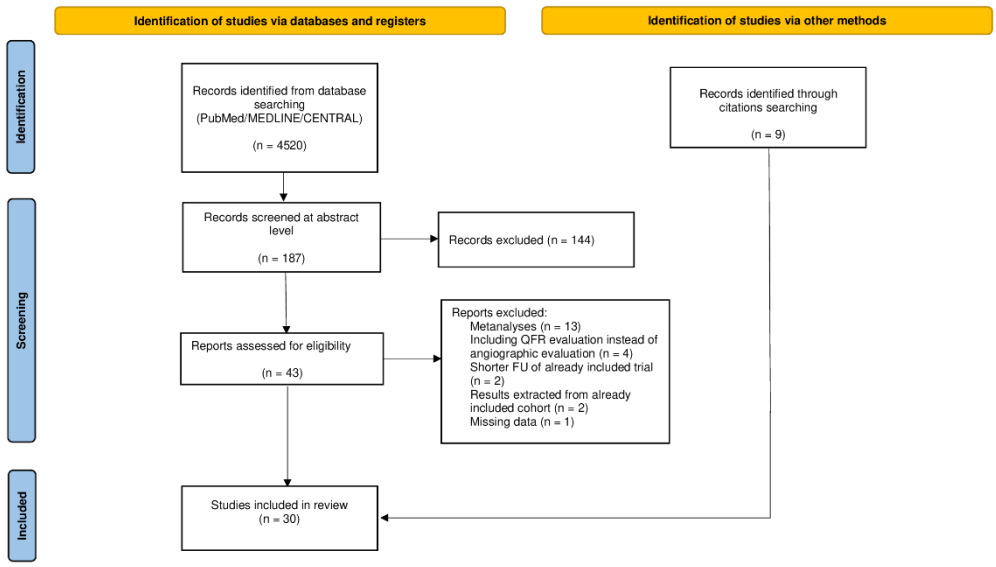
Study and year	FFR vs Angio	Periprocedurla MI definitions
Non-randomized studies		
Wrongpraparut et al. 2005 [23]	1 vs 2	Q wave/non-Q wave
Koo 2008 [24]	9 vs 16	N/A
Puymirat 2012 [25]	0 vs 24	UDMI
Di Serafino 2013 [26]	1 vs 18	N/A
Li 2013 [27]	N/A	N/A
Toth 2013 [28]	N/A	N/A
Frohlich 2014 [29]	N/A*	N/A
Di Gioia 2016 [35]	N/A	N/A
De Backer 2016 [36]	6 vs 13	UDMI
Sawant 2018 [13]	6 vs 3	N/A
Fournier 2018 [37]	N/A	N/A
Lunardi 2019 [11]	3 vs 7	UDMI
Di Gioia 2020 [14]	N/A	N/A
Parikh 2020 [38]	N/A	N/A
Völz 2020 [39]	N/A	N/A
Omran 2020 [42]	N/A	N/A
Wong 2021 [40]	N/A	N/A
Adjedj 2022 [41]	N/A	UDMI
Gerhardt 2023 [44]	N/A	N/A
Randomized studies		
Layland 2015 (FAMOUS-NSTEMI) [30]	5 vs 11	UDMI
Chen 2015 (DK-CRUSH VI) [31]	19 vs 20	Q wave/non-Q wave
Park 2015 (DEFER-DES) [32]	N/A	N/A
Van Nunen 2015 (FAME) [33]	12 vs 16	UDMI
Zhang 2016 [45]	N/A	N/A
Theusen 2018 (FARGO) [12]	N/A	UDMI
Toth 2019 (GRAFFITI) [10]	N/A	N/A
Puymirat 2021 (FLOWER-MI) [5]	7 vs 2	UDMI
Rioufol 2021 (FUTURE) [15]	N/A	N/A
Stables 2022 (RIPCORD-2) [16]	N/A	N/A
Lee 2022 (FRAME-AMI) [43]	3 vs 11	UDMI

FFR, fractional flow reserve; MI, UDMI, universal definition of myocardial infarction

*missing in the PSWM (propensity score weighted matching) adjusted cohorts

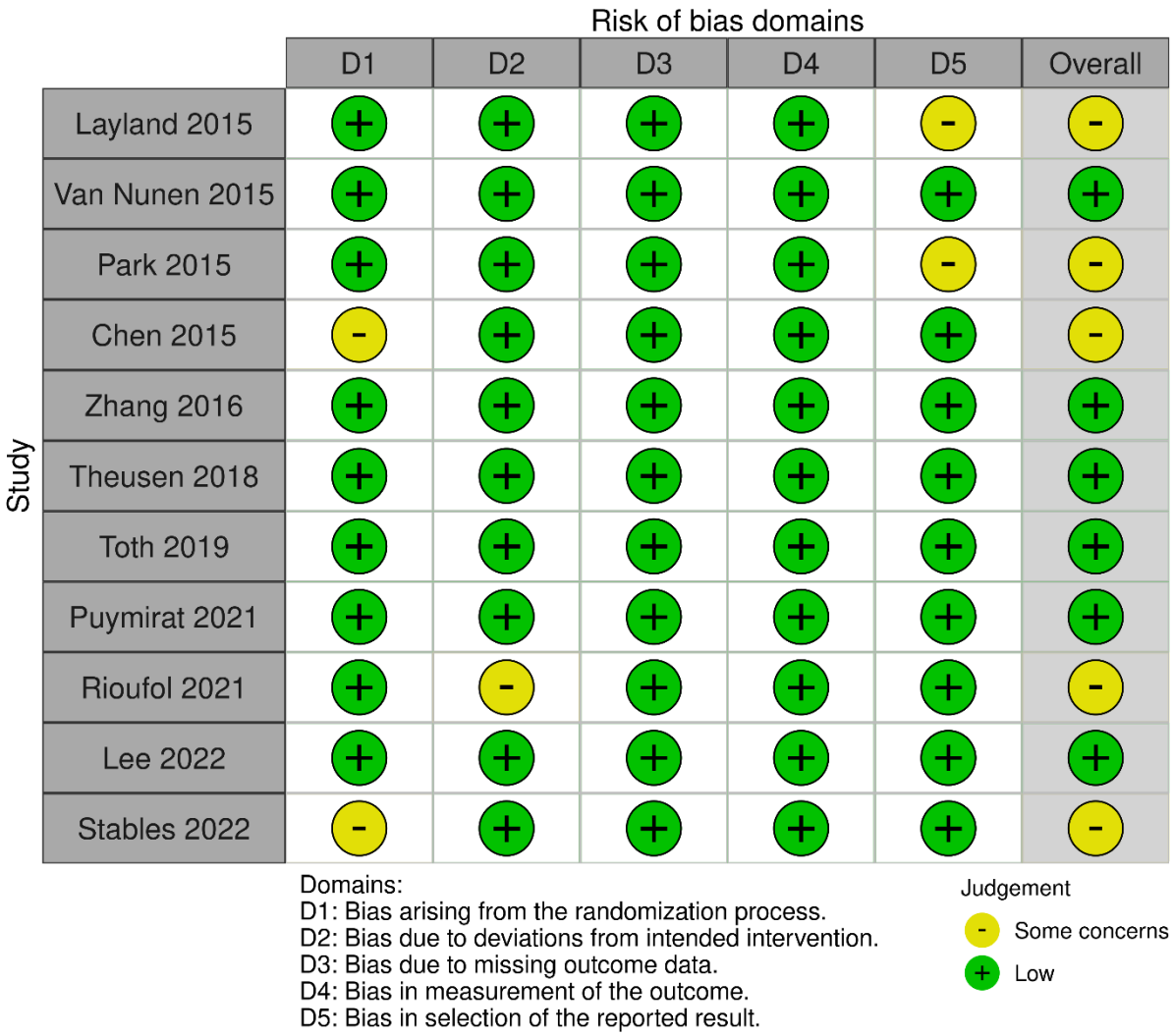
The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 1 of the supplementary data. PRISMA diagram



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

Figure 2 of the supplementary data. RoB 2 for RCTs diagram

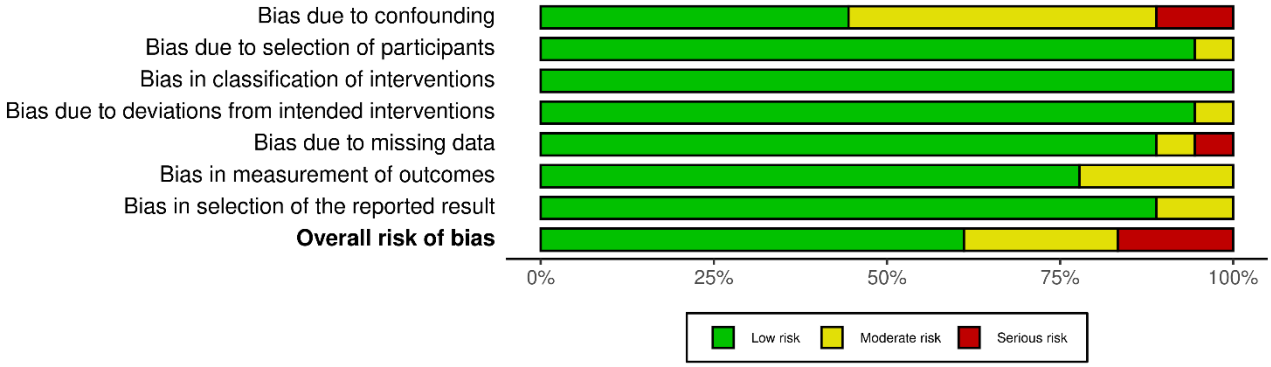


The bibliographic references mentioned in this figure correspond to: 2, 15, 16, 30, 31, 32, 33, 43, 45 Puymirat *et al.*[5], Toth *et al.*[10], Thuesen *et al.*[12], Rioufol *et al.*[15], Stables *et al.*[16], Layland *et al.*[30], Chen *et al.*[31], Park *et al.*[32], Van Nunen *et al.*[33], Lee *et al.*[43], Zhang *et al.*[45.]

RCT (randomized clinical trials).

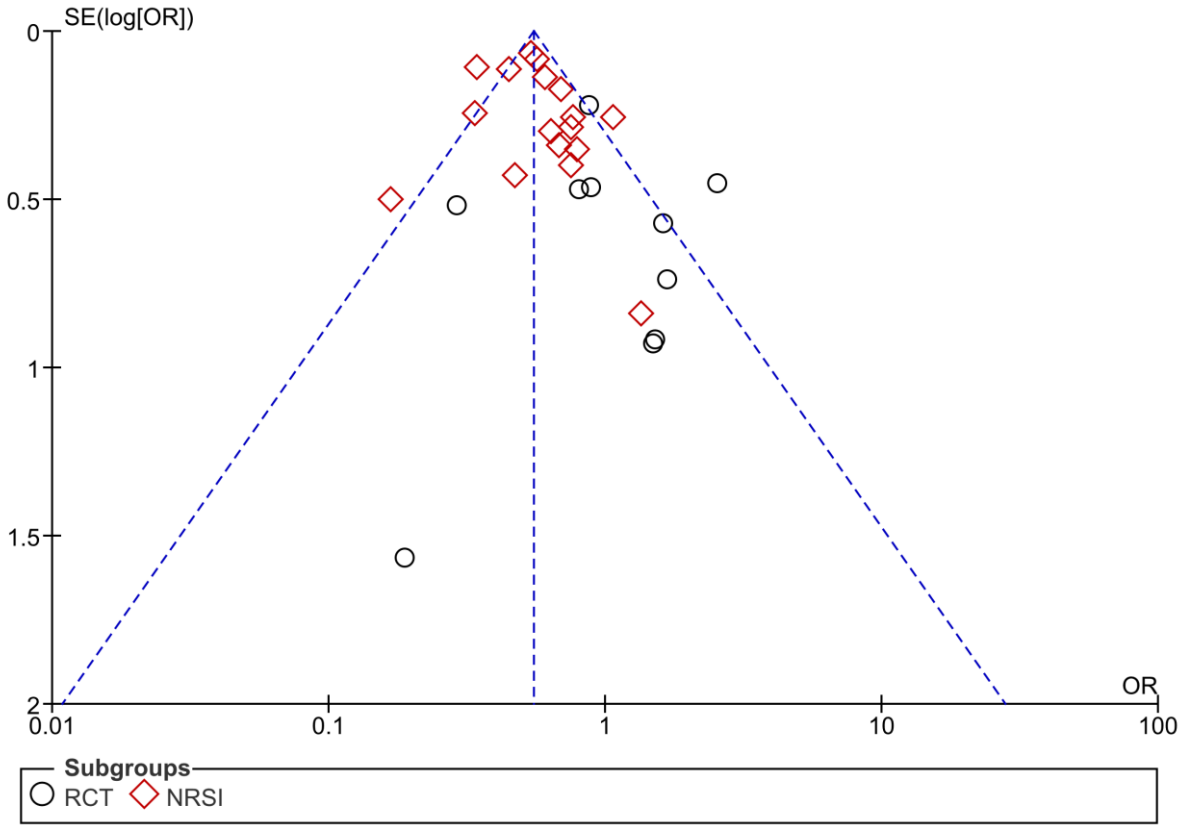
The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 3 of the supplementary data. ROBINS-I for NRSI diagram



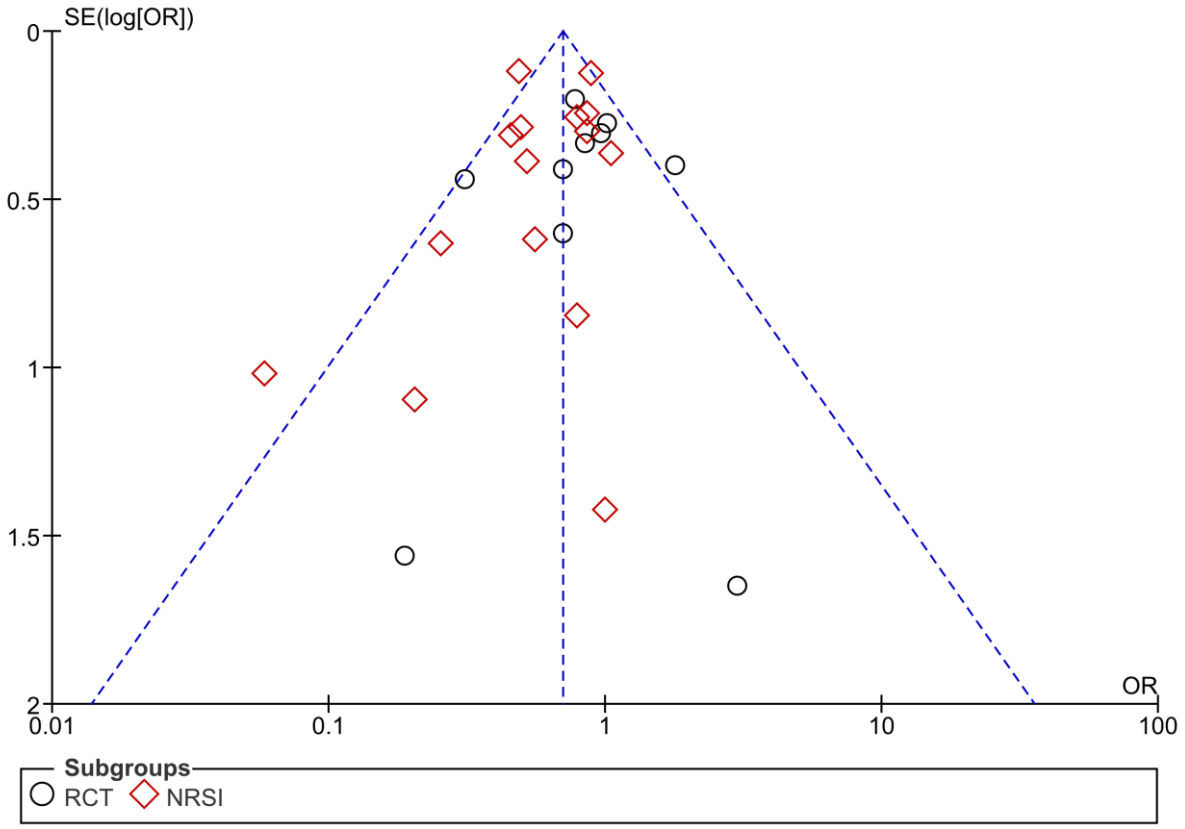
NRSI, non-randomized studies of intervention.

Figure 4 of the supplementary data. All-cause mortality funnel plot (Egger's test for primary analysis: *P* = .288; Egger's test for secondary analysis: *P* = .301)



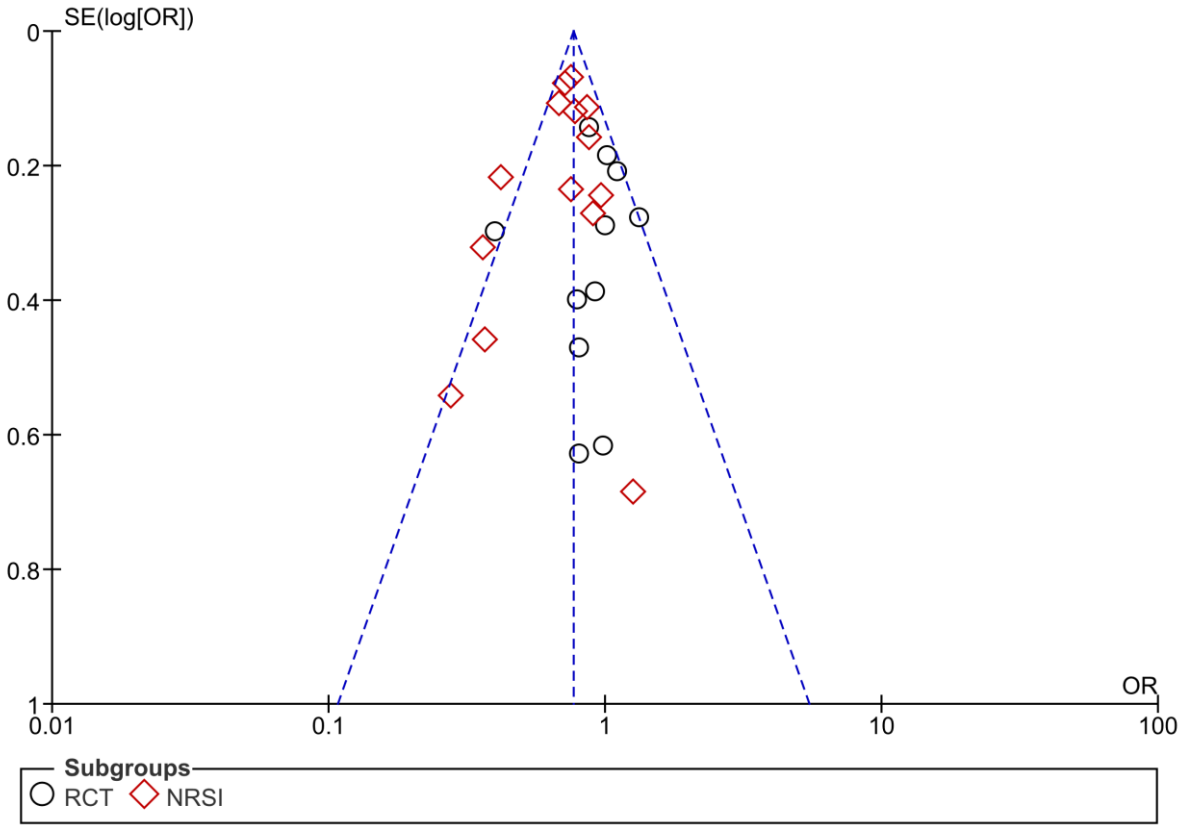
NRSI, non-randomized studies of intervention; OR, odds ratio; RCT, randomized clinical trials.

Figure 5 of the supplementary data. MI funnel plot (Egger's test for primary analysis: *P* = .628; Egger's test for secondary analysis: *P* = .506)



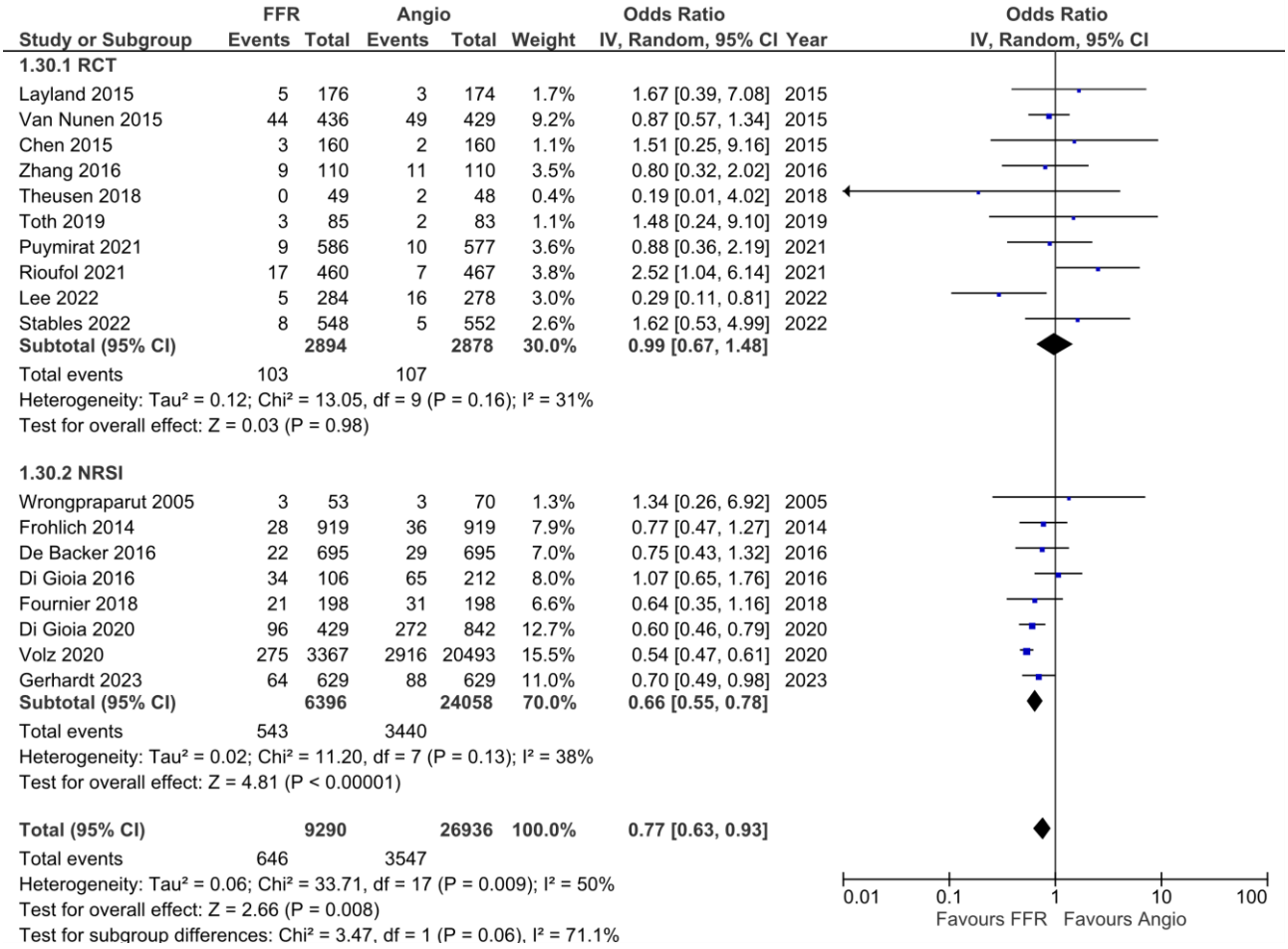
NRSI, non-randomized studies of intervention; OR, odds ratio; RCT, randomized clinical trials.

Figure 6 of the supplementary data. MACE funnel plot (Egger's test for primary analysis: *P* = .886; Egger's test for secondary analysis: *P* = .619)



NRSI, non-randomized studies of intervention; OR, odds ratio; RCT, randomized clinical trials.

Figure 7 of the supplementary data. Secondary analysis for all-cause mortality

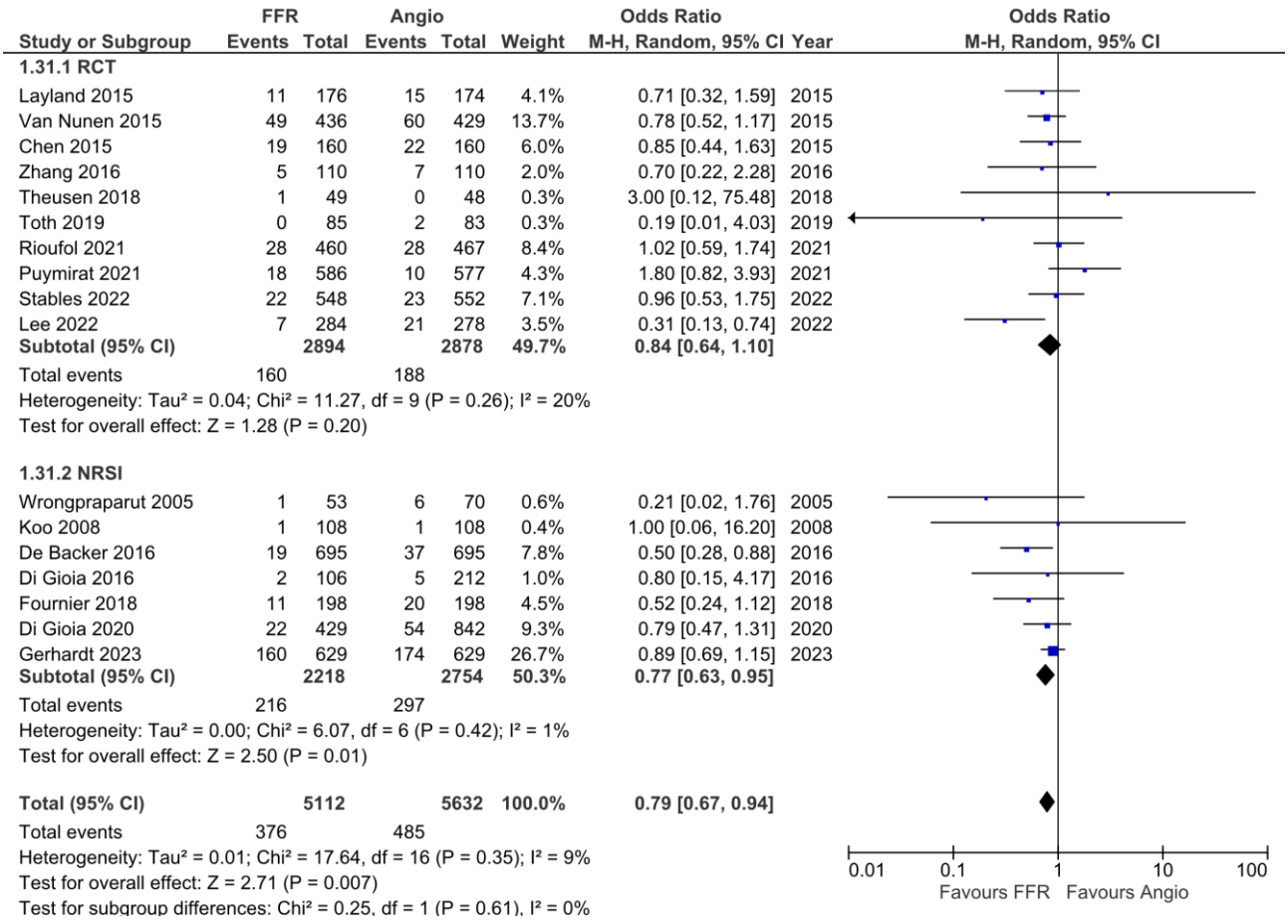


95%CI, 95% confidence intervals; FFR, fractional flow reserve; NRSI, non-randomized studies of intervention; RCT, randomized clinical trials.

The bibliographic references mentioned in this figure correspond to: Puymirat *et al.*[5], Toth *et al.*[10], Thuesen *et al.*[12], Di Gioia et al.[14], Rioufol et al.[15], Stables et al.[16], Wongpraparut [23], Fröhlich *et al.*[29], Layland *et al.*[30], Chen *et al.*[31], Van Nunen *et al.*[33], Di Gioia *et al.*[35], De Backer *et al.*[36], Fournier *et al.*[37], Völz *et al.*[39], Lee *et al.*[43], Gerhardt *et al.*[44], Zhang *et al.*[45].

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 8 of the supplementary data. Secondary analysis for MI

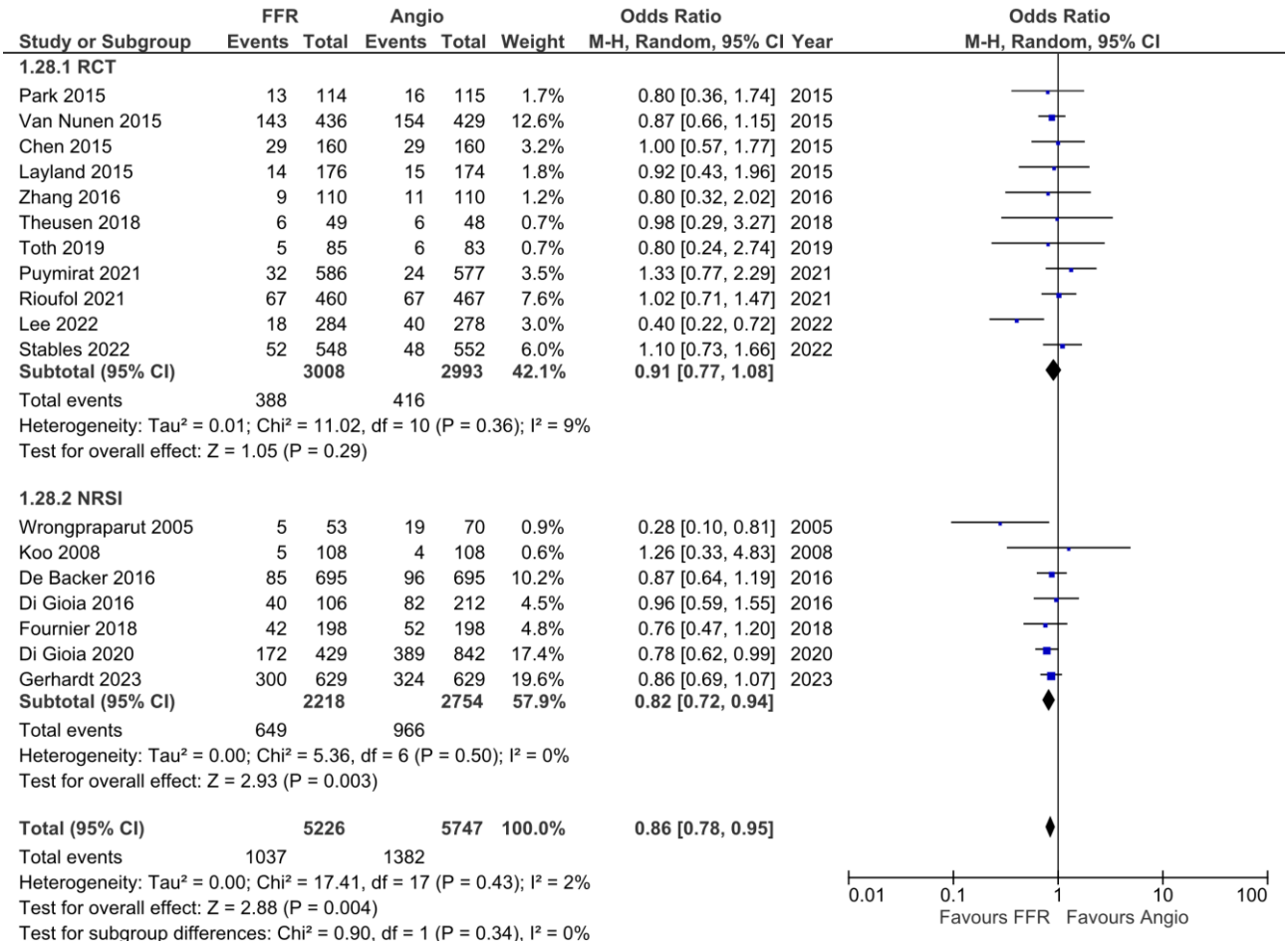


95%CI, 95% confidence intervals; FFR, fractional flow reserve; NRSI, non-randomized studies of intervention; RCT, randomized clinical trials.

The bibliographic references mentioned in this figure correspond to: Puymirat *et al.*[5], Toth *et al.*[10], Thuesen *et al.*[12], Di Gioia *et al.*[14], Rioufol *et al.*[15], Stables *et al.*[16], Wongpraparut *et al.*[23], Koo *et al.*[24], Layland *et al.*[30], Chen *et al.*[31], Van Nunen *et al.*[33], Di Gioia *et al.*[35], De Backer *et al.*[36], Fournier *et al.*[37], Lee *et al.*[43], Gerhardt *et al.*[44], Zhang *et al.*[45.]

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 9 of the supplementary data. Secondary analysis for MACE

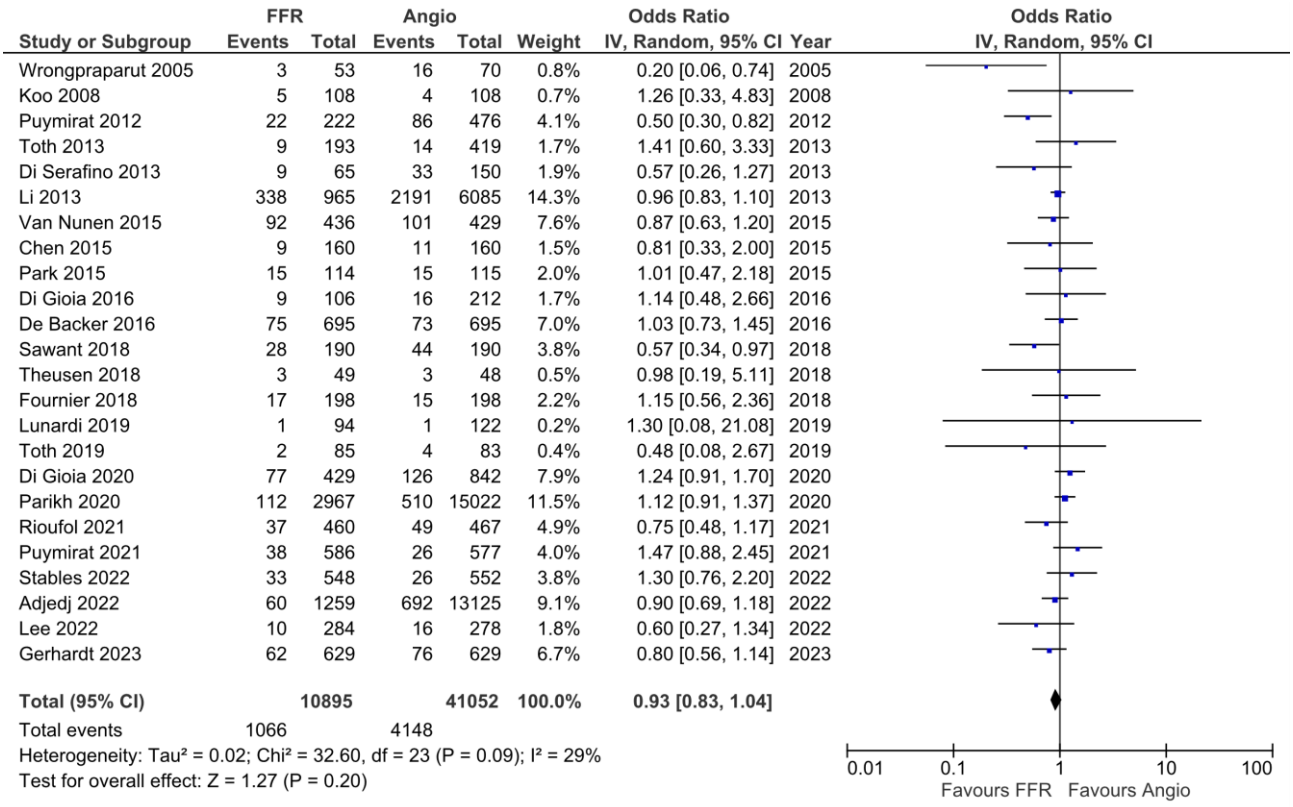


95%CI, 95% confidence intervals; FFR, fractional flow reserve; NRSI, non-randomized studies of intervention; RCT, randomized clinical trials.

The bibliographic references mentioned in this figure correspond to: Puymirat *et al.*[5], Toth *et al.*[10], Thuesen *et al.*[12], Di Gioia *et al.*[14], Rioufol *et al.*[15], Stables *et al.*[16], Wongpraparut *et al.*[23], Layland *et al.*[30], Chen *et al.*[31], Park *et al.*[32], Van Nunen *et al.*[33], Di Gioia *et al.*[35], De Backer *et al.*[36], Fournier *et al.*[37], Lee *et al.*[43], Zhang *et al.*[45].

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 10 of the supplementary data. Forest plot analysis for any revascularization

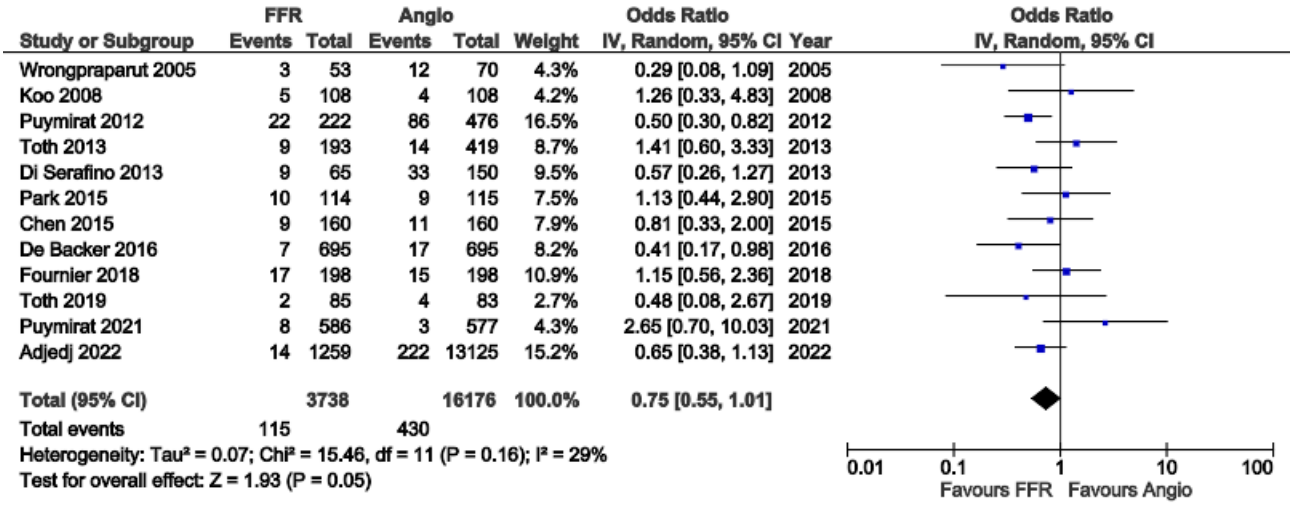


95%CI, confidence intervals; FFR, fractional flow reserve; NRSI, nonrandomized studies of intervention; RCT, randomized clinical trials.

The bibliographic references mentioned in this figure correspond to: Puymirat *et al.*[5], Toth *et al.*[10], Lunardi *et al.*[11], Thuesen *et al.*[12], Sawant*et al.*[13], Di Gioia *et al.*[14],Rioufol *et al.*[15], Stables *et al.*[16], Wongpraparut *et al.*[23], Koo *et al.*[24], Puymirat *et al.*[25], Di Serafino *et al.*[26], Li *et al.* [27],Toth *et al.*[28], Chen *et al.*[31], Park *et al.*[32],Van Nunen *et al.*[33], De Backer *et al.*[36], Fournier *et al.*[37], Parikh *et al.*[38], Adjedj *et al.*[41], Lee *et al.*[43], Gerhardt *et al.*[44].

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 11 of the supplementary data. Forest plot analysis for TVR/TLR (fixed model)

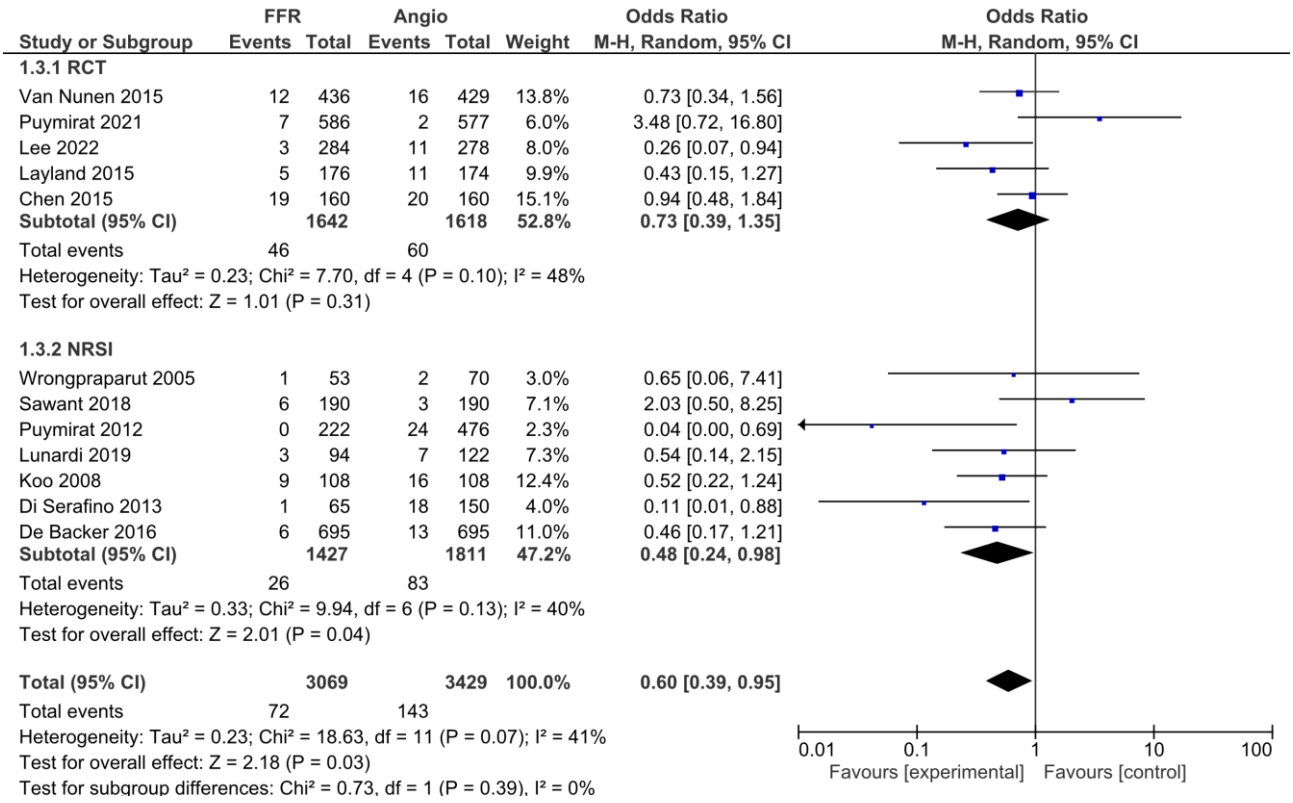


95%CI, confidence intervals; FFR, fractional flow reserve; TLR, target lesion revascularization; TVR, target vessel revascularization**.**

The bibliographic references mentioned in this figure correspond to: Puymirat *et al.*[5], Toth *et al.*[10], Wongpraparut *et al.*[23], Koo *et al.*[24], Puymirat *et al.*[25], Di Serafino *et al.*[26], Toth *et al.*[28], Chen *et al.*[31], Park *et al.*[32], De Backer *et al.*[36], Fournier *et al.*[37].

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.

Figure 12 of the supplementary data. Forest plot analysis for periprocedural MI



95%CI, 95% confidence intervals; FFR, fractional flow reserve; MI, myocardial infarction; NRSI, non-randomized studies of intervention; RCT, randomized clinical trials.

The bibliographic references mentioned in this figure correspond to: Puymirat *et al.*[5], Lunardi *et al.*[11], Sawant *et al.*[13], Wongpraparut *et al.*[23], Koo *et al.*[24], Puymirat *et al.*[25], Di Serafino *et al.*[26], Layland *et al.*[30], Chen *et al.*[31], Van Nunen *et al.*[33], De Backer *et al.*[36], Lee *et al.*[43].

The bibliographic citations included in the supplementary data correspond to the reference list included in the article.