Low Penetration of FFR (1A Class) in Real Practice; Why and How to Overcome?

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FFR (or iFR) Guideline

AHA/ACC Guideline 2021

Recommendations for the Use of Coronary Physiology to Guide Revascularization With PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 5.

COR	LOE	Recommendations
1	A	1. In patients with angina or an anginal equivalent, undocumented ischemia, and angiographically intermediate stenoses, the use of fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) is recommended to guide the decision to proceed with PCI.[1-6]
3: No benefit	B-R	2. In stable patients with angiographically intermediate stenoses and FFR >0.80 or iFR >0.89, PCI should not be performed.[7-10]

ESC Guideline 2018

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

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Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI

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ABSTRACT

BACKGROUND

The instantaneous wave-free ratio (iFR) is an index used to assess the severity of coronary-artery stenosis. The index has been tested against fractional flow reserve (FFR) in small trials, and the two measures have been found to have similar diagnostic accuracy. However, studies of clinical outcomes associated with the use of iFR are lacking. We aimed to evaluate whether iFR is noninferior to FFR with respect to the rate of subsequent major adverse cardiac events.

METHODS

We conducted a multicenter, randomized, controlled, open-label clinical trial using the Swedish Coronary Angiography and Angioplasty Registry for enrollment. A total of 2037 participants with stable angina or an acute coronary syndrome who had an indication for physiologically guided assessment of coronary-artery stenosis were randomly assigned to undergo revascularization guided by either iFR or FFR. The primary end point was the rate of a composite of death from any cause, nonfatal myocardial infarction, or unplanned revascularization within 12 months after the procedure.

RESULTS

A primary end-point event occurred in 68 of 1012 patients (6.7%) in the iFR group and in 61 of 1007 (6.1%) in the FFR group (difference in event rates, 0.7 percentage points; 95% confidence interval [CI], −1.5 to 2.8; P=0.007 for noninferiority; hazard ratio, 1.12; 95% CI, 0.79 to 1.58; P=0.53); the upper limit of the 95% confidence interval for the difference in event rates fell within the prespecified noninferiority margin of 3.2 percentage points. The results were similar among major subgroups. The rates of myocardial infarction, target-lesion revascularization, restenosis, and stent thrombosis did not differ significantly between the two groups. A significantly higher proportion of patients in the FFR group than in the iFR group reported chest discomfort during the procedure.

CONCLUSIONS

Among patients with stable angina or an acute coronary syndrome, an iFR-guided revascularization strategy was noninferior to an FFR-guided revascularization strategy with respect to the rate of major adverse cardiac events at 12 months. (Funded by Philips Volcano; iFR SWEDEHEART ClinicalTrials.gov number, NCT02166736.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Götberg at the Department of Cardiology, Clinical Sciences, Lund University, Skåne University Hospital, 222 41 Lund, Sweden, or at matthias.gotberg@med.lu.se.

*A complete list of participating centers and investigators in the Instantaneous Wave-free Ratio versus Fractional Flow Reserve in Patients with Stable Angina Pectoris or Acute Coronary Syndrome (iFR-SWEDEHEART) trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on March 18, 2017, at NEJM.org.

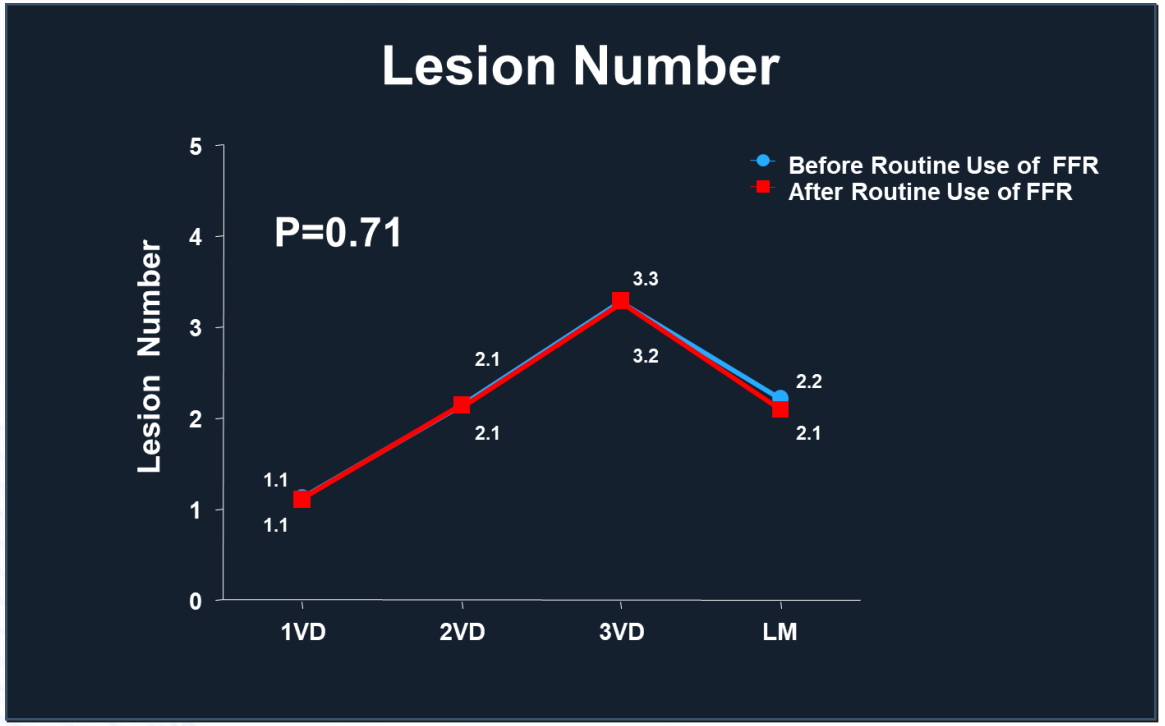
N Engl J Med 2017;376:1813-23.
DOI: 10.1056/NEJMoa1616540

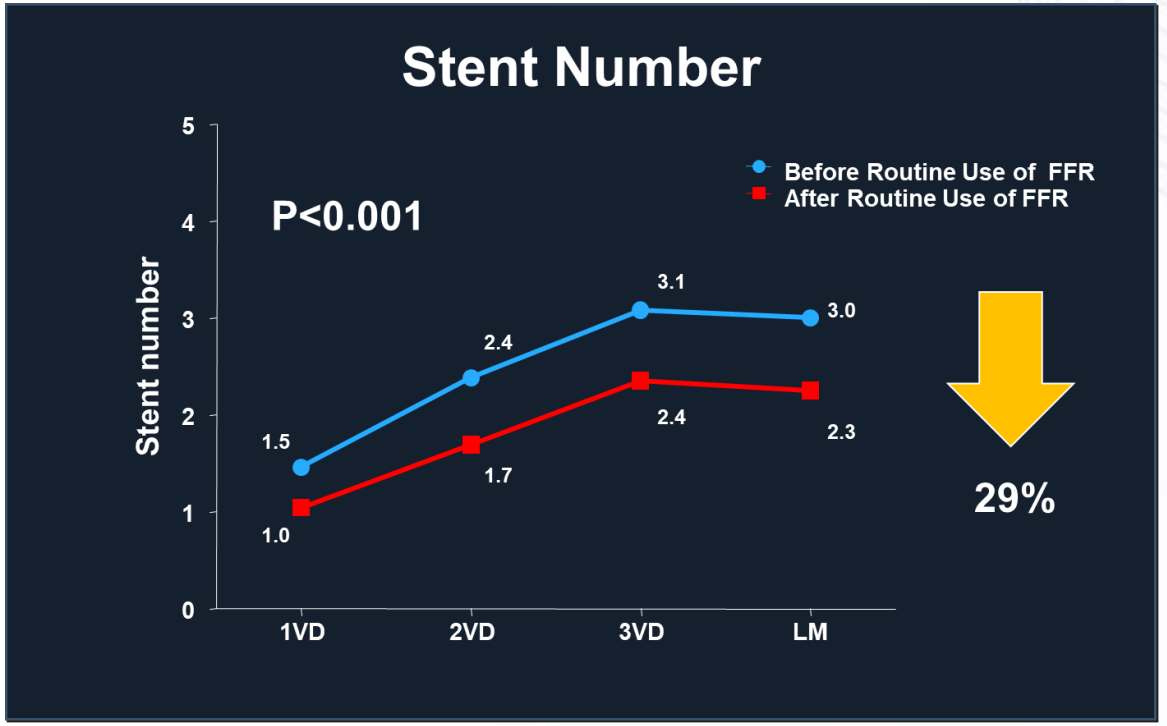
FFR (or iFR)

- Minimum Scientific and Ethical Safeguards to Avoid Unnecessary PCI
- No Benefit of PCI: FFR > 0.80 or iFR >0.89

Clinical Benefit of FFR (1)

ASAN PCI Registry

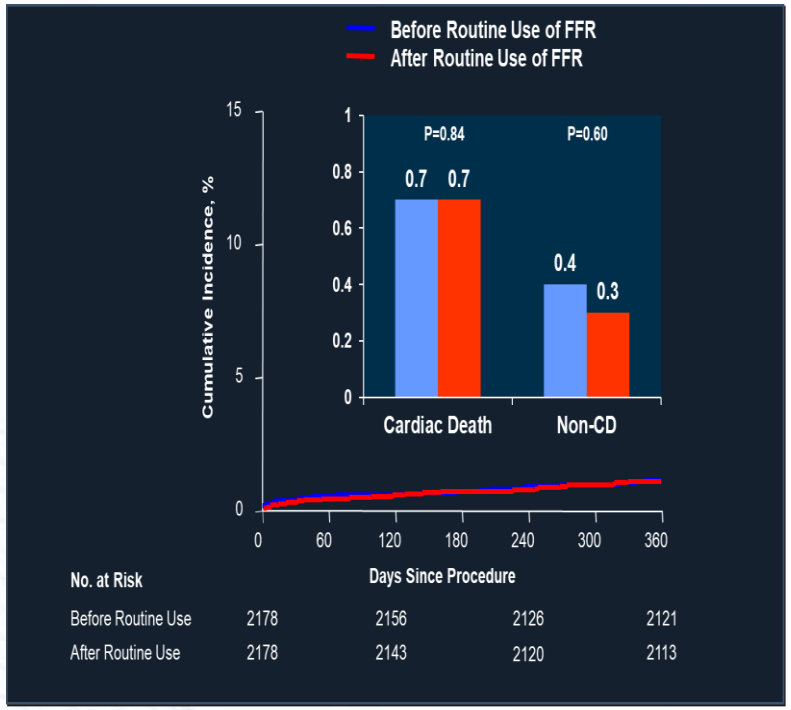




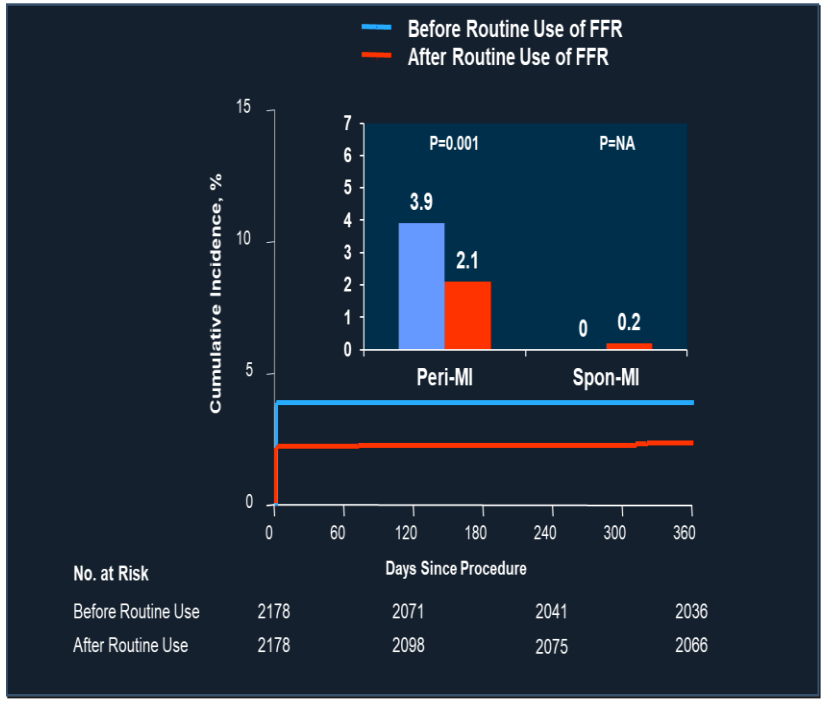
Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

Clinical Benefit of FFR (2)

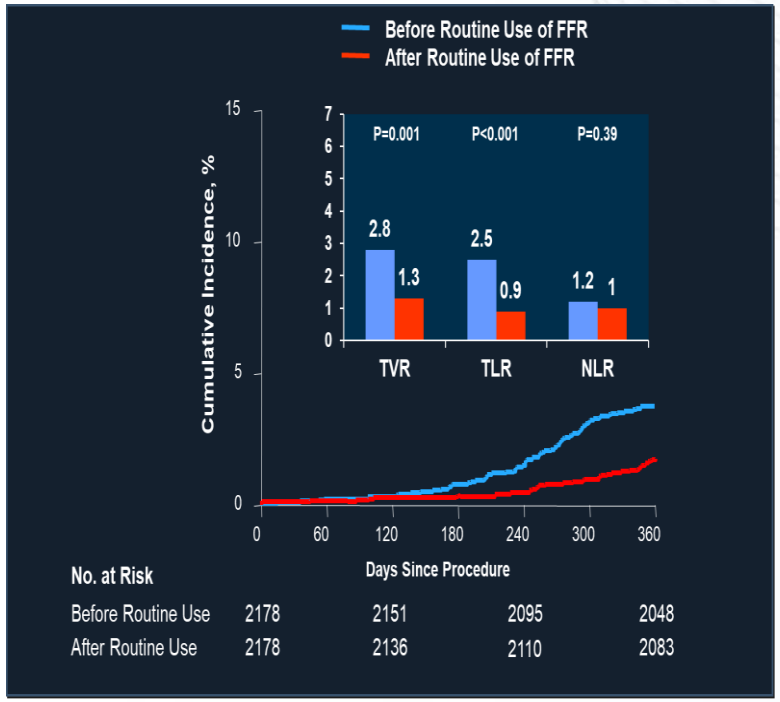
Death



Myocardial Infarction



Repeat Revascularization

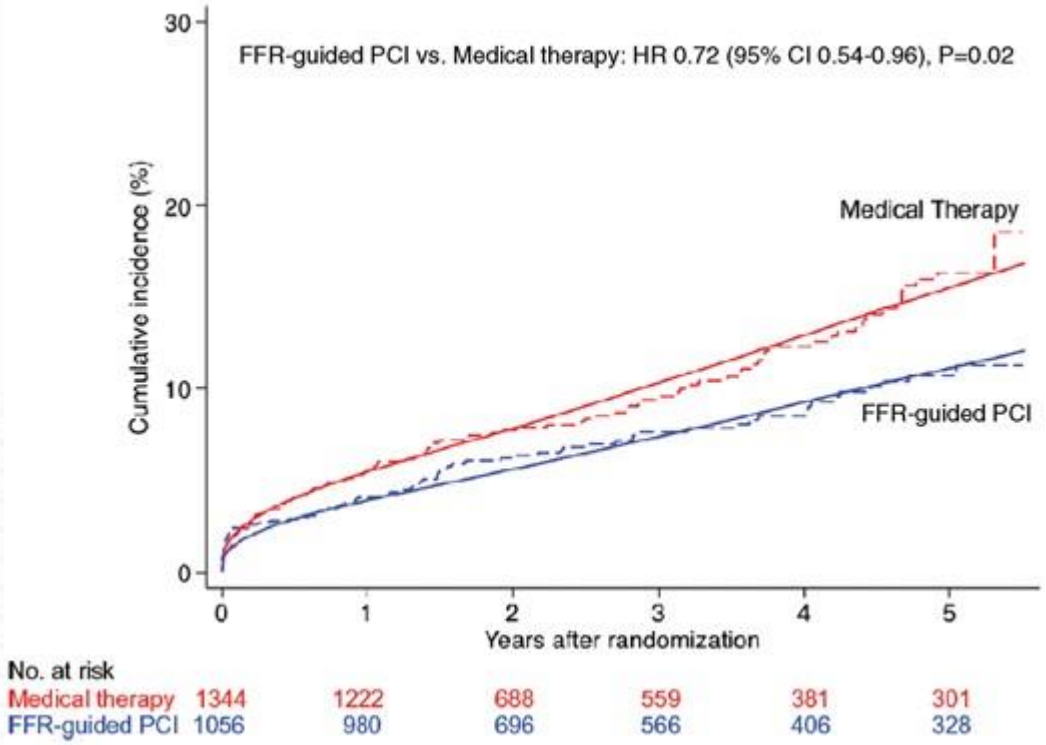


- The benefit of FFR guided PCI is primarily due to
  1) The reduced number of stents used per patients
  2) The subsequent decreased risk of peri-procedural MI and repeat revascularization

Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

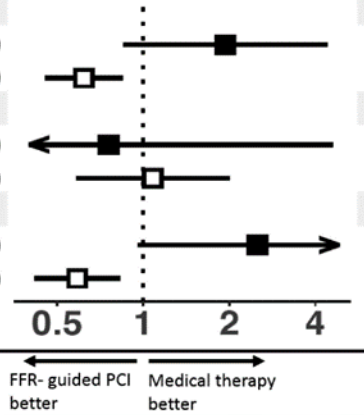
Clinical Benefit of FFR (3)

Meta-analysis from FAME2, DANAMI, COMPARE-Acute



Reduction of Spontaneous Myocardial Infarction

	HR (95% CI)	P-value	P-value for interaction
Cardiac death or myocardial infarction			0.003
Day 0 to 7	1.94 (0.85 to 4.42)	0.12	
Day 8 to maximum follow-up	0.62 (0.46 to 0.85)	0.003	
Cardiac death			0.83
Day 0 to 7	0.76 (0.12 to 4.60)	0.76	
Day 8 to maximum follow-up	1.08 (0.58 to 2.01)	0.81	
Myocardial infarction			0.001
Day 0 to 7	2.51 (0.96 to 6.57)	0.06	
Day 8 to maximum follow-up	0.59 (0.42 to 0.83)	0.002	



Eur Heart J . 2019 Jan 7;40(2):180-186.

Why the Penetration of FFR is Low ?

Revascularization in Stable Angina

PCI Failure or Trial Failure ?

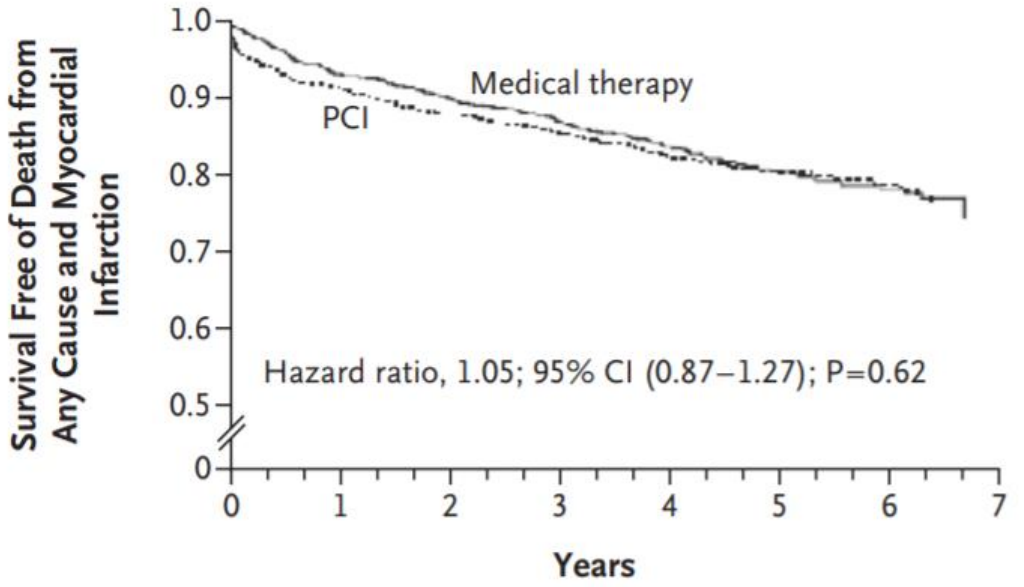
COURAGE

FAME2

ISCHEMIA Trial

COURAGE Trial

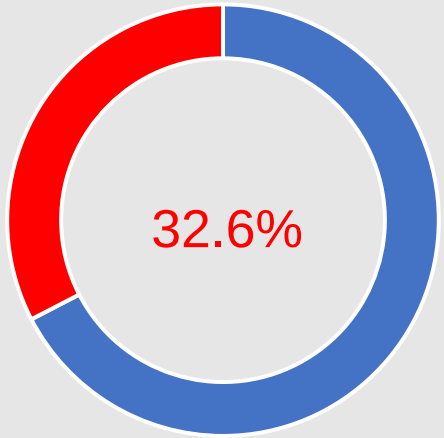
Death from Any Cause and MI



No. at Risk

Medical therapy	1138	1017	959	834	638	408	192	30
PCI	1149	1013	952	833	637	417	200	35

Revasc. During FU in Medication Group



Spontaneous MI

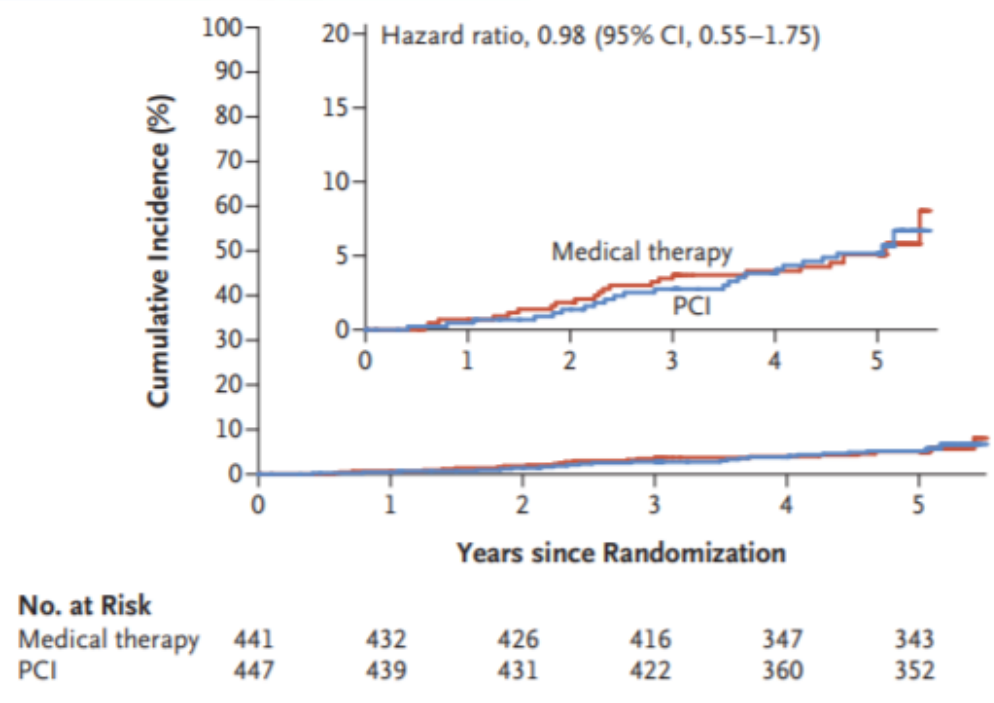
Medication: 119

PCI: 108

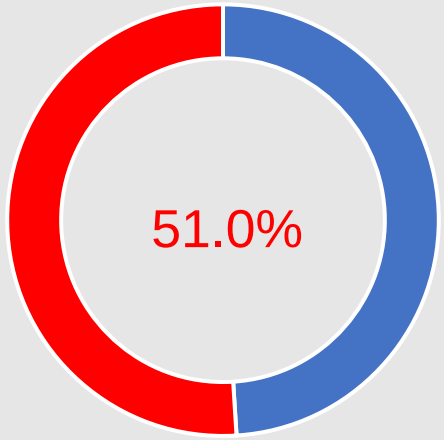
Boden et al. New Engl J Med 2007;356:1503-16.

FAME 2 Trial

Death from Any Cause



Revasc. During FU in Medication Group



Spontaneous MI

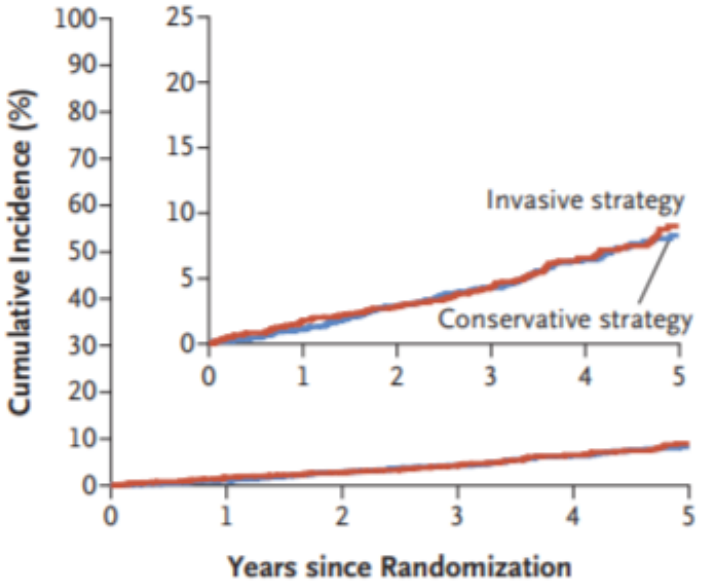
Medication: 54

PCI: 29

P. Xaplanteris et al. N Engl J Med 2018;379:250-9

ISCHEMIA Trial

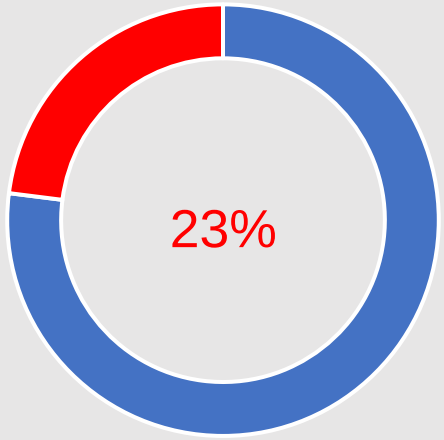
Death from Any Cause



No. at Risk

Conservative strategy	2591	2548	2065	1445	844	349
Invasive strategy	2588	2518	2061	1431	827	317

Revasc. During FU in Medication Group



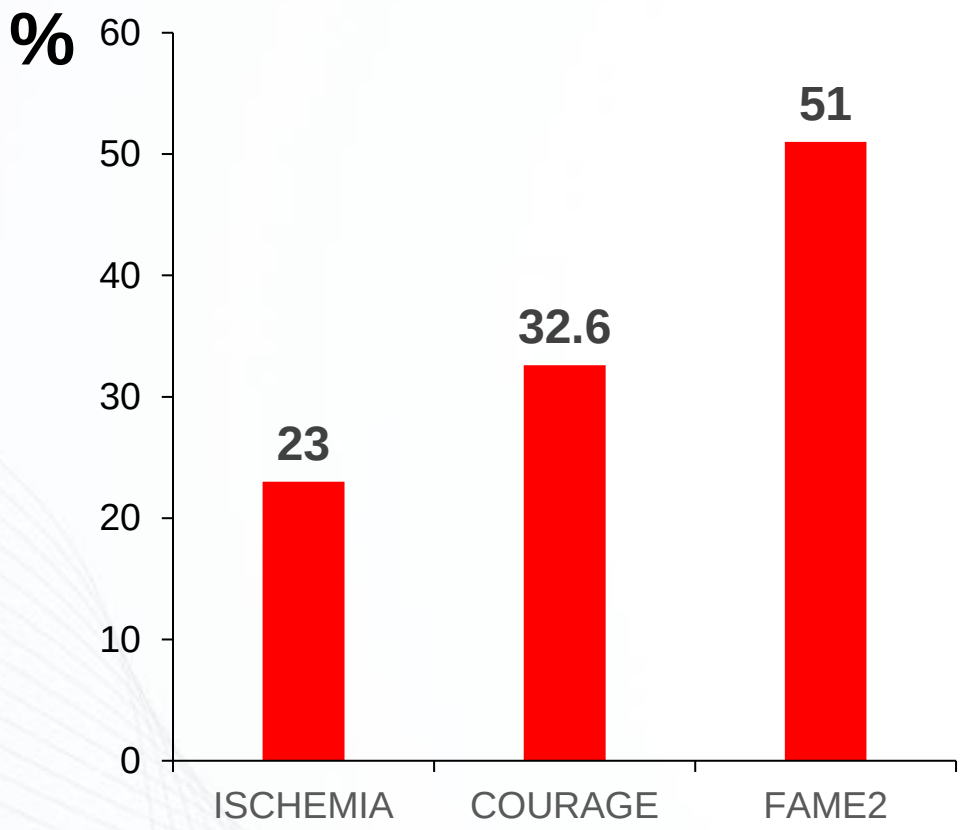
Spontaneous MI

Medication: 196

PCI: 130

Boden et al. New Engl J Med 2007;356:1503-16.

Revascularization in Medication Group



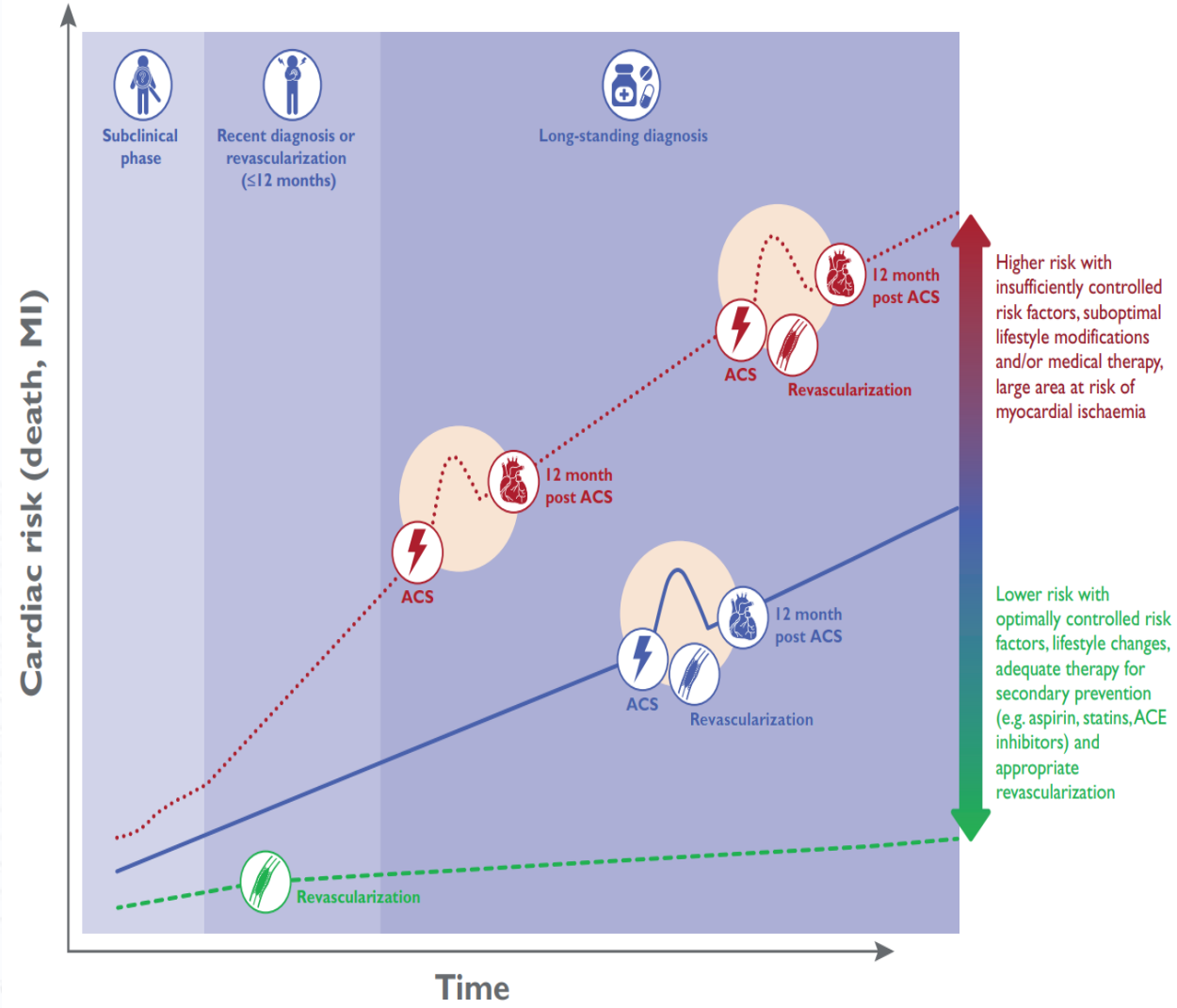
Reduction of Spontaneous MI

	Hazard Ratio
COURAGE Trial	≈ 0.89 (?)
FAME2 Trial	0.62 (0.39-0.99)
Meta*	0.59 (0.42-0.83)
ISCHEMIA Trial	0.67 (0.53-0.83)
COMPLETE Trial	0.68 (0.53-0.86)

Non culprit lesion revascularization in STEMI with MV

* Meta-analysis from FAME2, DANAMI, COMPARE-Acute
Eur Heart J . 2019 Jan 7;40(2):180-186.

Natural History of Stable Angina Patients with Moderate to Severe Ischemia Under OMT



The ISCHEMIA perspective

Rapid progression or Rupture

7.6% - sMI

1.2% - uAP admission

2591 patients under OMT

85% - No Event

Regression or Adaptation

Severe IHD that Can Affect Worse Prognosis Were Excluded in the Trials

Major Exclusion Criteria

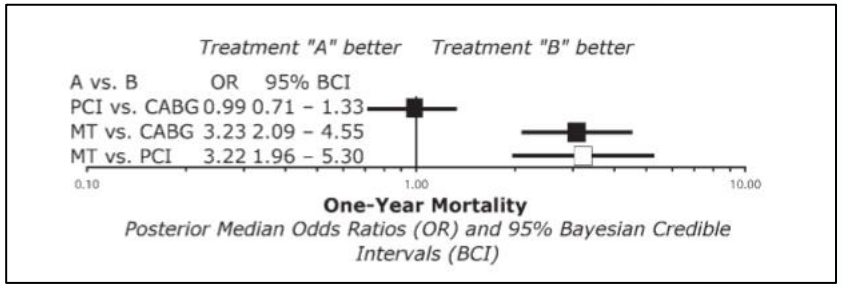
COURAGE
- Persistent CCS IV
- High-risk stress test
- LM disease
- EF <30%
- Refractory HF

FAME II
- CABG indicated
- LM disease
- LVEF <30%

ORBITA
- Multi-vessel ds
- LM disease
- LV dysfunction

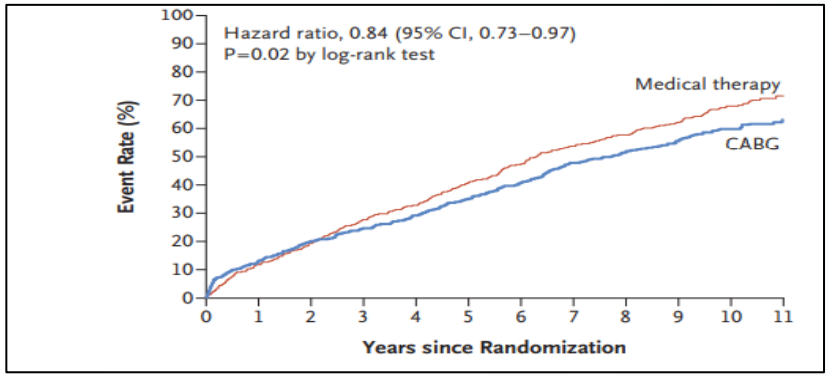
ISCHEMIA
- NYHA III-IV HF
- Refractory Angina
- LM disease
- EF <35%

Left Main Coronary Stenosis: Meta-analysis



Circulation. 2013;127:2177-2185

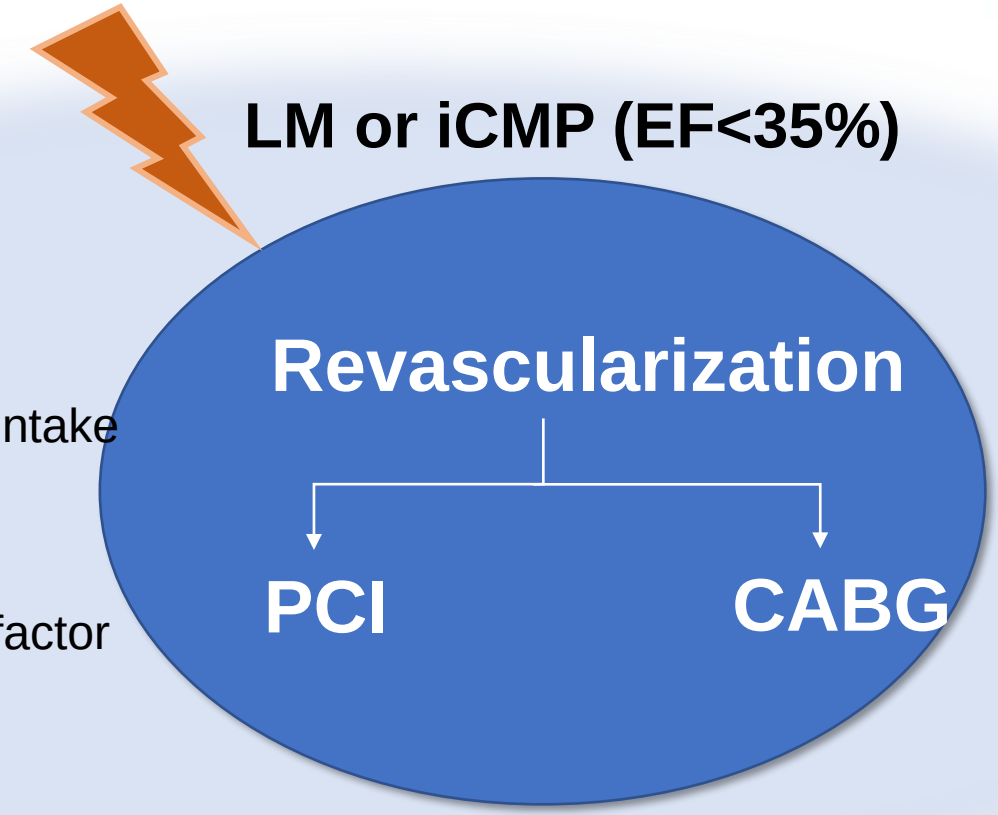
Ischemic cardiomyopathy (EF < 35%): STICH Trial



N Engl J Med 2016;374:1511-20

Treatment of SIHD

OMT plus Risk Factor Modification (Default Treatment)

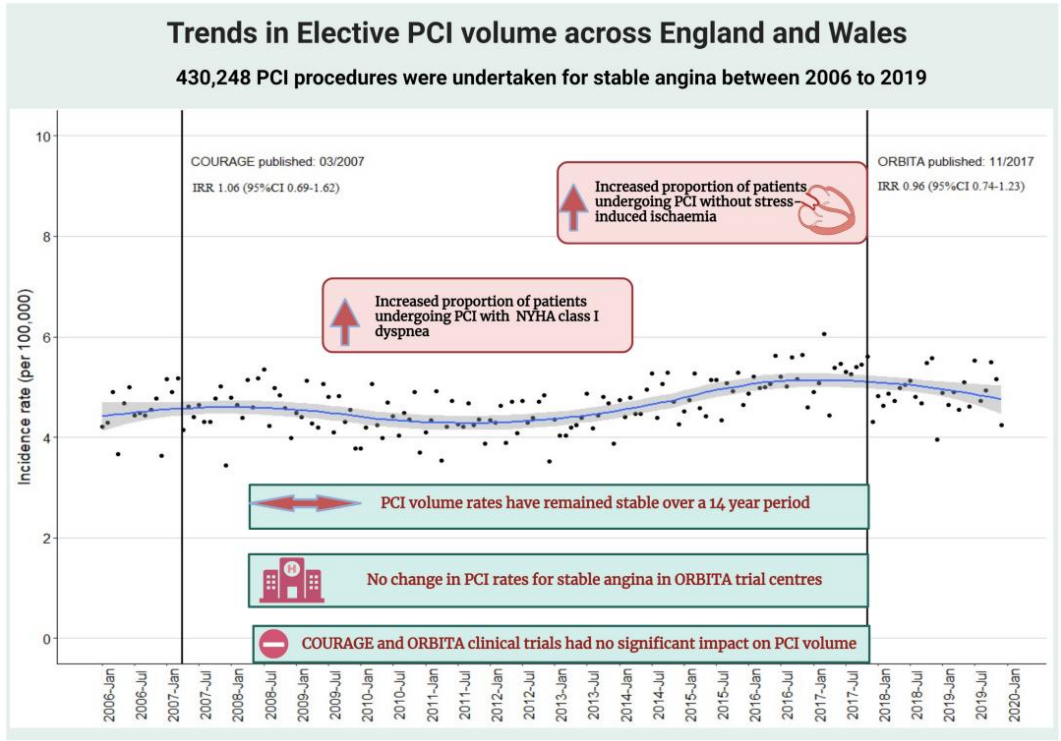


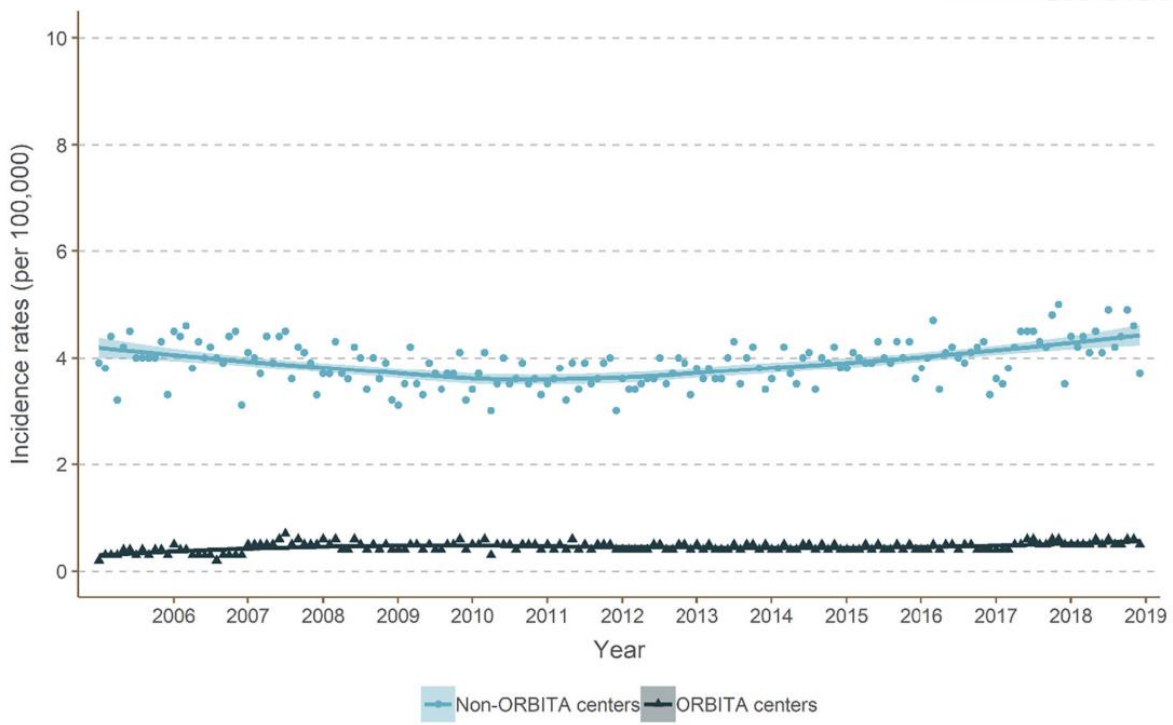
Behavioral risk factor
- Smoking cessation
- Physical activity
- Reduced saturated fat intake

Physiologic risk factor
- BP control
- Lipid control
- BMI control

Pharmacologic Targets
- Aspirin
- Statin
- Ezetimibe
- ACEi/ARB
- Beta blocker

Impact of COURAGE and ORBITA Trials



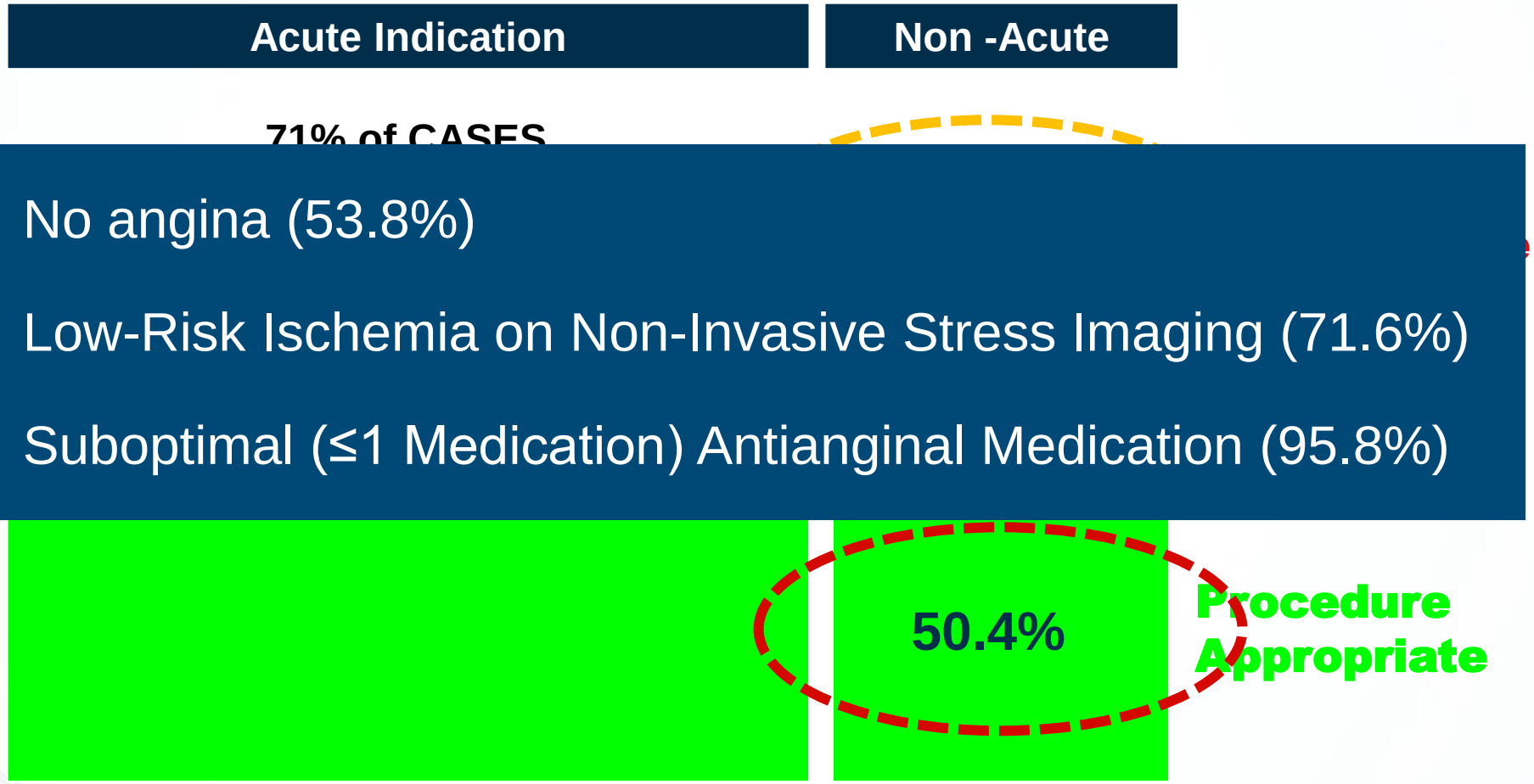


J Am Heart Assoc. 2022;11:e025426. DOI: 10.1161/JAHA.122.025426

Doctors (Humans) are like that.
They don't change easily.

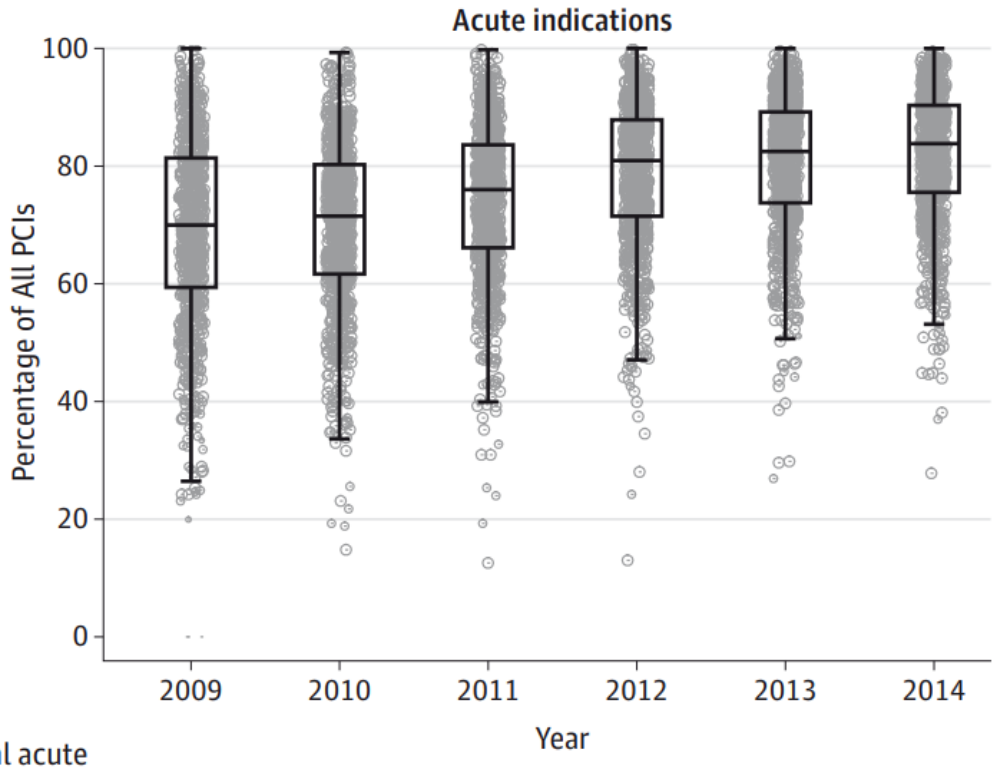
Appropriateness of PCI

From NCDR CathPCI Registry(N=500,154)

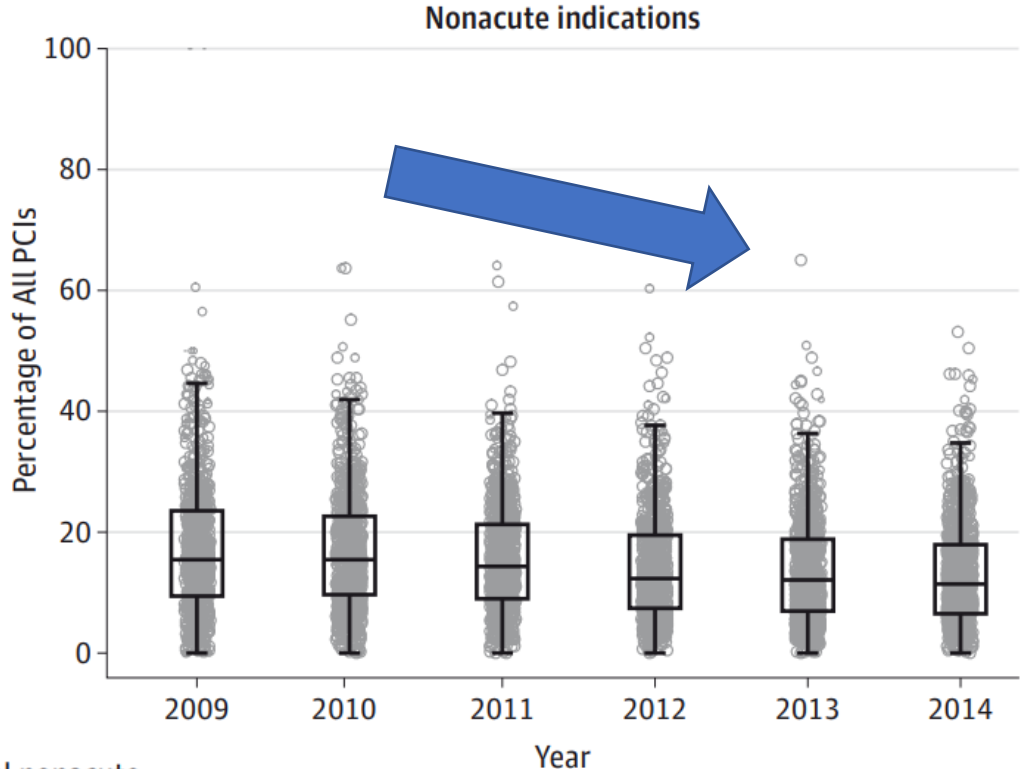


JAMA 2011;306(1):53-61

Since the publication of the Appropriate Use Criteria for Coronary Revascularization in 2009, there have been significant reductions in the volume of nonacute PCI



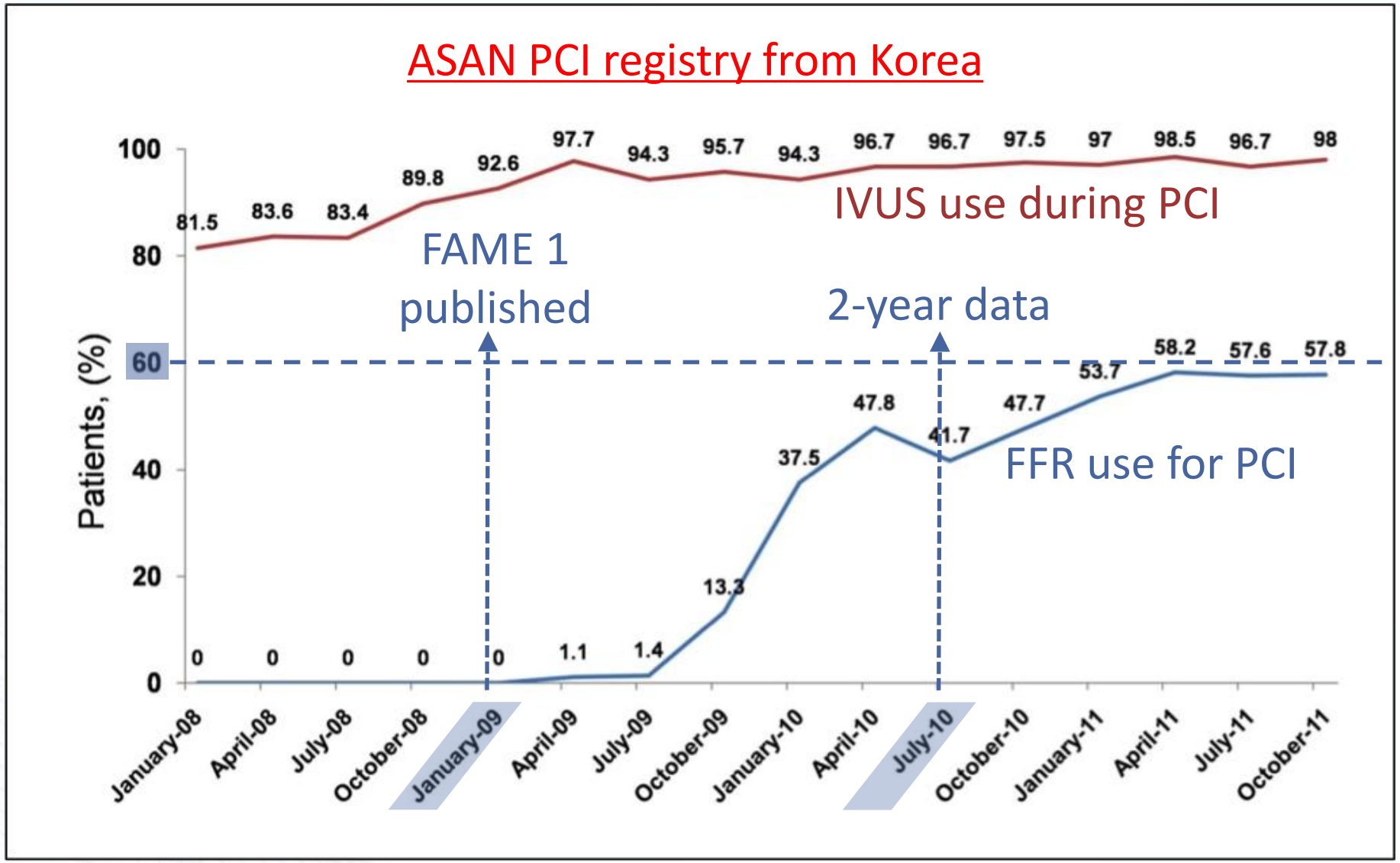
Hospital acute PCI volume, median No. (IQR)	2009	2010	2011	2012	2013	2014
	177 (101-289)	402 (246-629)	389 (255-614)	407 (264-627)	401 (262-620)	403 (265-620)



Hospital nonacute PCI volume, median No. (IQR)	2009	2010	2011	2012	2013	2014
	39 (20-72)	84 (46-151)	72 (39-127)	60 (34-107)	55 (29-100)	53 (27-98)

JAMA. 2015;314(19):2045-2053

Current Status of FFR Penetration (1)



Use of FFR wire (Abbott)

2019Y: 1238

2020Y: 1096

2021Y: 1214

2022Y: 1196

Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

Current Status of FFR Penetration (2)

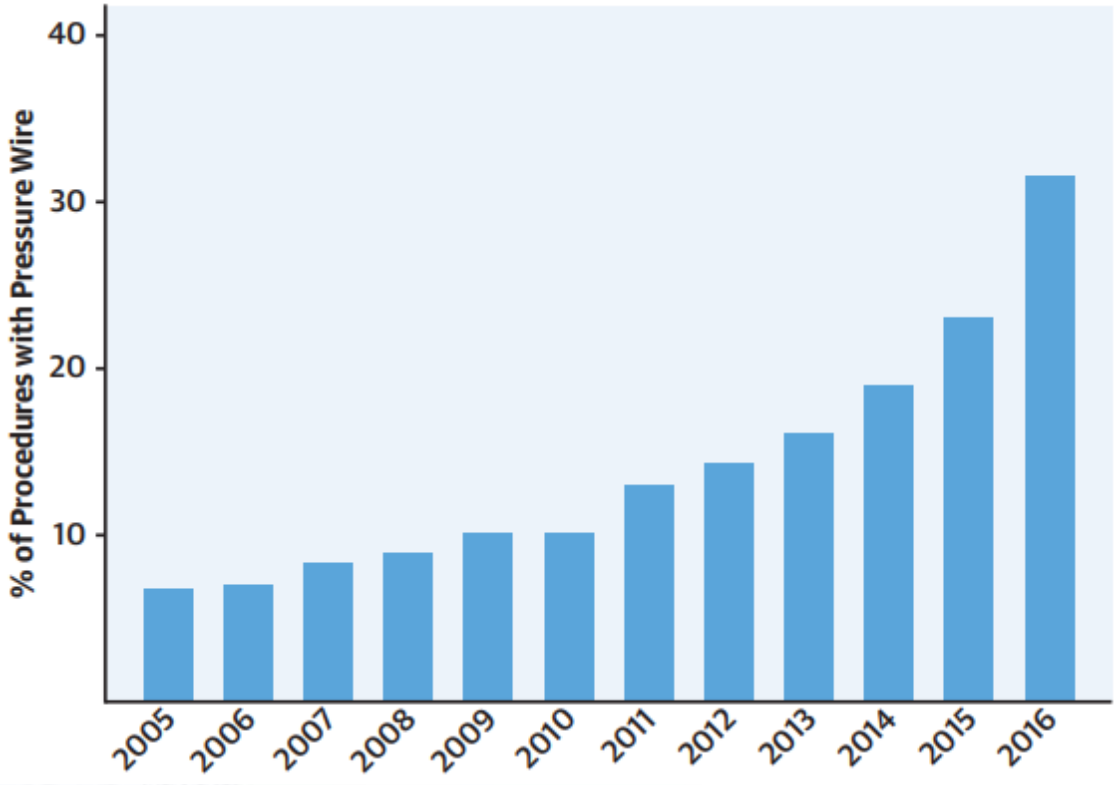
TABLE 1 Public Reporting of Coronary Physiology Uptake

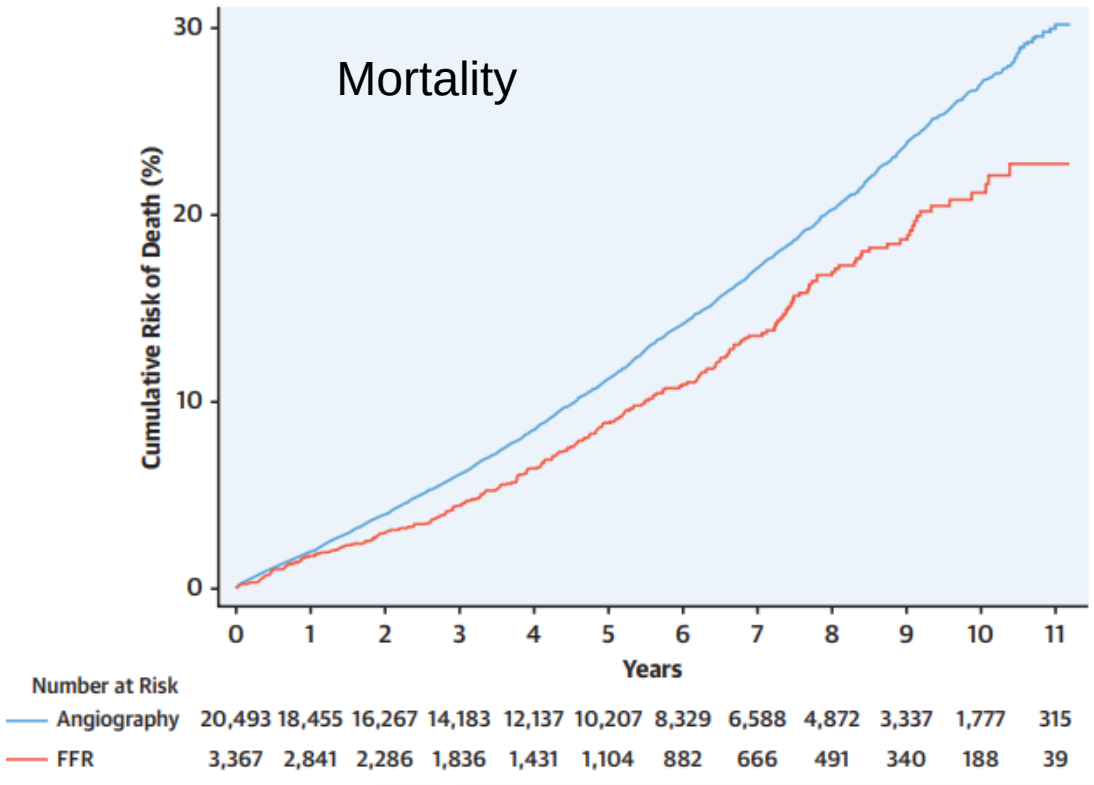
Country (Ref. #)	Year	PW	PCI	PW/PCI	Temporal Change	Hospital-Level Reporting?
Sweden (9)	2017	NR	NR	26%	3.1-fold in 10 yrs	Yes
United Kingdom (10)	2016	18,811	100,483	19%	3.5-fold in 8 yrs	Yes
Italy (11)	2016	11,000	218,751	5%	1.4-fold in 4 yrs	Yes
Europe EAPCI (12)	2015	NR	889,957	16%	2-fold in 5 yrs	Per country
United States (13)	2014	3,465*	NR	31%	3.8-fold in 5 yrs	No
Australia (14)	2015	NR	3,869	19%	100-fold in 9 yrs	Per state

Gradually, People Are Changing.

Current Status of FFR Penetration (3)

SCAAR Registry (>30%)

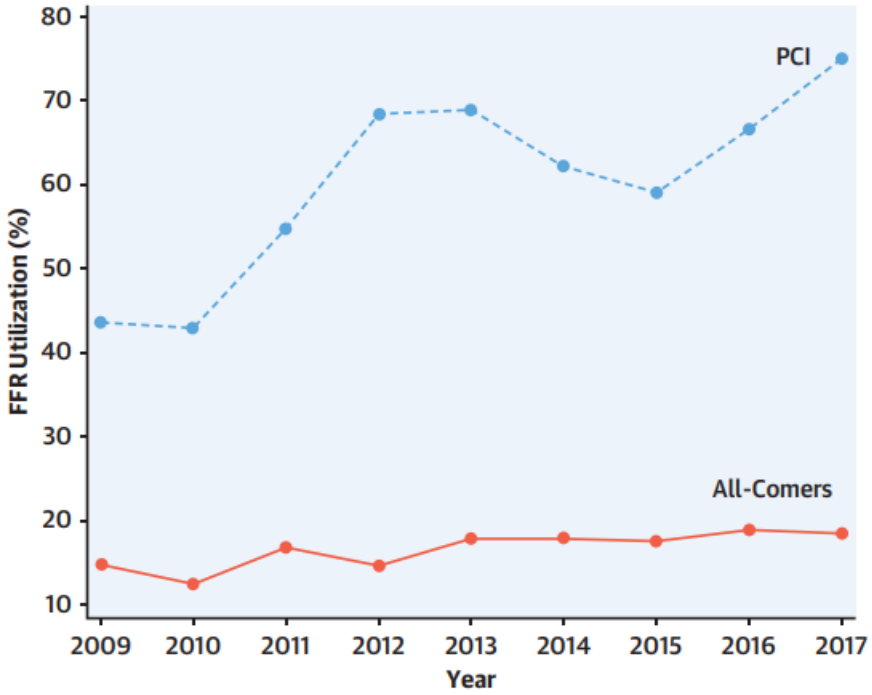


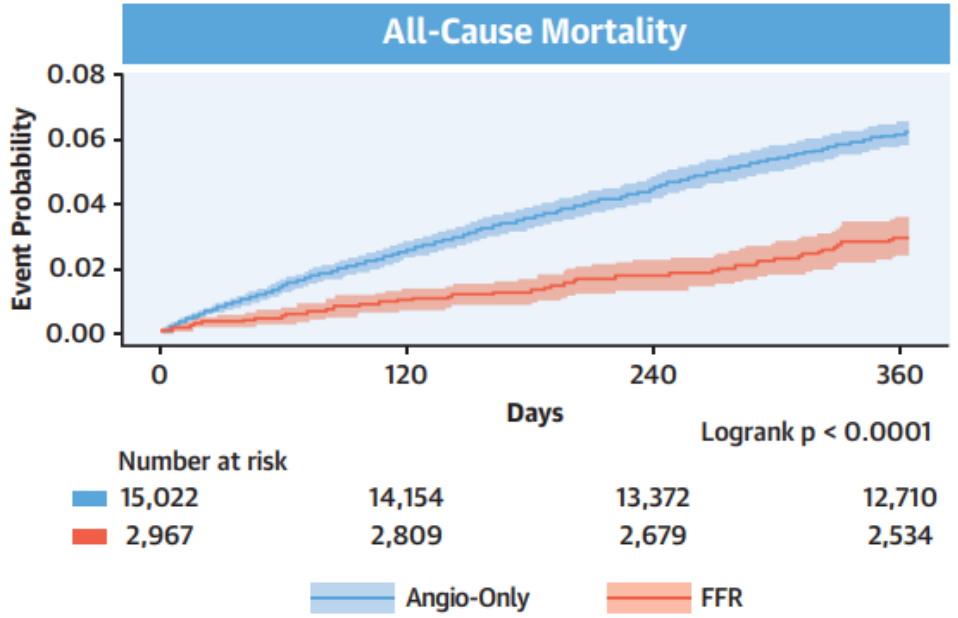


J Am Coll Cardiol 2020;75:2785–99

Current Status of FFR Penetration (4)

Veterans Affairs Registry (>70%)

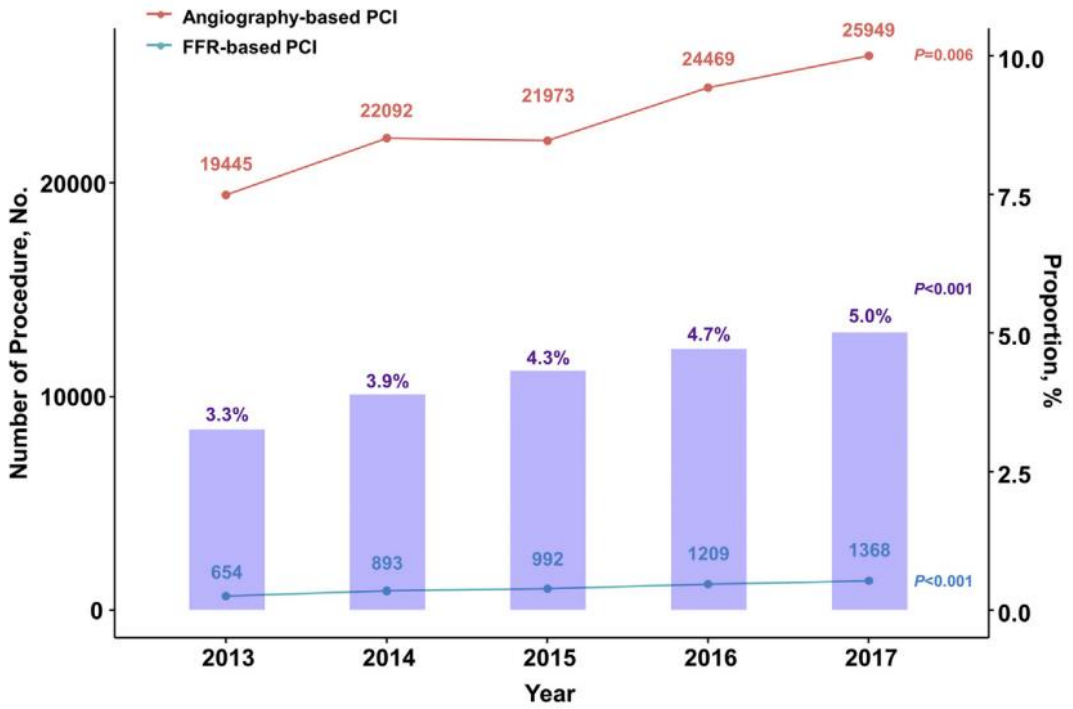


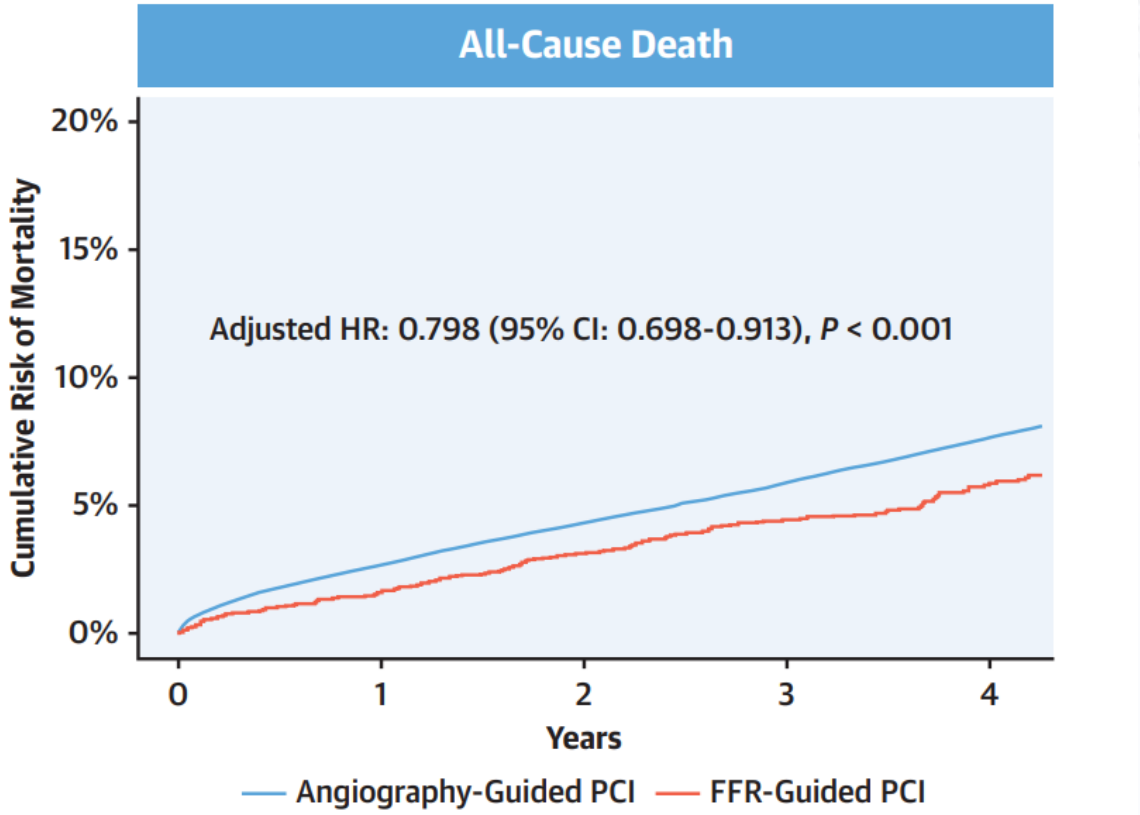


J Am Coll Cardiol 2020;75:409–19

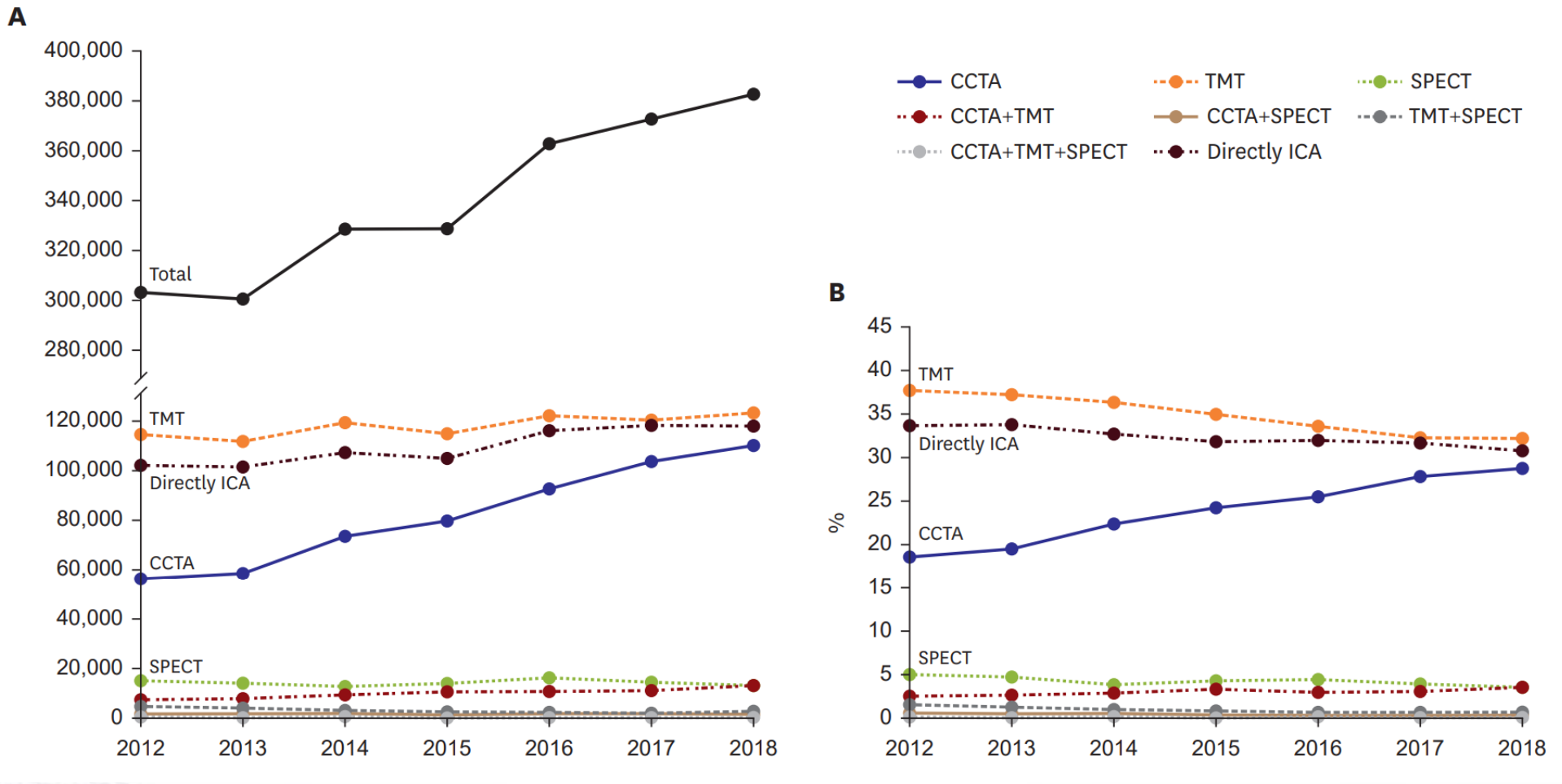
Current Status of FFR Penetration (5)

The ***Korea*** National Health Insurance Service Database (5% !!)





Nationwide Trends of Gatekeeper to Invasive Coronary Angiography in Suspected Coronary Artery Disease



Korean Circ J. 2022 Nov;52(11):814-825

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EDITORIAL COMMENT

Coronary Psychology

Do You Believe?*

Nils P. Johnson, MD, MS,[a] Bon-Kwon Koo, MD, PhD[b]

"Why don't physicians follow clinical practice guidelines?" That question—the title of a broad data review and synthesis (1)—remains as valid today as it was almost 20 years ago when posed. The Cabana et al. (1) framework connected 3 major steps along a path: knowledge (understanding what do to), attitude (believing that it should be done), and behavior (actually doing it). At each step, potential barriers can thwart the desired action. Given the enormous evidence base supporting coronary physiology, its perceived underuse in clinical practice has led to a multitude of explanatory theories, including hyperemic drugs, wire properties, and reimbursement. In this issue of *JACC: Cardiovascular Interventions*, the ERIS study from Italy (2) provides an important opportunity to examine new and old data for each of these hypothetical barriers.

SEE PAGE 1482

claimed it was due to a knowledge barrier ("I do not understand enough about FFR"). Additionally, <5% of responses identified attitude barriers, for example "I do not trust FFR." Instead, the dominant responses focused on reimbursement and the time necessary to perform the procedure. A logical conclusion from this survey was that we should focus on environmental barriers to improve the penetrance of coronary physiology.

However, surveys may not accurately reflect behavior, as recently demonstrated by polling miscues in the United States election and the Brexit vote. A subsequent European study called the ISIS study (4) asked interventional cardiologists to make clinical decisions when provided with an angiogram showing an intermediate lesion in a stable patient. Importantly, the decisions were to be made "assuming ideal world conditions, without considering any financial restrictions or local regulations, but only after the

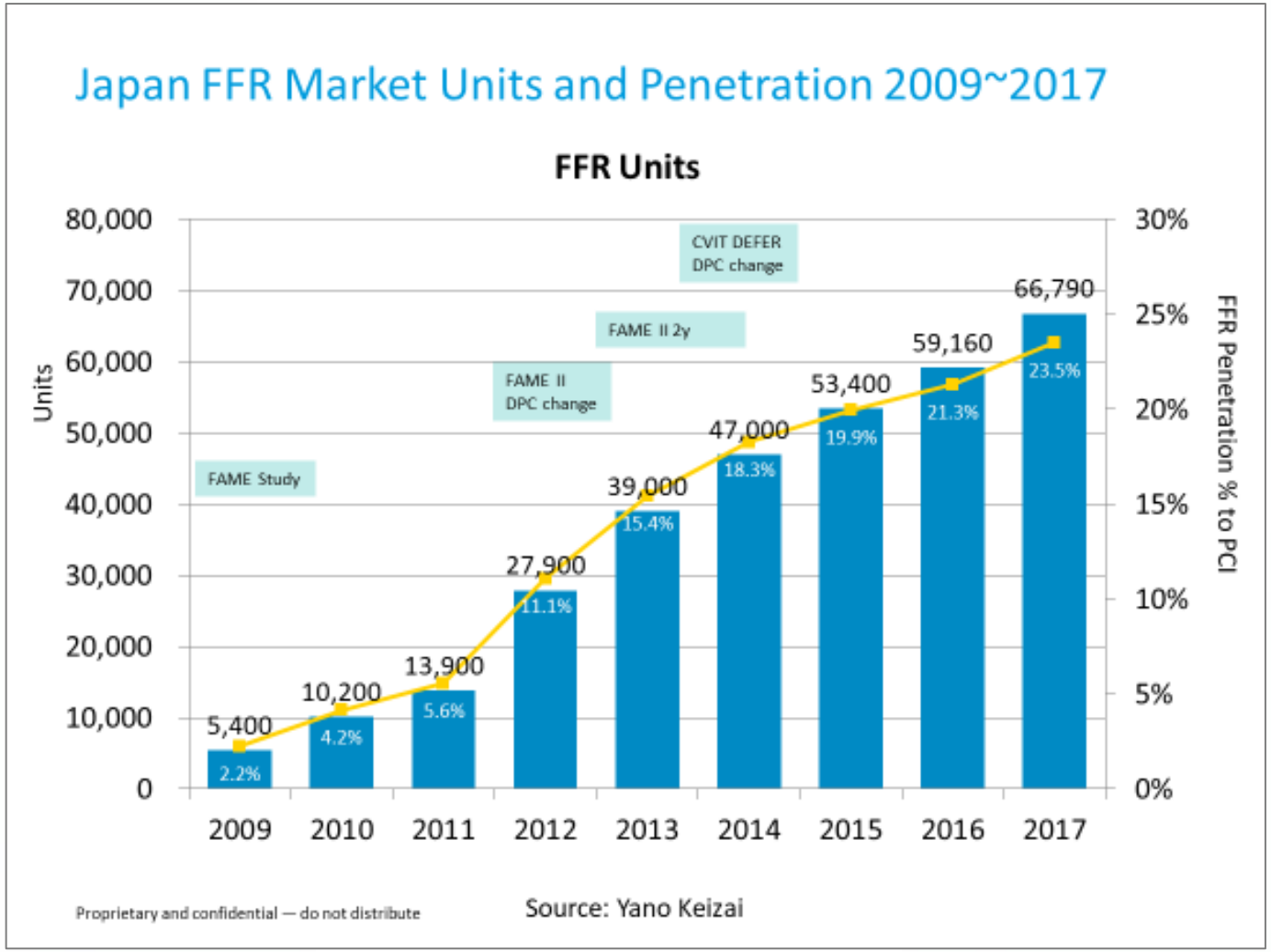
Coronary *psychology*

What *really works?*

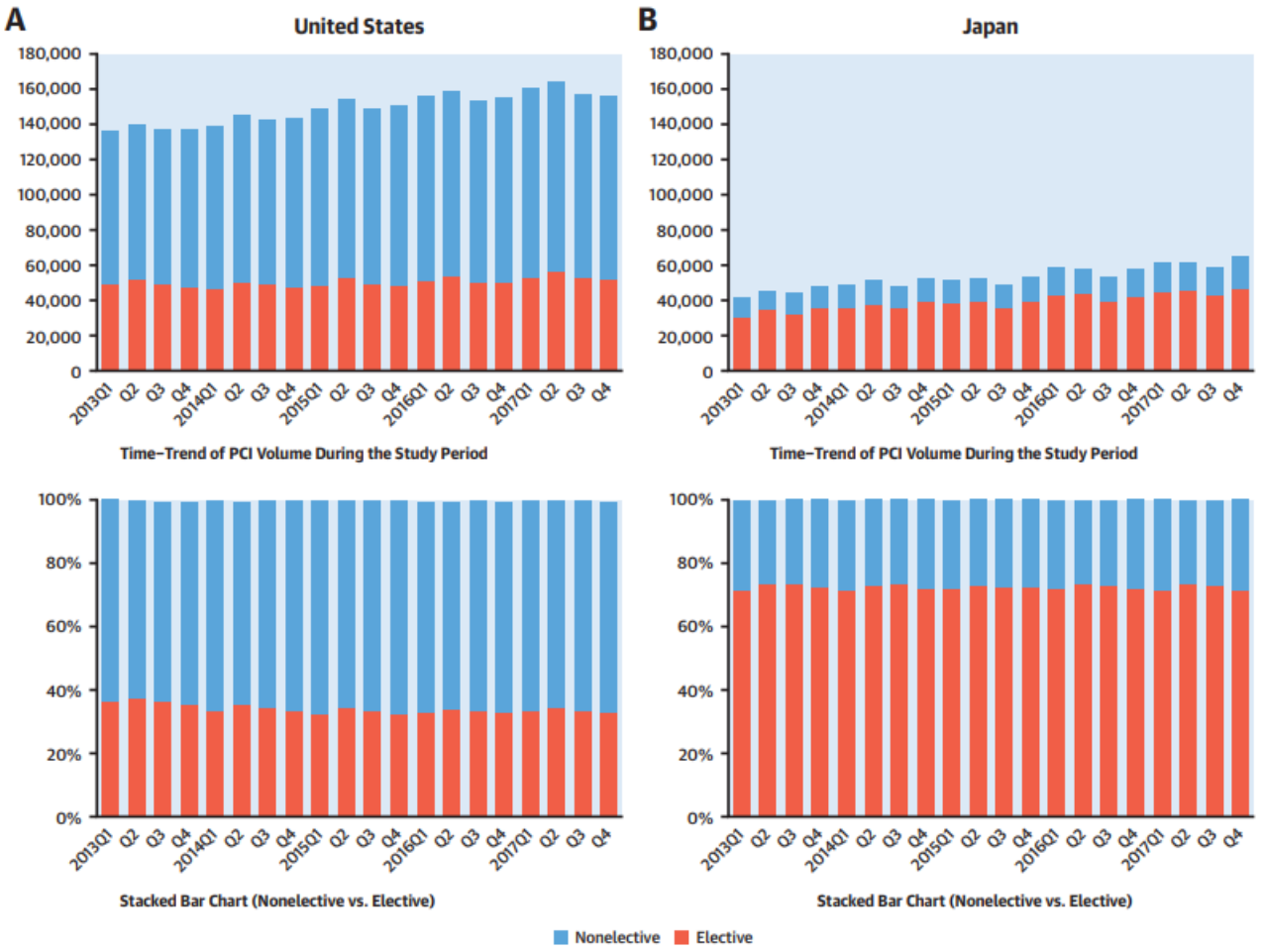
- more studies/trials
- training or conferences
- guideline or consensus
- insurance reimbursement
- media coverage
- legal action
- public registry
- simplify (avoid hyperemia)
- better wires

How to Overcome Low Penetration of FFR?

Current Status of FFR Penetration (6)

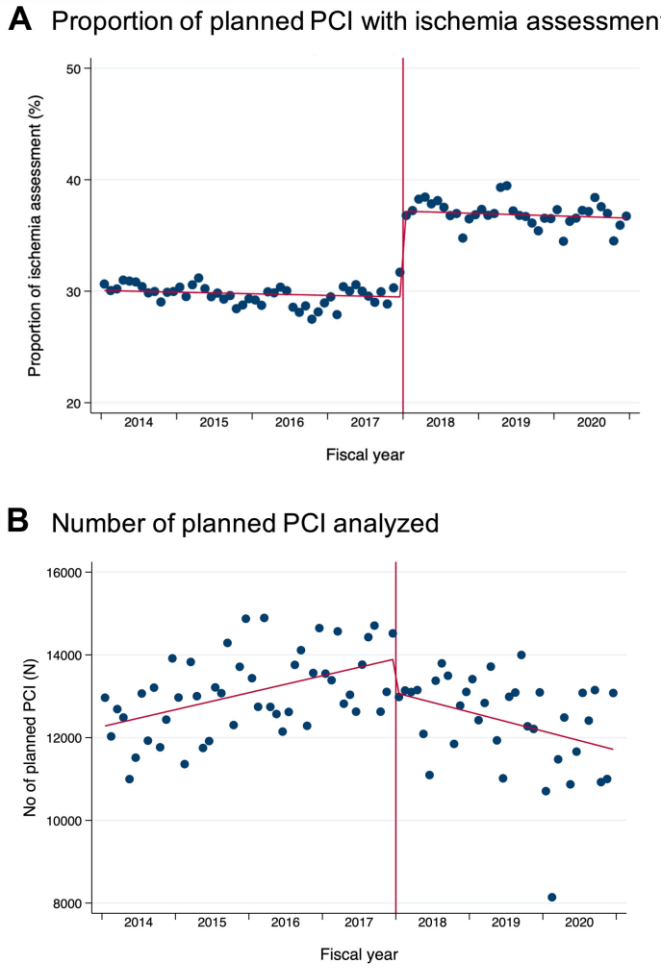


PCI Trend in US and JAPAN



Inohara, T. et al. J Am Coll Cardiol. 2020;76(11):1328-40.

The Policy Change for Ischemia Assessment in Japan



The Japanese Ministry of Health, Labour, and Welfare introduced a new reimbursement policy: to reduce unnecessary PCIs, ischemia assessment (**unless stenosis was very tight**) was required for planned PCI beginning in April 2018

Although the database did not include test results of ischemia assessment or details of PCI-associated complications, the total number of planned PCIs decreased without an increase in all-cause mortality after implementation of the new reimbursement policy.

Our results have a potential clinical benefit because the policy change led to a reduction in the number of unnecessary PCIs in patients with coronary artery disease

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