

Chest Pain Evaluation – Possible versus Probable: No Test, Stress Test or CT Angio?

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Relationships With Industry

I have two industry relationships relevant to this presentation.

All relationships with industry may be found online:

<http://www.dcri.duke.edu/research/coi.jsp>

Abbott

Akros

Alere

Bristol-Meyers Squibb

CardioDx

Edwards Lifesciences

Elsevier

Fabric Genomics

GE Healthcare

Gilead

HeartFlow

Host Response

Ibis Biosciences

Interleukin Genetics

Kowa

Novartis

Origin Commercial Advisors

Pappas Ventures

Singulex

UpToDate/Kluwer

Verily Life Sciences

23and Me

Which Test is Best for Stable Chest Pain ?

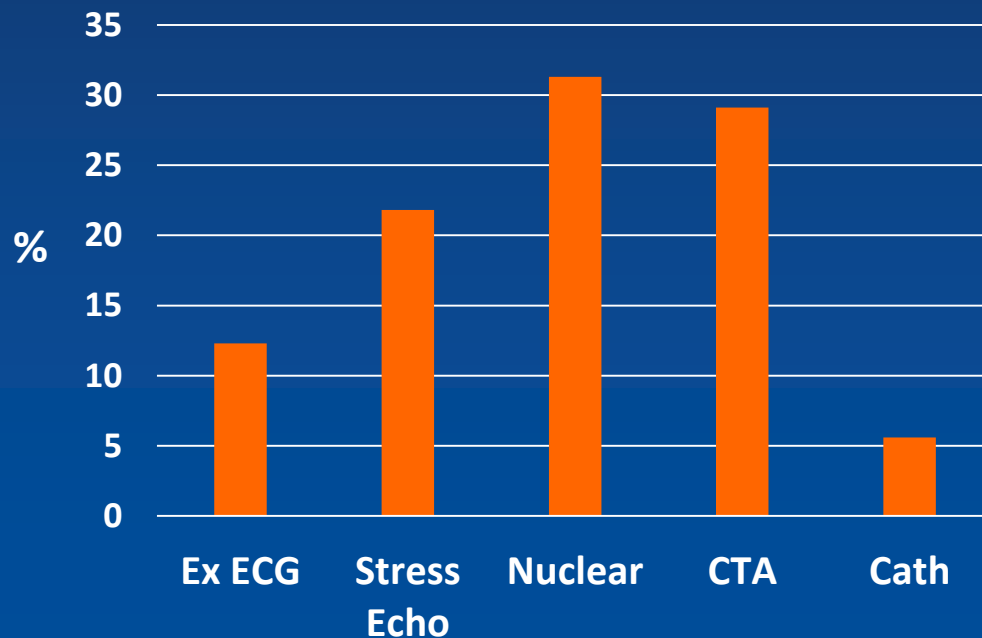
Evolution of Thinking About Testing Goals

- Hypothesis circa 2008-15: Simple shift from stress testing to CTA in all patients might improve outcomes
 - Two large pragmatic RCTs in 2015: SCOT-Heart, PROMISE
- Evolving data in 2017: It's not so simple
 - Different tests provide different information
 - Sensitivity and specificity trade-offs vary by patient risk
 - Demographic and comorbid subgroups matter
 - Goals of testing also matter, whether diagnostic (for obstructive CAD) or risk stratification (for long term care)
- Hypothesis circa 2017: **Precision Testing**
 - Selective use of different test modalities as determined by individual patient risk, clinical goals, test info provided

Pre Course Question



- 61 yo woman with atypical chest pain
- Risk factors: Diabetes, obesity, hypertension, hyperlipidemia, osteoarthritis
- What is the best test to assess chest pain?



Confidence in Test Choice

- Yes - 71%
- No - 29%

SCOT – Heart Top Line Conclusions

- In patients presenting with suspected angina due to coronary heart disease, the **addition** of CTA to ETT and usual care
 - Increases the diagnosis of CHD
 - Improves preventive treatment
 - Does not change cath rate but increases cath yield
 - Tends to increase revascularizations
 - Increases costs by 32% over usual care (stress testing)
- CTA reduces CV death/MI by 50% after implementation delay
 - Biologically plausible given improved preventive care and more accurate cath referral

PROMISE Top Line Conclusions

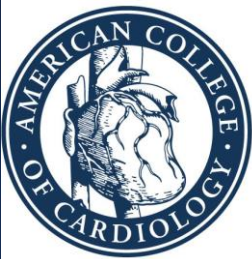
- In current real world care, stable or non-acute chest pain patients currently being evaluated for suspected CAD using noninvasive testing have a very low event rate
- This low event rate was not affected by test choice
- CTA was associated with
 - Improved preventive care
 - More invasive testing, higher cath yield
 - More revascularization
 - Similar costs when used instead of stress testing
- Given the similar clinical outcomes: CTA is a reasonable alternative strategy to stress testing as a first line investigation in stable chest pain

What We Have We Learned From PROMISE and SCOT-Heart in 2017

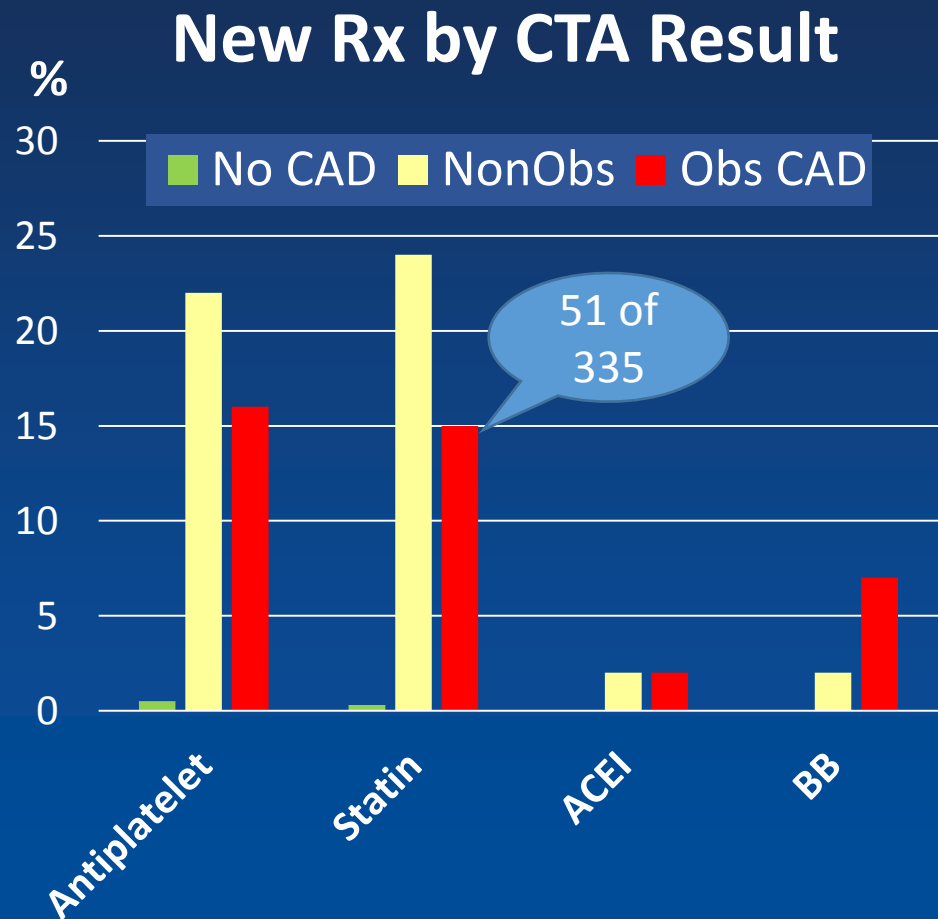
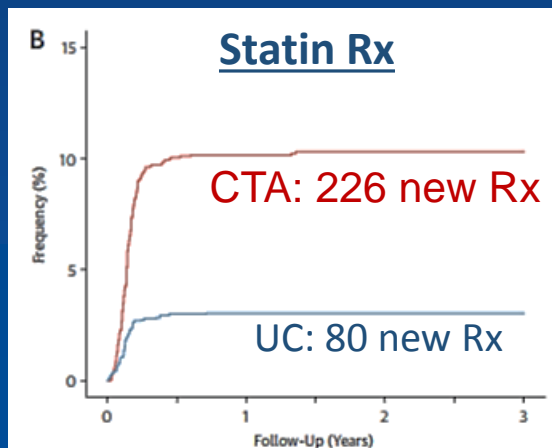
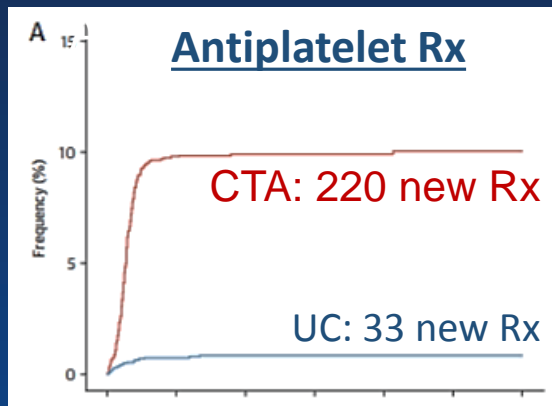
- The population being tested in the current era has:
 - High risk factor burden (average RF = 3)
 - Low rate of obstructive CAD (10-20%)
 - Low event rates (<1% /y for CV death/MI)
- The population being cathed in the current era has:
 - Low rate of obstructive CAD (<50% fxnl testing; 70-80% CTA)
 - Low rate of revascularization (<50% caths; 5-10% overall)
- There is no single, obvious 'best' testing strategy
 - No testing is an appealing option
 - More precise cath lab referral needed
 - One size does not fit all: More info needed on testing goals and subgroups to aid in testing decisions in individual pts

Going Beyond Simple Test Substitution: How Does CTA Inform CP w/u in 2018?

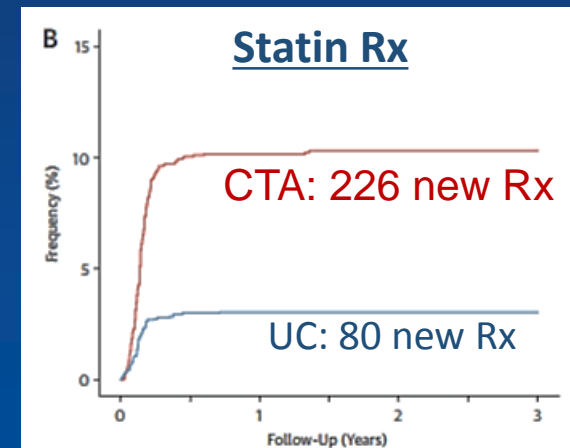
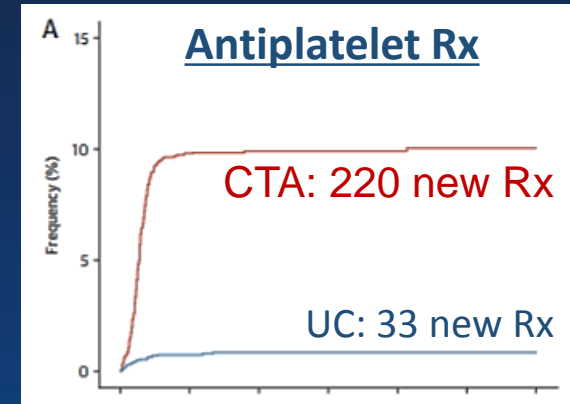
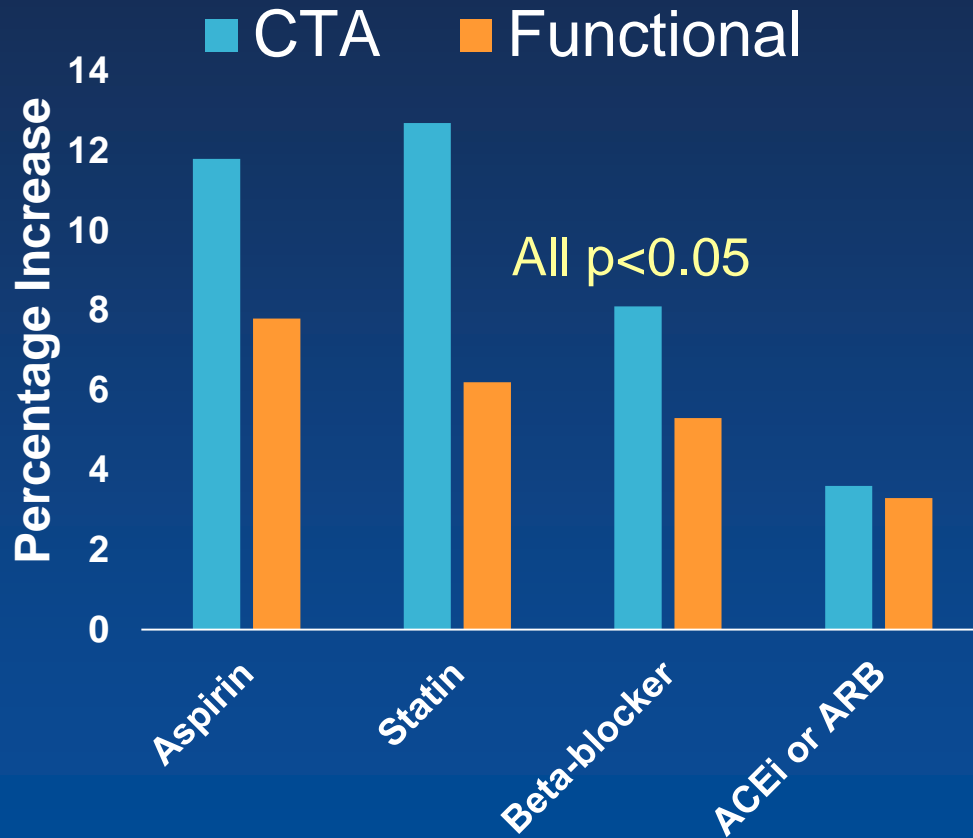
- Can we improve preventive care?
- Which pts are at lowest and highest risk?
- Which pts might benefit from deferred testing?
- Can we reduce unneeded caths/improve cath yield?
- Can we improve pt selection for revascularization?
- Can we practice '**precision testing**'?
 - Tailoring diagnostic strategies to individual patient risk, testing goals and test performance in relevant subgroups



Use of Coronary Computed Tomographic Angiography to Guide Management of Patients With Coronary Disease



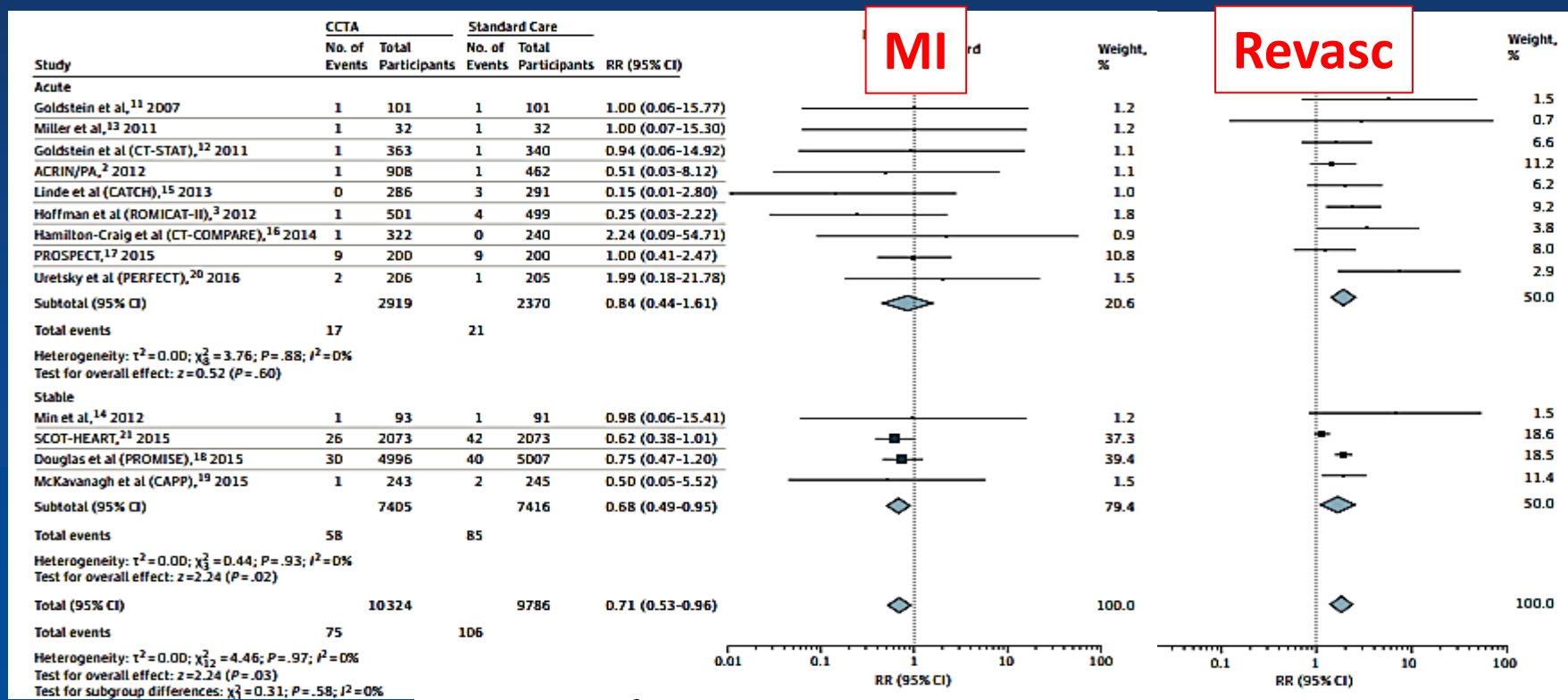
Changes in Preventive Medications



Coronary Computed Tomography Angiography vs Functional Stress Testing for Patients With Suspected Coronary Artery Disease

A Systematic Review and Meta-analysis

- Meta-analysis of 9 acute CP (n=5289); 4 stable CP (n=14,821)
- No difference in death or CV hosp (RR 0.93; 0.98)
- Reduced MI (RR, 0.71); More cath; revasc (RR 1.33; 1.86)
- More frequent new CAD Dx; Greater ASA, statin use



Low Risk Subgroups: Deferred Testing ?

■ **In support** of a deferred testing strategy

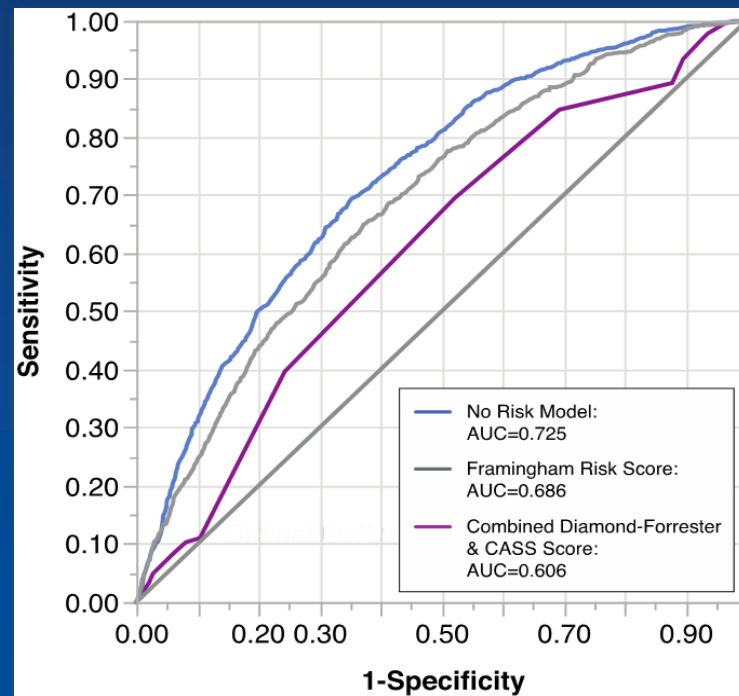
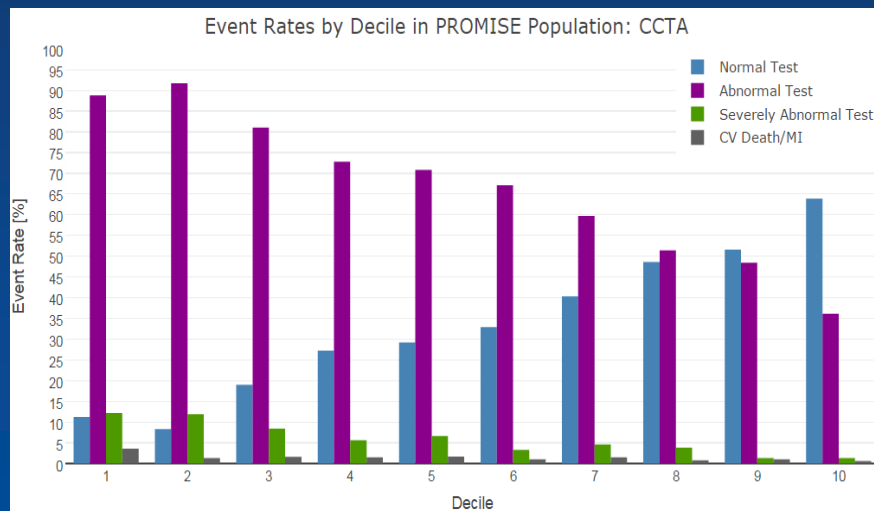
- Very low annual event rates in PROMISE, SCOT-Heart (1-2%/yr)
- Obstructive (revascularizable) CAD is infrequent (10-20%)
- Similar outcomes with revascularization vs med Rx (eg COURAGE)
- Excellent preventive and anti-anginal therapeutics available

■ **Against** a deferred testing strategy

- ACC/AHA GL recommend testing for non-acute chest pain (Class IA)
- No supporting prospective data: A deferred testing strategy has never been evaluated even in an observational setting for outcomes or costs
- Not testing may miss LM/3VD for whom revascularization is lifesaving
- Not testing may require multiple visits/medication changes
- Patient/Provider preferences for action/answers; Physician liability

Identification of Patients With Stable Chest Pain Deriving Minimal Value From Noninvasive Testing The PROMISE Minimal-Risk Tool, A Secondary Analysis of a Randomized Clinical Trial

- 4631 pts receiving CTA; 27% w/o CAC, stenosis or events
- Predict 'No Risk' using 10 clinical variables; C statistic 0.725
- Improvement over FRS (AUC 0.69) and D-F (AUC 0.61)
- Validated in SCOT-Heart; C statistic 0.805

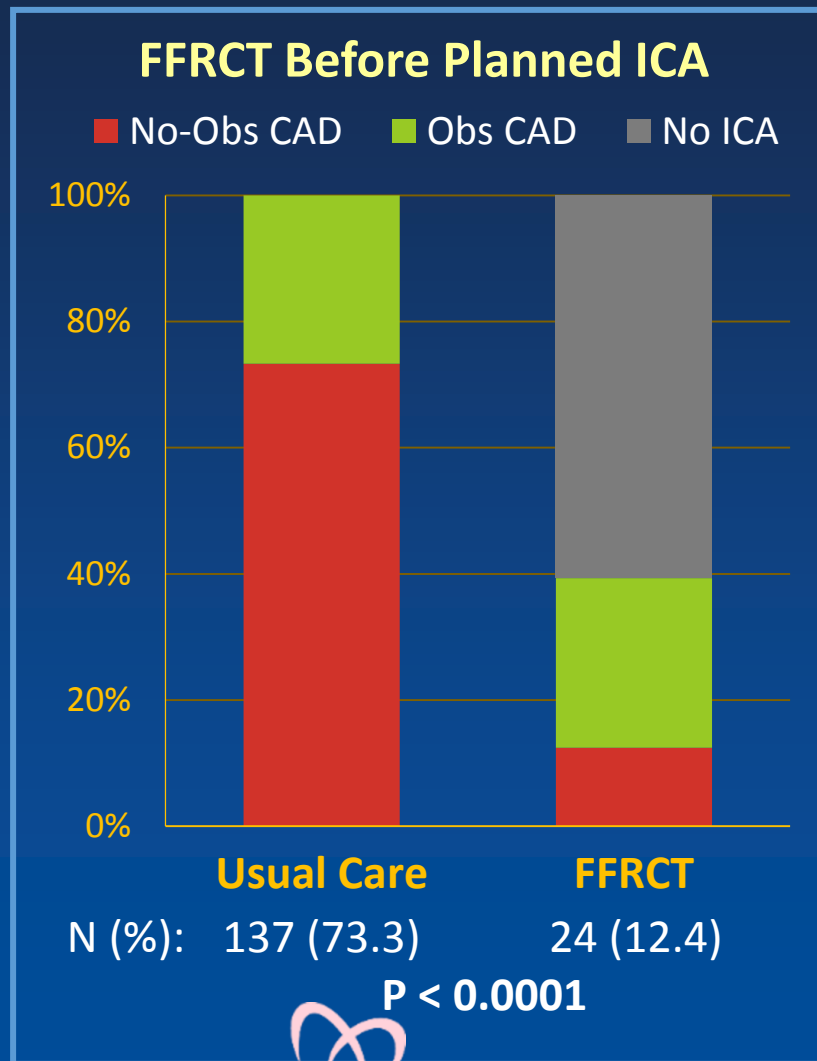
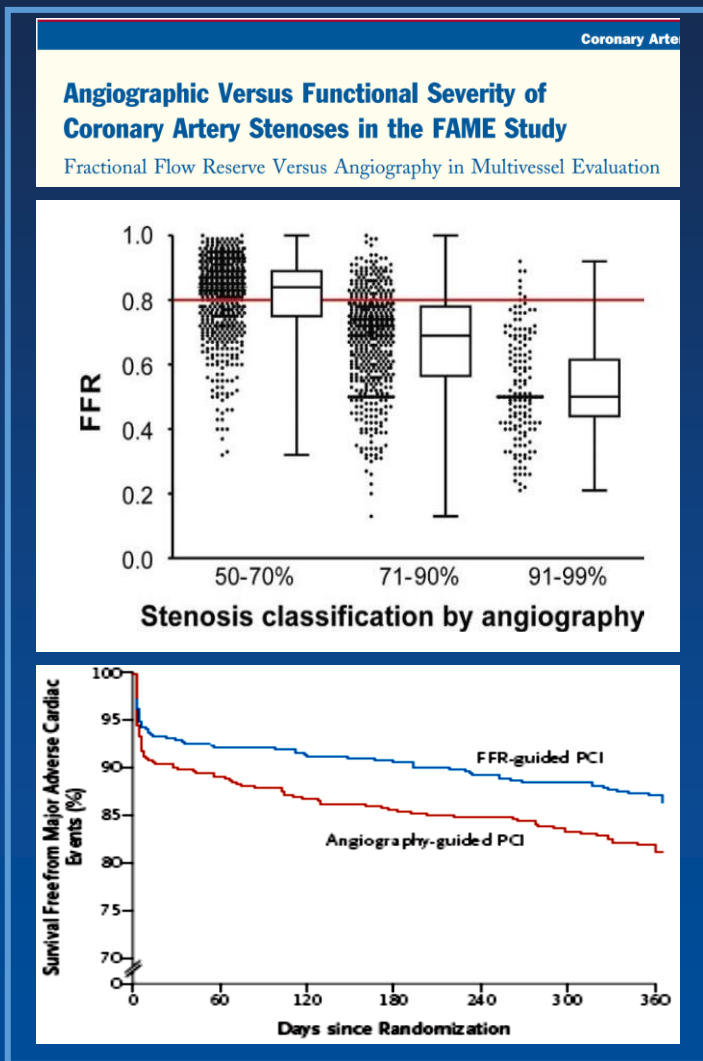


JAMA Cardiol 2017
PromiseRiskTools.com
Intl J Cardiology 2017



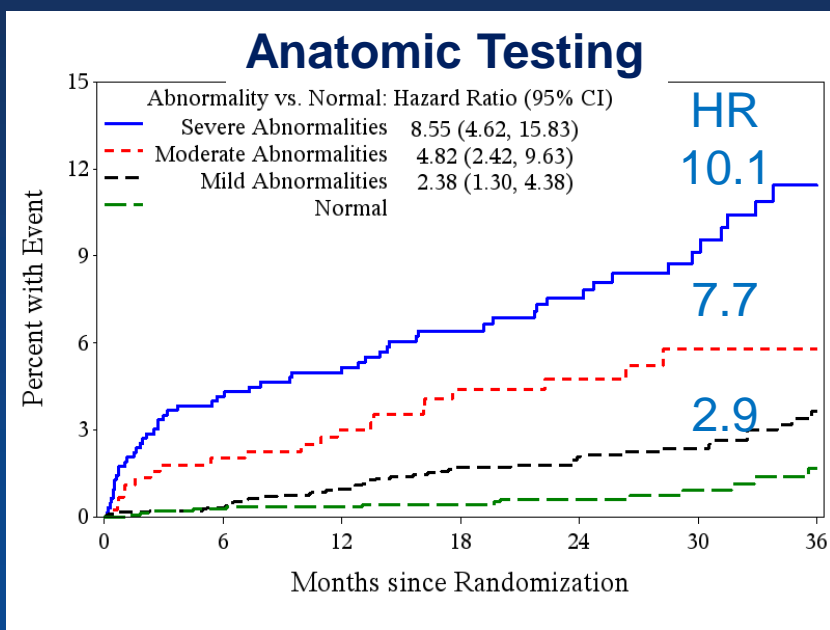
Coronary Anatomy ≠ Physiology

FFR for Managing CAD and Cath Lab Triage



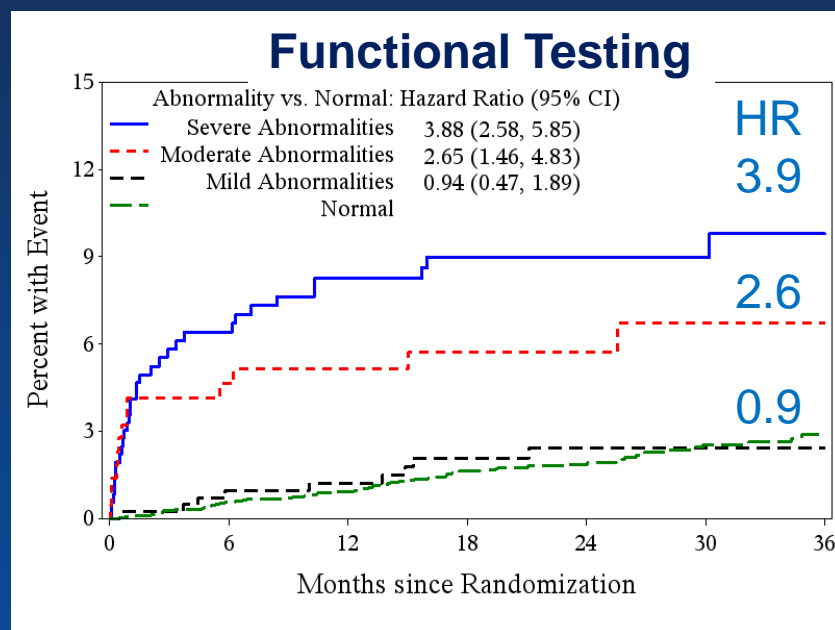
The Importance of Non Obstructive CAD for Prognosis

Composite of Death, MI, and Unstable Angina



Coronary CTA: Moderate CAD >50%

C-Index 0.725 (0.683, 0.766)

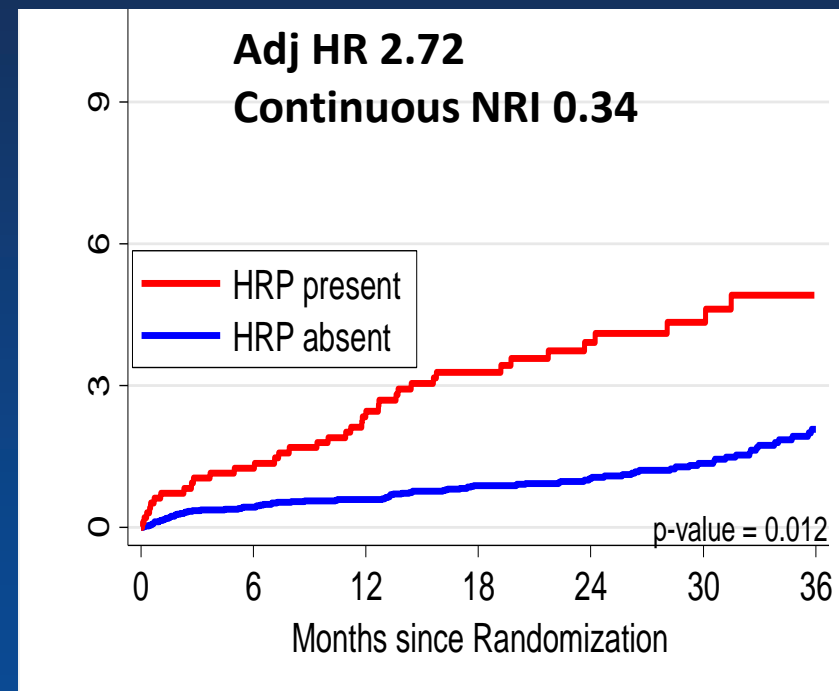


Any stress positive for ischemia

0.643 (0.593, 0.694) p=0.014

High-Risk Plaque Predicts Events in Stable CP: PROMISE Data

- Prevalence of HRP: 15.3% patients (676/4415)
 - Positive remodeling (93%)
 - Low CT attenuation (33%)
 - Napkin-ring sign (25%)
- Overall 25 mo event rate (Death, MI, UA): 3.0%
 - + HRP: 6.4% (43/676)
 - - HRP: 2.4% (88/3739)



How Does CAC Compare to Stress Testing for Diagnosis and Prognosis?

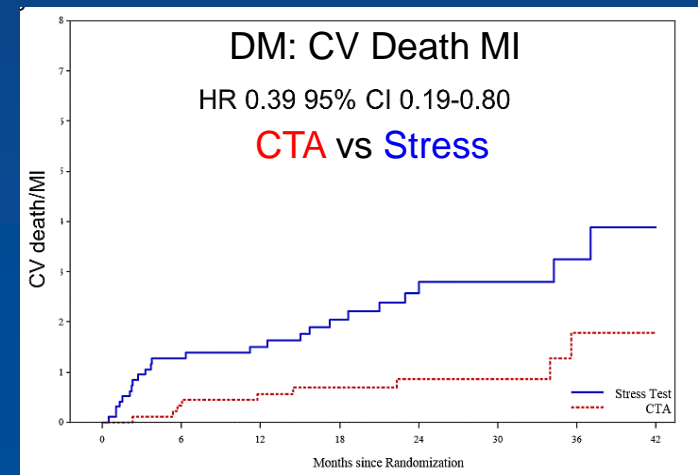
- Coronary artery calcium (CAC) is an established predictor of future cardiovascular events in asymptomatic individuals
- CAC: recommended for use as the initial diagnostic test in stable chest pain/suspected CAD but few prospective data
 - Provides surrogate data on plaque presence and severity
 - CAC vs CTA: No NTG or BB, less expensive, less radiation
- How does CAC compare to functional testing in estimating prognosis in symptomatic patients?
 - What is the predictive value of CAC for MACE ?
 - How does the prognostic ability of CAC compare to stress testing ?

Sensitivity and Specificity of CAC vs. FT for MACE

- A 'positive CAC' (any CAC > 0) was more **sensitive** than a positive FT for predicting events (84% vs. 43%, $p < 0.001$)
- Conversely, an abnormal FT was more **specific** than positive CAC for predicting events (79% vs. 35%, $p < 0.001$)
- Increasing the 'positive' CAC cut point improves specificity, at the expense of sensitivity
 - A cut point of CAC ≥ 100 increased specificity to 67%, while reducing sensitivity to 61%
 - A cut point of CAC > 400 increased specificity to 85%, while reducing sensitivity to 31% (similar test performance as stress testing)

High Risk Subgroups: Diabetes

- DM (n=2144): ↑ HTN, Hyperlipidemia, PAD, BMI vs Non DM
- DM: 38% more likely to have + test (= stress or CTA)
- DM: Worse outcomes than Non DM
 - Death/MI/UA: aHR 1.57 (1.18 - 2.09)
 - CV death/MI: aHR 1.54 (1.02 - 2.32)
- DM: Better outcomes with CTA vs Stress
 - Death/MI/UA: aHR 0.72 (0.46-1.15)
 - CV death/MI: aHR 0.37 (0.18 - 0.77)
- Non DM: Similar outcomes of CTA vs stress



Summary:

Emerging Evidence for the Role of CTA

- More improvement in preventive care
- No better than stress for lowest risk pts: Defer testing?
- Improves use of invasive testing, esp with FFRCT and HRP analyses; Unknown impact on revascularization/events
- CTA and CAC are more sensitive / less specific for plaque
- Both CTA and CAC provide better prognostic data in non obstructive CAD, but similar data in obstructive CAD
- Improves outcomes in diabetics, a high risk group

Have These Trials Changed Guidelines?

New UK NICE GLs Strongly Favor CTA, FFR_{CT}

- Final Guideline (Nov 2016): Chest Pain (CG95)
 - CTA more cost-effective than SPECT in diagnosing CAD over the range of pre-test probability of CAD (10-70%)
 - Recommendations for initial testing
 - Typical angina without known CAD: CTA
 - Prior history of CAD: Functional testing with imaging
 - Pretest probability of CAD $\geq 70\%$: Invasive catheterization
- Final Tech Assessment (Feb 2017): HeartFlow Technology for FFR_{CT}
 - Safe, accurate option for stable CP pts w 10% to 90% risk of CAD
 - Use of HeartFlow FFR_{CT} may lead to cost savings of £214 per patient (\$262), or > £9.1 million (\$11.1M) annually across the NHS

<https://www.nice.org.uk/guidance/cg95>

<https://www.nice.org.uk/guidance/mtg32/chapter/1-Recommendations>

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- Hypothesis circa 2018: **Precision Testing**

2018 and Beyond: Precision Diagnostic Testing

- **Precision Diagnostic Testing:** Selective use of different test modalities as determined by individual patient risk, clinical goals, test info provided
 - CTA and stress testing are both useful but provide different data and address different questions
 - Use growing evidence to tailor diagnostic strategies to individual patient needs
- *Stay tuned for further refinement.....*

THANK YOU