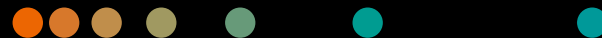


High-Sensitivity Cardiac Troponin I

Signature Healthcare

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Circulation

ESC/ACC/AHA/WHF EXPERT CONSENSUS DOCUMENT

Fourth Universal Definition of Myocardial Infarction (2018)

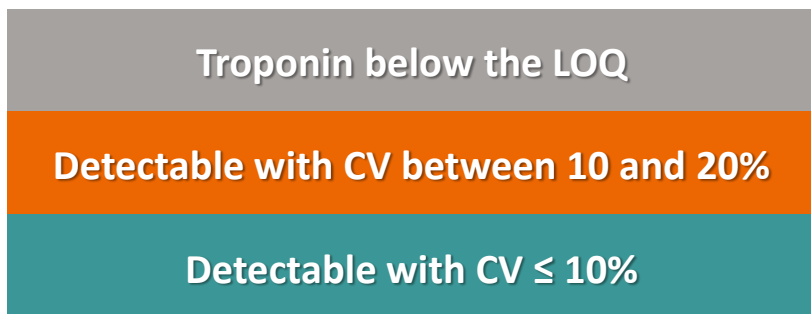
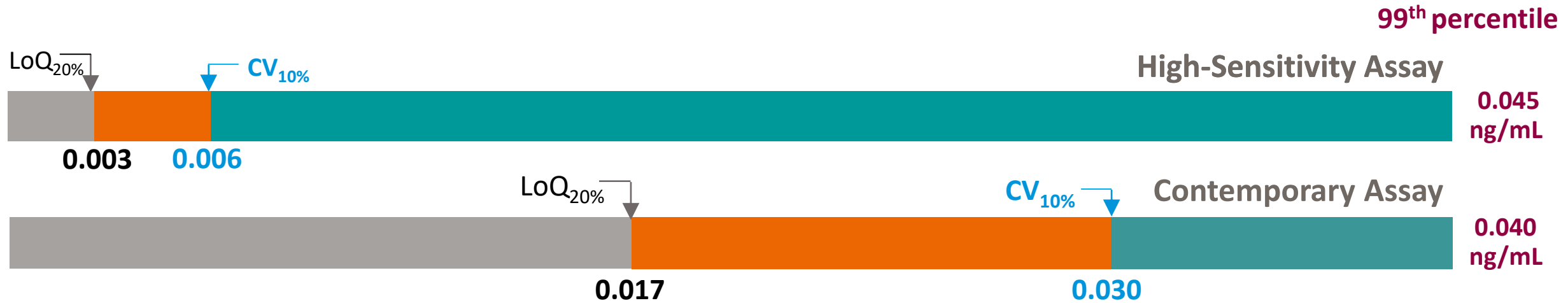
Definition of High Sensitivity Troponin

- The %CV at the 99th percentile should be $\leq 10\%$.
- At least 50% of healthy individuals should have measurable concentrations above the Limit of Detection (LoD) and below the 99th percentile.
- Sex-specific 99th percentiles are established.

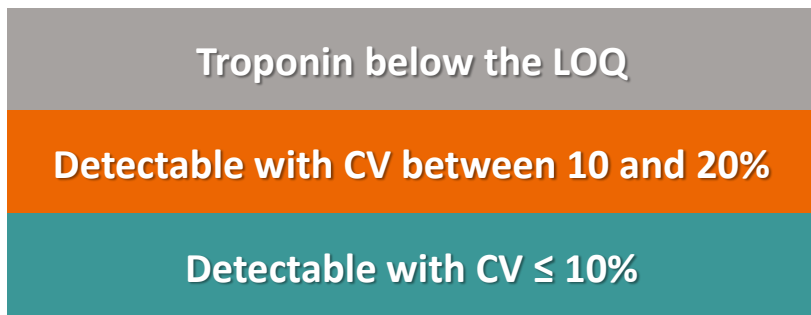
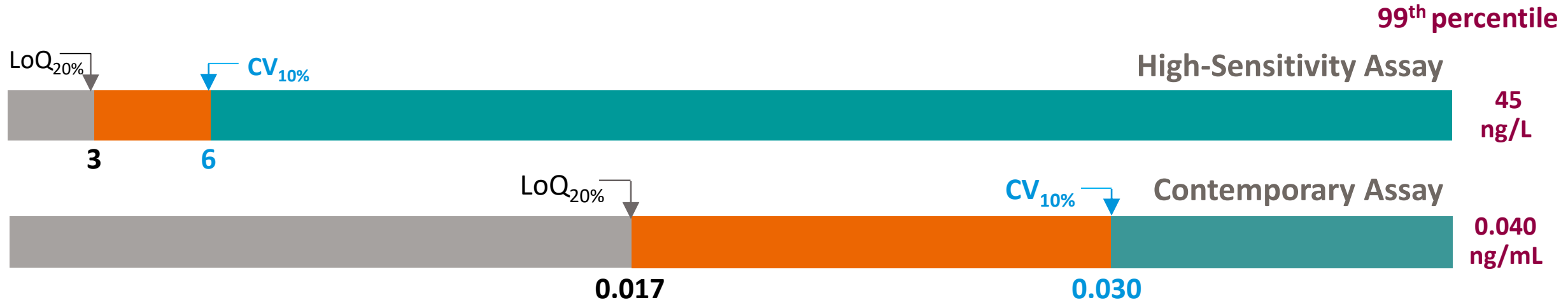
Why do we need high sensitivity troponin?

1. Better precision offers improved discrimination at diagnostic decision levels
2. Allows for the detection of smaller infarcts
3. Allows for the potential use of accelerated diagnostic protocols (ADP) for the more rapid triage of patients
4. The use of ADPs can reduce ED wait times and shorten patient turnaround times in the ED
5. More efficient and potentially better patient care

How does a contemporary troponin assay compare to a high sensitivity troponin?



How does a contemporary troponin assay compare to a high sensitivity troponin?

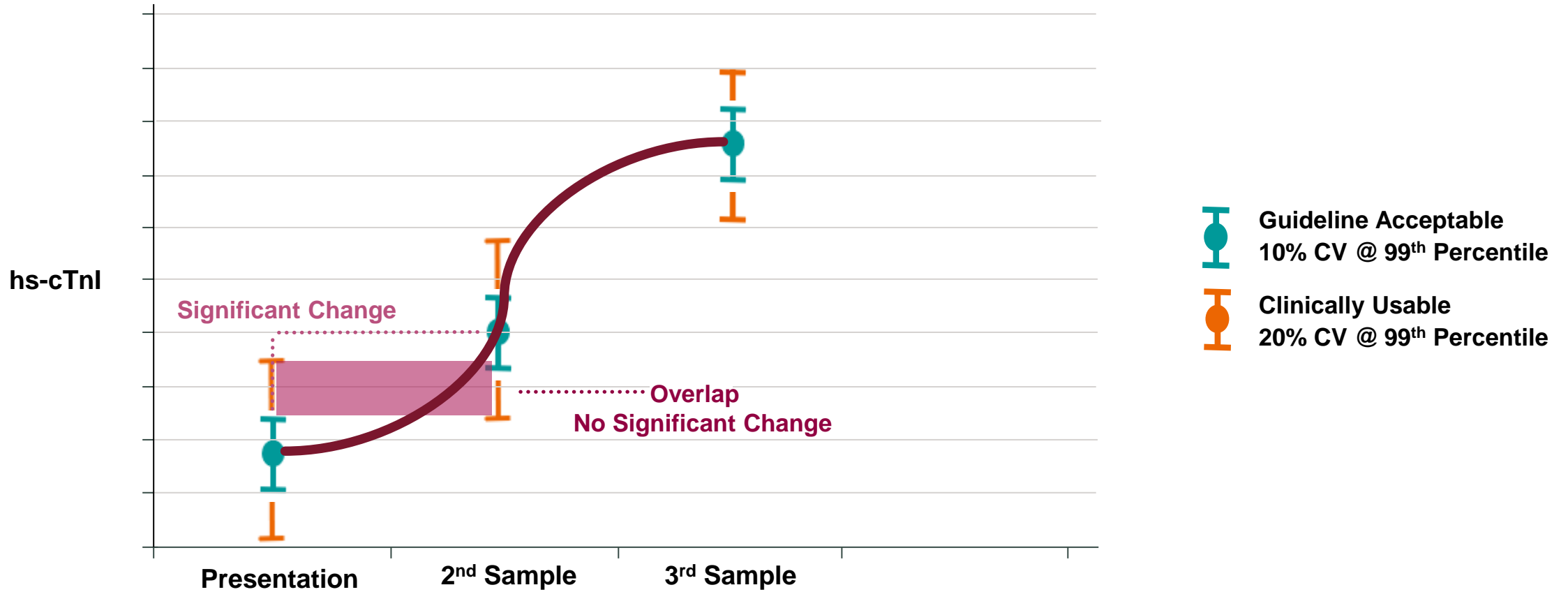


High Sensitivity Troponin Units Change

- From ng/mL to **ng/L**
- 1000 fold change
- Whole numbers

- Cardiac troponin is the preferred biomarker for the evaluation of myocardial injury, and high-sensitivity assays are **recommended for routine clinical use**.
 - The definition of MI includes a significant **rise and/or fall** pattern of troponin results
 - Used along with **clinical interpretation** (e.g. History, ECG, HEART Score, etc.)
- High Sensitivity Troponin assays support the use **accelerated diagnostic protocols** of 0 to 1 hour or 0 to 2 hours
- Definition of **“significant change”** (rise and/or fall) relative to 99th percentile value
 - If the patient’s result is <99th percentile: delta at least 50-60% of the 99th percentile
 - If the patient’s result is >99th percentile: delta at least 20% of the 99th percentile
 - Absolute changes are assay dependent but appear superior to relative percent changes

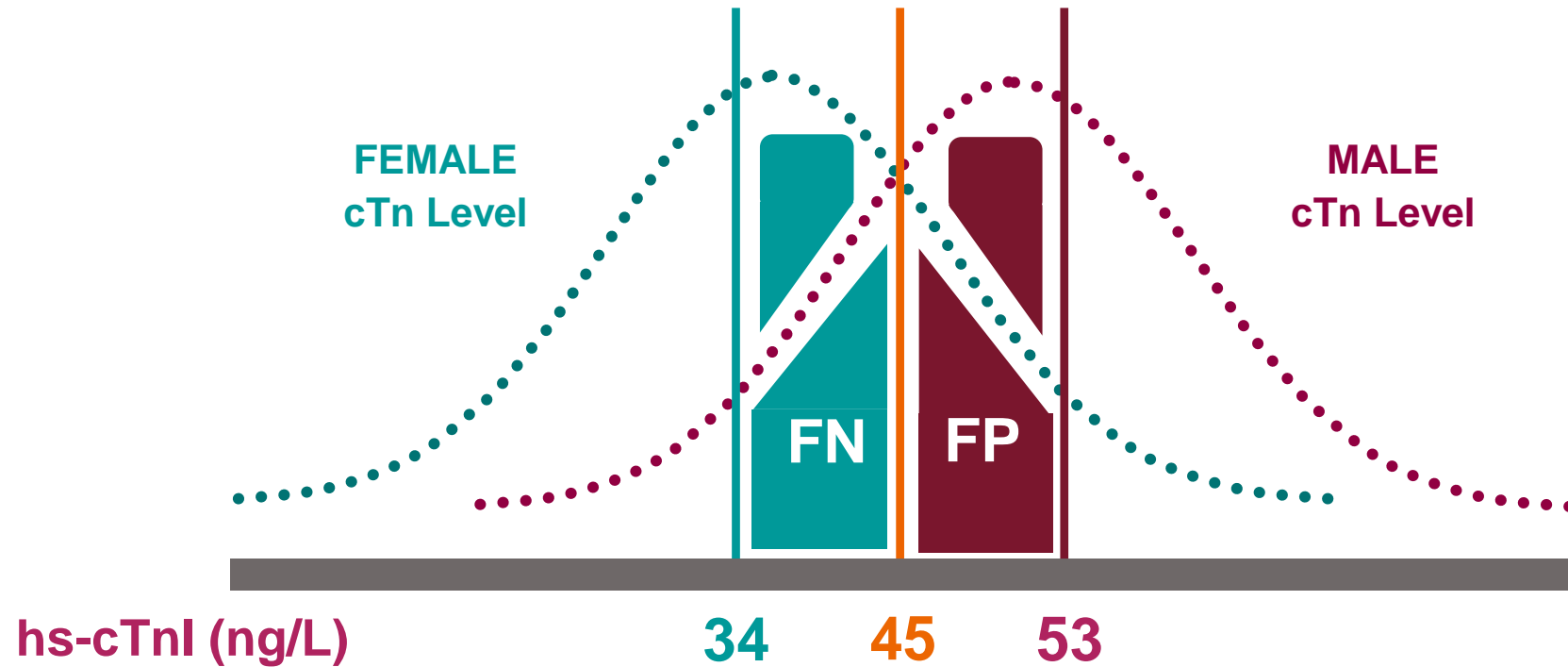
Comparison: Guideline Acceptable vs. Clinically Usable Troponin Assays



Options for Using the 99th Percentile

1. **Combined** male and female
 - Atellica 45 ng/L (ng/L)
2. **Sex specific**
 - Atellica male: 53 ng/L
 - Atellica female: 34 ng/L
3. **Assays are not alike** ... different analytical sensitivity and 99th percentile

Pros and Cons of using sex-Specific 99th Percentiles



High-Sensitivity Troponin Using Sex-Specific Cutpoints

Patients with Suspected ACS (n = 1126)		
Men (n = 622; 55%)		Women (n = 504; 45%)
High Sensitivity Troponin Classification Using a Single Cutpoint		
n = 142 (23%)	Type 1 MI	n = 80 (16%)
n = 30 (5%)	Type 2 MI	n = 25 (5%)
n = 15 (2%)	Myocardial Injury	n = 23 (5%)
n = 20 (3%)	Unstable Angina	n = 8 (2%)
n = 425 (67%)	Others	n = 368 (73%)
High Sensitivity Troponin Classification Using Sex-Specific Cutpoints		
n = 131 (21%)	Type 1 MI	n = 111 (22%)
n = 28 (5%)	Type 2 MI	n = 28 (6%)
n = 12 (2%)	Myocardial Injury	n = 28 (6%)
n = 22 (4%)	Unstable Angina	n = 6 (1%)
n = 429 (69%)	Others	n = 331 (66%)

p < 0.021

p < 0.001

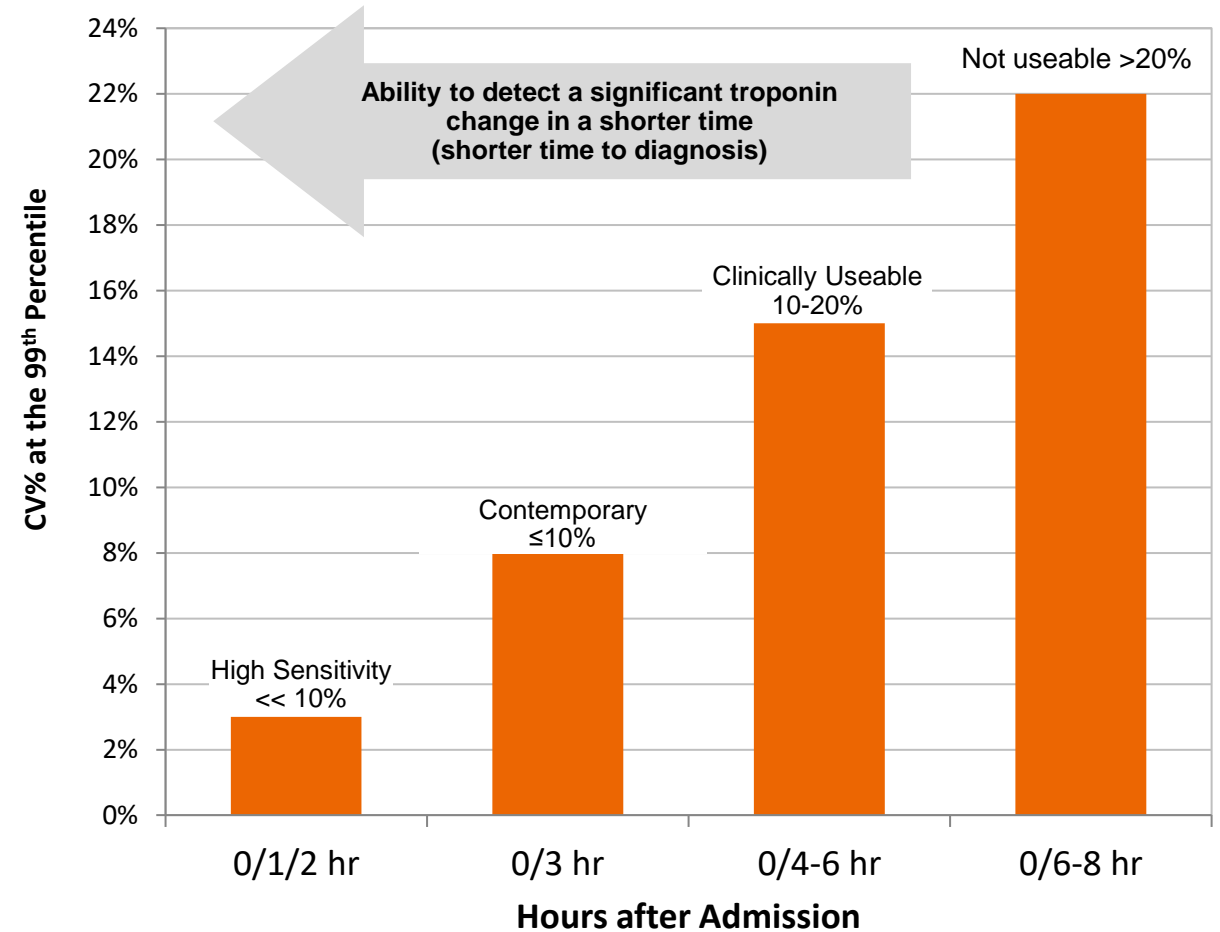
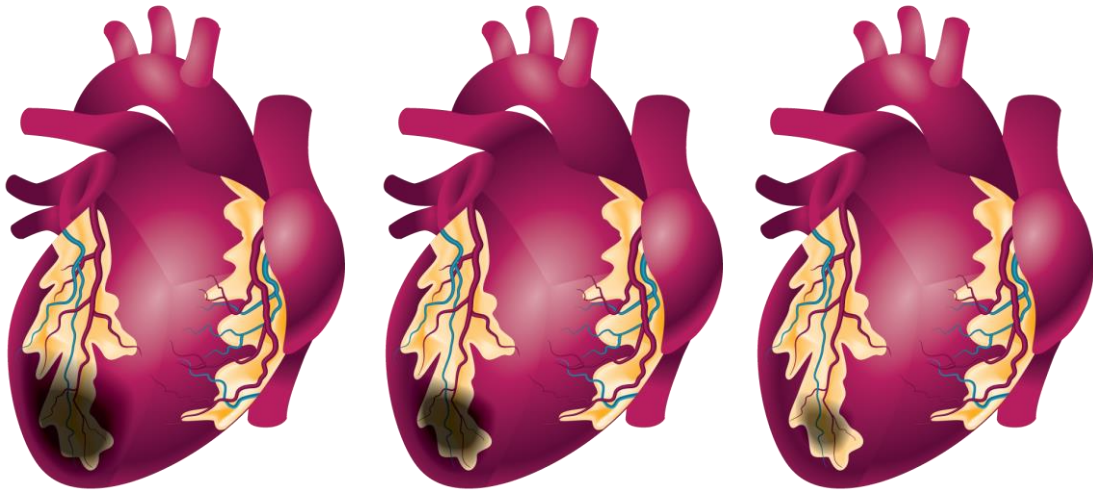
Diagnosis by consensus between the two cardiologists through in-depth review of source documents.

The Clinical Significance of High Sensitivity Troponin

Cardiac troponin assays are the preferred biomarkers for the evaluation of myocardial injury, and high-sensitivity assays are recommended for routine clinical use.

4th Universal Definition of MI JACC August 2018

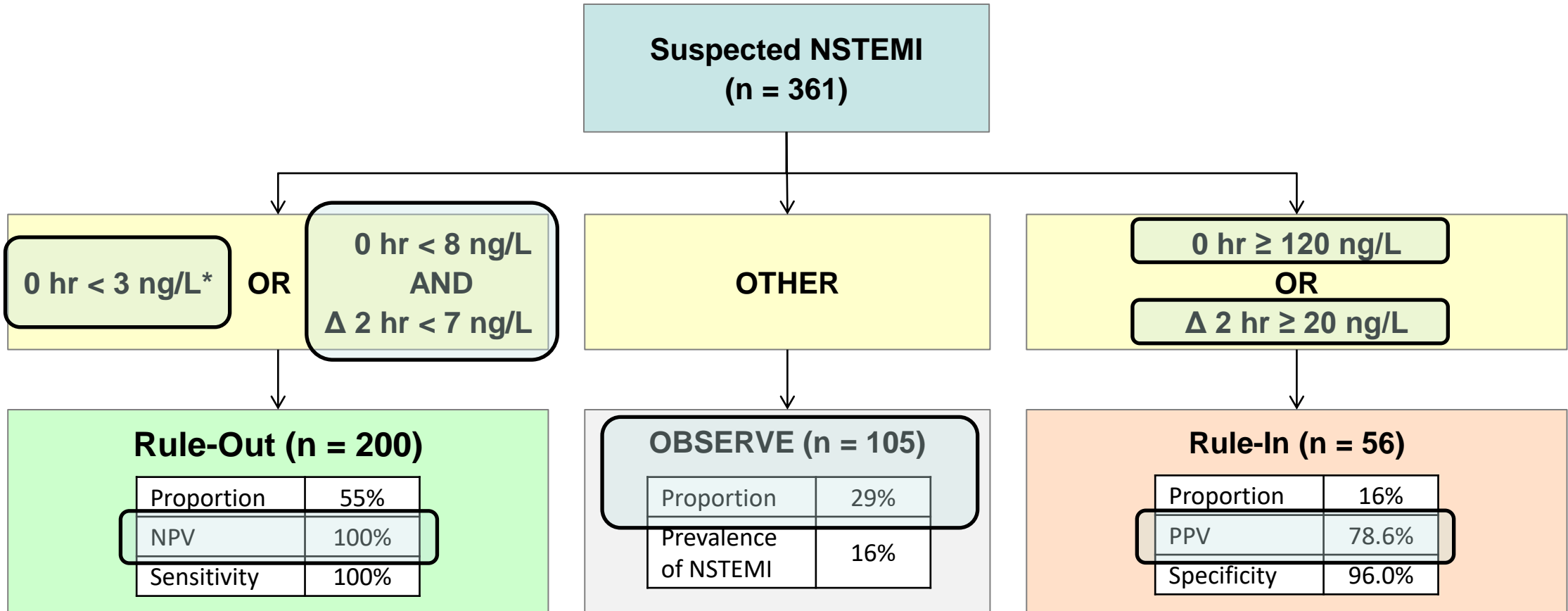
Ability to Detect Smaller Areas of Necrosis



NSTEMI Evaluation Algorithms using High-Sensitivity cTn

- **Analytical sensitivity and precision** are both important considerations when selecting a evaluation protocol.
- If you are dealing with **very early presenters** (<3 hours CPO), you may be able to make an earlier diagnosis based on the trajectory of the troponin result for those with high clinical suspicion; however, AMI should not be ruled out until sufficient time has passed from onset of symptoms.
- The institution needs to **determine and/or “fine tune” the algorithm** used based on their individual patient population and the clinical goals of the medical staff.

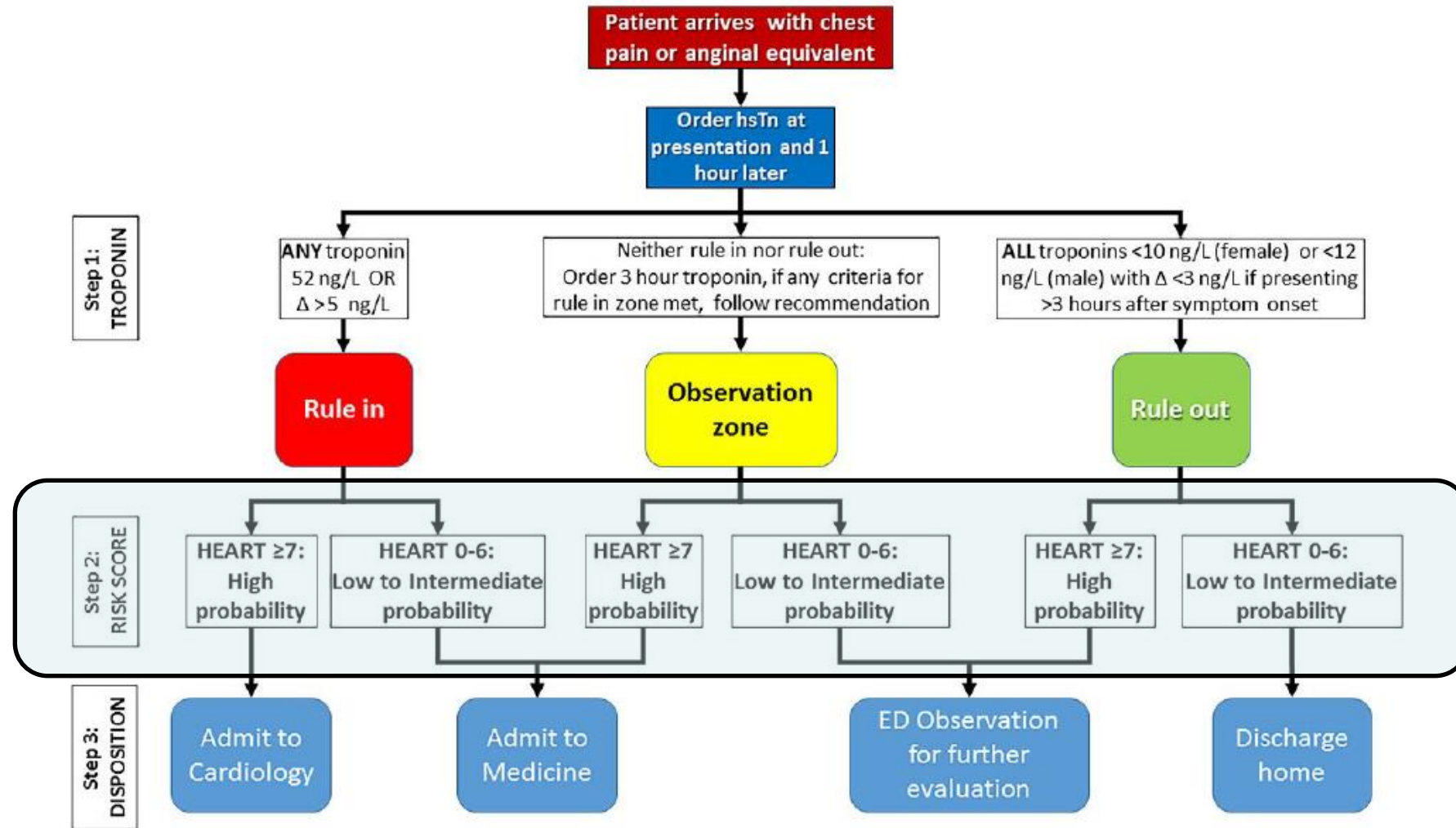
Clinical Performance of the Centaur hs-cTnI Assay using the 0/2 hr Testing Protocol - APACE



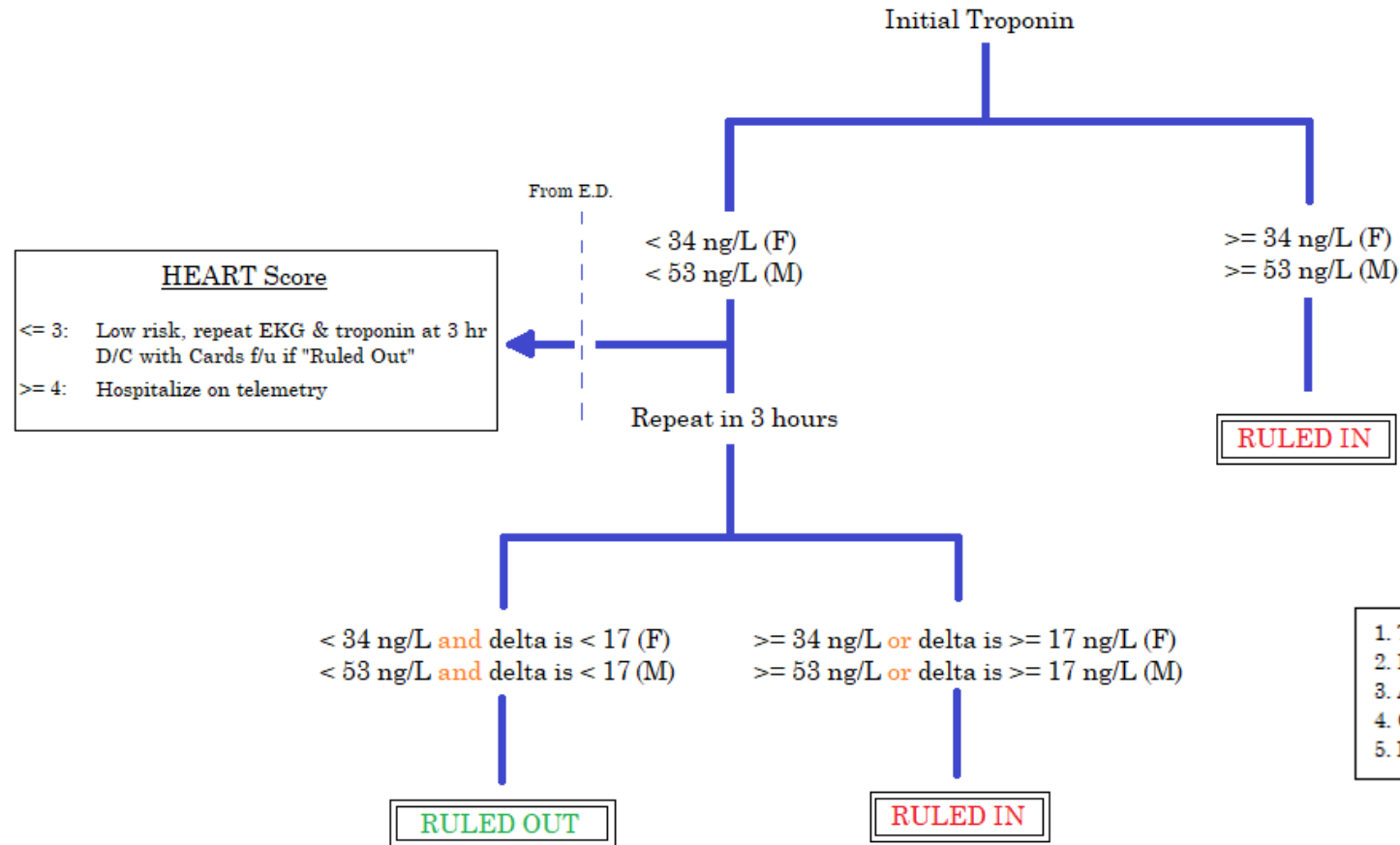
Note: The Centaur TNIH assay is not intended to be used in isolation; results should be interpreted in conjunction with other diagnostic tests and clinical information. Results may vary according to the prevalence of AMI in the population being tested and other factors that may influence assay performance.

*If chest pain onset >3h before presentation to the ED

Massachusetts General Hospital Pathway



High Sensitivity Troponin Assay

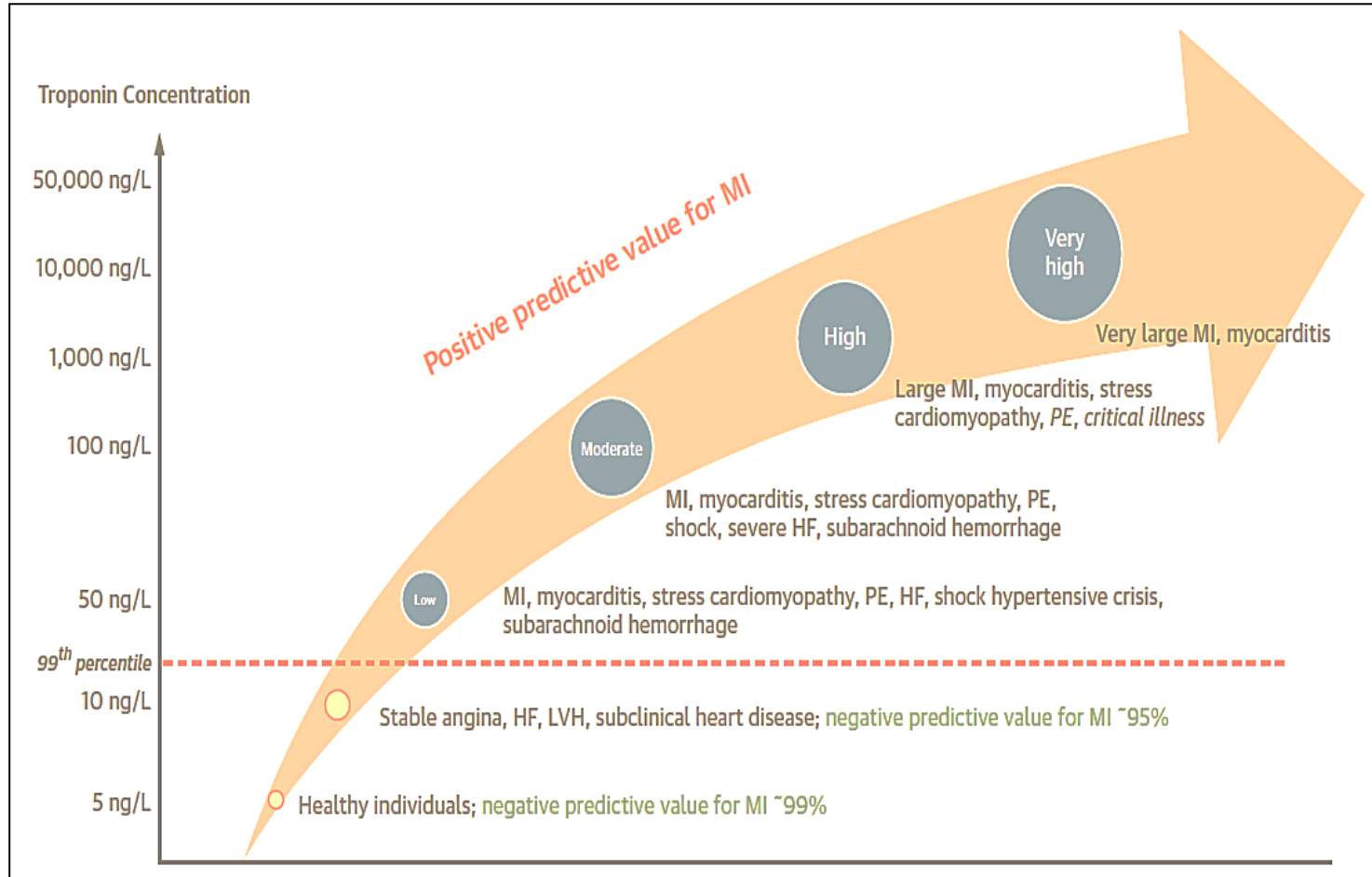


KEY

1. This assay is gender specific (birth sex)
2. F = female; M = male
3. A normal initial troponin gives the T component of HEART score a zero
4. Clinical judgment supersedes algorithm
5. Delta is the difference between first and second troponin

Higher Troponin Values are More Consistent with AMI

A broader differential diagnosis associated with lower-range elevations of hs-cTn begins to narrow as concentrations are higher.



Diagnosis	Peak hsTnI (ng/L)
Type 1 MI	855 (104 – 6755)
Type 2 MI	125 (48 – 604)
Acute Injury	74 (37 – 307)
Chronic Injury	55 (34 – 145)

9,115 patients with an elevated hsTnI results
Chapman et al Circulation. 2020;141:161–171

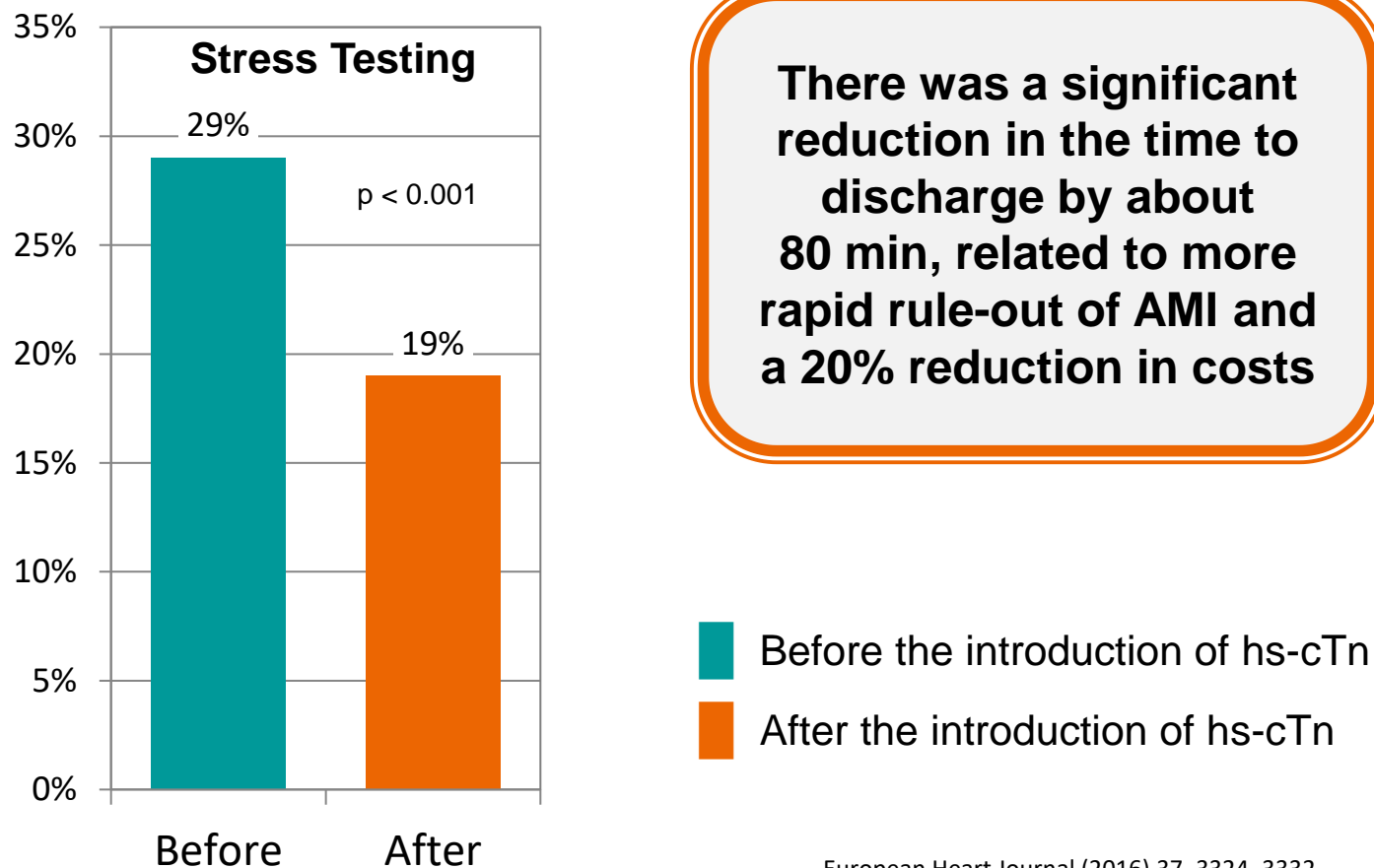
“False Positive” Troponin Results

- In the absence of overt myocardial ischemia, elevated cTn levels are often labelled as ‘false-positive’ hs-cTn results.
- This term should be avoided, as most of these unexpected hs-cTn elevations are ‘true positive’ for myocardial injury (rather than MI) and reflect previously undetected or underestimated cardiac disease including valvular heart disease, heart failure, and chronic coronary artery disease.
- Many cardiac and non-cardiac disorders may lead to substantial amounts of cardiomyocyte injury and thereby hs-cTn elevations.
- It is important to note that cTn elevations universally portend a worse prognosis than otherwise similar patients without a cTn elevation, irrespective of the underlying disease.
- This is true regardless of whether the patient has heart failure, renal dysfunction, gastrointestinal bleeding, sepsis, respiratory disease, pulmonary embolism, subarachnoid hemorrhage, or stroke or whether the patient is asymptomatic without known cardiovascular disease.
- Obviously, the medical consequences of cardiomyocyte injury as quantified by cTn elevations will be highly individualized and different from that in patients with MI.

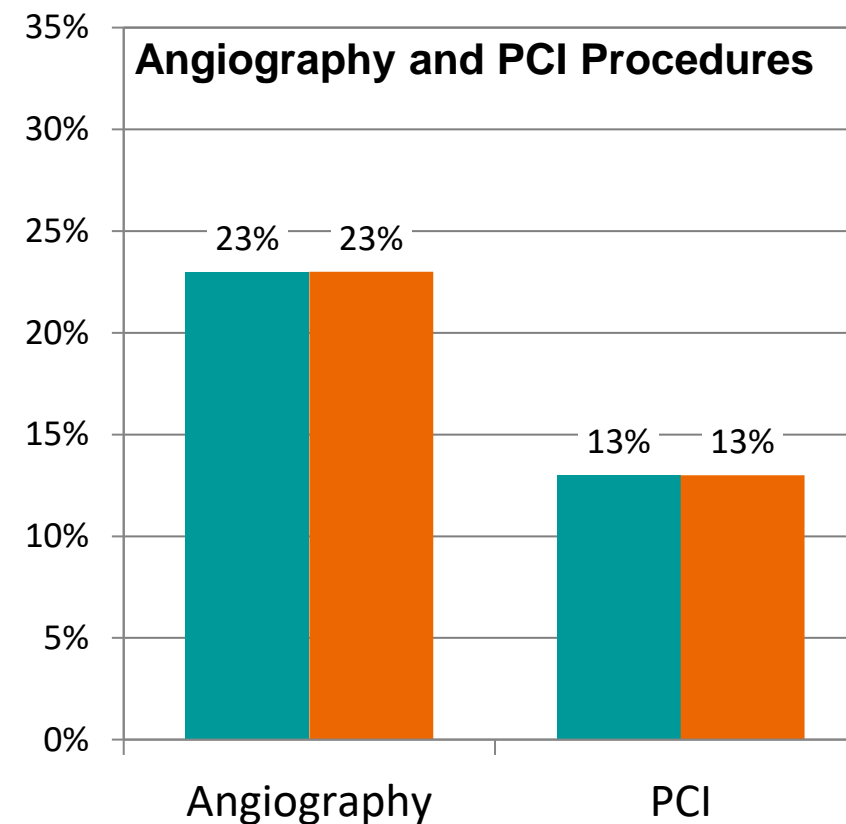
Procedures after the Implementation of hs-cTn

2,544 patients presenting to the ED with symptoms suggestive of AMI before and after the introduction of hs-cTn

There was a significant reduction in the percentage cardiac stress tests



There was also no increase in the percent of patients who underwent coronary angiography or PCI



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Q&A