Stress Testing: Classic is the Best

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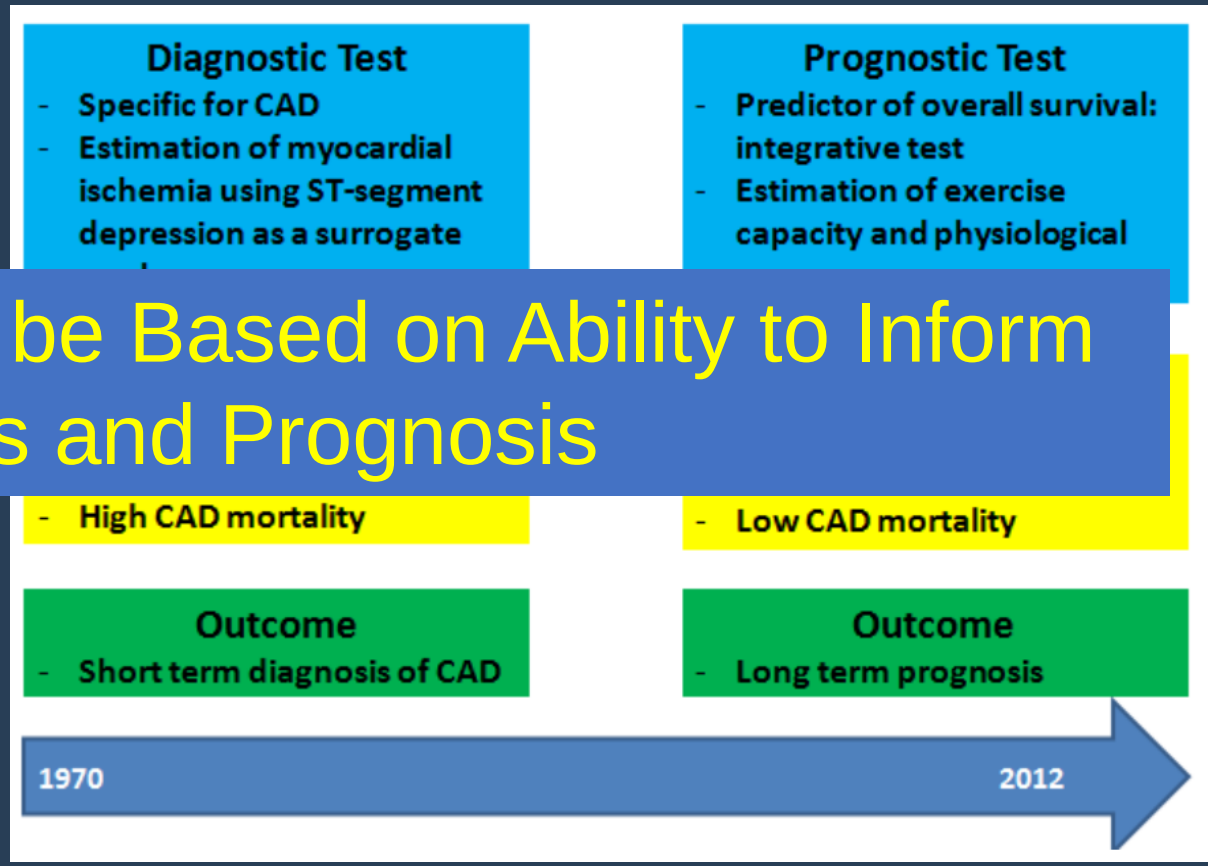
Disclosures

- Grants and Contracts: Society of Thoracic Surgeons, American College of Cardiology, National Institutes of Health (SBIR and R01), Cytokinetics, Food and Drug Administration (NESTcc), Abbott Vascular, Boston Scientific

- Advisory Boards / Consulting: Janssen, Edwards LifeSciences, American College of Physicians

Goals of Stable Chest Pain Evaluation

- Diagnosis:
  - Non Cardiac
  - Epicardial CAD
  -
  -
  - Other Cardiac Etiologies
- Prognosis



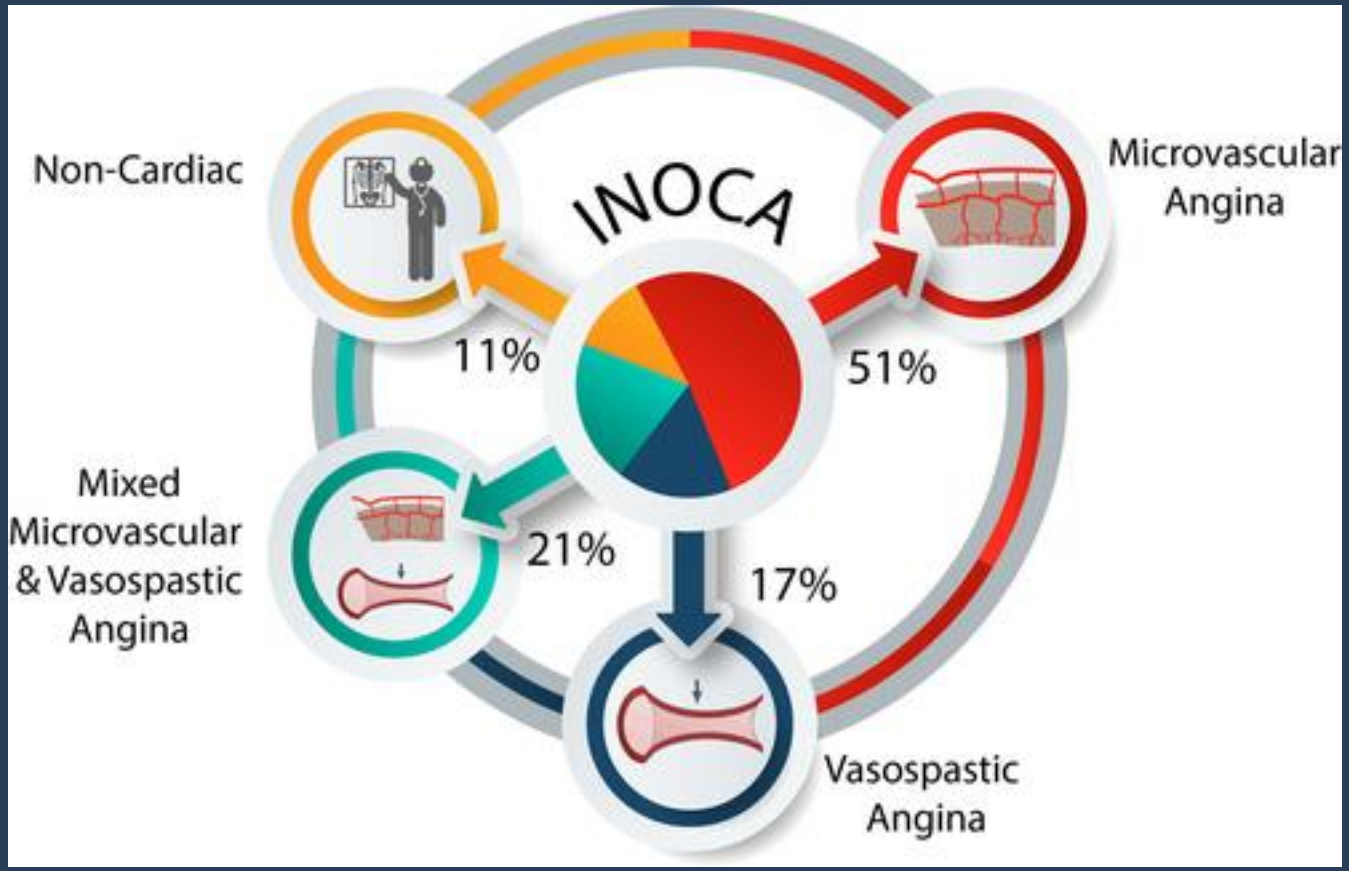
Choice of Test Should be Based on Ability to Inform Diagnosis and Prognosis

Charansonney et al. Discovery Medicine 2012

Diagnosis of Chest Pain

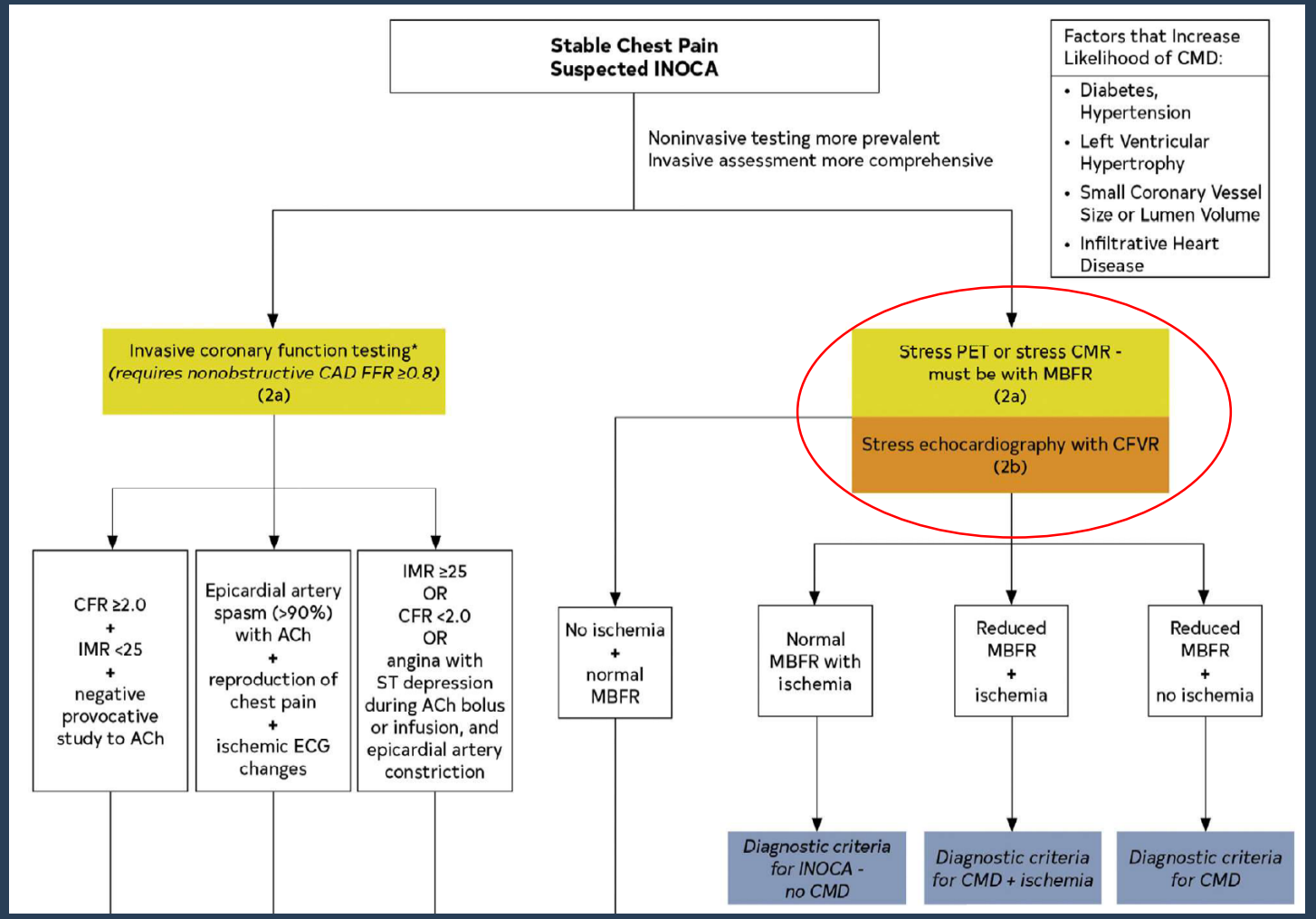
INOCA

- ~ 3-4 million patients with INOCA in the US
- More prevalent in women than men
- Most common causes are CMD and vasospasm



Circ Cardiovasc Interv. 2019;12:e008126

Diagnosis of INOCA



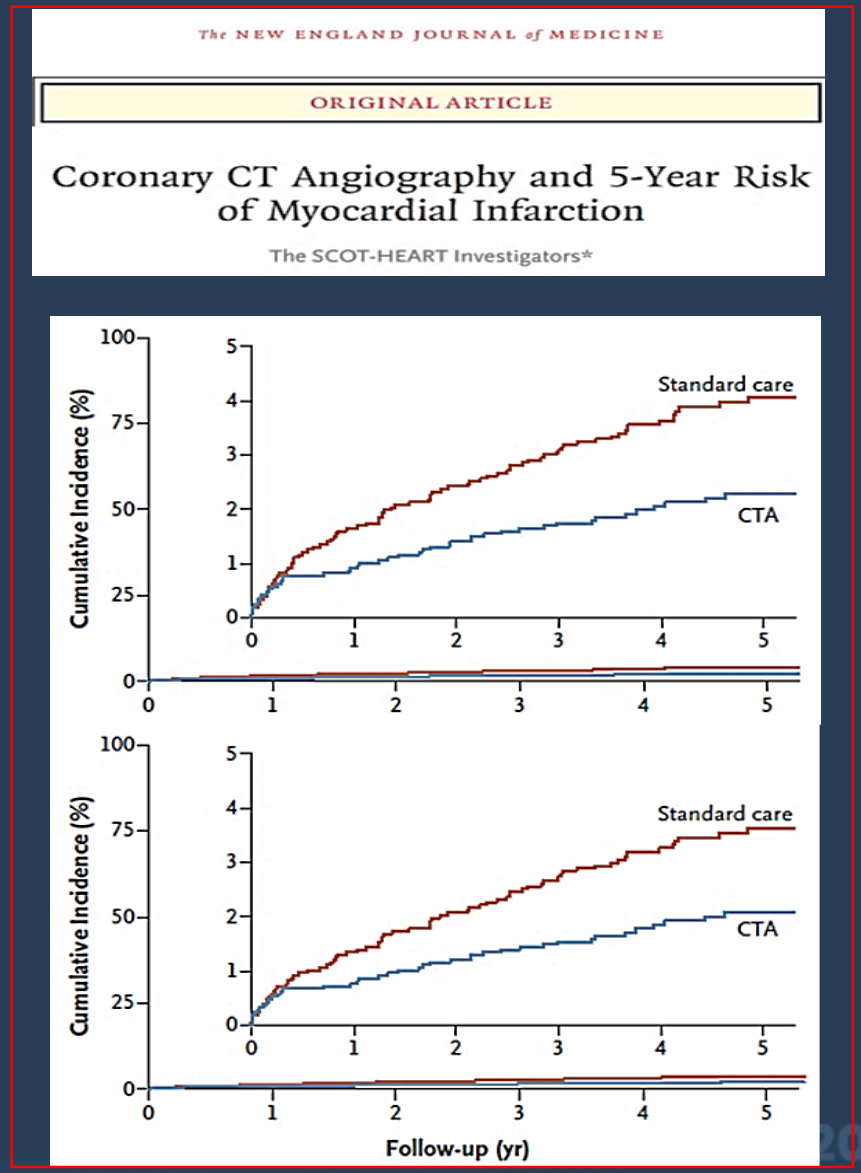
Gulati et al. JACC 2021

Diagnosis of Epicardial CAD and Prognosis

Randomized Studies of CT vs. Stress Testing

SCOT-HEART

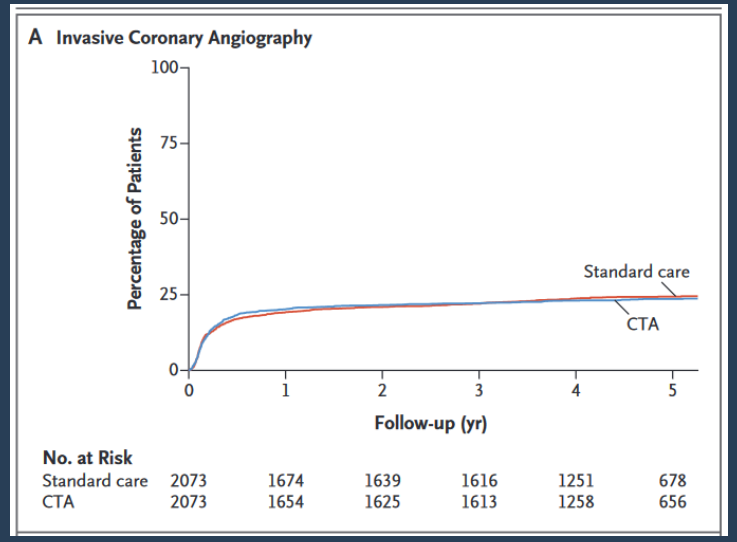
- Enrolled 18-75 yo referred by pcp to dedicated chest pain clinic
- 10-year risk of 17±12% by ASSIGN risk score
- Standard care = mostly EET
- 41% ↓ in CV Death /MI at 5 y
- But…

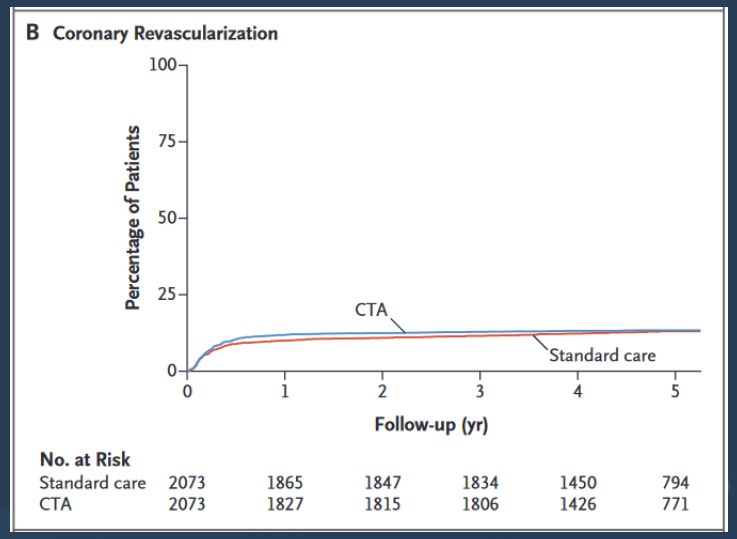


Randomized Studies of CT vs. Stress Testing

SCOT-HEART

- No substantial difference in ICA or revascularization
- Diagnosis of CAD at 6 weeks changed in 1% of patients in usual care and 27% in CTA
- Medication changes!!

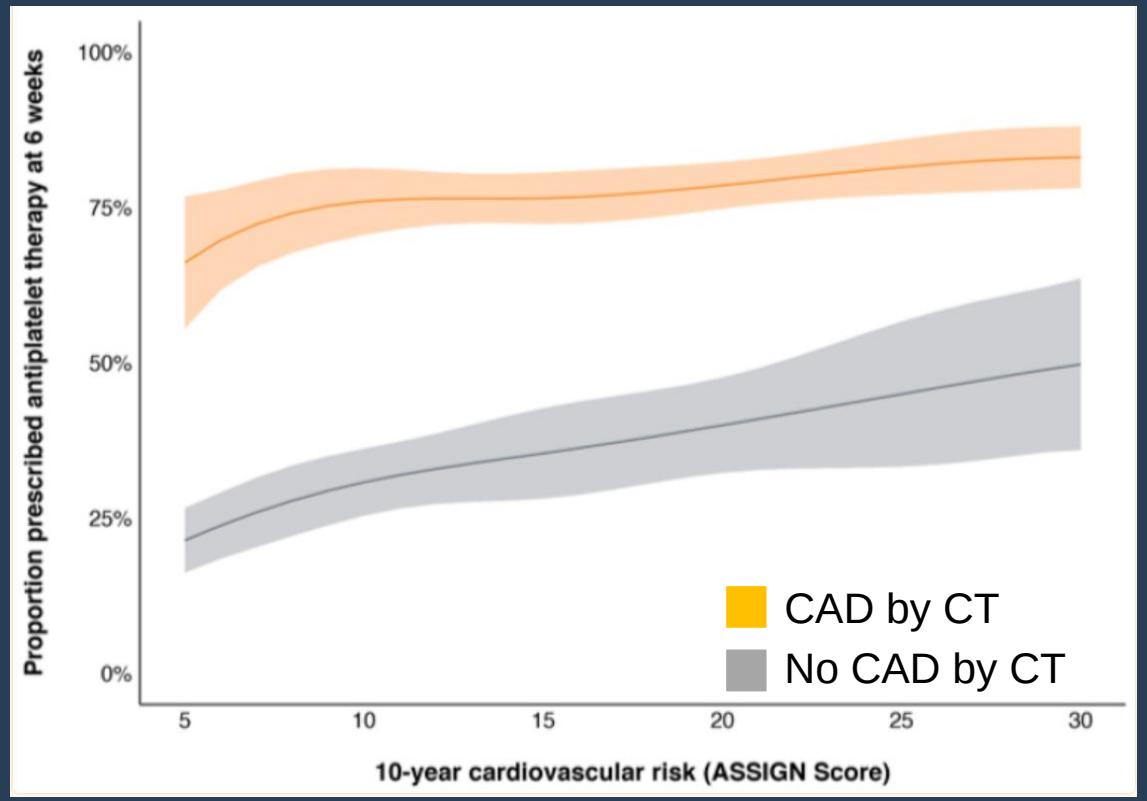




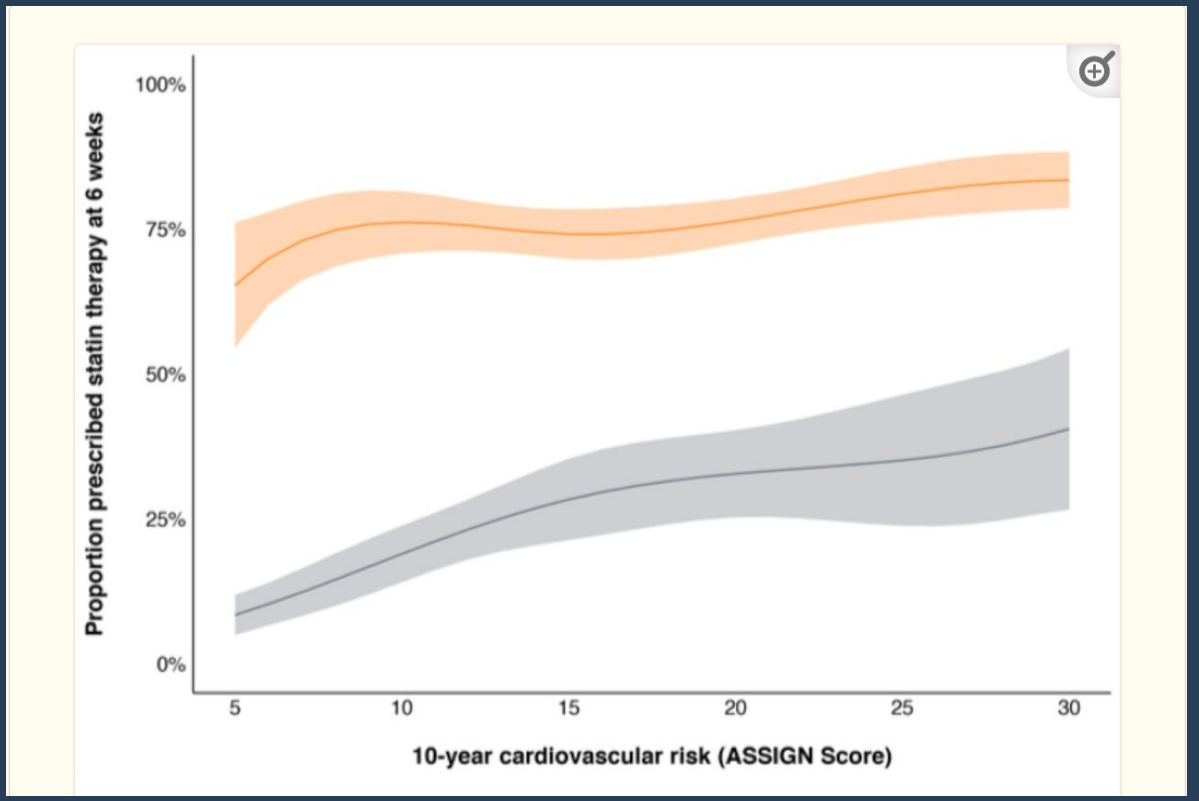
Randomized Studies of CT vs. Stress Testing

SCOT-HEART

Antiplatelet Therapy at 6 weeks



Statin Therapy at 6 weeks



Adamson et al. J Cardiovasc Comput Tomogr. 2019

Randomized Studies of CT vs. Stress Testing

SCOT-HEART

Circulation

CHOLESTEROL CLINICAL PRACTICE GUIDELINES

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/
AGS/APhA/ASPC/NLA/PCN
Management of Blood Cho

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

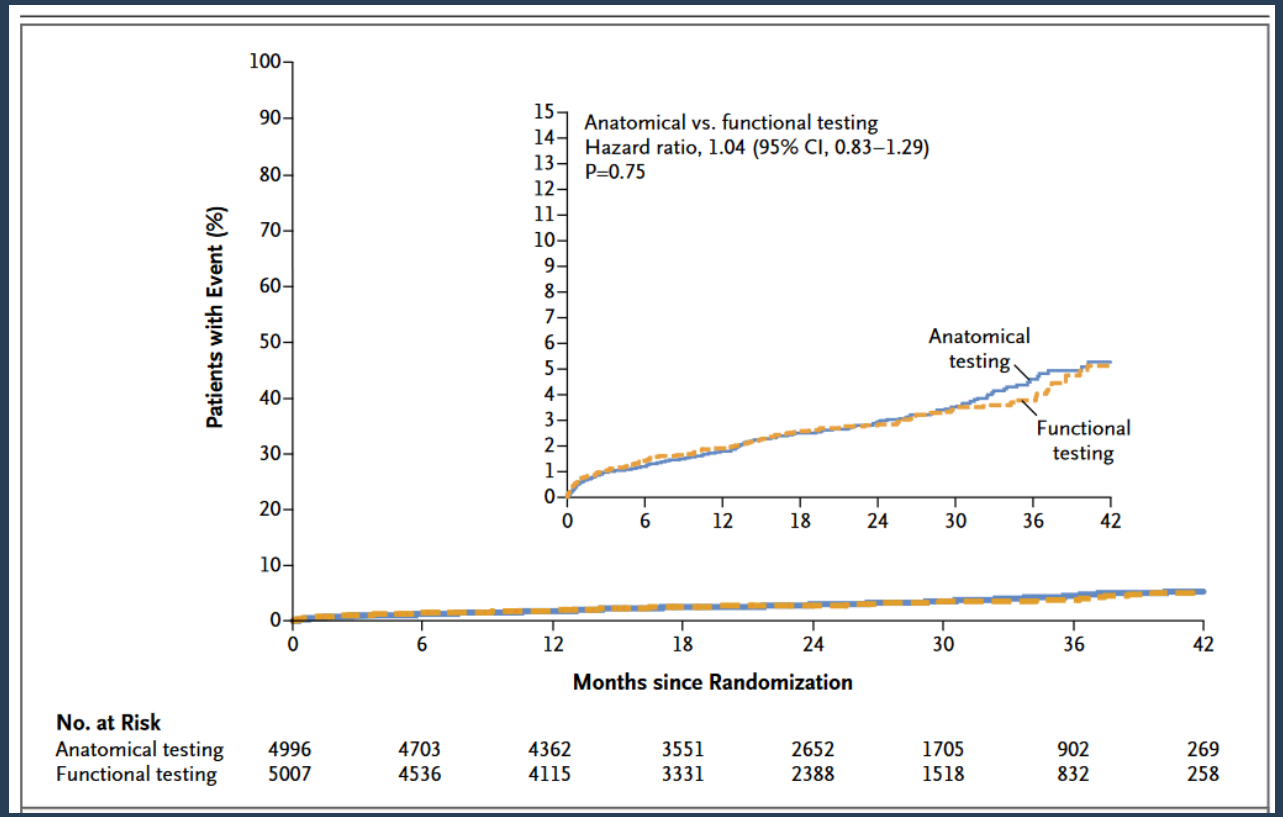
Clinical Practice Guideline

Paul K. Whelton, Robert M. Carey, Wilbert S. Aronow, Donald E. Casey, Karen J. Collins, Cheryl Dennison Himmelfarb, Sondra M. DePalma, Samuel Gidding, Kenneth A. Jamerson, Daniel W. Jones, Eric J. MacLaughlin, ... SEE ALL AUTHORS

Randomized Studies of CT vs. Stress Testing

PROMISE Trial

- 10,003 symptomatic patients w/o known CAD
- Median f/u of ~ 2 yrs
- No difference in all-cause death/MI/UA/procedural complication
- Resulted in more ICA in CT Arm (4.3% vs. 3.4%)

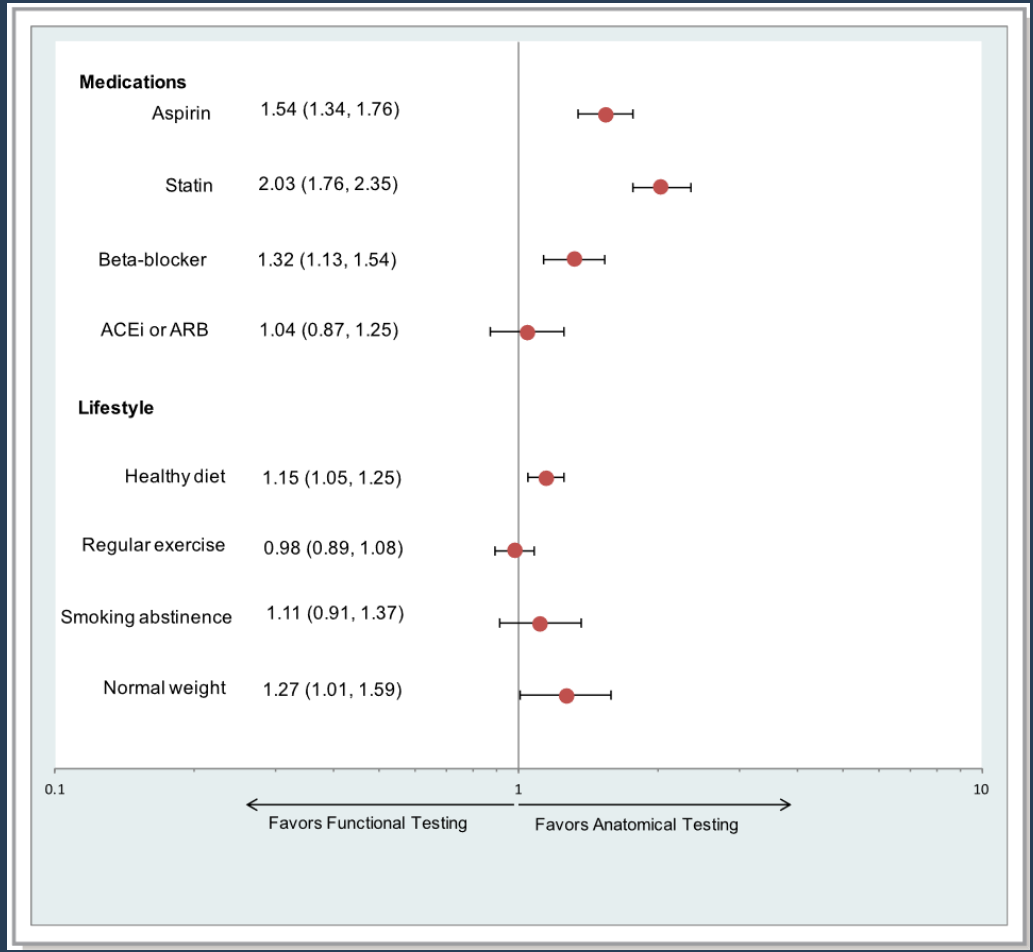


Douglas PS et al. NEJM 2015

Randomized Studies of CT vs. Stress Testing

PROMISE Trial: Medication Changes

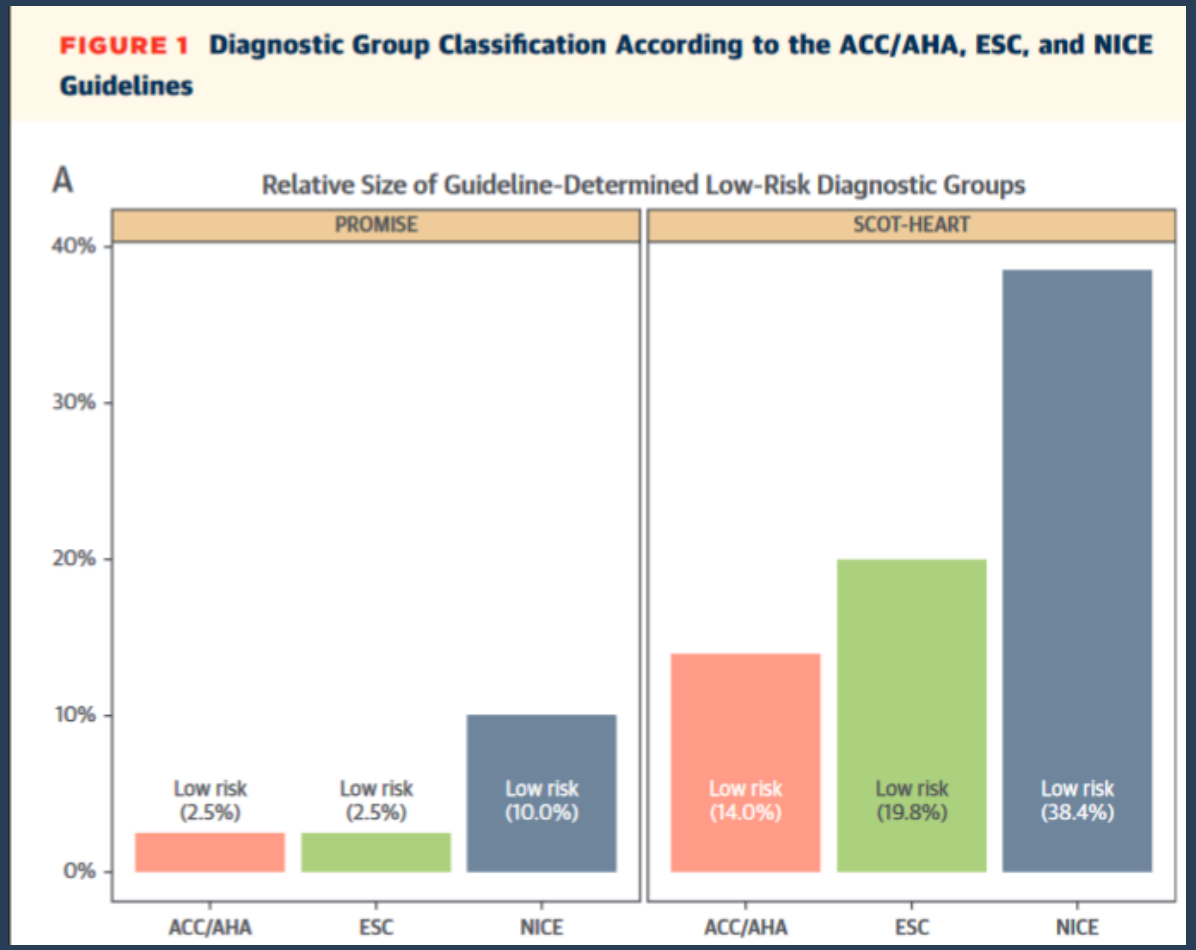
- CT associated with increased preventive therapies at 60-days
- Yet similar event rates between arms ~ 2 yrs
- Prevention guidelines have lowered the threshold for treatment!



Ladapo et al. Circ Cardiovascular Imaging 2016

Performance in Intermediate Risk Patients?

- PROMISE and SCOT-Heart had a substantial number of low-risk patients.
- CCTA vs Functional Stress Testing in Intermediate Risk Only?

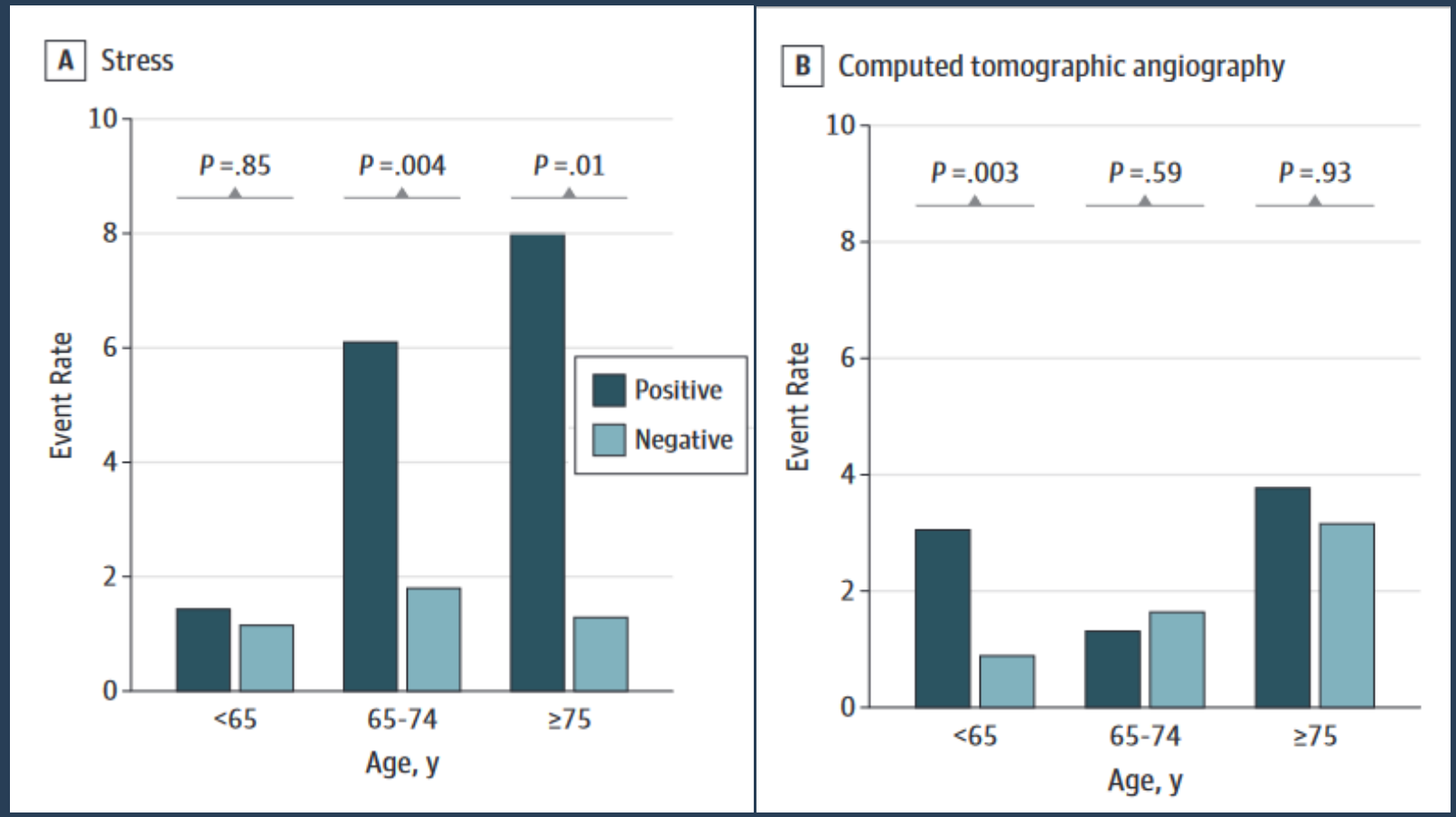


Adamson et al. JACC Imaging 2018

What About Age?

Association Between Age and Outcome in the PROMISE Trial

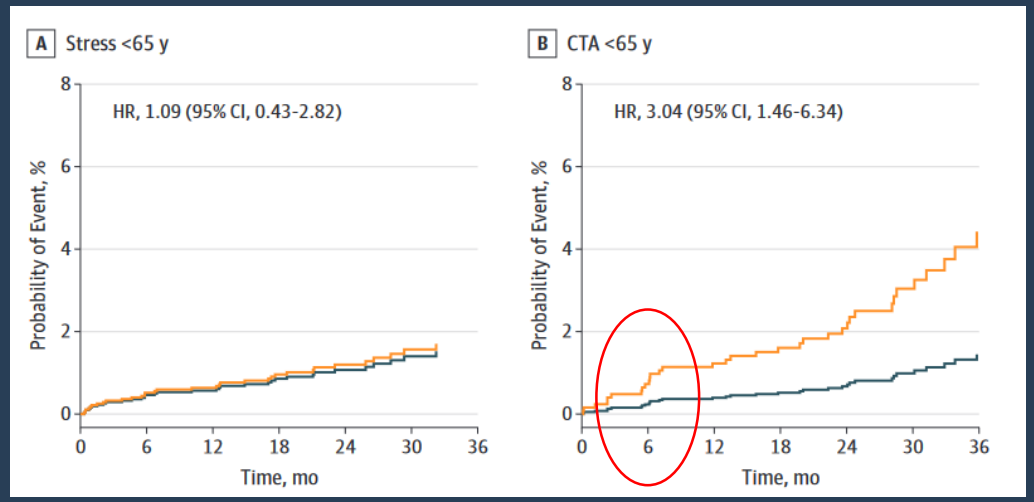
Primary Outcome of: CV death and MI

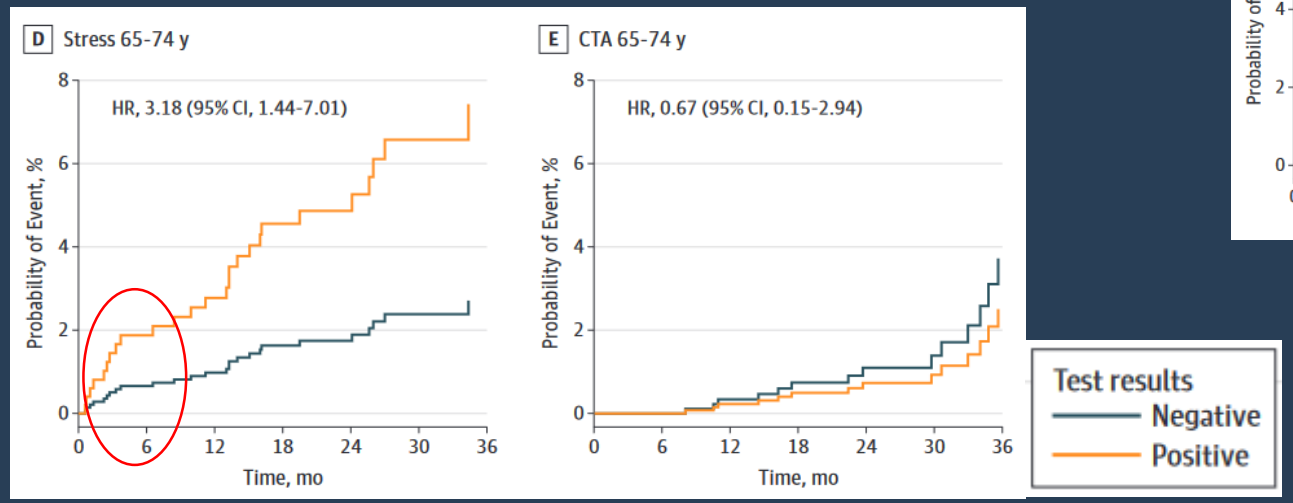


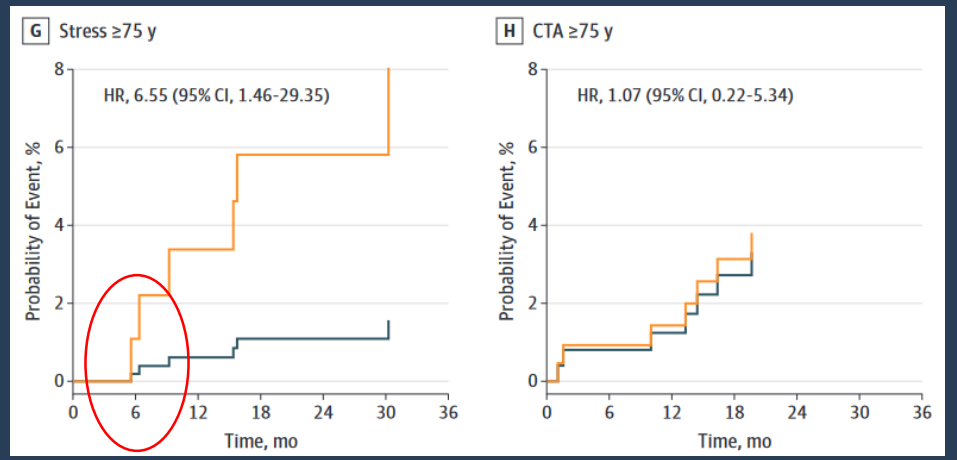
Lowenstern et al. JAMA Cardiology 2020

What About Age

Time to Event Based on Age and Test Modality in the PROMISE Trial







Lowenstern et al. JAMA Cardiology 2020

Age

Association Between Age and CV Death/MI Based on Test Positivity

Comparison	Event Rate (No. of Events/Sample Size), No. (%)		Unadjusted		Adjusted[a]	
	High Risk[b]	Low Risk[b]	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Interaction between test results, test modality, and age group				.01		.01
<65 y						
Positive vs negative in stress	5 (1.43)	32 (1.15)	1.17 (0.46-3.00)	.74	1.09 (0.43-2.82)	.85
Positive vs negative in CTA	10 (3.05)	26 (0.89)	3.48 (1.68-7.22)	<.001	3.04 (1.46-6.34)	.003
65-74 y						
Positive vs negative in stress	10 (6.10)	16 (1.80)	3.55 (1.61-7.83)	.002	3.18 (1.44-7.01)	.004
Positive vs negative in CTA	2 (1.31)	14 (1.64)	0.78 (0.18-3.43)	.74	0.67 (0.15-2.94)	.59
≥75 y						
Positive vs negative in stress	4 (8.00)	3 (1.29)	7.10 (1.59-31.74)	.01	6.55 (1.46-29.35)	.01
Positive vs negative in CTA	2 (3.77)	6 (3.16)	1.16 (0.23-5.76)	.85	1.07 (0.22-5.34)	.93

Lowenstern et al. JAMA Cardiology 2020

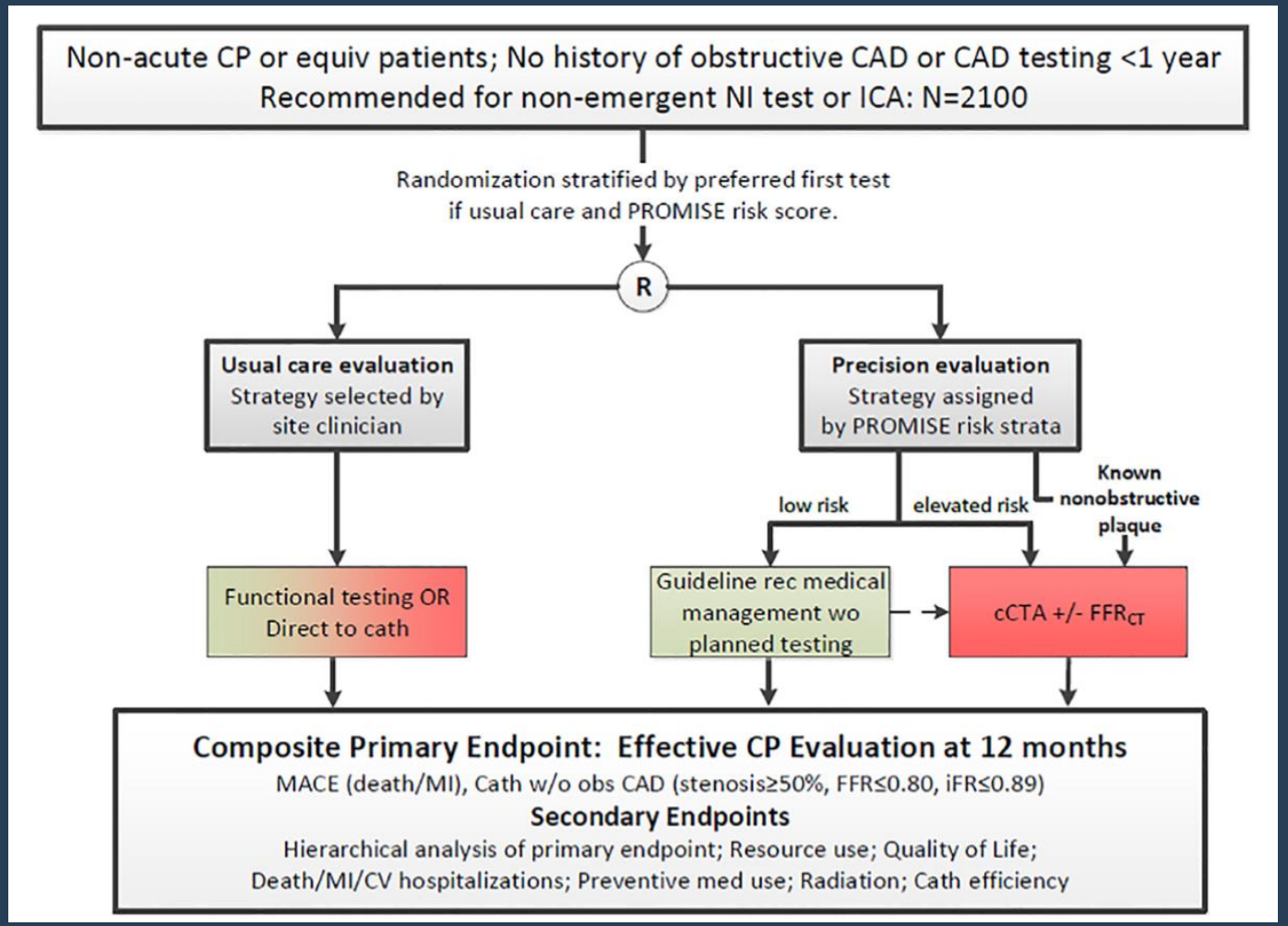
What About CT-FFR?

Does FFR_{CT} Make CTA Better? PACIFIC, PLATFORM, ADVANCE, AARHUS

- PACIFIC: FFR_{CT} correlates better with invasive FFR than other NI tests
- PLATFORM: Observational study
  - Adding CTA+FFR_{CT} →XL'd 61% planned caths and ↓ no obs CAD 73% → 12%
  - No impact on safety; Cost saving
- ADV
  - A
  - No events if FFR_{CT} >0.80
- Aarhus: Single center cohort
  - CTA+FFR_{CT} driven algorithm:
  - FFR_{CT} > 0.80 → OMT; FFR_{CT} ≤ 0.80 → OMT +/- Cath proved safe

Needs Randomized Data

RANDOMIZED DATA FOR CT ± FFR: PRECISE TRIAL



Nanna et al. AHJ 2022

Conclusions

- Testing in stable chest pain must focus on diagnosis and prognosis
- CTA is currently limited relative to CMR or PET in diagnosis of INOCA or Microvascular Dysfunction
- CTA is better at diagnosing non-obstructive disease and prompting medication changes
- Despite this, no difference in outcomes in PROMISE and SCOT-HEART and findings may be less relevant with changes in prevention guidelines and no testing strategies for low-risk patients

Conclusions II

- Stress Testing may be superior to CTA in older patients (? Higher risk patients)
- CTA alone is associated with more ICA in most studies
- Does existing CT-FFR data solve this problem?
- The PRECISE Trial will evaluate usual care intervention vs. PRECISION TESTING with:
  - No upfront testing for low-risk
  - CT+/- FFR for intermediate and above risk