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DEBATE: Which is the Better Test? CTA vs. Nuclear Stress: Nuclear Stress

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The CardioVascular Center
Tufts Medical Center

Professor of Medicine and Radiology
Tufts University School of Medicine

RWI: GE Healthcare, Heartflow, Medtrace

Anterior Wall Ischemia 1973

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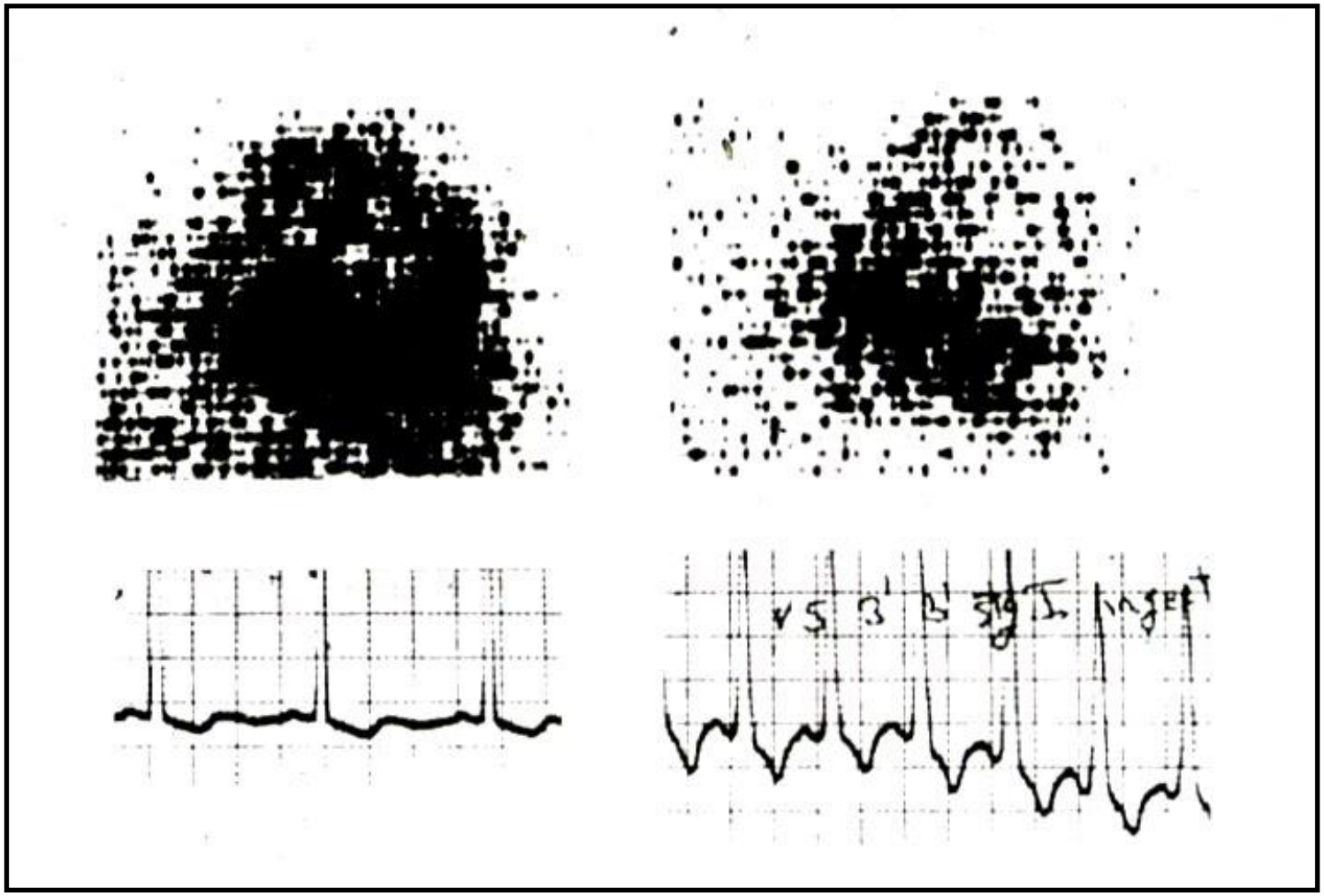

Zaret BL et al. *N Engl J Med*. 1973

Anterior Wall Ischemia 2020

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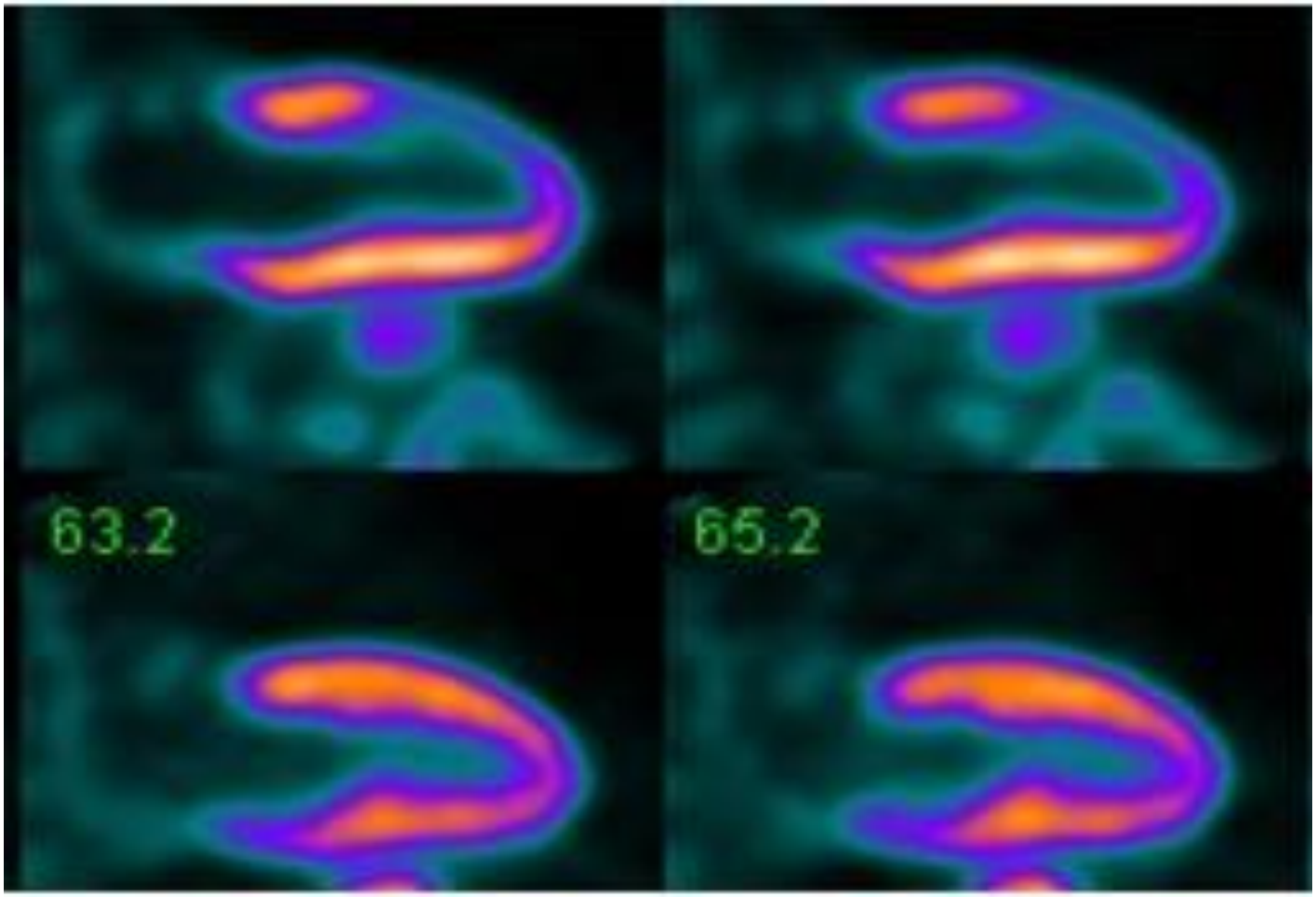

Maddahi et al. JACC 2020

AHA/ACC Imaging Guidelines: Levels of Evidence

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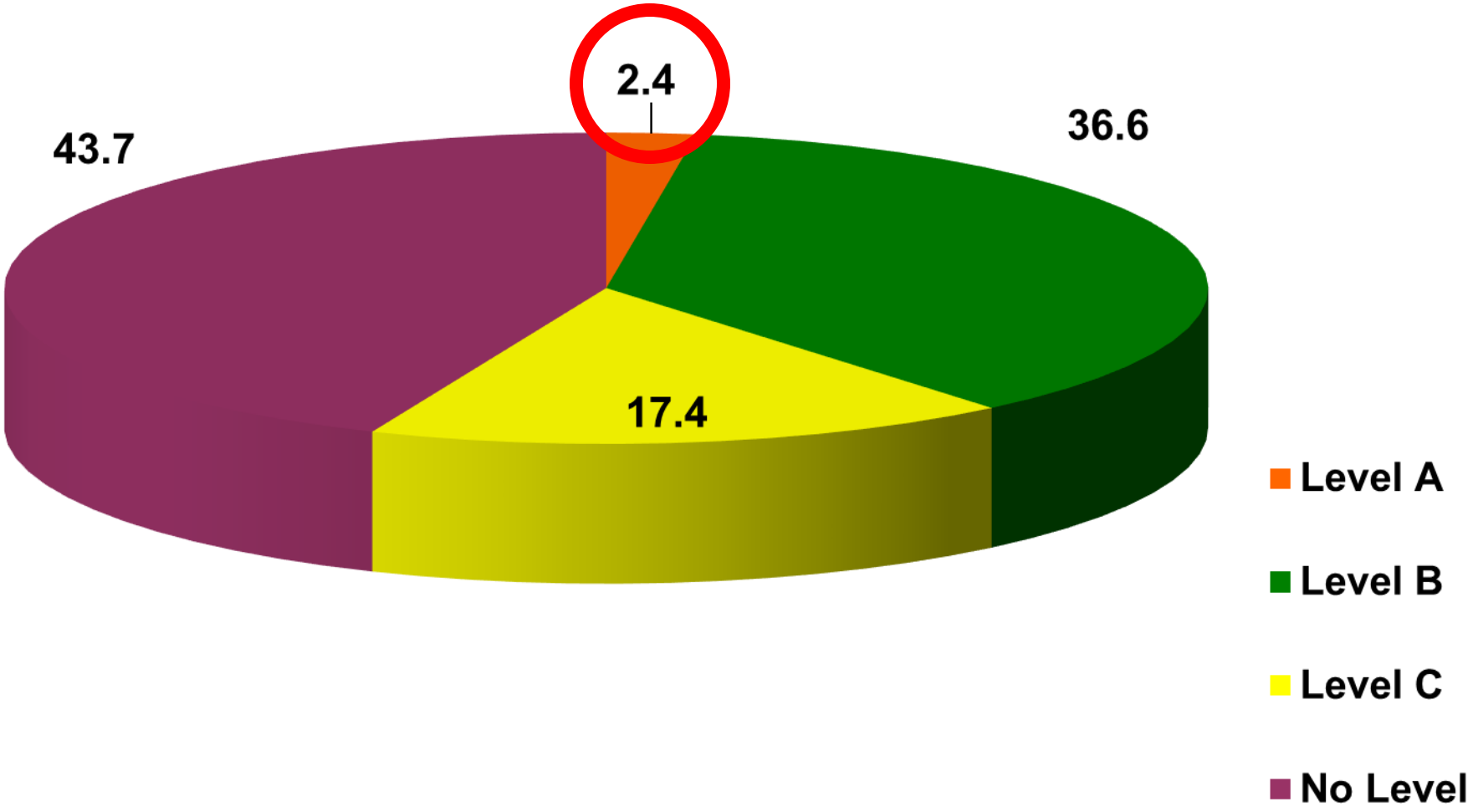

Tricoci et al, JAMA 2009

2021 ACC/AHA Chest Pain Guidelines

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Recommendations for Intermediate-High Risk Patients With Stable Chest Pain and No Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 29 and 30.

COR	LOE	Recommendations
		Index Diagnostic Testing
		Anatomic Testing
1	A	1. For intermediate-high risk patients with stable chest pain and no known CAD, CCTA is effective for diagnosis of CAD, for risk stratification, and for guiding treatment decisions.[160,238-248]
		Stress Testing
1	B-R	2. For intermediate-high risk patients with stable chest pain and no known CAD, stress imaging (stress echocardiography, PET/SPECT MPI or CMR) is effective for diagnosis of myocardial ischemia and for estimating risk of MACE.[124,245,249-270]

Gulati et al, Circ, JACC 2021

Evidence for Imaging

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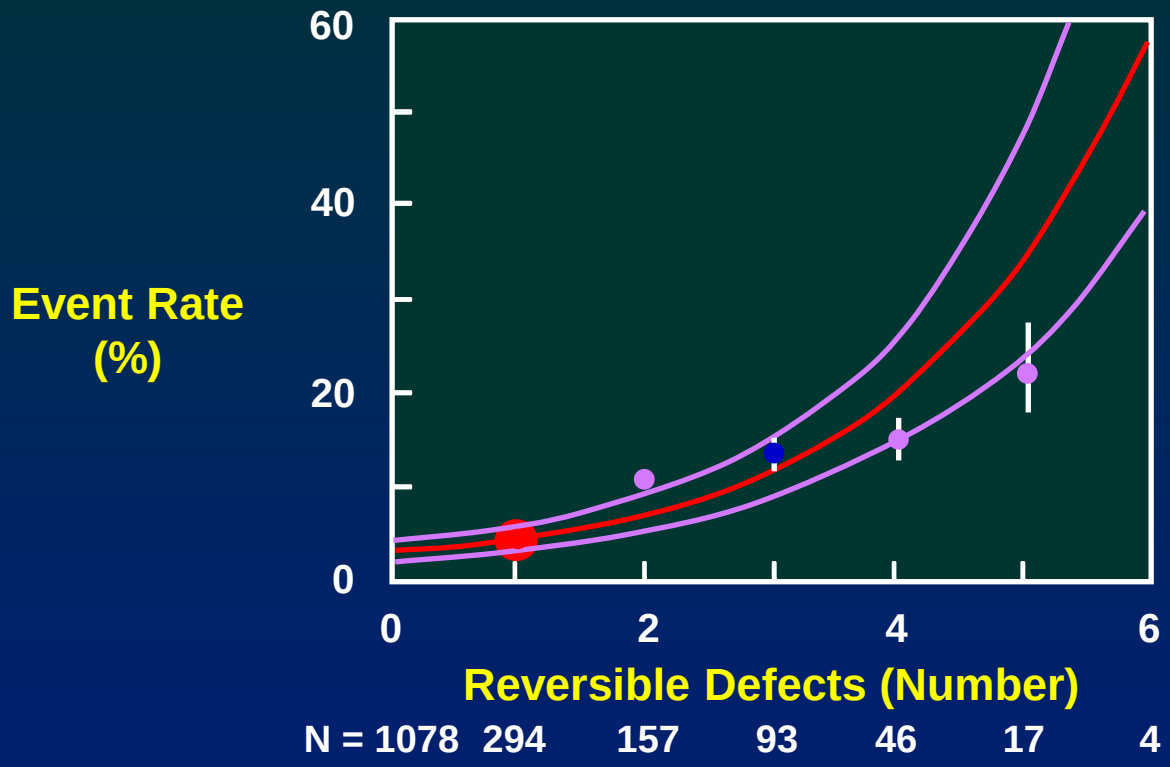
- **Diagnostic Efficacy : sensitivity, specificity, PPV, NPV, accuracy, AUC for dx, LRs**

MPI ✓ Str Echo ✓ CT Angio ✓ CMR ✓

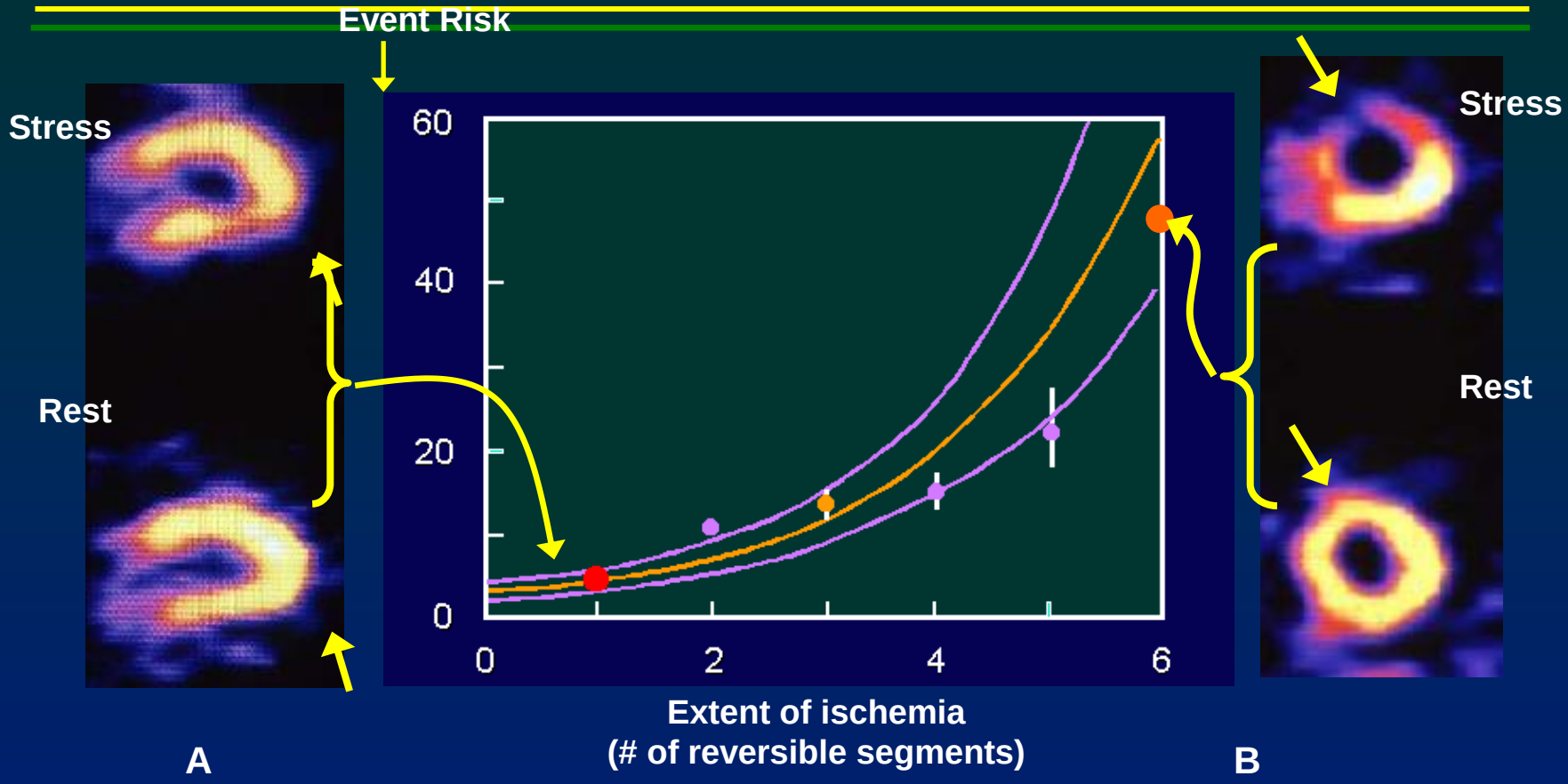
- **Prognostic Efficacy : relation of imaging findings to outcomes**
  - **The extent of abnormality is associated w risk of unfavorable outcome during follow-up**

MPI ✓ Str Echo ✓ CT Angio ✓ CMR ✓

Prognostic Value of the Extent of Inducible Ischemia



Ladenheim MI et al. *J Am Coll Cardiol* 7:464, 1986.



Adapted from Ladenheim et al et al, JACC 1986

Strategy Controlled Large Outcome RCTs

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- **PROMISE - CCTA vs Functional Imaging (~65% MPI, ~25% stress echo, ~10% stress ECG)**
  - **No difference in outcomes associated with the imaging approach**

NEJM 2015

- **SCOT-HEART – CCTA vs SoC (mostly stress ECG)**
  - **Lower NFMI associated with CCTA arm**

NEJM 2018

Which Approach? "Anatomic" (CCTA)? or "Functional" (Stress Testing)?

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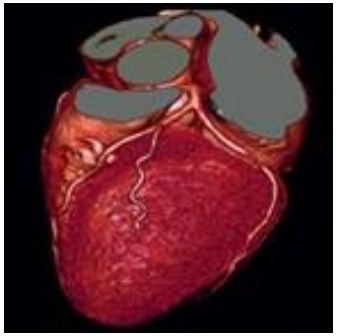
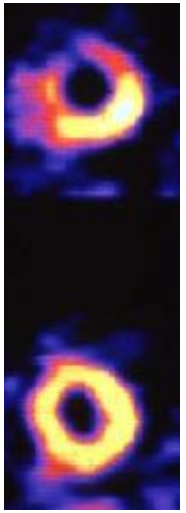
- CTA has evolved technically
  - Higher PPV and NPV for CAD
  - Could reduce unneeded invasive testing and improve outcomes
  - Ability to detect a broader spectrum of CAD, including non-obstructive disease
- The impact of the information derived from an initial strategy of noninvasive anatomic versus fxnl test data on subsequent management and clinical outcomes in stable CP pts is unknown





PROMISE Trial Design

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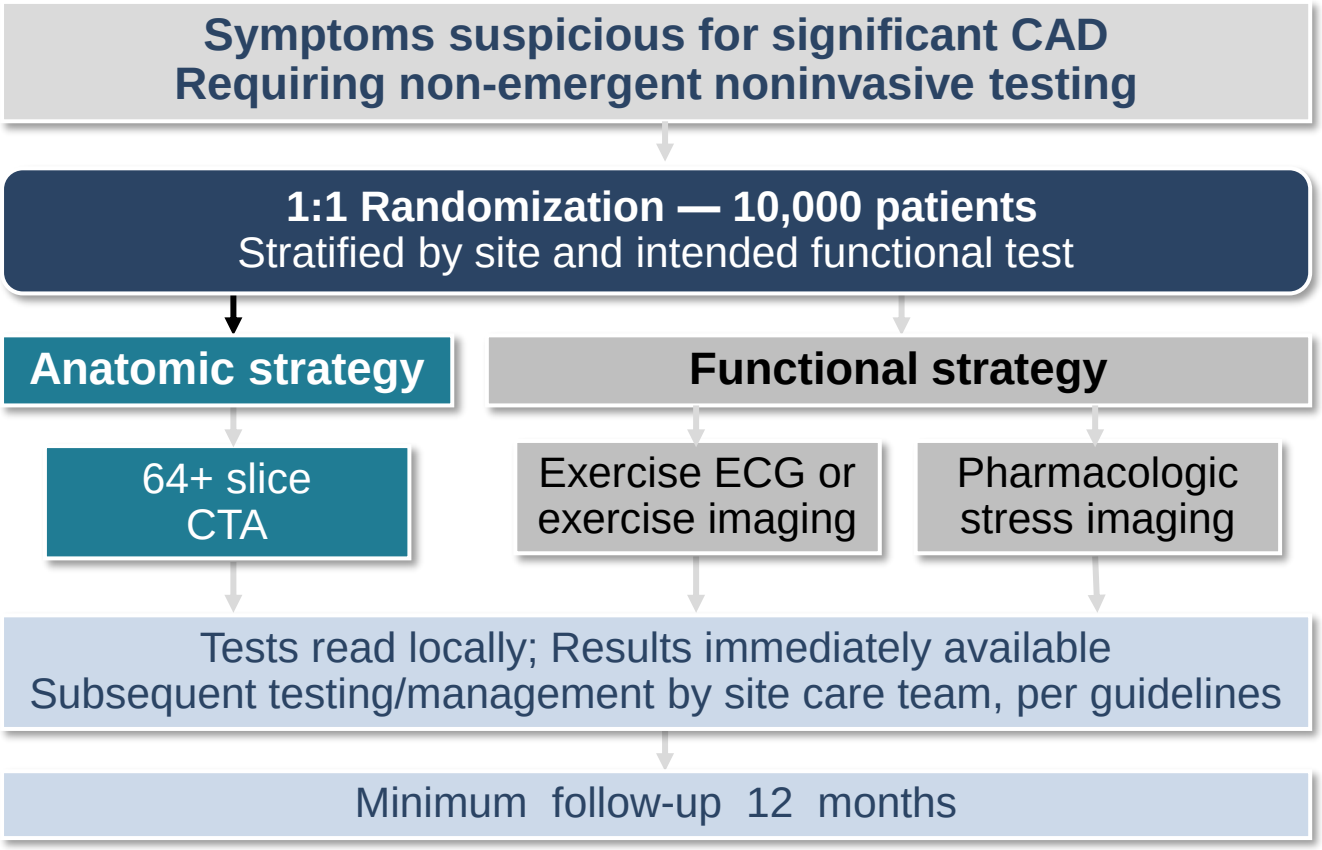
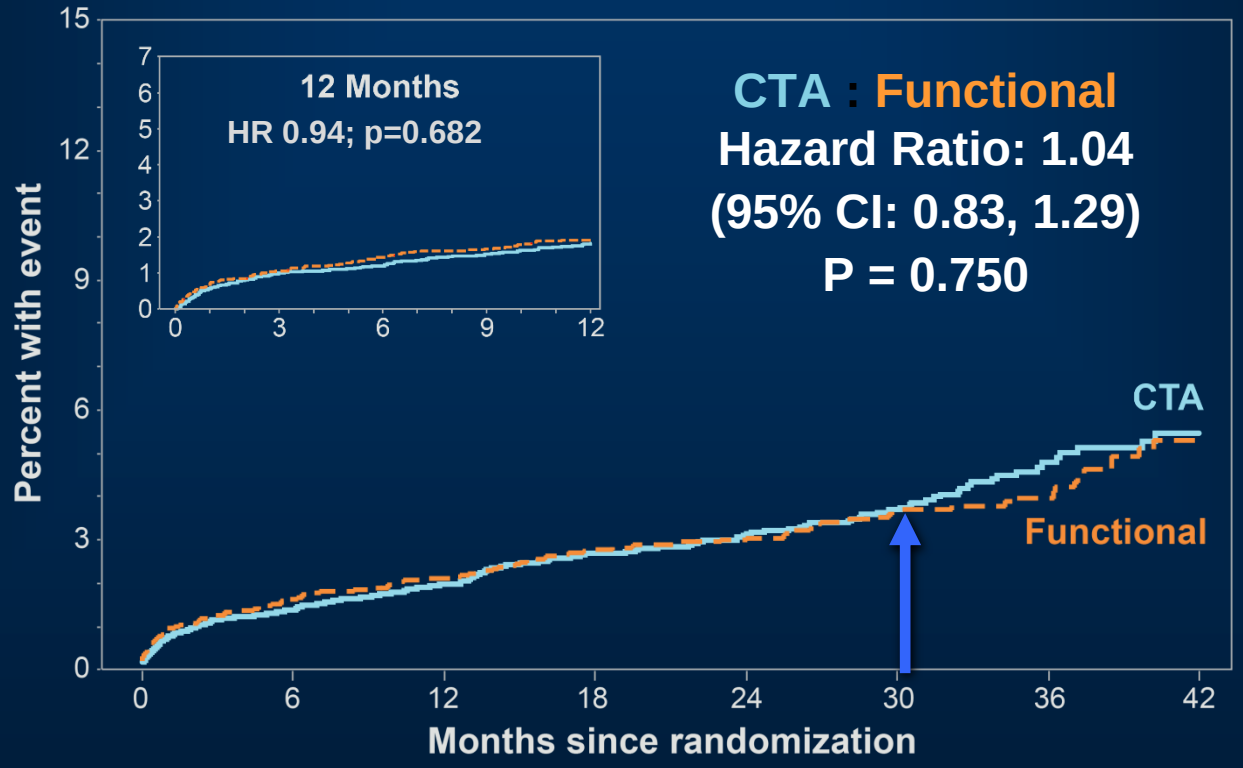


“Effectiveness”

Primary Endpoint:
Death, MI, Unstable Angina, Major Complications



# at risk	Baseline (0)	6 Mo.	12 Mo.	18 Mo.	24 Mo.	30 Mo.	36 Mo.	42 Mo.
CTA	4996	4703	4362	3551	2652	1705	902	269
Functional	5007	4536	4115	3331	2388	1518	832	258

promise

Douglas et al NEJM 2015

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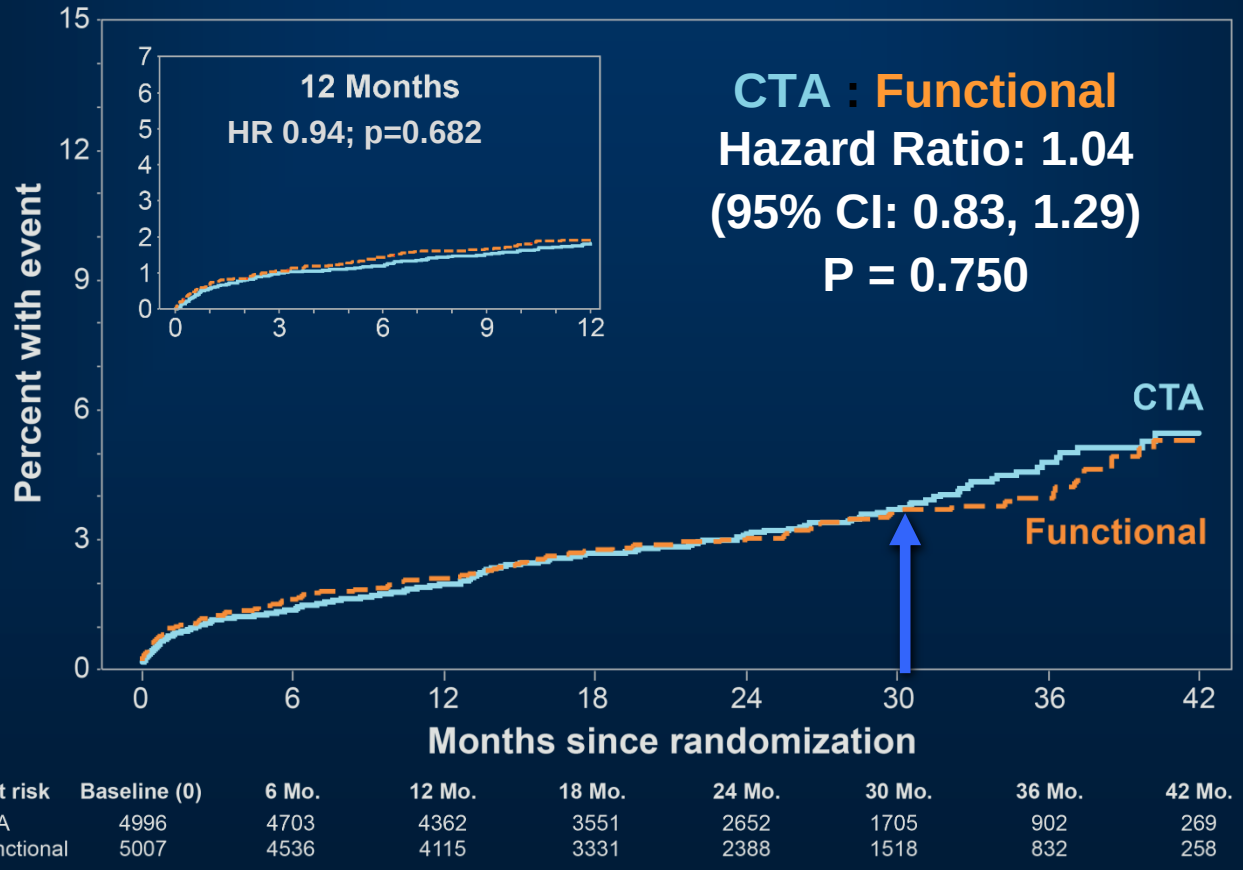

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P=NS for non-inferiority

Note event rate <8% at 2.5 yrs

promise

Douglas et al NEJM 2015

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Recommendations for Intermediate-High Risk Patients With Stable Chest Pain and No Known CAD
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Gulati et al, Circ, JACC 2021

Defer Testing in Low-Risk Subjects ?

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5.1.2. Low-Risk Patients With Stable Chest Pain and No Known CAD

Recommendations for Low-Risk Patients With Stable Chest Pain and No Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 27 and 28.

COR	LOE	Recommendations
1	B-NR	1. For patients with stable chest pain and no known CAD presenting to the outpatient clinic, a model to estimate pretest probability of obstructive CAD is effective to identify patients at low risk for obstructive CAD and favorable prognosis in whom additional diagnostic testing can be deferred.[228-232]

Gulati et al, Circ, JACC 2021

Temporal Trends in the Frequency of Inducible Ischemia

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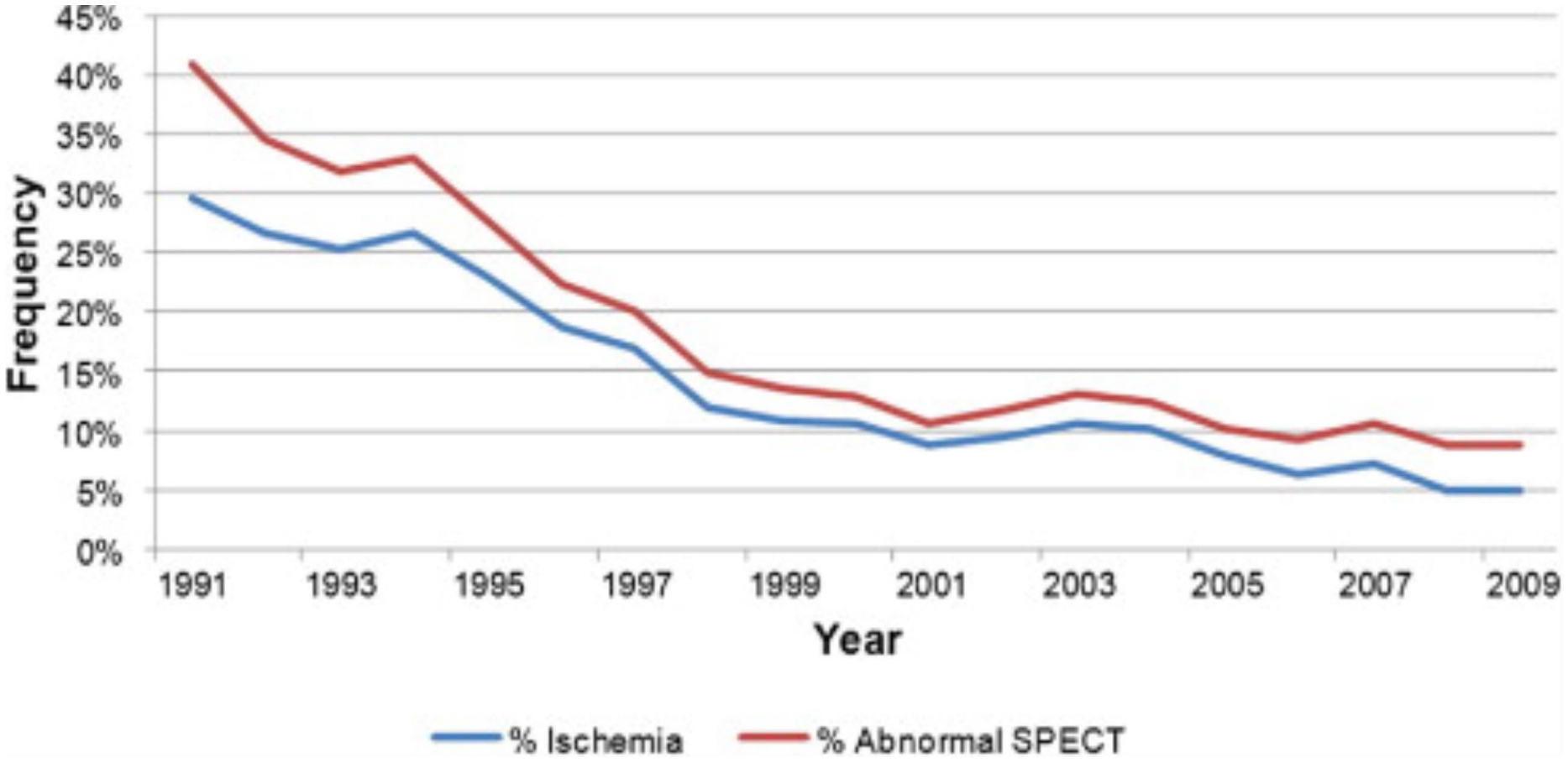

Rozanski et al. J Am Coll Cardiol. 2013

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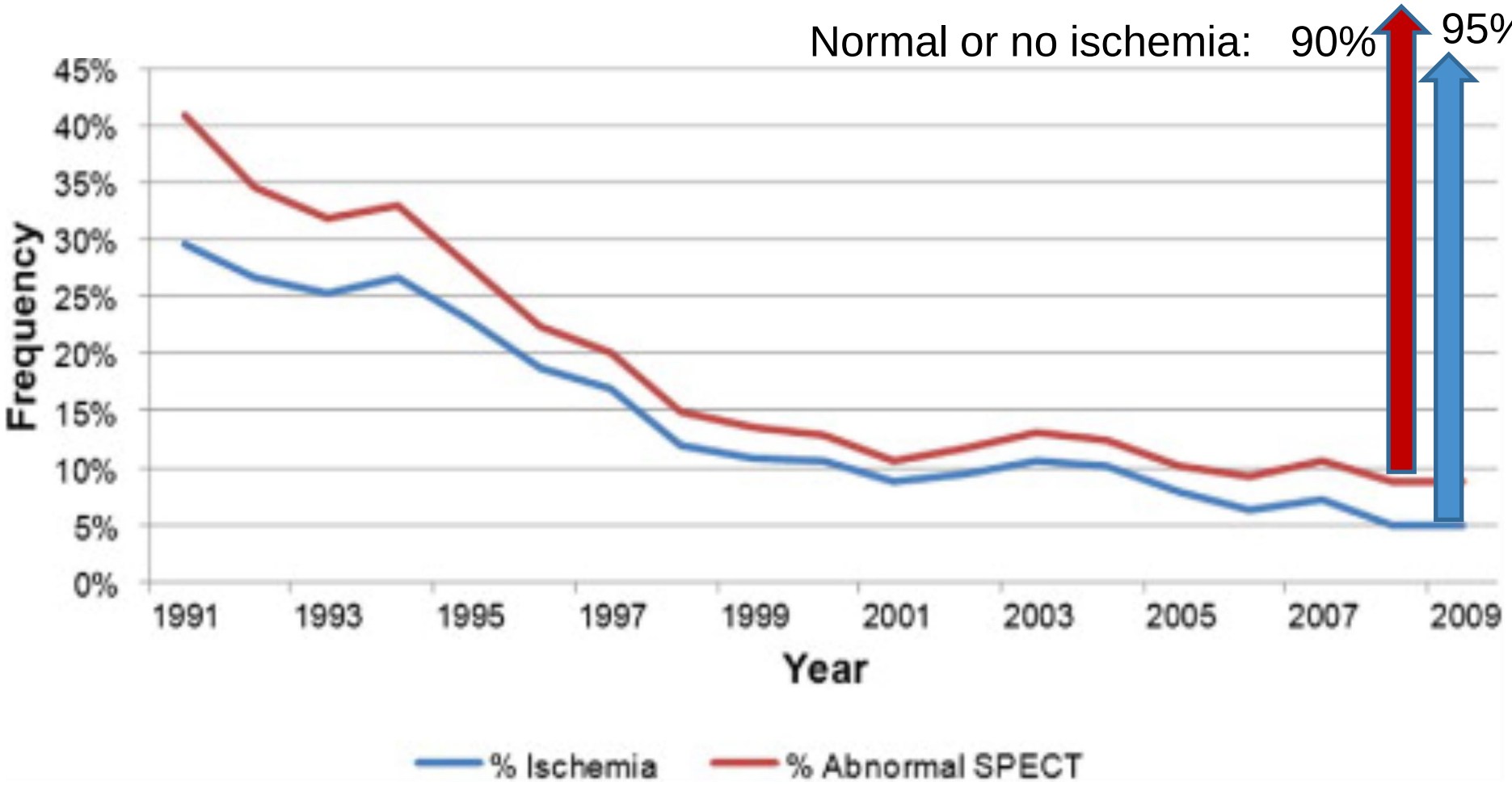

Rozanski et al. J Am Coll Cardiol. 2013

Can Pre-Test Data Identify Pts Destined to Have Normal Testing and No Events?

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The PROMISE "Minimal-Risk" Model

	Odds Ratio [95% CI)	P-value
Age [per 5 year decrease)	1.50 [1.41, 1.60]	<0.0001
Female sex	2.59 [2.13, 3.15]	<0.0001
Racial/ethnic minority	1.29 [1.05, 1.58]	<0.0137
No hypertension	1.54 [1.29, 1.85]	<0.0001
No dyslipidemia	1.43 [1.19, 1.72]	<0.0001
Never smoker*	1.66 [1.39, 1.98]	<0.0001
No family history of CAD	1.33 [1.06, 1.68]	<0.0001
No diabetes	1.47 [1.23, 1.77]	0.0141
Symptoms unrelated to physical/mental stress**	1.47 [1.23, 1.77]	0.0069
HDL [per 5 point increase]	1.04 [1.01, 1.07]	0.0123

Table 2. Predictors of No Risk in the final derivation model
Model derivation c-statistic = 0.73; model validation c-statistic = 0.73.
Odds ratios >1.00 indicate increased probability of No Risk for every 5 unit increase/decrease in continuous variables and when comparing category shift in categorical variables.
*versus ever smoking
**versus Symptoms related to physical/mental Stress

Fordyce, Udelson, et al.
***JAMA Cardiol* 2017**

Can Pre-Test Data Identify Pts Destined to Have Normal Testing and No Events?

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The PROMISE "Minimal-Risk" Model

76%

Predicted Probability of No Risk

The likelihood of being 'No Risk' [a normal diagnostic test and no clinical events (Death, MI, or Hospitalization due to Unstable Angina) within 25 months] in a patient with the reported constellation of risk factors is: 76%

What type of non-invasive test are you considering for your patient?

- (•) CCTA
- ( ) Functional Stress Test

View Event Rate Results from Selected Test

10th decile

PROMISE patients who underwent a CCTA diagnostic test and were in the 10th decile experienced the following event rates:

Likelihood of Given Test Results:

Normal (No CAD):
63.9%

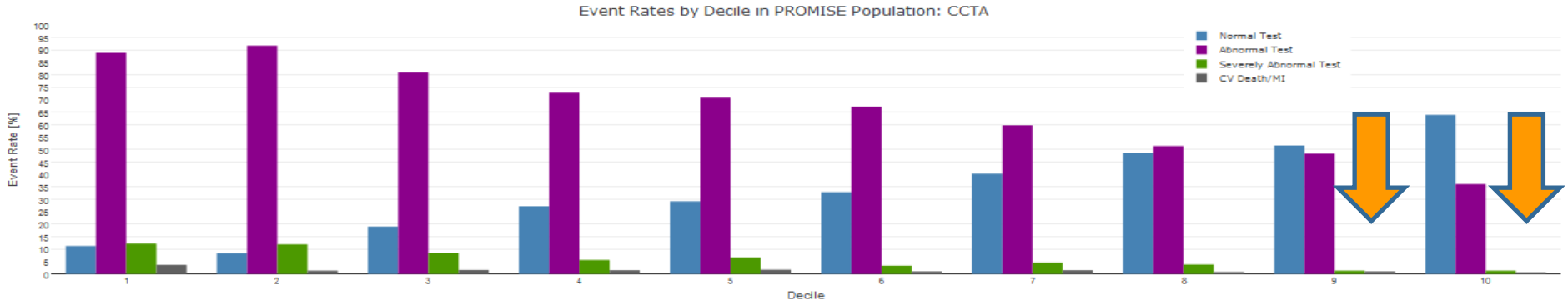
Abnormal (CAD present):
36.1%

Severely Abnormal (2 or more vessel disease (>=70%) or >=50% in left main stenosis or >=70% proximal LAD stenosis):
1.3%

Clinical Outcomes:

Cardiovascular Death/MI:
0.5%

The plot below exhibits the impact of the predicted probability and associated decile on the likelihood of given test results and CV Death/MI. Mouse over the various deciles to view the predicted rate of test results and clinical events.



PRECISE Trial: Prospective Randomized Trial of the Optimal Evaluation of Cardiac Symptoms and Revascularization

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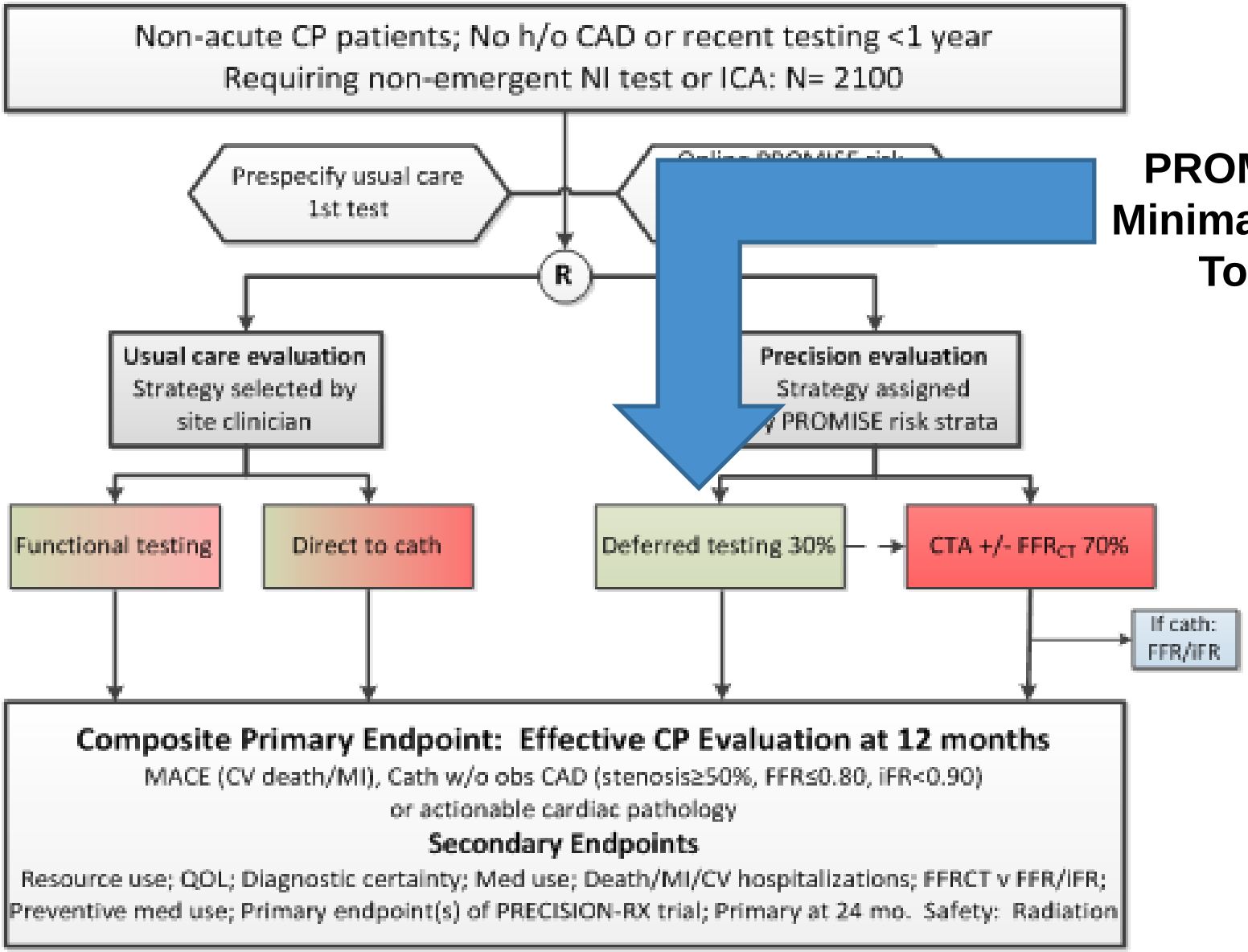

PROMISE Minimal Risk Tool

PRECISE Trial: Prospective Randomized Trial of the Optimal Evaluation of Cardiac Symptoms and Revascularization

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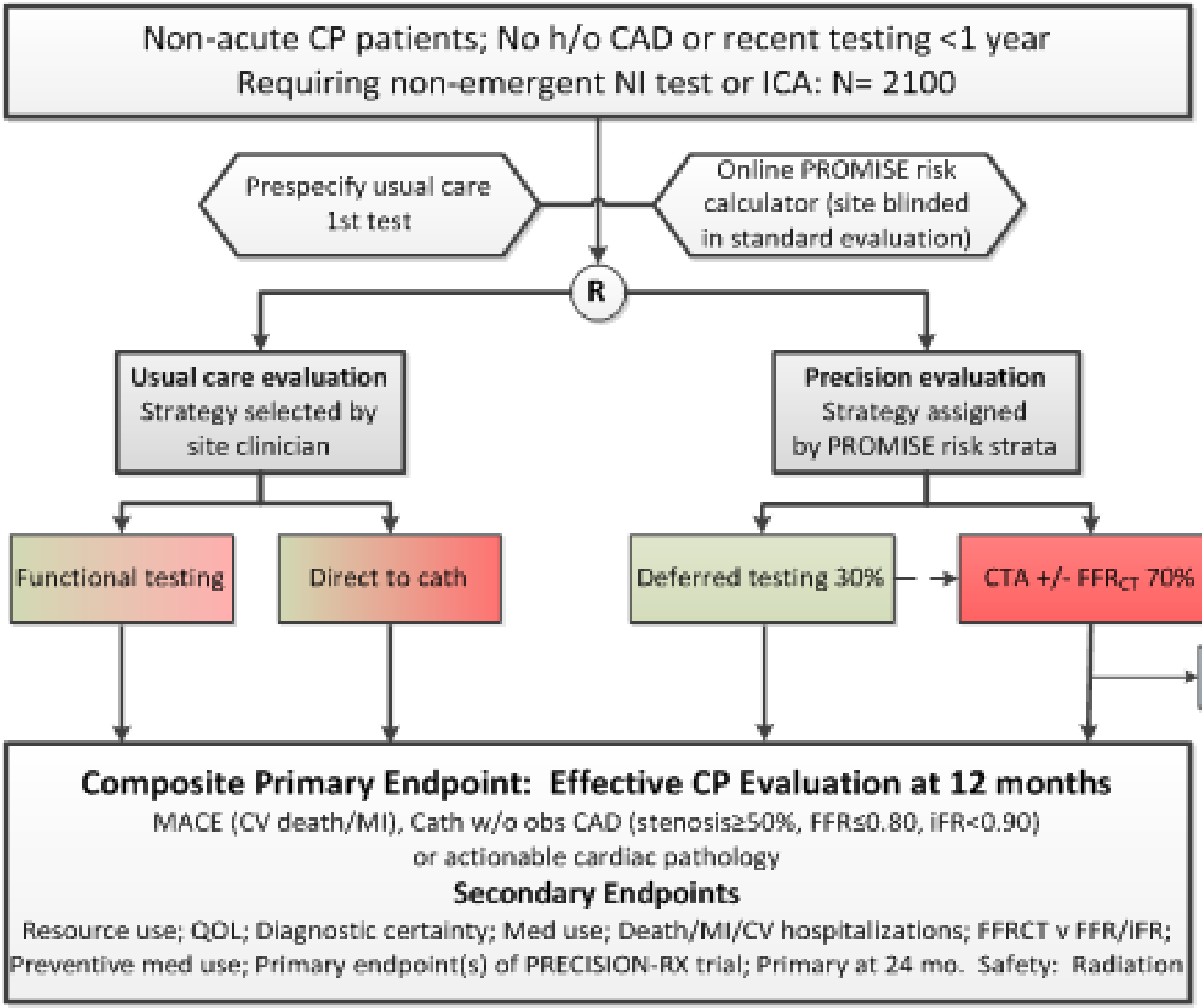

Enrollment completed

Topline Results AHA 2022

Deferred testing results ACC 2023

How Do Providers Choose an Imaging Modality to Test Their Patients ?

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- They do what is familiar from training
- They use what is most available at their center/practice
- They use what they understand and are comfortable with
- Trust in the readers
- Financial considerations

What Moves the Needle ?

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- **Published studies ? Guidelines? (Debates?)**

Modalities	Sensitivity				Specificity				+LR	−LR	DOR	SROC curve AUC
	Sensitivity	I^2 (%)	Q value	P	Specificity	I^2 (%)	Q value	p				
PET	0.85 [0.80, 0.89]	90.24 [87.55, 92.93]	286.87	<0.01	0.86 [0.81, 0.89]	77.88 [70.19, 85.58]	126.61	<0.01	5.9 [4.6, 7.7]	0.17 [0.13, 0.23]	34 [25, 47]	0.92 [0.89, 0.94]
SPECT	0.83 [0.81, 0.85]	92.81 [92.07, 93.55]	2350.03	<0.01	0.77 [0.74, 0.80]	93.69 [93.07, 94.32]	2679.42	<0.01	3.6 [3.3, 4.1]	0.22 [0.20, 0.25]	16 [14, 19]	0.87 [0.84, 0.90]
CMR	0.86 [0.84, 0.88]	84.53 [81.56, 87.50]	491.31	<0.01	0.83 [0.81, 0.86]	84.29 [81.26, 87.32]	483.76	<0.01	5.2 [4.5, 6.0]	0.17 [0.14, 0.20]	31[24, 40]	0.92 [0.89, 0.94]

CMR, cardiac magnetic resonance; SPECT, single-photon emission computed tomography; PET, positron emission tomography; MPI, myocardial perfusion imaging; +LR, positive likelihood ratio; −LR, negative likelihood ratio; DOR, diagnostic odds ratio; SROC, summary receiver operating characteristic; AUC, area under the SROC curve.

"Our meta-analysis indicates that CMR and PET present better diagnostic performance for the detection of CAD as compared with SPECT."

Xu et al, Front CV Med 2021

If Dr. Lepor Wins the Debate, Should I Switch ?

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High barriers to change…

- **May need new equipment – huge expense**
- **May need new readers – or re-train readers**
- **May need to re-educate referring providers**
- **Is there an ROI to all of this, either financially or in patient care ?**

Do Better Performance Characteristics (Sens and Spec) Result in Better Outcomes ?

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In one integrated health system:

- **Pts referred for SPECT MPI (n=6,777) 2011-12**
- **Pts referred for Rb-PET MPI (n=7,817) 2014-15**

Knight et al JCI Insight 2018

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	SPECT era	PET era	p
• Cath rate by day 60	9.7%	13.2%	<0.001
• % "obstructive" CAD*	71%	79%	<0.001
• Revasc rate	47%	57%	<0.001
• 1 yr outcome (D/MI)	similar		

*Any stenosis ≥ 70%

Knight et al JCI Insight 2018

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Assumed cost-effectiveness: SPECT better

Knight et al JCI Insight 2018

What if Reimbursement for Stable CP Work-Up was Fixed ?

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- **Out-pt w stable CP ?**
- **Here's $750….**

Pre-test LK:

Very Low	Low	Int	High
PROMISE Min-Risk score=> Don't test	CAC Screen => CCTA	CTA ± FFR Ex fxn img	Ex Fxn Img PET w CFR Stress CMR

Nuclear Imaging in Chronic Coronary Syndromes

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- **SPECT MPI is a very mature field**
- **Readers/referring providers generally understand strengths and limitations**
- **Despite publications showing PET/CCTA/CMR slightly better performance, SPECT MPI still widely performed**
- **Displacement costs high**
- **Future developments *may* make PET more accessible**