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Non-Invasive Imaging: Risk Assessment

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Module 2
Non-Invasive Imaging Evaluation of the Symptomatic Patient

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Talk Outline

1. List of available non-invasive cardiac imaging modalities
2. Results from clinical trials
   - PROMISE
   - SCOT-HEART
   - ISCHEMIA
3. European Society of Cardiology Guidelines
4. New ACC/AHA Chest Pain Guideline

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Available Non-Invasive Cardiac Imaging Modalities

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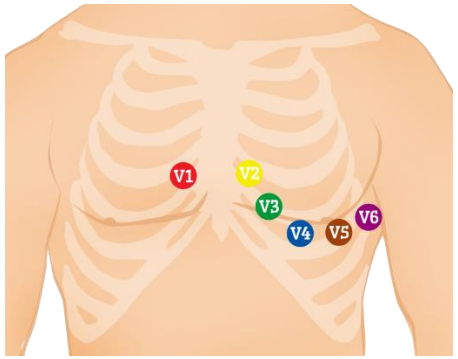
Definition of “Stable Chest Pain”

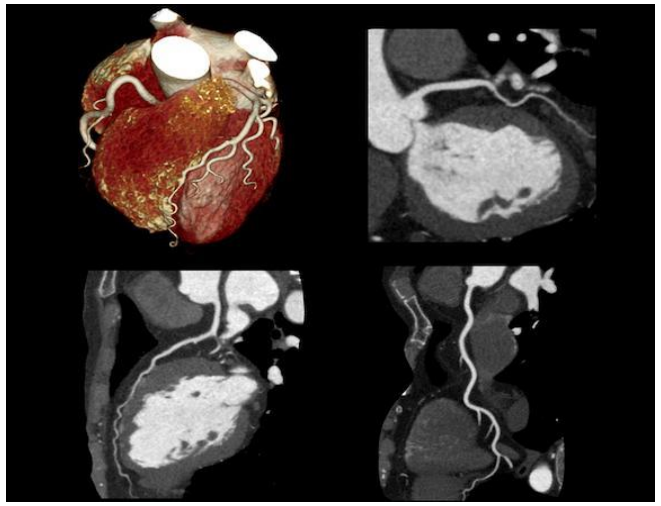
- All chest pain that is not an acute coronary syndrome
- Chest pain should be considered stable when symptoms are chronic and associated with consistent precipitants such as exertion or emotional stress.
- This includes EKG-negative, cardiac enzyme-negative chest pain presenting in emergency settings



12-lead EKG

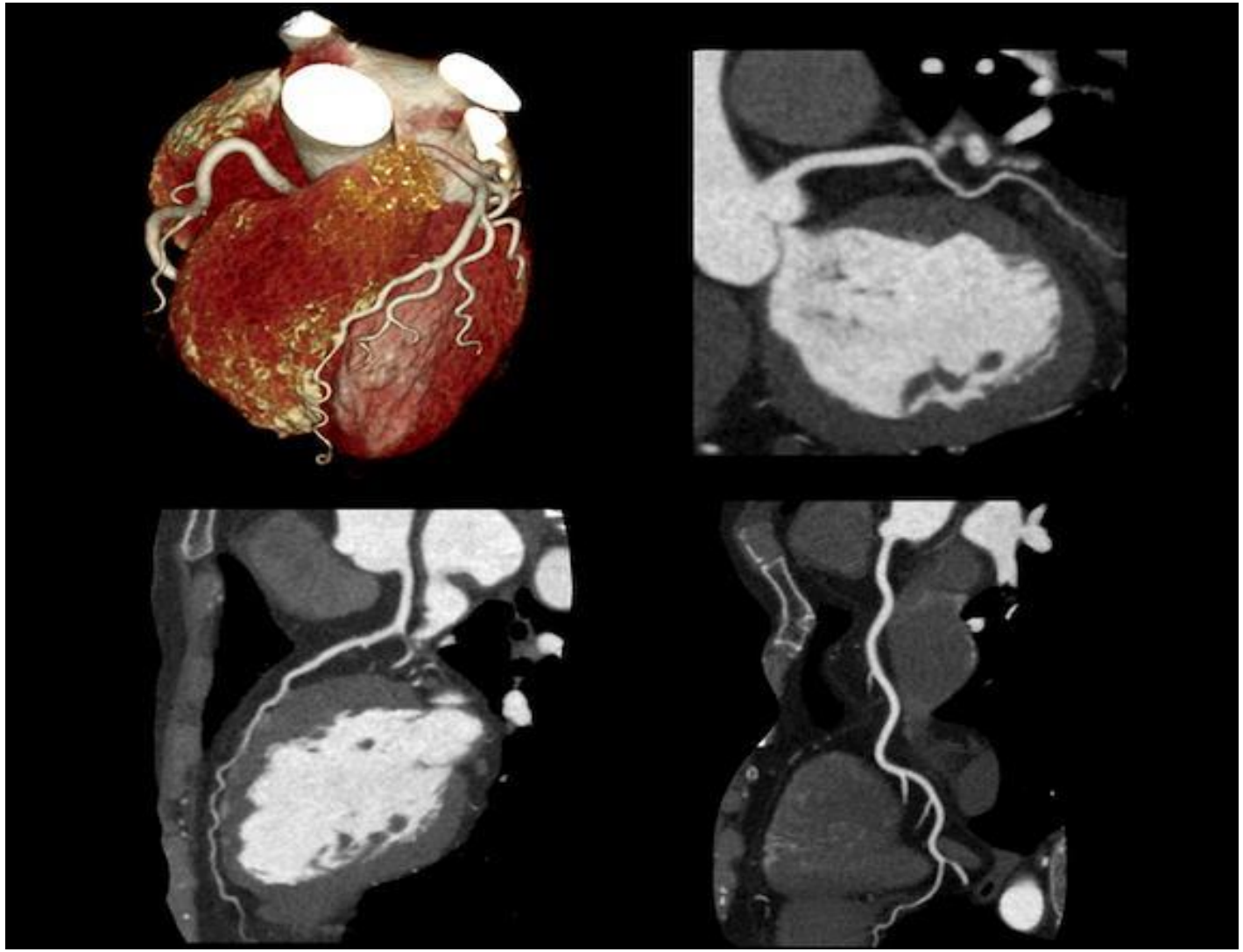
- Cheap, rapid, non-invasive assessment of electrical signature of the heart
- Most useful in **symptomatic** patients for assessing acute coronary injury/ischemia and arrhythmia
- *Limited value in asymptomatic patients – not recommended for use in everyday cardiometabolic practice*
- *No clear role in routine risk assessment in primary prevention; only left ventricular hypertrophy has independent prognostic value*
- Pros: fast, cheap, can be diagnostic of myocardial injury, useful as a one-time baseline measure
- Cons: many findings non-specific, no role in routine primary prevention

General Categories of Chest Pain Evaluations/Tests

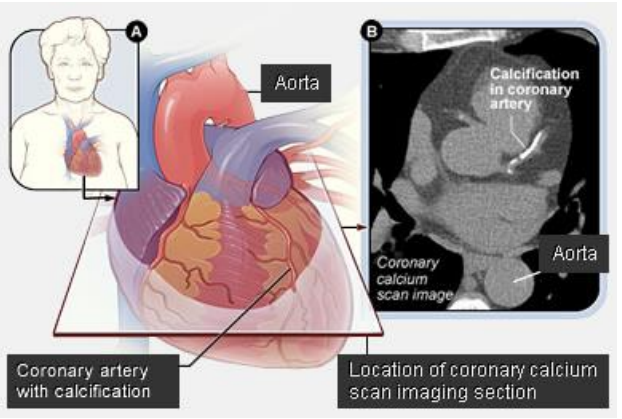


- **Anatomical Approach**
  - Assessment of the coronary arteries, assessment of coronary plaque
- **Functional Approach**
  - Assessment for signs/symptoms of ischemia (lack of blood flow to myocardium)

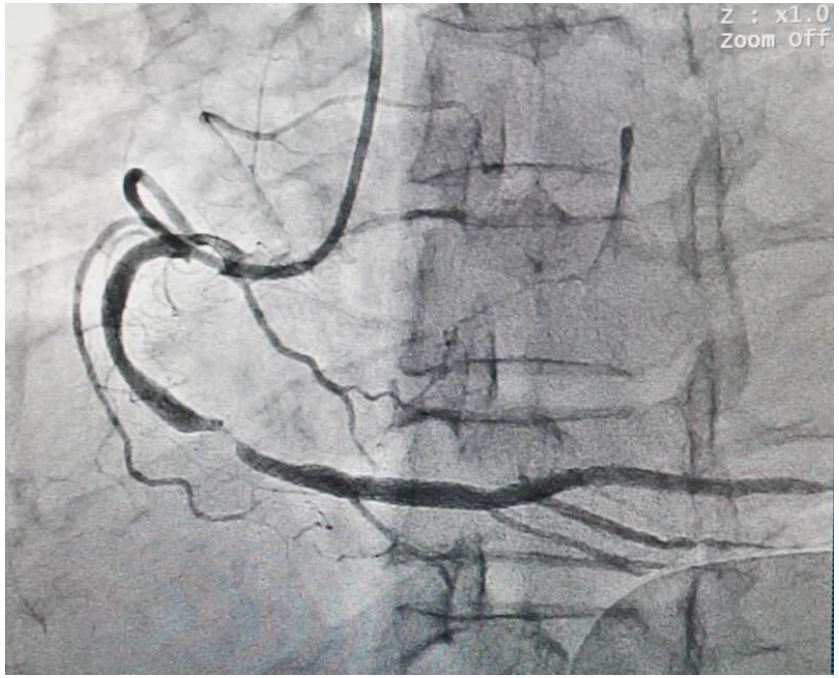
Anatomic Assessment of the Coronary Arteries



Coronary CT (cardiac-gated, dedicated heart CT)



- Can be non-contrast or with IV contrast
- Non-contrast: **Coronary Calcium Score** (evaluate for atherosclerosis burden in coronaries, aortic valve, and aorta)
- Contrast: **Coronary CTA** (mimics invasive angiography, + can reveal early plaque & specific plaque phenotypes)
- Pros: fast, amazing pictures, very high NPV
- Cons: need heart rate control, contrast, can be limited by severe coronary calcification

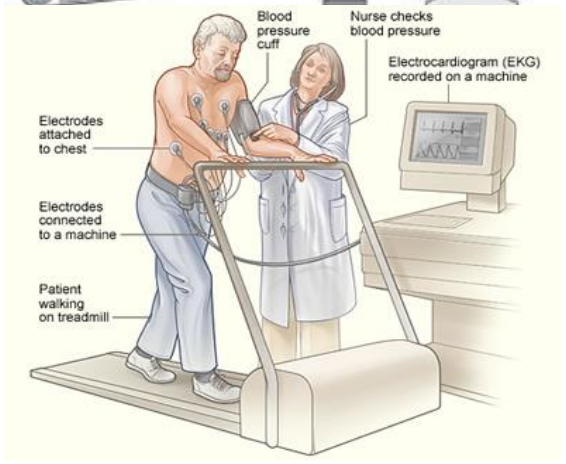


Invasive Coronary Angiography ("cardiac catheterization")

- Gold standard for assessing lumen stenosis
- Can intervene on critical coronary lesions after initial diagnostic procedure
- Complication rate is usually less than 1% and the risk of mortality of 0.05% for diagnostic cardiac cath.
- Pros: definitive assessment of obstructive coronary artery disease
- Cons: Invasive, expensive, cannot see early plaque or plaque phenotypes

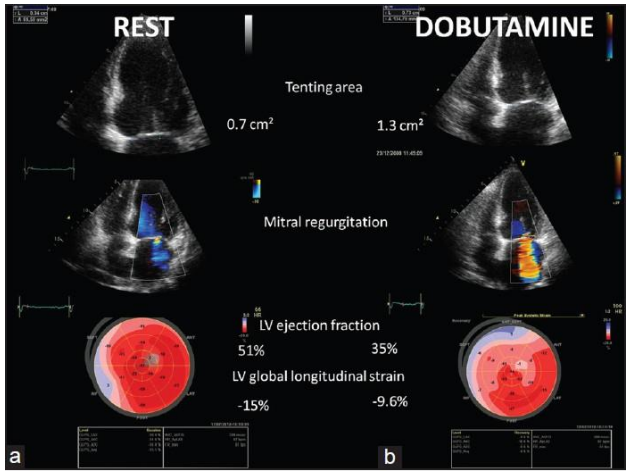
Functional Assessment of the Coronary Arteries

Stress EKG ("Treadmill stress test")



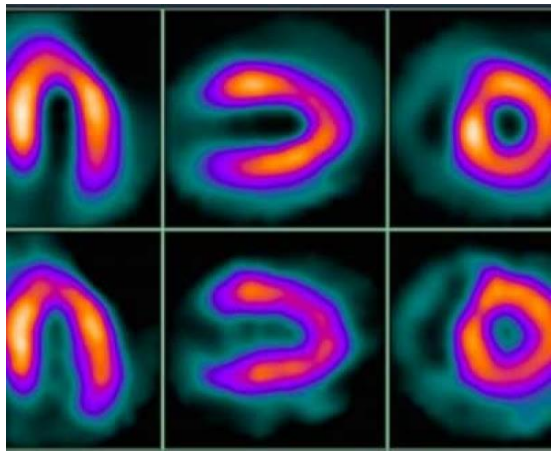
- Bruce or modified Bruce protocol
- Real-time assessment for ischemic EKG changes
- Also provides on data on patient's functional capacity
- Pros: simple, cheap, mimics "real-world" exercise
- Cons: Not always easy to interpret, limited by baseline EKG changes, not available to those who can't exercise, fairly high false positive rate □ layered testing, sensitivity also low

Stress ECHO ("Treadmill or Dobutamine stress test")



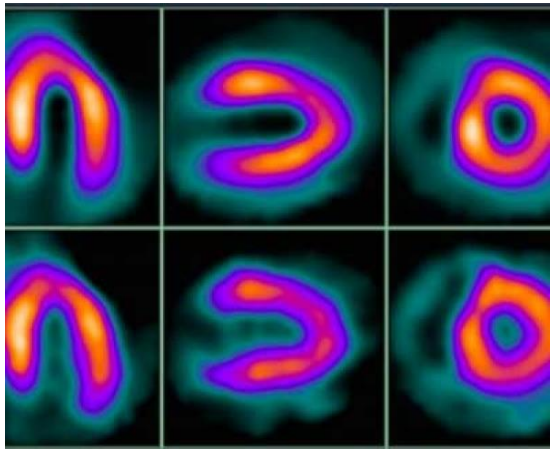
- Exercise or pharmacologically-induced (positive inotrope/chronotrope) stress
- Looks for stress-induced wall motion abnormalities
- **Late** assessment of the ischemic cascade
- Pros: treadmill □ functional capacity, less need for special equipment, **high specificity**, good yield for left main/proximal LAD disease ("critical anatomy")
- Cons: limited by baseline wall motion abnormalities, **limited sensitivity**, almost always negative

SPECT Imaging
(single nuclide emission computed tomography)
("Nuclear stress test")



- Exercise or pharmacologically-induced (mostly vasodilator, regadenason) stress
- Looks for regional differences in **perfusion**
- **Early** assessment of the ischemic cascade
- Pros: treadmill functional capacity, **higher sensitivity**, much better for ischemia **localization**
- Cons: ++ radiation, + cost, limited by obesity and GI uptake of tracer, can miss "balanced ischemia", **limited sensitivity** many false positives

PET Imaging ("PET stress test")



- Pharmacologically-induced (mostly vasodilator, regadenason) stress
- Can **quantify** myocardial blood flow
- Can be combined with viability testing
- Pros: will not miss balanced ischemia, much less sensitive to body habitus, more consistent imaging
- Cons: + radiation, +++ cost, limited by availability of tracer, unavailable in small hospitals

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Clinical Trial Results

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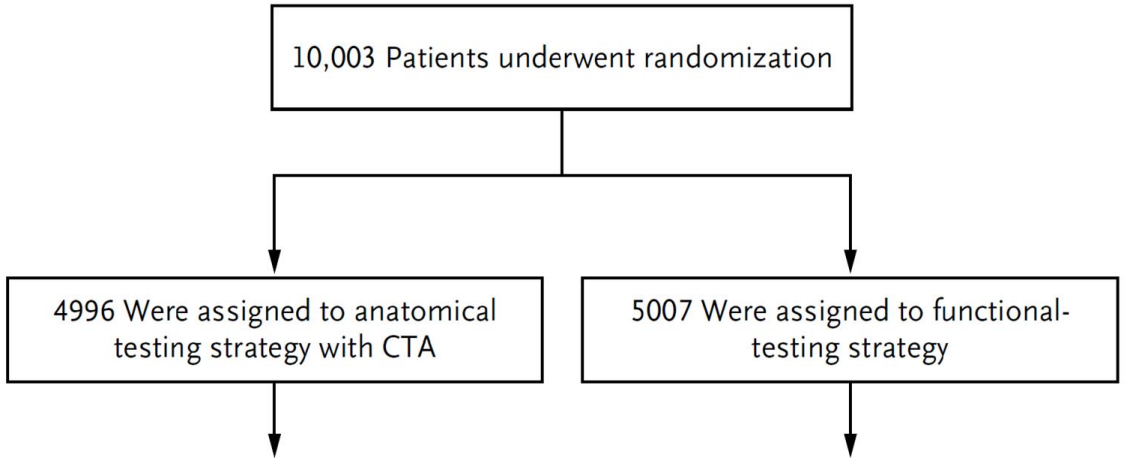
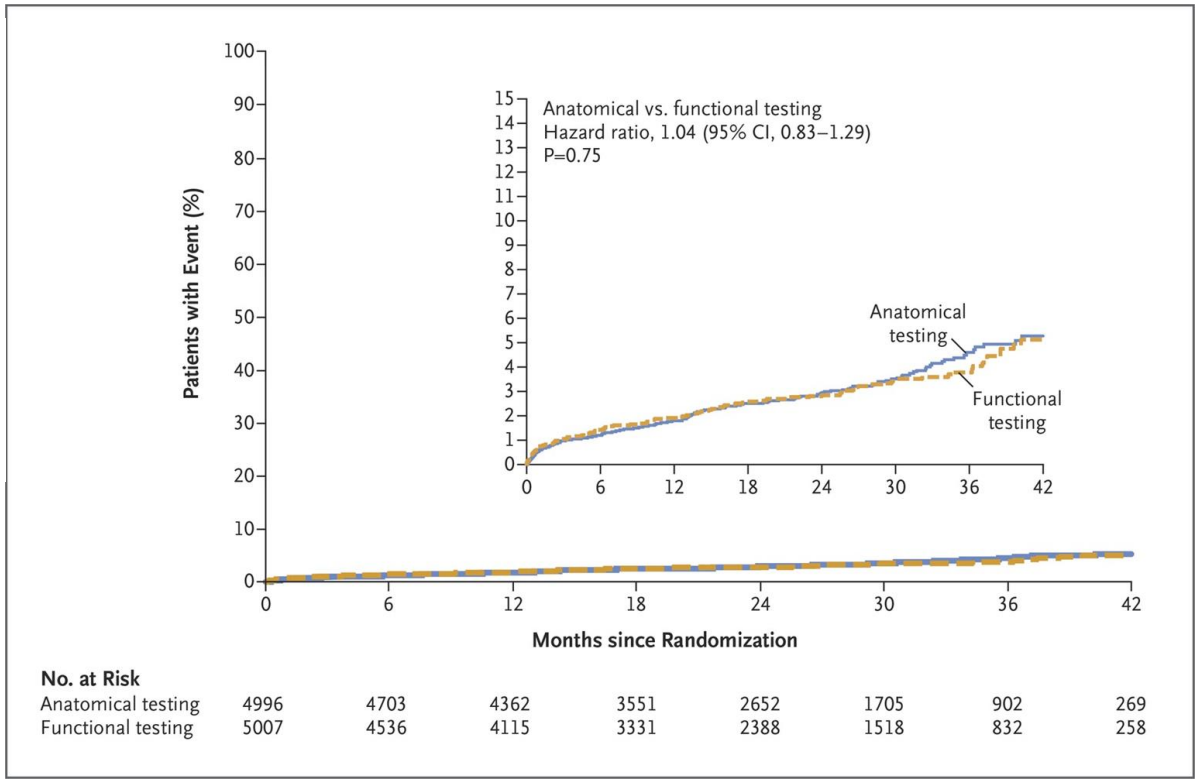
CLINICAL
TRIAL

PROMISE Trial
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., et al., for the PROMISE Investigators





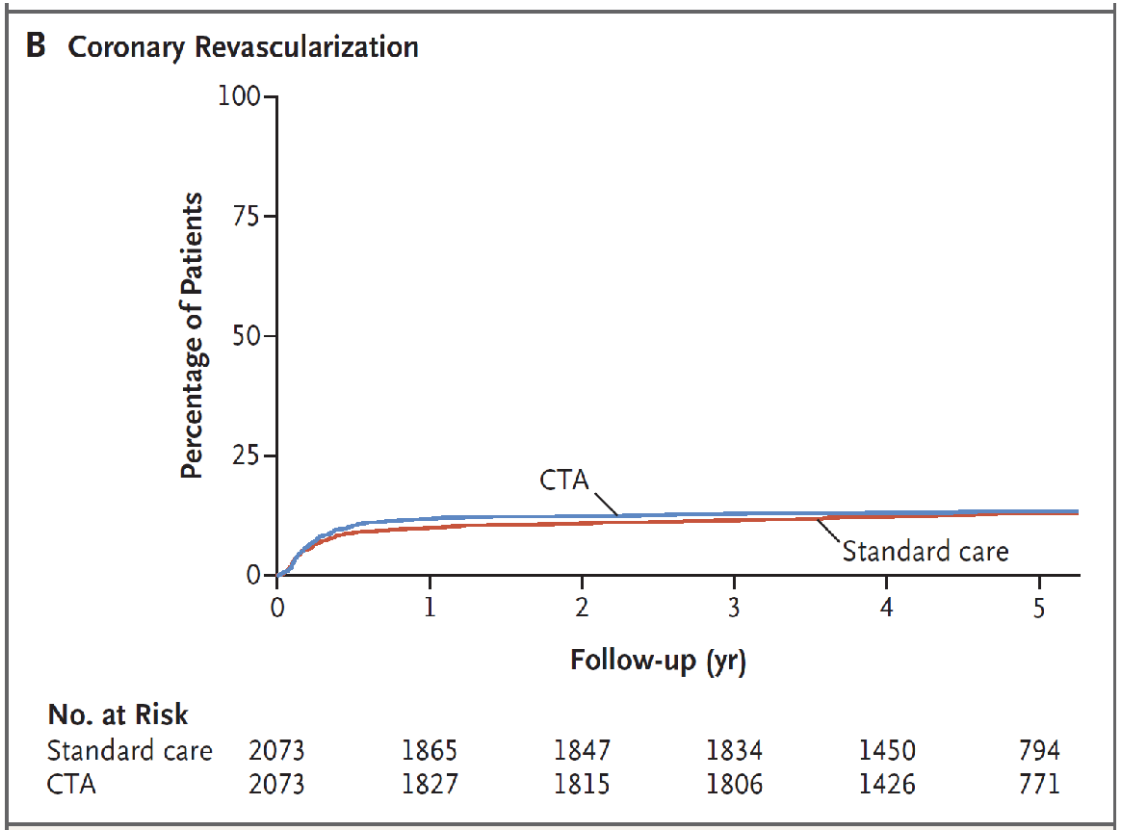
Douglas et al, *NEJM* 2015

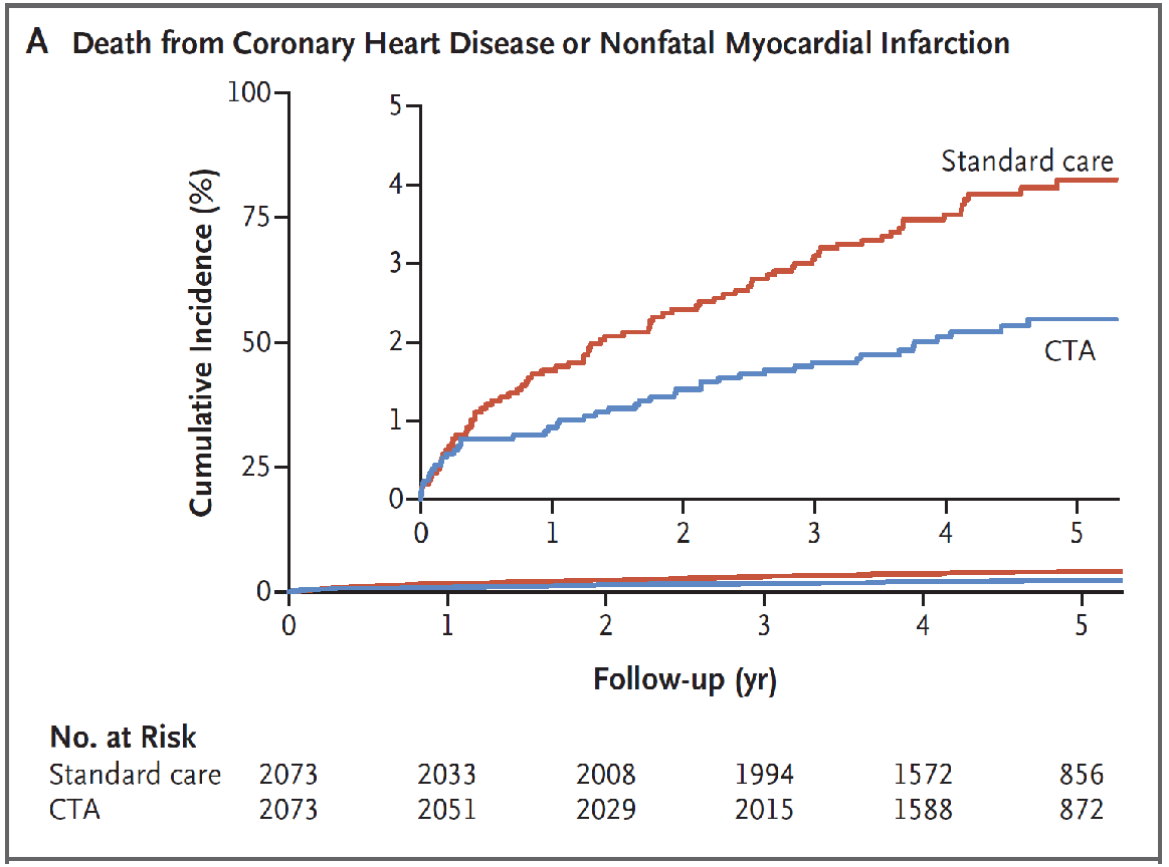
SCOT-HEART Trial

Coronary CT Angiography and 5-year Risk of Myocardial Infarction

The SCOT-HEART Investigators

In an open-label, multicenter, parallel-group trial, we randomly assigned 4146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2073 patients) or to standard care alone(2073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow-up.





SCOT-Heart Investigators, *NEJM* 2018

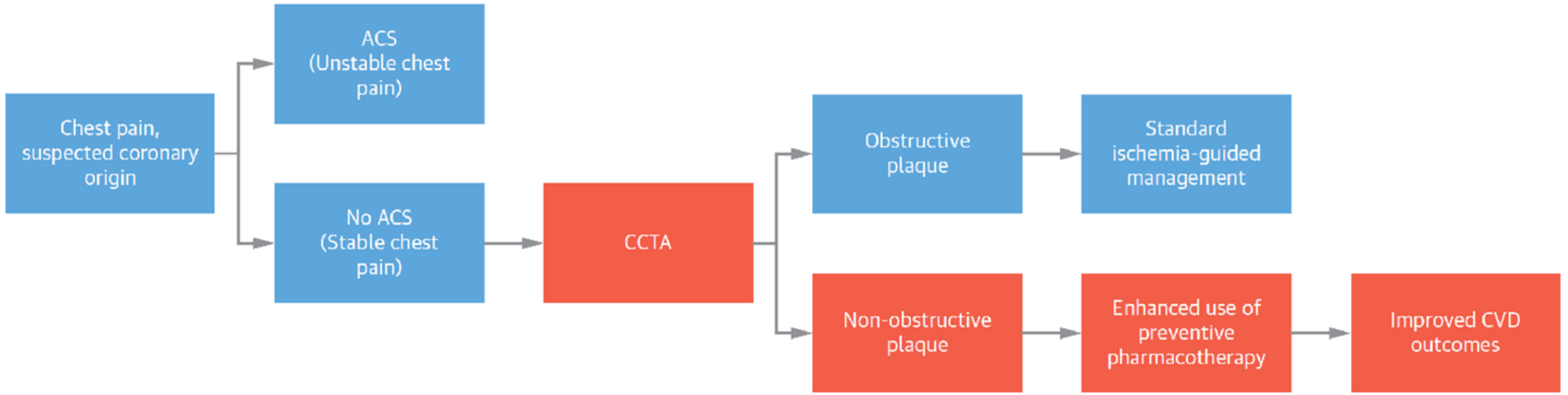
Editorial Comment

Coronary CT Angiography in New-Onset Stable Chest Pain

Time for U.S. Guidelines to be NICEr

Michael J. Blaha, MD, MPH; Miguel Cainzos-Achirica, MD, MPH

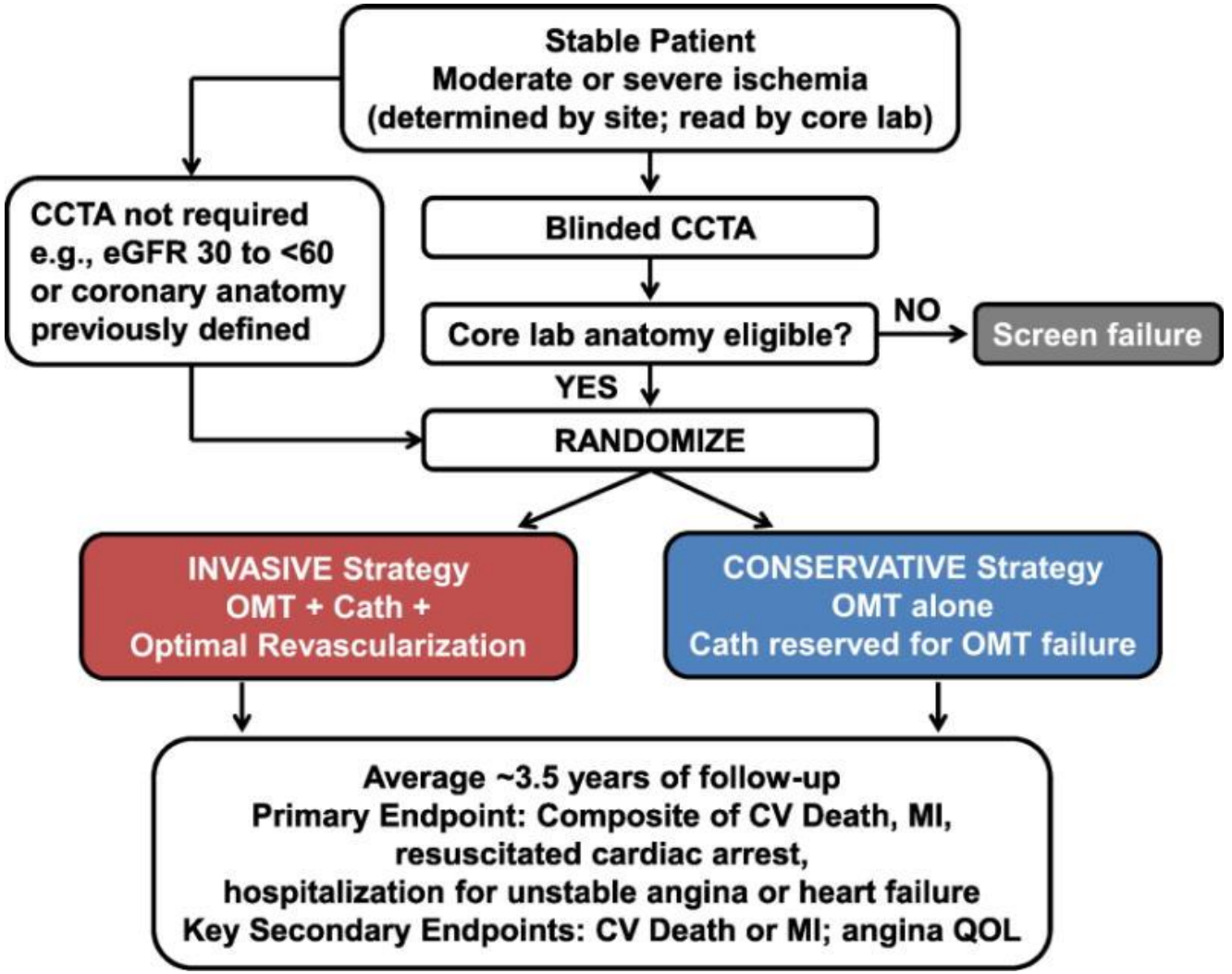
FIGURE 1 Framework for Improving Outcomes in New-Onset, Stable (i.e., Nonacute Coronary Syndrome) Chest Pain of Suspected Coronary Origin



ACS = acute coronary syndrome; CCTA = coronary computed tomographic angiography; CVD = cardiovascular disease.

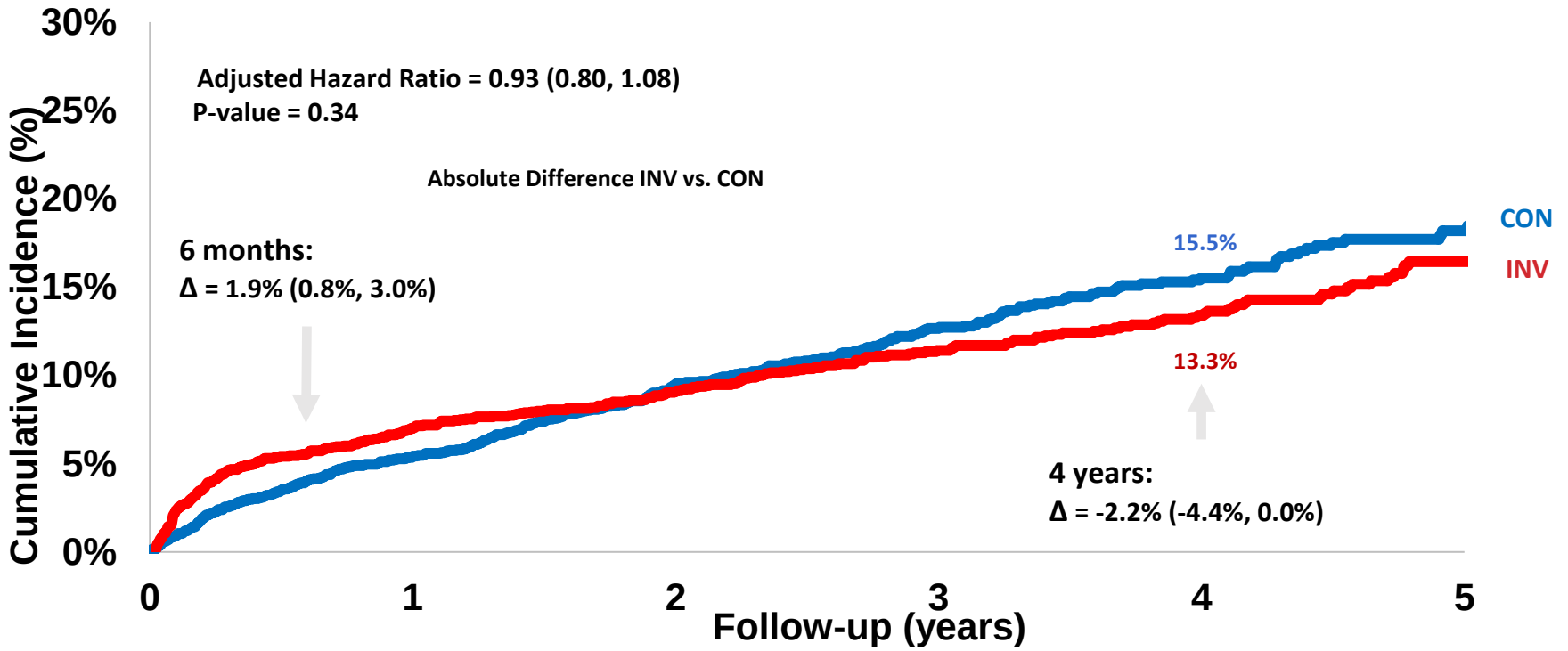
Blaha and Cainzos-Achirica, *JACC* 2019

ISCHEMIA Trial: Design



Maron et al, *American Heart Journal* 2018

Primary Outcome: CV Death, MI, hospitalization for UA, HF or resuscitated cardiac arrest

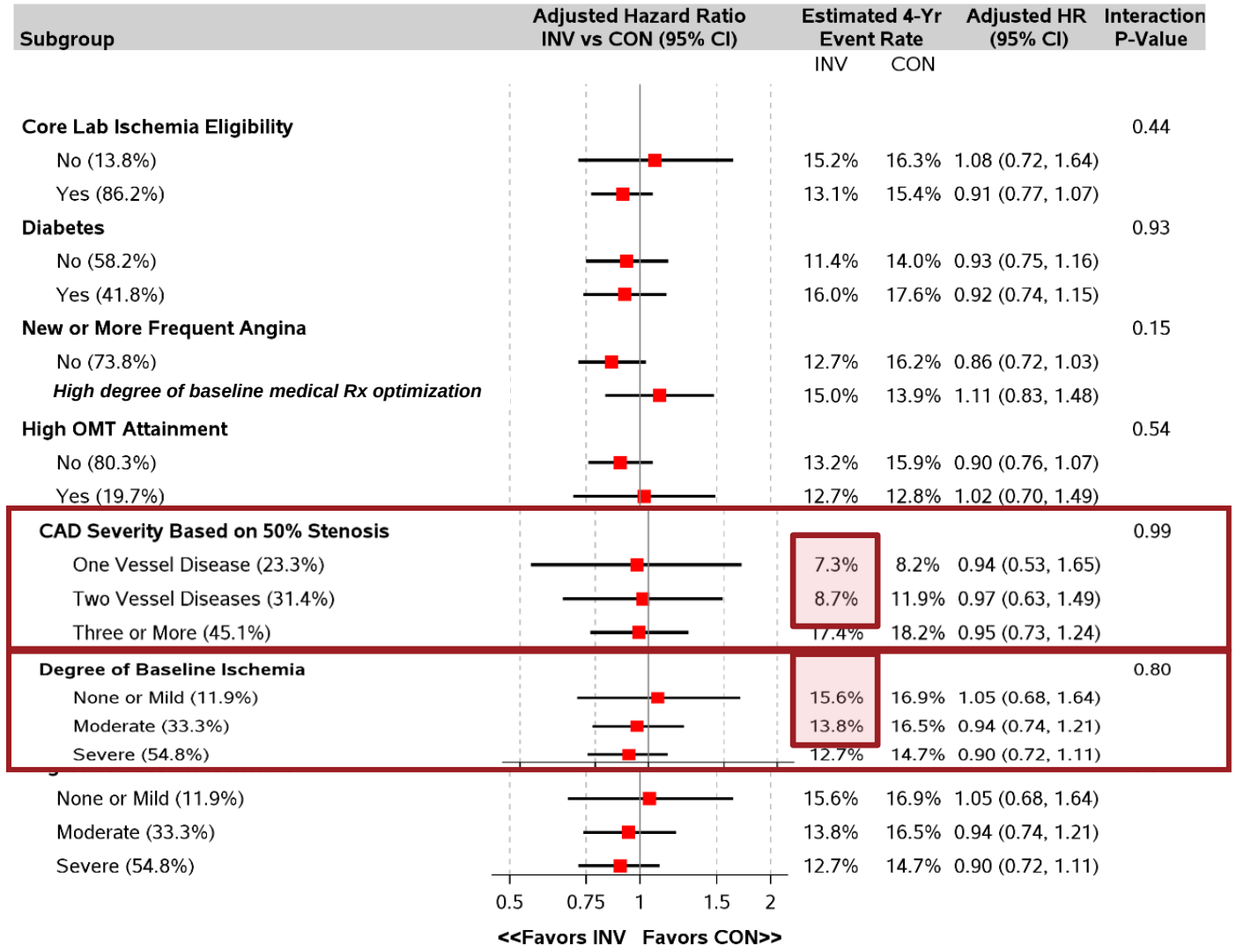


Subjects at Risk

CON	2591	2431	1907	1300	733	293
INV	2588	2364	1908	1291	730	271

Maron et al, *NEJM* 2020

Primary Endpoint
Pre-Specified Important Subgroups
There was no heterogeneity of treatment effect



Maron et al, *NEJM* 2020

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Guidelines

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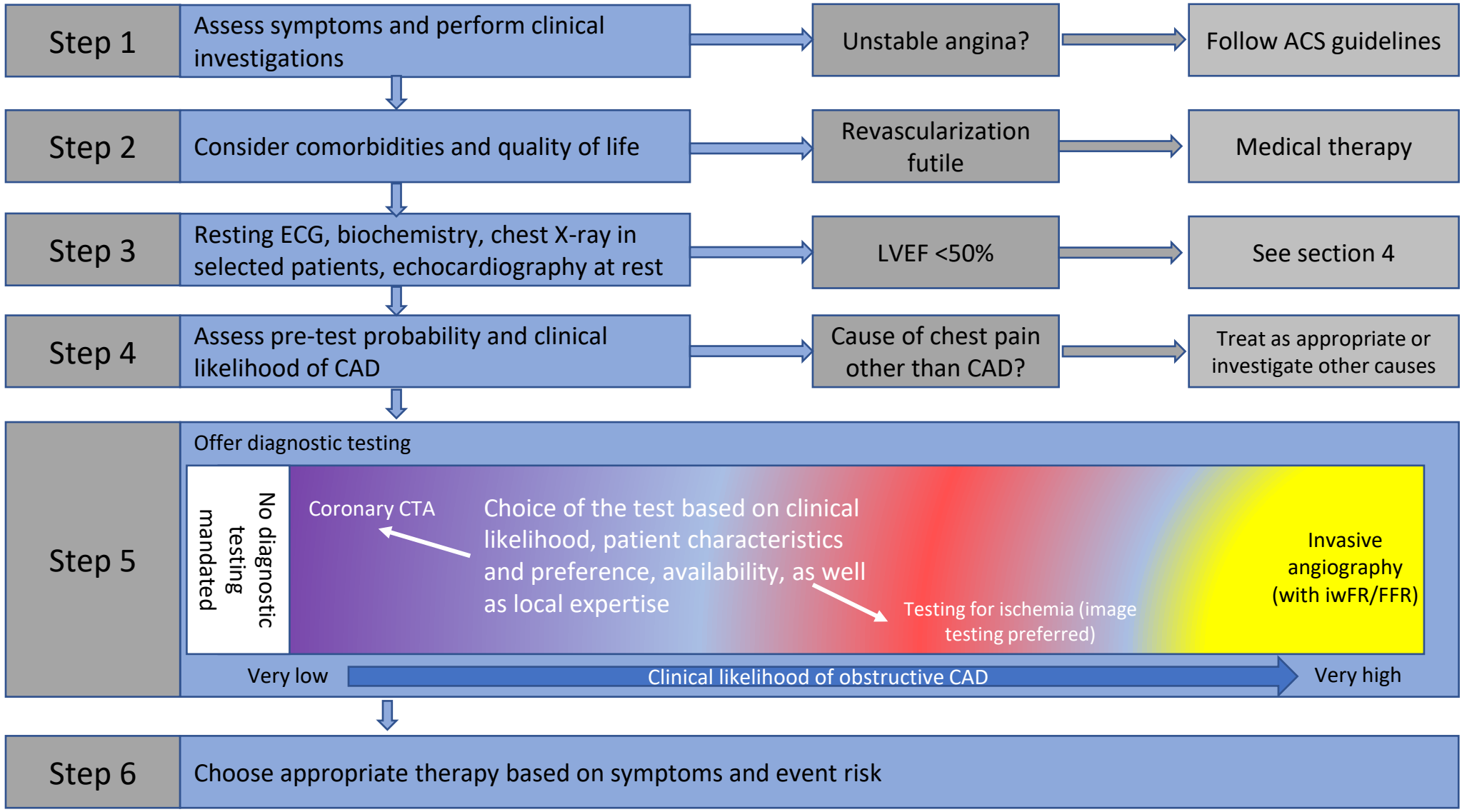
European Society of Cardiology 2019 Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes

Knuuti et al, *European Heart Journal* 2020

Approach For the Initial Diagnostic Management of Patients with Angina and Suspected Coronary Artery Disease



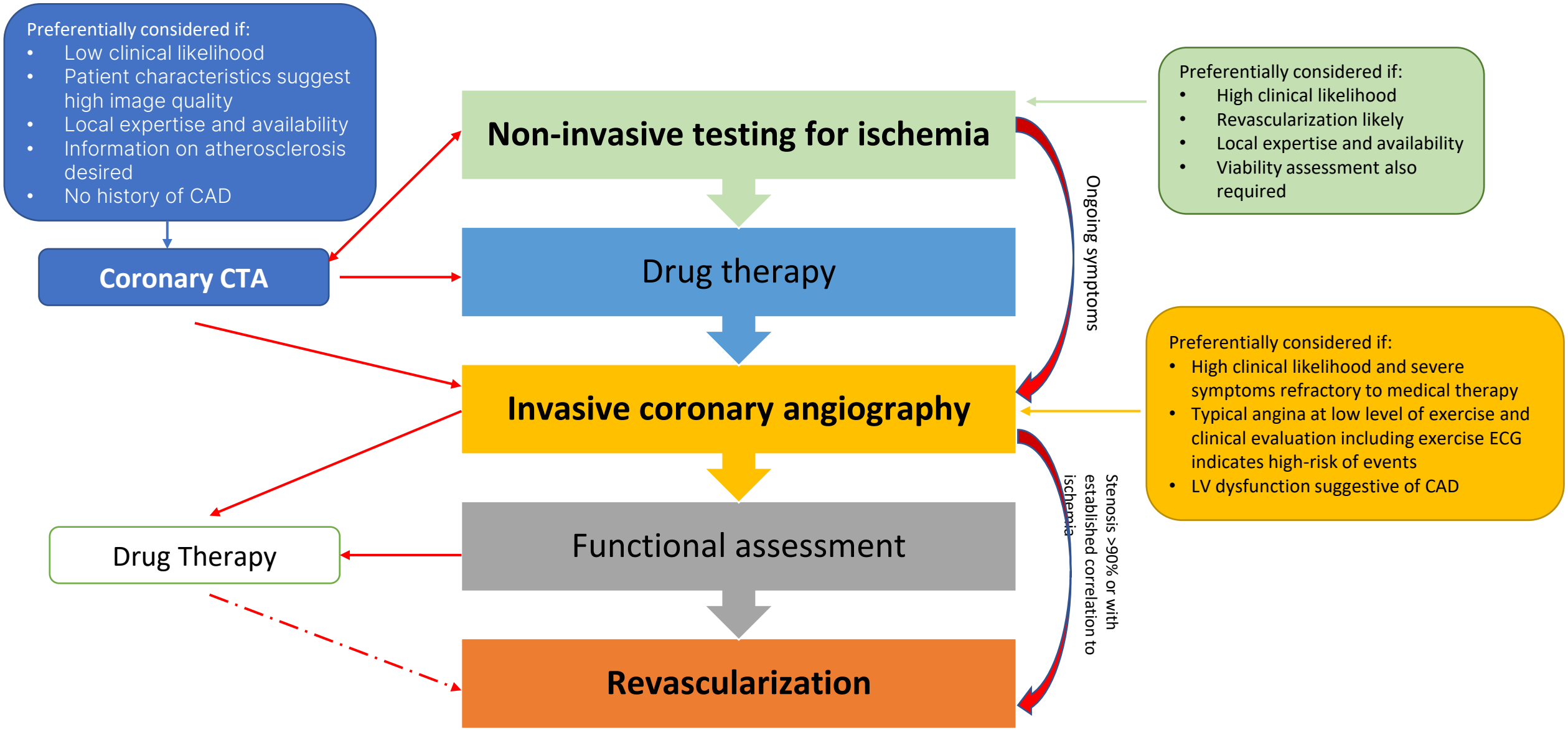
Adapted from Knuuti et al, *European Heart Journal* 2020

New Testing Recommendations

New Major Recommendations in 2019	
Basic testing, diagnostics, and risk assessment	
Non-invasive functional imaging for myocardial ischemia or coronary CTA is recommended as the initial test for diagnosing CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.	I
It is recommended that selection of the initial non-invasive diagnostic test be based on the clinical likelihood of CAD and other patient characteristics that influence test performance, local expertise, and the availability of tests.	I
Functional imaging for myocardial ischemia is recommended if coronary CTA has shown CAD of uncertain functional significance or is not diagnostic.	I
Invasive angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood and severe symptoms refractory to medical therapy, or typical angina at a low level of exercise and clinical evaluation that indicates high event risk. Invasive functional assessment must be available and used to evaluate stenoses before revascularization, unless very high grade (>90% diameter stenosis).	I
Invasive coronary angiography with the availability of invasive functional evaluation should be considered for confirmation of the diagnosis of CAD in patients with an uncertain diagnosis on non-invasive testing.	IIa
Coronary CTA should be considered as an alternative to invasive angiography if another non-invasive test is equivocal or non-diagnostic.	IIa
Coronary CTA is not recommended when extensive coronary calcification, irregular heart rate, significant obesity, inability to cooperate with breath-hold commands, or any other conditions make good image quality unlikely.	III

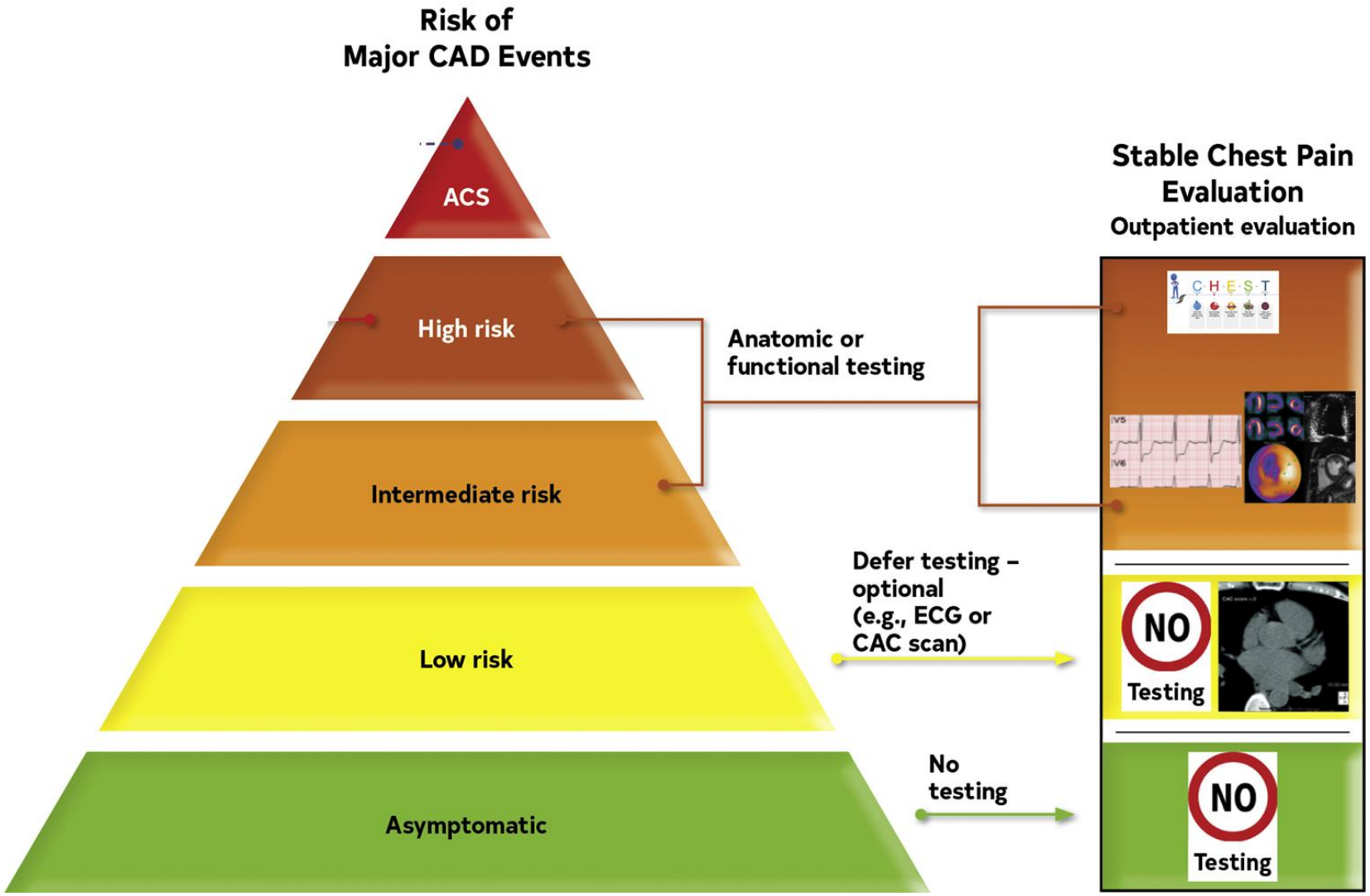
Adapted from Knuuti et al, *European Heart Journal* 2020

Main Diagnostic Pathways in Symptomatic Patients with Suspected Obstructive CAD



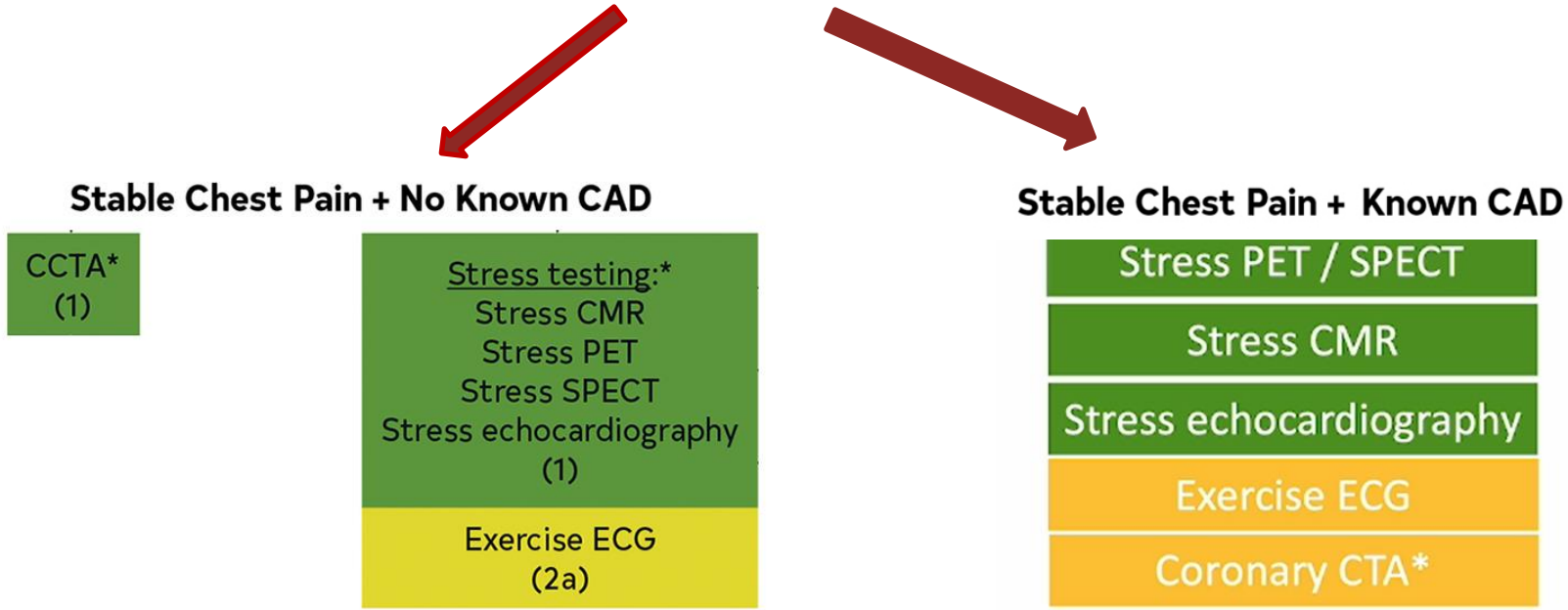
Adapted from Knuuti et al, *European Heart Journal* 2020

New ACC/AHA 2021 Chest Pain Guidelines



Gulati et al, *Circulation* 2021

Stable Chest Pain: Testing Options

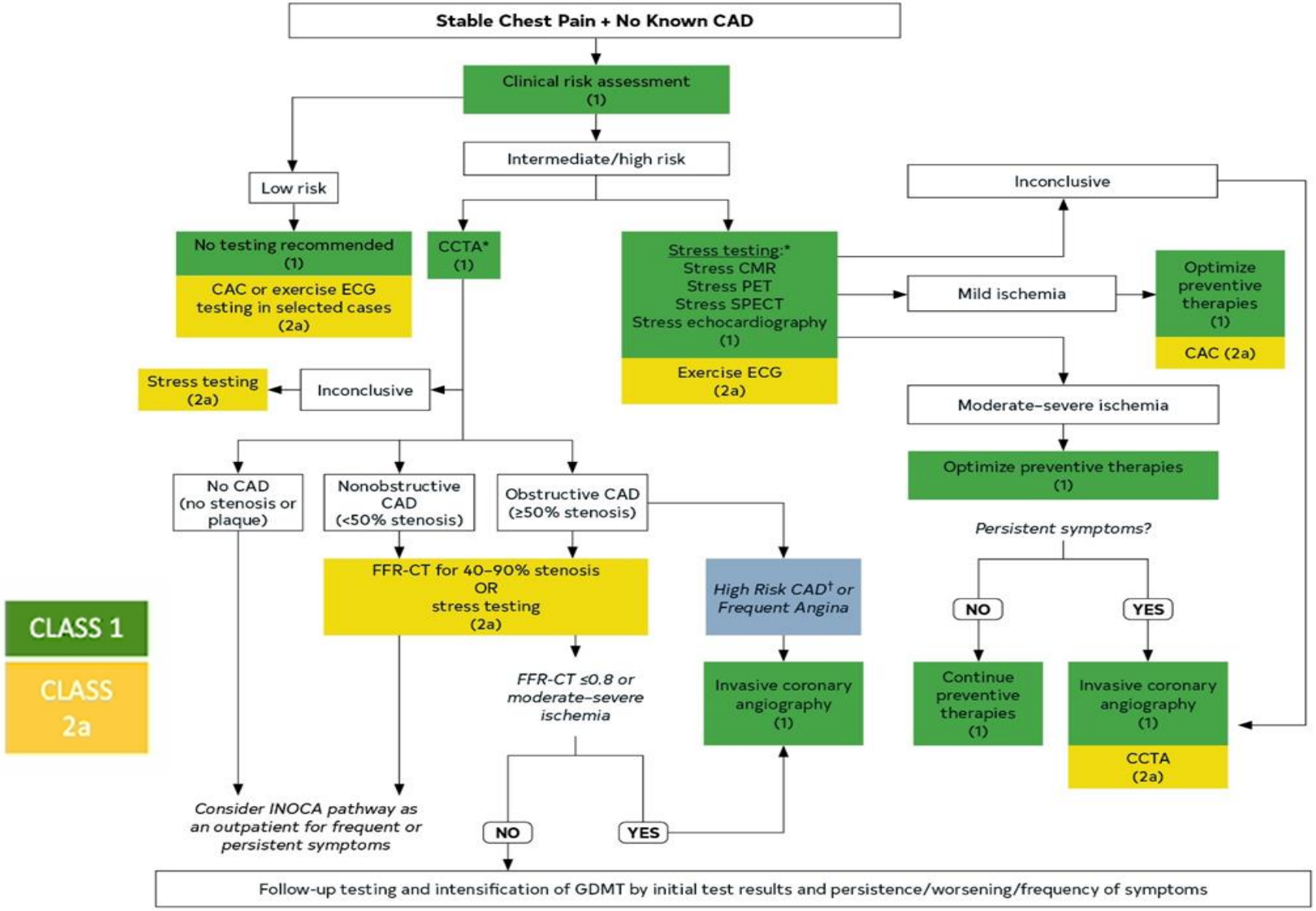


CLASS 1

CLASS 2a

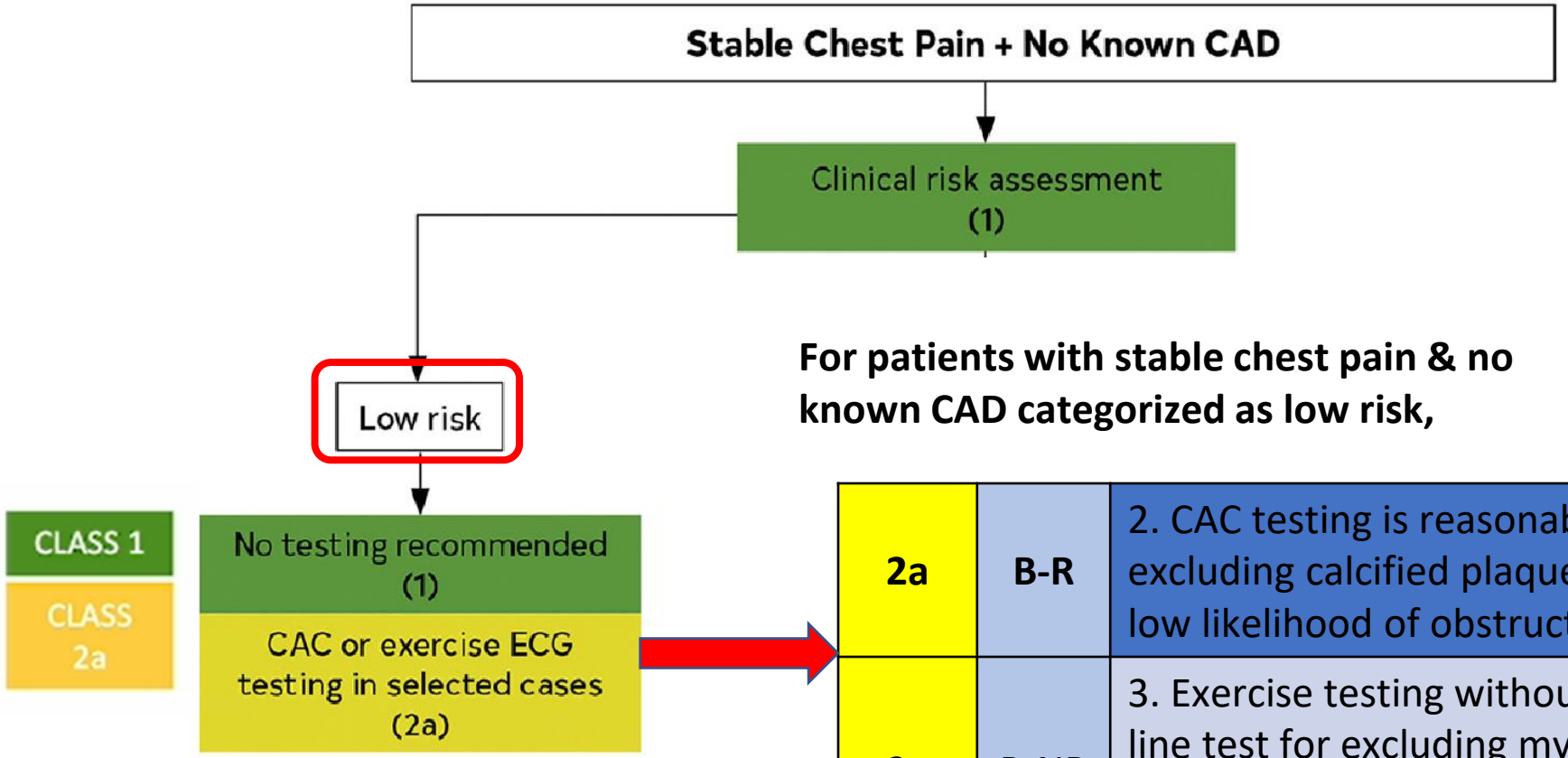
Gulati et al, *Circulation* 2021

Clinical Decision Pathway for Patients with Stable Chest Pain and No Known CAD



Gulati et al, *Circulation* 2021

Clinical Decision Pathway for Patients with Stable Chest Pain and No Known CAD

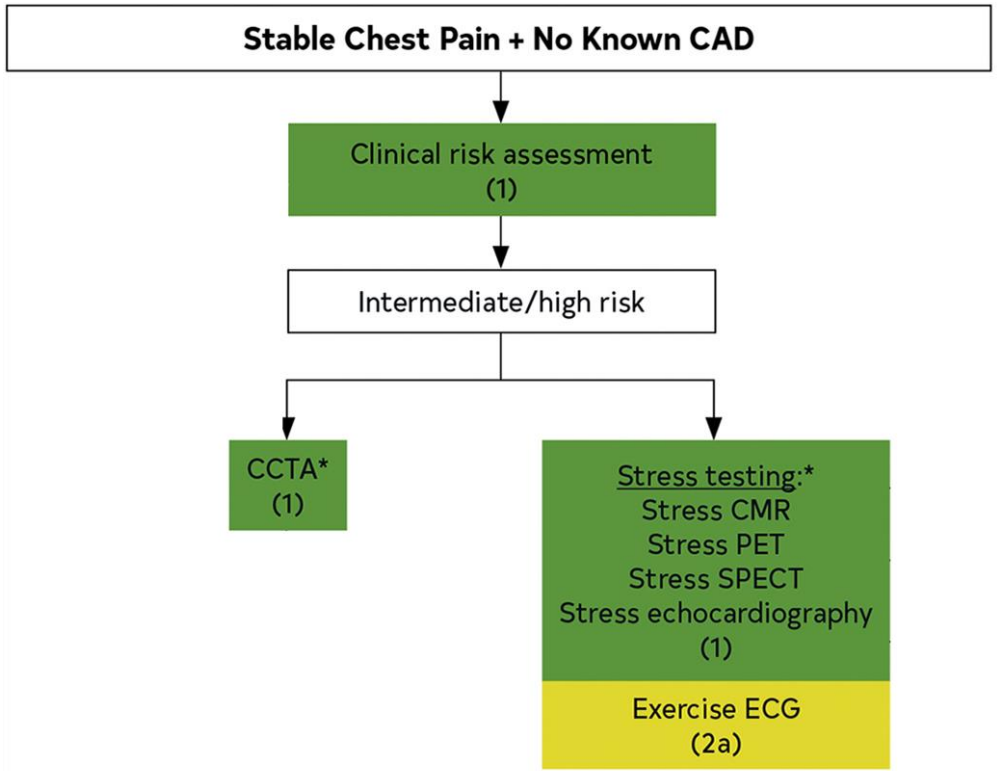


For patients with stable chest pain & no known CAD categorized as low risk,

2a	**B-R**	2. CAC testing is reasonable as a first-line test for excluding calcified plaque and identifying patients with a low likelihood of obstructive CAD.
2a	B-NR	3. Exercise testing without imaging is reasonable as a first-line test for excluding myocardial ischemia and determining functional capacity in patients with an interpretable ECG.

Gulati et al, *Circulation* 2021

Favors use of CCTA
• Rule out obstructive CAD • Detect Nonobstructive CAD
• High quality imaging and exert interpretation routinely available
• Age <65
• Prior functional study inconclusive
• Anomalous coronary arteries • Require evaluation of aorta or pulmonary arteries



Favors use of stress imaging
• Ischemia guided management
• High quality imaging and expert interpretation routinely available
• Age ≥65
• Prior CCTA inconclusive
• Suspect scar (especially if PET or stress CMR available) • Suspect coronary microvascular dysfunction (when PET or CMR available)

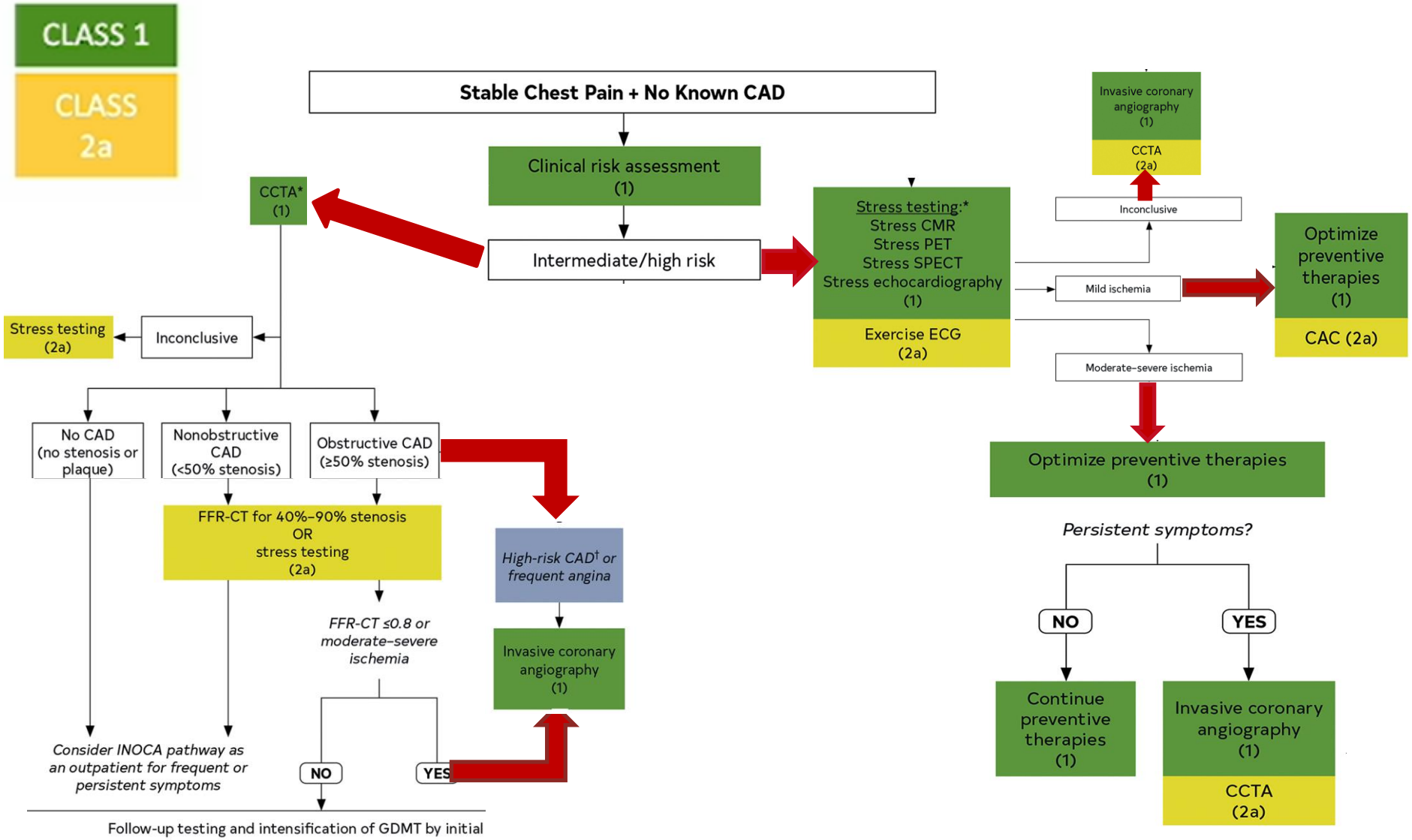
CLASS 1

CLASS 2a

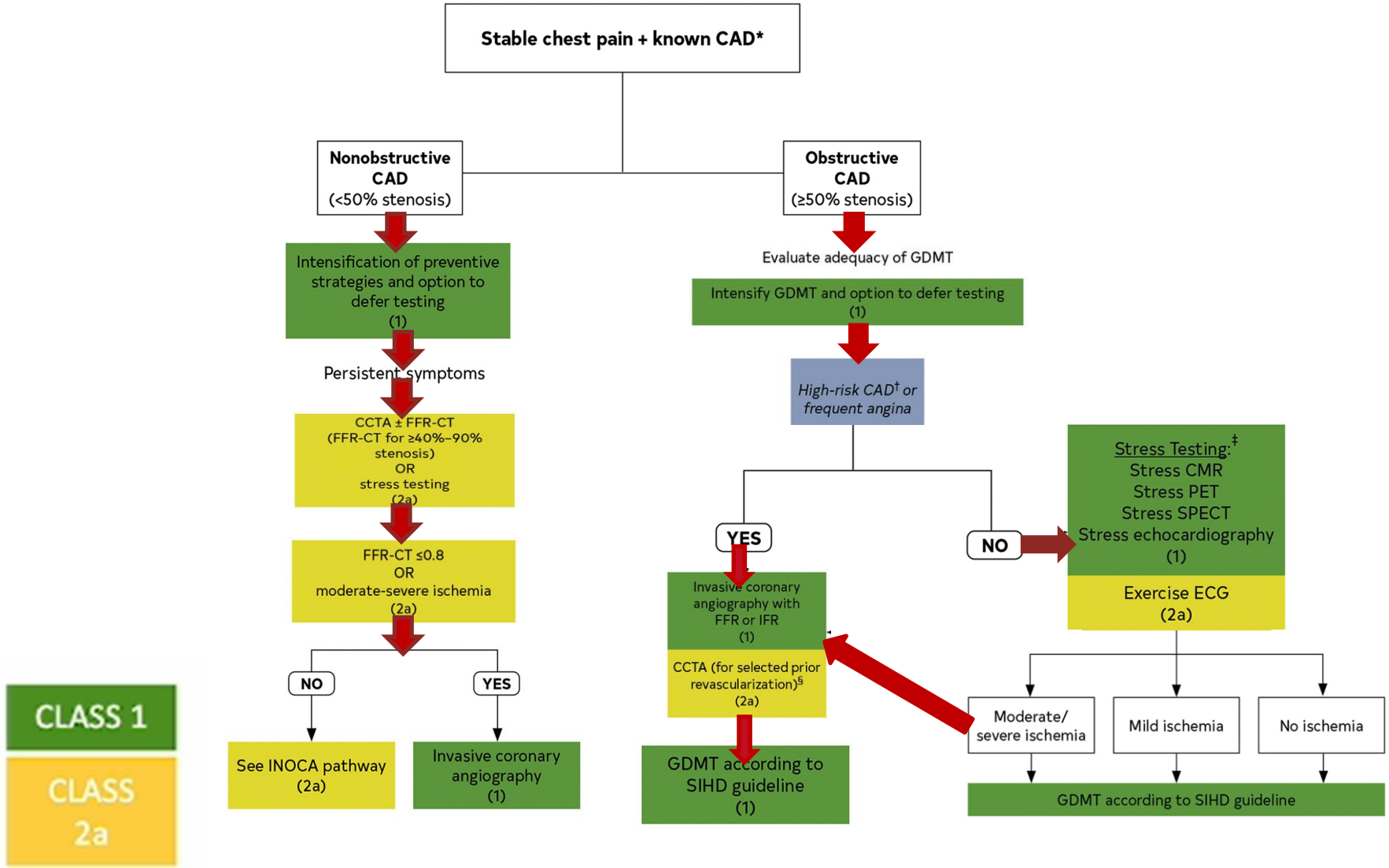
TABLE 7 Warranty Period for Prior Cardiac Testing

Test Modality	Result	Warranty Period
Anatomic	Normal coronary angiogram CCTA with no stenosis or plaque	2 y
Stress testing	Normal stress test (given adequate stress)	1 y

Gulati et al, *Circulation* 2021

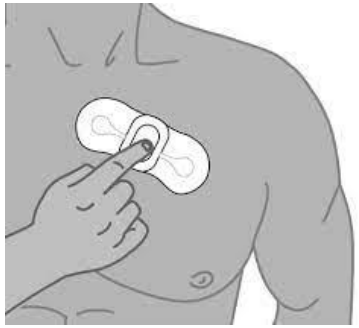


Gulati et al, *Circulation* 2021



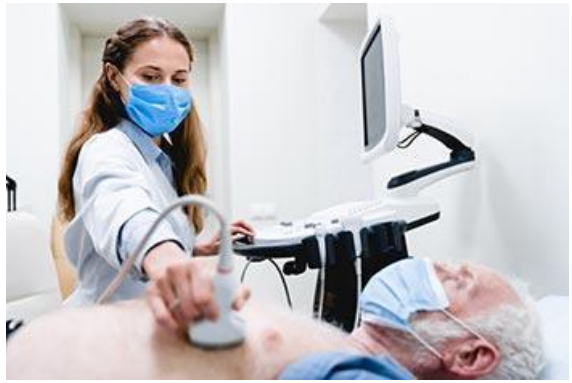
Gulati et al, *Circulation* 2021

Further non-invasive imaging evaluation for symptomatic patients found to have no coronary artery disease



Ambulatory EKG Monitoring

- Allows assessment for rhythm disorders in the “normal” everyday ambulatory home setting
- Coupled with symptom diary, can correlate symptoms with rhythm
- Can quantify PAC/PVC burden, time in atrial fibrillation
- Use in **symptomatic** patients with suspected intermittent arrhythmia
- No role in routine primary prevention – ectopy is not independently associated with cardiovascular risk
- Nowadays, can be done using a wireless patch inconspicuously placed on skin (after mailing directly to patient)
- Pros: easy to use, easy to conceal, home monitoring, reassurance
- Cons: ectopy burden not prognostic in asymptomatic patients



Resting 2D Echocardiography

- Non-invasive, ultrasound, relatively low cost
- Allows assessment of heart structure and function in real time
- Best tool to assess LVEF and for valvular heart disease
- Predominant use in **symptomatic** patients
- Screening – bicuspid aortic valve, conditions associated with cardiomyopathy, cardiotoxic drugs
- No role in routine primary prevention – low yield and does not provide independent value for risk assessment
- Pros: no radiation, functional assessment, relatively low cost
- Cons: operator dependent, limited by body habitus, no role in primary prevention

Conclusion

- Noninvasive and invasive diagnostic testing is a core component of the evaluation of patients with stable chest pain.
- CCTA can visualize and help to diagnose the extent and severity of nonobstructive and obstructive CAD, as well as atherosclerotic plaque composition. It can be a very useful risk assessment tool for patients with stable chest pain without known CAD.
- Exercise ECG involves graded exercise and can be used to define ischemia severity and for risk stratification purposes
- SPECT/PET stress test allows for detection of perfusion abnormalities, measures of left ventricular function, and high-risk findings, such as transient ischemic dilation and helps in ischemia guided management.
- Test selection for risk assessment would depend on various factors: patient characteristics & contraindications, local availability and expertise, and clinical preferences.