SOCIETY OF CARDIOVASCULAR PATIENT CARE

AN INSTITUTE OF THE AMERICAN COLLEGE OF CARDIOLOGY

Troponin and version 5 New Requirements: Implementing the Guidelines

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SOCIETY OF CARDIOVASCULAR PATIENT CARE

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Speaker Overview

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There are no disclosures

Objectives

Identify guideline-driven best practice recommendations on the use of biomarkers in the treatment of Acute Coronary Syndrome (ACS)

Review updates to the Myocardial Infarction (MI) Definition and Non-ST elevation Acute Coronary Syndromes (NSTE-ACS) guidelines

Discuss SCPC troponin turn-around-time (TAT) recommendations and documentation requirements

Share quality practices that optimize the care and outcomes of ACS patients

SCPC Position Statement: Laboratory

- **The Society does not promote or endorse lab based testing or point-of-care testing (POCT) rather focuses on processes and protocols for the identification and management of the Myocardial Infarction (MI) and Acute Coronary Syndrome (ACS) continuum.**
- **The Society provides guidance and education with the position that each facility is responsible to determine the vendor partnerships that best align to their hospital-specific processes, protocols and goals.**
- **Each hospital should be well versed in the latest guideline recommendations and ensure they have reviewed their protocols for Troponin, consistent with the assay(s) being used.**

Acute Coronary Syndrome (ACS)

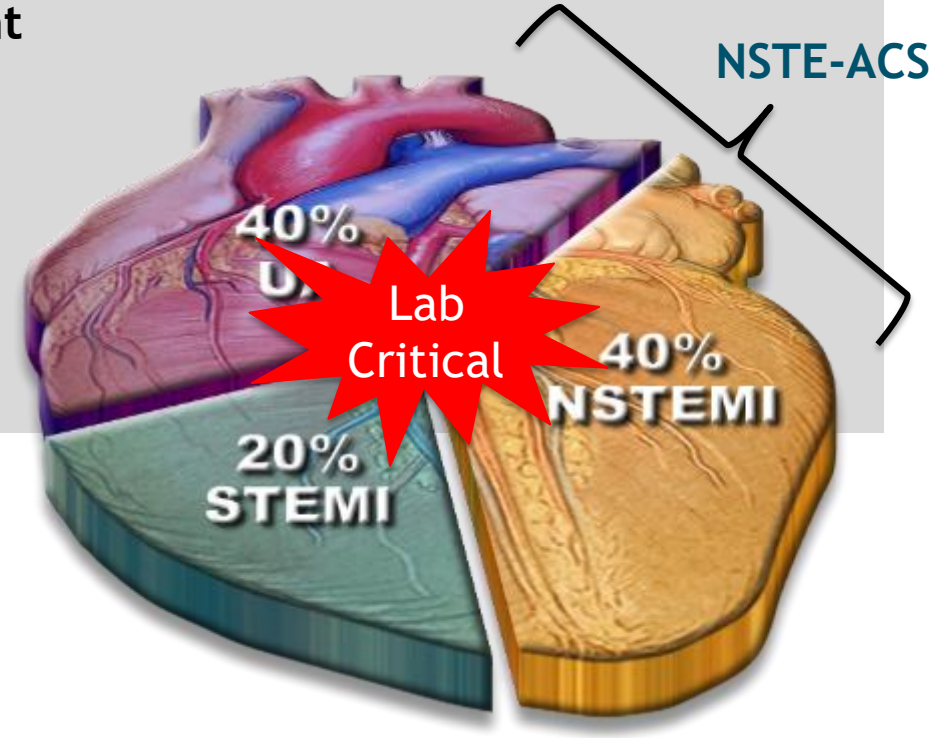
Per the 2014 guidelines…The new title, “Non–ST-Elevation Acute Coronary Syndromes” (NSTE-ACS) emphasizes the continuum between Unstable Angina (UA) and Non-ST Elevation Myocardial Infarction (NSTEMI). At presentation, patients with UA and NSTEMI can be indistinguishable and are therefore considered together in this Clinical Practice Guideline (CPG).

Estimated 5-8 million patients present to the ED annually for chest pain

20-25% diagnosed with Acute Coronary Syndrome

2,000,000

Low Risk/Observation Population:
The other 6,000,000+ people



Source: American Heart Association
Learn and Live

Definitions for Reperfusion

- **Percutaneous Coronary Intervention (PCI)** – most frequently used invasive method of treating the narrowing, or stenosis, of coronary arteries; performed in cardiac catheterization facilities (cath lab) at acute care hospitals
- **Primary PCI (PPCI)-** also known as (aka) emergency angioplasty, is a life-saving intervention performed during a heart attack (STEMI)
- **Non-primary PCI -** aka: elective angioplasty, scheduled intervention to relieve the narrowing of the artery; goal of preventing a heart attack from occurring in the future

Key Point: Facilities should ensure laboratorians are familiar with the protocols and facility diagnostic capabilities (cath lab, PPCI, thrombolytics, transfer) to address acute cardiac events.

Use explanations of the differences when working with Lab. Do not assume they know their role regarding the facility reperfusion strategy.

Guideline Updates:

"…As the field continues to absorb the guidelines, panelist and others advised laboratorians to take time to know the documents so they can have constructive discourse about them with physicians…"

Clinical Lab News, Feb 2014, vol 40, no 2

Updated MI Definition

Third Universal Definition of Myocardial Infarction (MI)

Kristian Thygesen, Joseph S. Alpert, Allan S. Jaffe, Maarten L. Simoons, Bernard R. Chaitman and Harvey D. White
Circulation. published online August 24, 2012

Key Points: First worldwide consensus document

- **TROPONIN (I or T) - preferred** biomarker overall
- Diagnosis of acute MI-**detection of a rise and/or fall**
- …99th percentile is ***designated*** **as the decision level** for **the diagnosis of MI** and must be determined for each specific assay with appropriate quality control in each laboratory
  - Assays with CV >20% at the 99th percentile URL should not be used
  - Blood samples for the measurement of cTn should be drawn on first assessment and repeated 3– 6 h later
  - Updated definitions for five different types of MI to include post-PCI and research

MI Definition: Follow-up Article

Clinical implications of the Third Universal Definition of Myocardial Infarction

White HD, Thygesen K, Alpert JS et al

Heart 2013;00:1–9. doi:10.1136/heartjnl-2012-302976

Summary:

- Comparative update from previous 2000 and 2007 Universal Definitions to the 2012 Third Universal Definition of MI
- Overview of the recommendations by category with a focus on clinical implications and practice considerations

"The new MI definition has important changes, which have been achieved by international consensus. It is hoped that they new definition will be embraced worldwide and be used to improve patient care."

Troponin Definitions Made Easy

Coefficient of variation –

When the test is run multiple times on the same sample how frequently do you get the same result? The standard answer is rarely, if ever.

So in real world terms, this is measured by running the sample at least 20 times and identifying the % of variation within that set of results.

The 3rd Universal of MI allows from 10% to 20%

99th percentile –

Troponin is fairly unique as one of the few analytes where a 99% reference range is recommended.

The reason for this recommendation is that the goal of early prediction is to pick up that result as early in the elevation cycle as possible.

In the case of **Analyzer X** the published 99th % is 0-0.07 ug/ml, meaning that when 100 "normal" patients with heart disease were tested 99 of the results fell between 0 and 0.07. Results outside that range would then be considered "positive".

Troponin Definitions Made Easy

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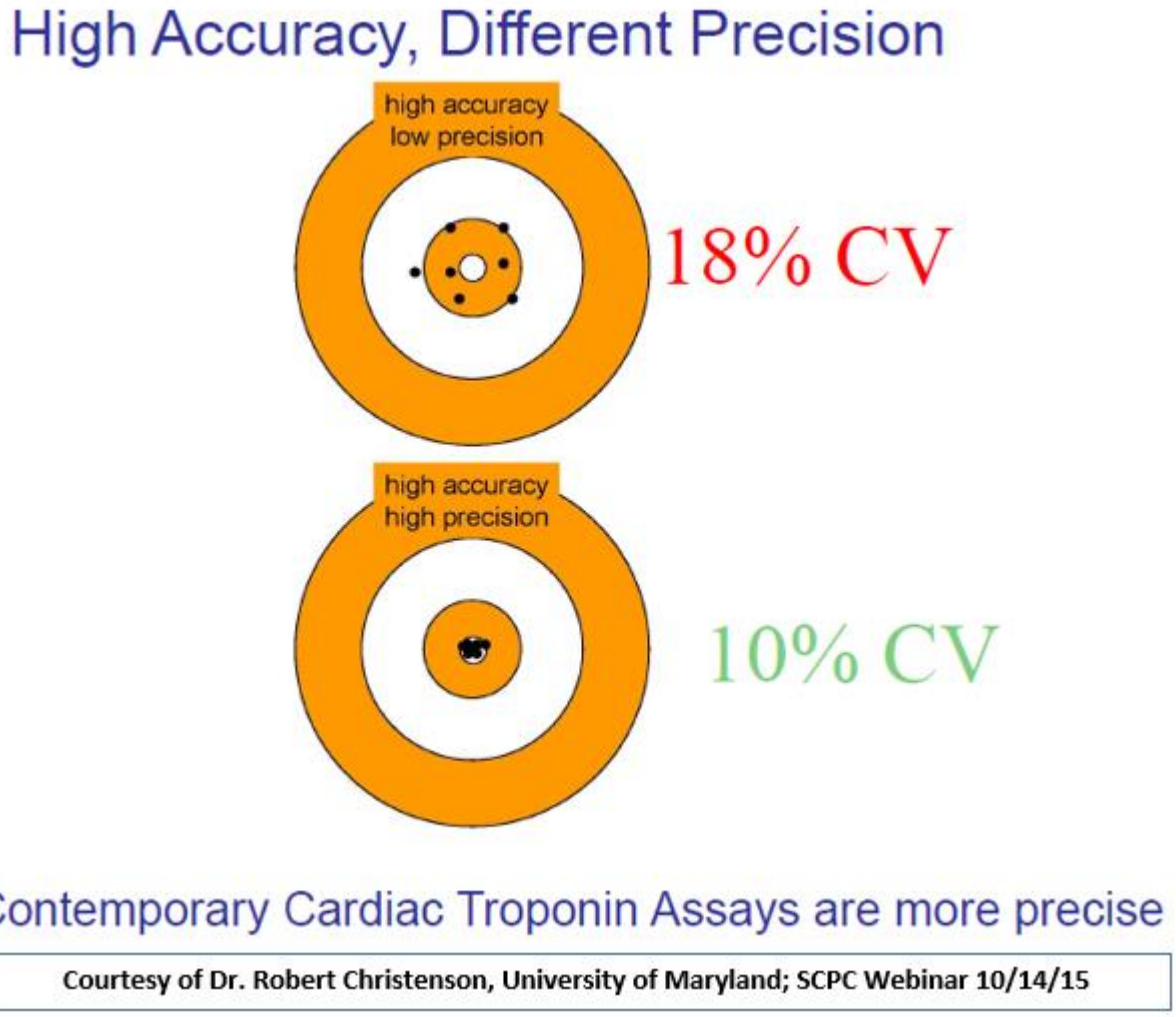


Understanding the definition of MI

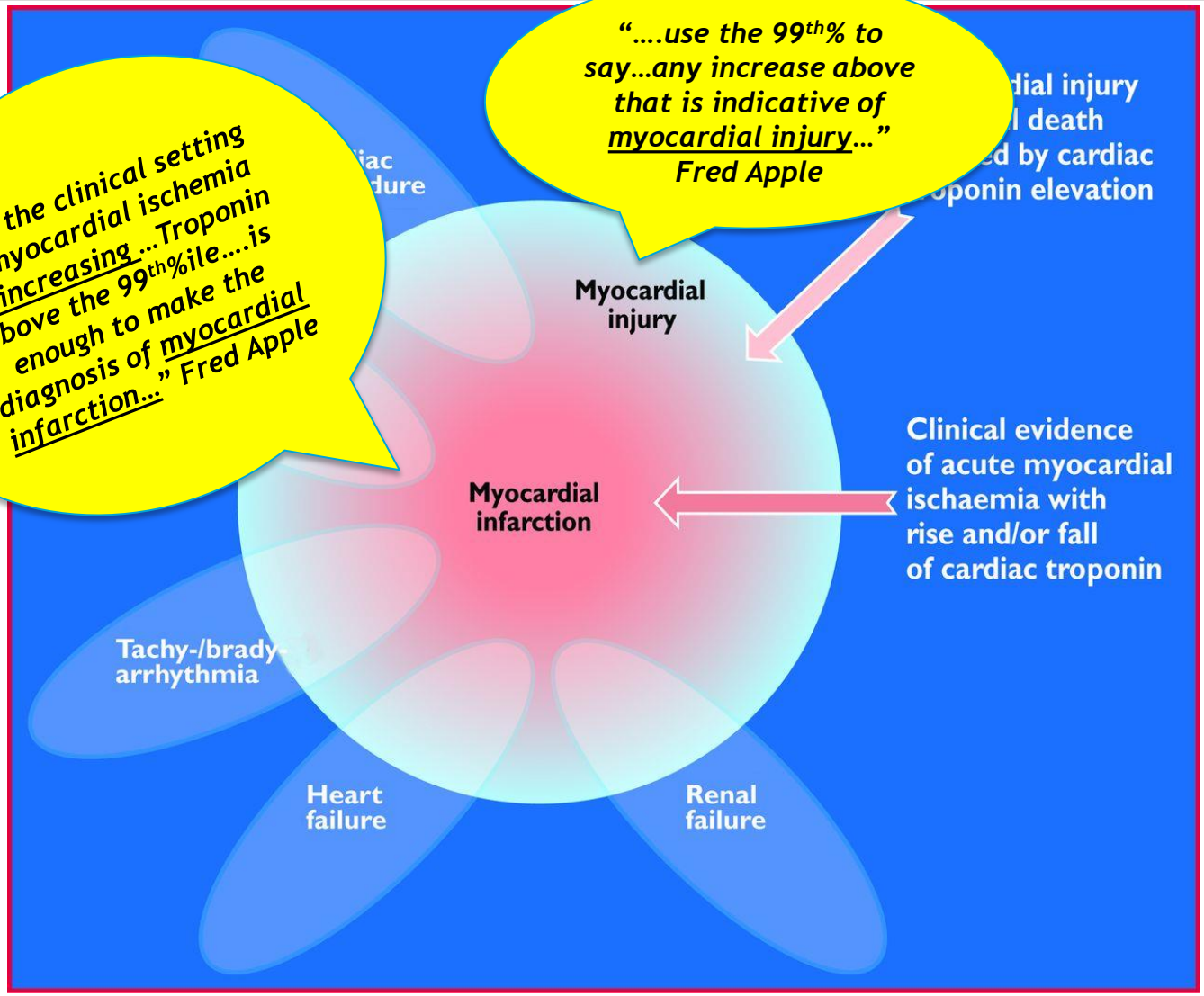
Dr. Fred Apple:

Currently, the guidelines are predicated on the 99th percentile of cardiac troponin, and we use that 99th percentile first to say, any increase above that is indicative of myocardial injury, number one.

Secondly, we use that cutoff to say that in the clinical setting of myocardial ischemia and an increasing cardiac troponin above the 99th percentile, those two criteria are enough to make the call of a diagnosis of myocardial infarction.

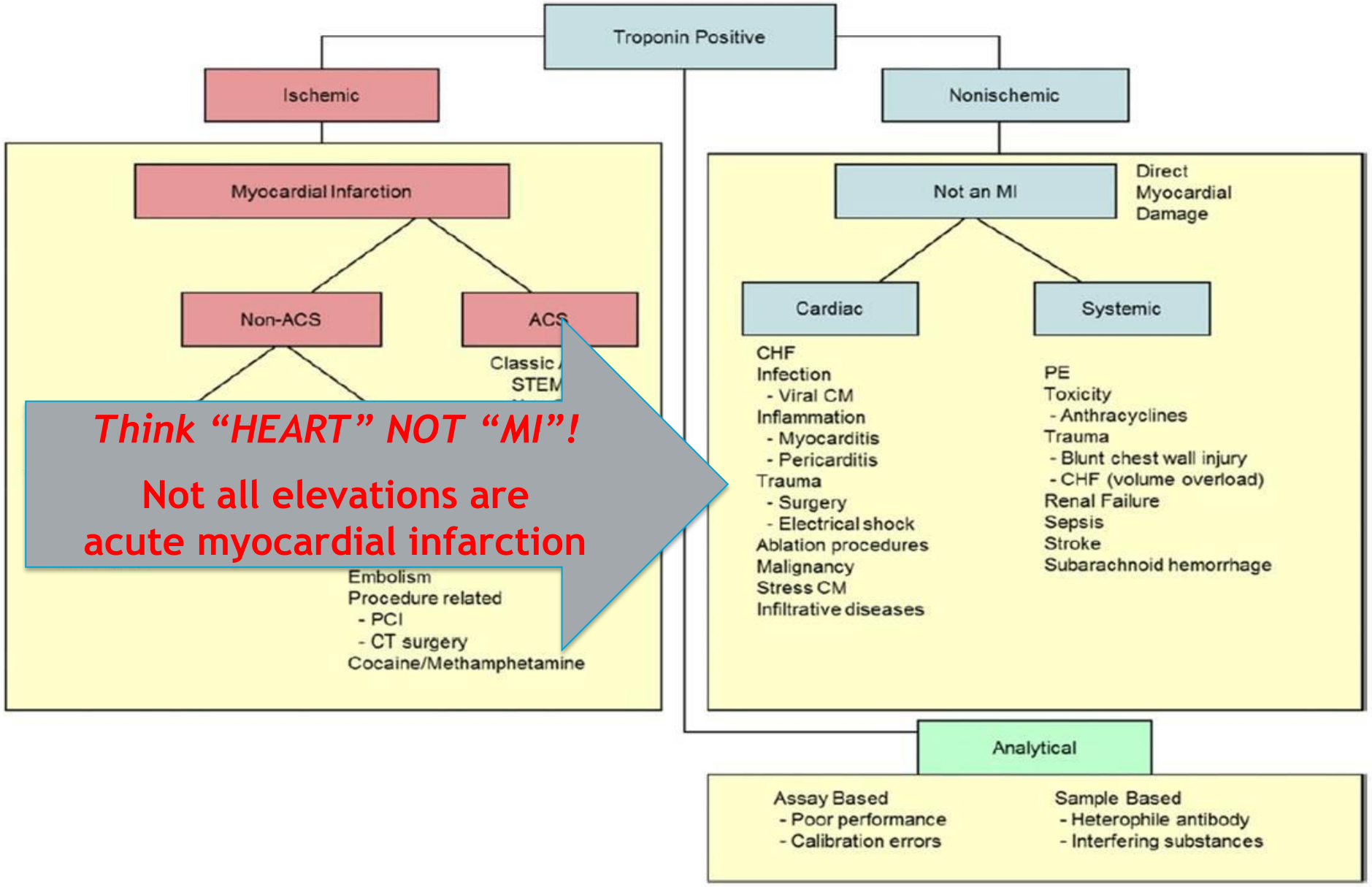
Clinical Chemistry PODCAST – May 2009 with Dr. Fred Apple –Professor of Laboratory Medicine in the Department of Laboratory Medicine and Pathology at the University of Minnesota and Medical Director of Clinical Laboratories and the Clinical Chemistry and Toxicology Laboratories at Hennepin County Medical Center

Third Universal Definition of MI



Thygesen K et al. Circulation 2012;126:2020-2035

American Heart Association
Learn and Live



ACCF 2012 Expert Consensus Document on Practical Clinical Considerations in the Interpretation of Troponin Elevations. (2012). Newby LK, Journal of the American College of Cardiology, 60 (23), 2012.

Explanation of the 99th Percentile

How to Interpret Elevated Cardiac Troponin Levels

Vinay S. Mahajan, and Petr Jarolim

Circulation: Volume 124(21):2350-2354; November 22, 2011

Summary:

- "The use of the 99th percentile cutoff for cTn positivity does not imply that 1% of the population suffers from myocardial damage.

- Rather, this cutoff is useful only when applied to patients with **a high pretest probability** of ACS.

- The clinician must interpret cTn results in the context of clinical history, ECG findings, and possibly cardiac imaging to establish the correct diagnosis.

- A positive troponin in the setting of a low pretest probability for ACS may be suggestive but clearly is not indicative of a coronary event."

Updated 2014 Non-ST-Elevation ACS

2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ. 2014 ACC/AHA guideline for the management of patients with non–ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines..
Circulation. published online September 2014

- A full revision of the 2007 ACCF/AHA clinical practice guidelines (CPG) for the management of patients with unstable angina (UA) and non–ST-elevation myocardial infarction (NSTEMI) and the 2012 focused update.
- The new title, "Non–ST-Elevation Acute Coronary Syndromes," emphasizes the continuum between UA and NSTEMI. At presentation, patients with UA and NSTEMI can be indistinguishable and are therefore considered together in this CPG.
- Supports the **Third Universal Definition of MI** for Troponin and Serial Testing

2014 Non-ST-Elevation ACS Guideline

Standing orders should no longer include:

CK-MB
MYO
Total CK

Class I

- **Cardia…nin (troponin I or T when a contemporary assay is used) levels should … presentation and 3 to 6 hours after symptom onset in all patient…ith symptoms consistent with ACS to identify a rising and/or falling …f Evidence: A)**
- **Additio…vels should be obtained beyond 6 hours after symptom onset in pati…oponins on serial examination when electrocardiographic ch…ntation confer an intermediate or high index of suspicion for A…e: A)**
- **If the tim…n onset is ambiguous, the time of presentation should be considered t…e of onset for assessing troponin values. *(Level of Evidence: A)***

Class III: No Benefit

- **With contemporary troponin assays, creatinine kinase myocardial isoenzyme (CK-MB) and myoglobin are not useful for diagnosis of ACS. *(Level of Evidence: A)***

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.*J Am Coll Cardiol*. 2014;64(24):e139-e228. doi:10.1016/j.jacc.2014.09.017.

Examples: Orders

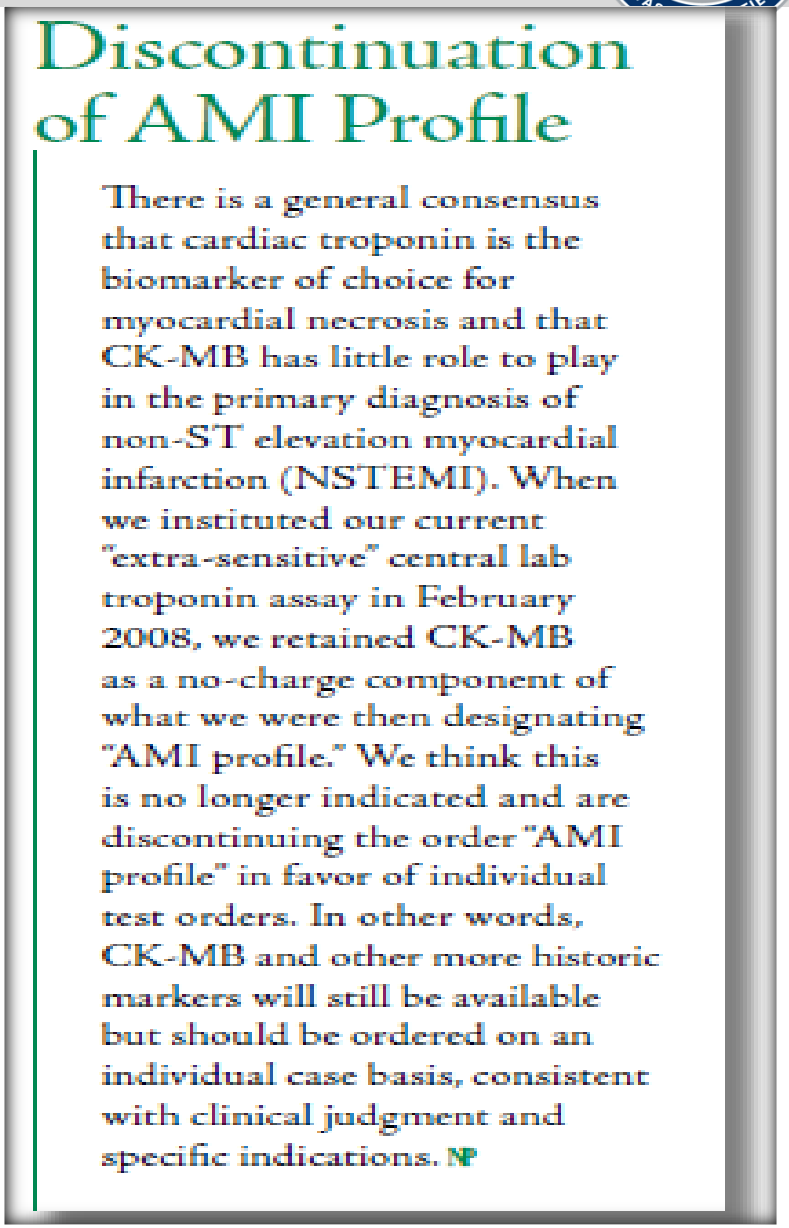
No pre-checked panel:
Serial strategy and use of 99th percentile consistent with guideline recommendations

Diagnostic:	ECG: ❑Repeat ECG at 3 hours and 6 hours after initial ECG, then ECG in am. ❑ECG at the following times: _____, _____, _____. Repeat ECG prn for symptoms suggestive of new, ongoing, or worsening chest pain or S/S of Acute Coronary Syndrome. *Notify physician.
	❑CXR-PA and Lat
	❑Other:_____
Labs:	Repeat Troponin-I at 3 hours and 6 hours after initial Troponin, Notify MD if Troponin greater than 0.06. ❑CK ❑CKMB ❑BMP in am ❑CBC in am ❑Fasting Lipid Panel in am ❑HgA1c in am ❑TSH in am ❑Other_____

Example: Laboratory Bulletin

Laboratory Bulleting with clear guidance to physicians.

Clinical Pathology News for the Medical Community
A Publication of Lexington Medical Center, October 2009
Source: web www.lexmed.com/medical_services/laboratory.htm



Discontinuation of AMI Profile

There is a general consensus that cardiac troponin is the biomarker of choice for myocardial necrosis and that CK-MB has little role to play in the primary diagnosis of non-ST elevation myocardial infarction (NSTEMI). When we instituted our current "extra-sensitive" central lab troponin assay in February 2008, we retained CK-MB as a no-charge component of what we were then designating "AMI profile." We think this is no longer indicated and are discontinuing the order "AMI profile" in favor of individual test orders. In other words, CK-MB and other more historic markers will still be available but should be ordered on an individual case basis, consistent with clinical judgment and specific indications. NP

MI Definition: Follow-up Article

How to Use High-Sensitivity* Cardiac Troponins in Acute Cardiac Care

Kristian Thygesen et al

European Heart Journal doi:10.1093/eurheart/ehs154 PDF online 2012

Summary Regarding Use of hsCardiac Troponin in Clinical Routine:

- Use 99th%ile concentration
- Serial testing…a minimum change of >20% in follow-up testing is required
- Blood sampling …admission and 3 h later…repeated 6 h after admission in patients of whom the 3 h values are unchanged but…clinical suspicion of A is still high
- Other markers, such as myoglobin or creatine kinase MB no longer needed

* High-Sensitive Troponin are not approved in the U.S.

Changing Perspectives of Turn-Around-Time (TAT) Tracking:
Accountability and Accreditation requirements

TAT Tracking: Healthcare Implications

July 2014 Clinical Laboratory News: Volume 40, Number 7

What Does Turnaround Time Say About Your Lab?

Key Quotes:

- " Every laboratorian knows that their colleagues in medicine see TAT as something almost as important as the quality of test results themselves."
- " In fact, surveys have found that 80% of labs get complaints about TAT."

TAT Tracking: Healthcare Implications

Studies and research support the following:

- Assessing the “whole process” (i.e.: arrival)
- Standardizing the definitions of turn-around-time (TAT)
- Assessing TAT with patient outcomes and length of stay

TAT Tracking: Healthcare Implications

Study by Ervasti et al, *Clin Chem Lab Med 2008*

Proposed new concepts for TAT in the diagnostic process:

As a "Patient-oriented" view or the "whole process"

- **Diagnostic TAT -** arrival to reporting of results
  - outcomes median 122 min
- **Clinical TAT** - arrival to order
- **Laboratory TAT -** order to report/resulted

TAT Tracking: Healthcare Implications

In *Academic Emergency Medicine*, *2010:17*, Hwang et al noted:

"Guidelines do not exist delineating times frames for when a troponin test should optimally be resulted in association with improved patient outcomes."

" Prolonged laboratory TAT may delay recognition of conditions in the acutely ill , potentially affecting clinician decision-making and the initiation of timely treatment."

- Outcomes median 107 minutes; "ordered to resulted"

.

SCPC Cardiac Biomarker Requirements

- Measuring TAT is and has been a guideline driven recommendation for many years
- No previous TAT requirements from any organization until…
  - 2012: CMS OP 16 requiring compliance for "Door-to-Result in 60 minutes"
    - initiated and then revoked
    - not reinstated to date
- SCPC requirement started in 2012
    - CPC to track and demonstrate improvements
- SCPC requirements continue to date
    - Review guideline compliance; patient-level data reviewed

Time is muscle – think HEART!

OLD	NEW
Door to ECG = 10 minutes	Door to ECG READ within 10 minutes
Door to Reperfusion = 90 minutes	Door to Reperfusion "*as soon as possible*"
	First Medical Contact (FMC) to Reperfusion < 90 minutes
TRANSFER: Door in - Door out = 30 minutes	Door in - Door Ready = 25 minutes
Door to Thrombolytics = 30 minutes	Same consideration; low utilization
Lab received to results = 60 minutes	Door to Troponin Results in 60 minutes (*facility sets % compliance - recommend setting at 75%)*
Order/Collect to results = 60 minutes	% compliance = 90%
NEW CONCEPTS: GOLDEN HOUR for the HEART	
STEMI is a heart trauma: think 60 minutes from "door"	
NEW GOAL: Door to Reperfusion in 60 minutes (60%)	
Troponin decision: think 60 minutes from "door"	

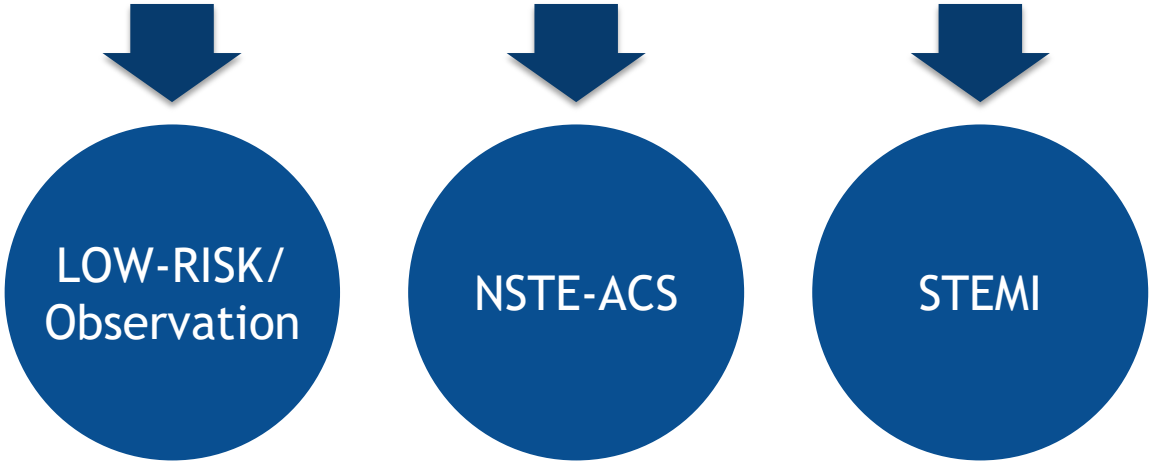
CPC: Patient Population Focus

Dual Challenge with Managing Chest Pain Patient Populations

Vague Symptomology

Combining 'Rule Out' Process with 'Diagnosis' Process
(treat as ACS until proven otherwise)

RISK STRATIFICATION IS THE KEY



CPC: RISK STRATIFICATION MODEL

Emergent Risk Assessment Must Include:

1. Symptomology Evaluation
2. ECG Completed and Read within 10 Minutes
3. Troponin: Turn Around Time (TAT)*
4. Risk Scoring Mechanism: ex. TIMI, GRACE, or other form founded in science

1. Facility Defined Evidence-Based Risk Stratification Model
2. Consistently Utilized and Documented by Facility's Providers (order-set, flowcharts, patient's chart)

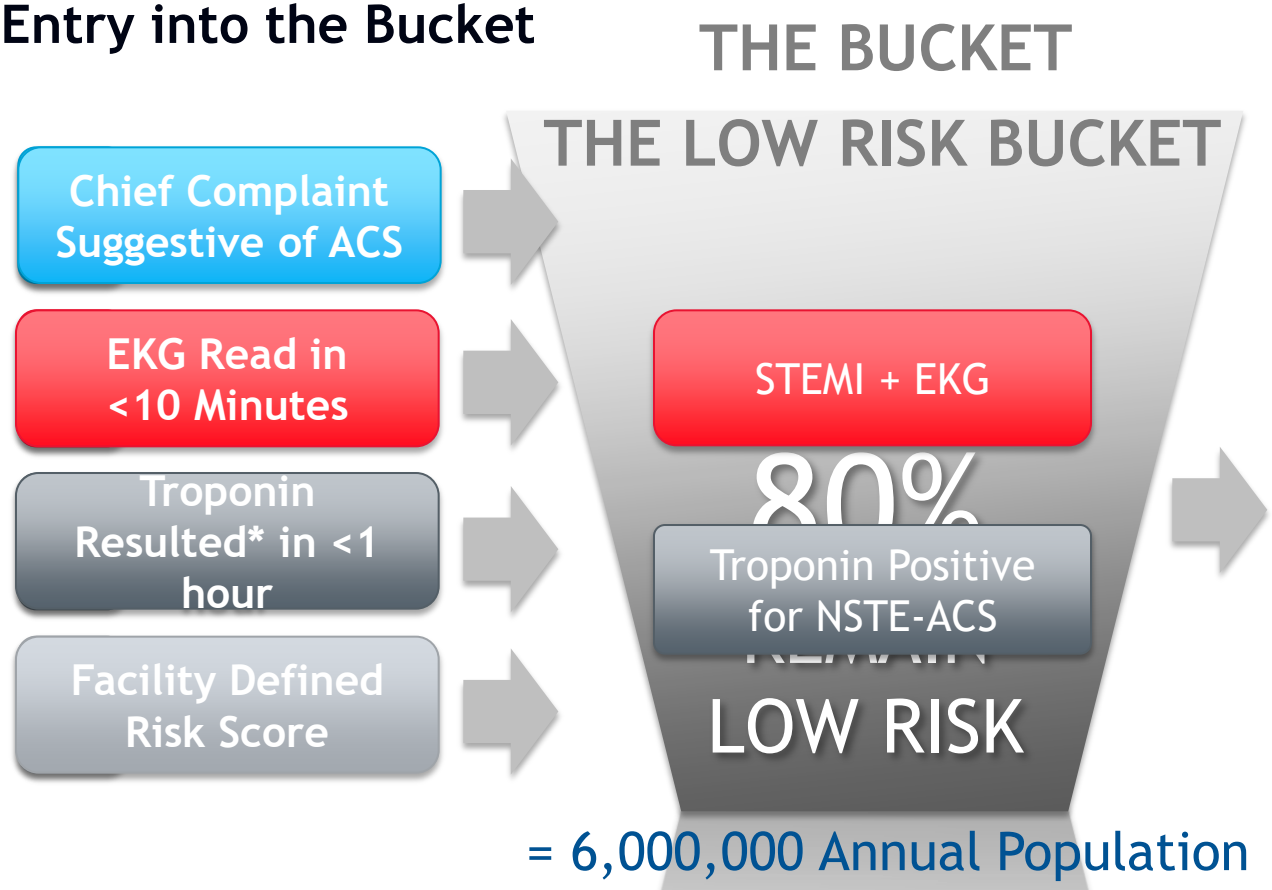
*Turn-around time requirements are explained in the appropriate accreditation tools

Risk Stratification: LOW-RISK

Emergent Risk Assessment Must Include:

- **Entry into the Bucket**

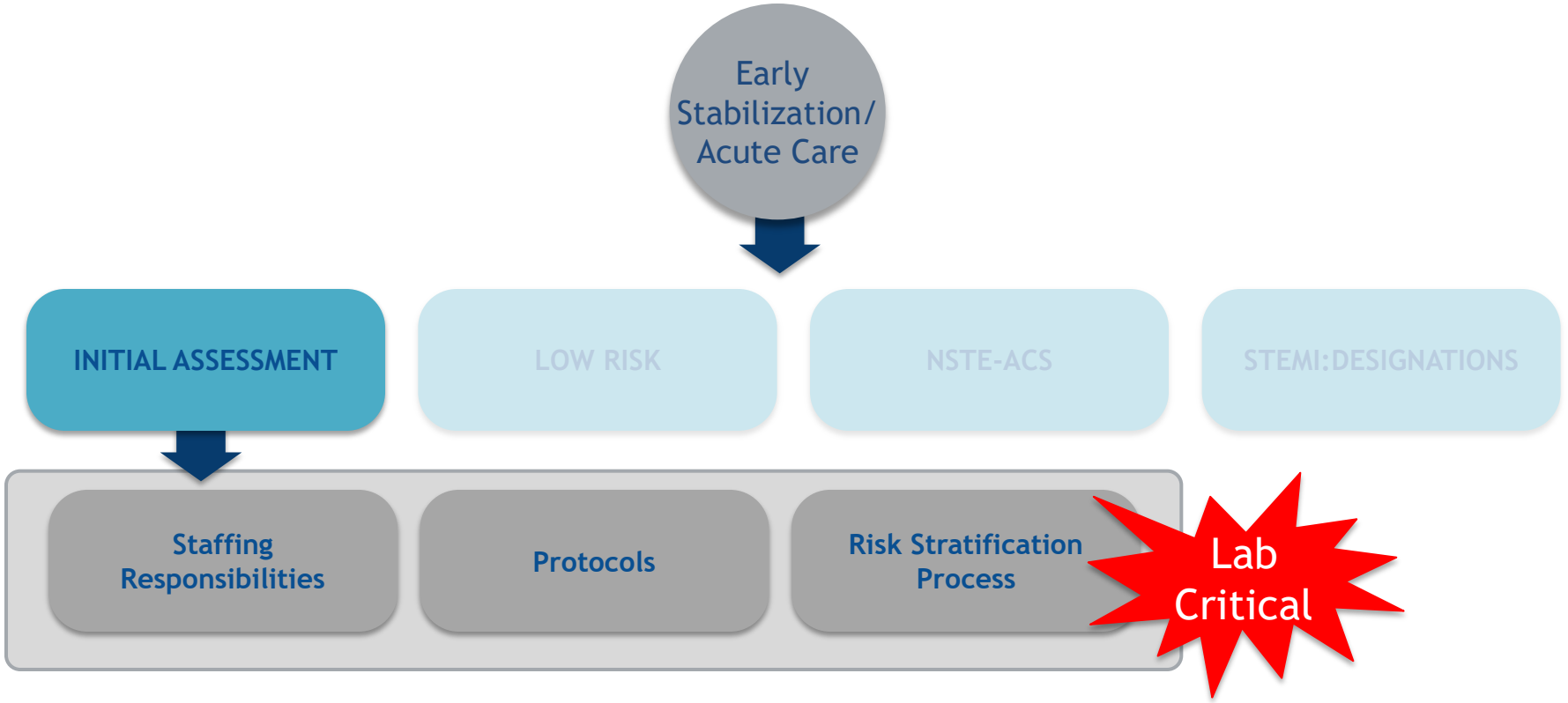
Removal from the Bucket



= 6,000,000 Annual Population

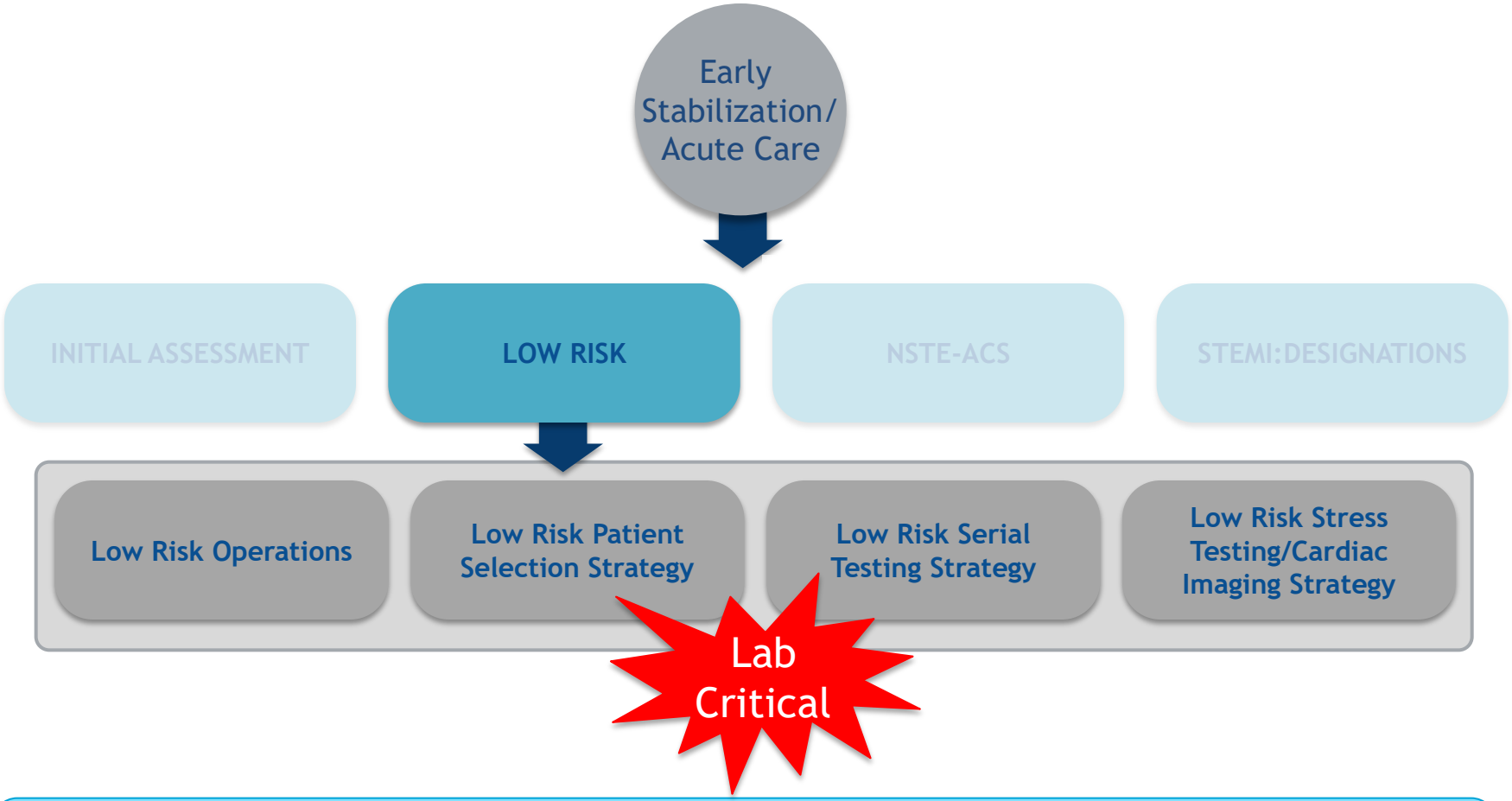
*Turn-around time requirements are explained in the appropriate accreditation tools

CPC v5: Framework



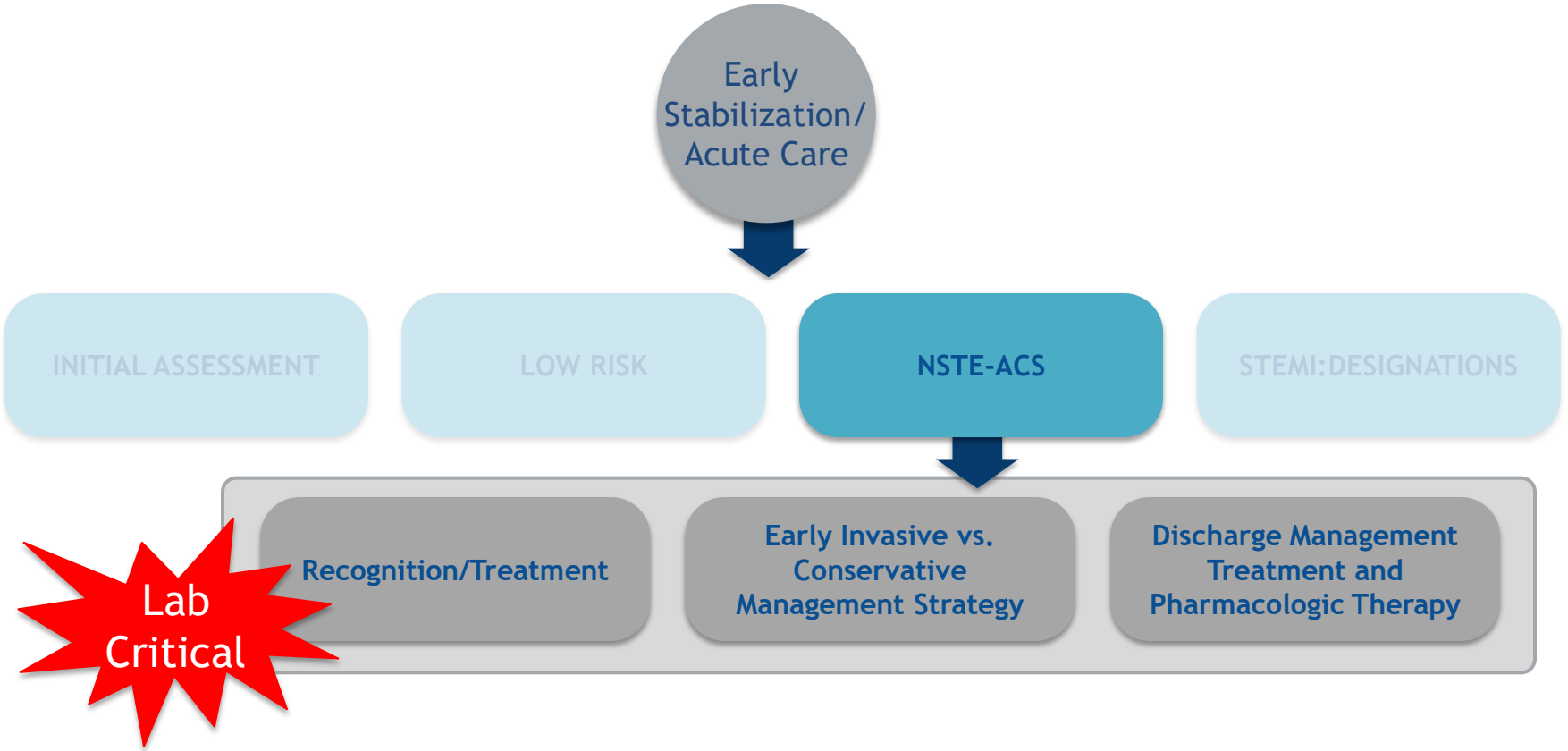
Laboratory participation for assistance with TAT tracking to assess PROCESSES; now begins at the "door" for both POCT and Central Lab and measured through "results"

CPC v5: Framework



Laboratory engagement in the LOW-RISK and NSTE-ACS processes of care for serial Troponin strategies is vital in multiple areas to include the entire ACS continuum for ED, Observation and In-Patient

CPC v5: Framework



Laboratory engagement in Risk Stratification strategies will be assessed to include adherence to the guidelines for standardization in timing, use of 99th%ile; eliminating outdated markers and "*gray-zone*"; providing interpretive results

Accreditation: Process Requirements

"To the extent that laboratory test TAT is only one factor impacting

ED length of stay and patient outcomes,

it is unlikely that POCT alone, in the absence of an interdepartmental approach to ED operations,

will produce measurable improvements in outcomes."

Lewandrowski, E. et al. Cardiac Marker Testing As Part Of An Emergency Department Point-of-Care Satellite Laboratory In A Large Academic Medical Center. Practical Issues Concerning Implementation. Point of Care. The Journal of Near Patient testing & Technology. 08/2002 Vol. 1, No.3, pp. 145-154.

CYLE III & IV: SCPC GENERAL FINDING

(results for discussion purposes only)

- Cycle III FIB data: n=700
  - 65% [illegible] 99th percentile
  - 50% [illegible]
- Cycle IV FIB data YTD
  - 77% using the 99th percen[illegible]
    - Of those, 87% -using manufa[illegible]ndations
  - 40% using POCT
    - Of those, 78% using Troponin only (no[illegible])

No previous validation of accuracy

Changing Perspectives: Literature Findings

Per Amsterdam et al in a Circulation 2010 article:

"Testing of Low Risk Patients Presenting to the ED with Chest Pain"

"…current studies have confirmed that contemporary troponin assays can identify the majority of MI's within 3 hours of ED arrival…"

IFCC Example

The International Federation of Clinical Chemistry (IFCC)

Supporting documentation on all assays specifications

Last update: Nov 2014

Website:
http://www.ifcc.org/ifcc-scientific-division/documents-of-the-sd/troponinassayanalyticalcharacteristics/

Commercially available assays - Company/ platform(s)/ assay	LoB [a] (µg/L)	LoD [b] (µg/L)	99th % (µg/L)	%CV at 99th %	10 % CV (µg/L)
Abbott AxSYM ADV	0.02		0.04	14.0	0.16
Abbott Architect	<0.01		0.028	14.0	0.032
Abbott Architect *STAT* hs-cTnI [e]	0.0007 - 0.0013	0.0011 - 0.0019	0.0262 M: 0.0342 F: 0.0156	4.0 M: 3.5 F: 5.3	0.0047
Abbott i-STAT	0.02		0.08	16.5	0.10
Alere Triage SOB	0.05		NAD	NA	NA
Alere Triage Cardio 3	0.002	0.01	0.02	17.0	0.04
Beckman Coulter Access Accu	0.01		0.04	14.0	0.06
bioMerieux Vidas Ultra	<0.01	<0.01	0.01	27.7	0.11
Mitsubishi PATHFAST cTnI [e]		0.001	0.020	5.2	0.0031
Mitsubishi PATHFAST cTnI-II [f]	0.002	0.008	0.029	5.0	0.014
Ortho VITROS Troponin I ES	0.007	0.012	0.034	10.0	0.034
Radiometer AQT90 FLEX TnI		0.0095	0.023	17.7	0.039
Radiometer AQT90 FLEX TnT		0.0080	0.017	15.2	0.026
Response Biomedical RAMP	0.03		0.1	20.0	0.21
Roche Cardiac Reader cTnT	0.03		NAD	NA	NA
Roche cobas h 232 TnT	0.05		NAD	NA	NA
Roche E 2010 /cobas e 411 / E 170 / cobas e 601 / 602 TnT (4th gen)	0.01		NAD	NA	0.03
Roche E 2010/cobas e 411 / E 170 / cobas e 601 / 602 hs-TnT		0.005	0.014	10.0	0.013
Roche E 2010/cobas e 411 / Roche E 170/cobas e 601 / 602 cTnI		0.16	0.16 [c]	NA	0.3
Siemens ADVIA Centaur® TnI-Ultra™	0.006		0.04	8.8	0.03
Siemens Dimension® EXL™ TNI	0.010	0.017	0.056	10.0	0.05
Siemens Dimension® RxL CTNI	0.04 [d]		0.07	15 - 22	0.14
Siemens Dimension VISTA® CTNI	0.015		0.045	10.0	0.04
Siemens IMMULITE® 1000 Turbo [e]	0.15		0.30	14	0.59
Siemens IMMULITE® 1000 [e]	0.1		0.19	11	0.22
Siemens IMMULITE® 2000 XPi [e]	0.2		0.29	10.3	0.32
Siemens IMMULITE® 1000 Turbo [f]	0.15		NA	NA	0.64
Siemens Stratus® CS cTnI	0.03 [d]		0.07	10.0	0.06
Tosoh ST AIA-PACK	0.06		0.06 [c]	8.5	NA

CPC v5: Framework

EC4.M1d: Serial troponin strategy is defined in an evidenced-based standardized protocol that is **consistent with the assay used.** Supporting documentation must include:		
EC4.M1d1	Manufacturer and assay used in central lab	
EC4.M1d2	Manufacturer and assay used for POC testing	
EC4.M1d3	Decision cut point for positive test for both central lab and POC (*where applicable*)	
EC4.M1d4	Decision cut point for negative test for both central lab and POC (*where applicable*)	
EC4.M1d5	99th percentile for both central lab and POC *(where applicable)*	
EC4.M1d6	Coefficient of variation at the 99th percentile for both central lab and POC *(where applicable)*	
EC4.M1d7	Protocol and policies define the standardized timing used	

CPC v5

Lab specific assessments are now part of the tool

For both CENTRAL LAB and POC Troponin

Troponin assessment:

- Manufacturer
- Analyzer
- 99th Percentile
- Coefficient of Variation at 99th%
- Review use of outdated assays

- Reviewing ***Interpretive Comments*** to ensure they are current to the guidelines
- Reviewing ***Instructions for Use IFU*** to validate Troponin precision
  - IFU document language are rarely updated due to FDA rules
  - Ensuring facilities are not using or referencing outdated WHO criteria from IFU
  - More current assays include current guideline language in IFU

CPC v5

For both CENTRAL LAB and POC Troponin

- Participation requirement by Lab personnel in CPC meetings
- Definition of baseline timing for serial strategy (ie: ED arrival versus 1st lab draw)
- Nursing staff whose focus is on the ACS patient (STEMI/ NSTE-ACS/ LOW-RISK) must receive annual education on cardiac biomarkers (CBM)

- **NEW-MANDATORY Requirement = 50% participation in CPC (or appropriate) committee meetings**
- **Defined protocols & policies of serial strategy throughout the hospital stay continuum**
- **NEW-Educational requirement for CBM – Lab assistance to create education to show hospital compliance of guidelines**

CPC v5

Lab specific assessments are now part of the tool to ensure communication and evaluation takes place

For both CENTRAL LAB and POC Troponin

- Metrics of trends for Troponin TAT - **arrival to result**
  (ACS patients beyond STEMI)
- % compliance TAT **arrival to result** in 60 minutes

- **SCPC ACD and hospital metrics**
- **More stringent than the current guideline requirements**
- **No compliance standard set at this time; no industry compliance standards set however the process is assessed from "door to result"**

Follow-up Article: MI and Serial Strategy

Cardiac Troponin Serial Ordering Recommendations: For Today and Tomorrow

Sara Love, PhD and Fred Apple, PhD

Clinical Lab News, May 2014, vol 40, no. 5

Summary:

- Implementation practices by facility addressing updated 2012 MI definition and the use of the 99th percentile and serial strategies

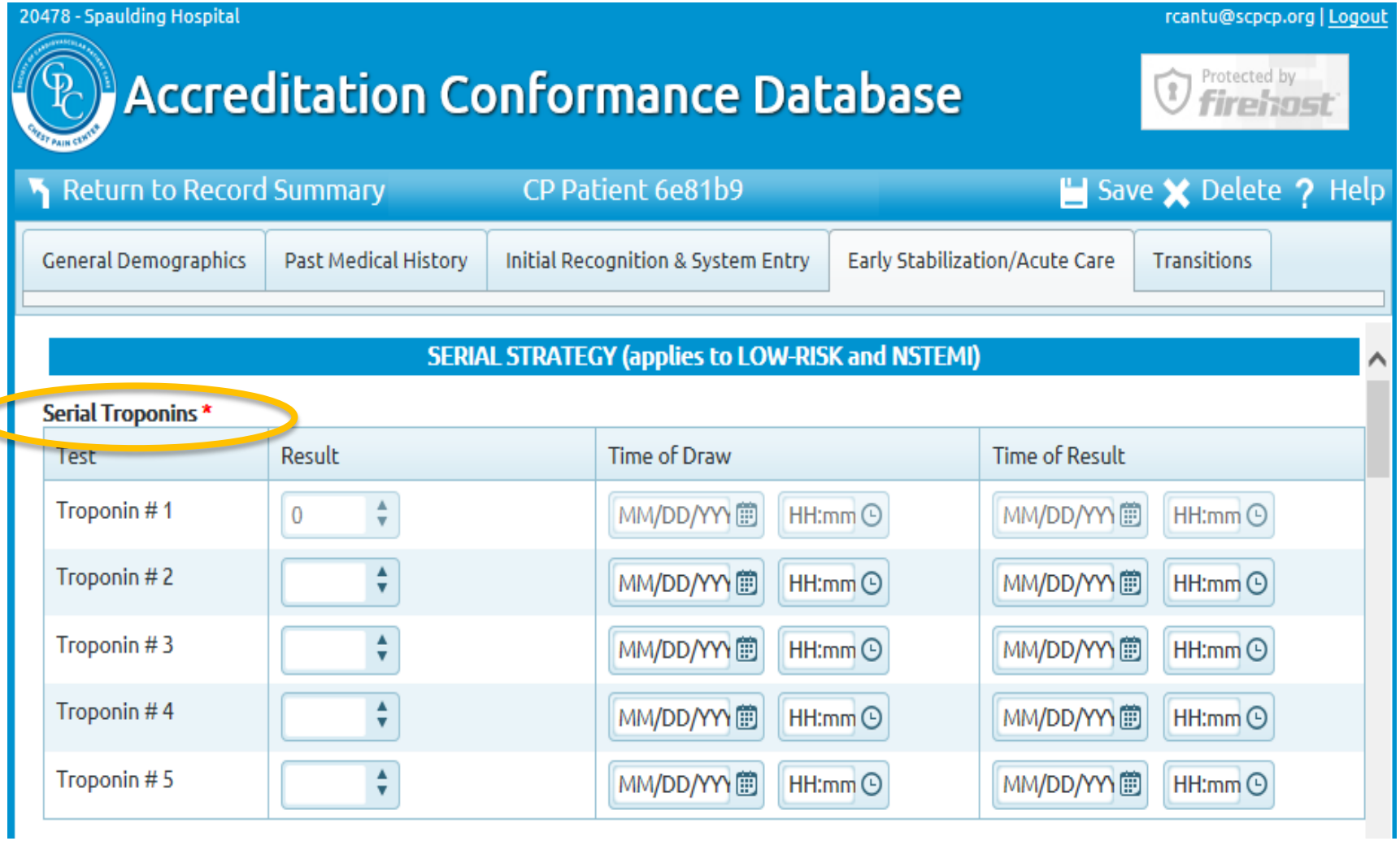
"….serial cTn ordering is a critical component of acute MI diagnosis readily understood in terms of timing, frequency and duration of cTn measurements…"

CPC v5: Serial Strategy Assessment

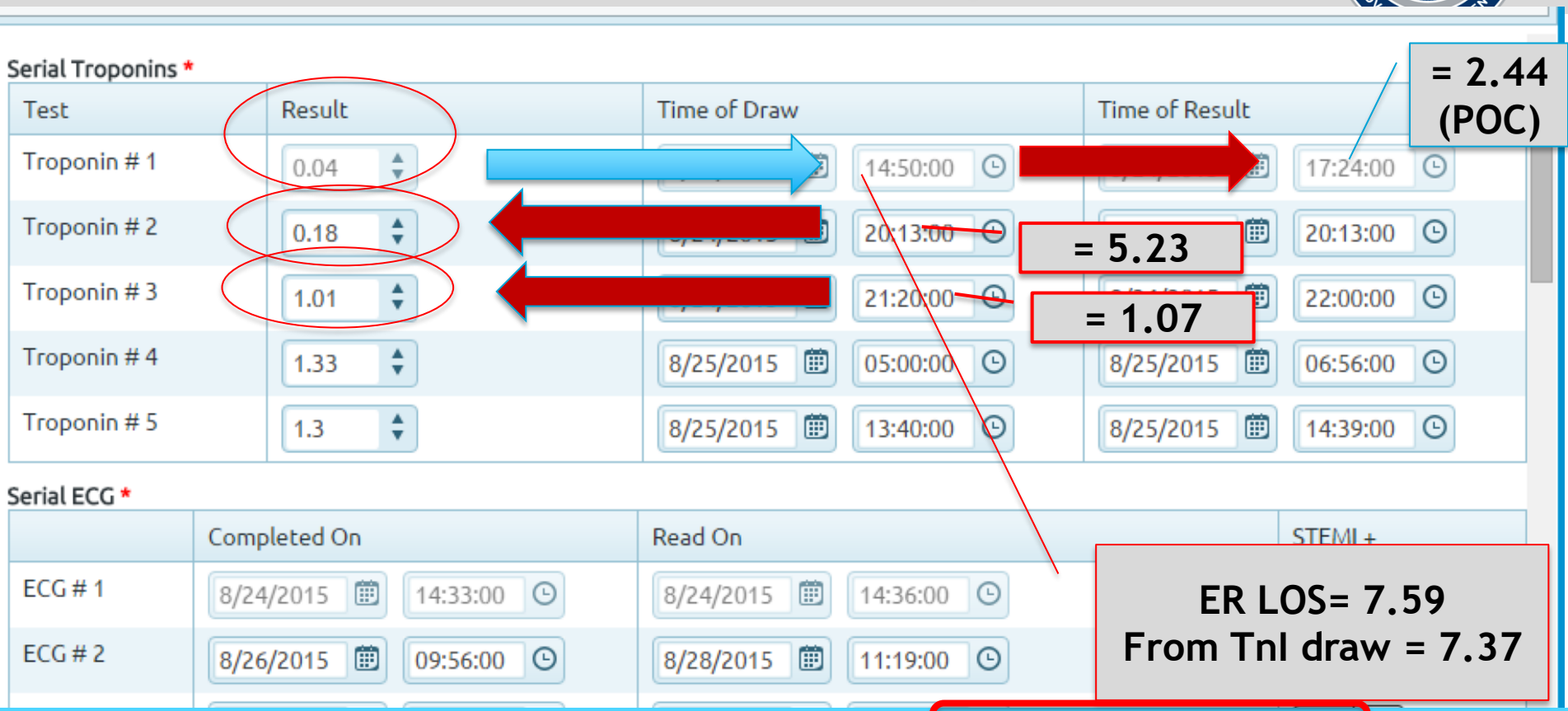
Facilities may still use a 0-6-12 strategy however it will most likely be listed as an "*opportunity*" for review and consideration to accelerate the diagnostic protocol per the updated guideline recommendations and impact on length-of-stay (LOS)

EC4.M1d7	Policies, protocols or orders for Troponin testing demonstrating the facility serial strategy. Facilities cannot use a serial strategy that is q8x3 as this is no longer the recommendation in the guidelines. The serial strategy must be standardized as demonstrated on the order-sets and flowcharts. Also refer to EC4M4a2.
EC4.M4a2	Timing between serial troponins are standardized throughout the facility *(Examples of timing strategy may include: 0, 2, 6 - 0, 3, 6 - 0, 3, etc. Duration of serial strategy may also be as short as three 3 hours using sensitive troponins, or troponin deltas if provocative cardiac testing or imaging takes place)*

v5: Serial Troponin Line Item Evaluation



CPCv5: TROPONIN Case Study



Assay: **Troponin I ED POC**

Negative: ≤ 0.08 / Positive: ≥ 0.09

Assay: **Troponin I Central Lab**

Negative: ≤ 0.045 / Positive: ≥ 0.05

Facility serial strategy: 0-3-6

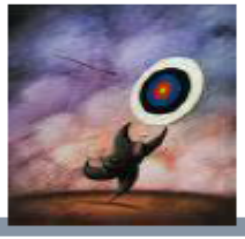
EMS: CP/SOB – arrival at **14:28**

First ECG - Negative

ED Disposition to In-Pt at **22:27**

The infamous “Gray Zone” of Troponin Testing

cTn History—A Moving Target



In early studies, first-generation assays did not consistently out-perform the then-gold standard CK-MB in sensitivity or analytical precision NACB guidelines for cardiac biomarkers, published in 1999

- Two cutpoints,
  - ROC curve used to establish acute MI decision limits.
  - They "Gray Zone" was born
  - Elevations below AMI curve were mainly labeled as false positives or ignored.
  - Risk Stratification was a concept few were believing in at this point.

"That set the stage for using whatever cutoff you want, and the field has never recovered from it,"

Jaffe et al, Clinical Chemistry 2008

2005

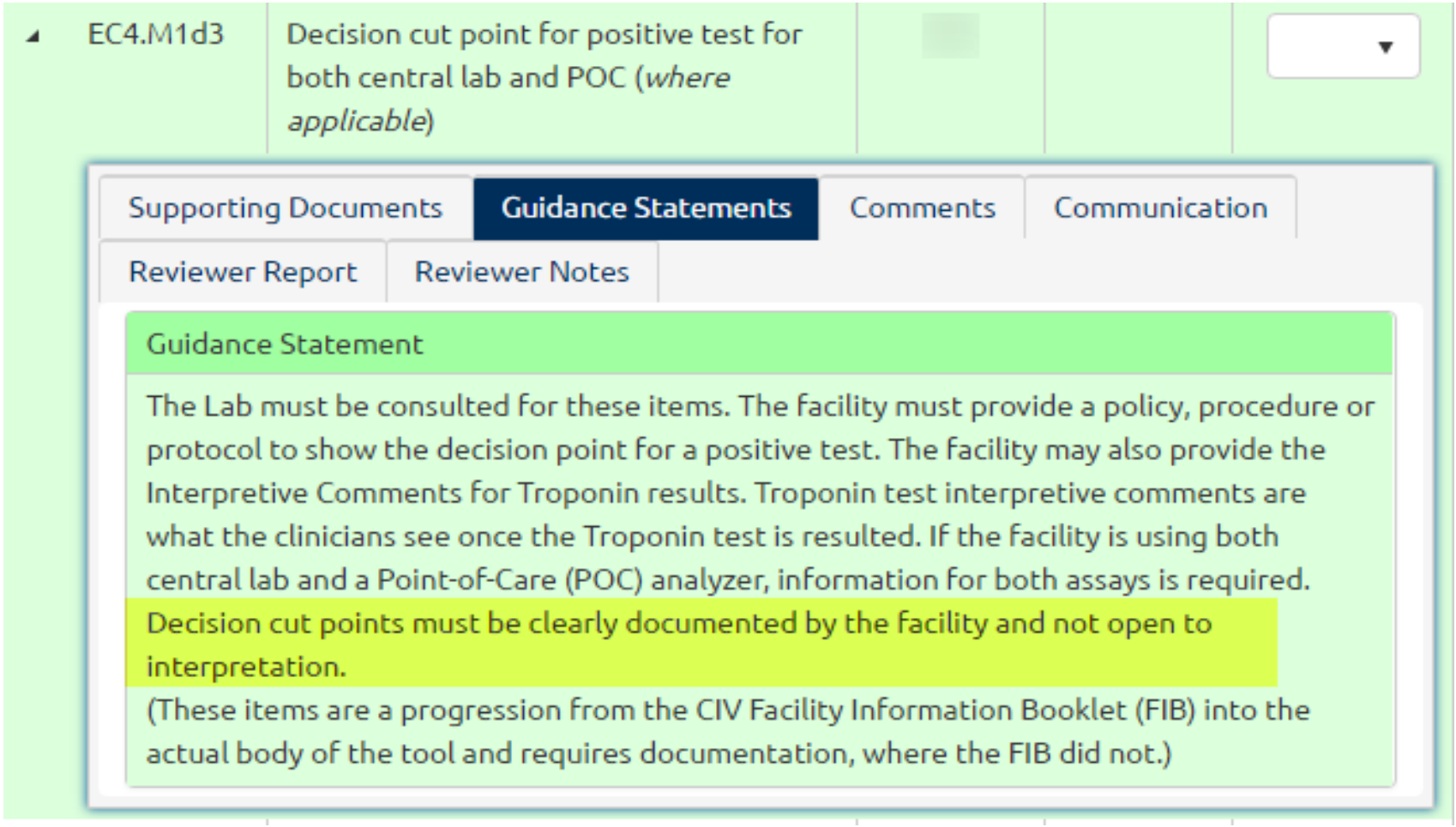
- Introduced the concept of elevations greater than the 99%tile (of a well patient population) with a Coefficient of variation [CV] of 10% or <.
  - Only one or two assays could meet this requirement at that time.
- It did however force the diagnostic industry to a goal of assay performance (moving closer to standardization [harmonization?])

NACB Guidelines Published In 2007

- Represented the first attempt to get all cardiac testing standardized.

Excerpt from internet presentation n.d. "Cardiac Markers: Why all the Confusion?" by R. Heitsman, Radiometer, National Accounts Manager

CP v5 Guidance Language



Interpretive Comments – Assessment of "Gray Zone"

(from actual hospital reporting of results)

- **TROPONIN T (TnT) 0.01 – 0.05** mg/L
- Indicates minimal myocardial damage which with the appropriate clinical and ECG findings may be of prognostic significance in patients with ACS. However levels within this range may also be due to non-ACS causes *e.g. pulmonary embolus, heart failure, CRF, severe sepsis etc.*
- In ACS TnT starts to rise at 3-4h and reaches maximum sensitivity at 12-18h post symptoms and can remain elevated for up to 7-8 days. For exclusion of ACS levels should not be taken before 12h post symptoms.
- **TnT >0.05** mg/L would support a diagnosis of AMI

Using the 99th% ile for decision point? Need more information (see IFCC or other document)

Using a "Gray Zone"? No, there is a negative and a positive

Interpretive Comments – Assessment of "Gray Zone"

TROPONIN I

- <0.04 No evidence of myocardial damage provided sample is at least 12h post symptoms (event).
- 0.04 – 0.48 Suggest minor myocardial damage provided at least 12h post event
- >0.49 Indicates major myocardial damage

- **Using the 99th% ile for decision point? Need more information**
  (see IFCC or other document)
- **Using a "Gray Zone"? YES**

Interpretive Comments – Assessment of "Gray Zone"

TROPONIN I

- <0.04 : Troponin appears normal or minor myocardial damage or other cause
- >0.04 : Consistent with Myocardial Infarction

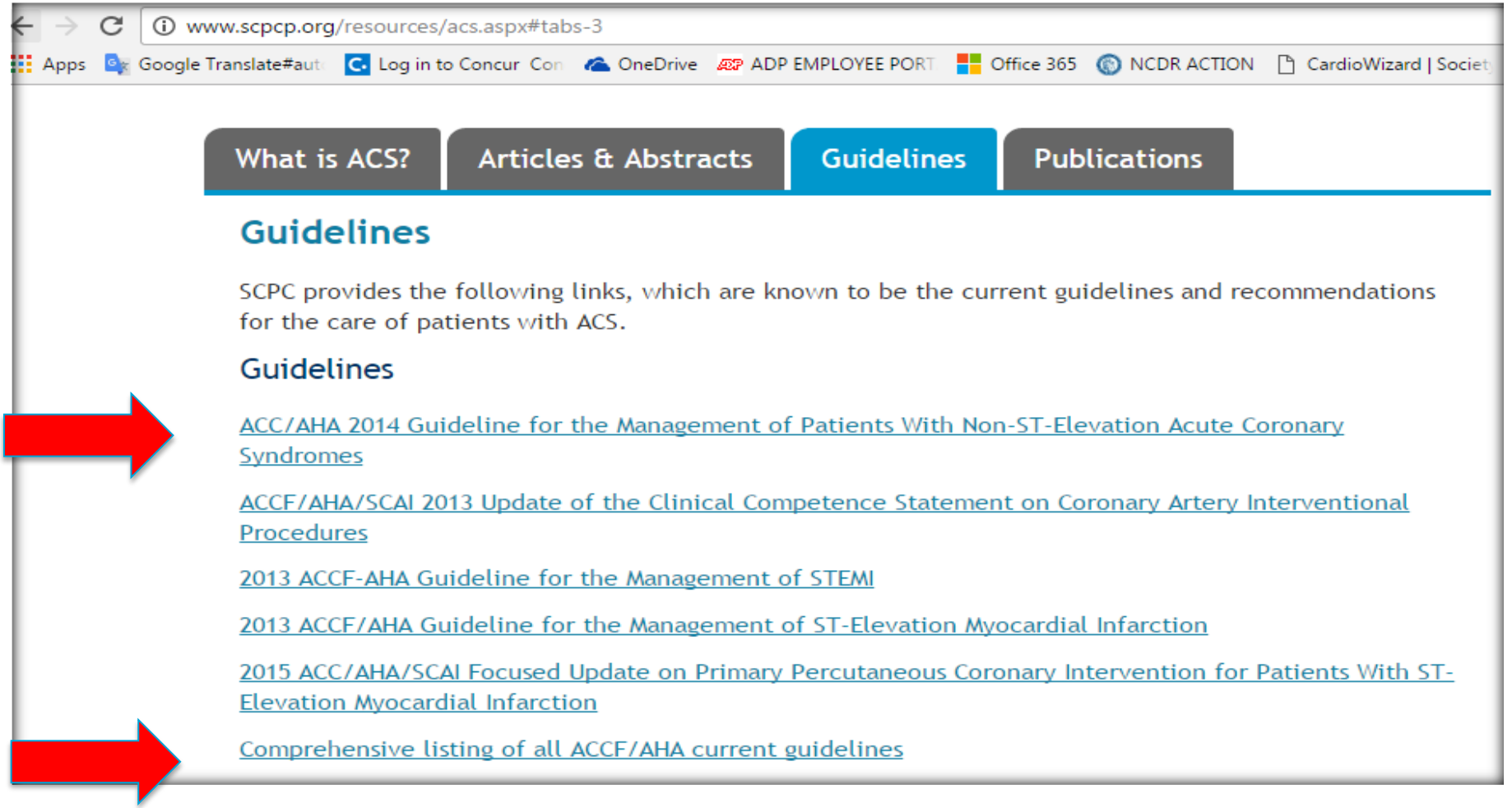
This information is based on the recommendations of the **2012 Third Universal Definition of Myocardial Infarction** for Troponin to be at least one value above the 99th percentile upper reference limit.

- **Using the 99th% ile for decision point? Probably (see IFCC or other document) – also cite the source (may see website links or PDF links)**

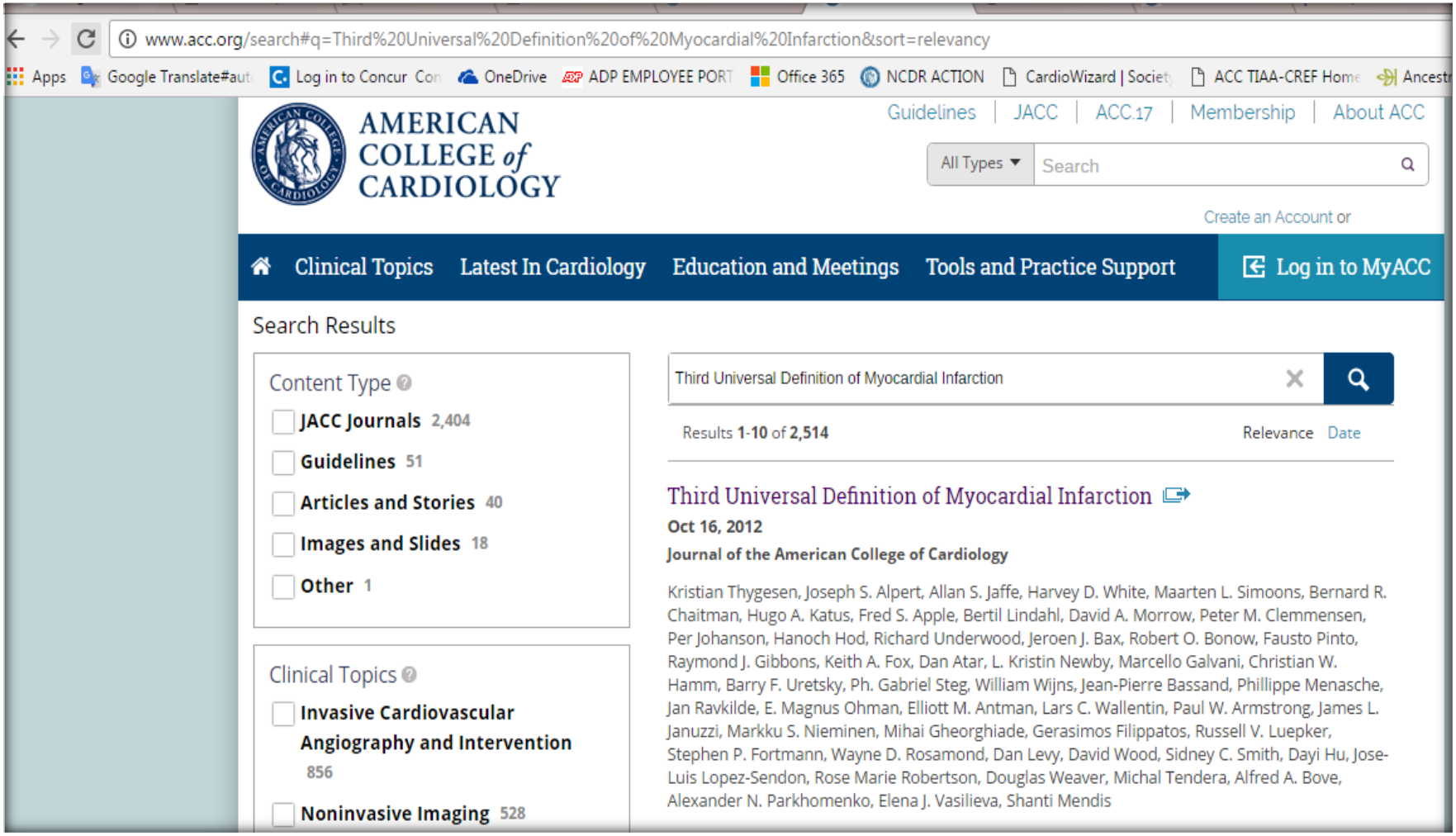
- **Using a "Gray Zone"? No, there is a negative and a positive**

RESOURCES: www.scpcp.org

SCPC Website: GUIDELINES



RESOURCES: www.acc.org



Science tells us what we can do

Guidelines tell us what we should do

Accreditation is the roadmap to implement the “should do”

Registries measure performance on the “should do”

Quality Initiatives & Education are the levers to improvement

SOCIETY OF CARDIOVASCULAR PATIENT CARE

AN INSTITUTE OF THE AMERICAN COLLEGE OF CARDIOLOGY

Thank you!

Ruth Cantu, BSN, RN

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