Complete Revascularization: The Future Mode of Revascularization in STEMI

Alan C. Yeung, MD
Li Ka Shing Professor of Medicine
Chief, Division of Cardiovascular Medicine
Stanford University School of Medicine

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

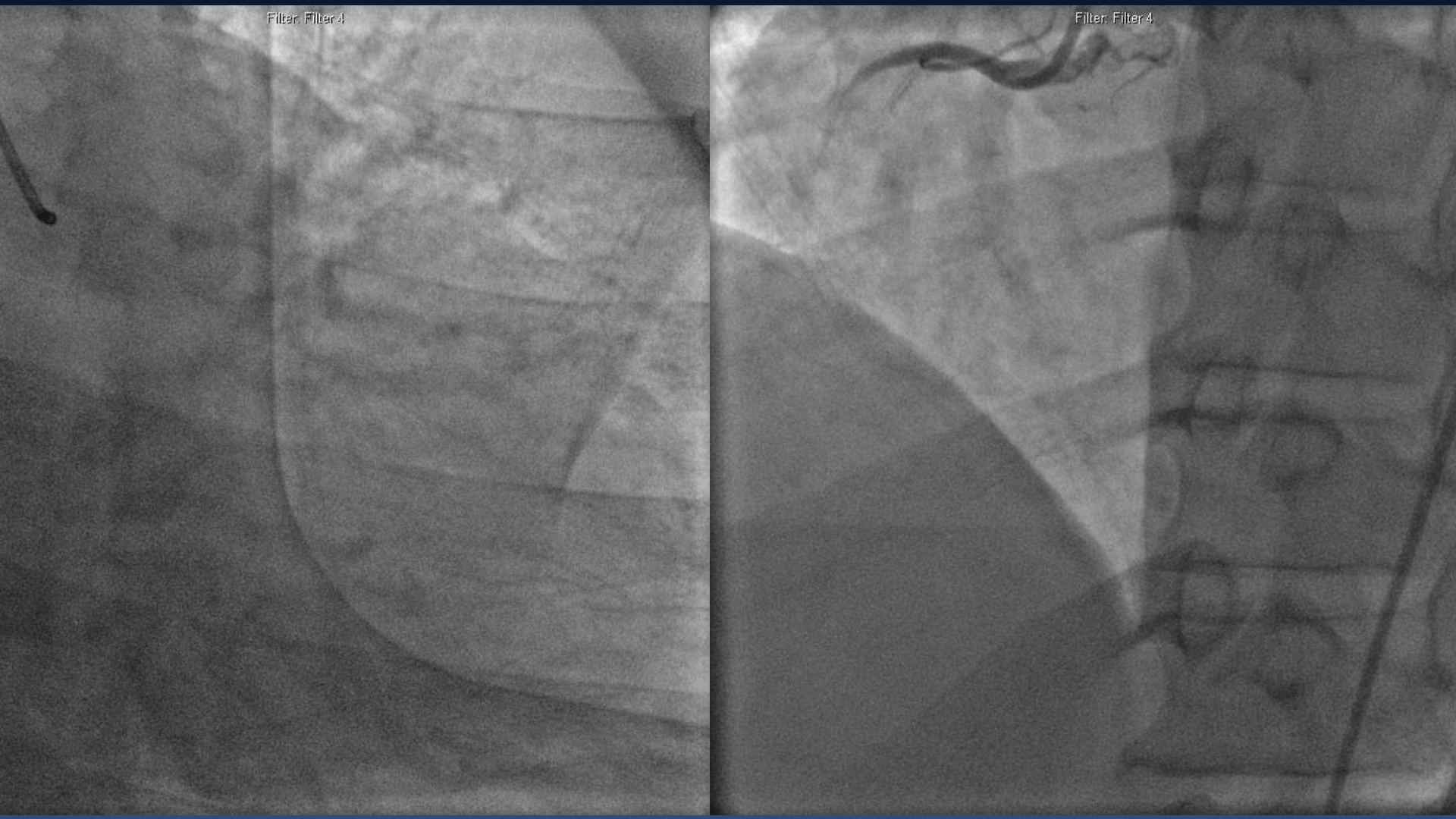
Affiliation/Financial Relationship	Company
• Grant/Research Support	• Edwards Lifesciences, Abbott
• Grant/Scientific Advisory Board	• Medtronic, Abbott
• Executive Physician Council	• Boston Scientific Corp

Multivessel Disease in Patients with STEMI Undergoing Primary PCI

- Is present in 40% - 50% of patients
  - ~10% of patients may have simultaneous plaque ruptures
- Is associated with a worse short-term and late prognosis
- **How to treat is controversial**
  - Multivessel PCI during the index primary PCI
  - Multivessel staged PCI (? optimal timing)
    - Multivessel PCI guidance: Angio vs. FFR guided?
  - Conservative approach (recurrent symptoms or +ETT)

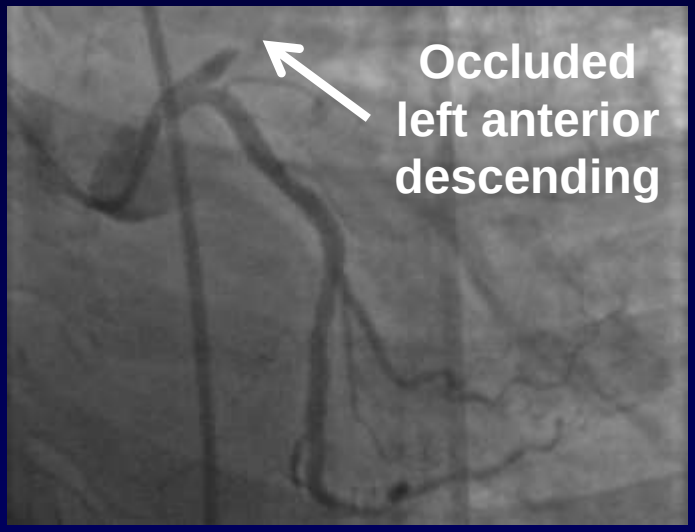
Cannon CP, et al. *N Engl J Med* 2001;344:1879–87

STEMI: *Multivessel vs. Culprit PCI*



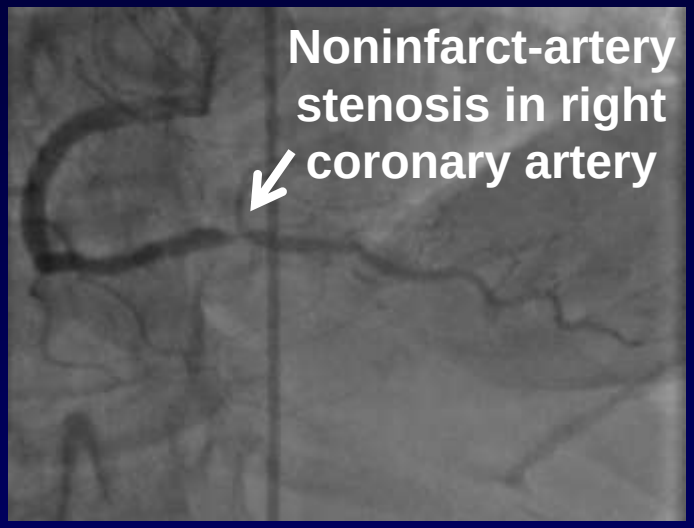
Background

Patient with acute ST elevation myocardial infarction



Infarct-artery PCI

certain benefit

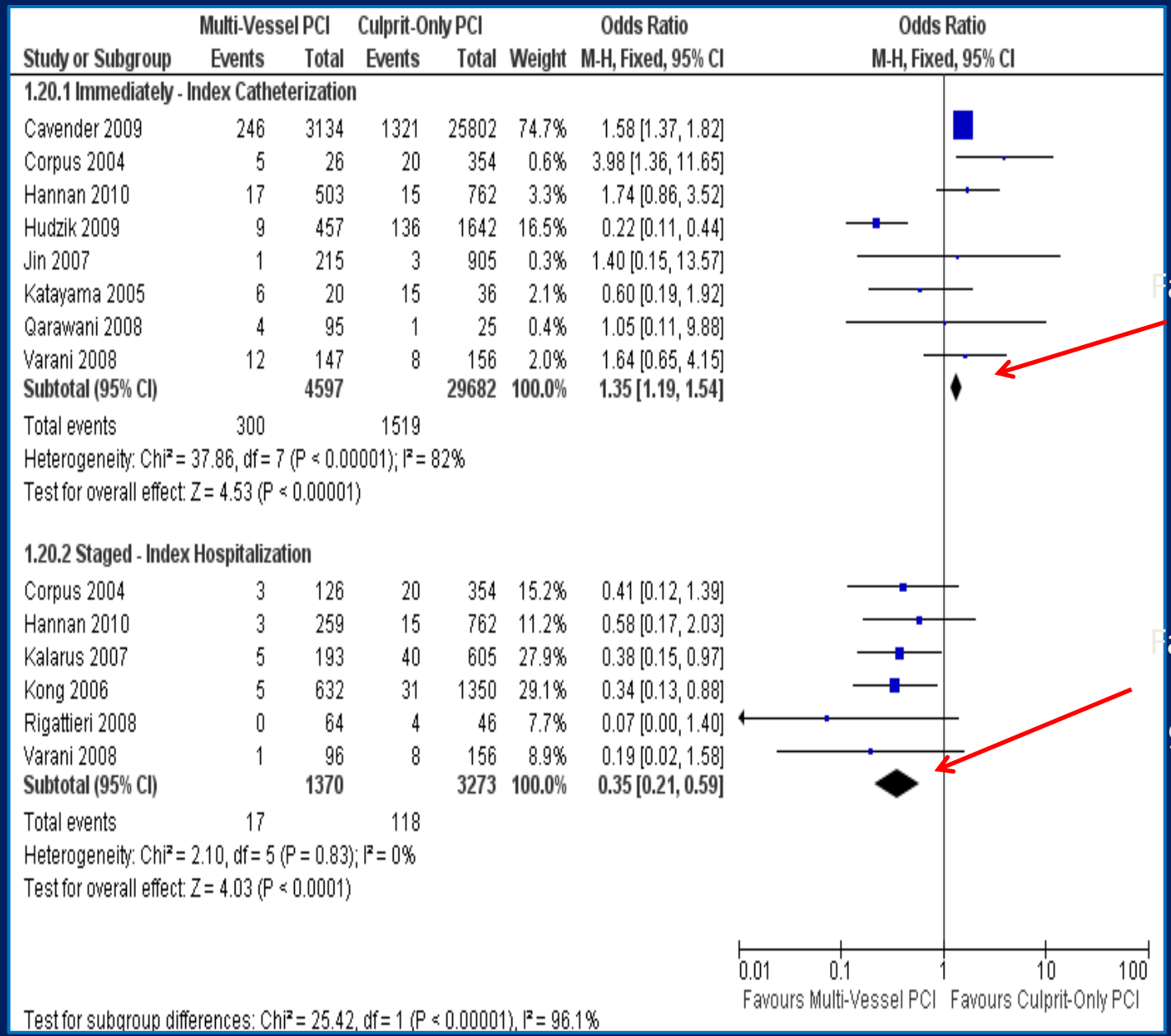


Preventive PCI
during same procedure

uncertain benefit

Large Meta-Analysis of (Mostly) Observational Data: Same sitting PCI harmful, staged PCI possibly beneficial

Bainey K, Am Heart J 2013



N=34,279

Same-Sitting:
Favours culprit-only
HR 1.35
95% CI 1.19-1.54
P<0.00001

Staged
Favours COMPLETE
HR 0.35
95% CI 0.21-0.59
P<0.0001

Preventive Angioplasty in Acute Myocardial Infarction (PRAMI)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Preventive Angioplasty in Myocardial Infarction

David S. Wald, M.D., Joan K. Morris, Ph.D., Nicholas J. Wald, F.R.S., Alexander J. Chase, M.B., B.S., Ph.D., Richard J. Edwards, M.D., Liam O. Hughes, M.D., Colin Berry, M.B., Ch.B., Ph.D., and Keith G. Oldroyd, M.D., for the PRAMI Investigators*

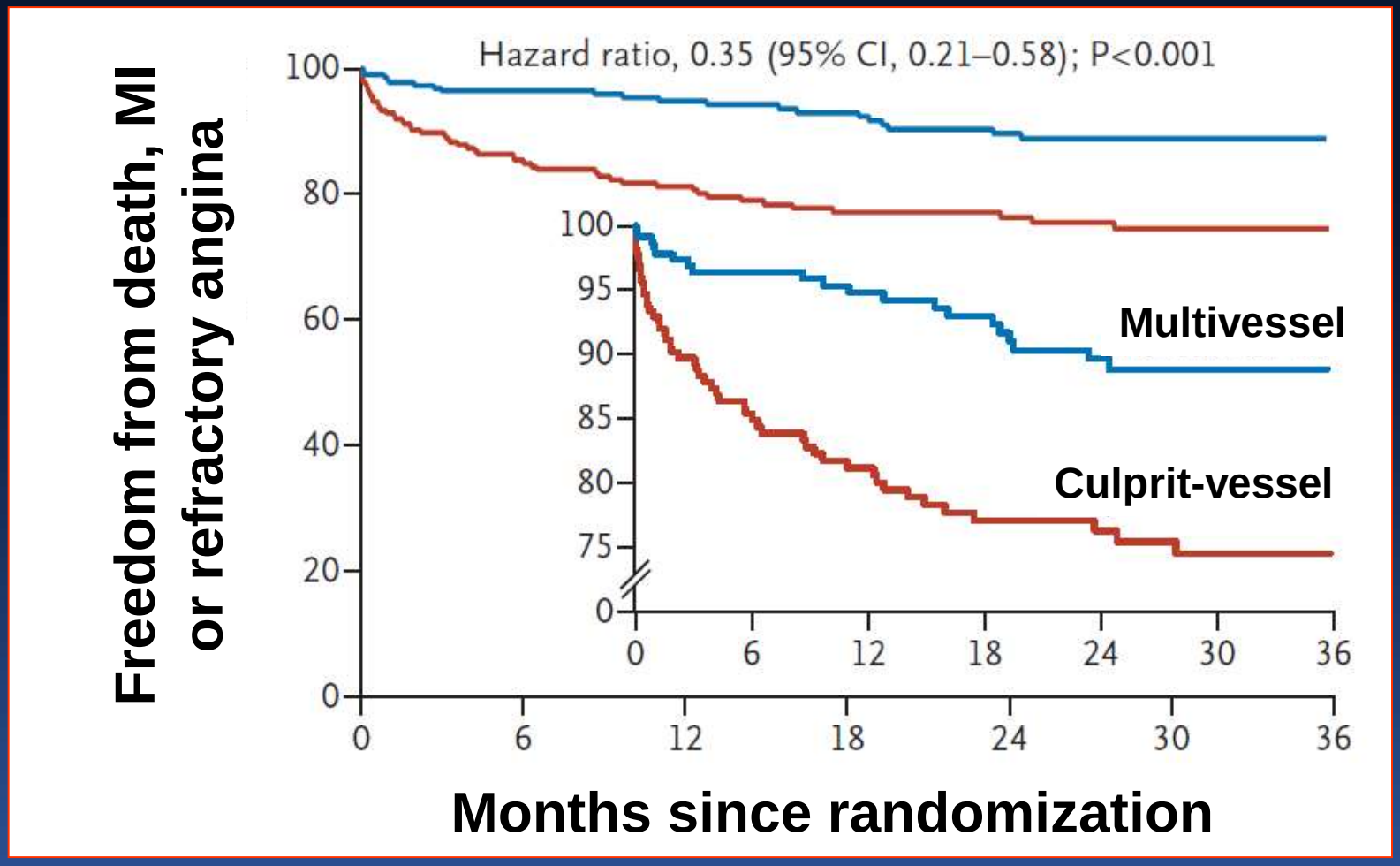
ABSTRACT

BACKGROUND

In acute ST-segment elevation myocardial infarction (STEMI), the use of percutaneous

Wald DS et al. N Engl J Med 2013;369:1115-1123

PRAMI: *Non-Infarct PCI during STEMI*



Wald DS et al. N Engl J Med 2013;369:1115-1123

PRAMI Trial

Variable	Preventive PCI (N=234)	Medical Rx (N=231)	HR (95% CI)	P value
Cardiac Death, MI, RFA	21	53	0.35 (0.21–0.58	<0·001
Cardiac death or MI	11	27	0.36 (0.18–0.73	0.004
All Death	12	16		NS
Cardiac Death	4	11	0.34 (0.11–0.73)	NS
RFA	12	30	0.35 (0.18–	<0.00

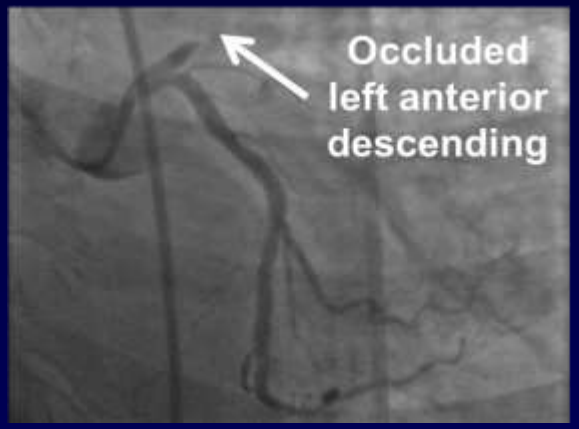
Wald NEJM 2013

PRAMI Study: Effect of Adding only 3 MI's to Preventive Angioplasty Group

	Preventive PCI N=234	Medical Therapy N=231	P value
PRAMI	7	20	0.007
PRAMI+3	10	20	NS

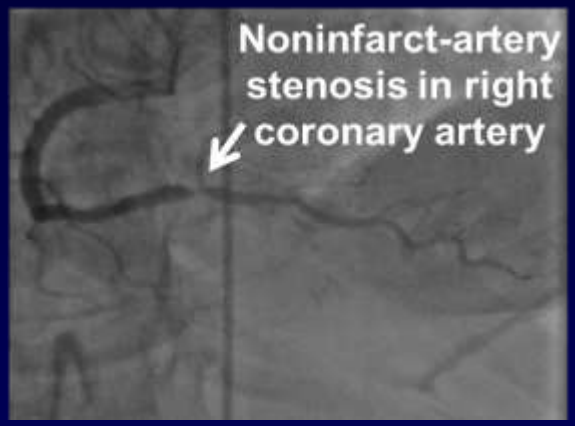
Post PRAMI

Patient with acute ST elevation myocardial infarction



Infarct-artery PCI

certain benefit



Preventive PCI
during same procedure

substantial

~~**uncertain benefit**~~

65% ↓ cardiac death / nonfatal MI / refractory angina

64% ↓ cardiac death / nonfatal MI

Guideline Summary

2013 US Guideline	
III: Harm	**PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise (Level of Evidence B).**
2014 ESC Guideline	
IIb	**Immediate revascularization of significant non-culprit lesions during the same procedure as primary PCI of the culprit vessel may be considered in selected patients (Level of Evidence B)**

O'Gara PT et al. *Circulation* 2013;CIR.0b013e3182742cf6.citation
Windecker S, et al. Eur Heart J 2014;35:2541–2619

Managing multi-vessel disease detected at P-PCI for STEMI:

The **C**omplete **v**ersus **L**esion-only **PR**imary PCI **T**rial (**CvLPRIT**)

Anthony H Gershlick

University Hospitals of Leicester

United Kingdom

On behalf of the CvLPRIT Investigators

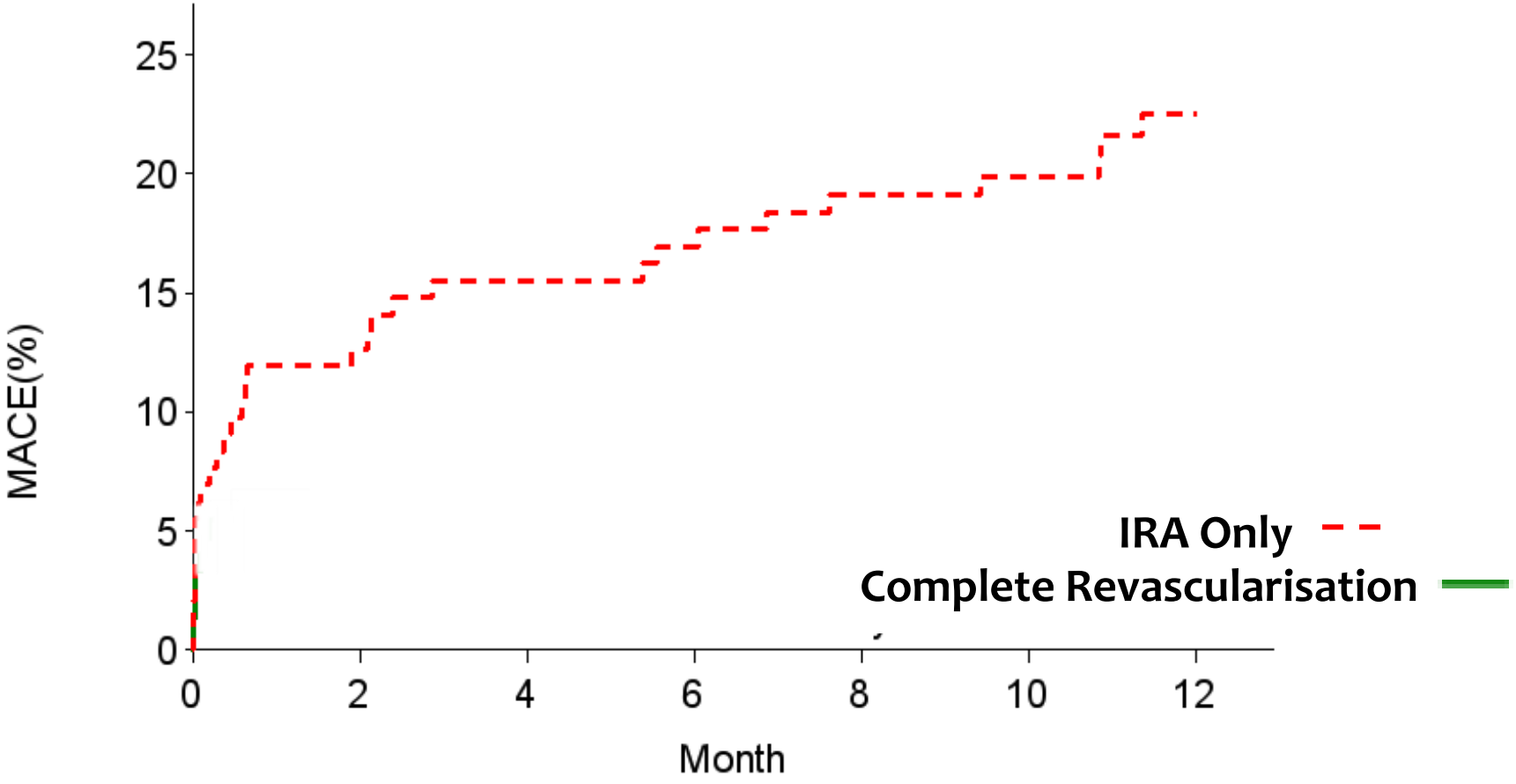
Jamal Nasir Khan, Damian J Kelly, John P. Greenwood, Thiagarajah Sasikaran, Nick Curzen ,Daniel J Blackman, Miles Dalby, Kathryn L Fairbrother ,Winston Banya, Duolao Wang, Marcus Flather, Simon L Hetherington, Andrew D Kelion , Suneel Talwar, Mark Gunning, Roger Hall , Howard Swanton ,Gerry P McCann

British Heart Foundation

NHS National Institute for Health Research

Results 1: Percent MACE at 12 months

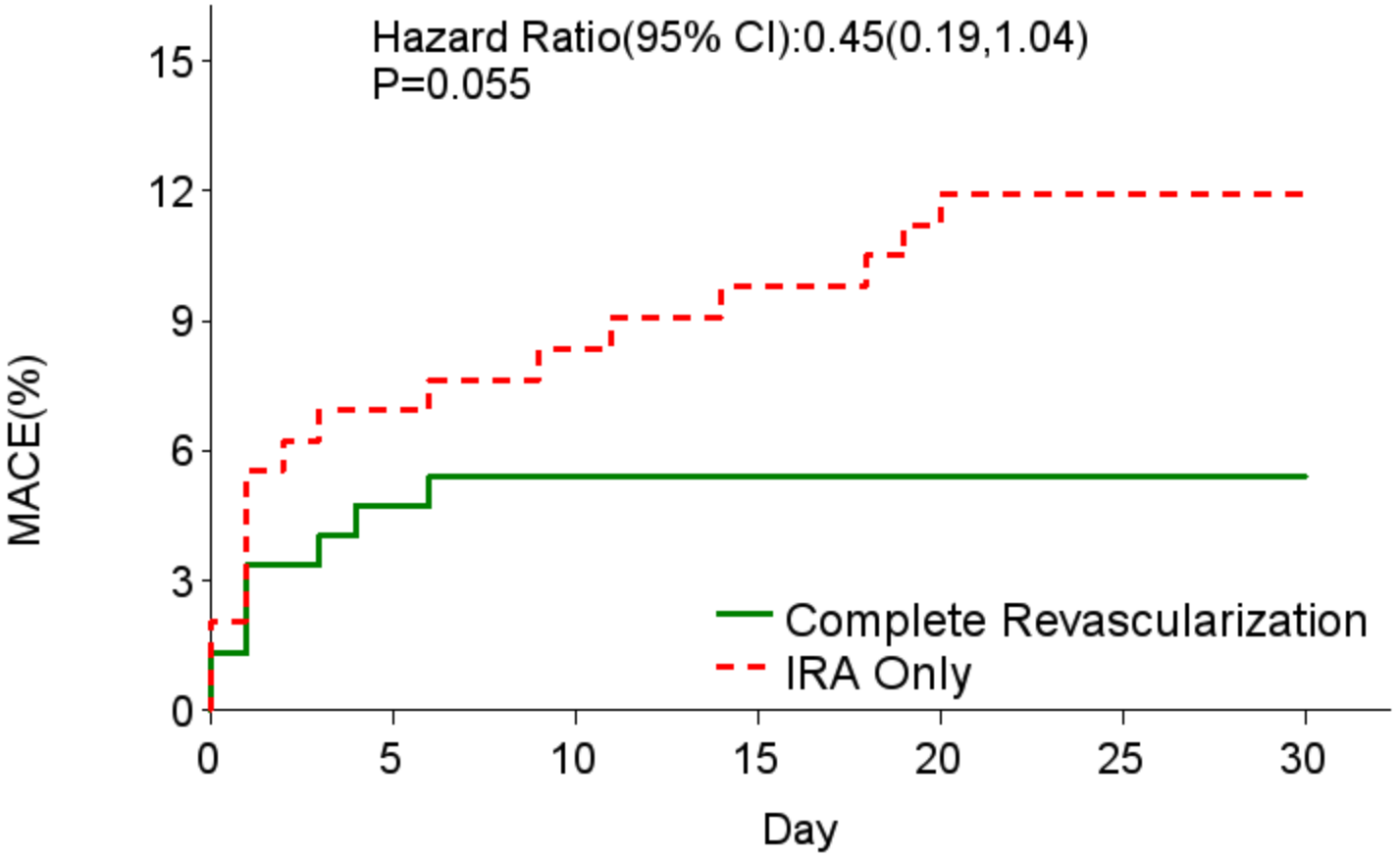
The primary endpoint composite of total mortality, recurrent MI, heart failure and ischaemia-driven revascularisation at 12 months



Number at risk:

Complete:150	131	129	128	125	108	73
IRA Only:146	122	118	116	111	98	68

MACE to 30 days



Number at risk:						
Complete:150	136	133	133	133	133	133
IRA Only:146	131	128	126	124	123	123

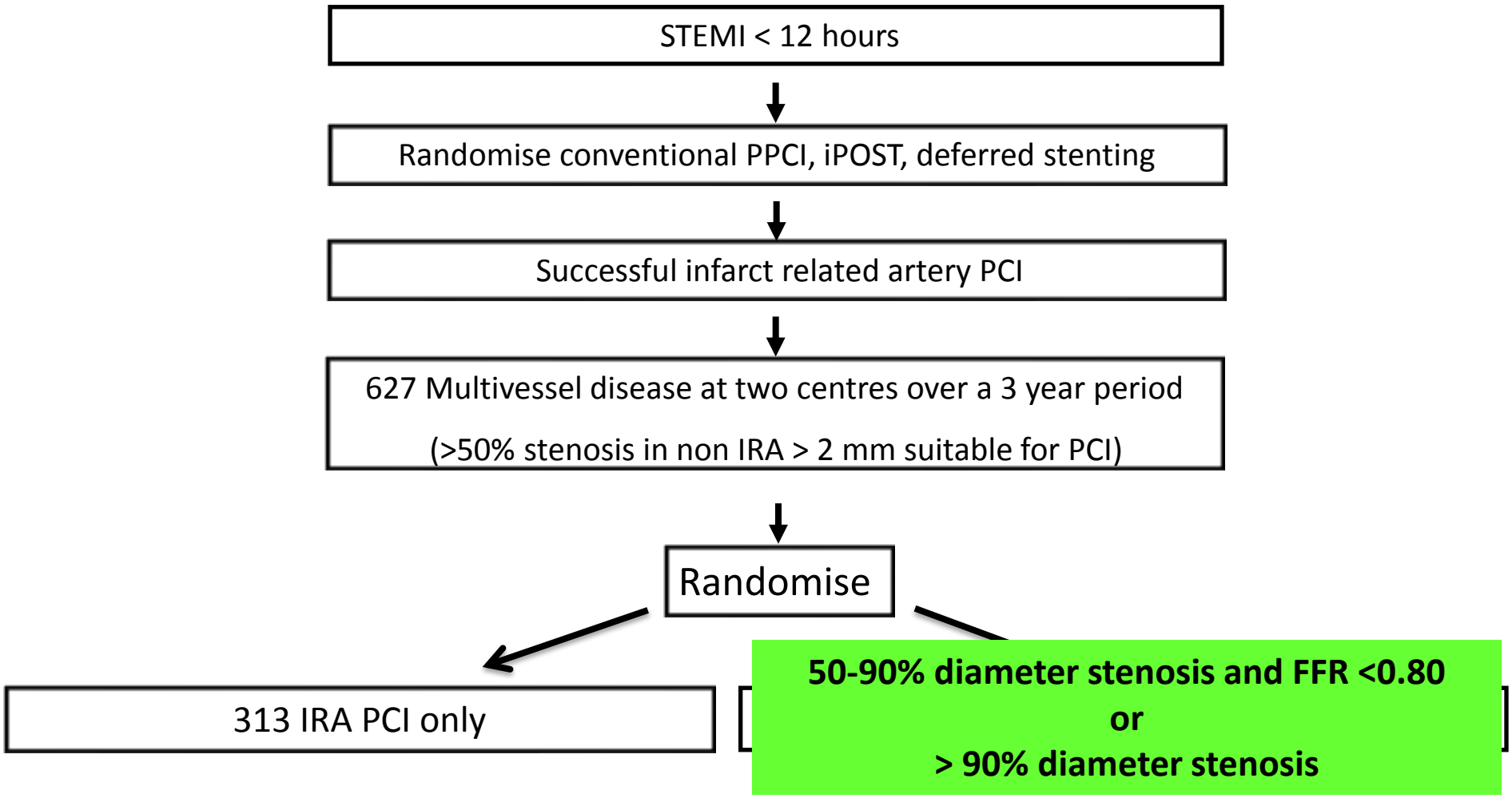
Cvlprit Trial

Variable	Medical Rx (N=146)	PCI (N=150)	HR (95% CI)	P value
MACE N= (%)	31 (21.2)	15 (10.0)	0.45 (0.24, 0.84)	<0·001
All-cause mortality	6 (4.1)	2 (1.3)	0.32 (0.06, 1.60)	0.14
Recurrent MI	4 (2.7)	2 (1.3)	0.48 (0.09, 2.62)	0.39
Heart failure	9 (6.2)	4 (2.7)	0.43	0.14

Gerschlick A. JACC 2017

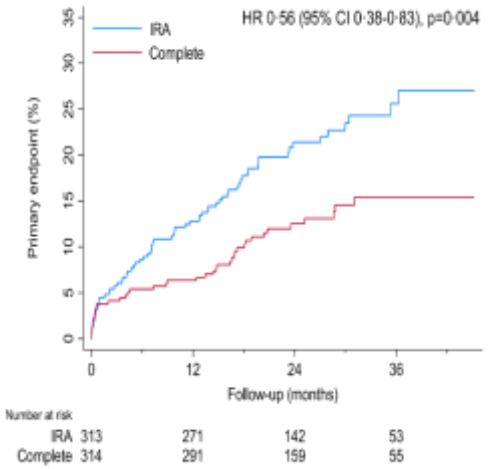
DANAMI3-TRIAL program[1]

[1] Høfsten *et al. Am Heart J 2015*

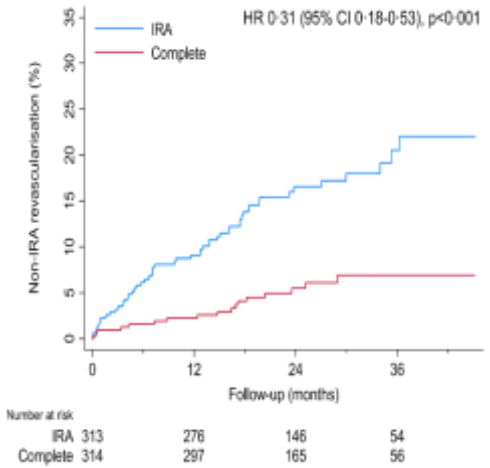


DANAMI3-PRIMULTI

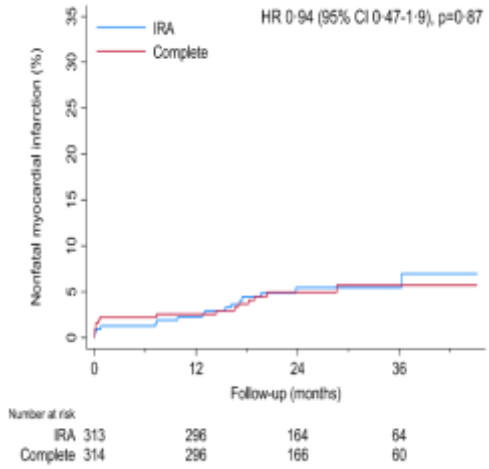
Individual components of primary endpoint



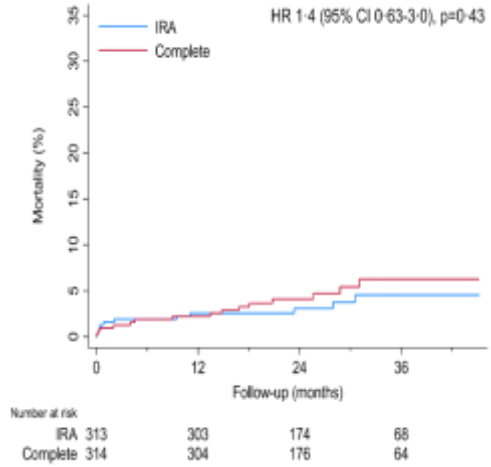
Composite



Revascularisation



Non fatal MI



All cause death

DANAMI3-PRIMULTI

DANAMI 3 – PRIMULTI Trial: FFR–Guided PCI reduced revasc with no difference in death or MI

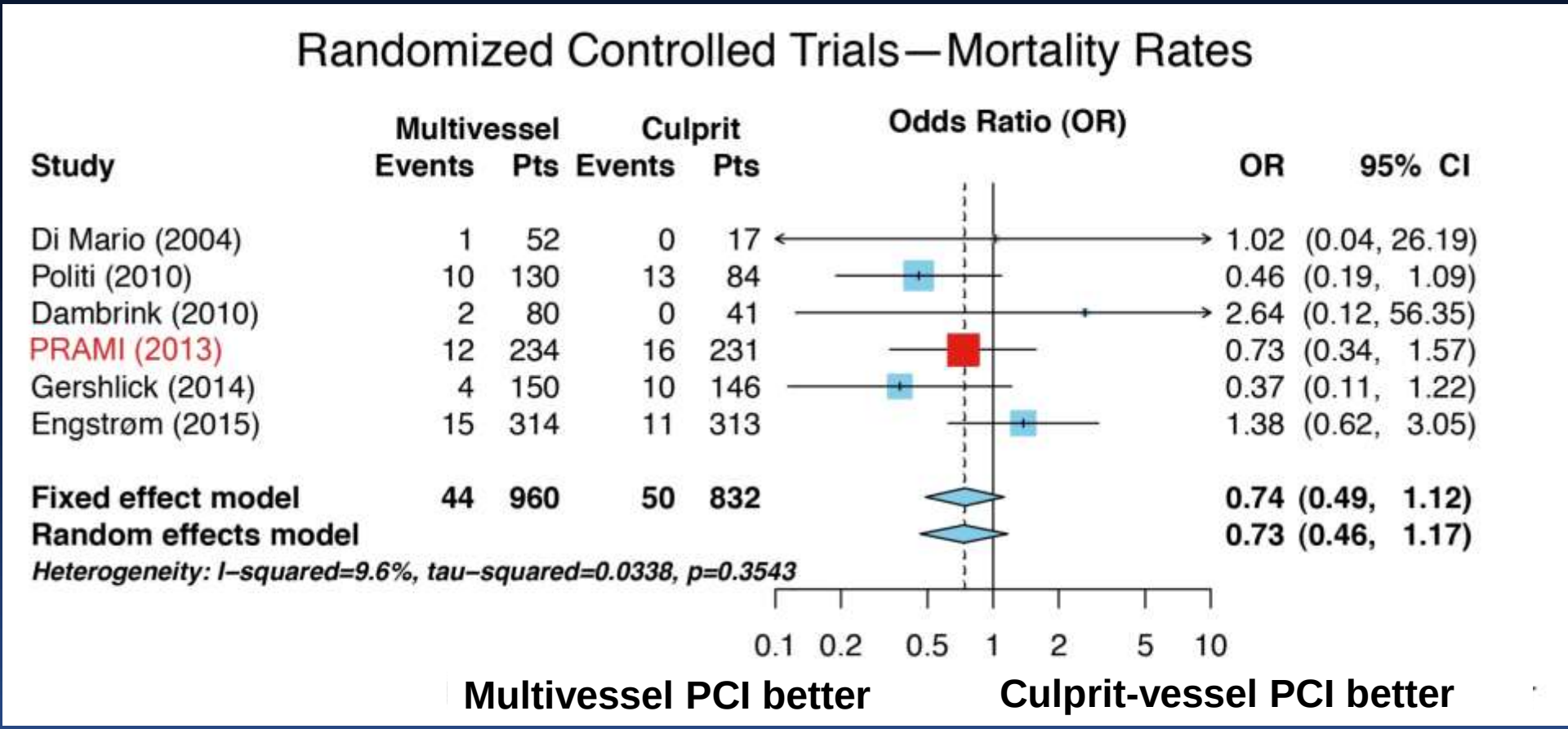
	IRA only (n = 313)	Complete revascularisation (n = 314)	HR [95% CI]	p
Primary endpoint	68 (22%)	40 (13%)	0·56 [0·38 – 0·83]	0·004
All-cause death	11 (4%)	15 (5%)	1·4 [0·63 – 3·0]	0·43
Nonfatal MI	16 (5%)	15 (5%)	0·94 [0·47 – 1·9]	0·87
Ischemia-driven revascularisation*	52 (17%)	17 (5%)	0·31 [0·18 – 0·53]	<0·001

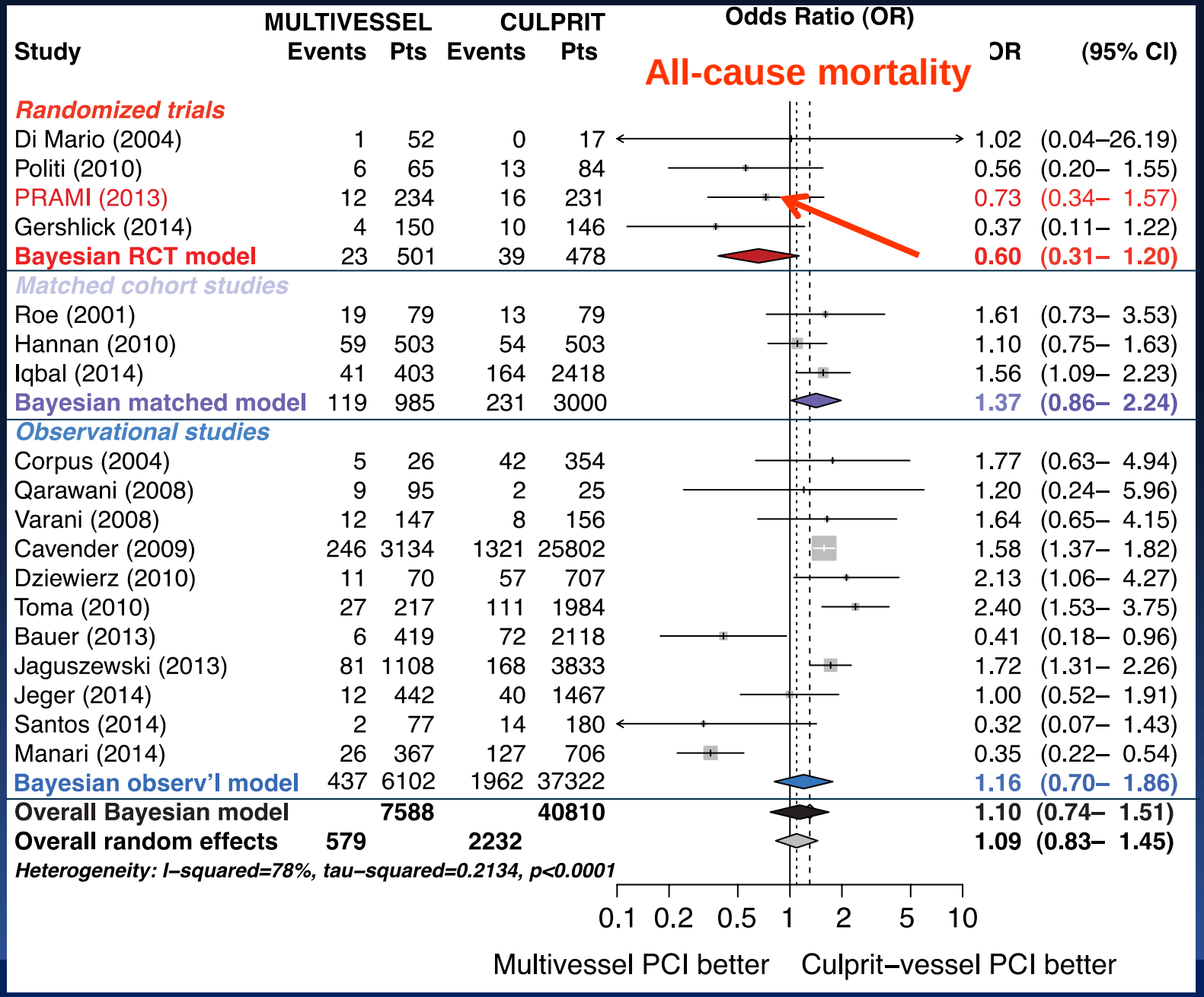
Engstrøm, Lancet 2015.

Contemporary RCTs of Culprit Only PCI vs Complete Revascularisation in Patients undergoing PPCI for STEMI

	PRAMI (n=465)	CvLPRIT (n=296)	PRIMULTI (n=627)
No patients per center per year	19	23	105
Lesion criteria	> 50% DS	> 70% DS or > 50% DS in 2 views	> 50% DS and FFR <0.80 or > 90% DS
Strategy for non-IRA lesions	Immediate	Immediate or staged within index admission	Staged within index admission
Primary endpoint	D/MI/refractory ischaemia	D/MI/HF/isch D R	D/MI/isch D R
Power (80%)	20% reduced to 14% (30% Rx effect)	37% reduced to 22% (40% Rx effect)	18% reduced to 13% (30% Rx effect)
Result	23% reduced to 9% (65% Rx effect)	21% reduced to 10% (55% Rx effect)	22% reduced to 13% (44% Rx effect)

PRAMI and Other RCTs





Bittl JA et al. Cathet Cardiovasc Interv 2015;86:Suppl 1;S15-22

Catheterization and Cardiovascular Interventions 86:S15–S22 (2015)

Outcomes after Multivessel or Culprit-Vessel Intervention for ST-Elevation Myocardial Infarction in Patients With Multivessel Coronary Disease: A Bayesian Cross-Design Meta-Analysis

John A. Bittl,[1*] MD, Jacqueline E. Tamis-Holland,[2] MD, Christopher D. Lang,[3] MD, and Yulei He,[4] PhD

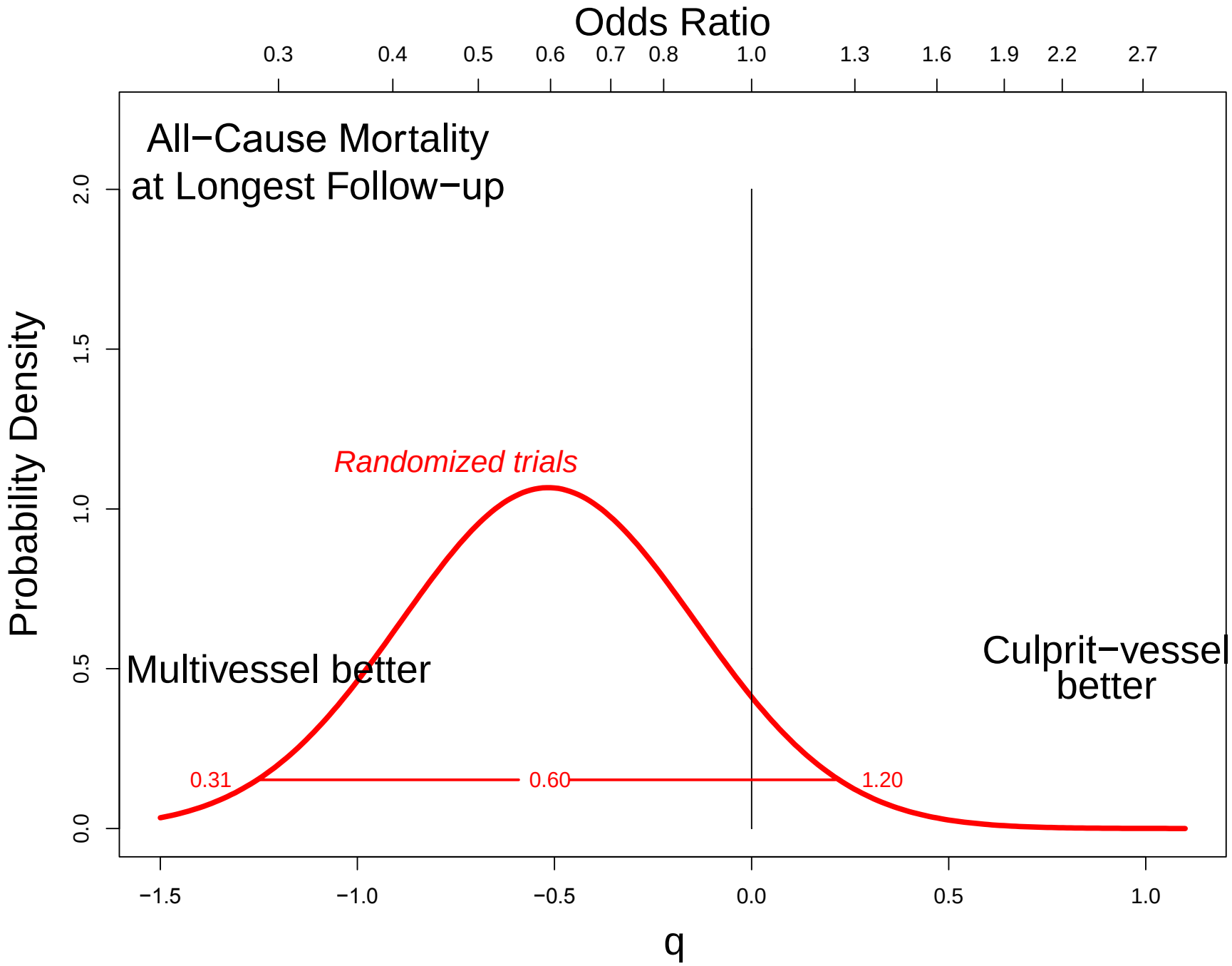
Introduction: During primary percutaneous coronary intervention (PCI), patients with ST-elevation myocardial infarction (STEMI) and multivessel coronary disease can undergo either multivessel intervention (MVI) or culprit-vessel intervention (CVI) only. Background: Randomized controlled trials (RCTs) support the use of MVI, but cohort studies support the use of CVI. Methods: We developed Bayesian models that incorporated parameters for study type and study outcome after MVI or CVI. Results: A total of 18 studies (4 RCTs, 3 matched cohort studies, and 11 unmatched observational studies) enrolled 48,398 patients with STEMI and multivessel CAD and reported outcomes after MVI or CVI-only at the time of primary PCI. Using a Bayesian hierarchical model, we found that the point estimates replicated previously reported trends, but the wide Bayesian credible intervals (BCI) excluded any plausible mortality difference

Evidence Synthesis

Bayesian cross-design meta-analysis

- **Allows studies of different designs to be analyzed together**
- **Generalizes results for the STEMI population by including evidence from RCTs and observational studies**
- **Identifies the true treatment effect of multivessel vs. culprit-vessel PCI, which is conditional on both study outcome and study design**

Spiegelhalter, Abrams, Miles: Bayesian Approaches to Clinical Trials and Health-Care. Wiley, 2004.


Odds Ratio
0.3
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0.6
0.7
0.8
1.0
1.3
1.6
1.9
2.2
2.7
All−Cause Mortality
at Longest Follow−up
Probability Density
2.0
1.5
1.0
0.5
0.0
Randomized trials
Multivessel better
Culprit−vessel
better
0.31
0.60
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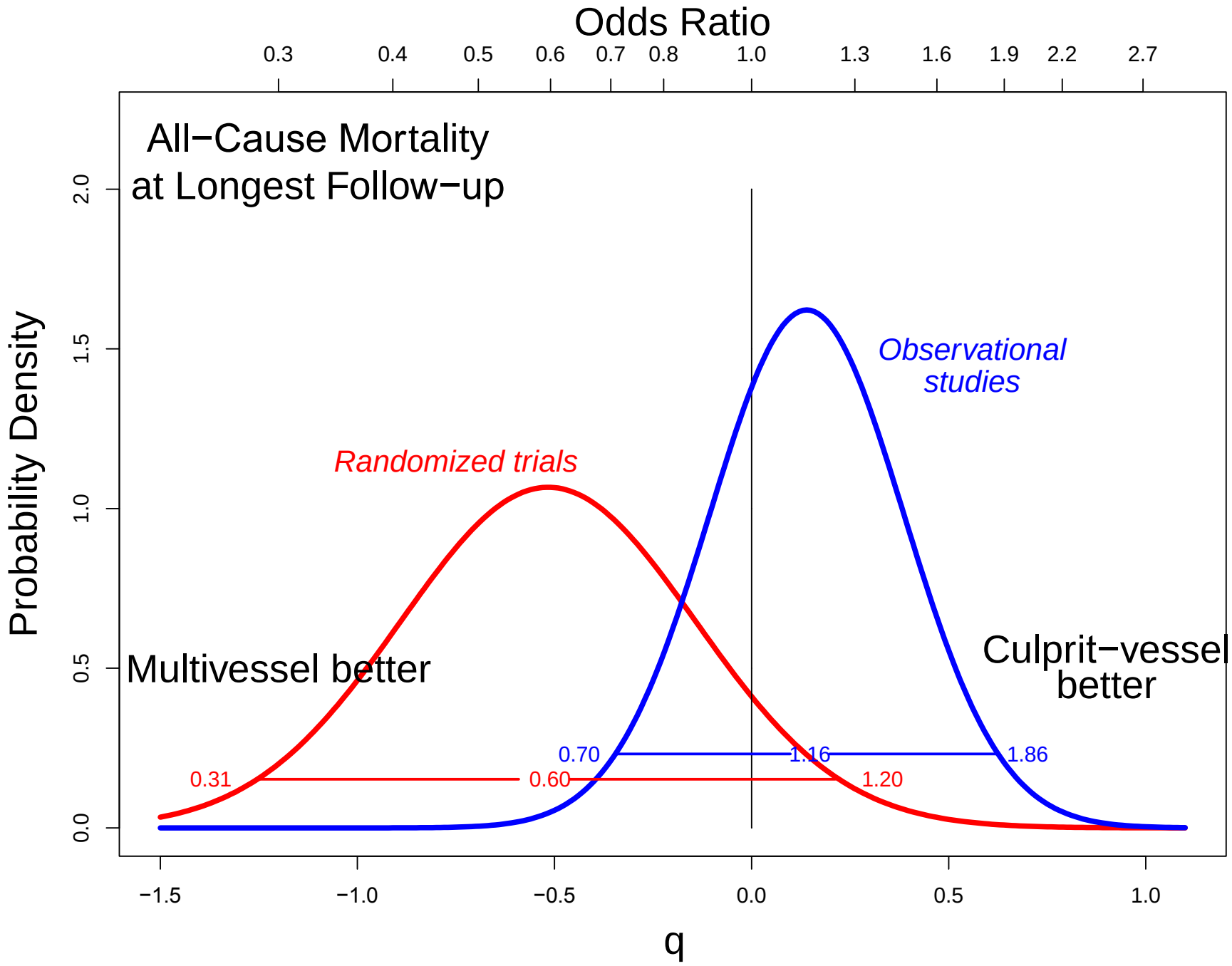
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0.0
Observational
studies
Randomized trials
Multivessel better
Culprit−vessel
better
0.70
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1.86
0.31
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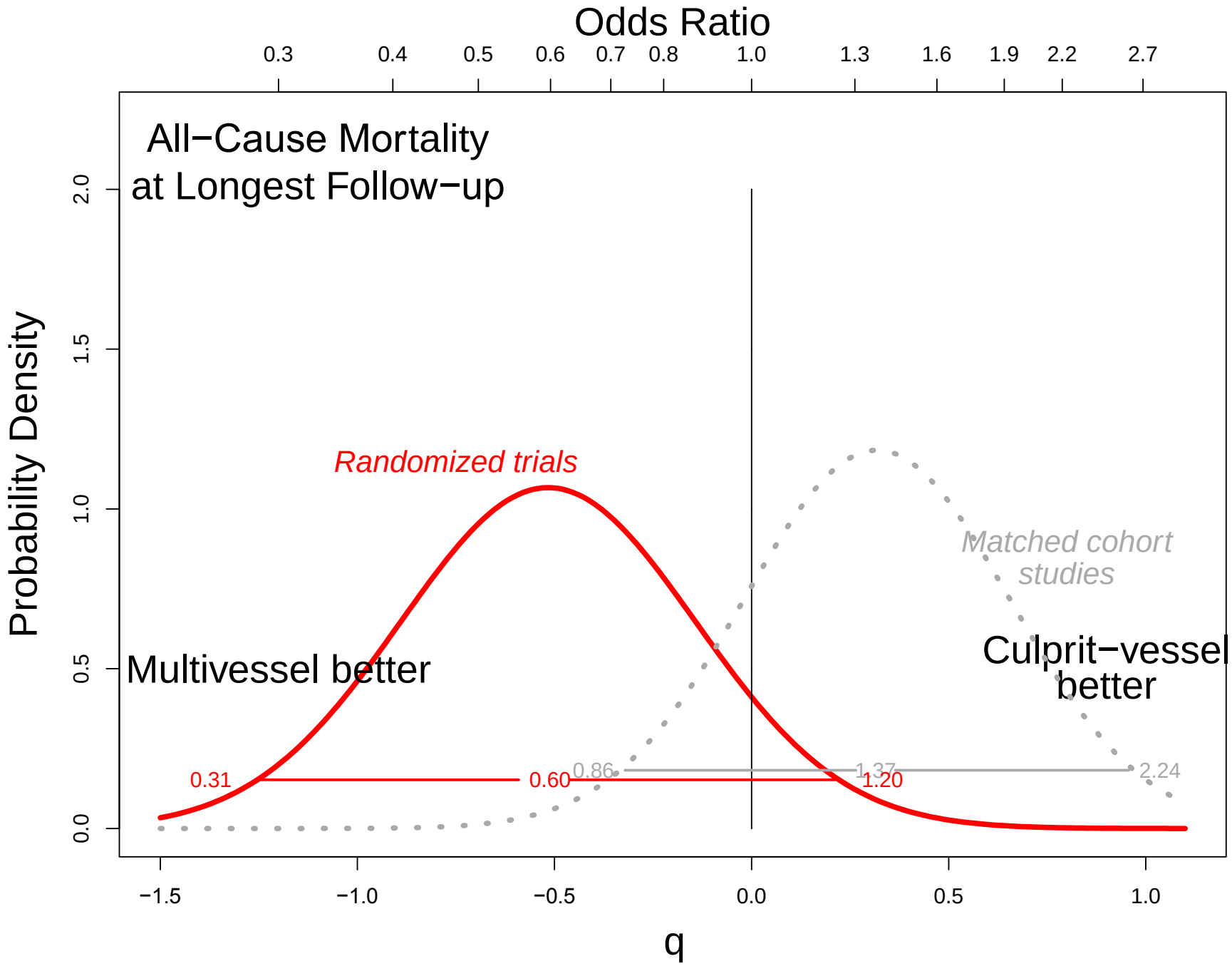
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Randomized trials
Matched cohort
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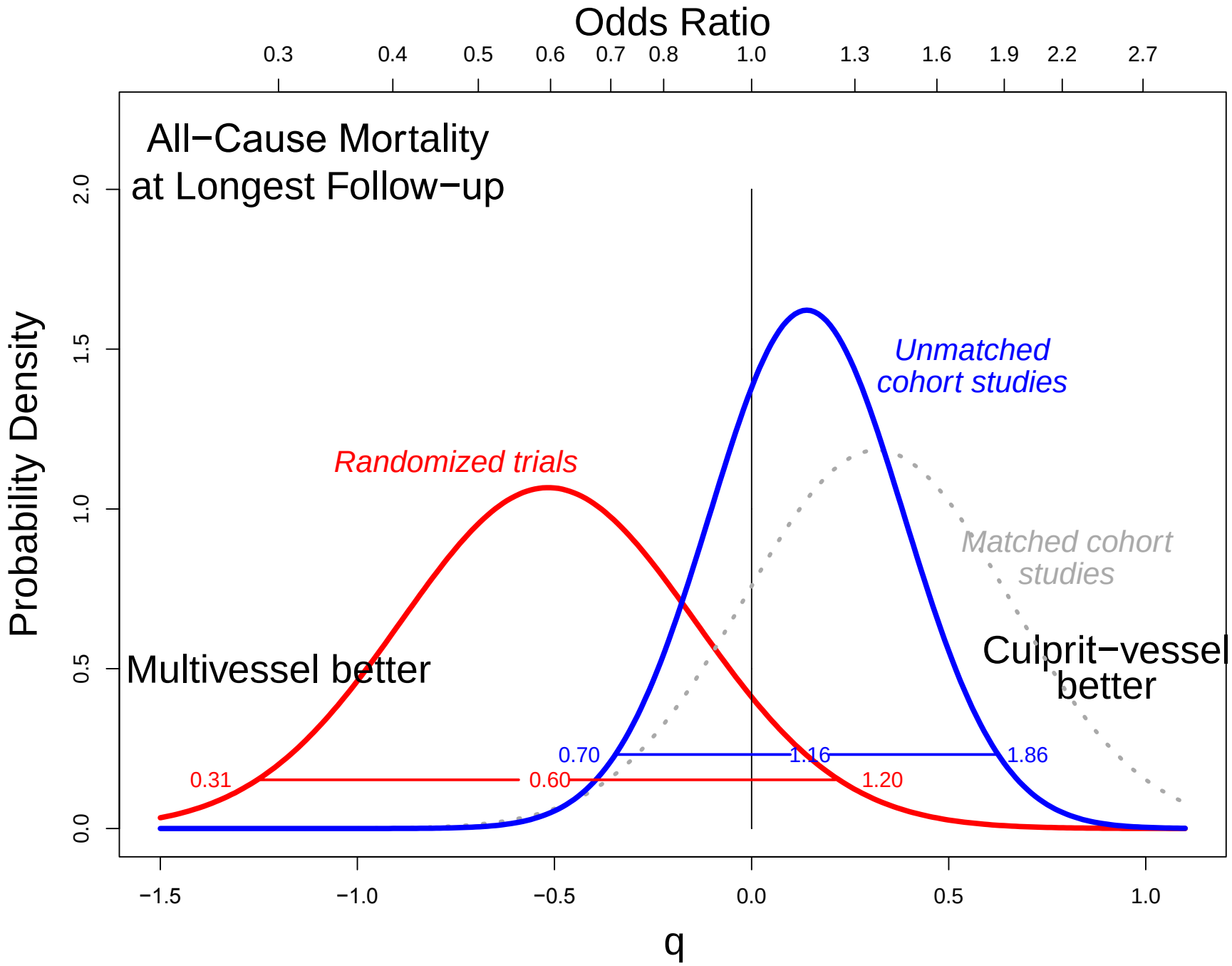
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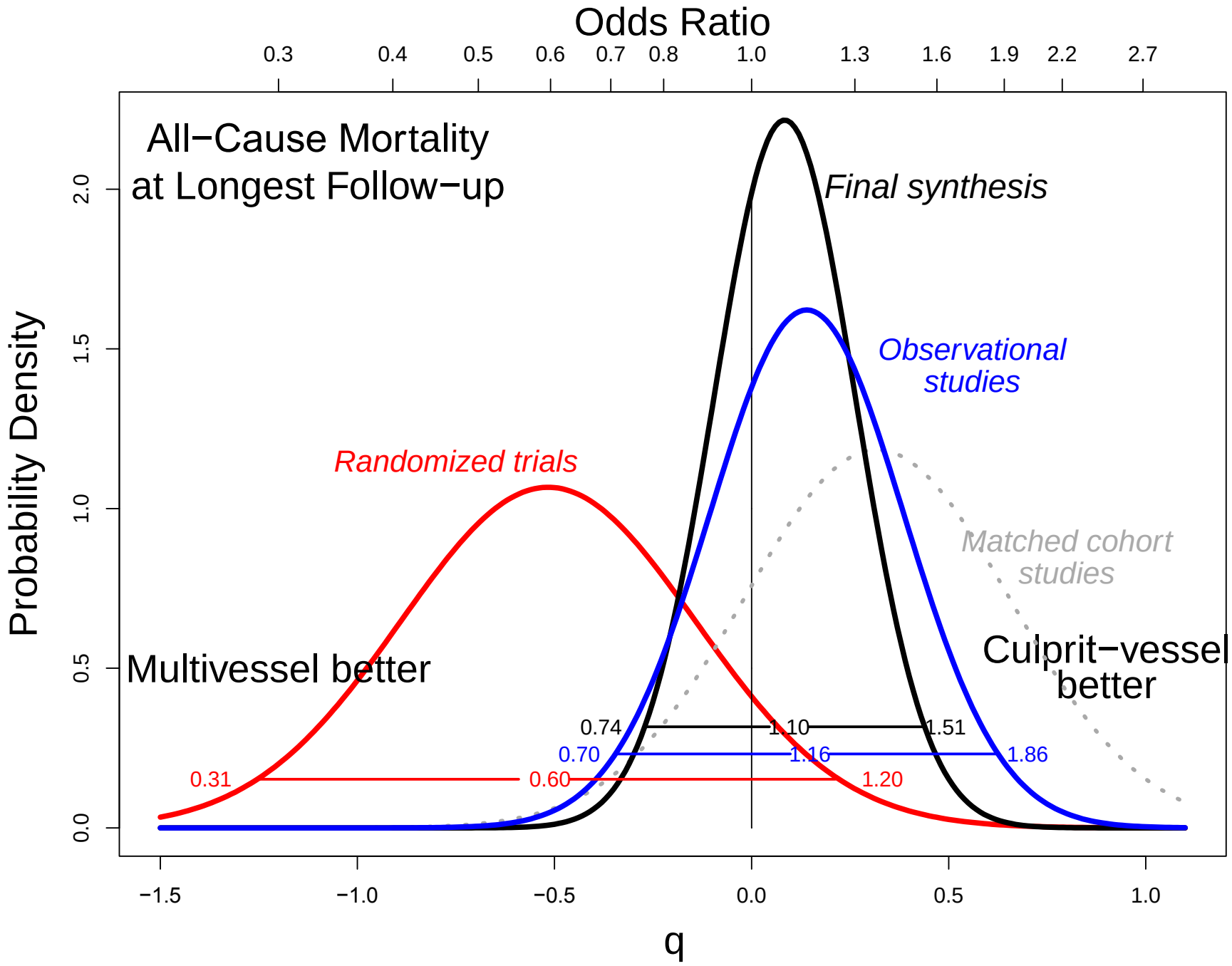
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All−Cause Mortality
at Longest Follow−up
Final synthesis
Observational
studies
Randomized trials
Matched cohort
studies
Multivessel better
Culprit−vessel
better
0.74
1.10
1.51
0.70
1.16
1.86
0.31
0.60
1.20
Probability Density
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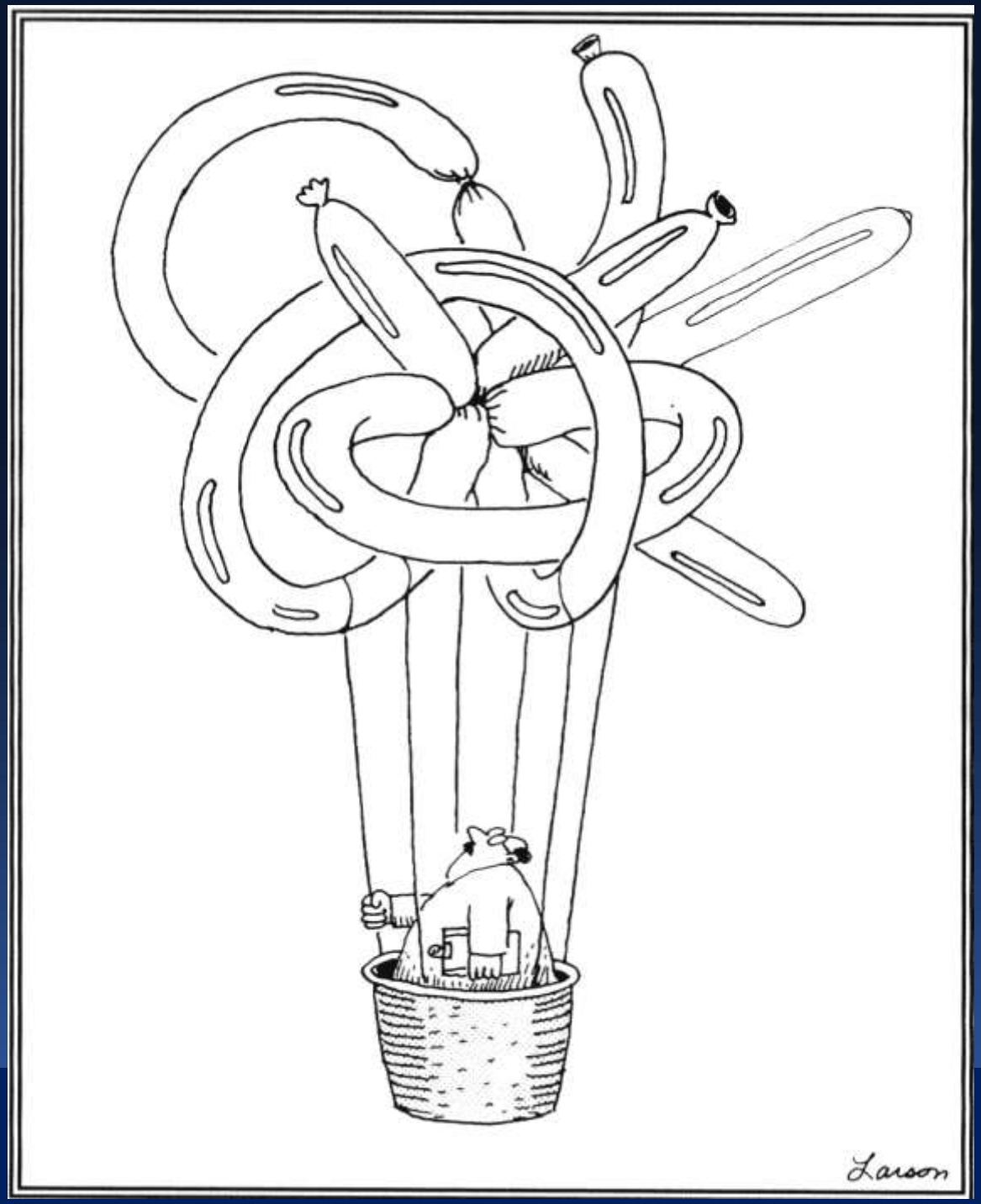

Larson

Bayesian: *Inductive Inference*

Neither multivessel PCI nor culprit-vessel PCI emerges as the preferred strategy in an analysis that accounts for study type and mortality differences

Bittl JA et al. Cathet Cardiovasc Interv 2015;86:Suppl 1;S15-22

A randomized, comparative effectiveness study of complete versus culprit-only revascularization strategies to treat multi-vessel disease after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction

COMPLETE Study Design

STEMI patients with successful culprit lesion PCI (primary, rescue or pharmaco-invasive) and ≥ 70% stenosis in at least one additional non-culprit lesion that is ≥2.5 mm

RANDOMIZED
(Stratified for intended timing of PCI)

Staged Non-culprit Lesion PCI plus OMT

Staged PCI of all suitable non-culprit lesions and ticagrelor, ASA and other OMT
N=1950

Optimal Medical Therapy Alone

No further revsac of non-culprit lesions and ticagrelor, ASA and other OMT
N=1950

ALL patients receive Optimal Medical Therapy (ASA, Ticagrelor, ACE/ARB, Statin, Beta Blocker) and Risk Factor Modification (smoking cessation, glycemic control, etc.)

Follow-up: Discharge, 6 Weeks, 6 Months, then annually up to 5 years

Primary Efficacy Outcome: Cardiovascular Death or new Myocardial Infarction (MI)
Key Secondary Outcome: Cardiovascular Death, new MI, or Ischemia-driven Revascularization

Crossover Criteria for Revascularization in OMT Group

1. Hospitalization for recurrent MI (STEMI or NSTEMI).

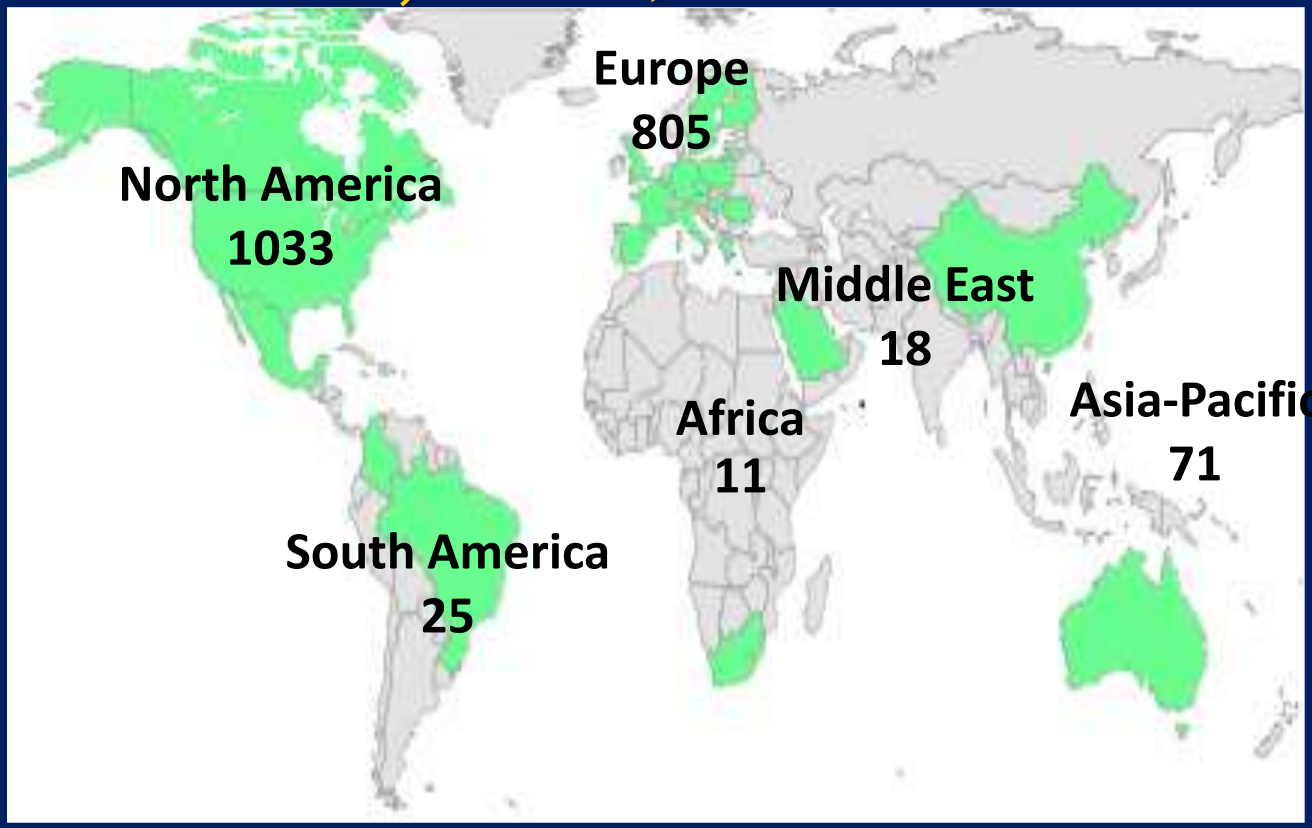
2. Hospitalization for hemodynamic instability or refractory ischemic HF (defined as Killip class ≥3).

3. Intractable angina (CCS Class 3 or 4 symptoms) despite OMT AND objective, proven and documented evidence of ischemia in the territory of one or more non-culprit vessels.

COMPLETE: Unique Features

- ✓ Global trial involving >120 high volume STEMI centers
- ✓ Powered to detect reductions in CV death or MI
- ✓ High proportion of DAPT with ASA and ticagrelor
- ✓ Very high proportion of DES use (EES-CoCr Promus series)
- ✓ Angiographic Core Lab (100% of all angiograms)
- ✓ OCT Non-culprit Lesion Substudy
- ✓ CTO Non-culprit Lesion Substudy
- ✓ CABG Surgery Registry

Global Trial Recruitment (as of October 1, 2015)



North America: Canada, Mexico, United States

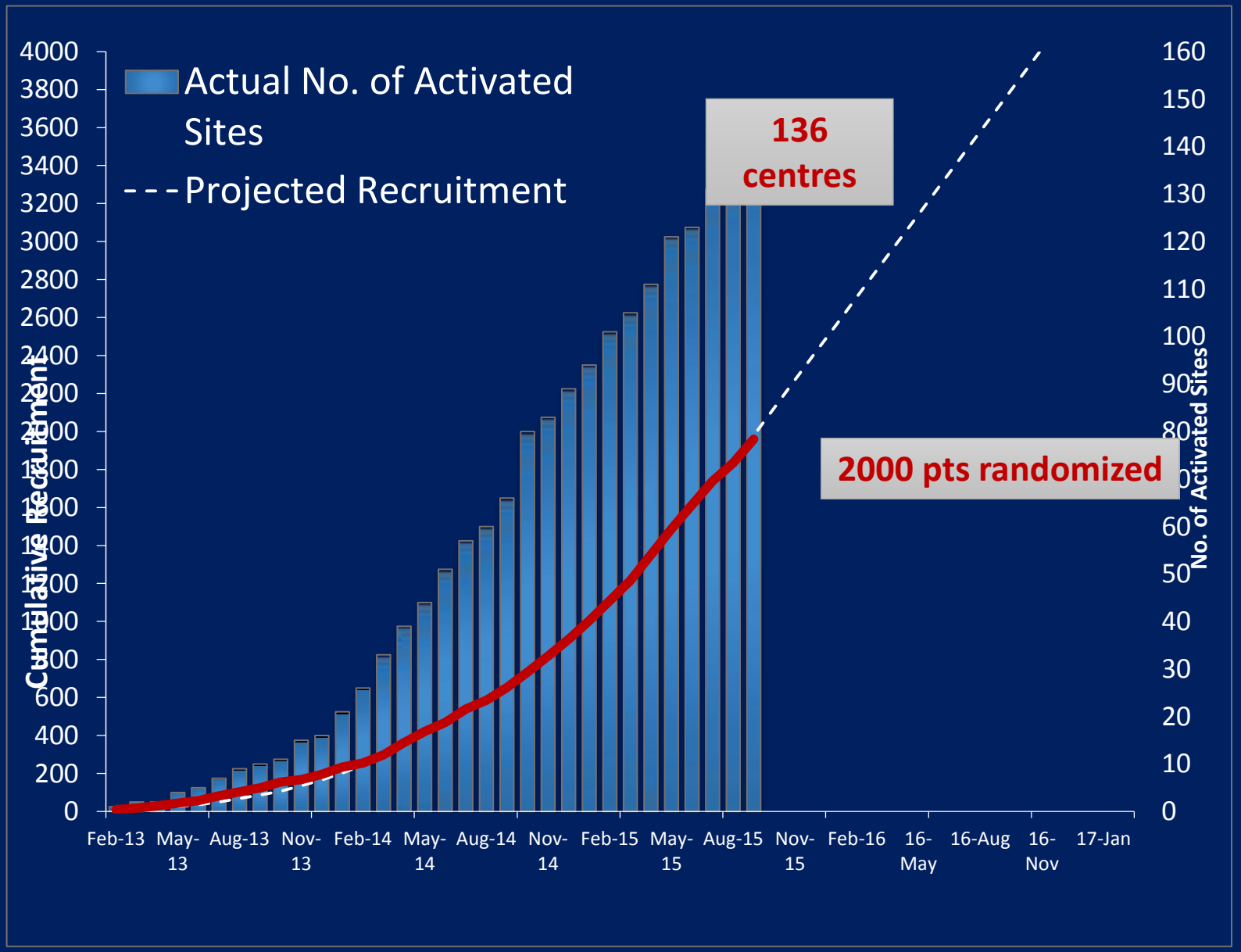
Europe: Austria, Belgium, Czech Republic, Finland, France, Germany, Greece, Hungary, Italy, Lithuania, Macedonia, Poland, Romania, Serbia, Spain, Sweden, UK

Asia-Pacific: Australia, China

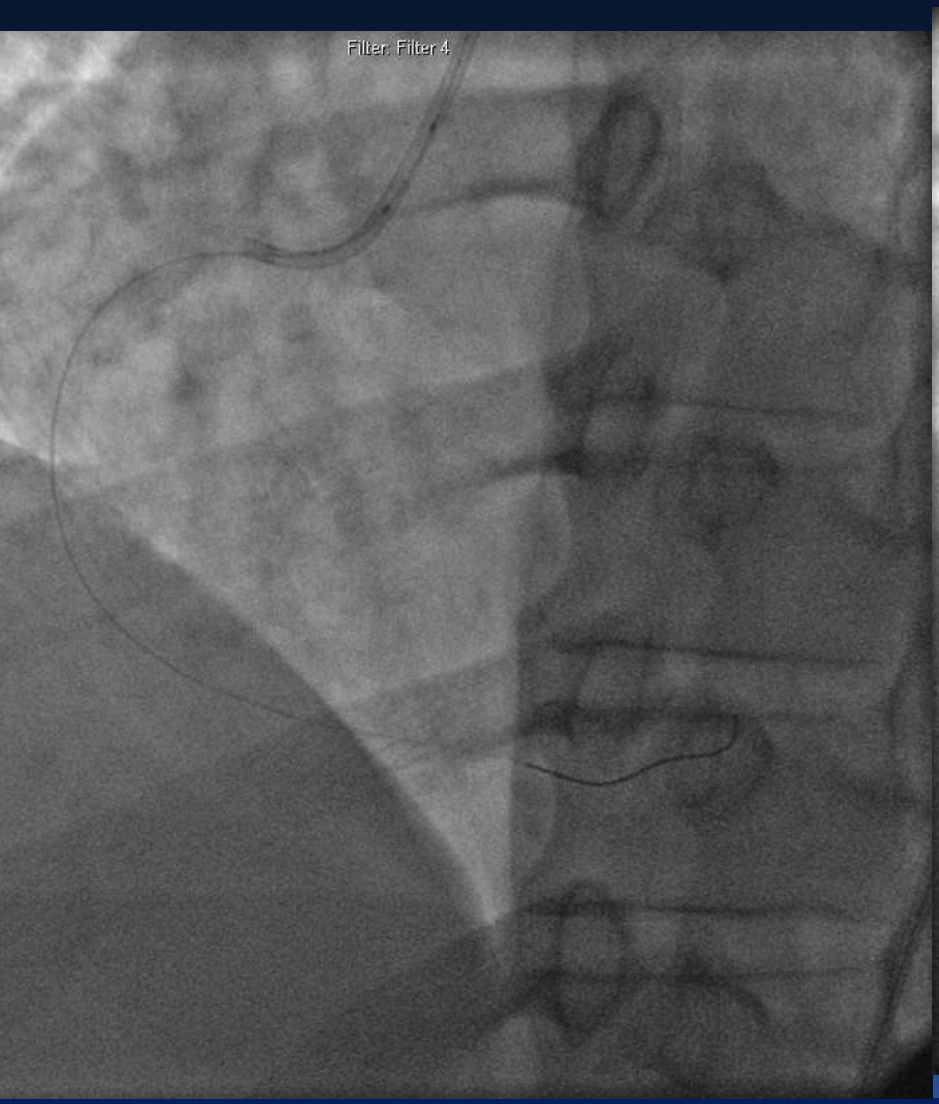
South America: Brazil, Colombia

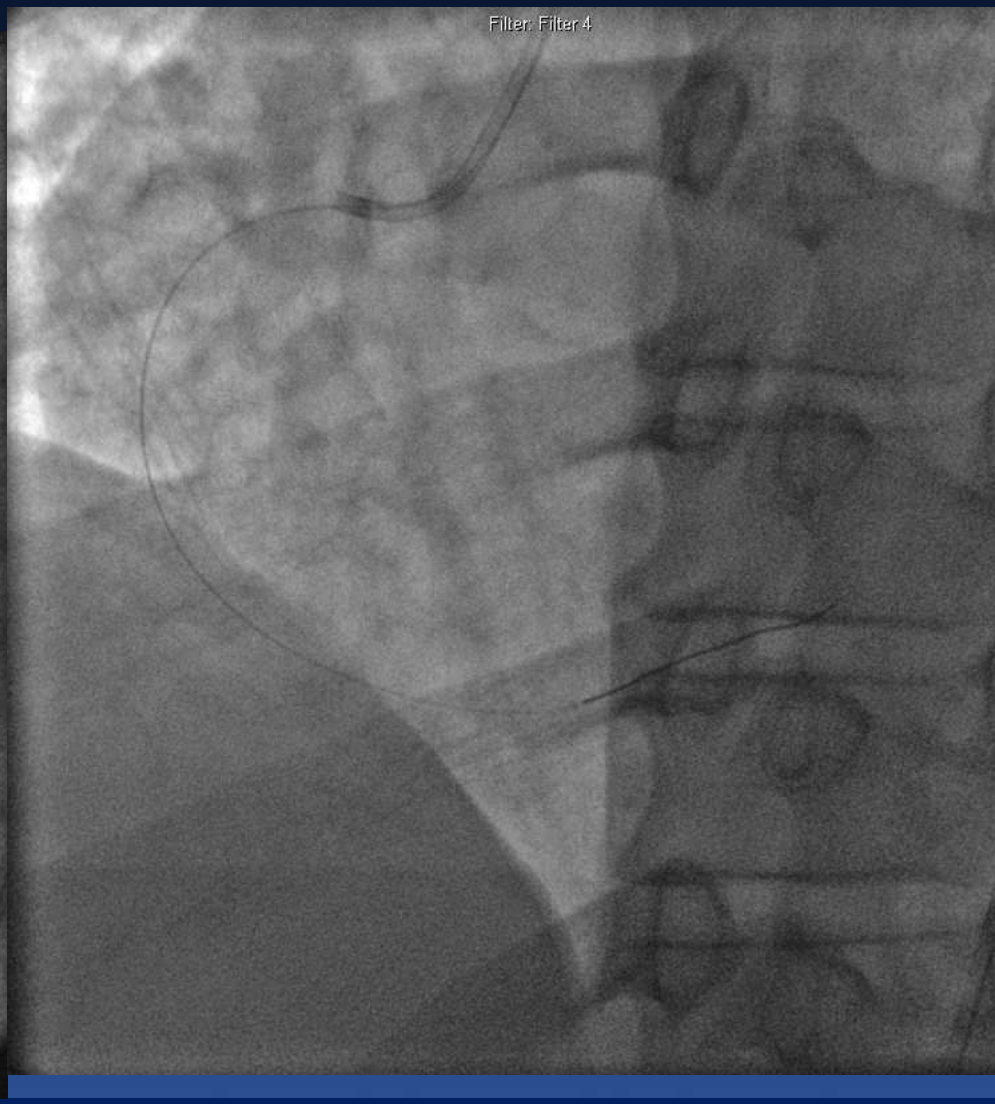
Africa/Middle East: Israel, Kuwait, Saudi Arabia, South Africa, Tunisia

Recruitment Update



STEMI: *Multivessel vs. Culprit PCI*





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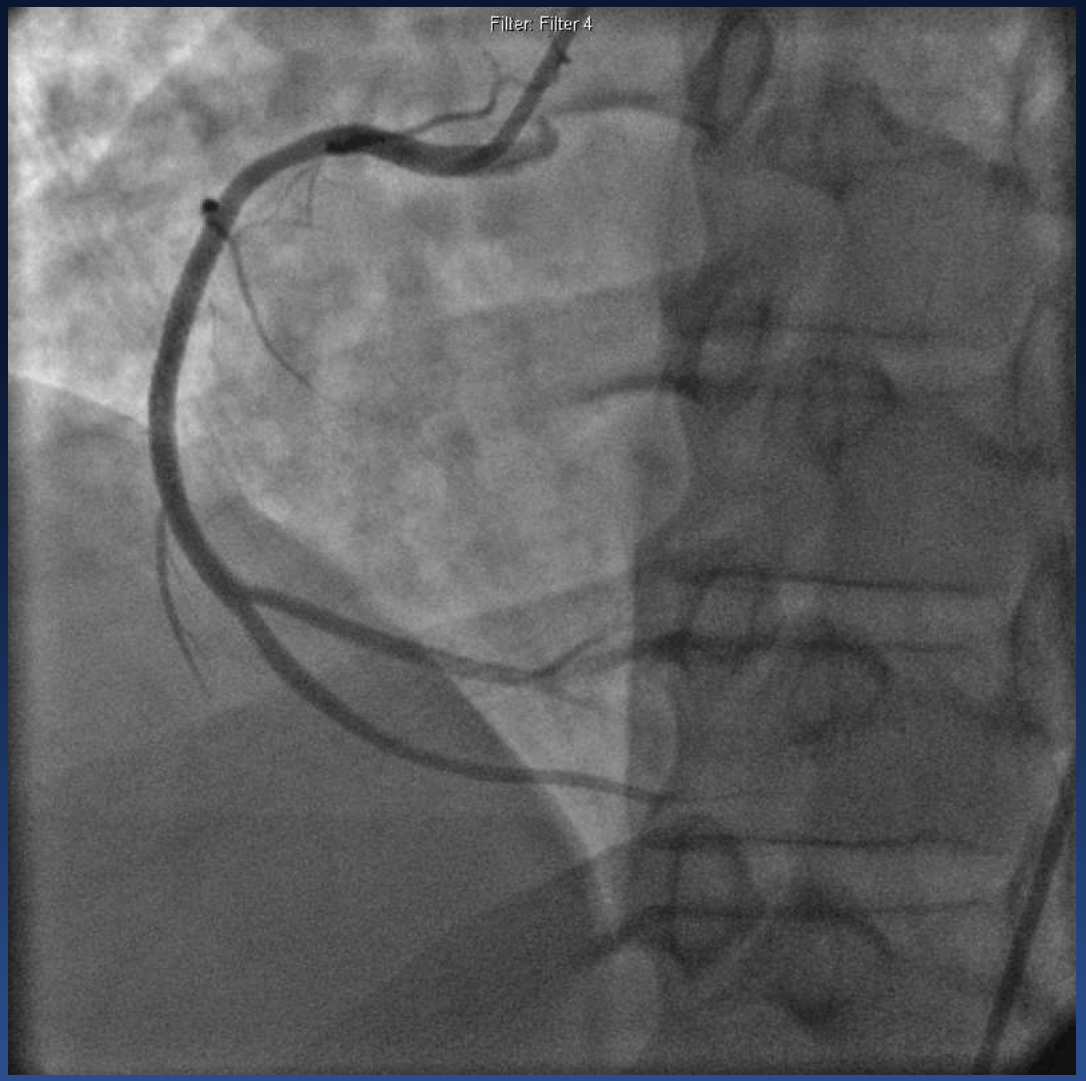

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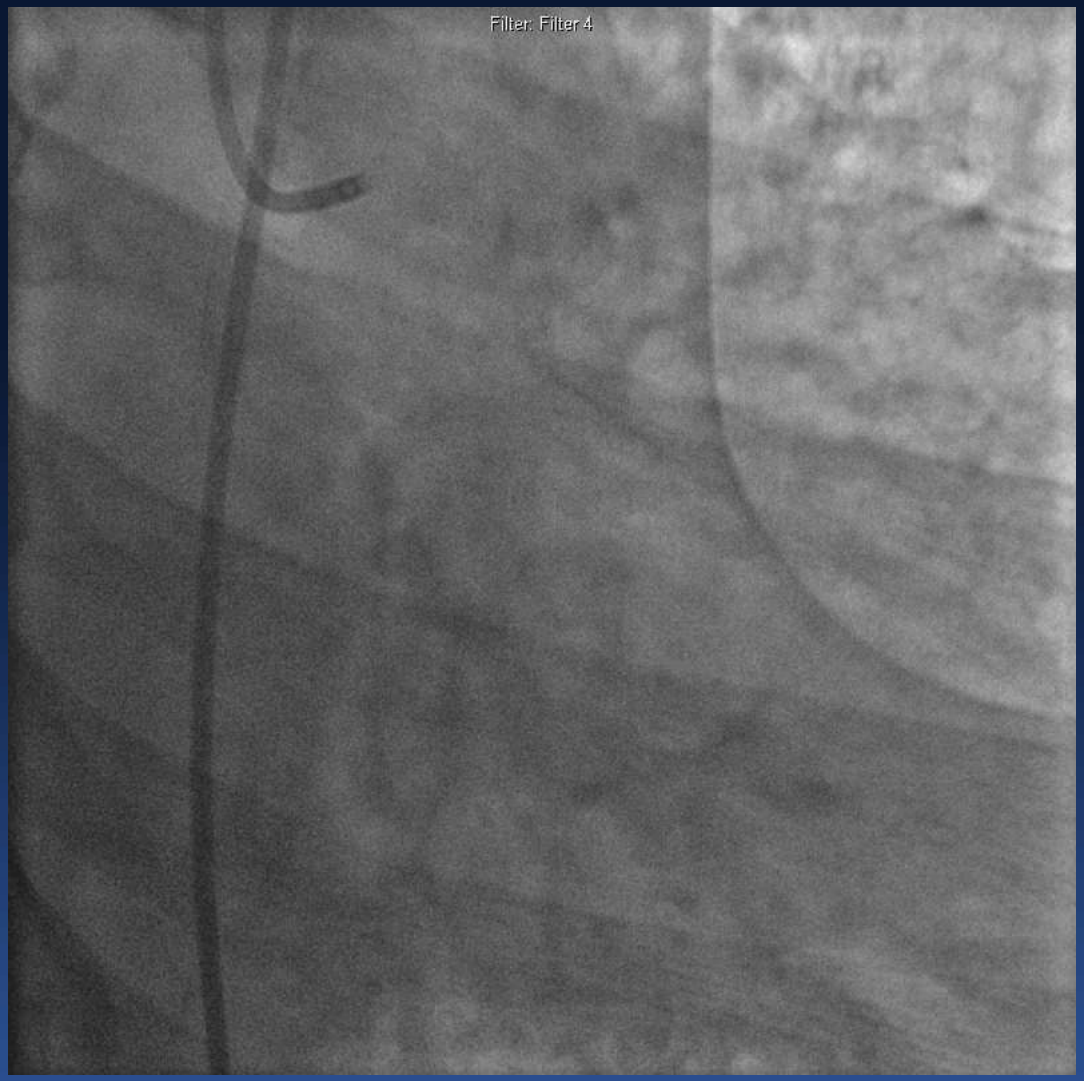

Take Home Message Until COMPLETE

- Culprit lesion should still be the focus
- If hemodynamically unstable, evidence of ischemia in other coronary territories, continue chest pain, should perform complete revascularization if possible (?CTO)
- If hemodynamically stable, other non-culprit lesion are proximal, relatively simple to fix (no rotablator, no bifurcation, no extreme tortuosity etc), can perform complete revascularization. Lesions should be severe (90%+)
- Staged procedure for renal dysfunction or long primary PCI duration.