



Pioneering better health for all

Topping Troponin

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18th September 2019

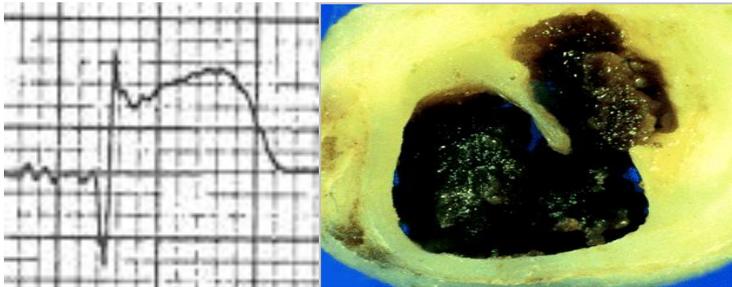
 @tomkaier



Suspected Acute Coronary Syndrome

- 23 million A+E attendances in England during 2015
- most common single symptom is chest pain
- 10% of all presentations
- Approx 15% (of 10%) have acute MI (85% no AMI)

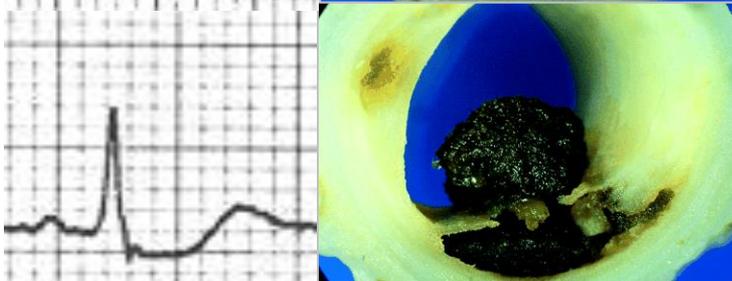
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Necrosis by closed **artery**

→ **STEMI**

2/3

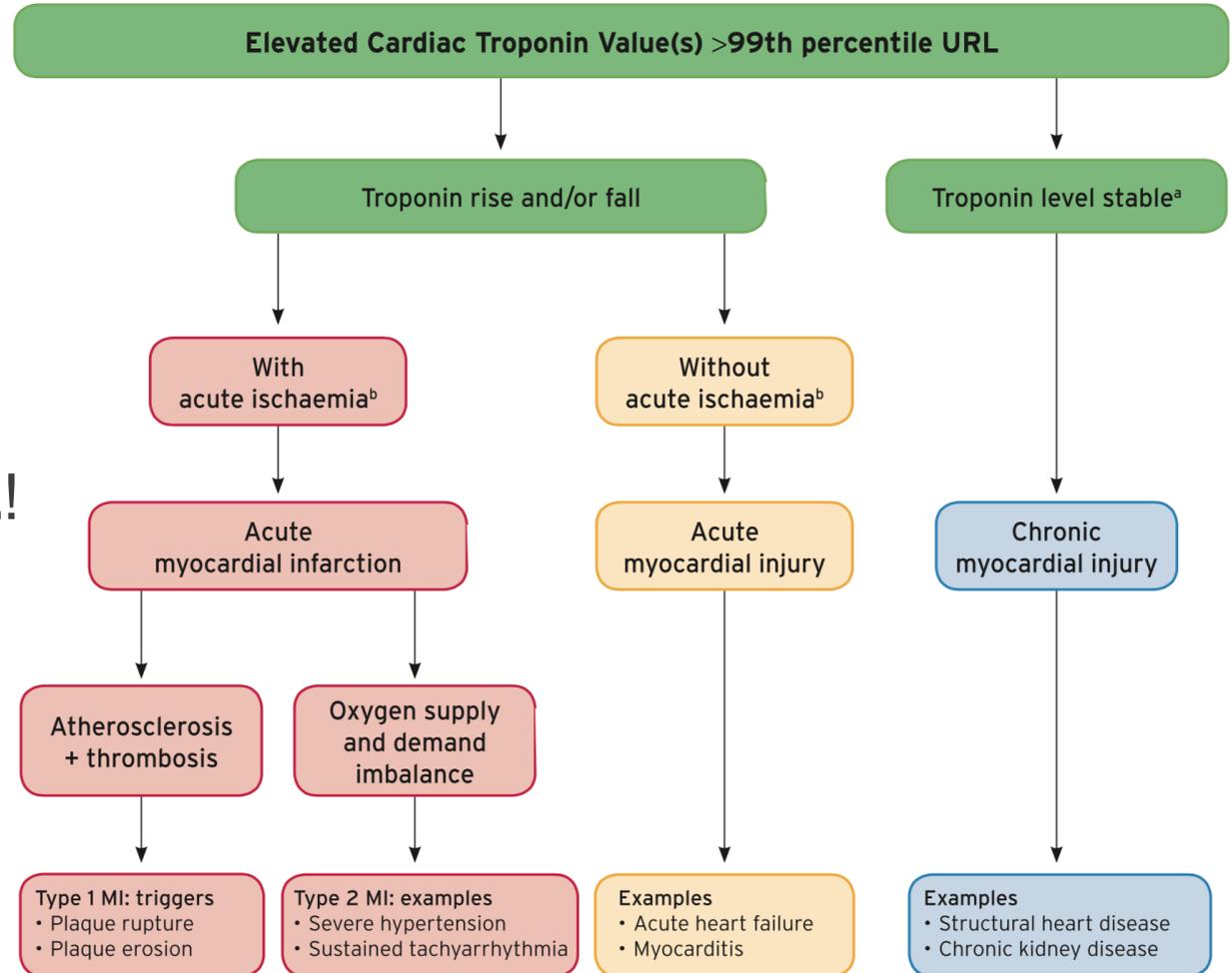


Necrosis by closed **muscle**

→ **NSTEMI**



Biomarker diagnosis

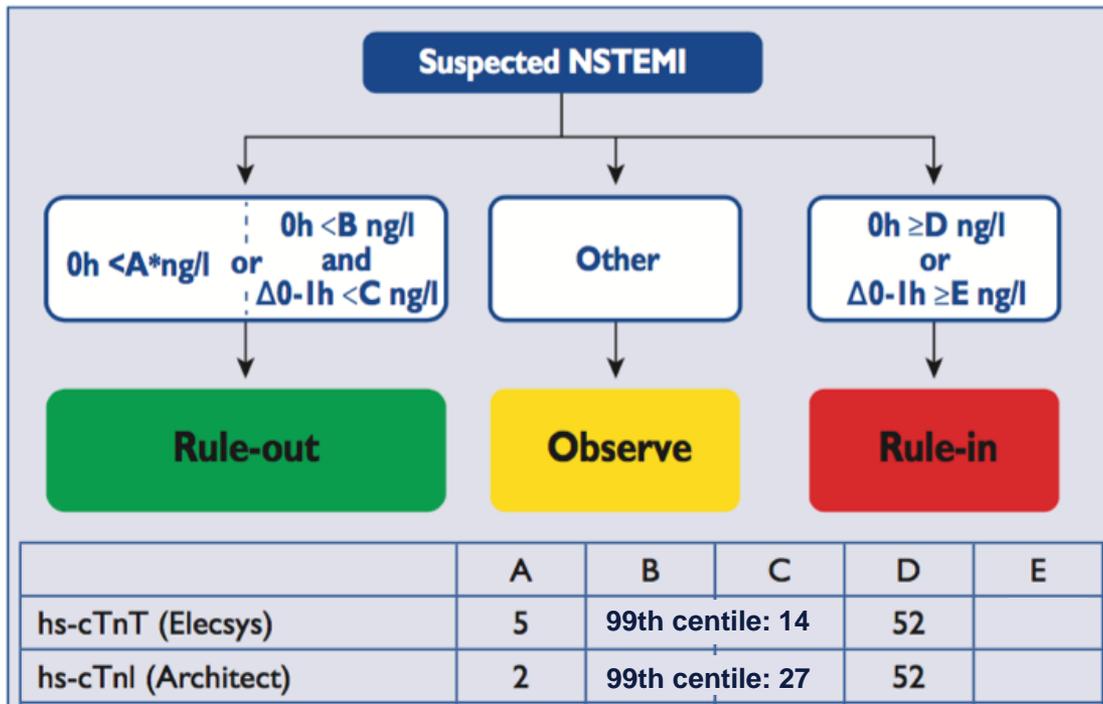


This is **UNIVERSAL!**

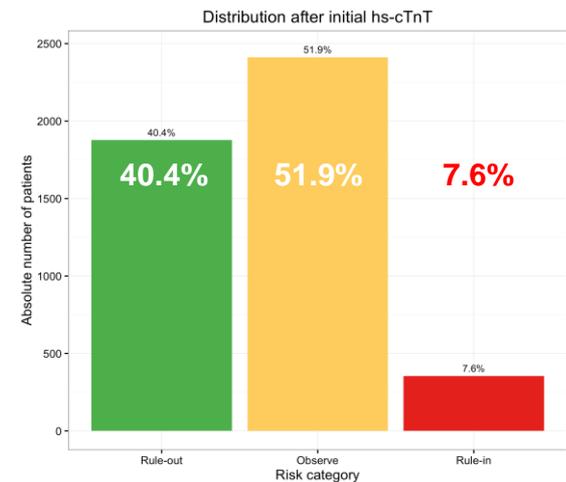
Thygesen K, et al *Journal of the American College of Cardiology*. 2018;72:2231–2264.



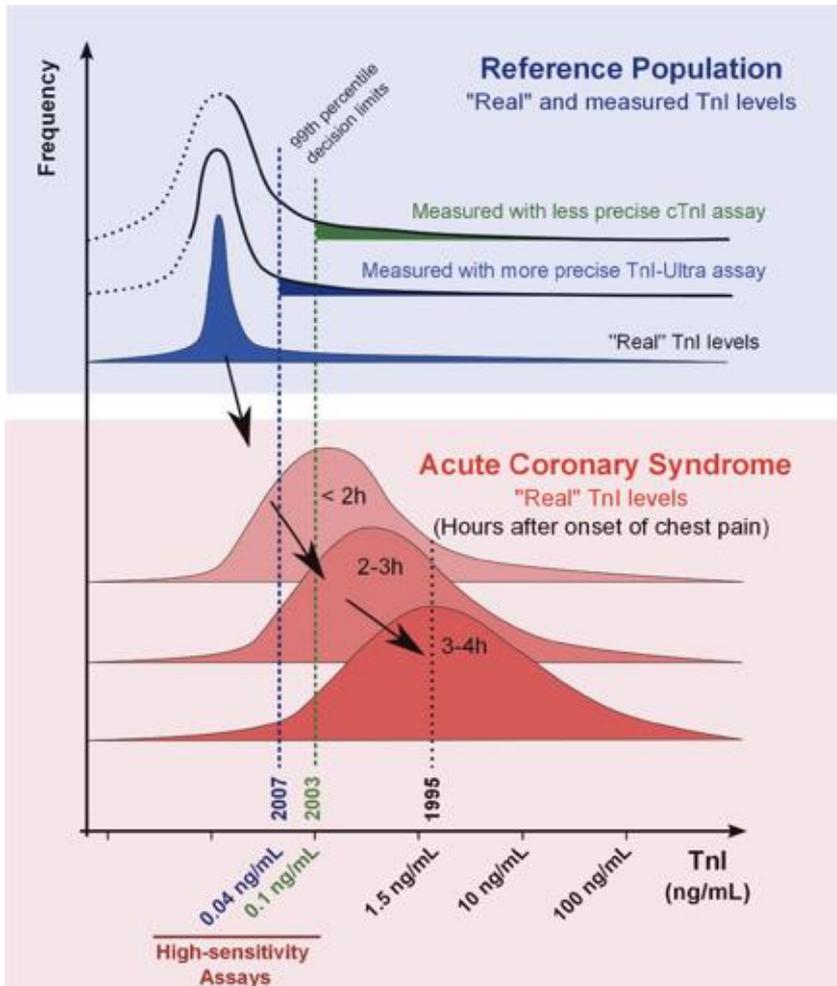
Suspected Non-ST elevation MI – real life



Single-centre, prospective cohort study at St Thomas' Hospital
n=4,644



Cardiac Troponin evolution



'When troponin was a lousy assay it was a great test, but now that it's becoming a great assay, it's getting to be a lousy test

Jesse RL. On the Relative Value of an Assay Versus That of a Test. *Journal of the American College of Cardiology*. 2010;55:2125–2128.

Based on Mahajan VS et al; *Circulation* 2011



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Sensitivity/Specificity Quagmire



0h 1h 2h 3h

6h 12h 24h

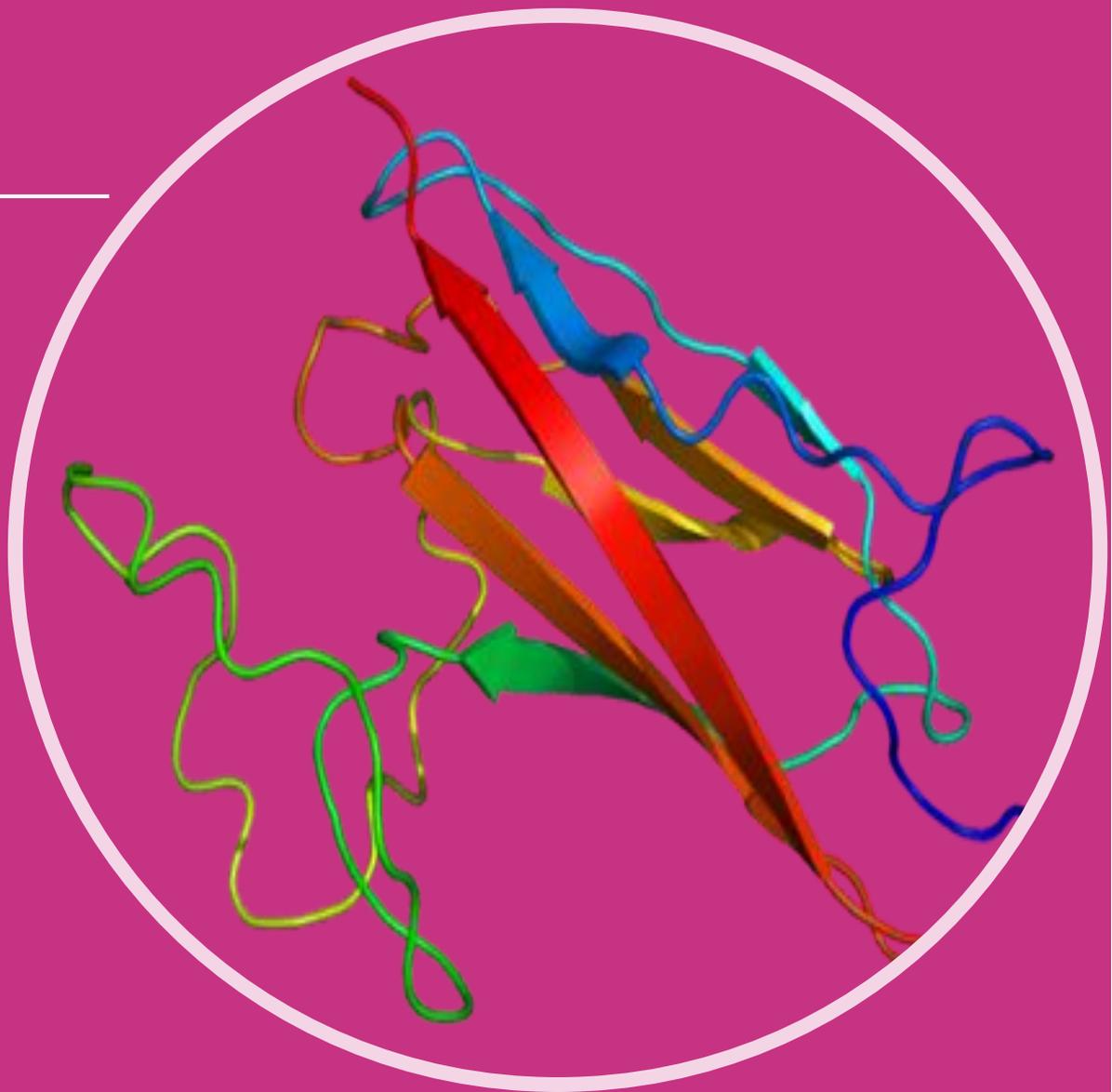
Need sensitivity

Don't want to discharge patients with AMI

Desire specificity

Don't want to use dAPT, heparin and angiography inappropriately

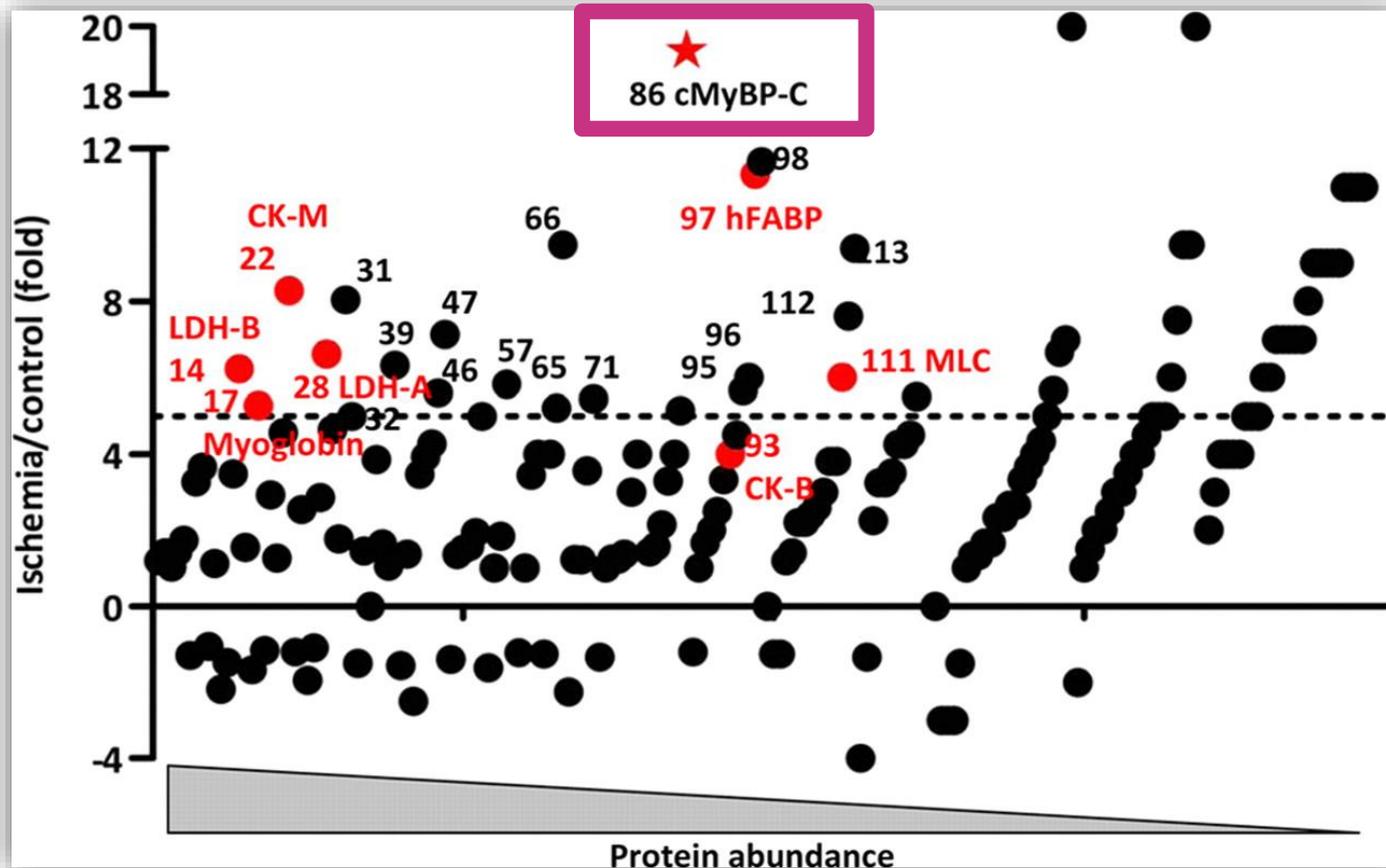
Can we do
better?





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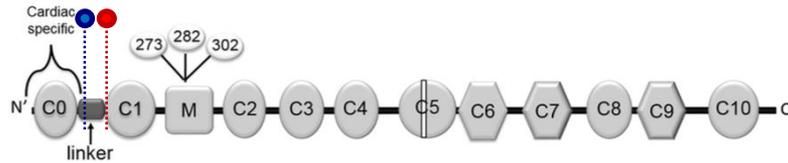
The discovery – cardiac myosin-binding protein C (cMyC)





cMyC – timed myocardial infarction

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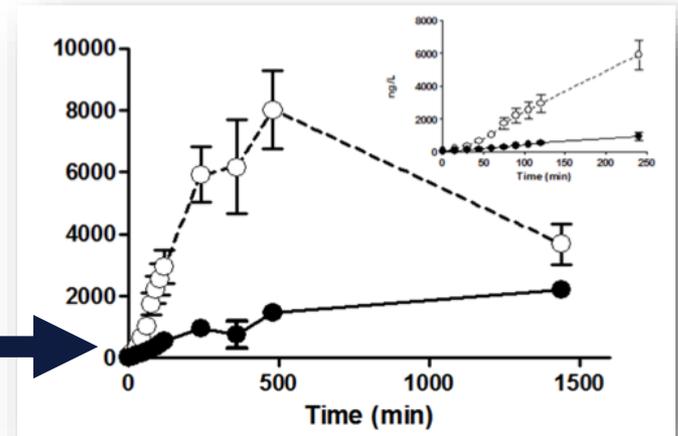
- 1A4
- 3H8



Alcohol Septal Ablation (n=20)

- Performed in patients with HCM to reduce muscle thickness in LV outflow tract
- Time to Peak concentration 9.7 ± 1.4 v 21.6 ± 1.4 hrs
- Rate of Rise 25.8 ± 1.9 v 4.0 ± 0.4 ng/L/min

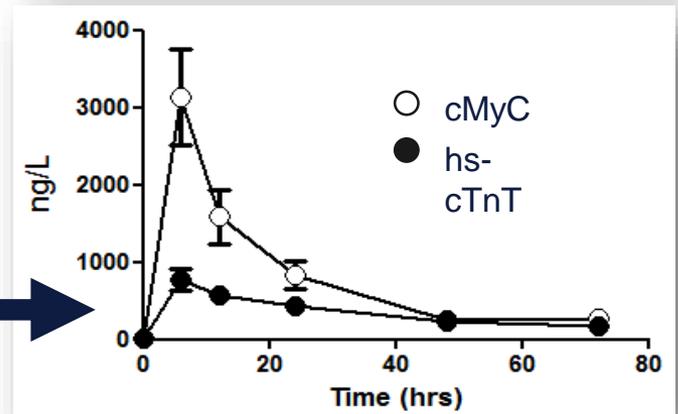
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Coronary artery bypass grafting, with serial measurements of cardiac markers (n=20)

- Decay half-time 5.5 ± 0.8 hrs v 22 ± 5 hrs
- Note: still on research platform – MesoScale Discovery (LLOD 80 ng/L)

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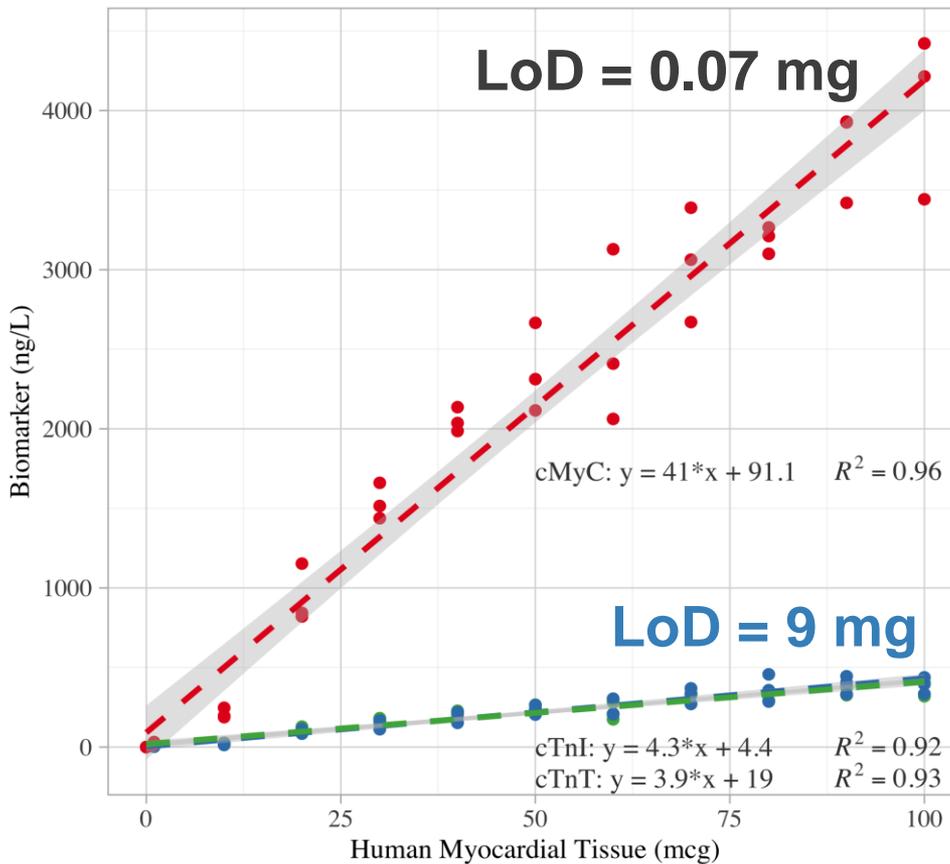




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How sensitive?

Biomarker release from human myocardium



Clinical Chemistry 63:5
990-996 (2017)

Proteomics and Protein Markers

Quantifying the Release of Biomarkers of Myocardial Necrosis from Cardiac Myocytes and Intact Myocardium



Biomarker

- cMyC
- hs-cTnI
- hs-cTnT

Biomarkers:

- hs-cTnT: increased 3.9 ng/L
- hs-cTnI: increased 4.3 ng/L
- cMyC: increased 41.0 ng/L per μg of human myocardium

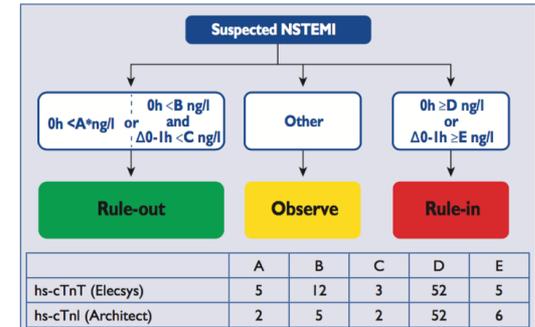
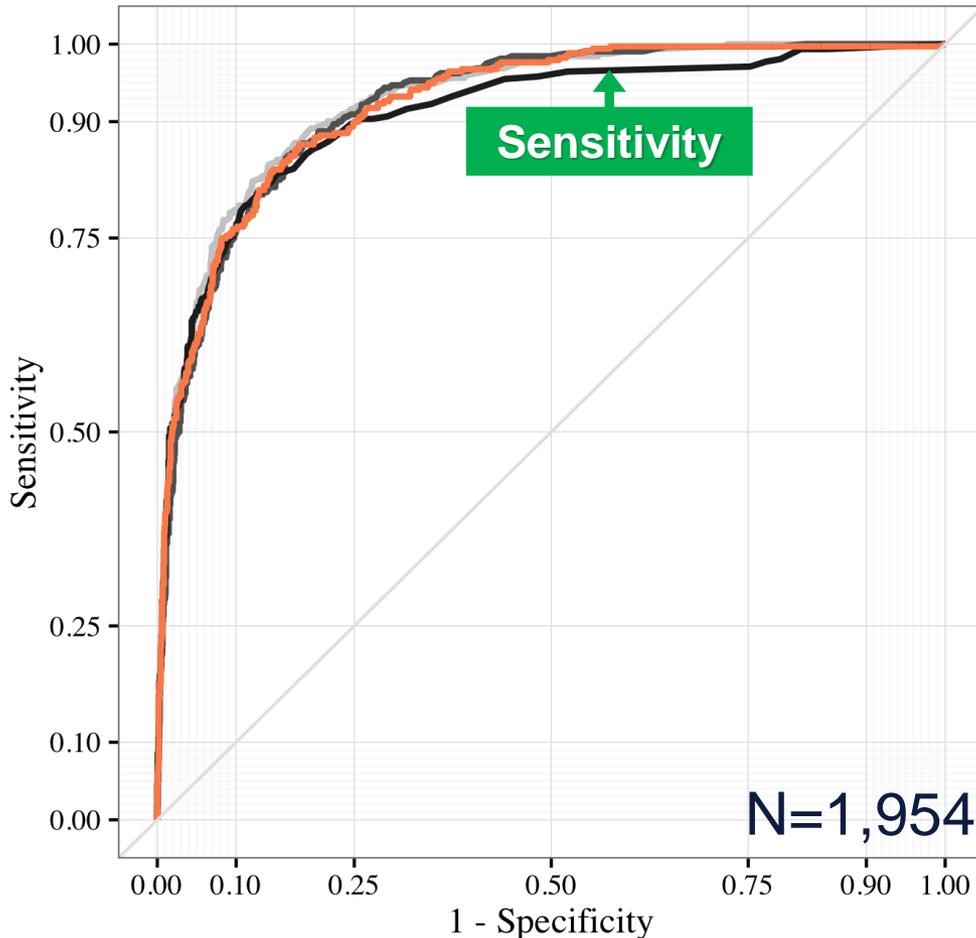
Kaier TE & Marjot J, et al. *Clin Chem.* 2017



Diagnostic performance

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ROC curves for individual biomarkers



Area Under the Curve

cMyC: 0.924

hs-cTnT 0.927

hs-cTnI 0.922

s-cTnI 0.909*

Median symptom time: 5 hrs

Rule-out: <10 ng/L

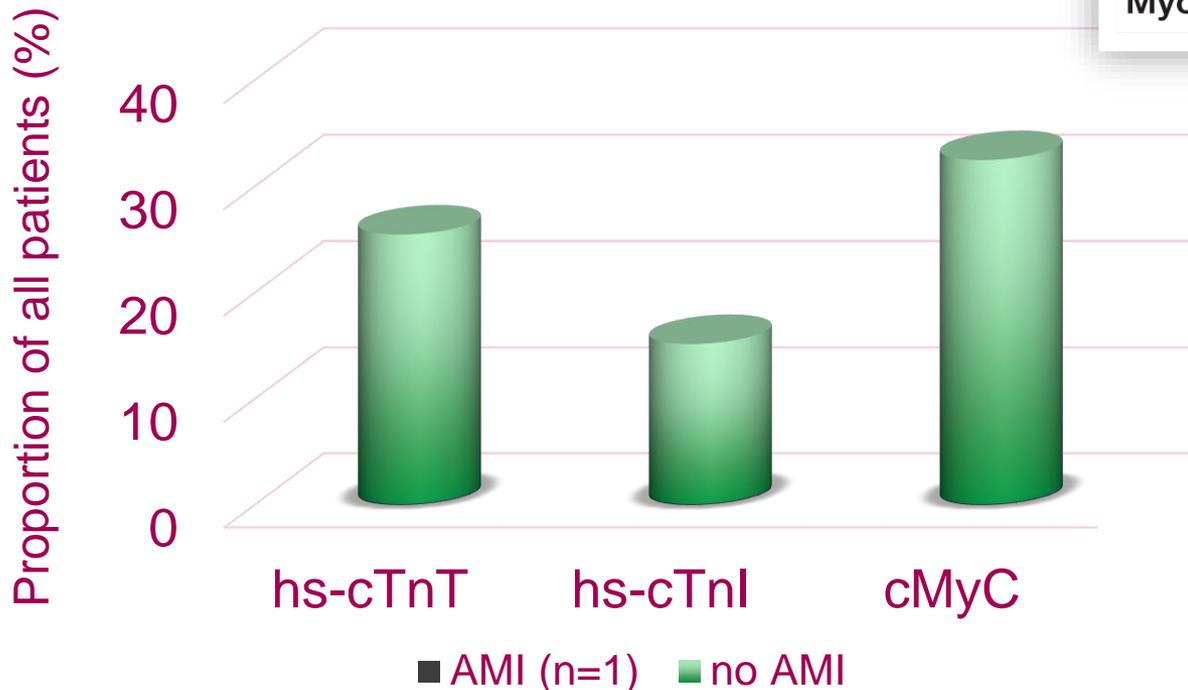
Rule-in: >120 ng/L



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Triage performance

Rule-Out



ORIGINAL RESEARCH ARTICLE



Direct Comparison of Cardiac Myosin-Binding Protein C With Cardiac Troponins for the Early Diagnosis of Acute Myocardial Infarction

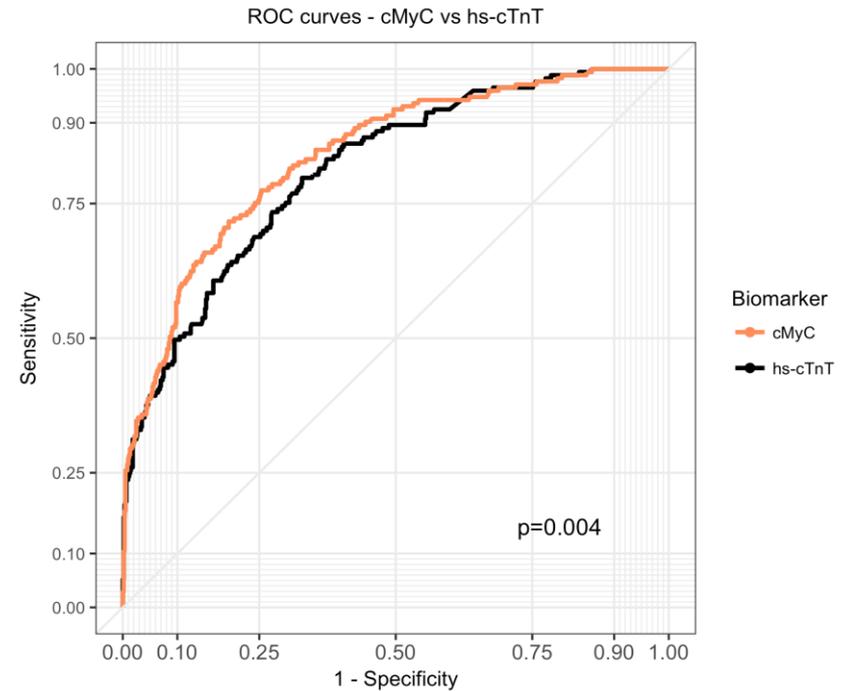
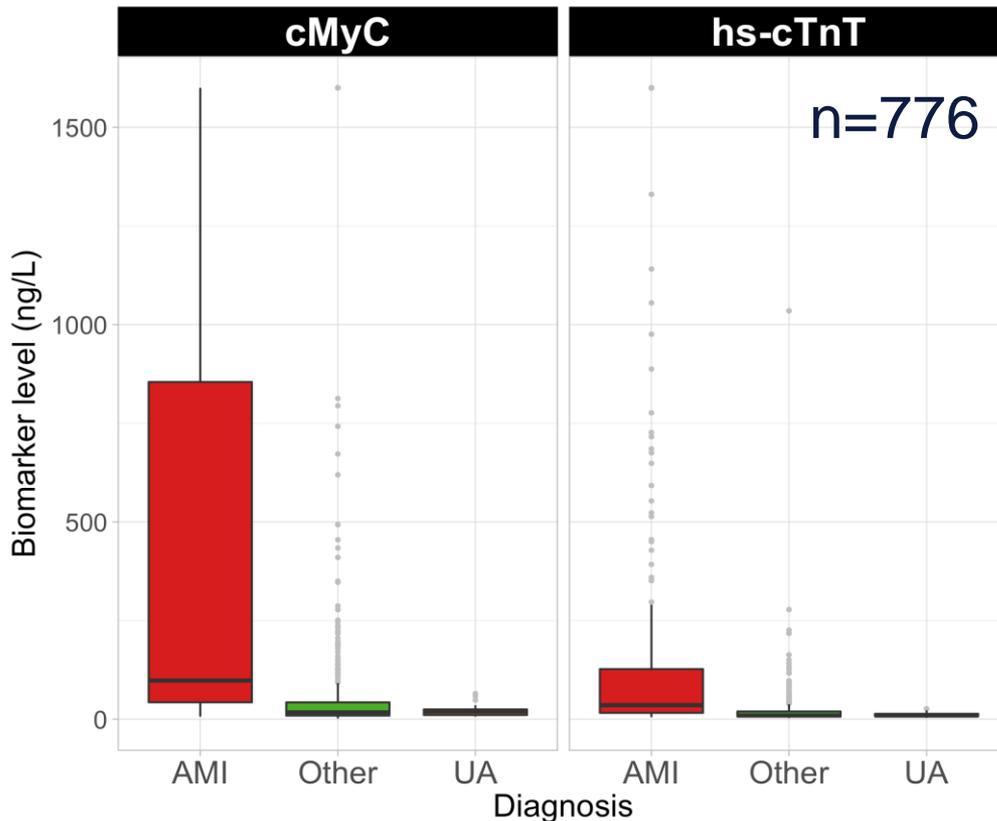
17% more patients ruled-out

St Thomas' Hospital:
1,000 bed days annually

Fewer patients in the observe zone!



Pre-hospital triage



Area under the Curve (AUC) for AMI:
cMyC 0.839 – rule-out (10 ng/L): Sens 96.5%
hs-cTnT 0.813* – POCT (50 ng/L): Sens 40.5%

Median symptom time: 70 mins (Other cohort: 5 hrs)

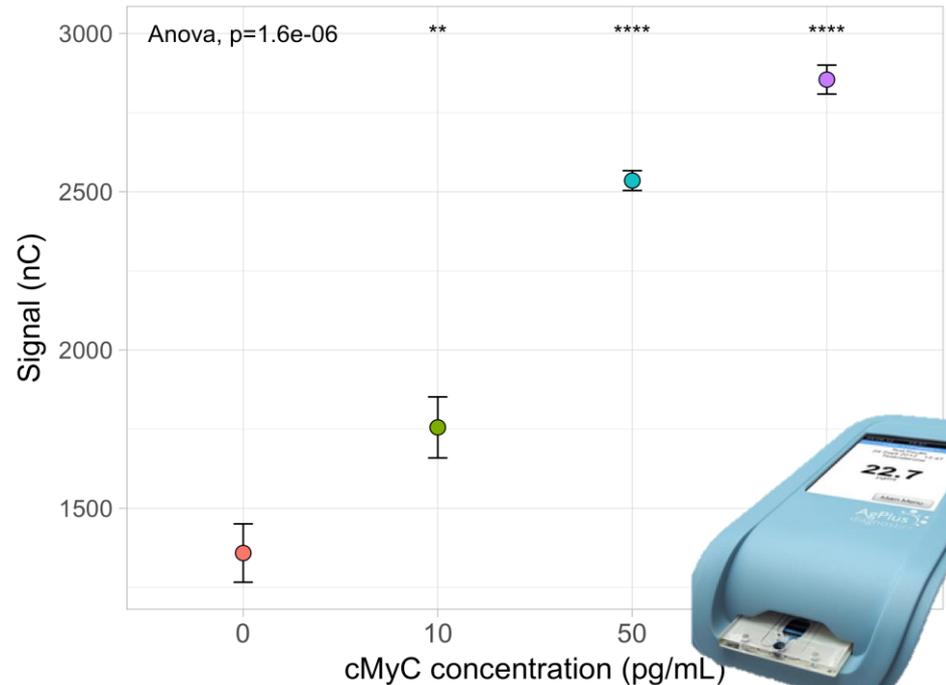
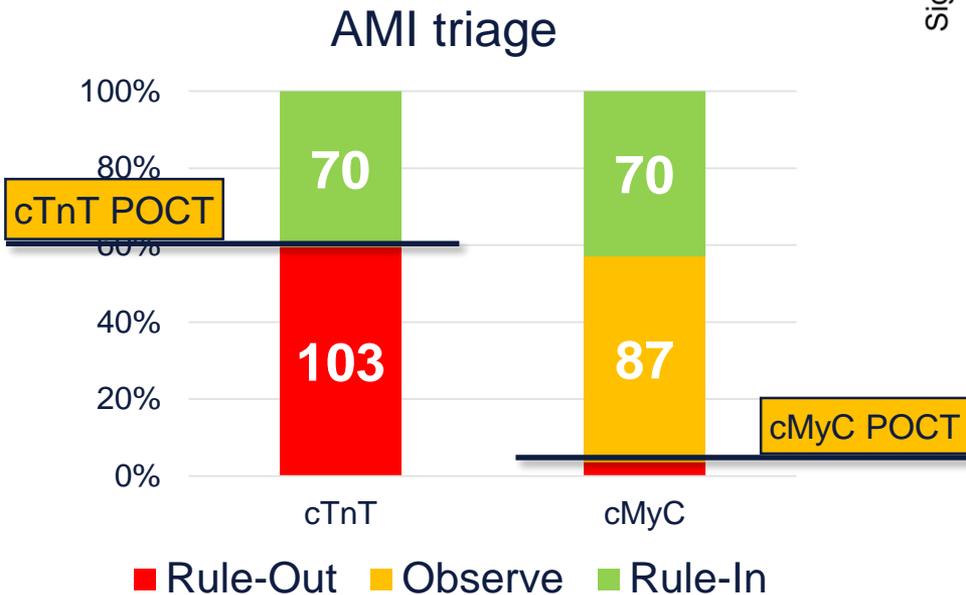


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cMyC on POCT – can it be done?

- King's Health Accelerator award 2017
- First foray into POCT of cMyC

Point-of-Care Test – 'almost there'



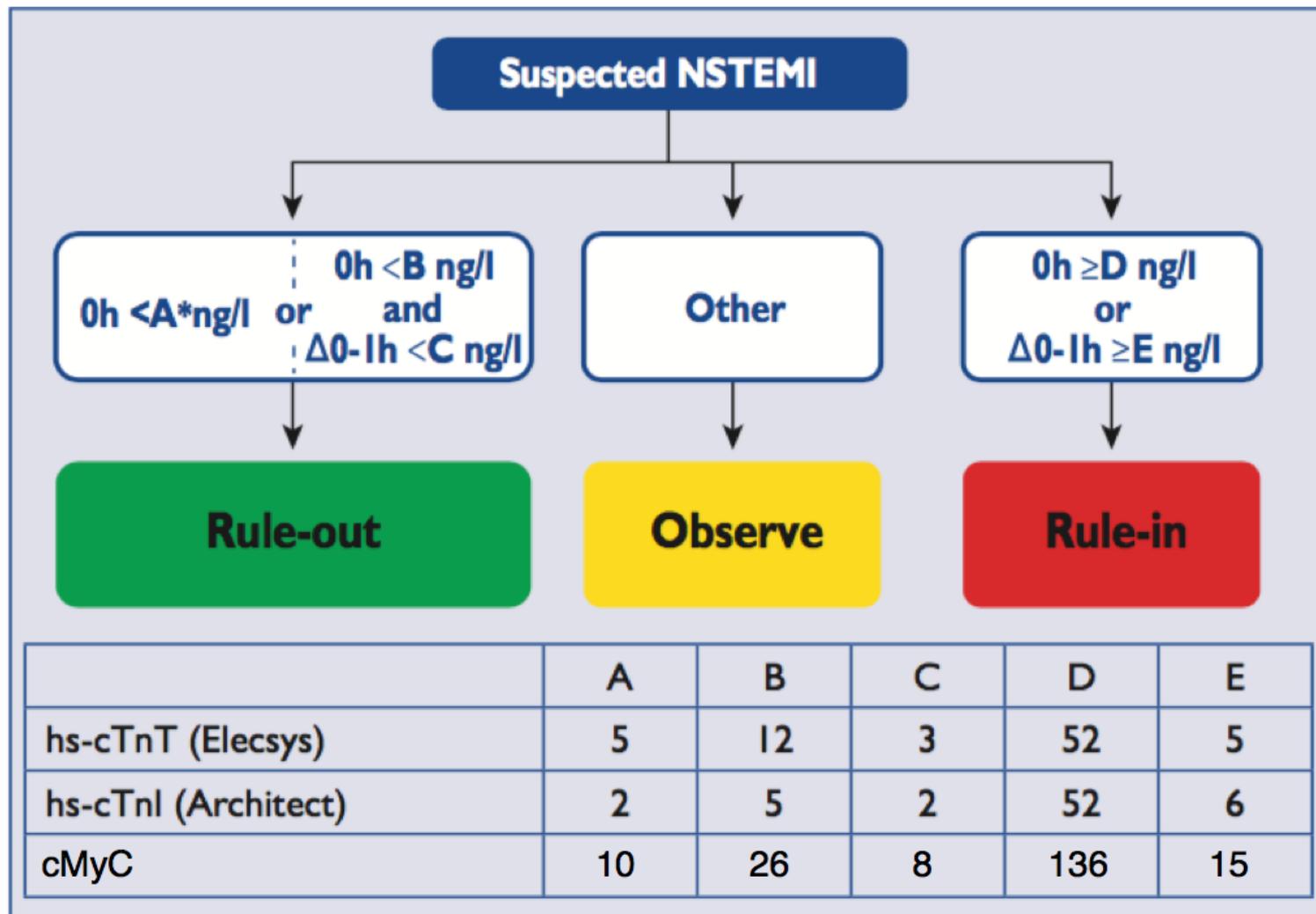
cMyC

Signal obtained for varying concentrations of C0C2 analyte at 10 mins incubation



Calibrating a new biomarker

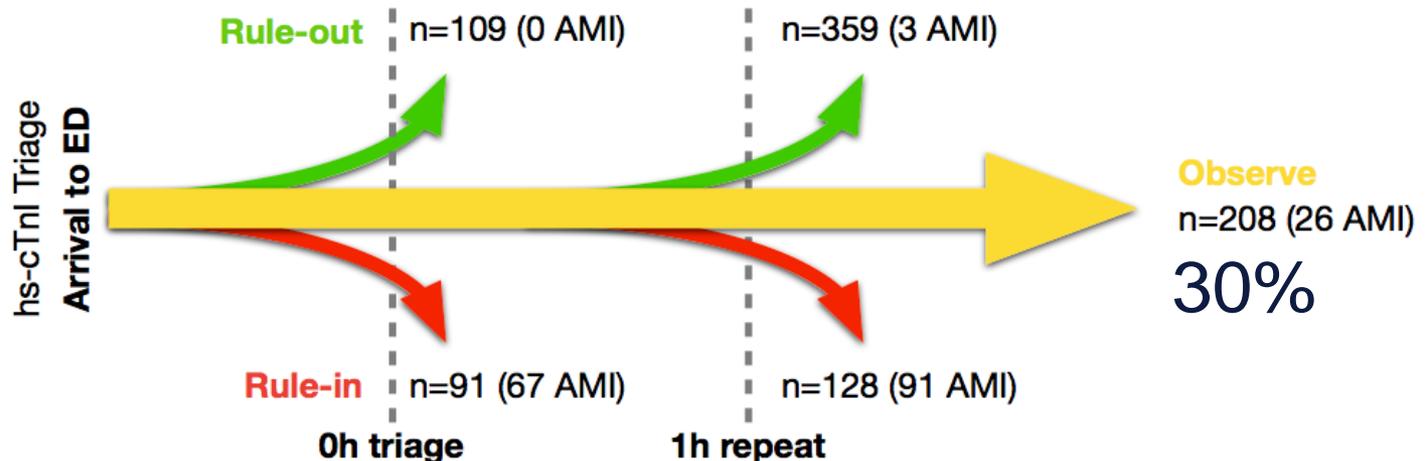
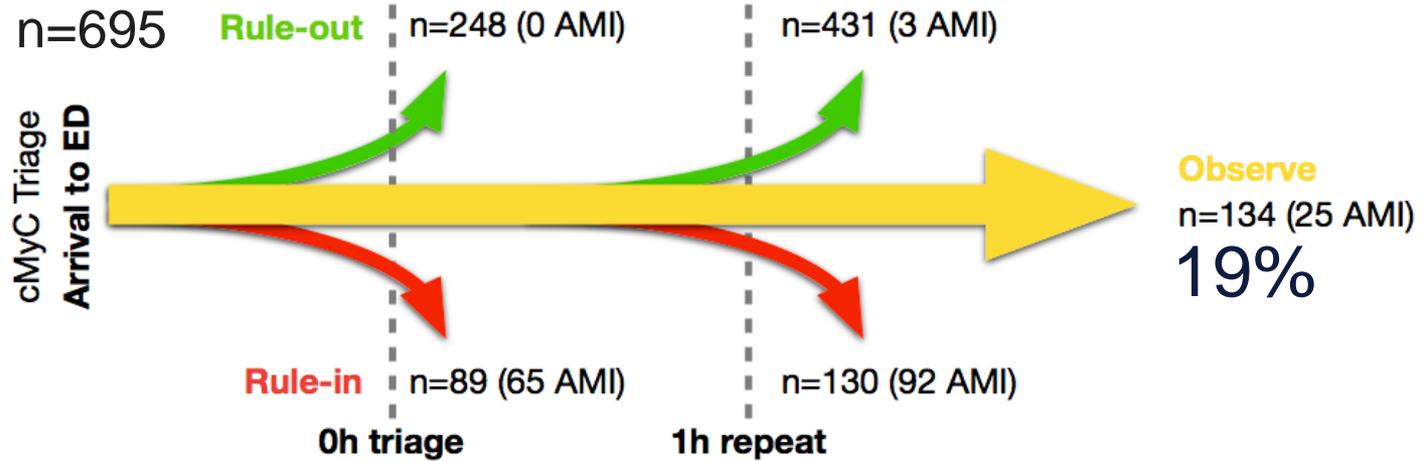
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cMyC 0/1h rule-out algorithm





Key findings & future

- cMyC is many times more abundant than cTn
- diagnostic accuracy of cMyC is at least as good as the leading cTn assays; better in early presenters
- cMyC can improve chest pain triage - earlier rule-out & rule-in, and fewer patients would need in-patient stay
- **Future:**
 - Clinical platform crucial for ongoing research
 - Partner with industry – e.g. antibodies to test cMyC release patterns
 - POCT remains very attractive concept



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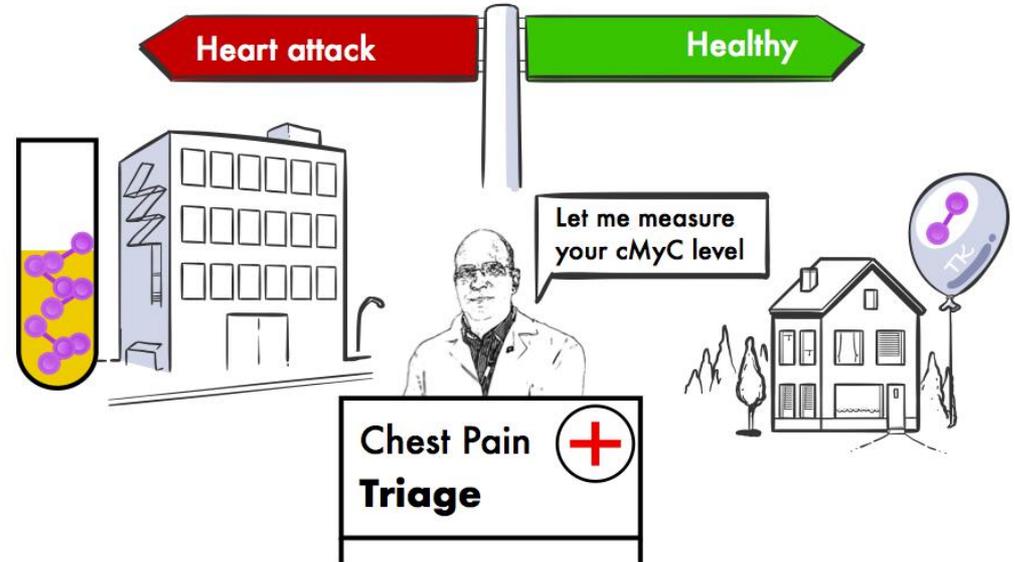
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 **cMyC** can **immediately** guide 40% more patients to their correct destination





Fundraiser

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<https://www.justgiving.com/fundraising/tomkaier>

