

Meta-analysis of Randomized CTO Trials *PCI vs. MEDICAL Rx*

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Stable angina, PCI with BMS, 1990's



Conventional Wisdom

Treatment Assumptions in CAD Management:

- Patients with symptomatic CAD and chronic angina who have significant coronary stenoses “need” revascularization
- Revascularization is required to improve prognosis
- PCI is less invasive than CABG surgery (i.e., is safer) and, therefore, should be selected

Stable angina, PCI, 2000's



6/99-1/04

Conclusions

- As an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, MI, or other major cardiovascular events when added to optimal medical therapy
- As expected, PCI resulted in better angina relief during most of the follow-up period, but medical therapy was also remarkably effective, with no between-group difference in angina-free status at 5 years

Stable angina, PCI, 2000's

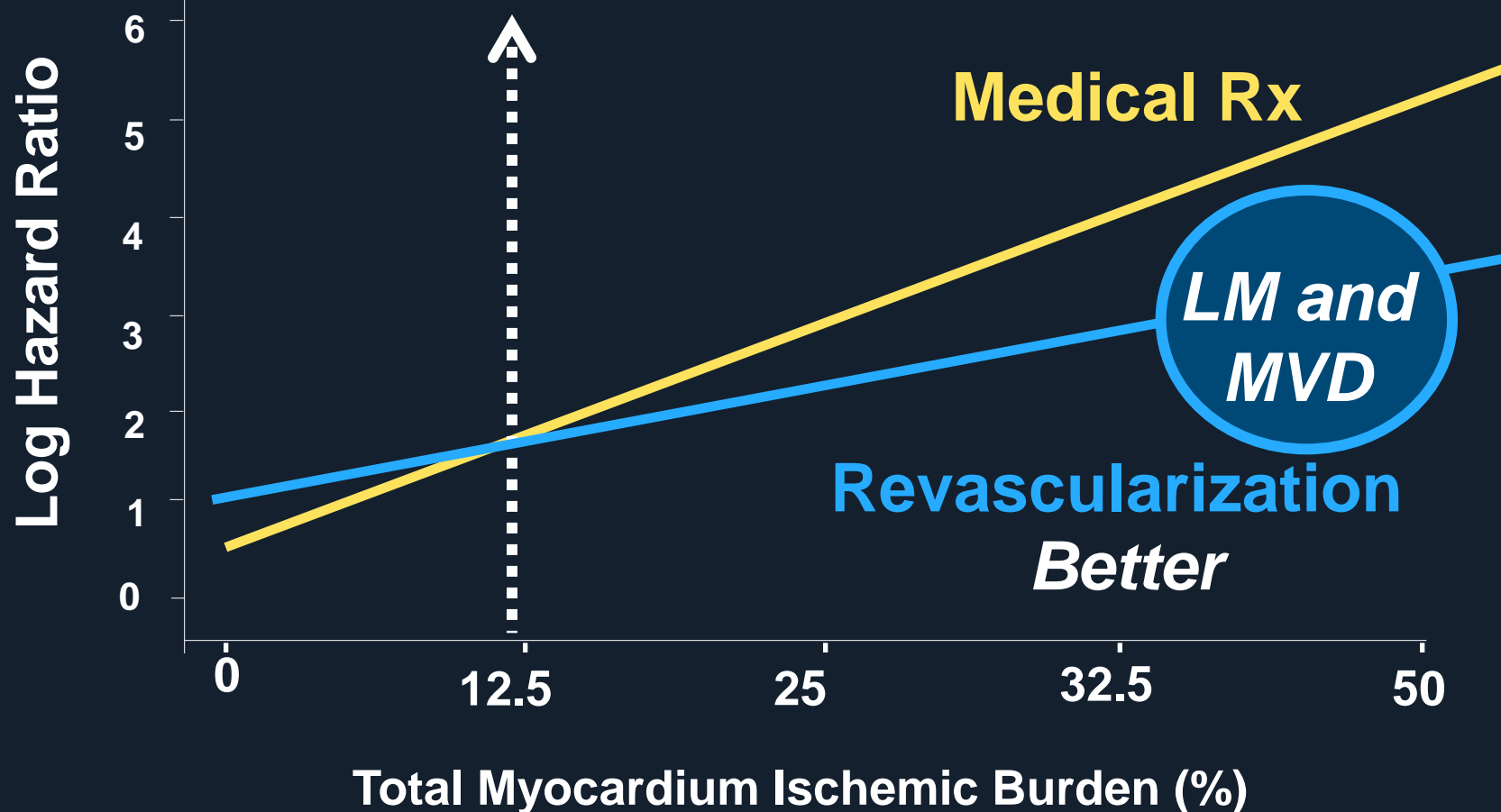


Implications

- Our findings reinforce existing ACC/AHA clinical practice guidelines, which state that PCI can be safely deferred in patients with stable CAD, even in those with extensive, multivessel involvement and inducible ischemia, provided that intensive, multifaceted medical therapy is instituted and maintained
- Optimal medical therapy and aggressive management of multiple treatment targets without initial PCI can be implemented safely in the majority of patients with stable CAD—two-thirds of whom may not require even a first revascularization during long-term follow-up

Survival Benefit of Revascularization

for Large Ischemic Burden >10%



Stable angina, CTO, 2010's

Prognosis, PCI vs. MEDICAL Rx **Is this an important issue?**

CTO is different from stenotic lesion

CTO was excluded from COURAGE

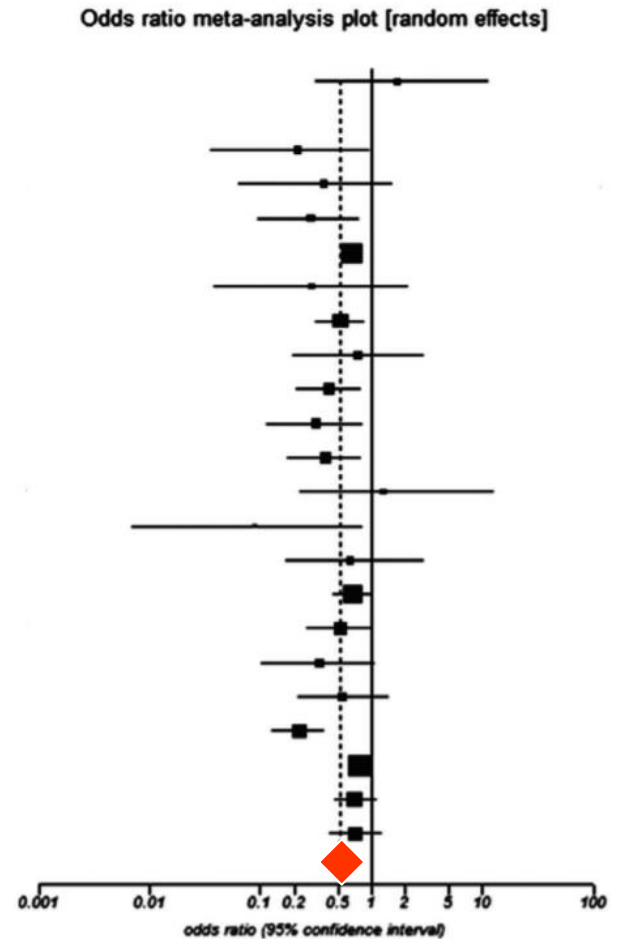
PCI technology has become superior

**Bunch of evidence from observational data
(different from pre-COURAGE situation)**

All-cause Mortality

Meta-analysis of CTO PCI (n=28,685)

Study	PCI Success		PCI Failure		Weight	Odds ratio [95%CI]
	Events	Total	Events	Total		
Finci	5	100	3	100	0.29	1.70 [0.32, 11.23]
Warren	0	26	0	18	0	* (excluded)
Ivanhoe	3	317	7	163	0.94	0.21 [0.04, 0.95]
Angioi	3	93	9	108	0.83	0.37 [0.06, 1.54]
Noguchi	7	134	15	92	1.74	0.28 [0.09, 0.78]
Suero	395	1491	180	514	20.22	0.67 [0.54, 0.84]
Olivari	3	286	3	83	0.47	0.28 [0.04, 2.16]
Hoye	37	567	36	304	4.50	0.52 [0.31, 0.87]
Drozd	7	280	5	149	0.65	0.74 [0.20, 3.01]
Arslan	19	117	37	115	3.21	0.41 [0.21, 0.80]
Aziz	9	377	12	166	1.67	0.31 [0.12, 0.83]
Valenti	17	344	17	142	2.35	0.38 [0.18, 0.83]
Labriole	7	127	2	45	0.29	1.25 [0.23, 12.81]
Chen	2	132	3	20	0.53	0.09 [0.01, 0.84]
Lee	8	251	4	82	0.60	0.64 [0.17, 3.00]
Mehran	74	1226	49	565	6.48	0.68 [0.46, 1.01]
Jolicoeur	22	213	24	133	2.72	0.52 [0.27, 1.03]
Yang	7	87	10	49	1.01	0.34 [0.10, 1.09]
Borgia	19	237	9	65	1.34	0.54 [0.22, 1.44]
Jones	26	582	44	254	6.01	0.22 [0.13, 0.38]
George S	492	10199	259	4240	35.78	0.78 [0.67, 0.91]
Yamamoto	92	1192	35	332	5.19	0.71 [0.47, 1.10]
Kim	56	2045	20	523	3.18	0.71 [0.41, 1.26]
TOTAL	1310	20423	783	8262	100.00	0.52 [0.43, 0.63]



Favors Success Favors Failure

CTO-PCI vs. Medical Rx, PMS matched studies

Coronary artery disease

ORIGINAL ARTICLE

Medical therapy, percutaneous coronary intervention and prognosis in patients with chronic total occlusion

Andrew Ladwir
Angela Hoye^{1,2}



Circulation Journal
Official Journal of the Japanese Circulation Society
<http://www.j-circ.or.jp>

ORIGINAL ARTICLE

Ischemic Heart Disease

Optimal Medical Therapy vs. Percutaneous Coronary Intervention for Patients With Coronary Chronic Total Occlusion

Jeong Ho
Taek Kyu Park,
Sang Ho



European Heart Journal (2015) **36**, 3189–3198
doi:10.1093/eurheartj/ehv450

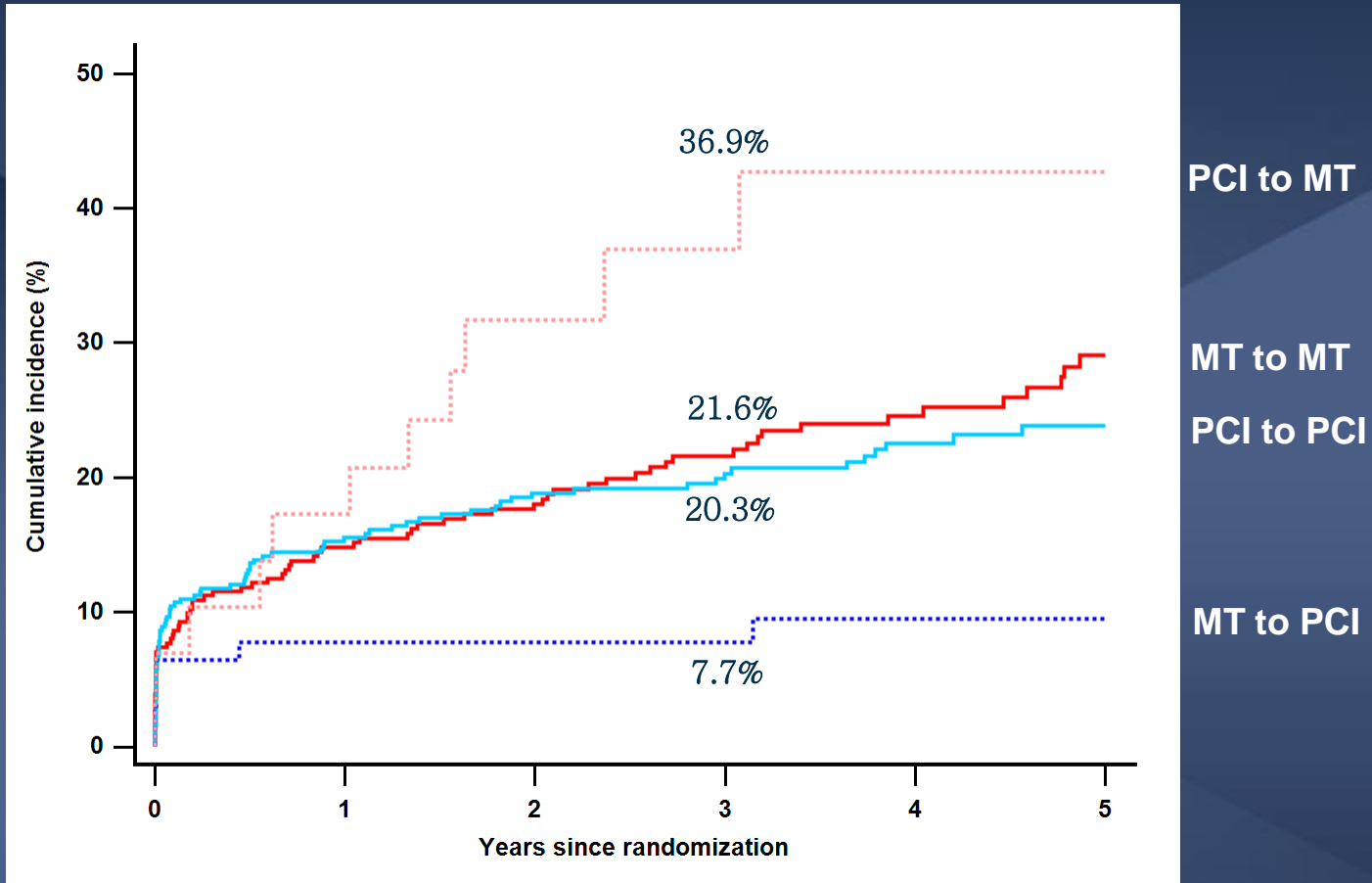
CLINICAL RESEARCH

Interventional cardiology

Management strategies in patients affected by chronic total occlusions: results from the Italian Registry of Chronic Total Occlusions

Salvatore D. Tomasello¹, Marouane Boukhris^{1†}, Simona Giubilato¹, Francesco Marzà¹, Roberto Garbo², Gaetano Contegiacomo³, Antonio Marzocchi⁴, Giampaolo Niccoli⁵, Andrea Gagnor⁶, Ferdinando Varbella⁶, Alessandro Desideri⁷, Paolo Rubartelli⁸, Angelo Cioppa⁹, Giorgio Baralis¹⁰, and Alfredo R. Galassi^{1*}

Subject to Bias, **worse than any other theme**



PCI to MT

MT to MT

PCI to PCI

MT to PCI

PCI to PCI	384	306	254	210	152	98
PCI to MT	29	25	16	13	10	8
MT to PCI	78	70	65	59	46	30
MT to MT	313	257	224	172	125	78

CTO-PCI vs. Medical Rx

5 Published **RCTs**

Percutaneous Intervention for
Concurrent Chronic Total Occlusions
in Patients With STEMI

The EXPLORE Trial



**A randomized multicentre trial to compare
revascularization with optimal medical
therapy for the treatment of chronic
total coronary occlusions**

Letters

RESEARCH CORRESPONDENCE
The IMPACTOR-CTO Trial



**A Randomized Trial to Assess Regional
Left Ventricular Function After Stent
Implantation in Chronic Total Occlusion**

The REVASC Trial



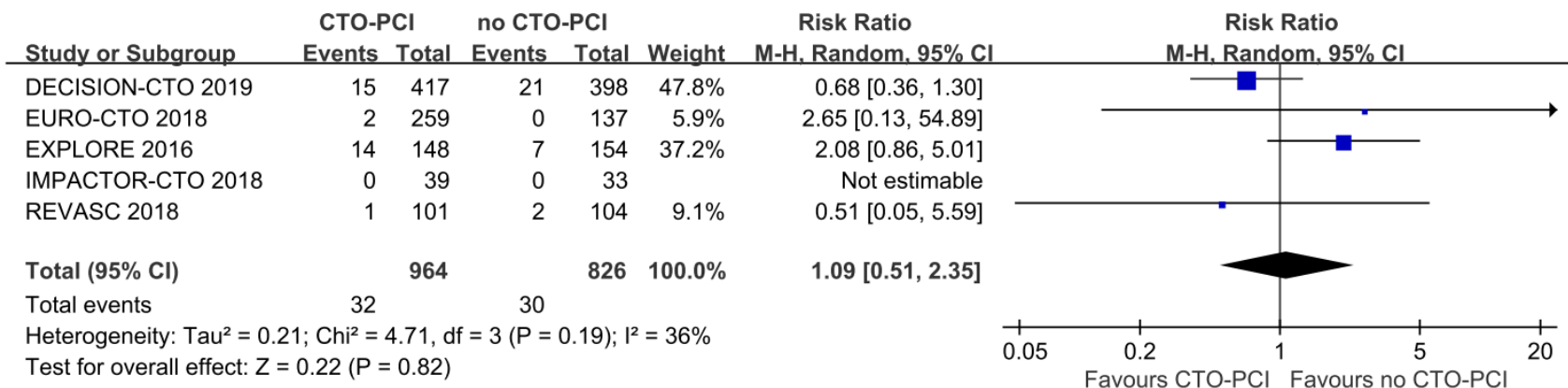
**Randomized Trial Evaluating Percutaneous
Coronary Intervention for the Treatment
of Chronic Total Occlusion**

The DECISION-CTO Trial

Features of RCTs

	Patients		Follow-up, Median, y	Patient subjects	Primary endpoint	Age, Mean, y	Men	DM	JCTO	TVD
	CTO-PCI	No CTO-PCI								
EXPLORE (2016)	148	154	3.9	STEMI c CTO	LVEF/LVEDV at 4 Mo cMR	60	85.1	15.6	2.0	42.7
EURO-CTO (2018)	259	137	1	Single CTO or CTO c MVD (Tx non-CTO lesion >4wks)	Change of SAQ	65.0	84.0	31.6	1.8	22.7
REVASC (2018)	101	104	1	CTO +/- non CTO lesion	Change in SWT at 6Mo cMR	66.5	90.5	31.5	2.0	55.6
IMPACTOR (2018)	39	33	1	Isolated RCA CTO	Change in MIB at 12Mo cMR	56.6	83.3			0
DECISION (2019)	417	397	4.0	CTO +/- non CTO lesion	MACCE	62.5	82.5	33.1	2.1	31.3

Meta-analysis Death



1.1.2 All-cause mortality

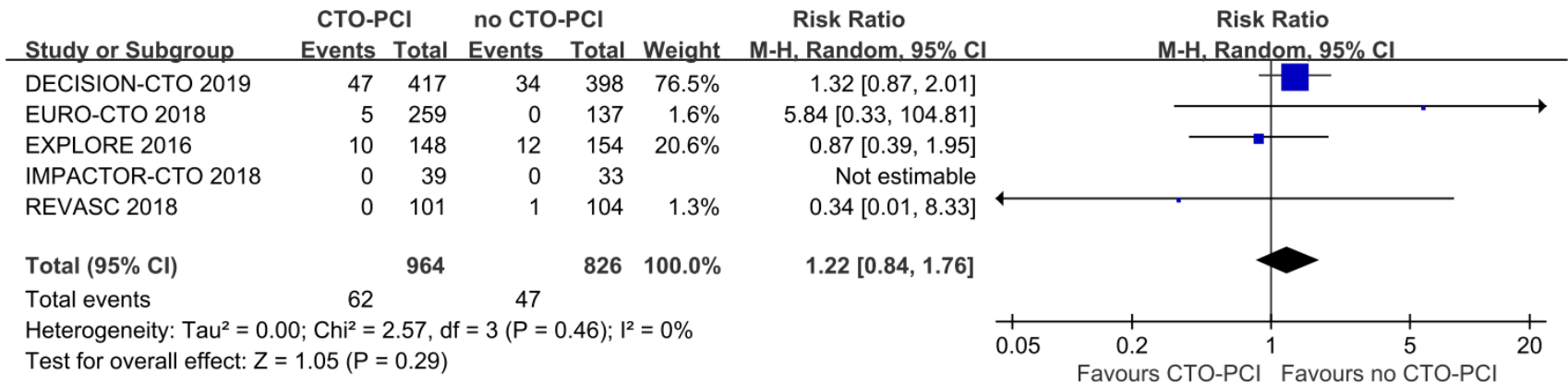
DECISION-CTO 2017	19	417	31	398	92.0%	0.58	[0.34, 1.02]	2017
IMPACTOR-CTO 2018	0	39	0	33		Not estimable		2018
REVASC 2018	1	101	2	104	5.0%	0.51	[0.05, 5.59]	2018
EUROCTO 2018	2	259	0	137	3.1%	2.65	[0.13, 54.89]	2018
Subtotal (95% CI)		816		672	100.0%	0.61	[0.36, 1.04]	
Total events	22		33					
Heterogeneity: Tau ² = 0.00; Chi ² = 0.95, df = 2 (P = 0.62); I ² = 0%								
Test for overall effect: Z = 1.83 (P = 0.07)								

1.1.3 Cardiovascular mortality

EXPLORE 2016	2	259	0	137	15.4%	2.65	[0.13, 54.89]	2016
DECISION-CTO 2017	8	417	14	398	54.0%	0.55	[0.23, 1.29]	2017
EUROCTO 2018	4	150	0	154	16.4%	9.24	[0.50, 170.12]	2018
REVASC 2018	0	101	1	104	14.2%	0.34	[0.01, 8.33]	2018
IMPACTOR-CTO 2018	0	39	0	33		Not estimable		2018
Subtotal (95% CI)		966		826	100.0%	1.04	[0.27, 3.99]	
Total events	14		15					
Heterogeneity: Tau ² = 0.69; Chi ² = 4.49, df = 3 (P = 0.21); I ² = 33%								
Test for overall effect: Z = 0.05 (P = 0.96)								

Meta-analysis

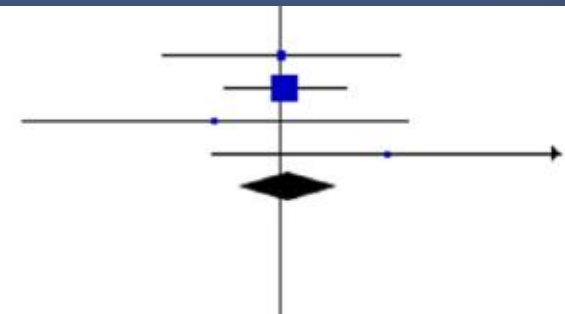
Myocardial Infarction



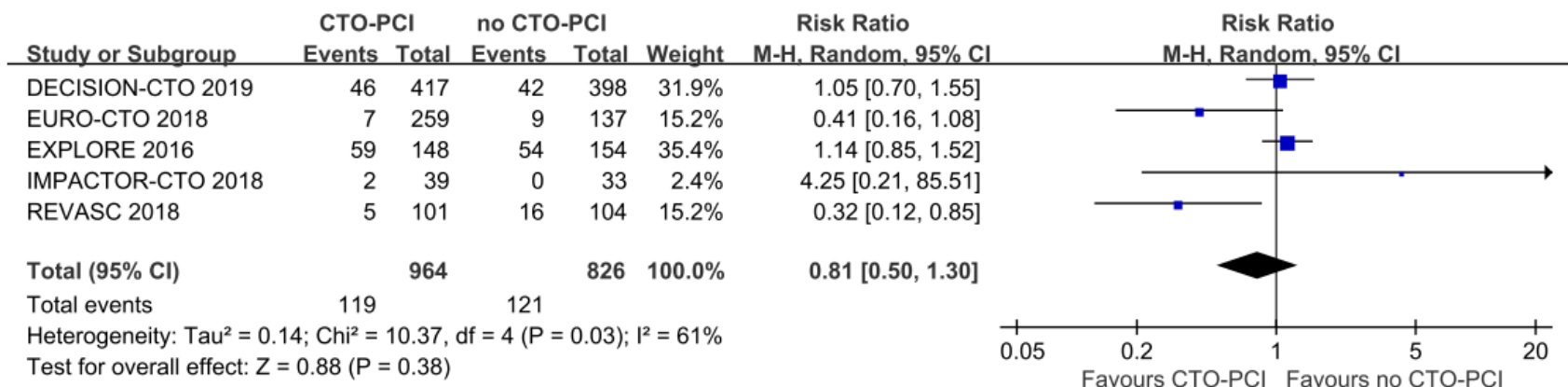
1.1.4 Spontaneous myocardial infarction

EXPLORE 2016	2	150	2	154	17.9%	1.03 [0.15, 7.19]	2016
DECISION-CTO 2017	8	417	7	398	67.3%	1.09 [0.40, 2.98]	2017
REVASC 2018	0	101	1	104	6.7%	0.34 [0.01, 8.33]	2018
EUROCTO 2018	5	259	0	137	8.1%	5.84 [0.33, 104.81]	2018
Subtotal (95% CI)		927		793	100.0%	1.15 [0.50, 2.61]	
Total events	15		10				

Heterogeneity: Tau² = 0.00; Chi² = 1.84, df = 3 (P = 0.61); I² = 0%
 Test for overall effect: Z = 0.32 (P = 0.75)

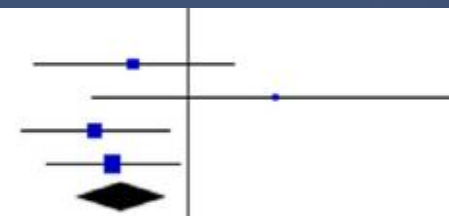


Meta-analysis Repeat Revasc & TVR

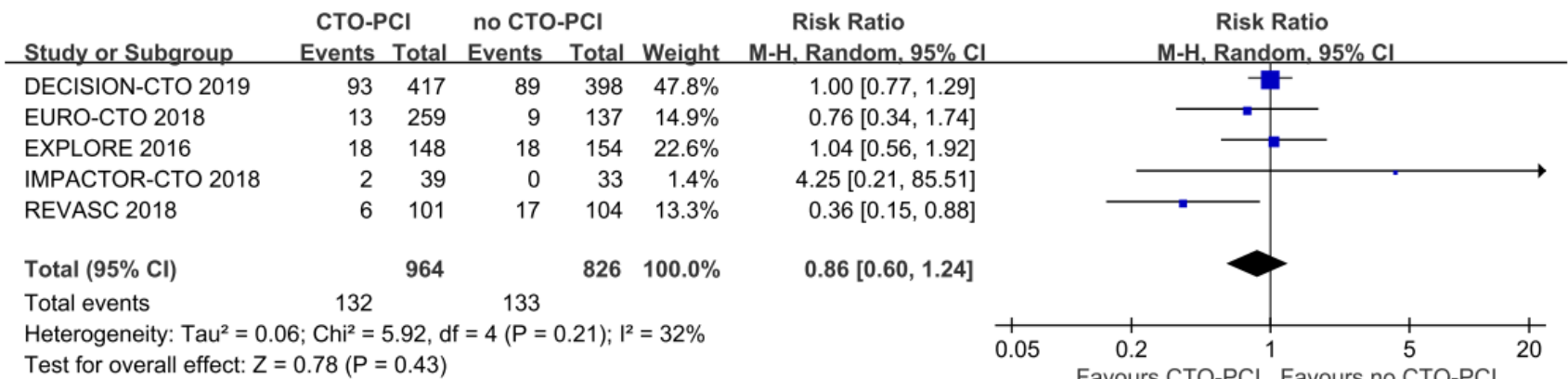


1.1.5 Target vessel revascularization

EXPLORE 2016	2	150	5	154	19.9%	0.41	[0.08, 2.08]	2016
IMPACTOR-CTO 2018	2	39	0	33	6.2%	4.25	[0.21, 85.51]	2018
REVASC 2018	3	101	14	104	33.1%	0.22	[0.07, 0.74]	2018
EUROCTO 2018	5	259	9	137	40.8%	0.29	[0.10, 0.86]	2018
Subtotal (95% CI)		549		428	100.0%	0.34	[0.16, 0.72]	
Total events	12		28					
Heterogeneity: Tau ² = 0.07; Chi ² = 3.35, df = 3 (P = 0.34); I ² = 10%								
Test for overall effect: Z = 2.81 (P = 0.005)								



Meta-analysis MACE



Meta-analysis Problems

- Still small number (1,792)

17.8% incidence of MACE in the MT group, 25% relative risk reduction in the PCI group, 5% type-a error, and 80% power ; 11,895

- Strategies for non-CTOs were relatively consistent, but Failed/Crossovers are problems

Do we know about the prognostic value of CTO-PCI?

We have to look at a CTO lesion working as a part of the whole coronary vessel and heart muscle

In part, Yes

Substantial part, No

Can we prove it?

For the meantime, unlikely
particularly for mortality

But we should not stop

ISCHEMIA-CTO

Native CTO

Myocardial ischemia assessed by nuclear imaging

3 Month OMT

Cohort A; Asymptomatic patients with >10% of myocardial ischemia
Cohort B; Symptomatic patients with >5% of myocardial ischemia

R

CTO-PCI
(N=750)

OMT
(N=750)

Cohort A: Composite endpoint of MACCE (all-cause mortality, stroke, myocardial infarction, clinically driven revascularization*), hospitalization for heart failure or incidence of malignant arrhythmias. (5-Year)
Cohort B; SAQ Quality of Life Assessment after 6 months.

NOBLE-CTO

A randomized registry

≥1 CTO lesion amenable to PCI
Symptoms and/or signs of reversible ischemia

R

Initial conservative Rx
with an option for
crossover after 6 months
(N=1000)

Initial interventional Rx
with medical optimization
(N=1000)

Primary Outcome; All-cause mortality (minimal FU 6-months), QOL assessment

Secondary Outcome; Reduction of myocardial perfusion defect, improvement of LVEF on cMR & Echocardiography

A call for active collaboration **5 Published *RCTs***

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