Critical Role of CT Coronary Angiography: Insight from PROMISE Trial– TCT AP 2015

Duke Heart Center 25 Duke Heart Center

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Disclosures

- Interventional cardiologist
- Research Grants:
  - NHLB, AHRQ, AstraZeneca, Pleuristem, Johnson and Johnson, Maquet / Datascope
- Advisory Board/Consulting:
  - Genzyme, Bayer, Baxter Healthcare, Ortho McNeil Jansen, theHeart.org, Medscape, Maquet, CSI technologies
- Professional Society Roles:
  - Member ACC/AHA AUC Task Force
  - Chair of Writing Group for ACC/AHA Coronary Revascularization Appropriateness Criteria
  - Chair of AHA Diagnostic and Interventional Cath Committee

Question # 1

- In patients with intermediate pre-test probability of coronary artery disease - what cardiovascular test should be done to diagnose and risk stratify for coronary artery disease?

What do the Guidelines Say?

- Chronic Stable Angina Guidelines - All patients with an interpretable ECG should get and Exercise Treadmill (Class I, level of evidence B)
- Radionuclide Guidelines - Patients with intermediate pre-test probability of disease and chest pain syndrome - Stress SPECT (Class I, Level of Evidence B)
- Echocardiography Guidelines - Patients with chest pain and intermediate pre-test probability - Stress Echo (Class I, no level of evidence noted)

AHRQ Systematic Review

Prepared by Duke Evidence-based Practice Center, Durham, North Carolina

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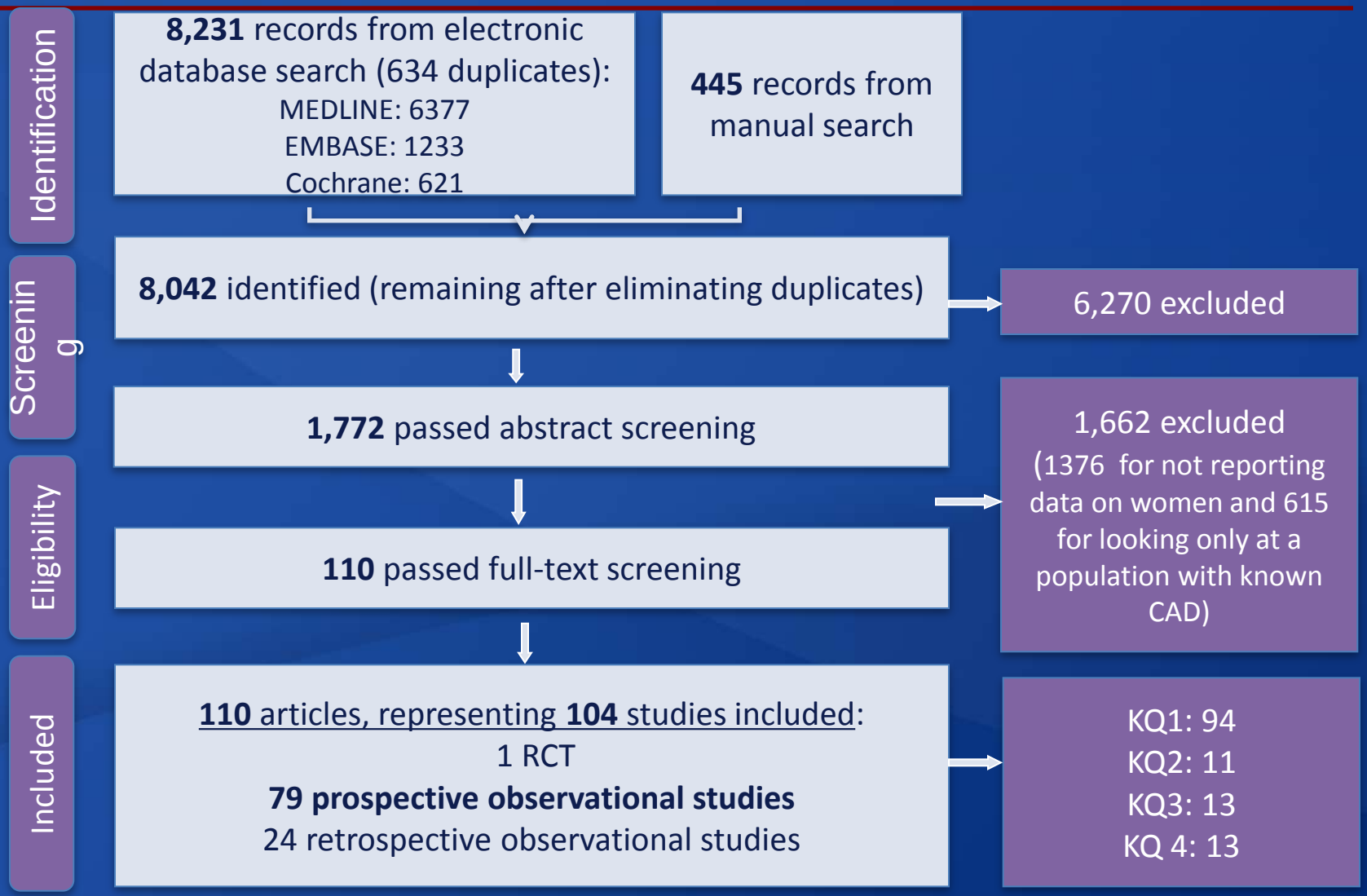
Dolor RJ, et al. Noninvasive Technologies for the Diagnosis of Coronary Artery Disease in Women. Agency for Healthcare Research and Quality, January, 2012. Rockville, MD. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Literature Search Results



Dolor RJ, et al. Agency for Healthcare Research and Quality 2012. Rockville, MD.

Summary of Key Findings (KQ1):
Diagnostic Accuracy of NITs in Women vs Men

Accuracy of NITs for diagnosing CAD in men compared with women from mixed populations

Modality	Studies	Sensitivity		p Value	Specificity		p Value
	n	Men	Women	Women vs. Men	Men	Women	Women vs. Men
ECG	20	64%	61%	0.57	81%	65%	0.007
ECHO	9	77%	78%	0.80	81%	86%	0.50
SPECT	11	88%	82%	0.36	74%	81%	0.47
CMR	3	86%	78%	0.53	72%	84%	0.12
CTA	7	97%	94%	0.36	89%	87%	0.87

Dolor RJ, et al. Agency for Healthcare Research and Quality 2012. Rockville, MD.

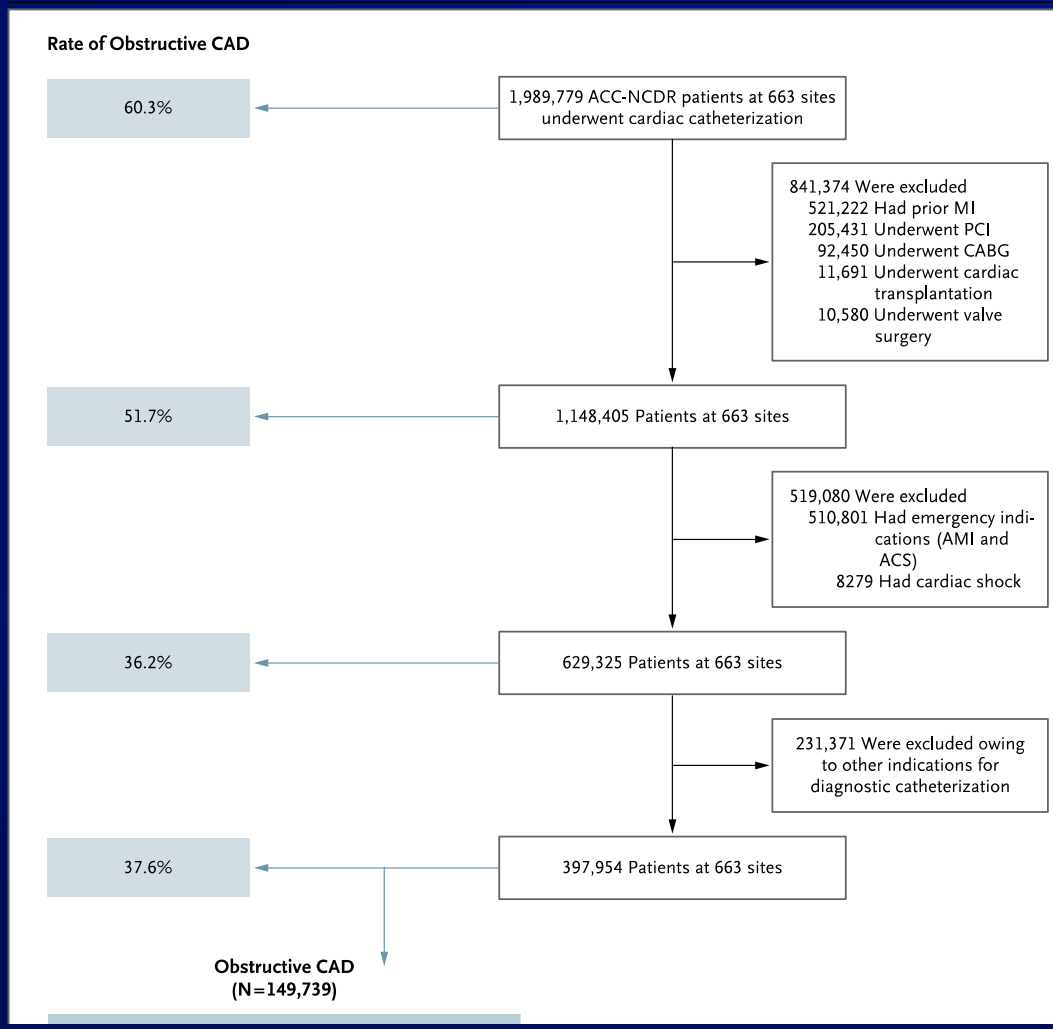
How do we currently perform – predicting obstructive coronary disease?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Low Diagnostic Yield of Elective Coronary Angiography

Manesh R. Patel, M.D., Eric D. Peterson, M.D., M.P.H., David Dai, M.S., J. Matthew Brennan, M.D., Rita F. Redberg, M.D., H. Vernon Anderson, M.D., Ralph G. Brindis, M.D., and Pamela S. Douglas, M.D.



- 38% Stenoses ≥50% LM or ≥ 70% epicardial
- 41% by any ≥ 50%
- 39% had all stenoses <20%

PROspective Multicenter Imaging Study for Evaluation of Chest Pain

ORIGINAL ARTICLE

Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease

Pamela S. Douglas, M.D., Udo Hoffmann, M.D., M.P.H., Manesh R. Patel, M.D., Daniel B. Mark, M.D., M.P.H., Hussein R. Al-Khalidi, Ph.D., Brendan Cavanaugh, M.D., Jason Cole, M.D., Rowena J. Dolor, M.D., Christopher B. Fordyce, M.D., Megan Huang, Ph.D., Muhammad Akram Khan, M.D., Andrzej S. Kosinski, Ph.D., Mitchell W. Krucoff, M.D., Vinay Malhotra, M.D., Michael H. Picard, M.D., James E. Udelson, M.D., Eric J. Velazquez, M.D., Eric Yow, M.S., Lawton S. Cooper, M.D., M.P.H., and Kerry L. Lee, Ph.D., for the PROMISE Investigators*

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Duke Clinical Research Institute

NIH National Heart, Lung, and Blood Institute

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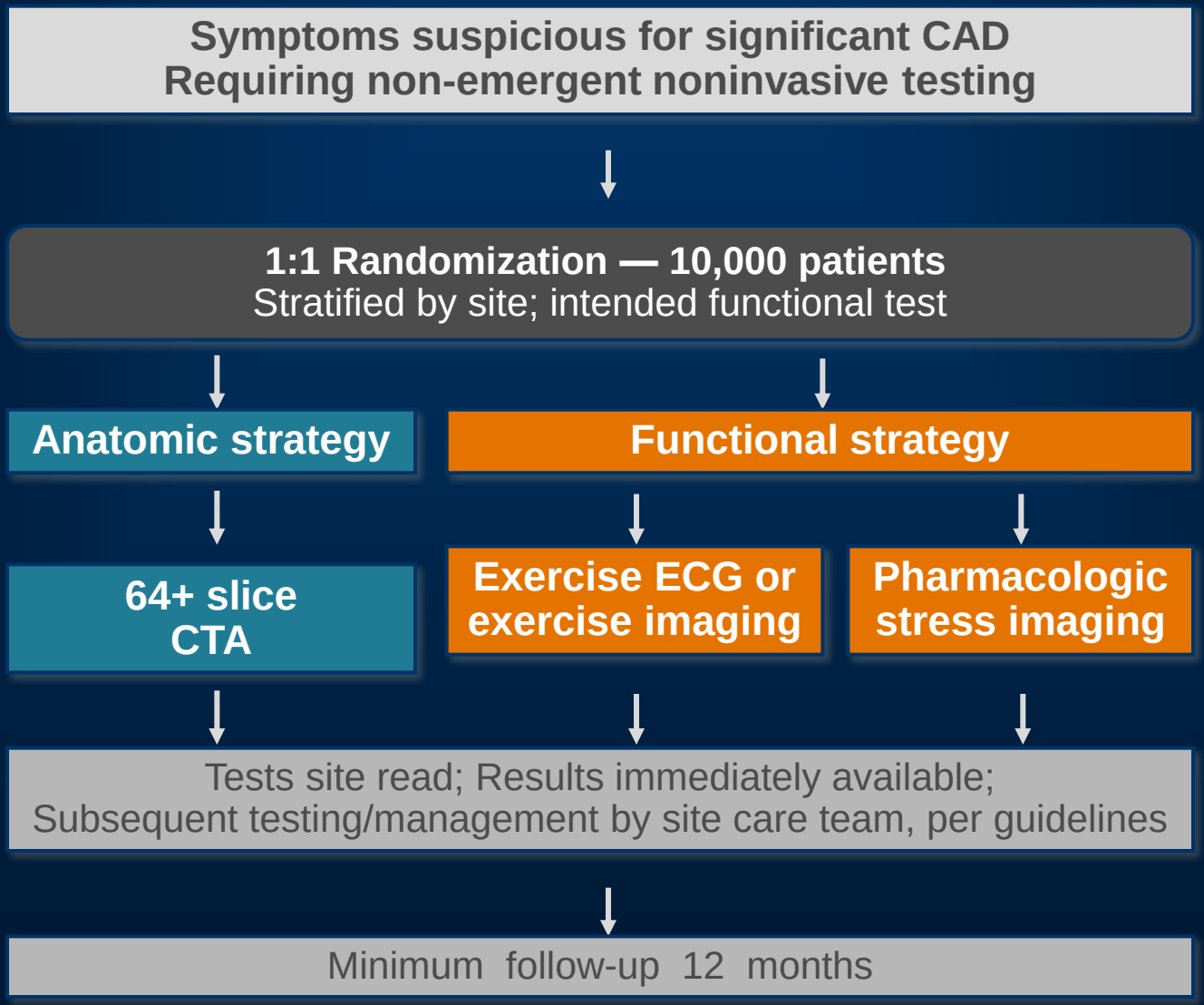
Background

- New onset chest pain accounts for approximately 4 million stress tests annually in the United States
- Limited randomized data to guide care
  - Little consensus about which test is preferable
  - Unknown impact of testing on health-related outcomes
- Current practice may include testing of very low risk populations and catheterization of patients without obstructive CAD

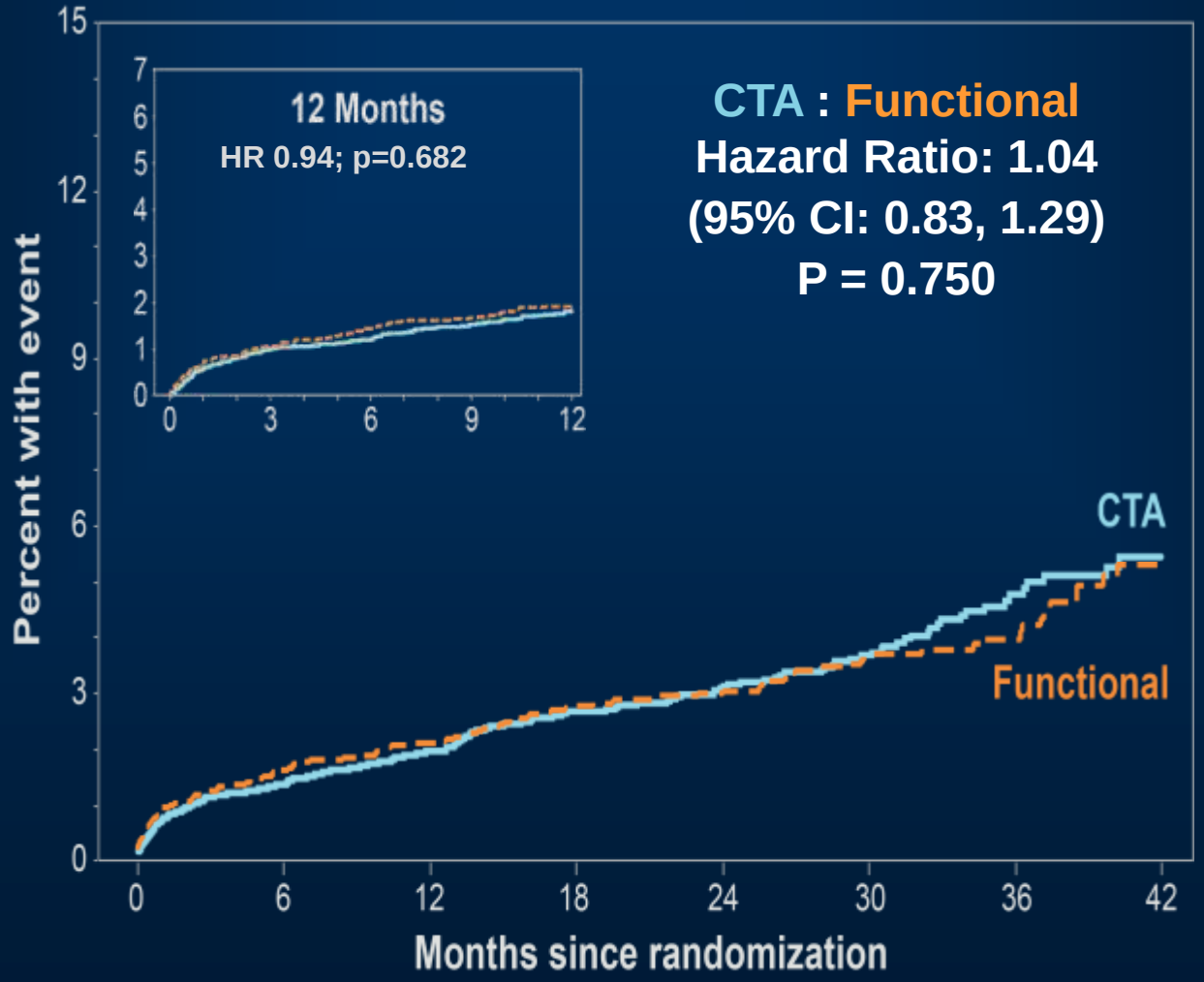
PROMISE Trial Design



Baseline Characteristics

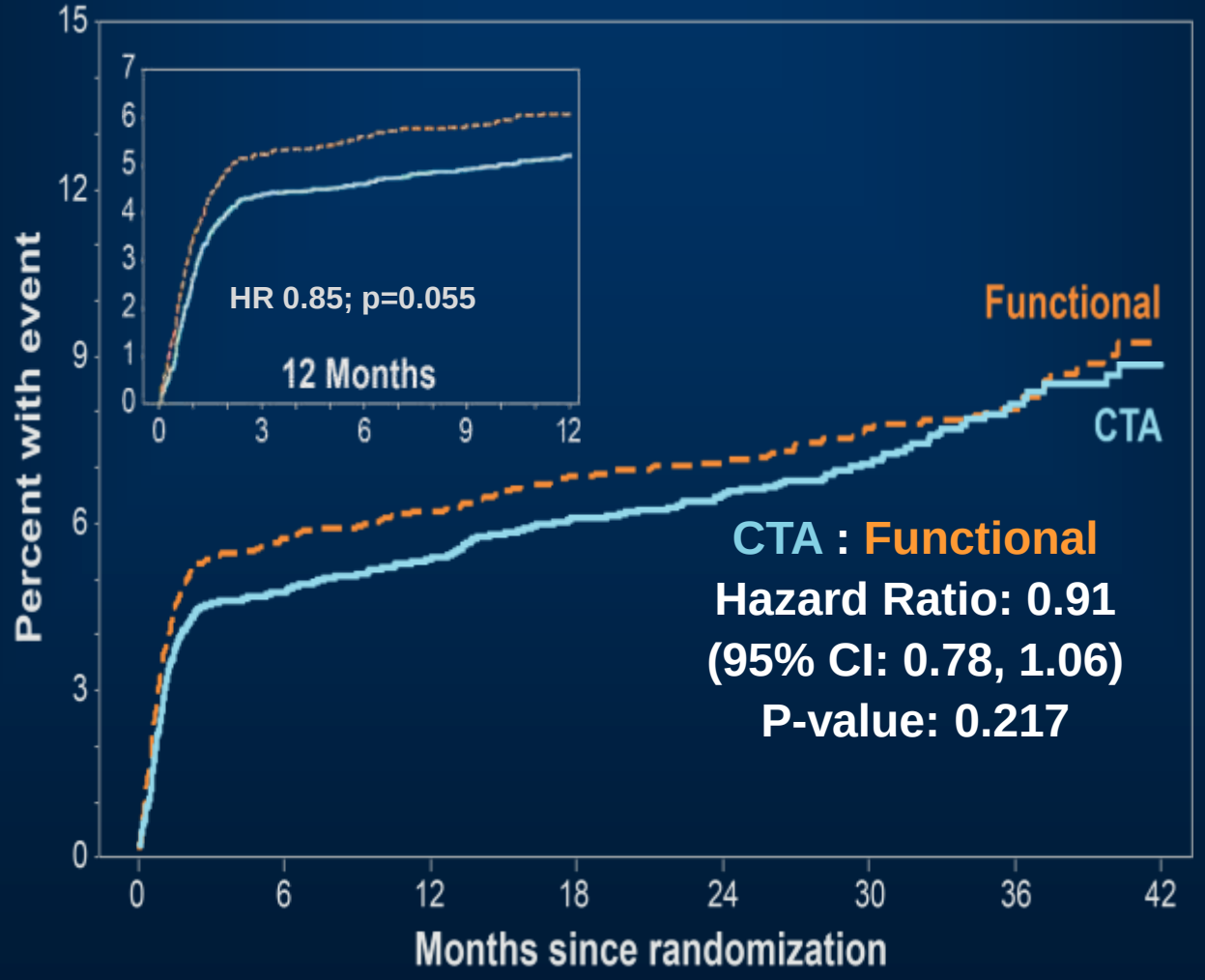
		CTA (n=4996)	Functional (n=5007)
Demographics	Age — mean ± SD, yrs	60.7 ± 8.3	60.9 ± 8.3
	Female sex — %	52	53
	Non-white race	16	15
Risk factors	Hypertension — %	65	65
	Diabetes — %	21	22
	Dyslipidemia — %	67	68
	Family hx premature CAD — %	33	32
	Current or past smoking — %	51	51
1° symptom	Chest pain or DOE — %	88	88
Anginal type	Typical or atypical — %	89	89
Pretest probability CAD	Diamond–Forrester/CASS — mean %	53.4	53.2

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



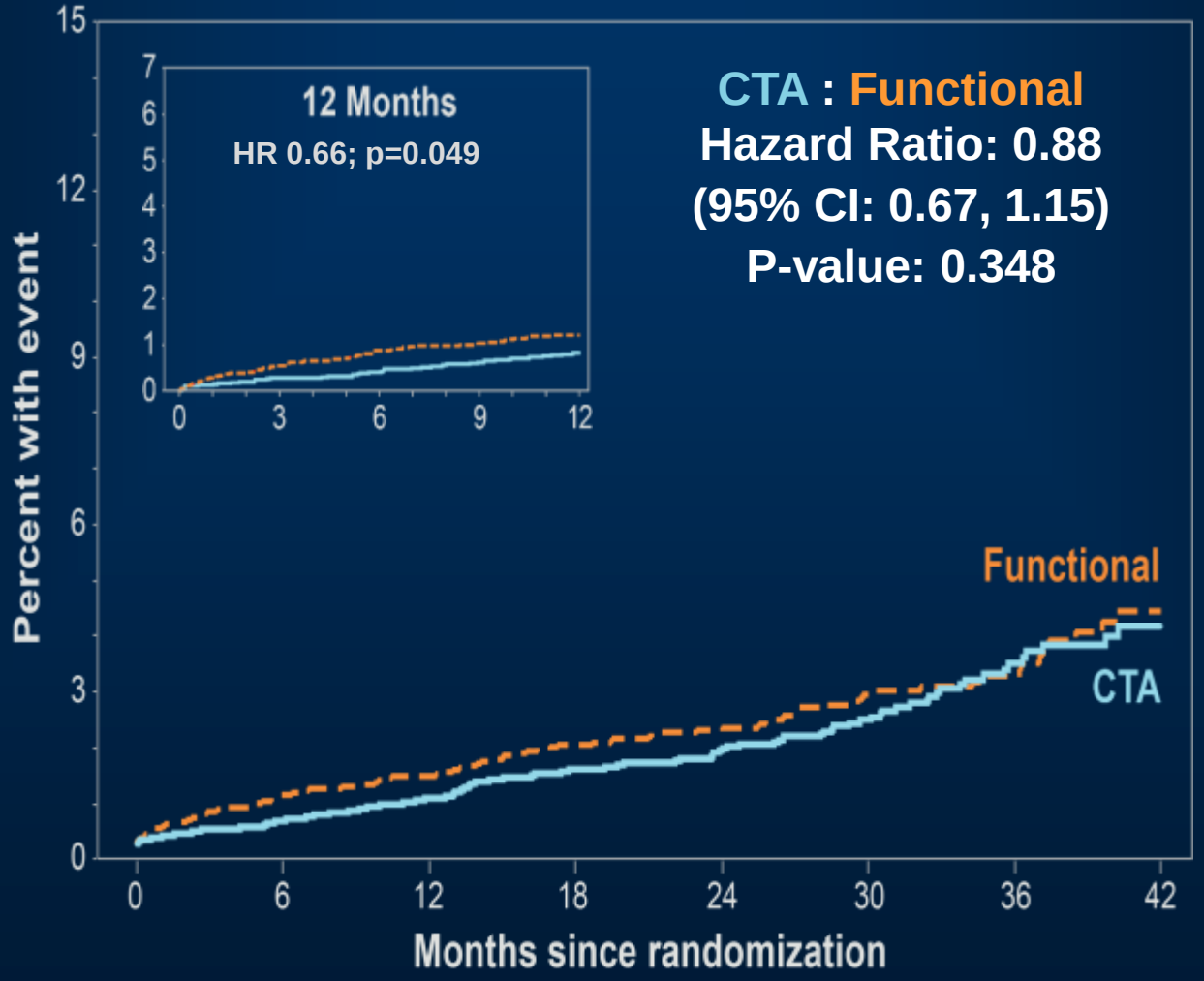
# at risk	Baseline (0)	6 Mo.	12 Mo.	18 Mo.	24 Mo.	30 Mo.	36 Mo.	42 Mo.
CTA	4996	4703	4362	3551	2652	1705	902	269
Functional	5007	4536	4115	3331	2388	1518	832	258

Secondary Endpoint:
Primary Endpoint + Catheterization w/o Obstructive CAD



# at risk	Baseline (0)	6 Mo.	12 Mo.	18 Mo.	24 Mo.	30 Mo.	36 Mo.	42 Mo.
CTA	4996	4540	4211	3430	2565	1645	868	255
Functional	5007	4341	3934	3179	2276	1438	781	244

Secondary Endpoint:
Death or Non-fatal MI



# at risk	Baseline (0)	6 Mo.	12 Mo.	18 Mo.	24 Mo.	30 Mo.	36 Mo.	42 Mo.
CTA	4996	4739	4409	3599	2686	1732	918	276
Functional	5007	4563	4148	3365	2415	1540	846	262

	CTA (n=4996)	Functional (n=5007)	Adj HR (95% CI)	P value
Primary endpoint composite	**164**	**151**	**1.04 (0.83–1.29)**	**0.750**
All-cause death	74	75		
Nonfatal MI	30	40		
Unstable angina hosp	61	41		
Major procedural complications	4	5		
Primary endpoint plus cath without obstructive CAD	**332**	**353**	**0.91 (0.78–1.06)**	**0.217**
Death or nonfatal MI	**104**	**112**	**0.88 (0.67–1.15)**	**0.348**
Death, nonfatal MI, or unstable angina hospitalization	**162**	**148**	**1.04 (0.84–1.31)**	**0.703**

Secondary Endpoint:
Catheterization Without Obstructive CAD ≤90 days

	CTA (n=4996)	Functional (n=5007)	P value
Invasive catheterization without obstructive CAD — N (%)	**170 (3.4)**	**213 (4.3)**	**0.022**
Invasive catheterization	609 (12.2%)	406 (8.1%)	
Revascularization	311 (6.2%)	158 (3.2%)	
CABG	72	38	

Secondary Endpoint:
Cumulative Radiation Exposure ≤90 days

Mean ± SD; mSv	CTA (n=4996)	Functional (n=5007)	P value
All patients	**12.0 ± 8.5**	**10.1 ± 9.0**	**<0.001**
No radiation exposure	4%	33%	
Intended nuclear test randomization stratum	12.0 ± 8.4	14.1 ± 7.6	<0.001
Intended stress echo randomization stratum	12.6 ± 9.0	1.3 ± 4.3	<0.001
Intended exercise ECG randomization stratum	10.4 ± 7.8	2.3 ± 5.4	<0.001

promise

Summary

- PROMISE enrolled a symptomatic, intermediate risk population for whom testing is currently recommended
- There is a low event rate in this contemporary population
- There were no significant differences in outcomes between an initial anatomic (CTA) or functional testing strategy with respect to the primary endpoint overall or in any subgroup
- An initial CTA strategy was associated with a lower rate of invasive catheterization without obstructive CAD
- Radiation exposure was higher in CTA arm overall, but lower in those patients for whom a nuclear test was specified pre-randomization as the intended functional test, but who were randomized to CTA

Conclusions

- Our results suggest that CTA is a viable alternative to functional testing
- These real-world results should inform noninvasive testing choices in clinical care as well as provide guidance to future studies of diagnostic strategies in suspected heart disease

ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease

A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons

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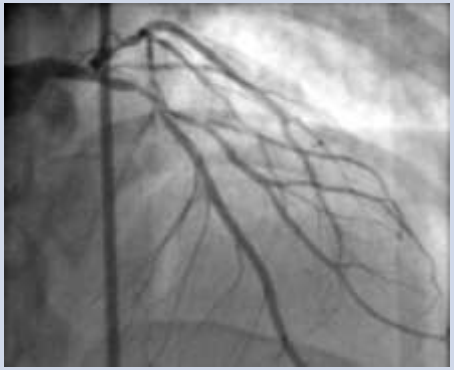
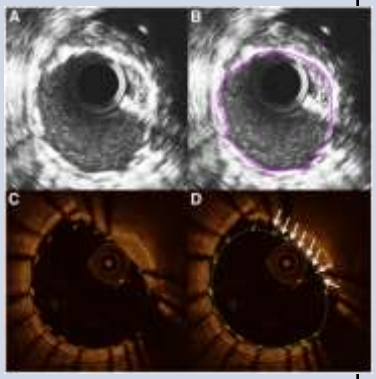
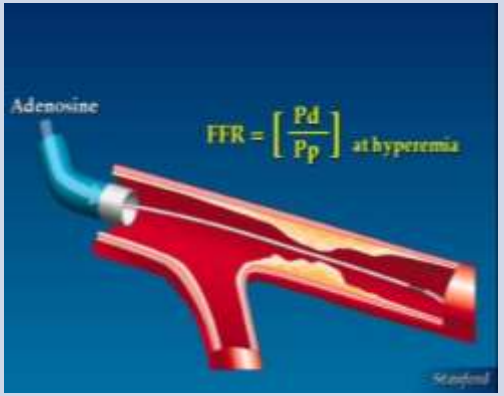
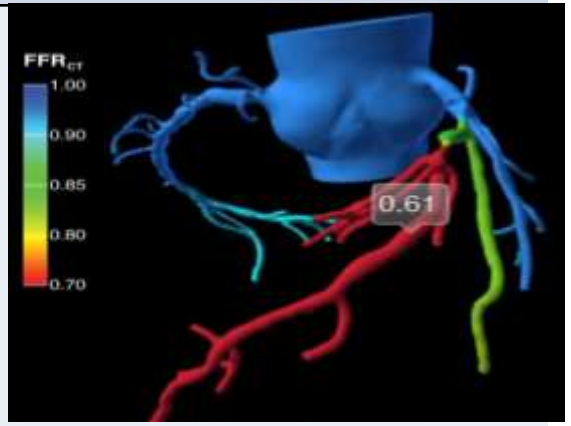
AUC will be informed by studies

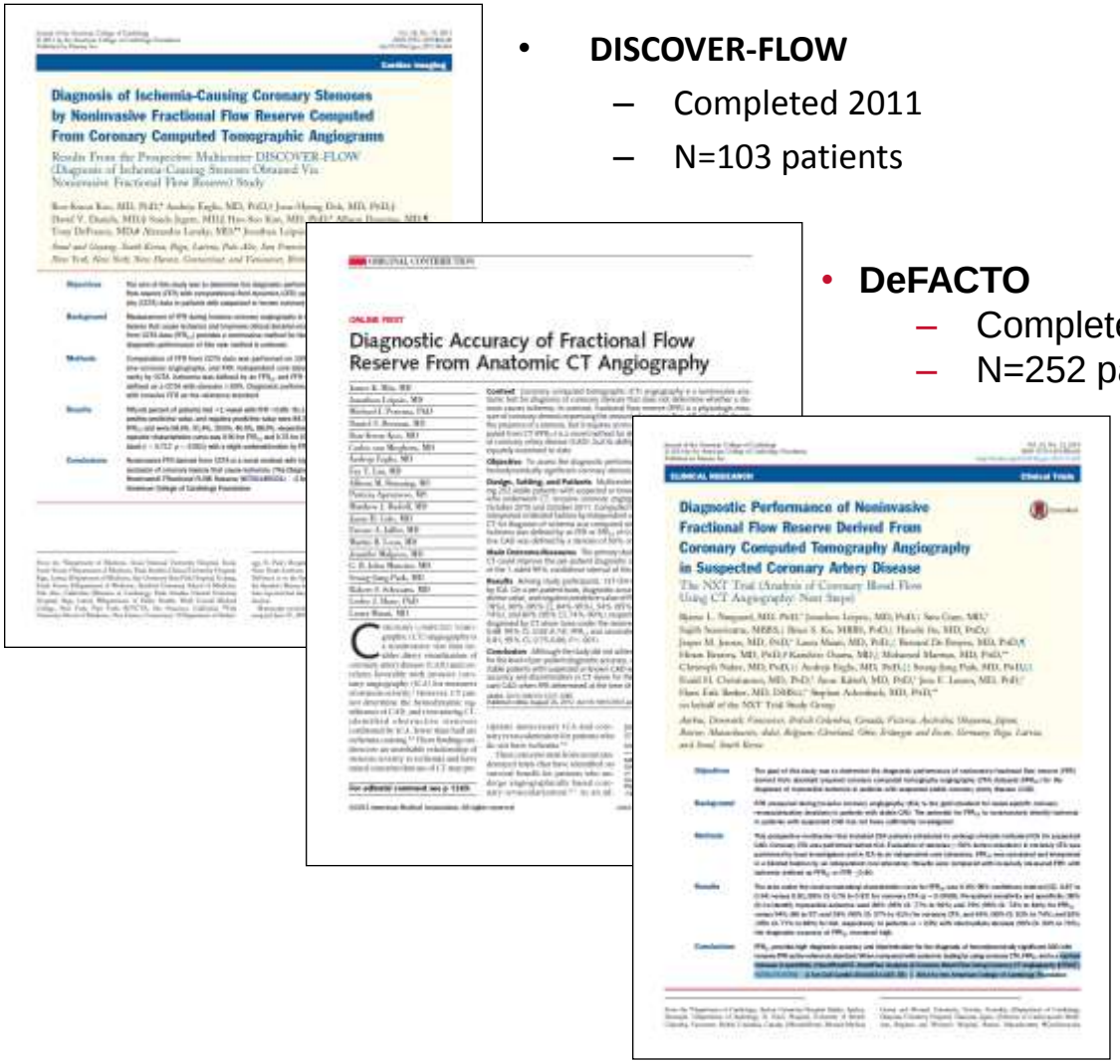
Table 1.1. Symptomatic

Refer to pages 16 and 17 for relevant definitions, in particular Table A and text for age, sex, symptom presentation, and risk factors relevant to each pre-test probability category								
Indication Text		**Exercise ECG**	**Stress RNI**	**Stress Echo**	**Stress CMR**	**Calcium Scoring**	**CCTA**	**Invasive Coronary Angiography**
1.	• Low pre-test probability of CAD • ECG interpretable AND able to exercise	A	R	M	R	R	R	R
2.	• Low pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	M	R	M	R
3.	• Intermediate pre-test probability of CAD • ECG interpretable AND able to exercise	A	A	A	M	R	M	R
4.	• Intermediate pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	A	R	A	M
5.	• High pre-test probability of CAD ECG interpretable AND able to exercise	M	A	A	A	R	M	A
6.	• High pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	A	R	M	A

Diagnosing anatomic and functionally-significant CAD

	ANATOMY	***FUNCTION***
	Identify obstructive CAD	***Identify lesion-specific ischemia that may benefit from PCI***
Invasive	 	
Non-invasive		

HeartFlow FFR_{CT} Clinical Trial Data is growing



- **DISCOVER-FLOW**
  - Completed 2011
  - N=103 patients
- **DeFACTO**
  - Completed 2012
  - N=252 patients
- **NXT**
  - Completed 2013
  - N=254 patients
  - 10 Worldwide Sites
    - Europe
    - Australia
    - Japan
    - Korea

3 major trials comparing FFR_{CT} to FFR in more than 600 patients

Conclusions

- CTA for chest pain is a viable alternative to stress testing and in the PROMISE trial showed
  - Less invasive cardiac catheterization without obstructive disease
  - Less radiation compared to Stress Nuclear
  - Favorable 1 year outcomes
- CT FFR is an emerging technology that may help patients with chest pain getting a CTA