Physiologic stenosis severity

Linking FFR value to clinical outcomes

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Health Science Center at Houston
Medical School

catharina
ziekenhuis

Disclosure Statement of Financial Interest

Within the past 12+ months, Nils Johnson has had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Organizations (alphabetical)
• Grant/Research Support (to *institution*)	• St Jude Medical (for CONTRAST study) • Volcano/Philips (for DEFINE-FLOW study)
• Educational organizations (travel support for academic meetings but *never honoraria*)	• ASNC (travel award 2007) • Canadian CPI (Montréal 2013-15) • CRF (TCT 2012-14, CPIIS 2014) • Emory (EPIC-SEC 2015) • ESC (ETP physiology courses 2013-15) • KSIC (annual meeting & IPOP 2015) • PCR (EuroPCR 2015) • SCAI (travel award 2010) • Stanford (physiology course 2015)

Nils Johnson has *never* personally received *any* money from *any* commercial company. Specifically, he does *not accept* commercial consulting, travel, entertainment, or speaking compensation *of any kind*.

ISCHEMIA Trial

ISCHEMIA Trial

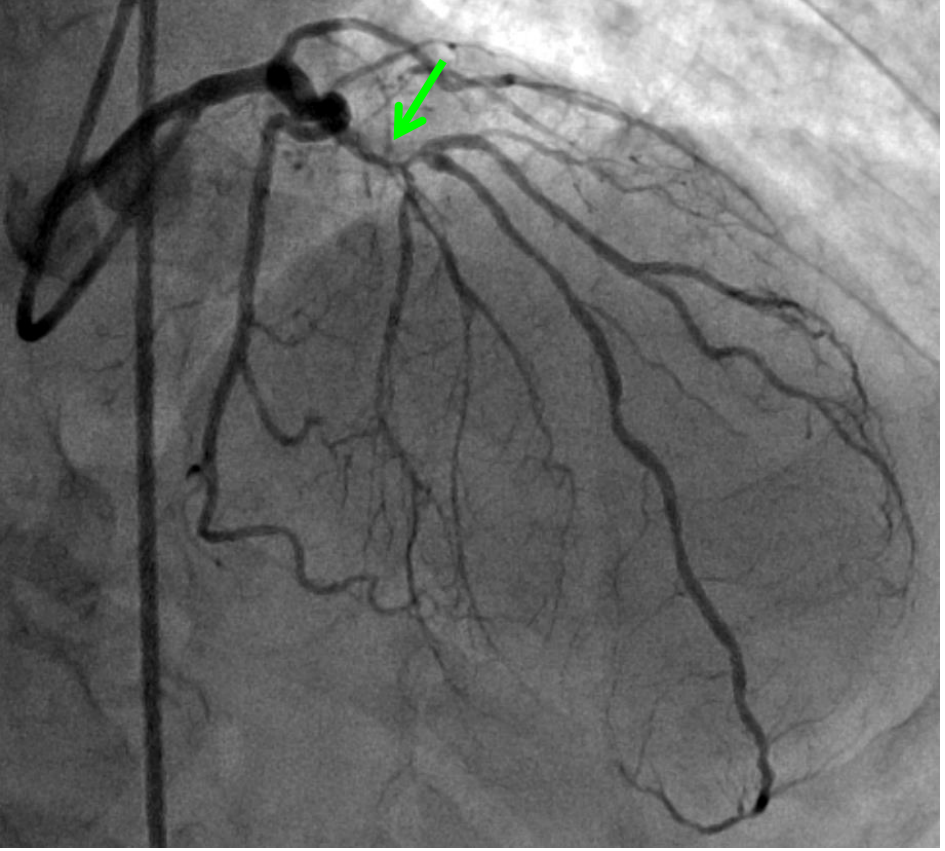
A message from Gregg W. Stone, MD

"As long as there is ***no difference in hard outcomes*** of death and myocardial infarction, I believe that revascularization for stable, ischemic heart disease is going to be ***relegated*** to primarily patients who have ***failed an initial medical approach***." – Gregg Stone

http://www.crf.org/ischemia.html (accessed June 16, 2015, with ***my emphasis added***)

71 year-old man

- *No symptoms* with typical daily activities
- Non-exertional chest discomfort, but *mild and brief*
- Classic but *mild angina once* when digging a ditch in very hot weather
- Treadmill showed *no angina* after 6:30 minutes of Bruce protocol



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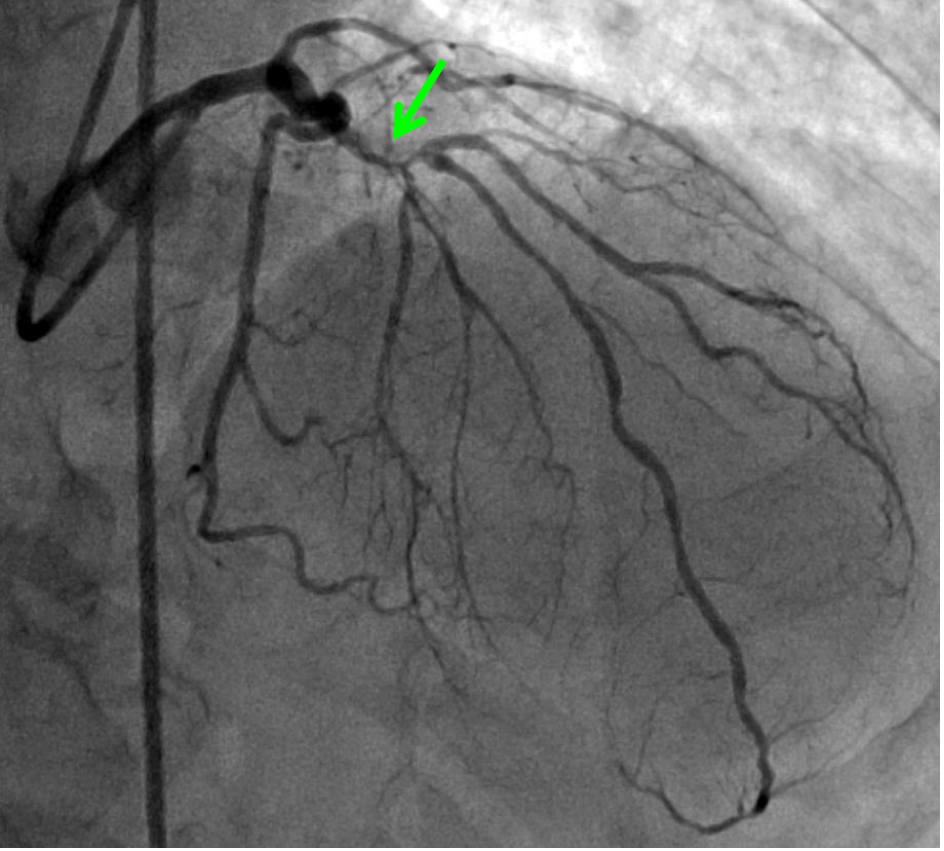
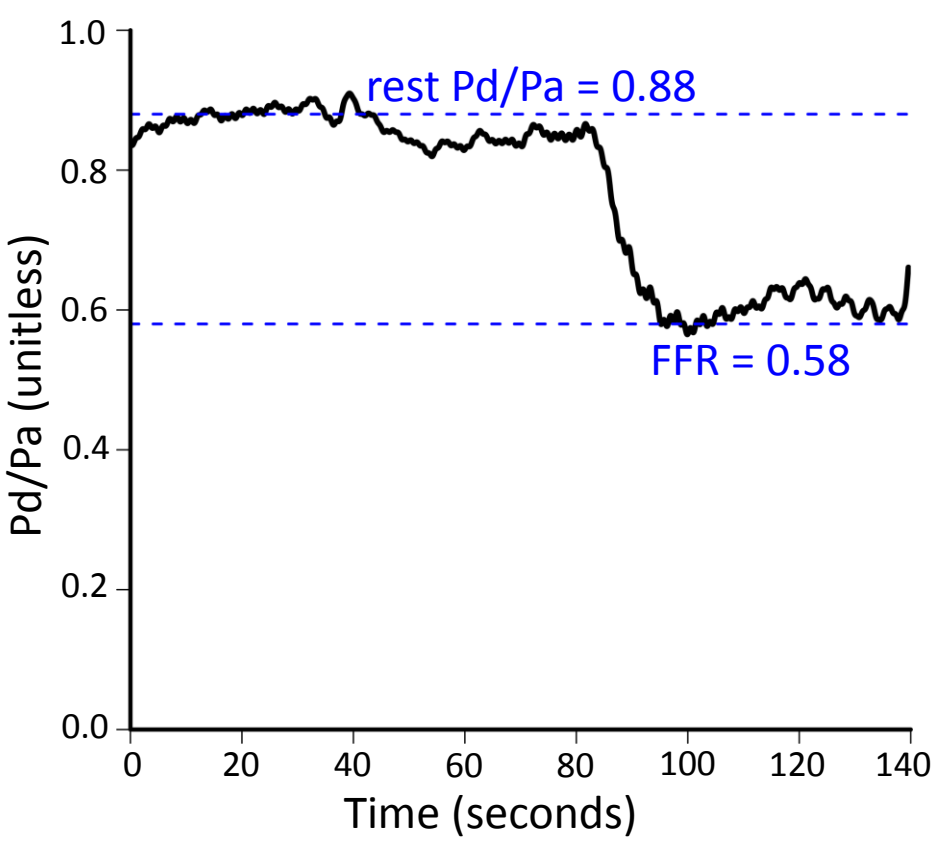
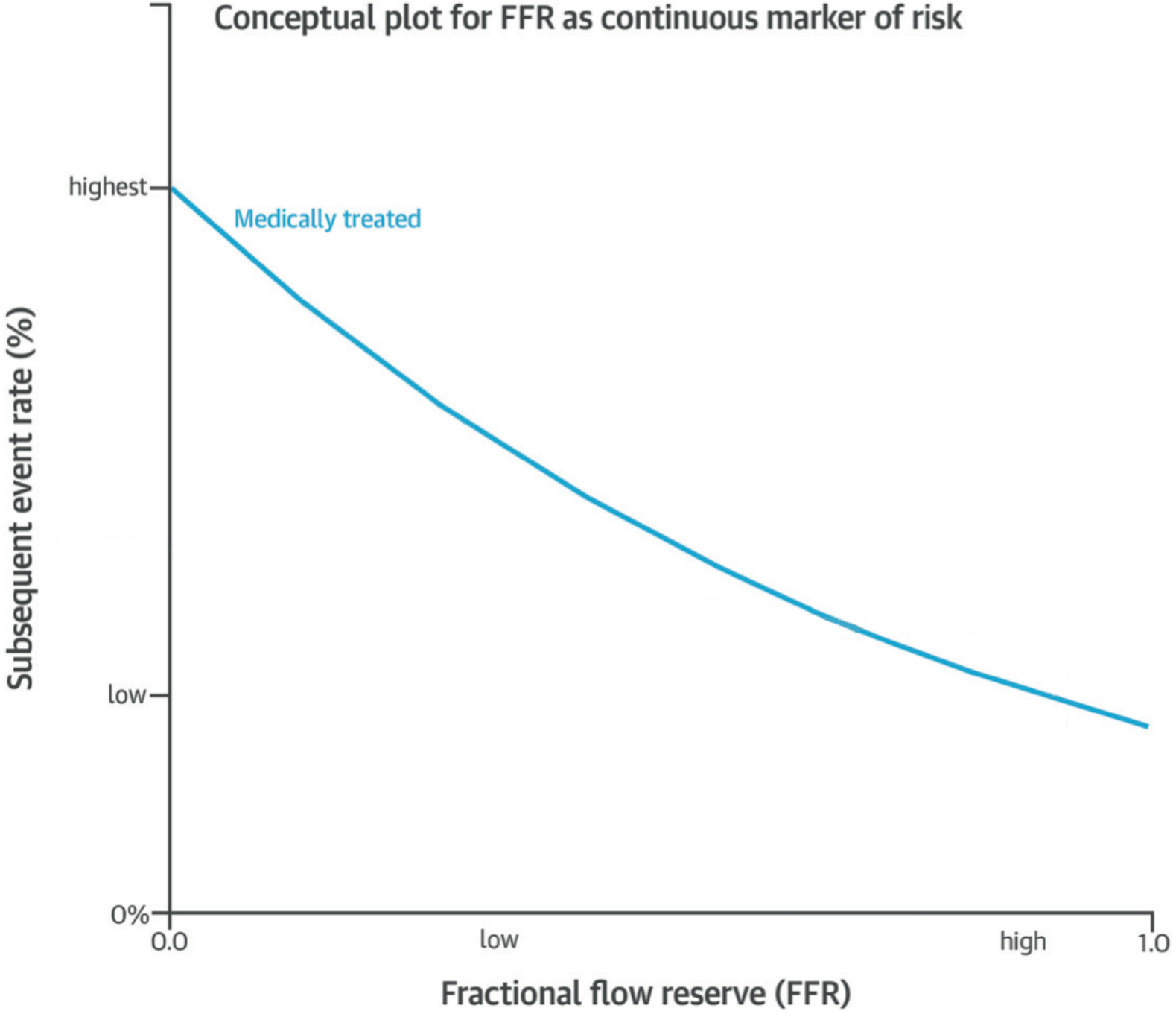


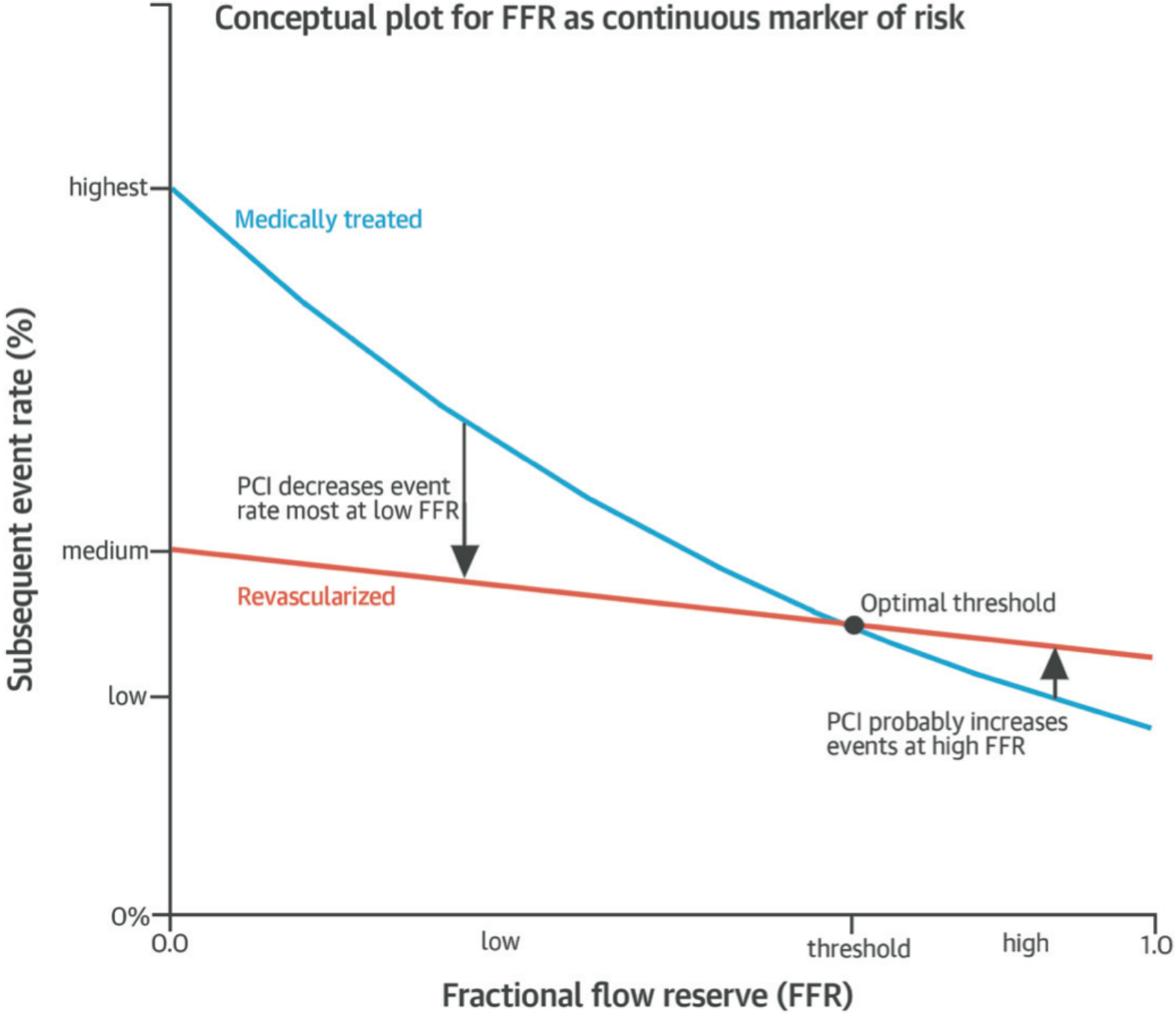


FFR = 0.58 in the proximal LAD

Can we really say *<u>nothing</u>*
about death & MI?



Johnson NP, *JACC*. 2014 Oct 21;64(16):1641-54 (Central Illustration, portion)



Johnson NP, *JACC*. 2014 Oct 21;64(16):1641-54 (Central Illustration)

Prognostic Value of Fractional Flow Reserve

Linking Physiologic Severity to Clinical Outcomes

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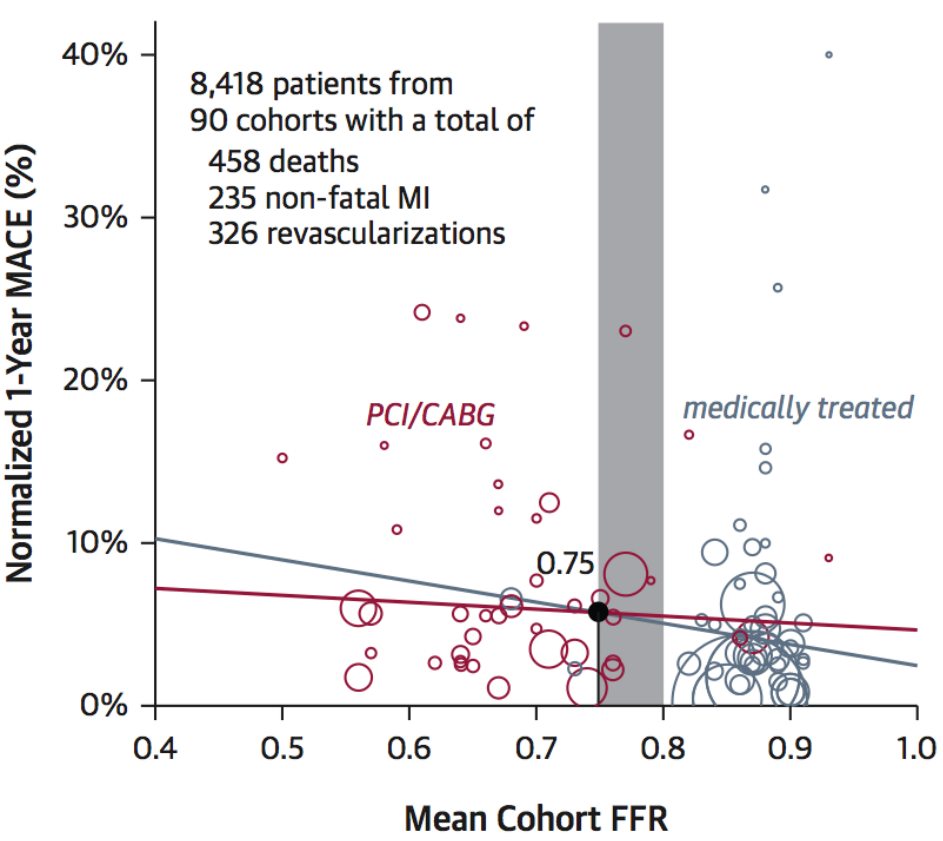
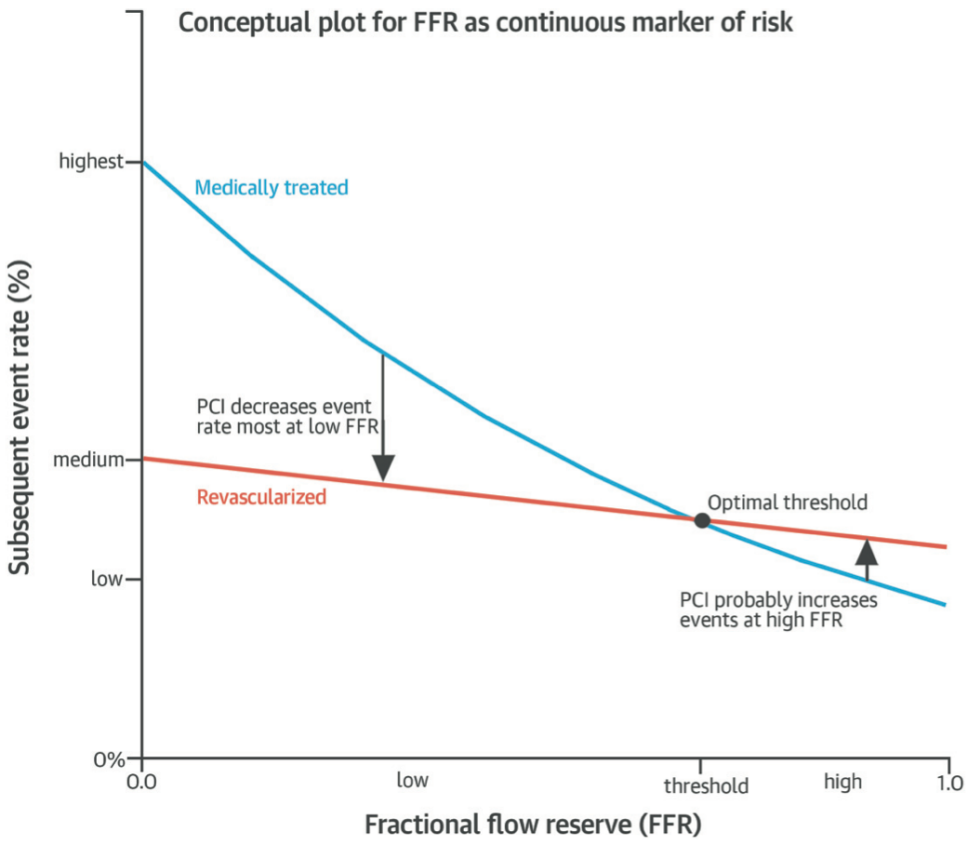
Johnson NP, *JACC*. 2014 Oct 21;64(16):1641-54.

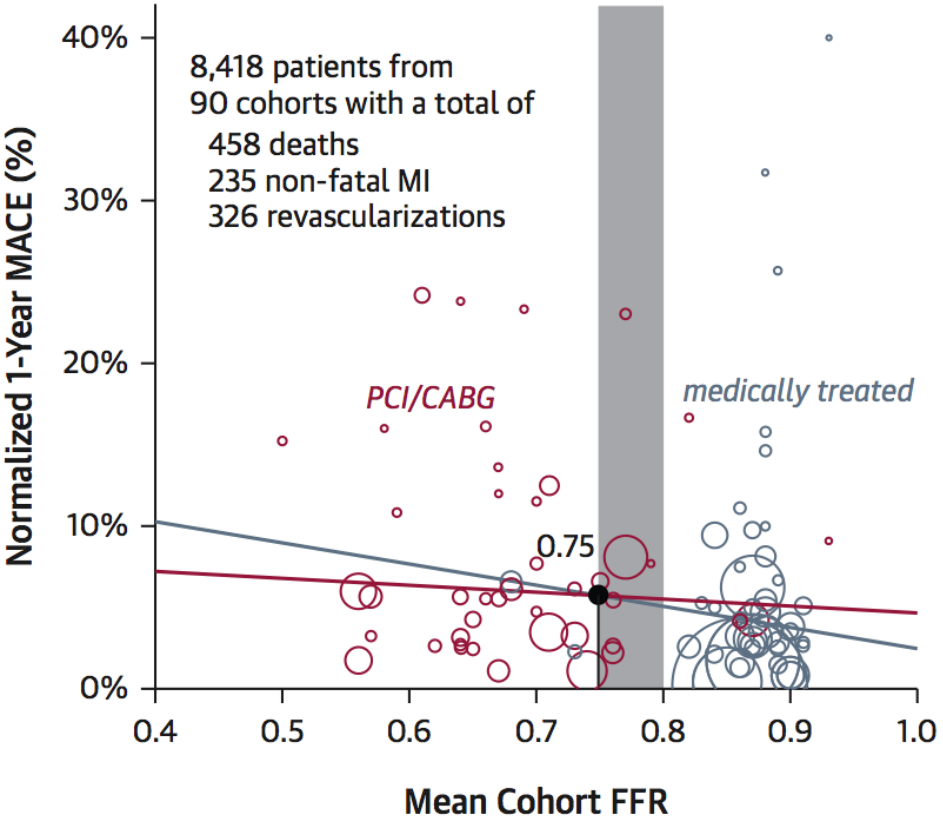


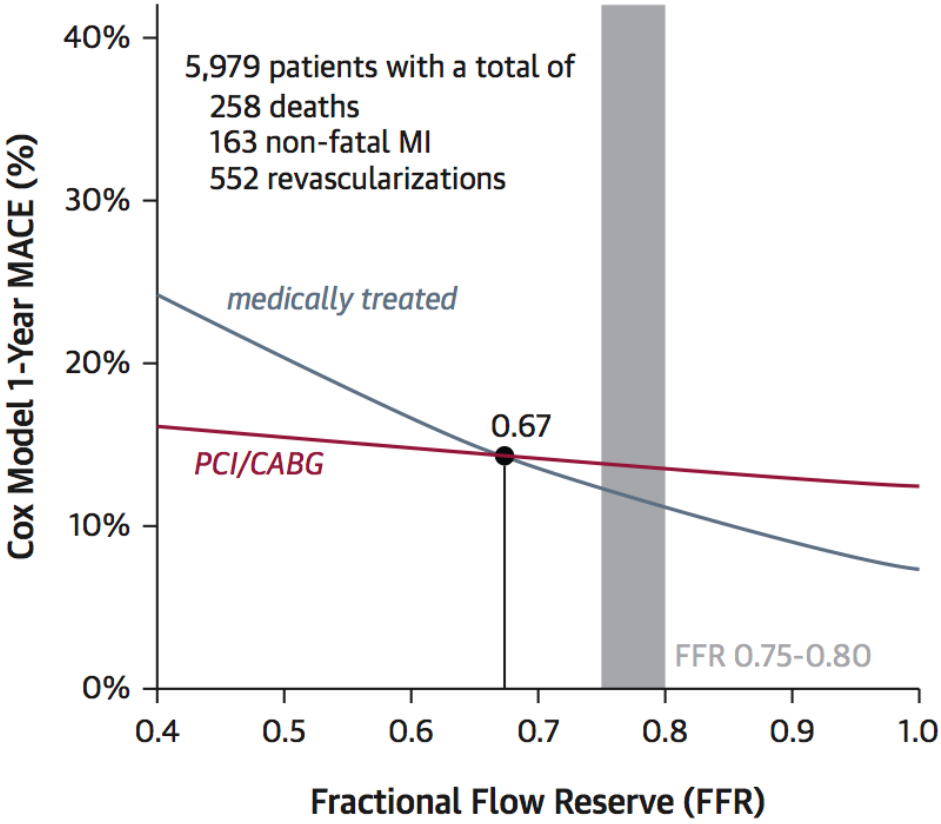


study-level analysis (8,418 patients)

continuum idea

Johnson NP, *JACC*. 2014 Oct 21;64(16):1641-54 (Figure 3A and central illustration)

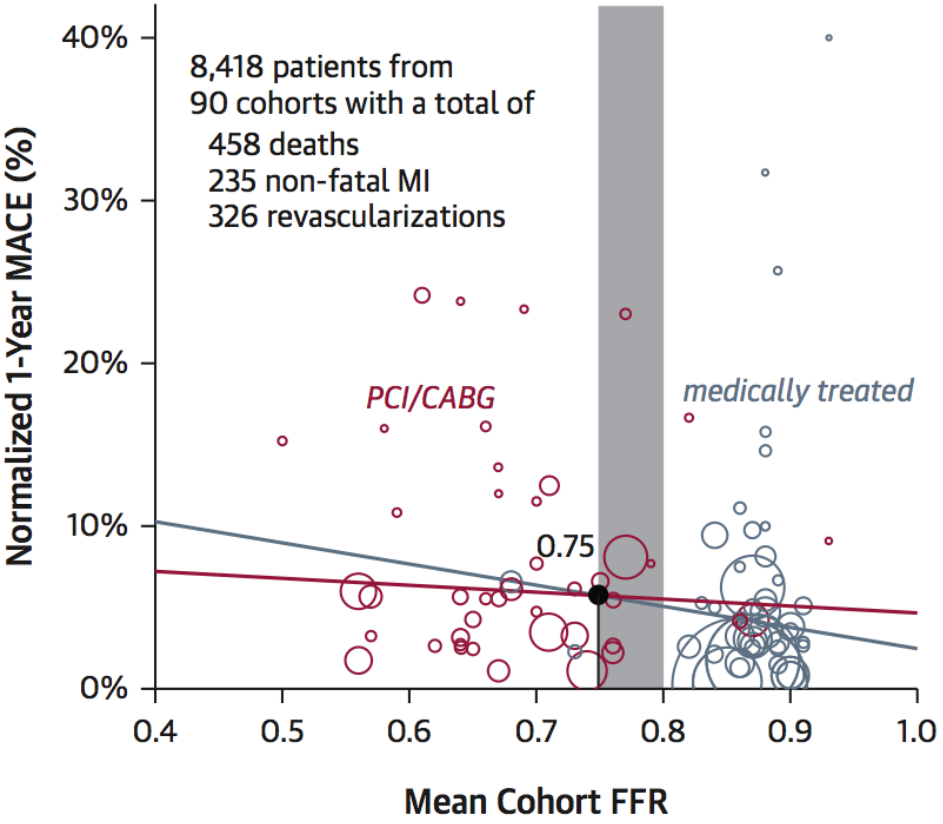


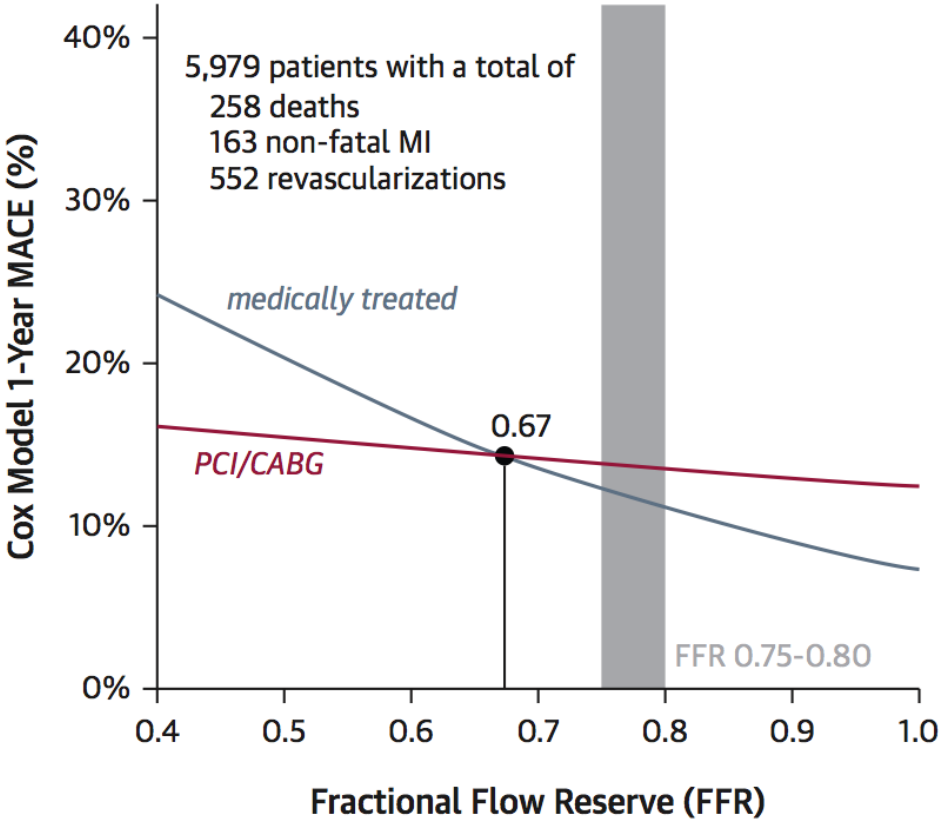


study-level analysis
(8,418 patients)

patient-level analysis
(5,979 patients)

Johnson NP, *JACC*. 2014 Oct 21;64(16):1641-54 (Figure 3)





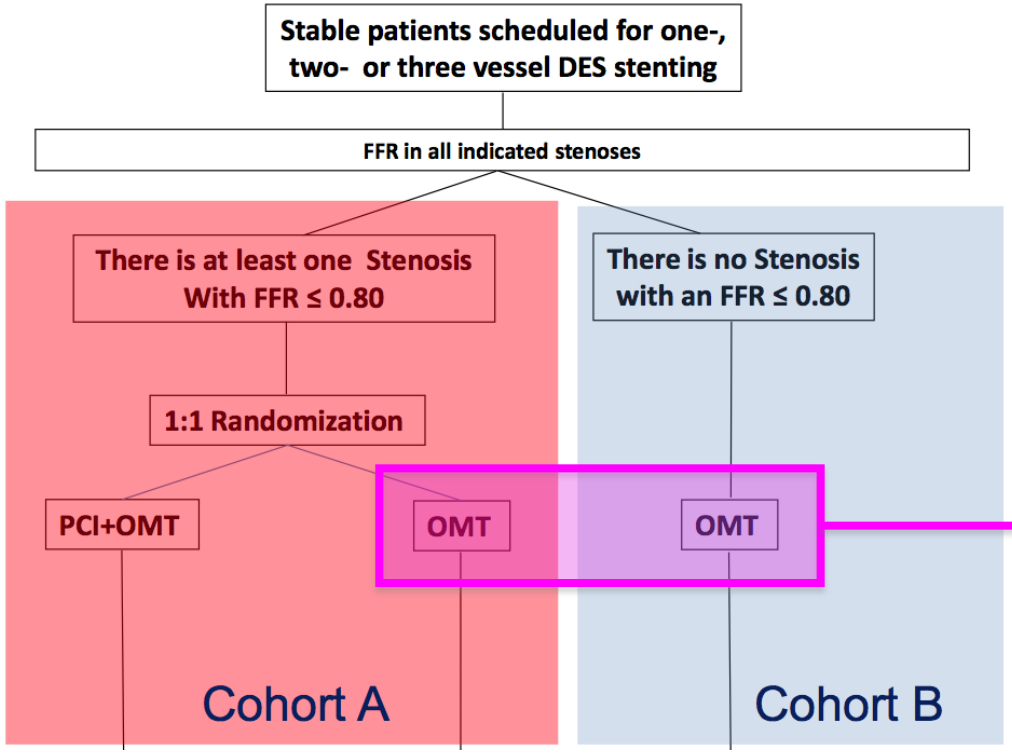
"Our data support the concept that *ischemia exists not as a dichotomous state, but rather as a graded continuum*."

Johnson NP, *JACC*. 2014 Oct 21;64(16):1641-54 (Figure 3 with *emphasized* quote from discussion)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

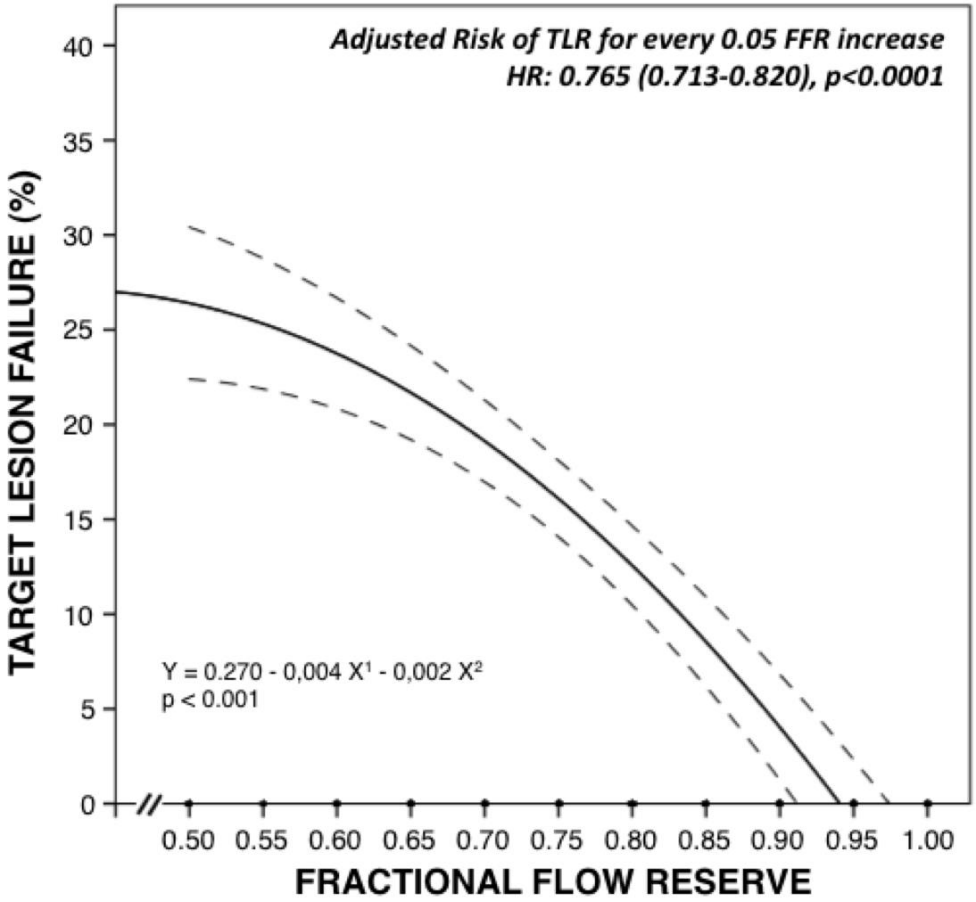
Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease



Subanalysis of lesions treated medically regardless of FFR

De Bruyne B, *NEJM*. 2014 Sep 25;371(13):1208-17 (*annotated* figure from protocol)

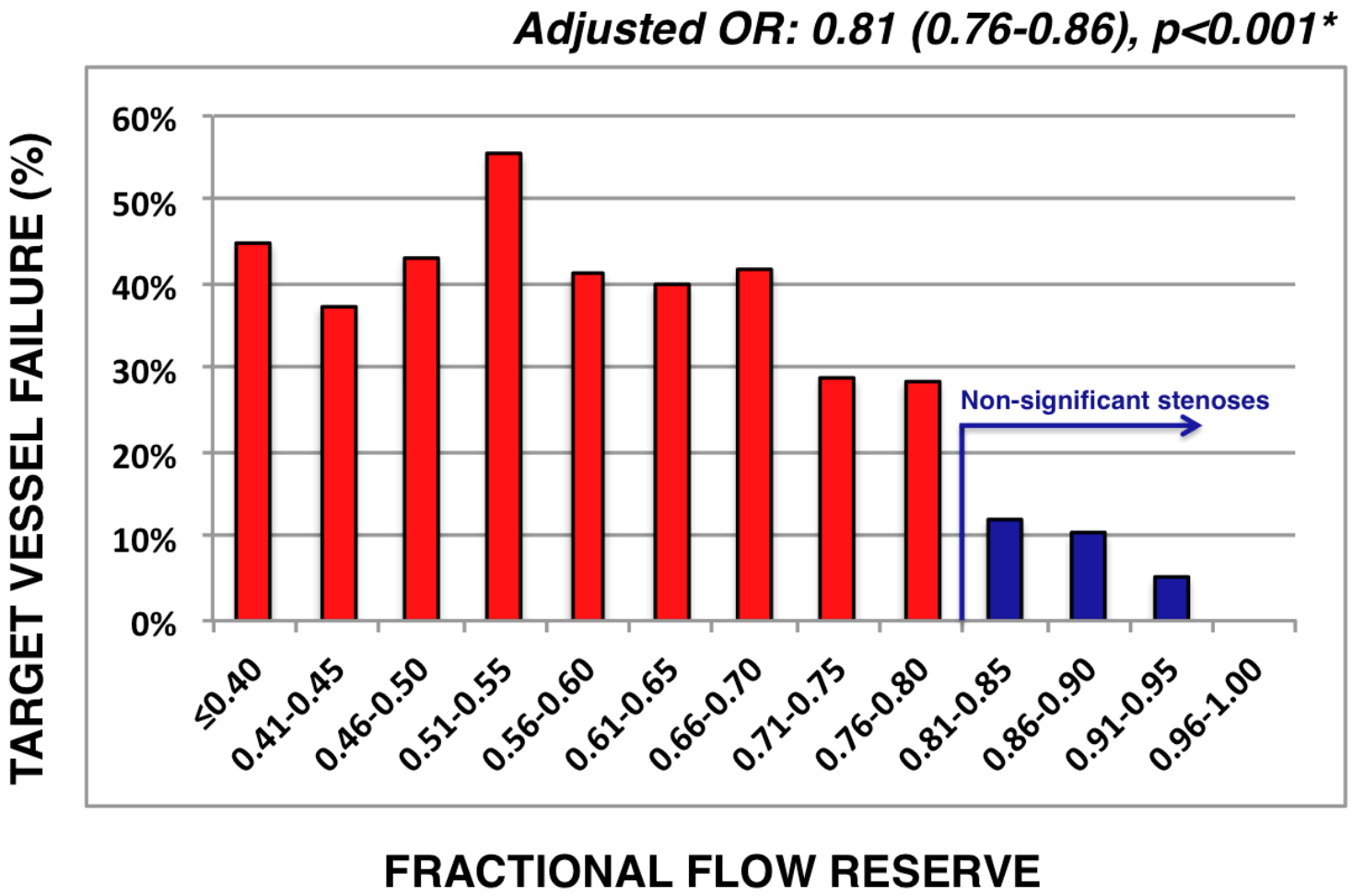
FAME 2 subanalysis



- 1,027 lesions treated medically
- 13.5% TLF during follow-up
- Binary comparison (p<0.001)
  - yes TLF: FFR = 0.63 ± 0.14
  - no TLF: FFR = 0.75 ± 0.16

Barbato E, ESC abstract P3978 from 2013

Rate of TVF for each 0.05 FFR reduction



Barbato E, ESC presentation in London, September 2, 2015 (slide #6)

ClinicalTrials.gov

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Home > Find Studies > Study Record Detail

Natural History of FFR-Guided Deferred Coronary Lesions (IRIS FFR-DEFER Registry)

This study is currently recruiting participants. (see Contacts and Locations)

Verified November 2015 by *CardioVascular Research Foundation, Korea*

Sponsor:
Seung-Jung Park

Collaborators:
CardioVascular Research Foundation, Korea
St. Jude Medical (Hong Kong) Limited

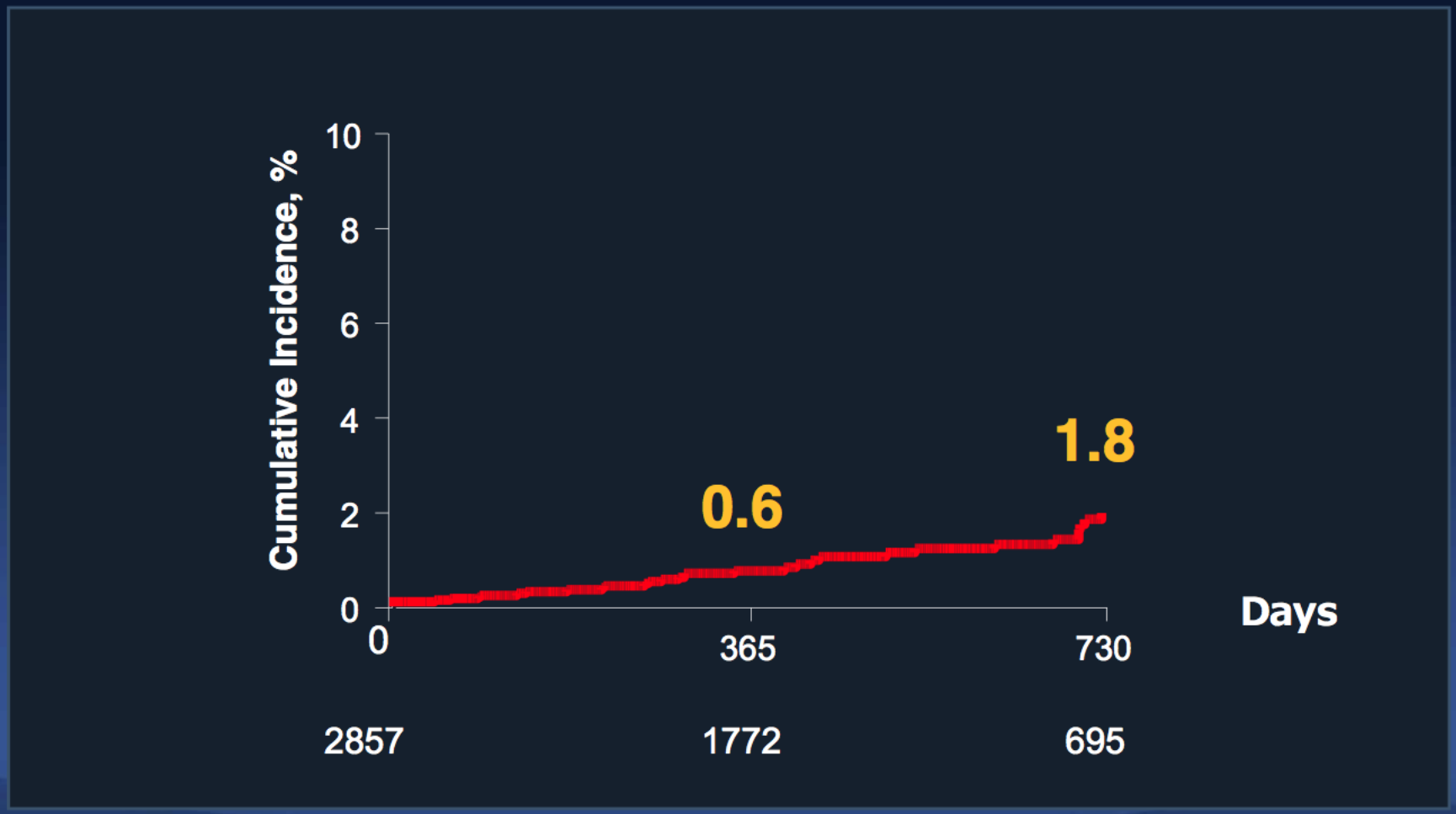
ClinicalTrials.gov Identifier:
NCT01366404

First received: June 2, 2011
Last updated: November 10, 2015
Last verified: November 2015
History of Changes

- Observational study
  - Enrolling about *10,000 patients* from *28 Korean sites*
  - *FFR>0.8* despite %DS>30% visually
  - Primary endpoint is *2-year MACE (CV death, MI, TVR)*

https://clinicaltrials.gov/ct2/show/NCT01366404. Accessed December 4, 2015.

Cardiac Death and MI at 2 Years
(2857 patients, 3534 DFERred lesions)



CardioVascular Research Foundation

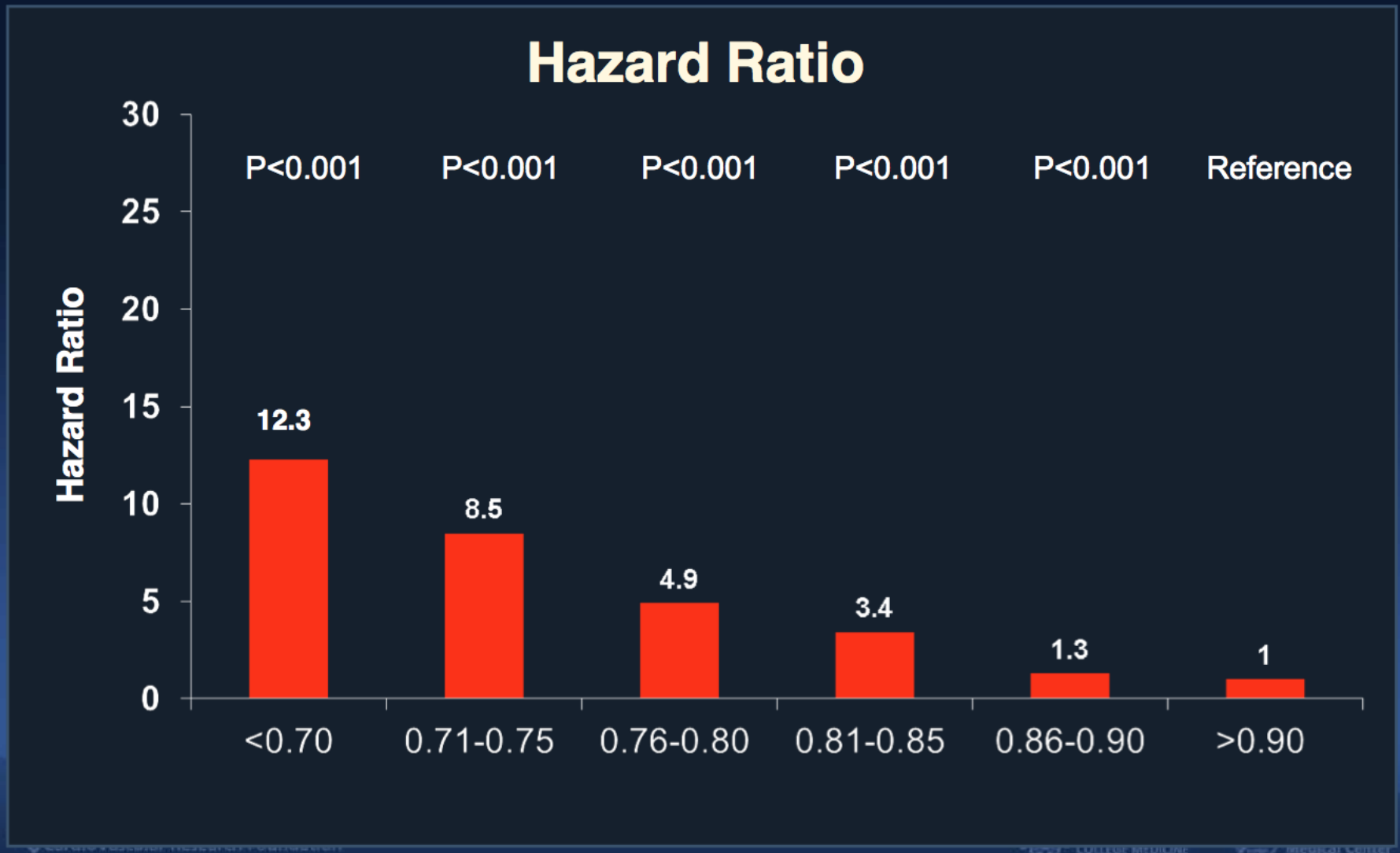
IRIS-FFR Registry, Preliminary Analysis 2015

UNIVERSITY OF ULSAN COLLEGE MEDICINE

ASAN Medical Center

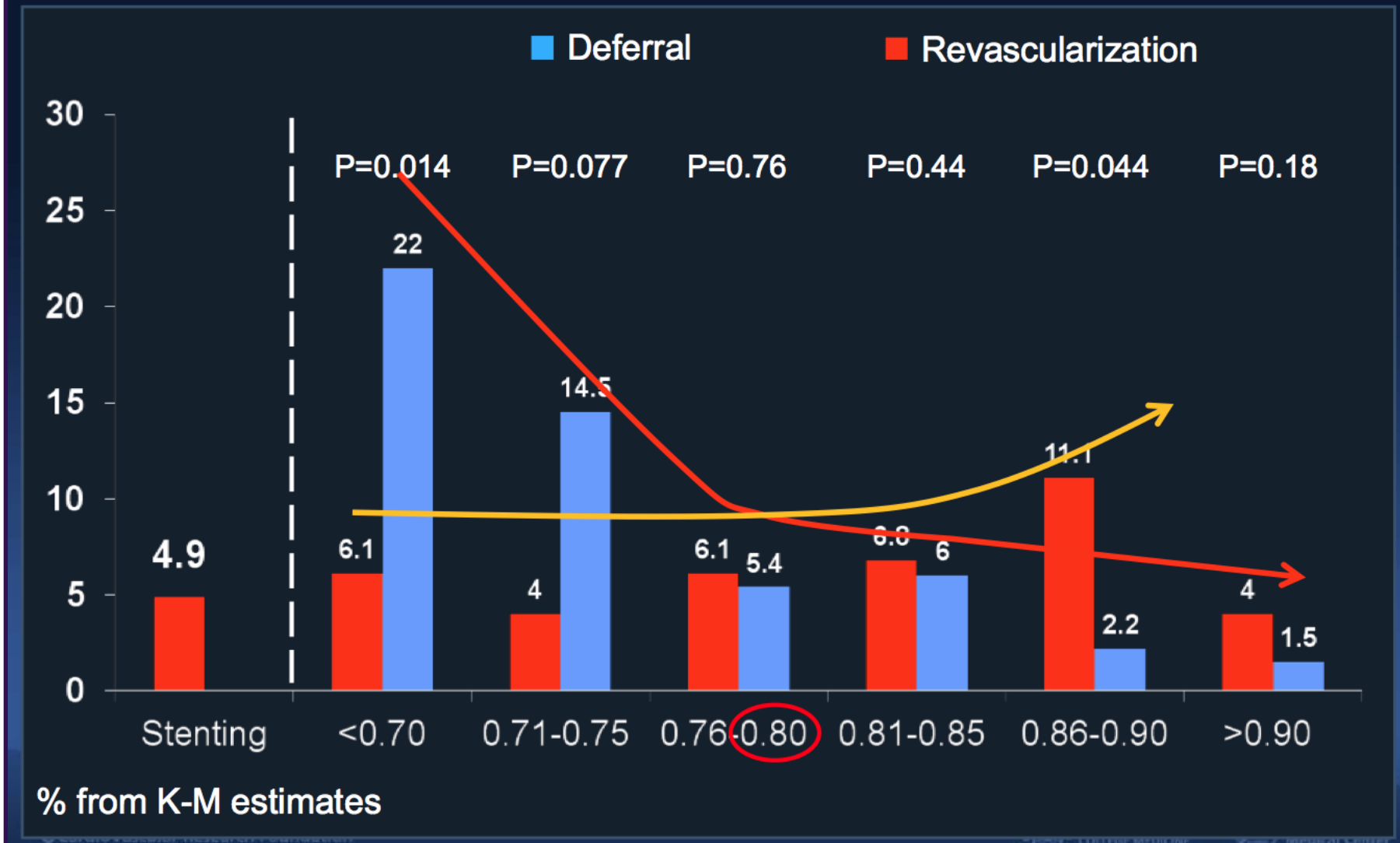
Park SJ, TCT-AP presentation in Seoul, April 29, 2015 (slide #23)

Repeated Intervention at 2 Years (per vessel)



Park SJ, TCT-AP presentation in Seoul, April 29, 2015 (slide #26)

Repeated Intervention at 2 Years (per vessel)



Park SJ, TCT-AP presentation in Seoul, April 29, 2015 (slide #27)

FFR Grey Zone and Clinical Outcome

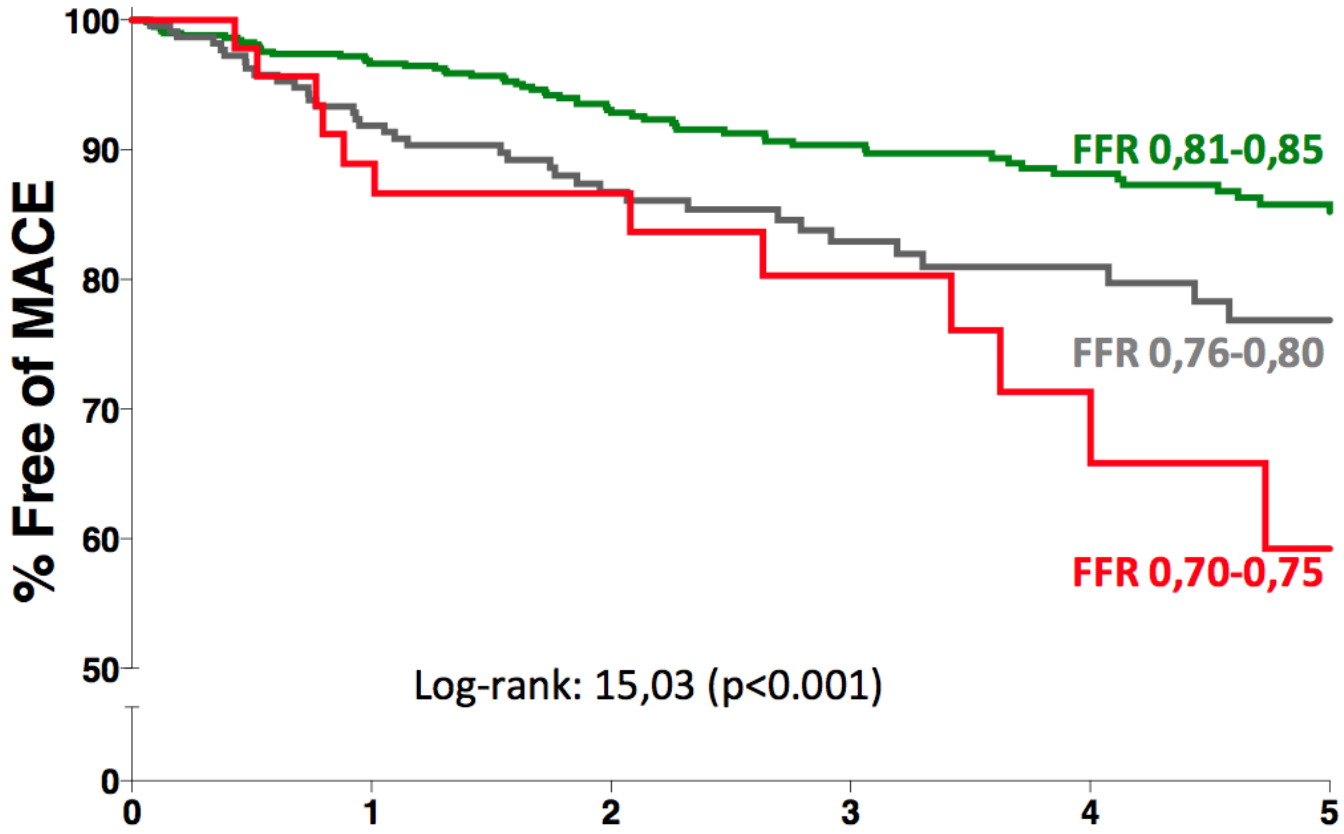
Julien Adjedj,
Vincent Floré, Giuseppe Di Gioia, Angela Ferrara, Mariano Pellicano, Gabor Toth, Bernard De Bruyne, Emanuele Barbato

Cardiovascular Centre Aalst
Belgium

Adjedj J, EuroPCR presentation in Paris, May 22, 2015.

MACE-Rate per FFR strata

Pts with MT (n=1010)



FFR 0,70-0,75	53	39	29	20	12	8
FFR 0,76-0,80	266	184	133	93	66	46
FFR 0,81-0,85	691	516	393	277	213	149

Adjedj J, EuroPCR presentation in Paris, May 22, 2015 (slide #9)

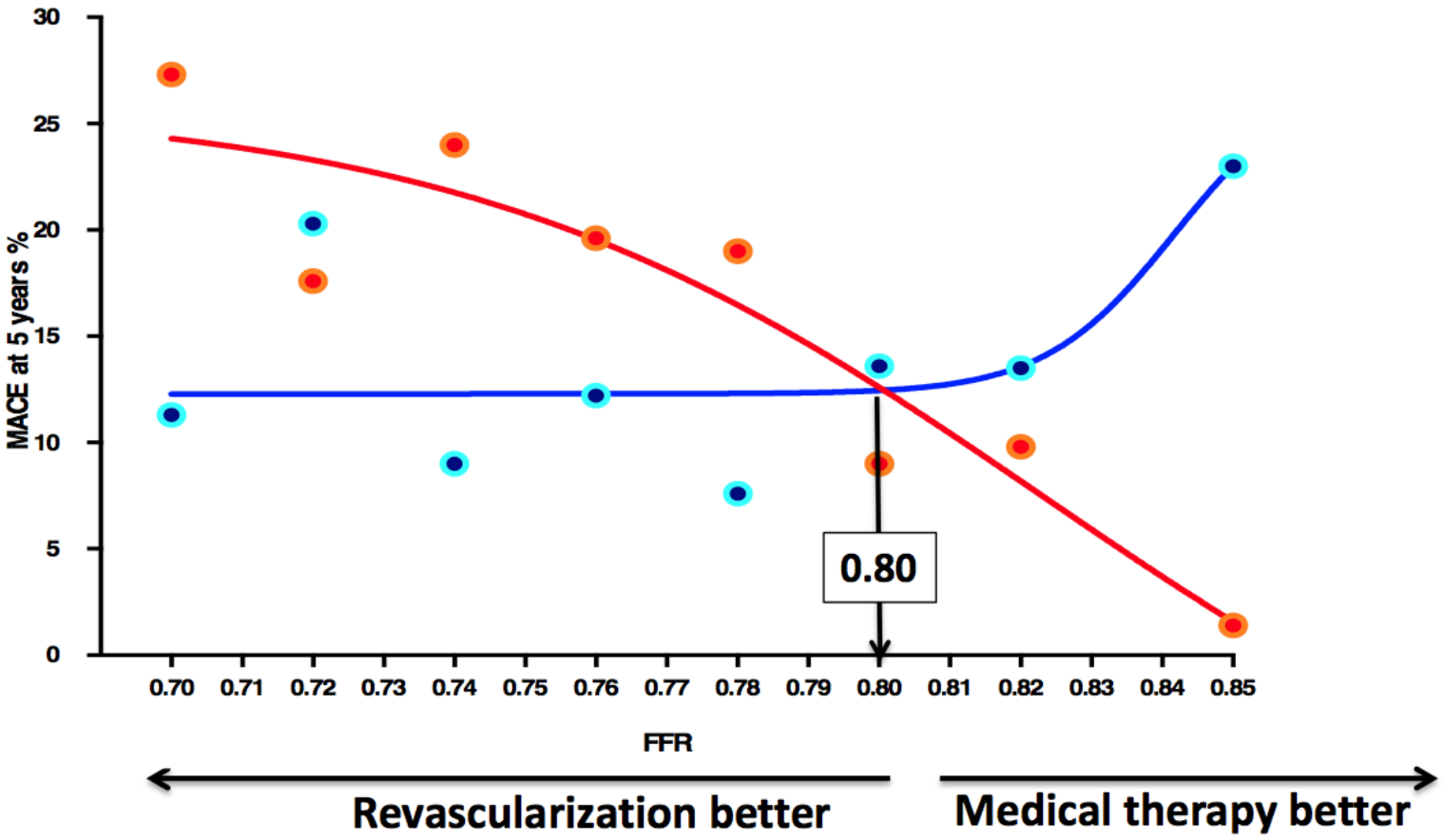
MACE-Rate per FFR strata

euro PCR 2015

Cardiovascular Center Aalst

Pts with MT (n=1010)

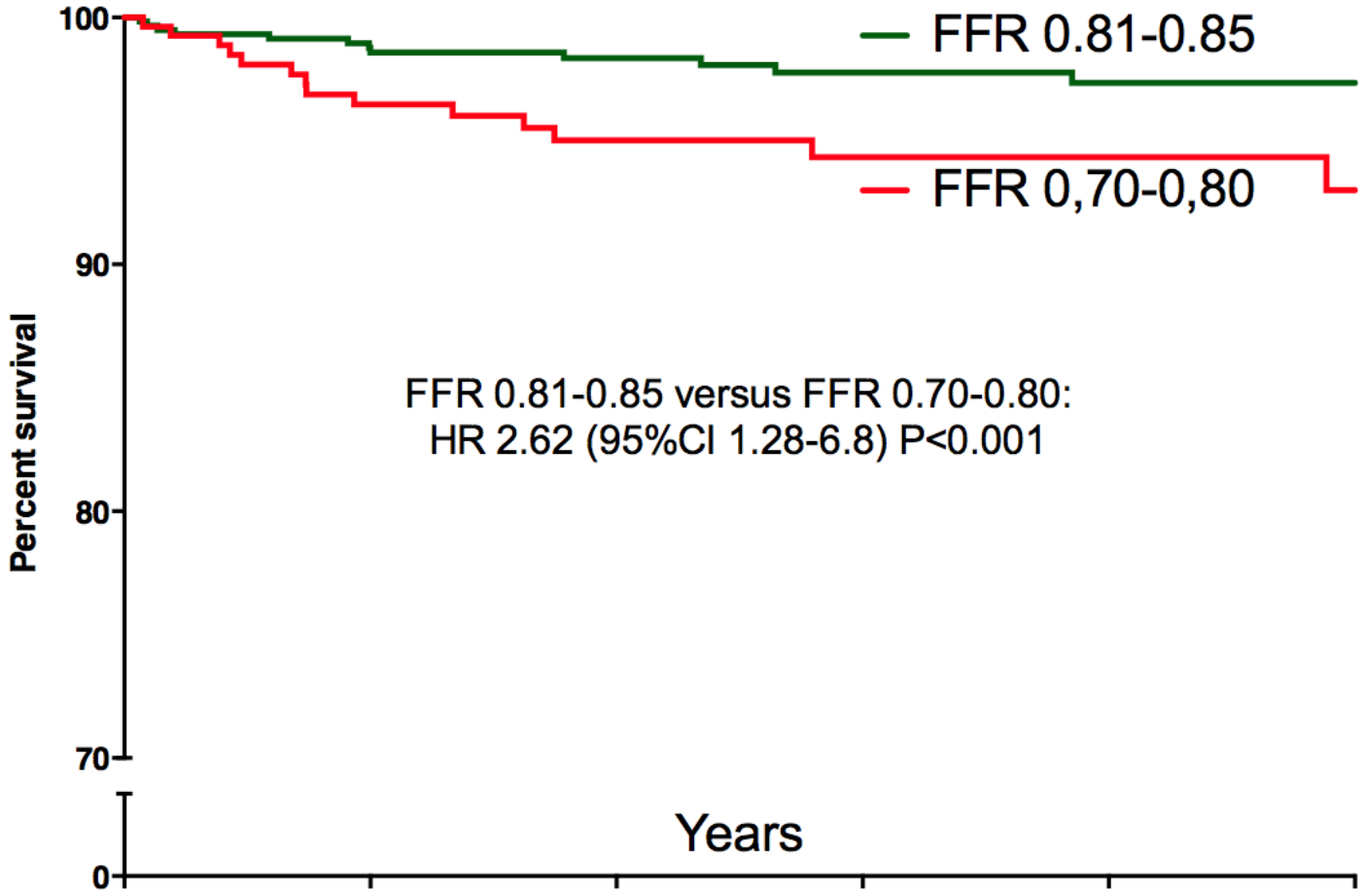
Pts with Revascularisation (n=449)



Adjedj J, EuroPCR presentation in Paris, May 22, 2015 (slide #12)

All Cause Death per FFR strata

Pts with MT (n=1010)



	0	1	2	3	4	5
FFR 0,70-0,80	319	228	175	124	92	67
FFR 0,81-0,85	691	518	411	292	227	164

Adjedj J, EuroPCR presentation in Paris, May 22, 2015 (slide #10)

European Heart Journal (2015) **36**, 509–515
doi:10.1093/eurheartj/ehu412

Risk model for estimating the 1-year risk of deferred lesion intervention following deferred revascularization after fractional flow reserve assessment

- 882 lesions deferred using FFR
  - *mean 0.87* ± 0.05

- During *4.0* ± 2.3 *years* of follow-up, *18% PCI*
  - reason: 19% MI, 46% UA, 34% stable angina
  - *0.8%/year acute MI* due to deferred lesion

Depta JP, *Eur Heart J*. 2015 Feb 21;36(8):509-15

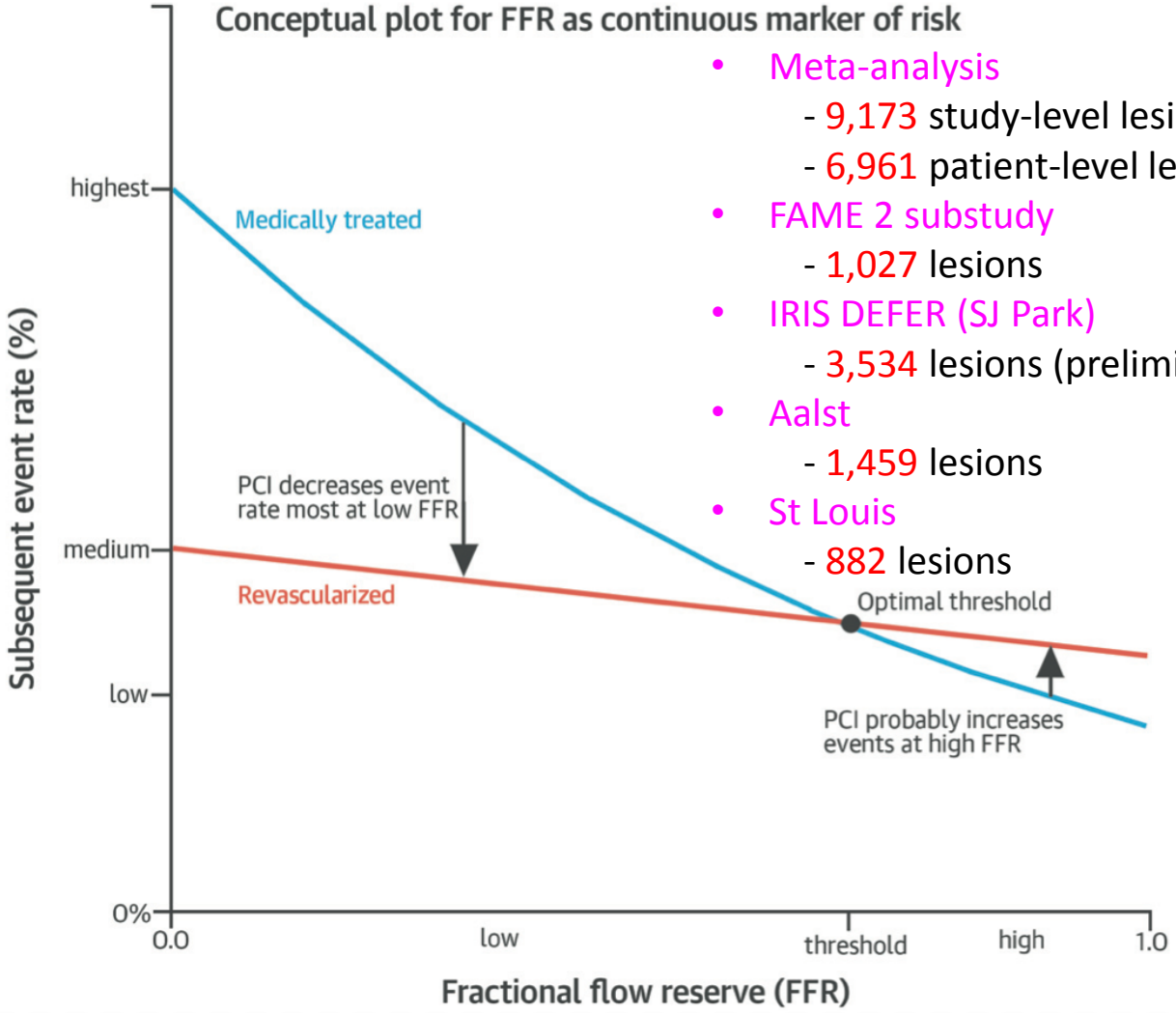
Table 5 **Multivariable predictors and 1-year β regression coefficients for freedom from DLI in the final[a] model**

	HR (95% CI)	*P*-value	*β* coefficients
Age (per 1-year increase)	0.98 (0.97–0.99)	0.005	−0.02075
Current/former smoker	1.49 (1.04–2.14)	0.03	0.39710
History of CAD or prior PCI	1.62 (1.05–2.49)	0.03	0.48086
Creatinine (per 1 mg/dL increase)	1.15 (1.08–1.22)	<0.001	0.13681
Multi-vessel CAD	1.68 (1.09–2.58)	0.02	0.51777
FFR value (per 0.05 unit decrease)	1.21 (1.03–1.42)	0.02	−3.81032

[a]The model was reduced using a stepwise variable selection technique. For prediction purposes, the 1-year baseline estimate of freedom from DLI for a patient with all covariates set to zero or to the reference group is 0.169. All abbreviations as shown in *Tables 1* and *2*.

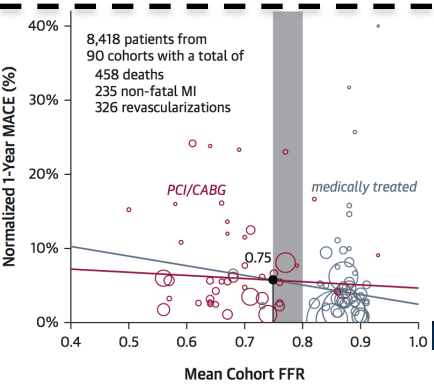
- Inverse relationship between FFR and outcomes
  - FFR *decrease of 0.05*, future PCI *increase of 21%*

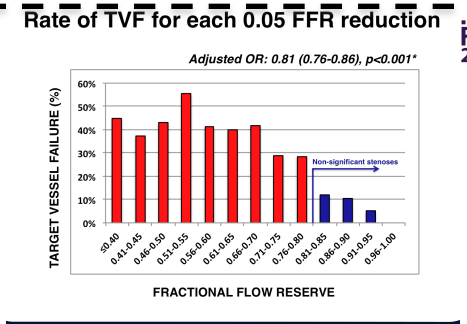
Depta JP, *Eur Heart J*. 2015 Feb 21;36(8):509-15 (Table 5)

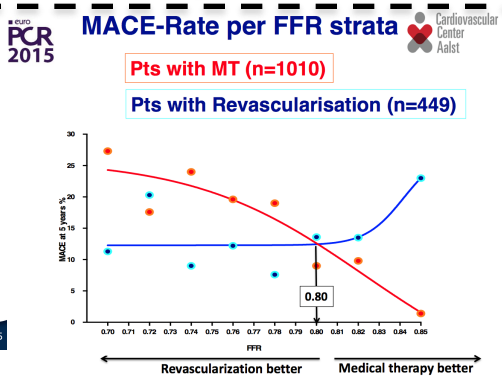


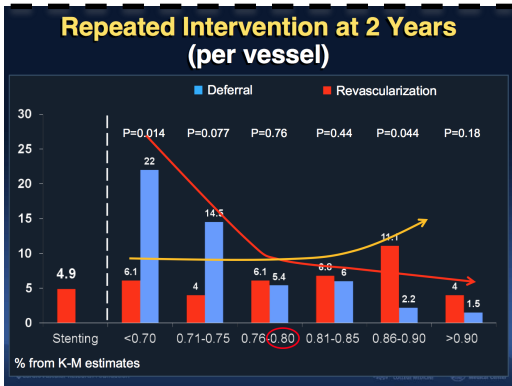
- Meta-analysis
  - 9,173 study-level lesions
  - 6,961 patient-level lesions
- FAME 2 substudy
  - 1,027 lesions
- IRIS DEFER (SJ Park)
  - 3,534 lesions (preliminary)
- Aalst
  - 1,459 lesions
- St Louis
  - 882 lesions

>15,000 lesions









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http://www.crf.org/ischemia.html (accessed June 16, 2015, with ***my emphasis added***)

does PCI reduce the incidence of MI and/or death, or is any derived benefit limited to relief of symptoms? This distinction in outcome definition is critical as if there is no penalty for delaying PCI until significantly limiting symptoms develop, then the case can be made for delaying intervention, thereby avoiding the, albeit small, risks posed by PCI.

VI

Percutaneous Coronary Intervention Versus Medical Therapy in Stable Coronary Artery Disease

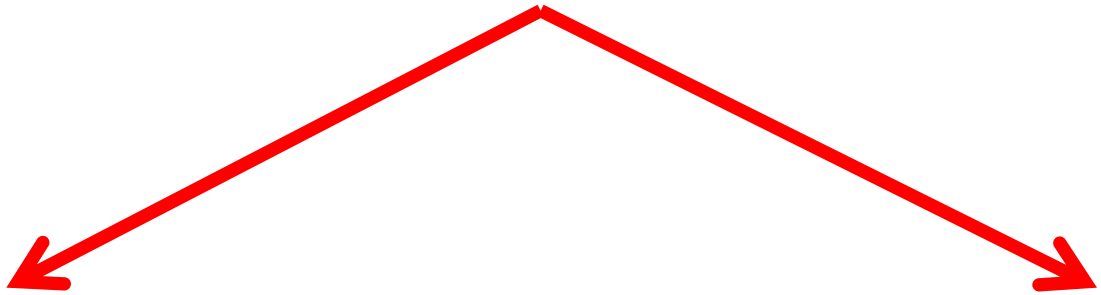
The Unresolved Conundrum

Stephen E. Epstein, MD, Ron Waksman, MD, Augusto D. Pichard, MD, Kenneth M. Kent, MD, Julio A. Panza, MD

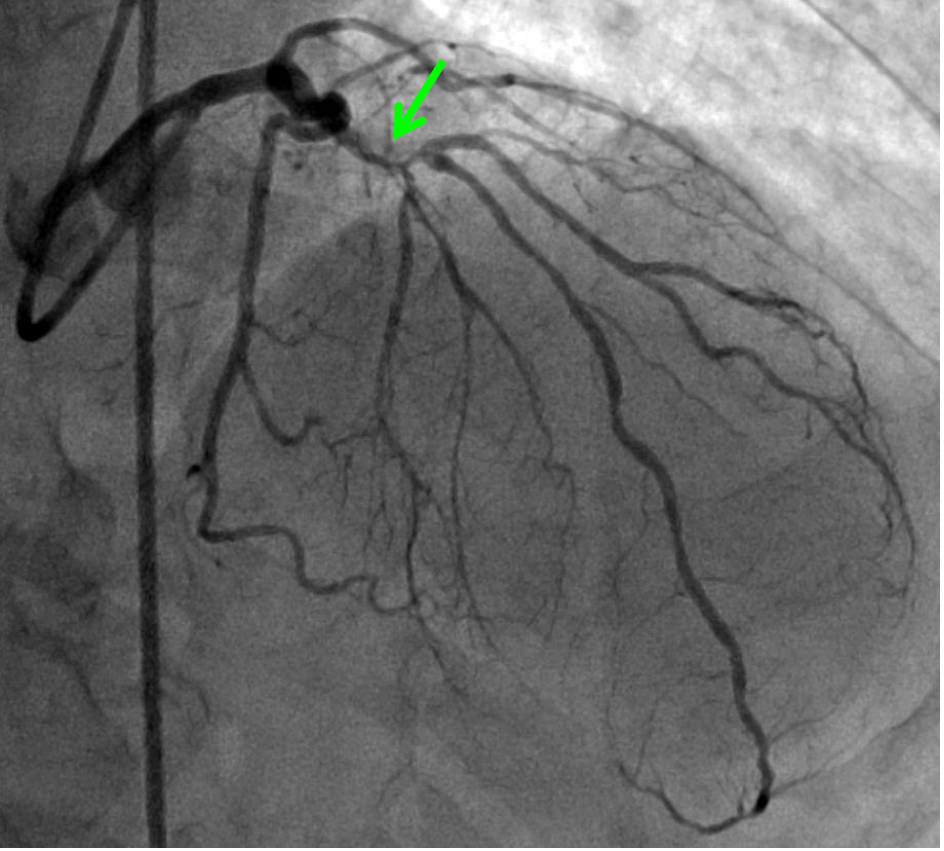
Washington, DC

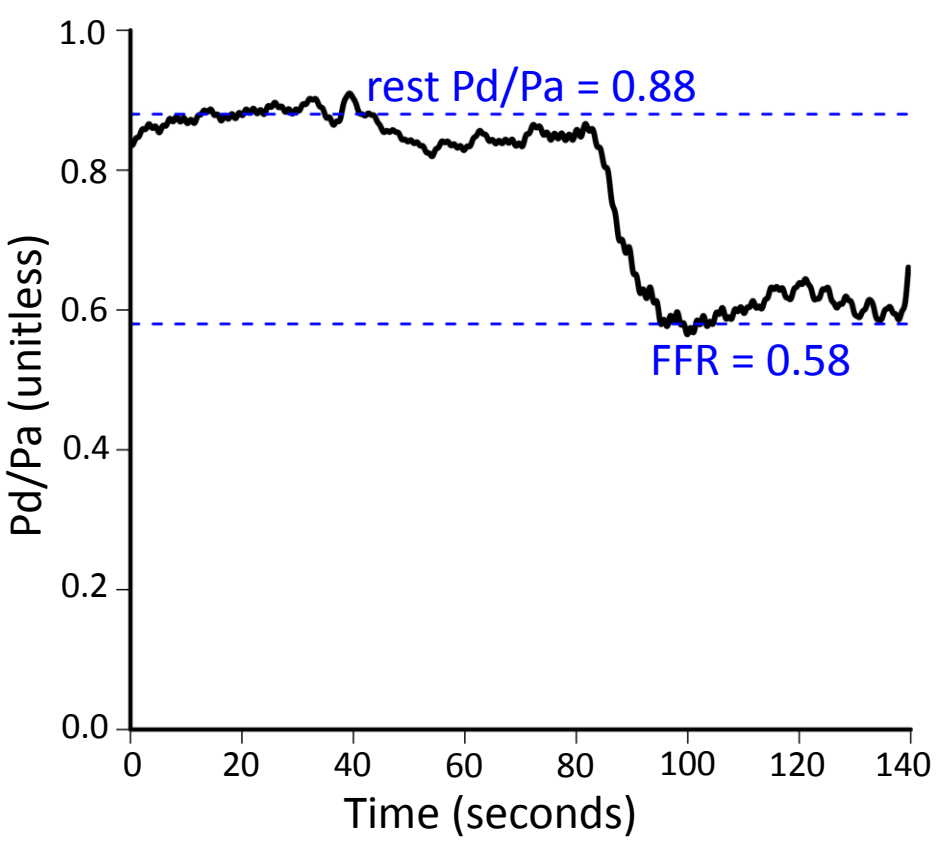
Epstein SE, *JACC Cardiovasc Interv*. 2013 Oct;6(10):993-8

PCI



symptoms prognosis





FFR = 0.58 in the proximal LAD

Can we really say *<u>nothing</u>*
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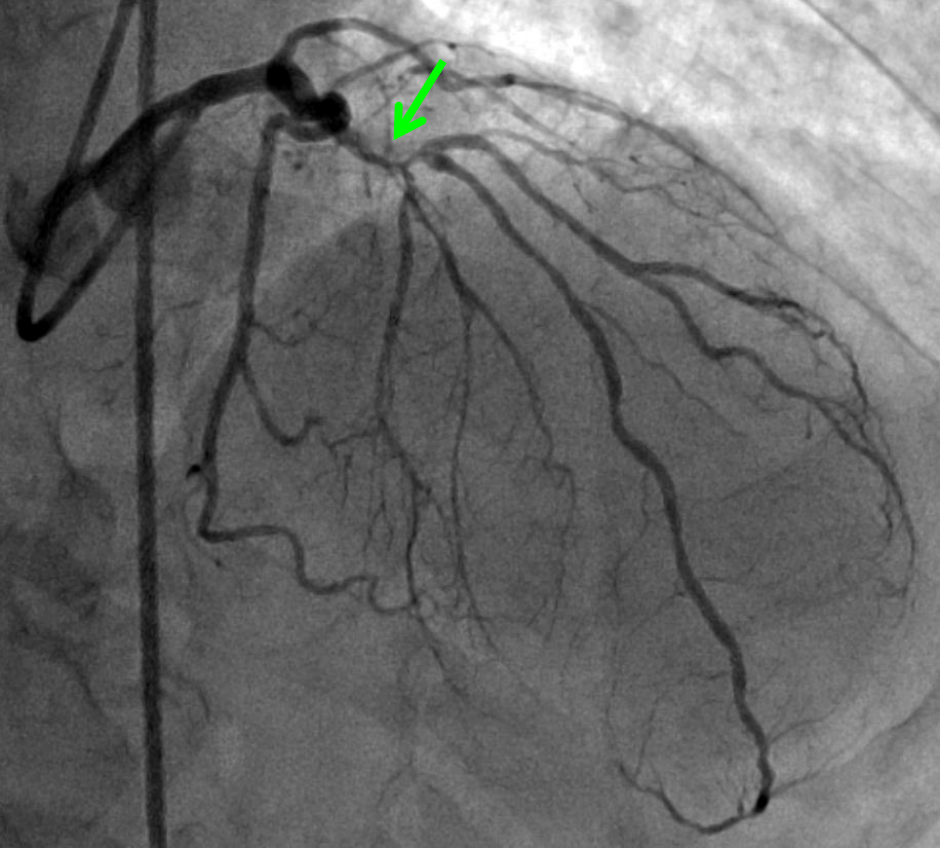

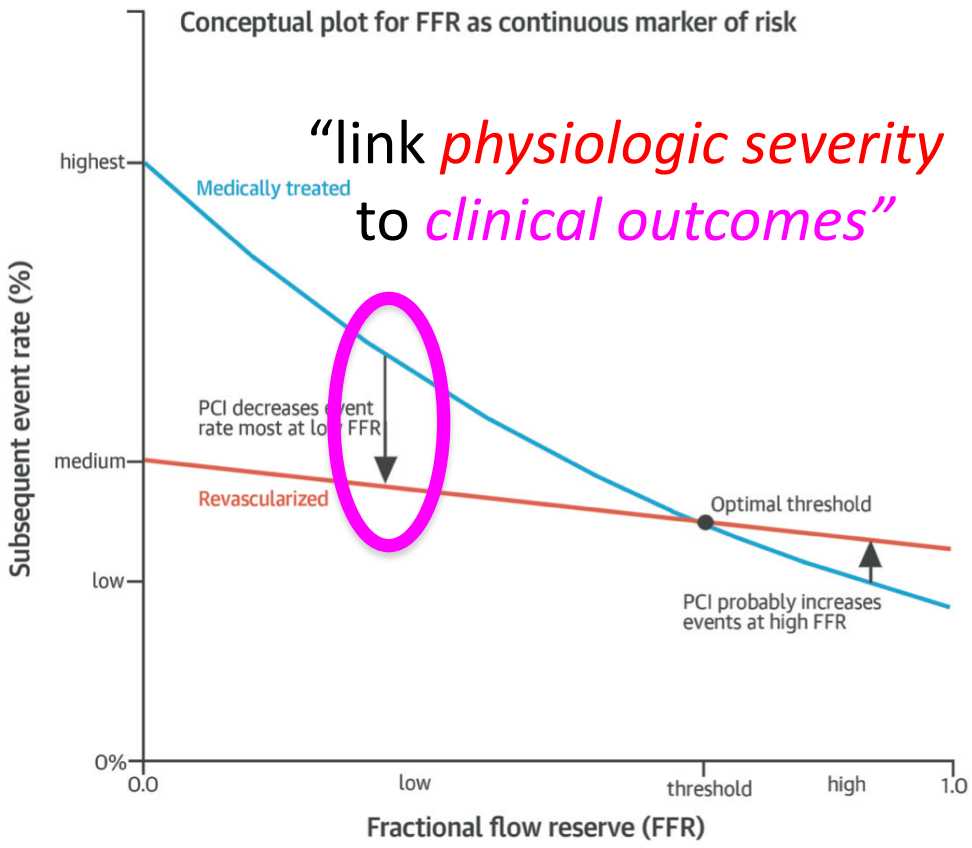

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Can we really say ~~*nothing*~~ about death & MI?