

**2009 Great Innovations in Cardiology
JMMC**

**5th Joint Meeting with Mayo Clinic
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**Interpretation and misinterpretation of
biomarkers in ACS:
Practical considerations**

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DISCLOSURE

Relevant Financial Relationship(s)

None

Off Label Usage

None

Acute Coronary Syndromes: 2 questions to answer in ER

- Are symptoms and signs due to ACS secondary to underlying obstructive CAD?
- What is risk of adverse event?
 - Death
 - MI or severe ischemia
 - Heart failure
 - Serious arrhythmia

Case #1

- 54 year old man presents after 2 episodes of severe chest pain while at work. First episode 3 hours ago.
- Past history of hypertension. Family hx of CHD. Prior smoker.
- ECG shows transient 1 mm ST depression V_{4-6}
- Patient now pain free

Case #1

What biomarker test(s) would you order?

- A. CK-MB
- B. Tn
- C. Tn and CK-MB
- D. Tn and hsCRP
- E. Tn and BNP
- F. Myoglobin

Cardiac Biomarkers in ACS

- Initial evaluation
 - Troponin I or T
 - CK-MB
 - Myoglobin
- Risk stratification
- Multiple biomarkers

Where to treat patient?
Selection of treatment

Biomarkers for Diagnosis of AMI

- Troponin I or T: **preferred**
 - Highly sensitive and specific for myocardial injury
- CK-MB: **unnecessary**
 - Less specific and less sensitive
 - Variability in quality control of assay
 - Can be misleading – don't ignore the Tn
- Myoglobin: **not widely used**
 - Very early marker; release can be erratic
 - Not specific to heart (skeletal muscle)

Why use Troponin?

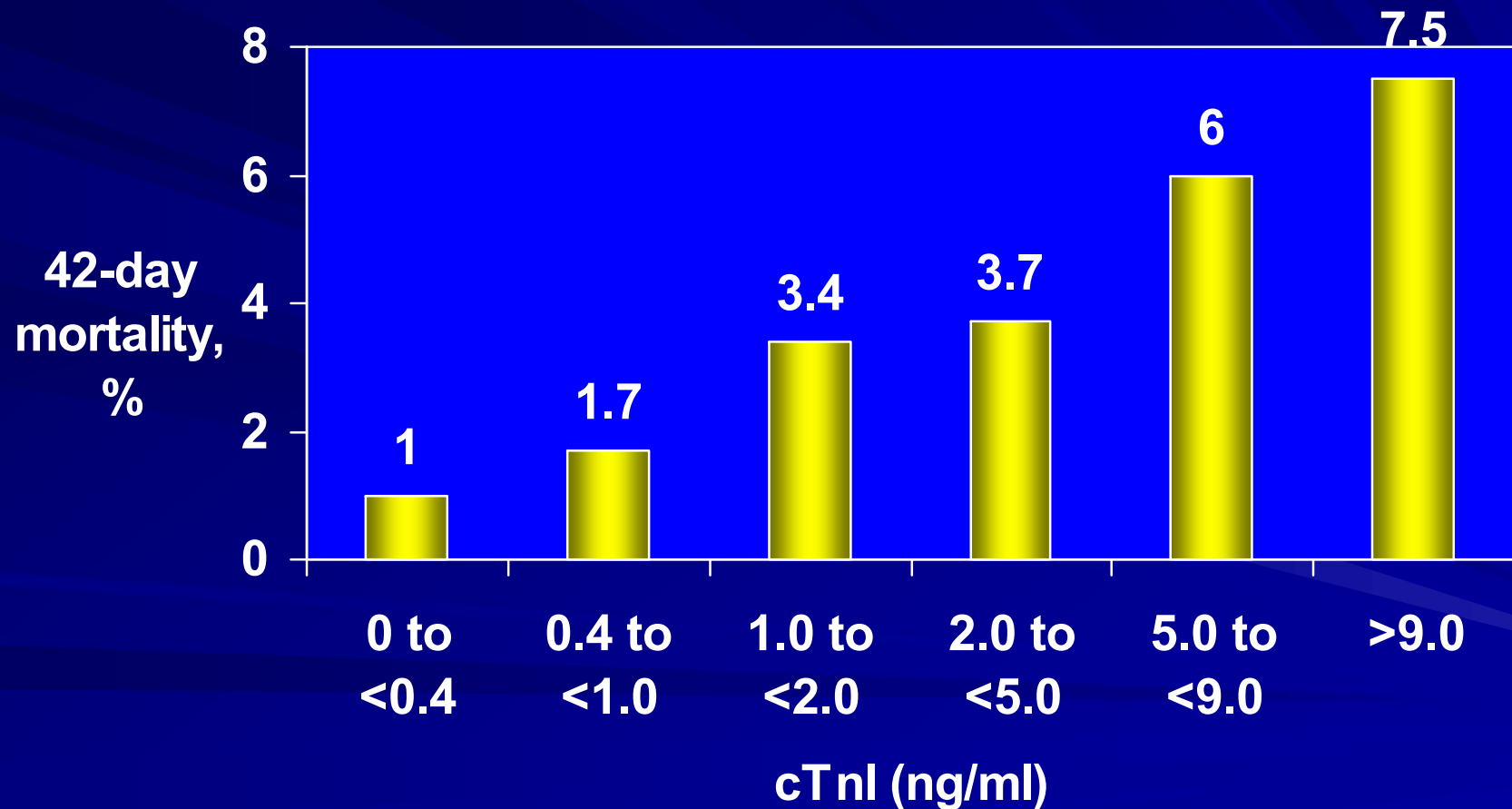
- Cardiac troponin I (cTnI) and T (cTnT)
 - Specific - found only in the heart
- Detectable within 3-12 hours of injury
 - but as early as 2 hours
- Remains detectable for 5-14 days
- Sensitivity – 1 g of muscle necrosis
- False negative – rare
 - Blocking antibodies to part of Tn molecule

Back to Case #1

Initial TnT 0.04 ng/mL and CK-MB 5. What would you do next?

- A. UFH $\pm$ eptifibatide, or clopidogrel, and plan on coronary angiogram within 24 hs
- B. Enoxaparin and clopidogrel then stress test
- C. CT angiogram
- D. Outpatient evaluation if next Tn no higher

Troponin Levels Predict Mortality in ACS (TIMI IIIB)



Diapositiva 10

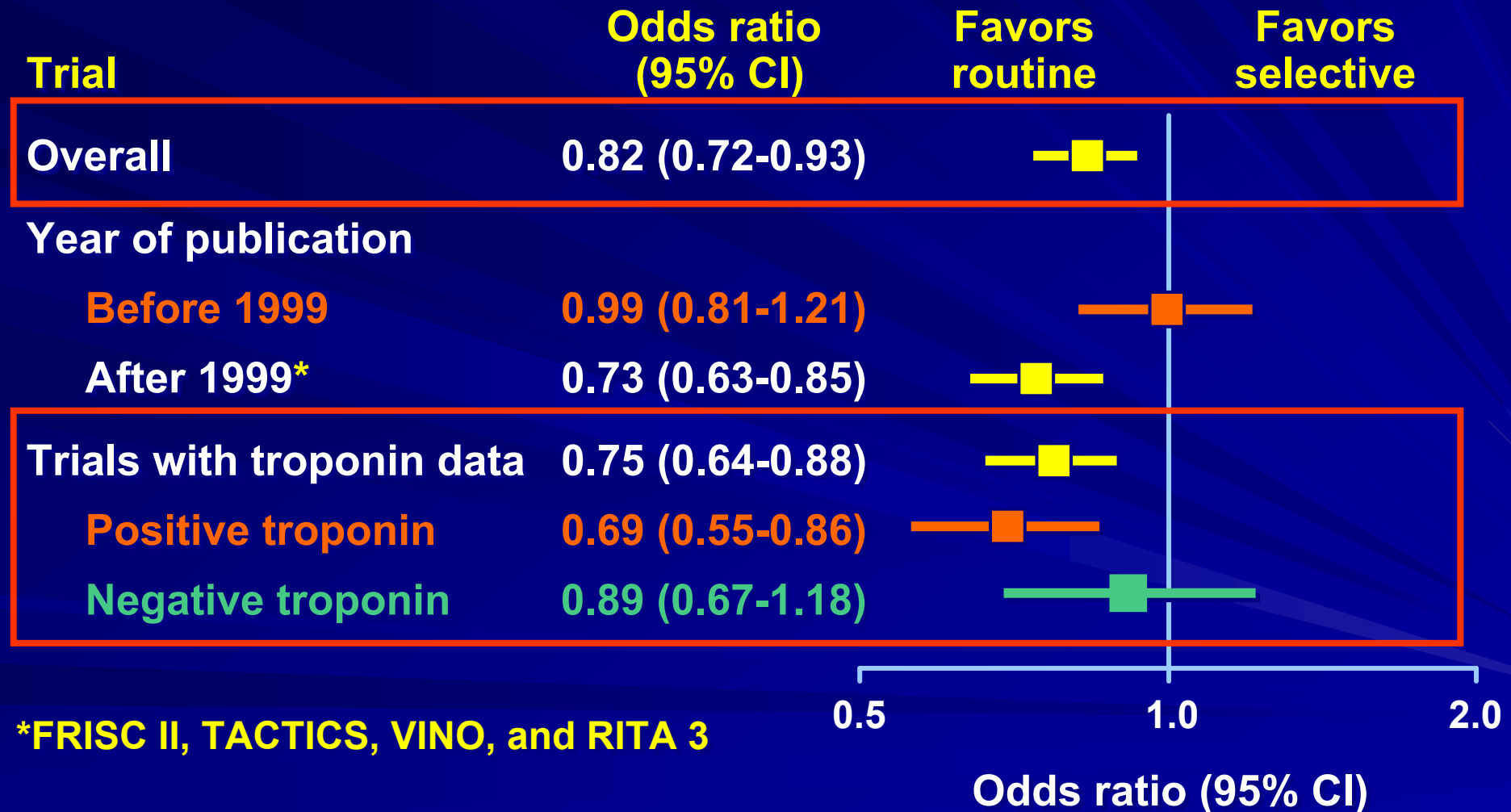
MB1

No threshold

Malcolm Bell; 25/09/2008

Routine vs Selective Invasive Strategies

Death/MI

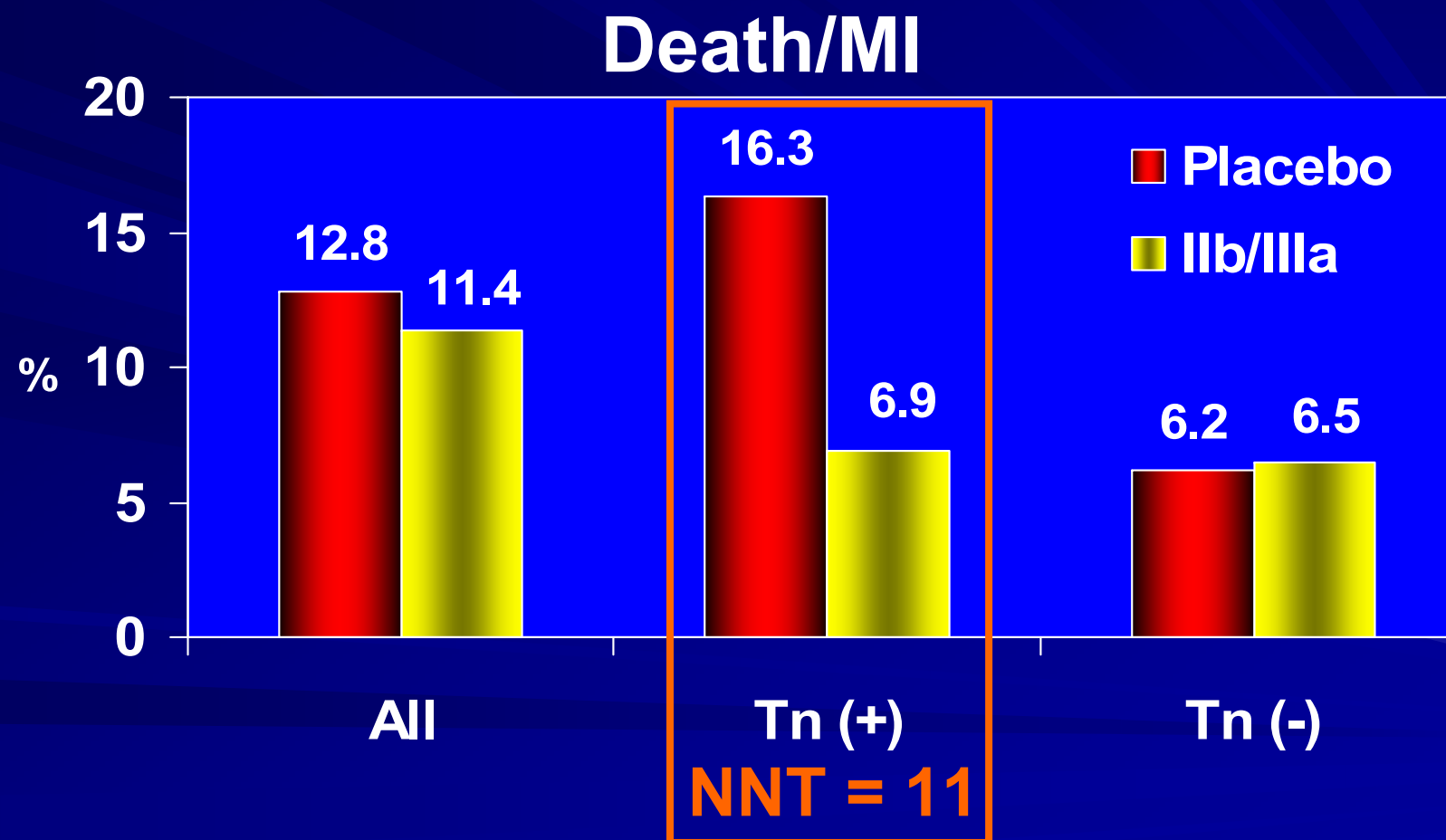


*FRISC II, TACTICS, VINO, and RITA 3

Mehta SR: JAMA, 2005

GP IIb/IIIa Efficacy in ACS Trials

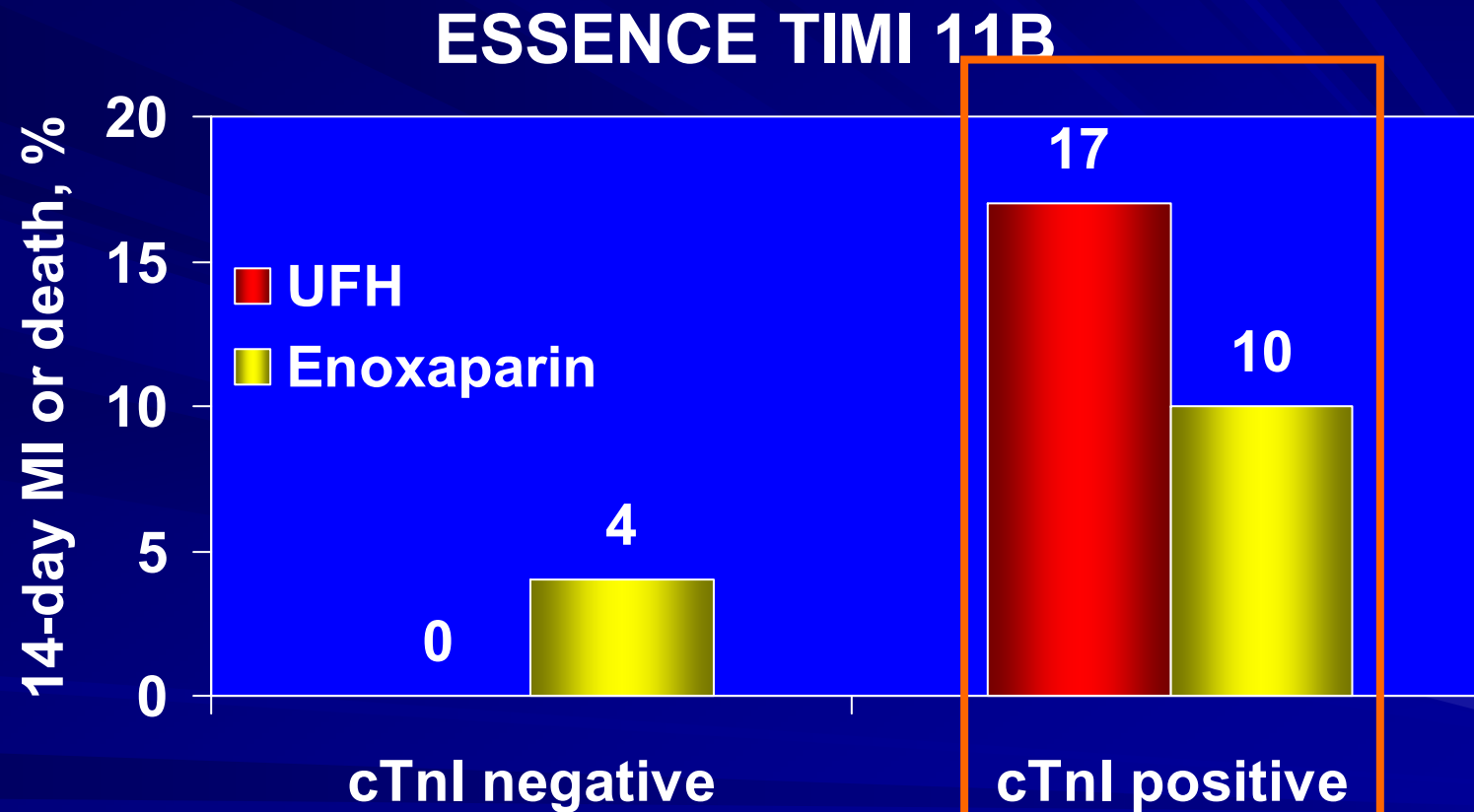
Troponin Status



Chew DP and Moliterno DJ: JACC 2000

LMWH Efficacy in ACS

Troponin Status



NNT = 14

Case #2

- 65 yr old man. Anterior STEMI treated with Primary PCI (DES) one year ago. Prostate surgery 3 months ago. Now returns to ED with chest discomfort and dyspnea. No clopidogrel.
- SBP is 80 mmHg, HR 100 bpm. SO_2 89%. T 37.0
- ECG - nonspecific T wave changes lateral leads and Q waves V1-4. CXR neg.
- Creatinine 1.8 mg/dL; TnT = 0.08 ng/mL
- Fluids and dopamine started

Case #2

What would you do next?

- A. Urgent coronary angiogram
- B. Begin eptifibatide and UFH, transfer to CCU and repeat TnT
- C. Check CK-MB to confirm elevated TnT
- D. None of the above

Case #2

With which drug, would the patient derive most benefit?

- A. Abciximab
- B. Bivalirudin
- C. tPA
- D. Clopidogrel
- E. Fondaparinux

Case #3

- 64 year old female presents to outside ED with a few hours of sudden onset dyspnea and rapid heart rate. Previously well.
- ECG – ST 105/min. TnT = 0.08 ng/mL
- ED physician requests transfer for further evaluation and Rx of NSTEMI

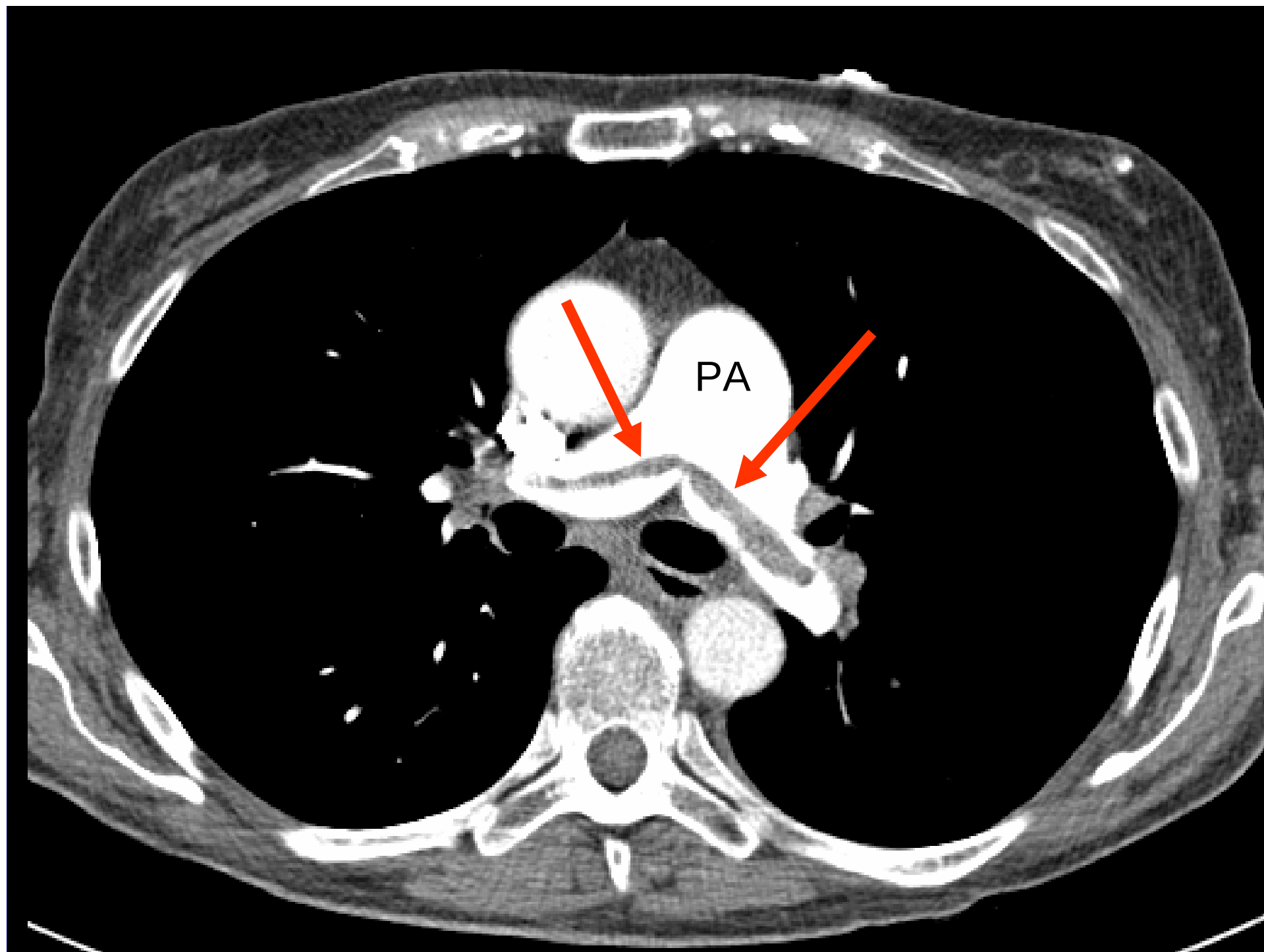
Case #3

What test would you order after patient arrival?

- A. Transthoracic echocardiogram
- B. Coronary angiogram
- C. CT angiogram
- D. Nuclear stress test
- E. Recheck Troponin in 3 and 6 hours

Cases #2 and 3

Diagnosis: Pulmonary embolism



Troponin Elevation and Pulmonary Embolism

- Very common – particularly with large PE
- Most powerful predictor of mortality

Case #4

- 80 year old female nursing home resident, presents with 2 days of worsening dyspnea and cough.
- PHx of AMI 10 years ago. Chronic renal failure
- She is barely responsive. RR 28/min. Temp 38.9C. SBP 75 mmHg
- ECG old inferior MI. TnT = 0.1 ng/mL. Creatinine 2.6 mg/dL

Case #4

The elevated troponin is likely related to which of the following:

- A. Chronic renal failure
- B. Sepsis secondary to pneumonia
- C. Recent NSTEMI
- D. CVA
- E. Any of the above

Troponin Elevation in End Stage Renal Disease

- It is real
 - not due to decreased Tn clearance
- Elevation is common
 - TnT 50%, TnI <10%
- Ominous!
 - Long term mortality 2 to 5 times higher*

*Khan NA: Meta-analysis - Circ 2005

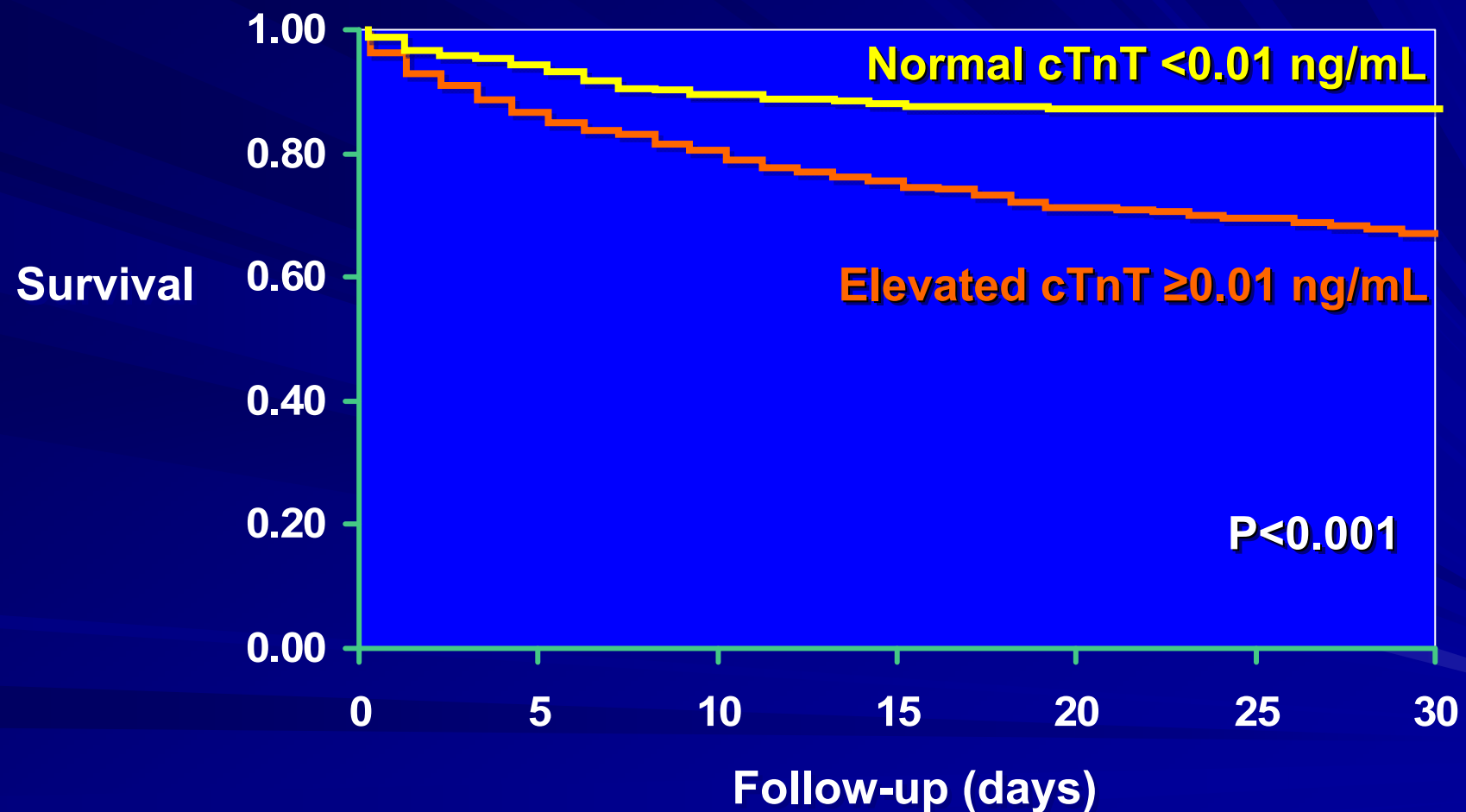
Utility of Troponin in ACS in Patients with Renal Failure

- Diagnosis of AMI
 - Valid (TnT and TnI)
 - Look for delta
- Powerful predictor of mortality*
- Even mild renal failure portends very high risk in itself*
- Don't use in isolation – clinical status!
It is just a lab test! Solve the puzzle!

*Aviles RJ (GUSTO IV): NEJM 2002

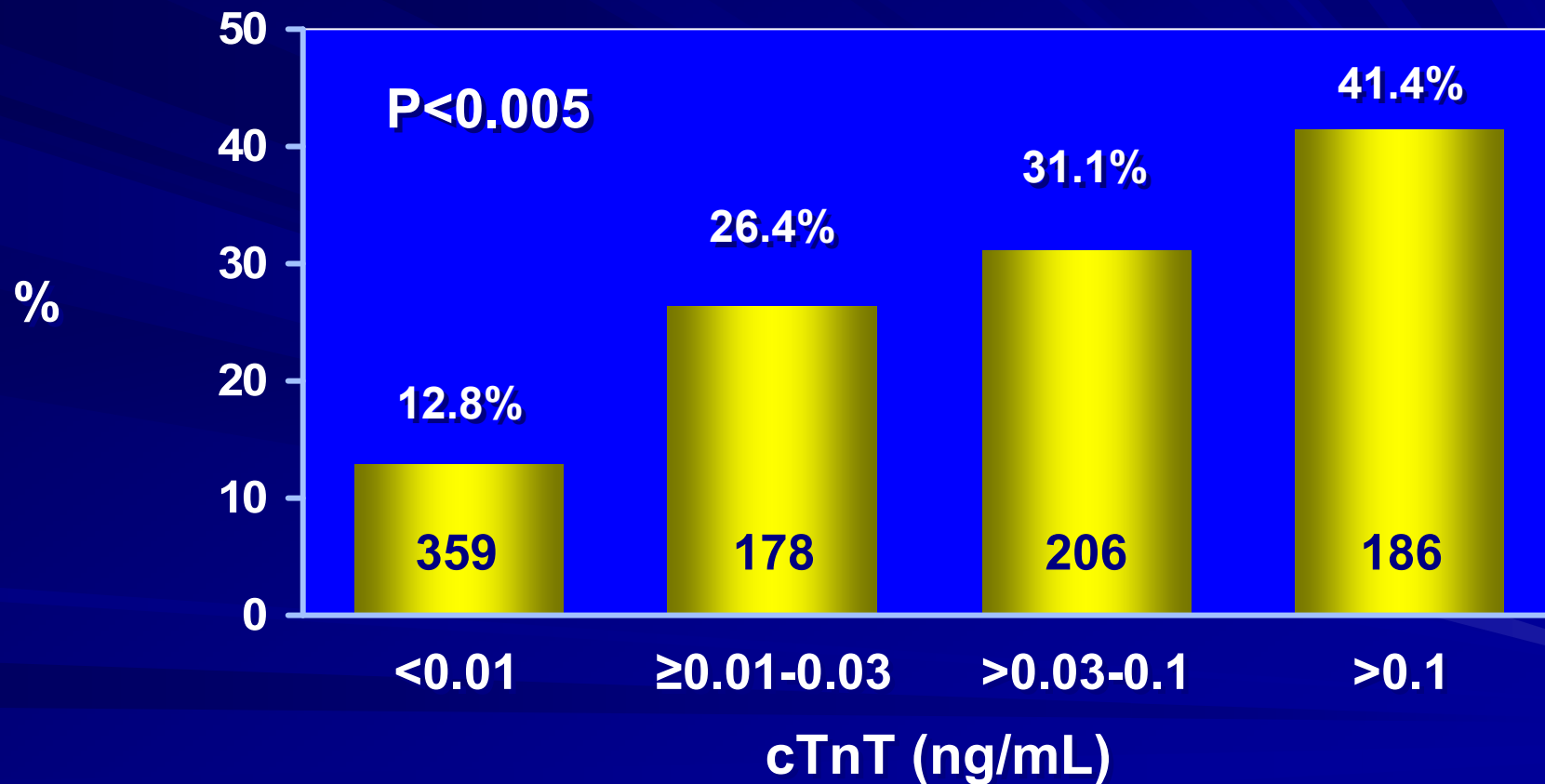
Short-Term Prognosis of Critically Ill Medical ICU Patients

Mayo Clinic



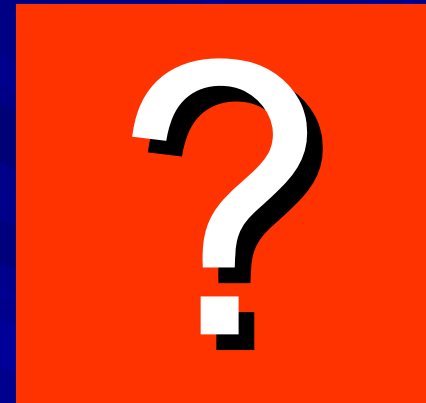
Mortality of Critically Ill Medical ICU Patients at 30 Days By cTnT Level

Mayo Clinic



Troponin Elevation in Critically Ill Patients

- CHD is uncommon
- Mechanisms – unknown
 - Inflammatory mediators
 - Myocardial demand ischemia
 - Inadequate O₂ delivery



Troponin Elevation in non ACS

■ Prognostic importance

- Don't ignore!

■ Evaluation and therapy

- Individualize
- Monitor carefully
 - Echo for LV function
- Rx underlying problem
- Evaluation for CHD? Timing?

If TnT >1.0

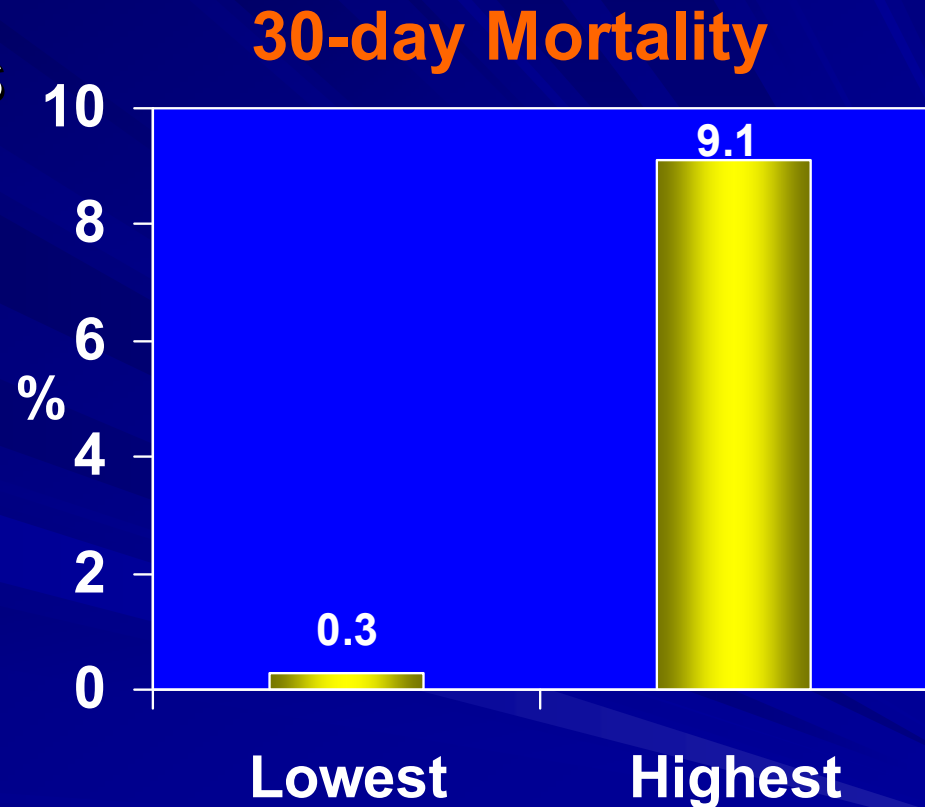
➤ **Myocarditis?**

➤ **AMI?**

Other biomarkers

hsCRP

- Inflammation, not necrosis
- Predicts early mortality*
- Role for routine measurement unclear
- CRP more common in women than men**



**Quartiles of both
CRP and TnT**

*GUSTO-IV. James SK: JACC 2003

**TACTICS-TIMI 18. Wiviott SD: Circ 2004

Use of BNP and NT-proBNP in ACS

- Rapidly rise in first 24 hrs
- Can remain elevated for weeks and months
- Higher in elderly, women and lower BMI
- Powerful predictors of subsequent mortality at any interval
 - Even if TnT is negative

Biomarkers in ER

- Suspect ACS – angina or angina equivalent
 - Clear guidelines: Tn = preferred
 - Role for additional markers unclear
- Non-ACS
 - Avoid indiscriminate use
 - Differentiate between ischemic and non ischemic causes of elevated Tn
 - Therapies are different!!

Troponin Release in Marathon Runners

2002 Boston Marathon



- 68% had increased troponin
 - >0.01 ng/mL
- 12% were severe
 - >0.075 ng/mL
- Unknown significance

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Medtronic Twin Cities Marathon Information

**Medtronic
Twin Cities Marathon**

Medtronic Twin Cities Marathon

October 4, 2009 in Saint Paul, MN

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[Question About Results?](#)