

Clinical Benefits of High Sensitivity Troponin

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Seguin, Texas
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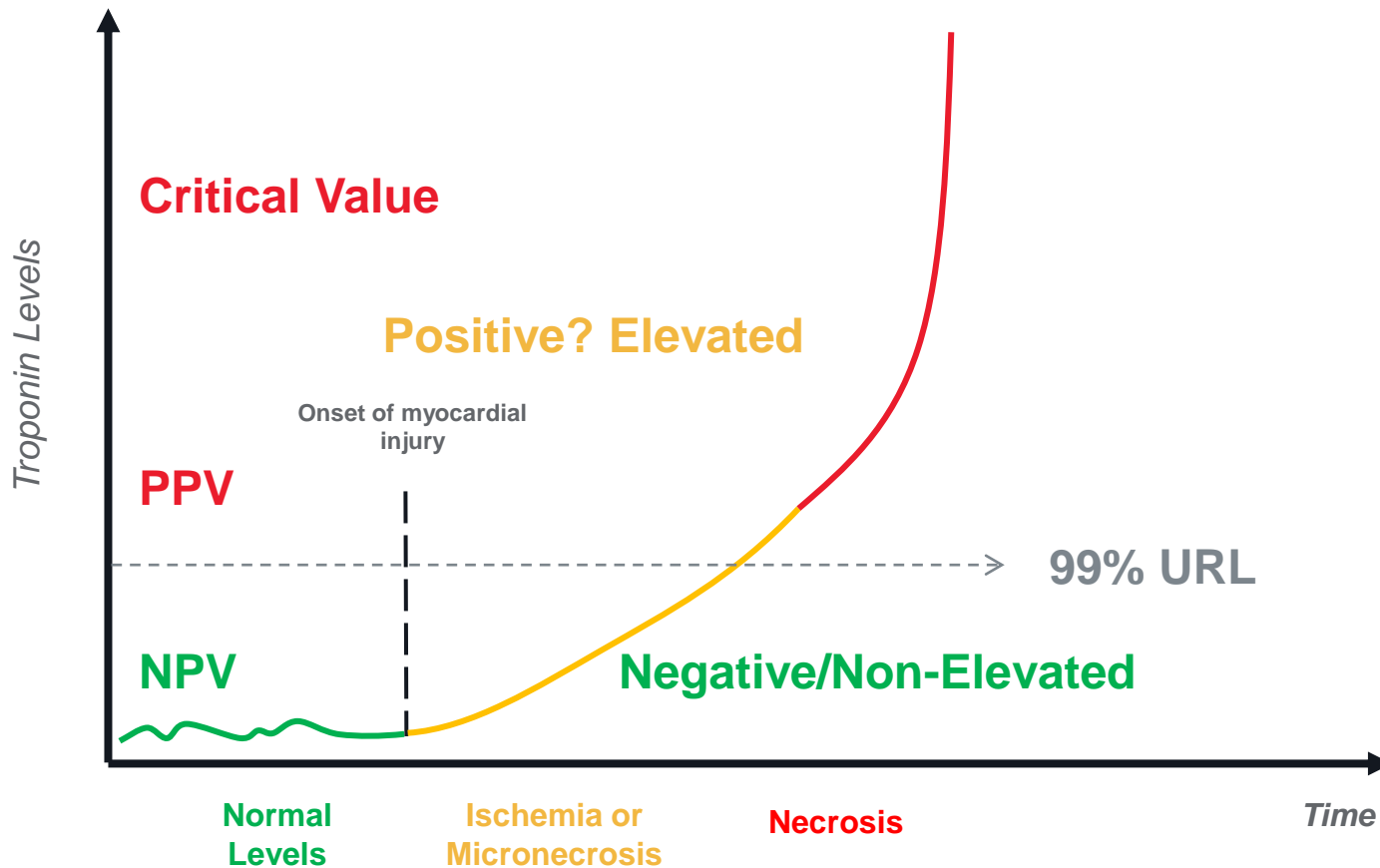
Areas of Focus

- > Physician Concerns:
 - Why should I do it?
 - ACC, AHA recommendation
 - AccuTnl+3 Sunset
 - How will it change what I do now?

- > Normalize Terminology

- > Accent Analytical Improvement and advantage to practice
 - Reported number acuity – better assessment of micronecrosis
 - Robust number on ~everyone
 - Info earlier in potential events
 - Decision making accelerated
 - **Delta provides clinical sensitivity**
 - **Improved clinical acuity in range >Cutoff to Critical value**

Normalizing Terminology



Troponin Testing for Clinicians

> Expectations:

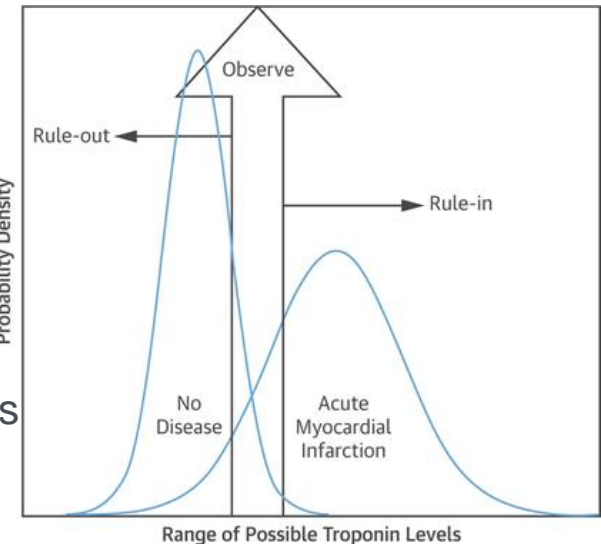
- 20% increase in reported results
- 4-5% of this group will be elevated
 - Mainly women and early presenters
 - Depending upon size of delta, many of these will be referred to cardiology in next 24-48 hrs
- Most patients ruled out quickly

> Emphasis:

- **>LOD – Critical Zone (Injury/MI)**
 - Delta provides clinical sensitivity
 - Absolute number, not percentage change
 - Resource allocation
 - HEART Score Usage

> References in the Gray Zone

- Boeddinghaus – Clin Chem 2019 Jul;65(7):893-904
 - “Yellow Zone”, 0-1 hr ADP
- Nestelberger – Clin Chem 2019 Nov;65(11):1437-1447
 - “Yellow Zone”, 0-2 hr ADP
- Baugh – Transition, Crit Pthwys Cardio 2020 Mar;18(1):1-4
 - “Grey Zone” & HEART Score (TnT)



Troponin Testing for Clinicians continued

- › Greenslade – J Clin Med 2020 Jun 16;9(6):1883-1895
 - 6 mos AccuTnl+3 – 6 mos hsTnl
 - 63K/61K patients
 - Outcomes
 - Primary –
 - i. Decreased Hospital LOS
 - ii. Increase in elevated cTn values
 - iii. **No** concomitant increase in cardiac admissions, invasive coronary procedures or diagnosis of AMI
 - Secondary –
 - i. Decreased ED LOS, 90-day CV mortality,
 - ii. Following adoption:
 - Decrease single cTn order.
 - Increased – dual cTn orders – **More Deltas**
 - iii. Increased detection of myocardial injury
 - Male 5%, Female 12%
 - Diagnostic rates remain unchanged
 - iv. Significant economic savings.

Guideline Recommendations

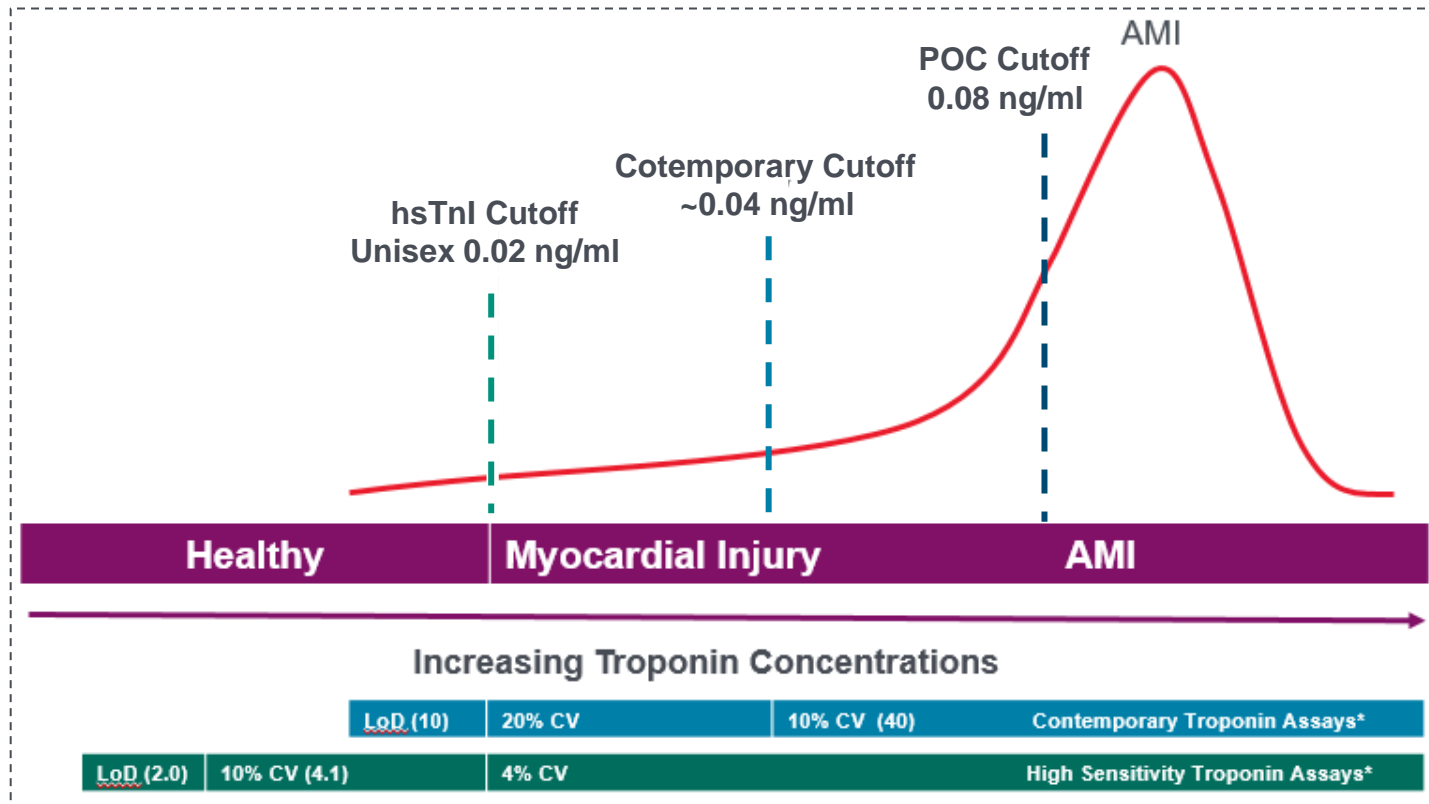
- > Thygesen et al 2019 Eur Heart Jnl 40, 237-269
 - Fourth universal definition of myocardial infarction
 - “cTnl and cTnT are the preferred biomarkers for the evaluation of myocardial injury, and **high-sensitivity (hs)-cTn assays are recommended for routine clinical use.**”
 - “Very low levels of hs-Tn on presentation or the lack of any change and persistently normal hs-cTn values over a 1-2 hour period after presentation have been advocated **to exclude acute myocardial injury, and MI as well.**”

- > AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Clinical Practice Guidelines
 - Gulati et al 2021 Circulation; 144:00-00 (November 2021)
 - Guideline for the Evaluation & Diagnosis of Chest Pain: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines
 - i. **High-Sensitivity Troponins Preferred**

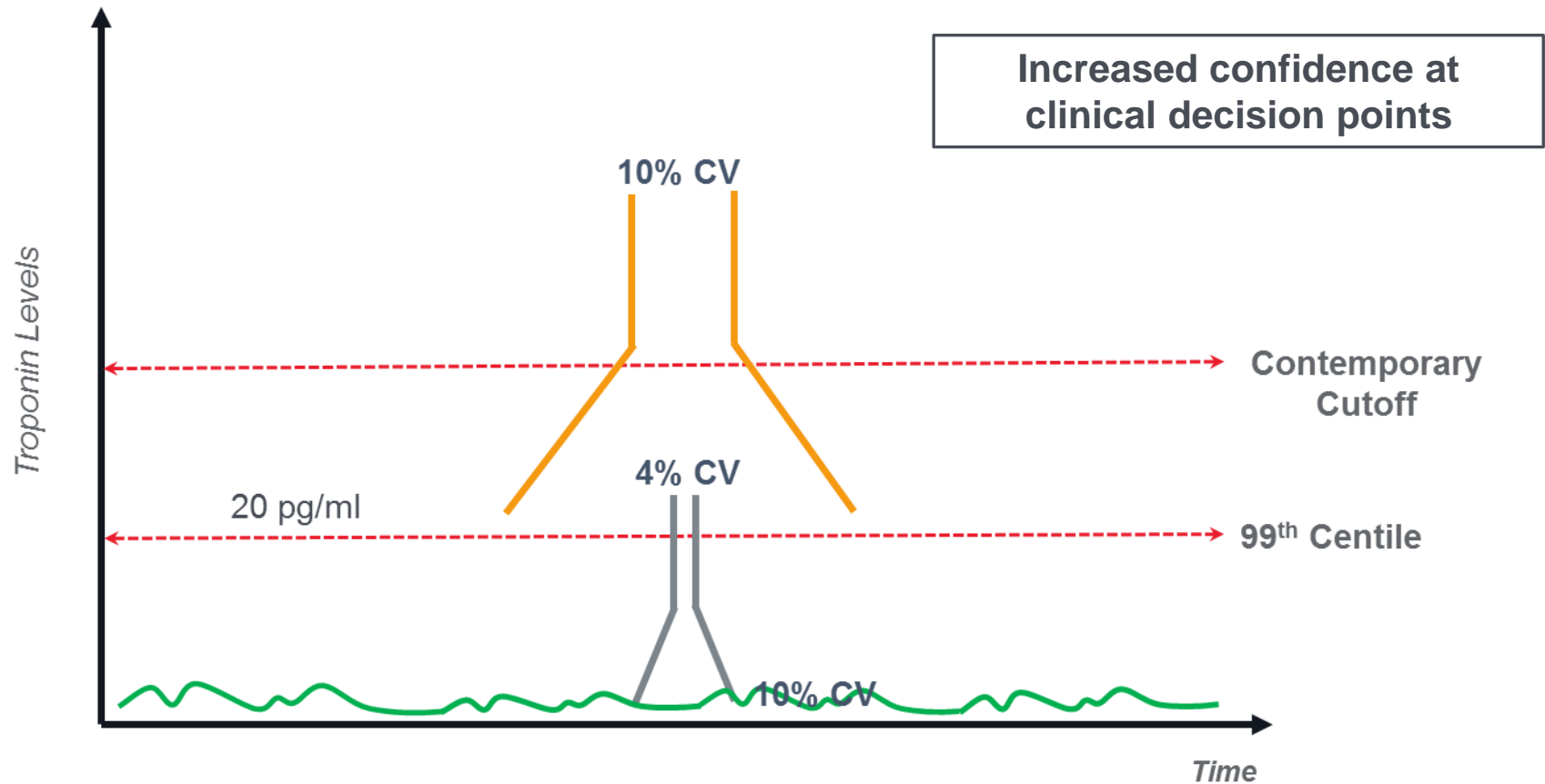


What Stays the Same

➤ 99th Percentile (URL)



Different: Improved Precision at 99th Percentile



What is Different?

- › **Enhanced Analytical Sensitivity**
- › **Units** – ng/ml to pg/ml.
 - **0.03 ng/ml is now a 30 pg/ml**
- › **Delta** Instead of Cutoff
- › Male/Female-Specific 99th Percentile URL
- › Troponin Number on Almost All Patients
- › Shorter Draw Protocols
 - 0-1, 0-2, 0-1-3

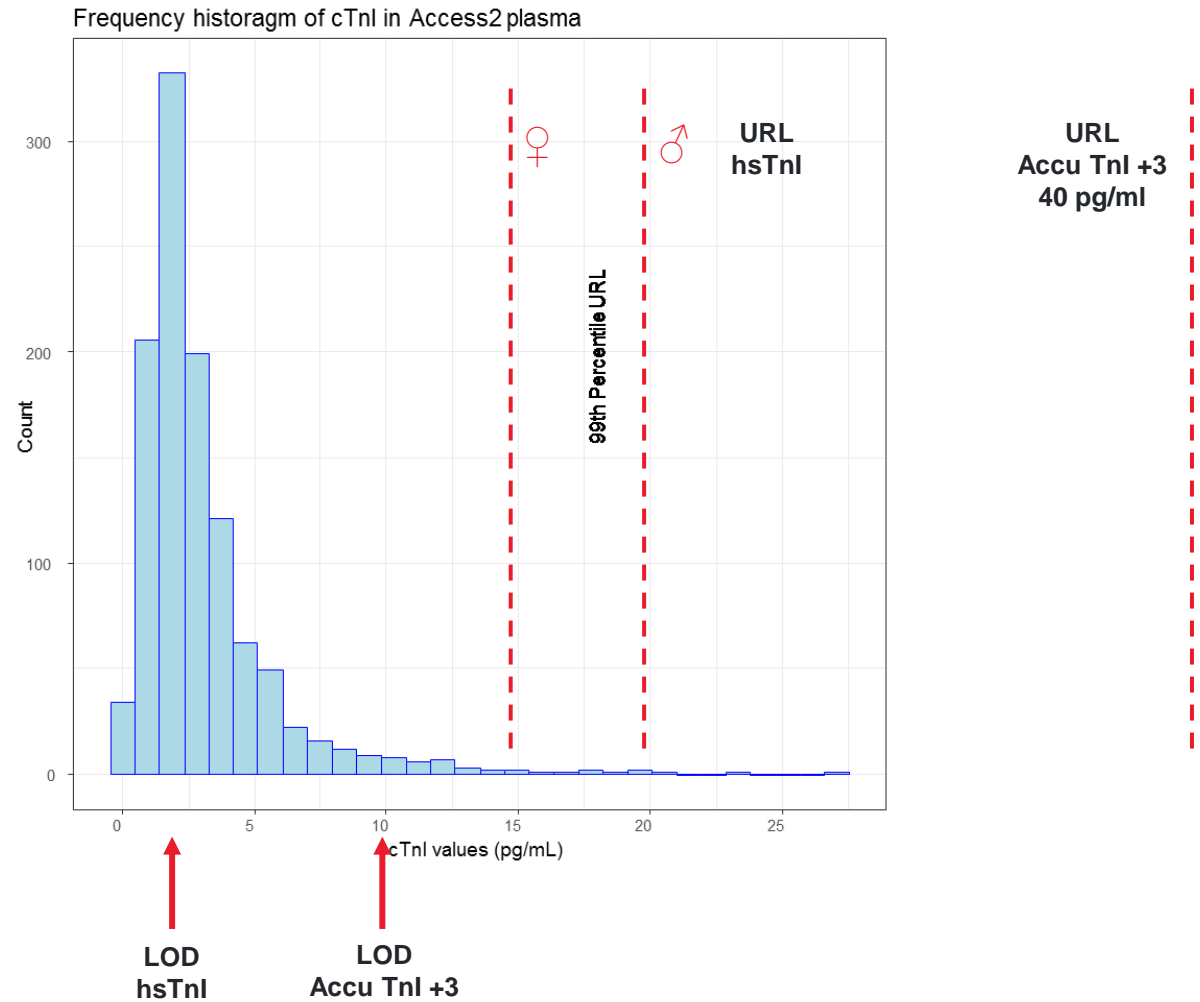
Parameter	AccuTnl +3*	Access hsTnl UniCel Dxl
LoD (pg/mL)	10	2.3
10% CV (pg/mL)	40	5.6
20% CV (pg/mL)	30	2.3

pg/ml

pg/ml

What is different?

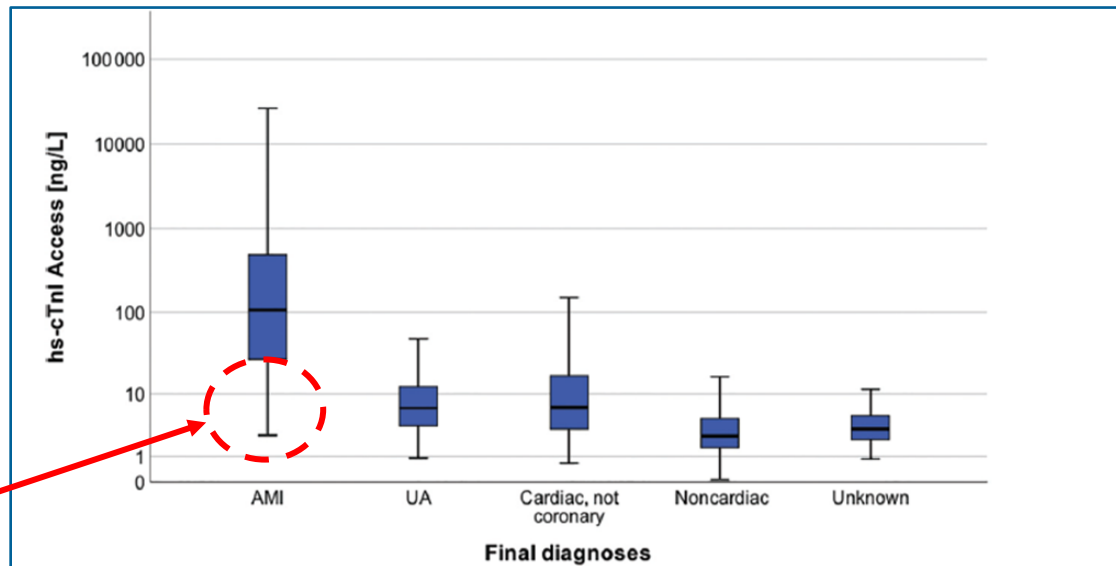
Reference Interval –
population distribution



Additional Values at Low End are Relevant

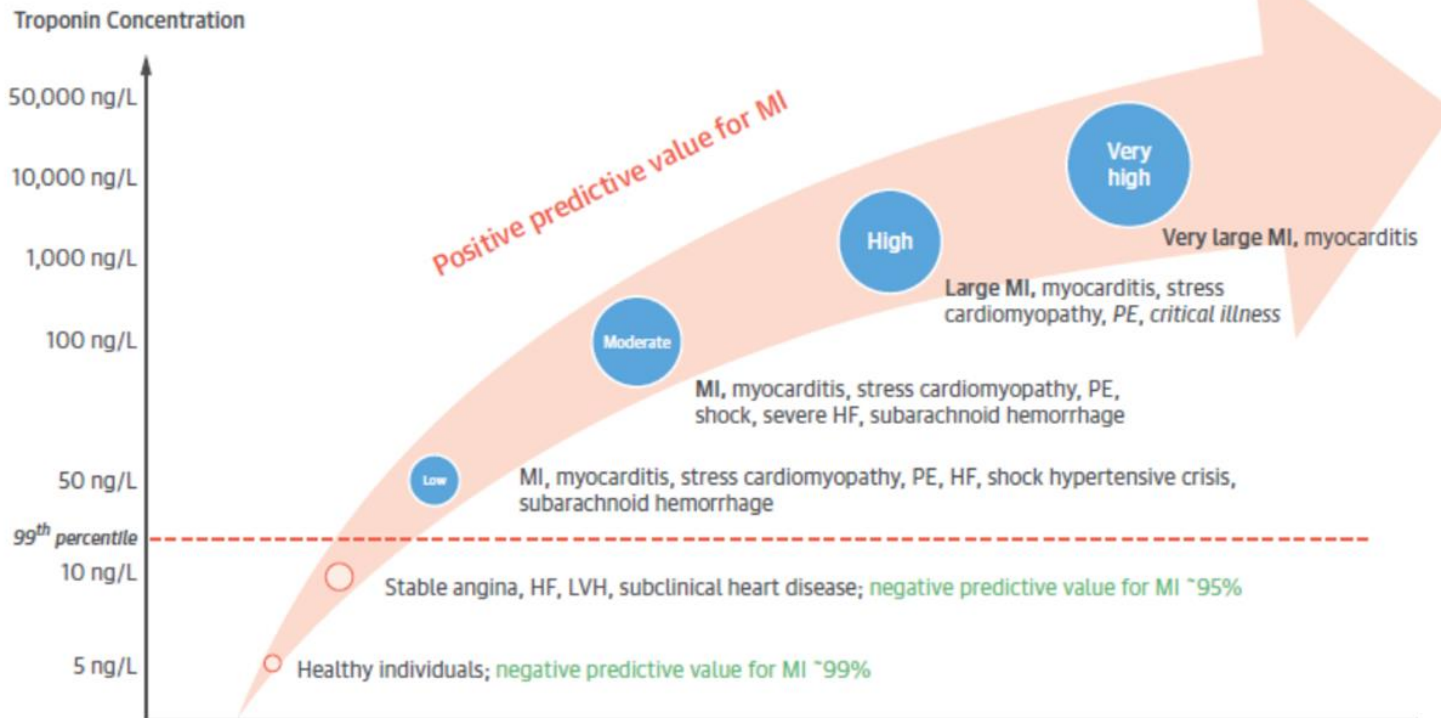
Approx 20% of AMI patients had initial Troponin BELOW 99th Percentile

Region where additional results due to hsTnI analytical sensitivity will be seen

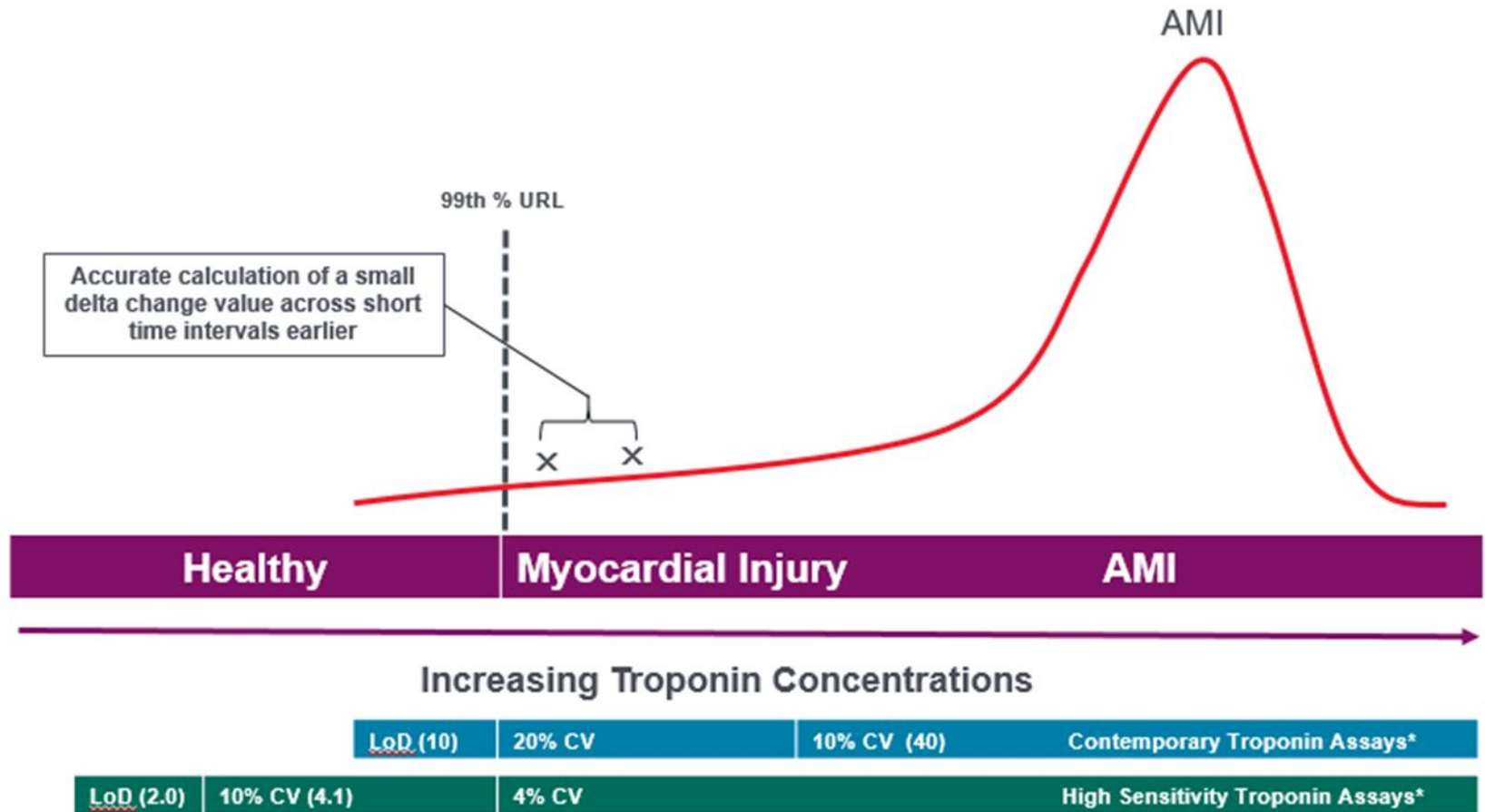


Hs-cTnI concentration at presentation vs. final diagnoses

The Spectrum of Troponin Values

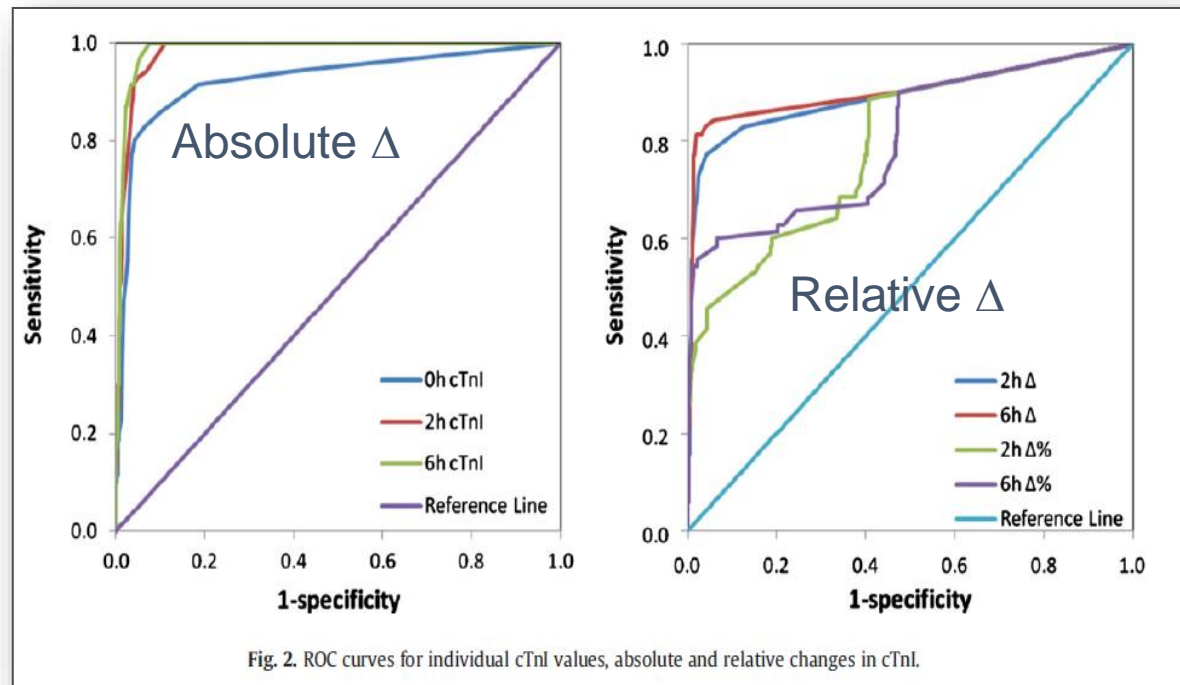


What is Different: Deltas

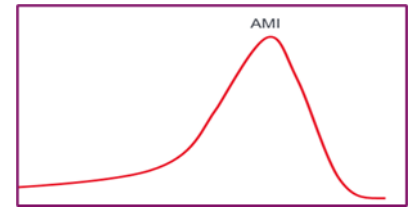


Absolute vs. Relative Delta

Delta troponin for the early diagnosis of AMI in emergency patients with chest pain.
Cullen 2013. Int J Cardiol 168(3):2602-8.



Case Study



> Contemporary Practice:

- 42 year old female presents to ED with nausea, vomiting, trouble breathing
- Normal sinus rhythm, left ventricle hypertrophy. 2nd ECG noted ST elevation
- Final Diagnosis:
 - Acute MI – STEMI
- Patient received IV tissue plasminogen activator

	Current assay (ng/mL)	Current assay (pg/mL)	hsTnI (pg/mL)
Baseline	<0.03	<30	14
3 hr.	<0.03	<30	36
6 hr.	0.63	630	562
12 hr.	26.43	26430	18762

> Emergent Practice:

- Baseline hsTnI level is above 99th percentile for females >12pg/mL
- 3hr troponin level also abnormal, including significant change as compared to baseline.
- This pattern is seen with early presenters.

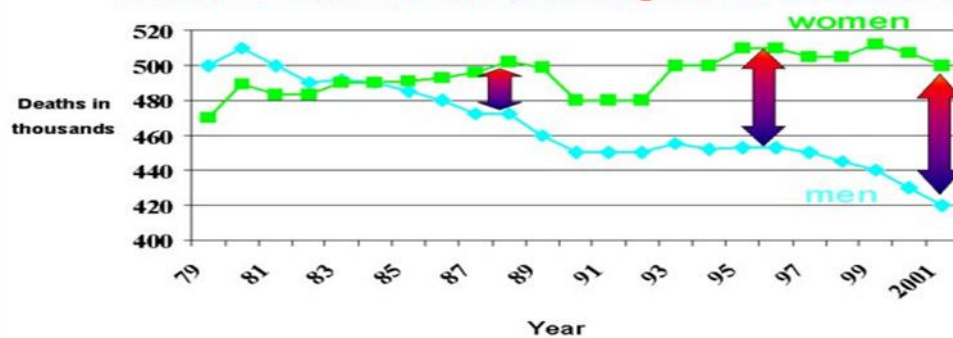


Who Benefits?



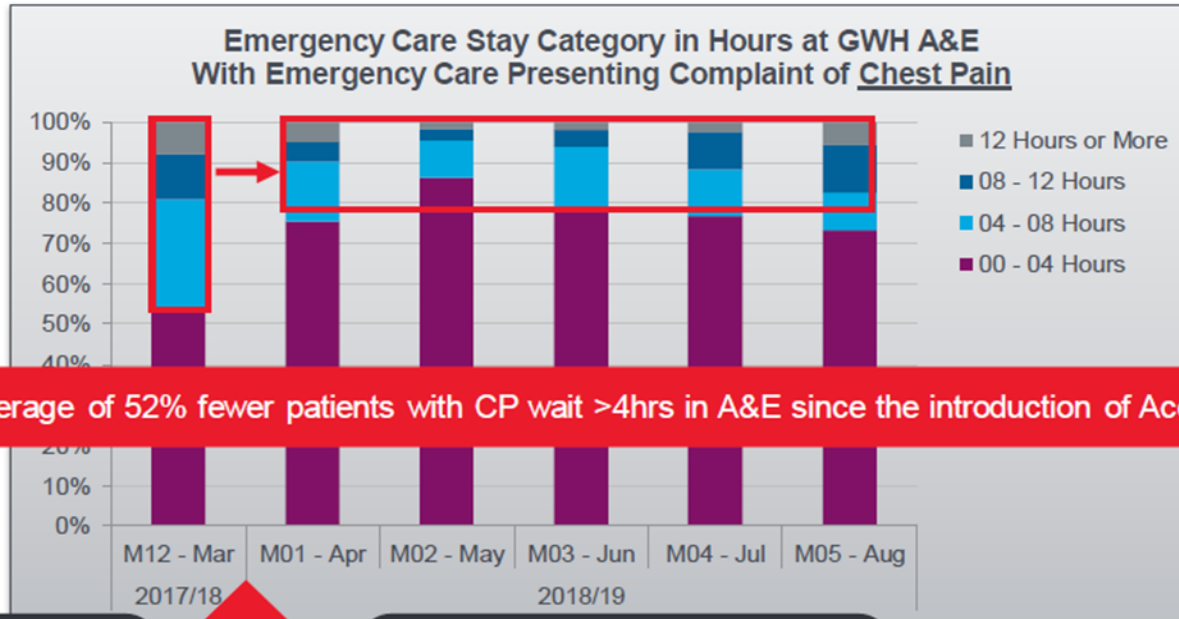
Cardiovascular Disease Mortality Trends

Women's rates are not declining in line with men's



Reduced Patient Waiting Time in the A&E

52% fewer patients presenting to A&E with chest pain are waiting longer than 4 hours following implementation of Access hsTnl in Q1 2018/19



An average of 52% fewer patients with CP wait >4hrs in A&E since the introduction of Access hsTnl

March 2018:
46% patients
with CP waited
>4hrs

Access
hsTnl
introduced
April 2018

April – August 2018:
Following introduction of Access
hsTnl an average of 22% patients
with CP waited >4hrs

Reference interval – 99th percentile URL: Dxl

UniCel Dxl (plasma) results:

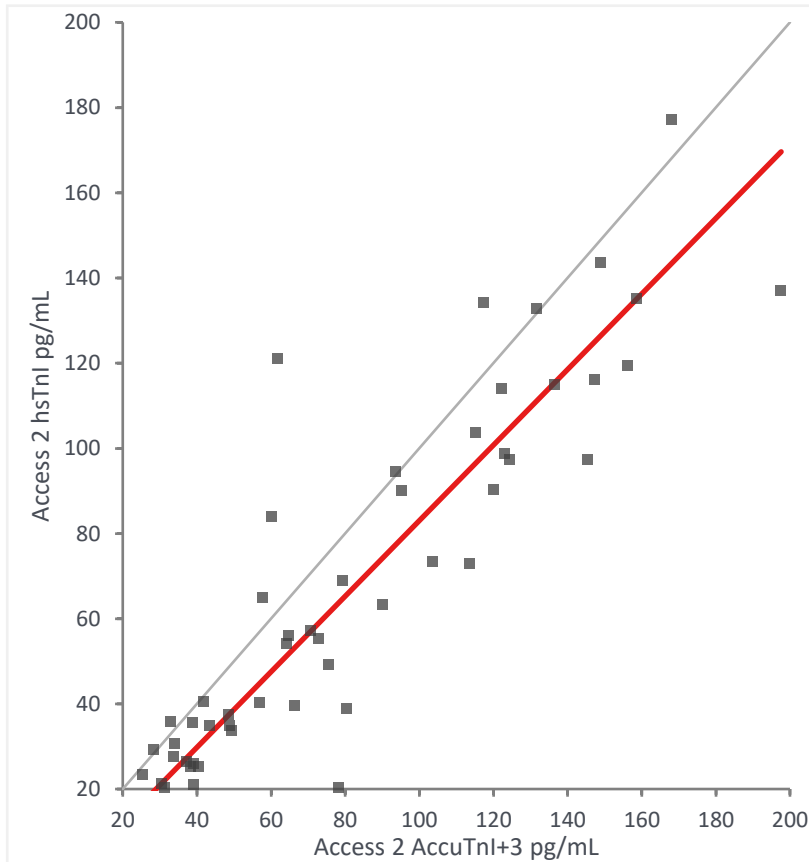
99 th Percentile URL	Access hsTnl	AccuTnl+3
Overall N = 1088	17.9 pg/mL	<30 pg/mL (<0.03 ng/mL)
Female N = 593	14.9 pg/mL	N/A
Male N = 495	19.8 pg/mL	N/A

Clinical trial – Results

- > Identifies most true AMI patients in as little as one hour post presentation
- > 99% NPV in as little as one hour after ED admission
- > Specificity
 - Increases with change from 30ng/L (AccuTnl+3) to 18ng/L (hsTnl).
 - For sex-specific cutoffs
 - Sensitivity & Specificity improve for females

99 th %URL cutoff, ng/L	Hours After Admission to ED	Sensitivity, %	Specificity, %	PPV, %	NPV, %
17.9 Overall	Baseline	88	89	58	98
	≥1-3 hour	94	90	54	99
	≥3-6 hour	94	90	55	99
	≥6-9hour	99	85	51	100
14.9 Females	Baseline	83	91	53	98
	≥1-3 hour	93	92	47	99
	≥3-6 hour	96	92	51	100
	≥6-9hour	100	88	45	100
19.8 Males	Baseline	89	87	61	97
	≥1-3 hour	96	88	57	99
	≥3-6 hour	94	88	58	99
	≥6-9hour	98	81	53	100

Medical Decision Point Correlation – 20-200 pg/ml



Range	Slope	Intercept	R	N
20 – 200 pg/mL	0.89	-5.7	0.90	51

Access 2 hsTnI vs Access 2 AccuTnI+3

Access 2 hsTnI	Access 2 AccuTnI+3	
	> 20 pg/mL (+)	≤ 20 pg/mL (-)
>17 pg/mL (+)	111	0
≤ 17 pg/mL (-)	6	19
	117	19

Concordance of $(111+19)/136 \times 100 = 96\%$

Cardiac Troponin Medical Cutoffs/Medical Decision Points

Rule In

- PPV – Critical Value

AMI

95% Confidence Limit

Trend

- Serial – Trend

Gray Zone

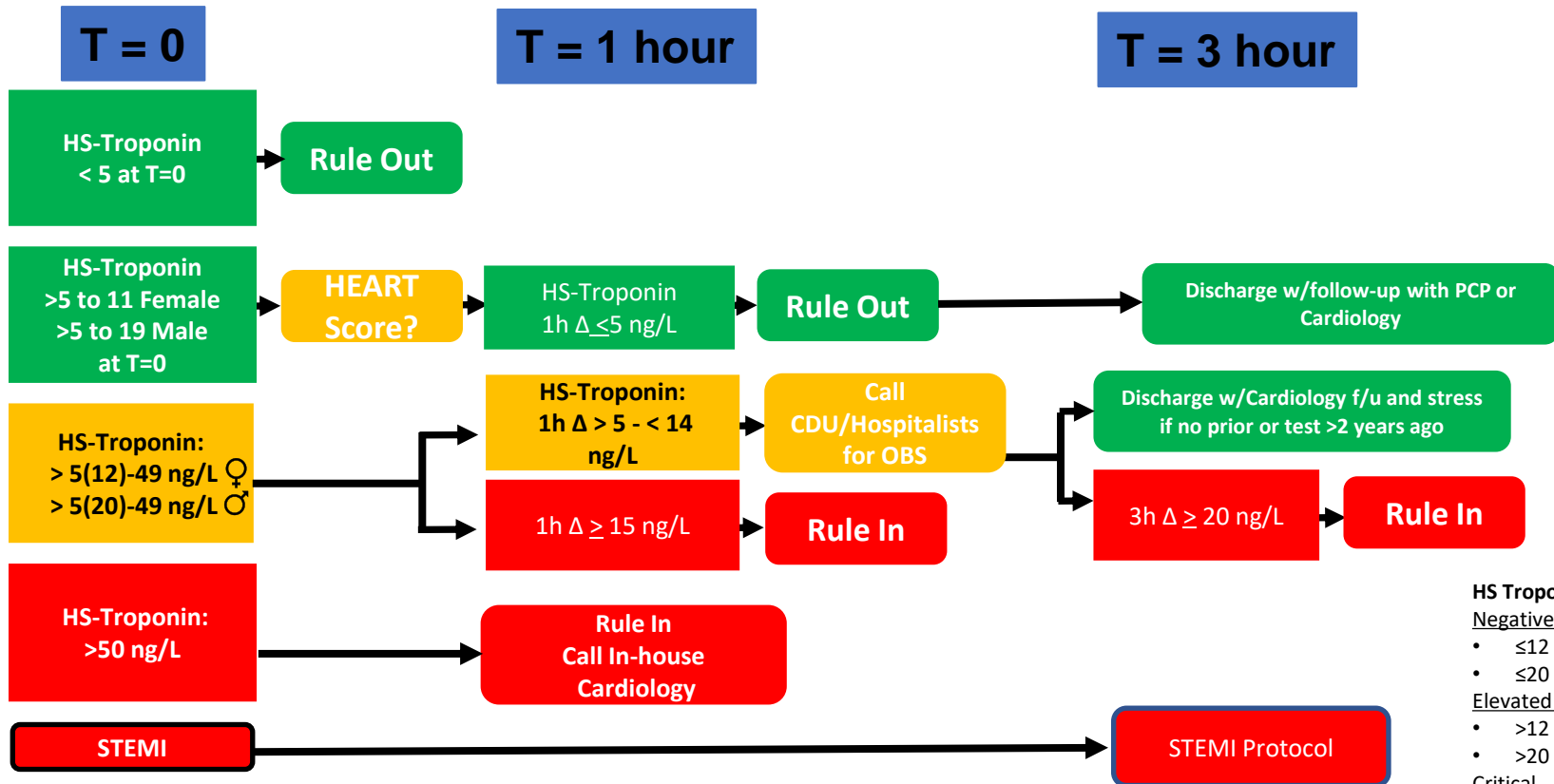
99% Cutoff

Rule Out

- Sgl – NPV
- Serial – Trend?

Normal
LOD - cutoff

ED Chest Pain Protocol



- HS Troponin Lab Definitions**
- Negative
- ≤12 ng/L (female)
 - ≤20 ng/L (male)
- Elevated
- >12 ng/L (female)
 - >20 ng/L (male)
- Critical
- ≥50 ng/L Male/Female

This protocol does NOT replace clinical judgement, but should be referred to as a best standard practice guideline.

hsTnI transition at St. Lukes Bethlehem, PA

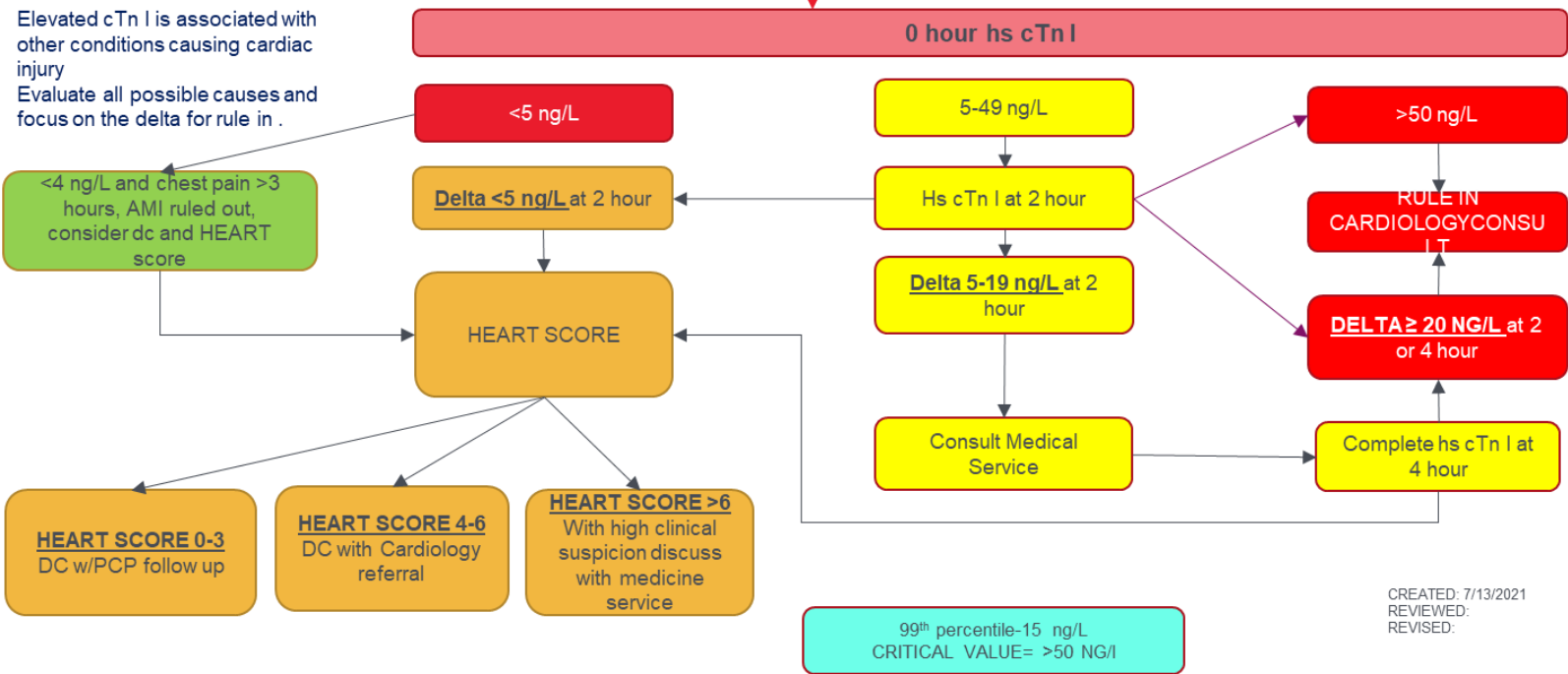


Acute Coronary Syndrome (ACS)

ECG reviewed by a provider within 10 minutes, repeat ECG with new or worsening chest discomfort and with each troponin draw, vital signs, continuous ST segment monitoring, IV, physical exam, CxR, consider Oxygen if sat <90%
hs Troponin I (hs cTnI) stat

STEMI criteria met?
Go to STEMI flowchart

Elevated cTn I is associated with other conditions causing cardiac injury
Evaluate all possible causes and focus on the delta for rule in .



CREATED: 7/13/2021
REVIEWED:
REVISED:

GUIDELINES DO NOT REPLACE THE PROVIDERS CLINICAL IMPRESSION
Not all chest pain is cardiac, consider all causes



SharpHealth Care Decision Making

High Sensitivity Troponin I – Result Algorithm

Clinical judgement supersedes the algorithm especially in high risk patients or patients with unusual symptoms or an unstable/concerning ECG.

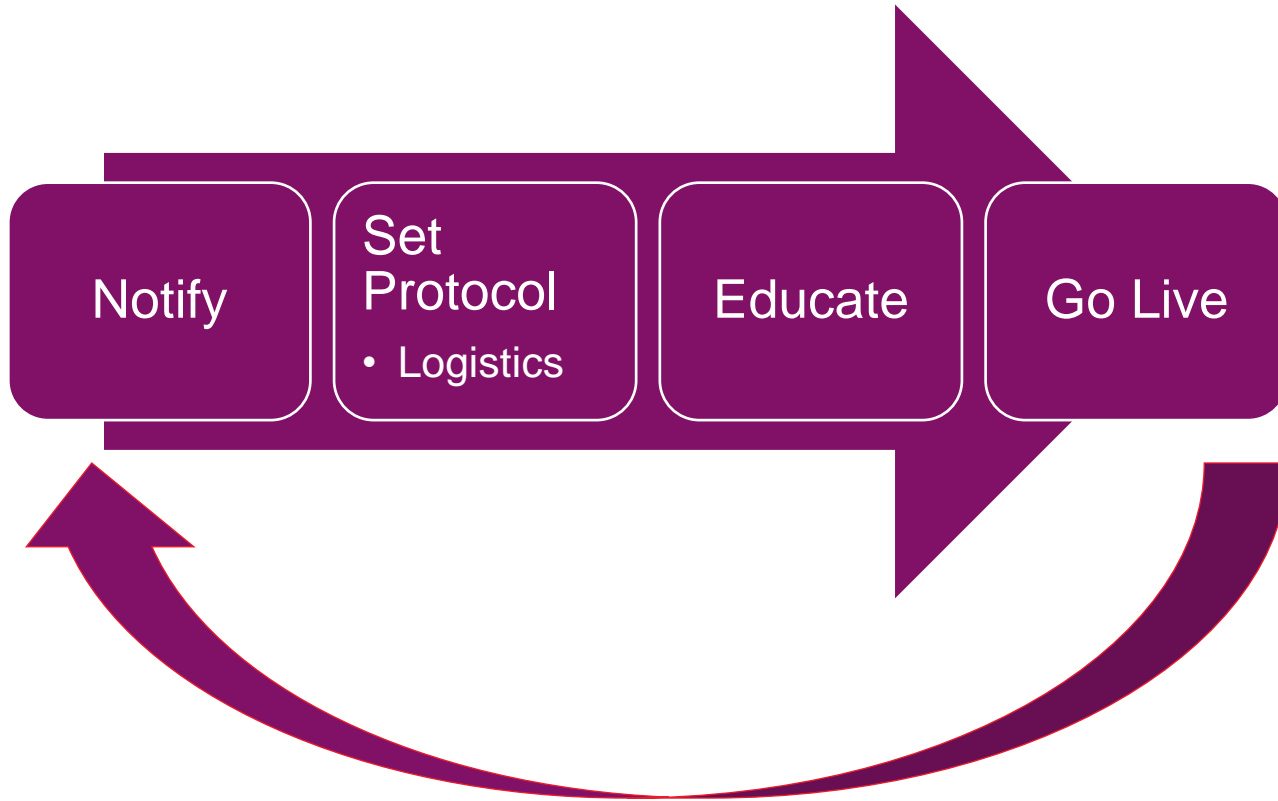
Draw Times	Move to Rule-Out AMI	Move to Rule-In AMI
0 hour	≤5.0 pg/mL	>99.0 pg/mL Males >75.0 pg/mL Females
<u>0 - 2 hours</u> <ul style="list-style-type: none"> ▪ >5.0 pg/mL and ▪ Below the Cutoff Male – 19.8 pg/mL Female – 14.9 pg/mL ▪ Significant HEART score/clinical presentation 	Δ <5.0 pg/mL*	Δ >15.0 pg/mL
<u>0 - 2 hours</u> <ul style="list-style-type: none"> ▪ Above the Cutoff Male – 19.8 pg/mL Female – 14.9 pg/mL 	Δ <5.0 pg/mL*	Δ >15.0 pg/mL

* Δ between 5-15 pg/mL need to be interpreted with clinical context

Possible Non-Ischemic causes of elevated troponins: Tachyarrhythmias, congestive heart failure, critically ill patients (sepsis, respiratory failure, inflammatory diseases, burns), pulmonary embolism or severe pulmonary hypertension, severe hypertension or hypotension, apical ballooning cardiomyopathy (Takotsubo Syndrome), stroke or subarachnoid hemorrhage, renal failure, myocarditis, myopericarditis, cardioversion or ablations, aortic stenosis, chest trauma, hypertrophic cardiomyopathy, coronary spasm, hypothyroidism, infiltrative cardiomyopathy, extreme exertion, drug toxicity (some chemotherapies).

Reference: Clinical Use of High-Sensitivity Cardiac Troponin in Patients with Suspected Myocardial Infarction
R Twerenbold et al. J Am Coll Cardiol 70 (8), 996-1012. 2017.

hsTn Implementation in the Clinic



Physician buy-in is critical
Audit, assess, communicate, repeat



THANK YOU



Move healthcare forward.

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