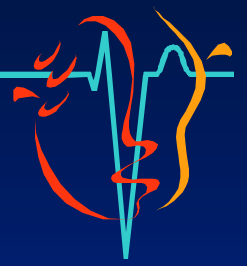
The Next Generation

Navigating the transition in clinical thresholds and diagnostic accuracy

Professor Patrick Twomey

Uses of an investigation/test



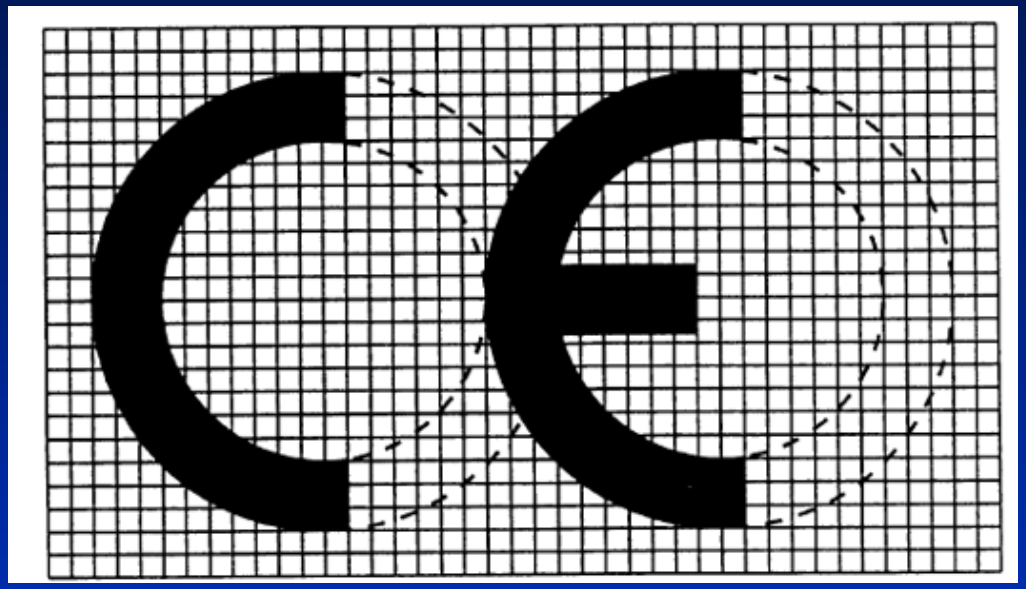
- (Targeted) Screening
- Case finding
- Diagnosis
- Prognosis
- Management
- Rule in
- Rule out

The Standards for Reporting of Diagnostic Accuracy Studies (STARD) checklist

- **Published in 13 biomedical Journals in 2003 * Updated in 2015 – 30 criteria * Adopted by over 200 biomedical journals since**

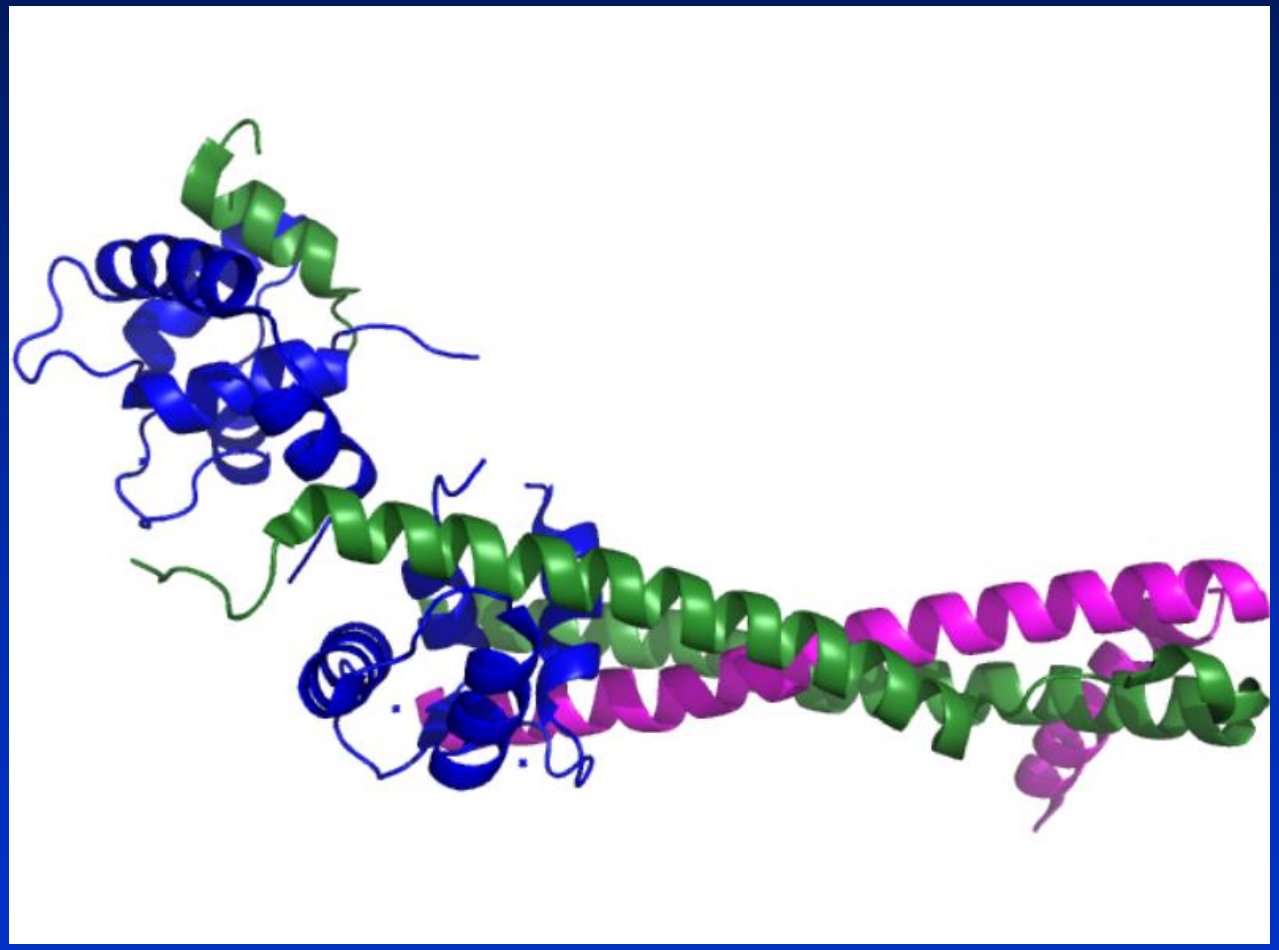
Test methods	10a	Index test, in sufficient detail to allow replication
	10b	Reference standard, in sufficient detail to allow replication
	11	Rationale for choosing the reference standard (if alternatives exist)
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing prespecified from exploratory
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing prespecified from exploratory
	13a	Whether clinical information and reference standard results were available to the performers or readers of the index test
	13b	Whether clinical information and index test results were available to the assessors of the reference standard

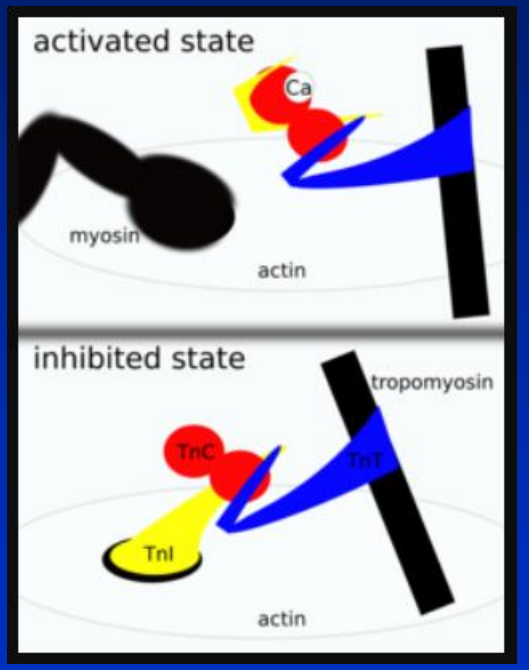
NCPP and CE Marking: Dec 2026



Each CE Marked assay has a manufacturer intended use

Troponin T or I (Tn T or I)





Intended Use Generation 6

- **Tn T is a marker of heart muscle injury used "as an aid in the differential diagnosis of acute coronary syndrome to identify necrosis, e.g. acute myocardial infarction (AMI)", not a specific diagnosis in itself**

Intended use

Immunoassay for the in vitro quantitative determination of cardiac troponin T in human serum and plasma.

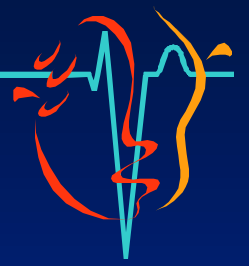
This assay can be used as an aid in the differential diagnosis of acute coronary syndrome to identify necrosis, e.g. acute myocardial infarction (AMI); and as an aid for early discharge and outpatient management for patients suspected of acute coronary syndrome (ACS).

The test is further indicated for the risk stratification of patients presenting with suspected acute coronary syndrome.

Roche Product Information Notice Information Only 11/03/2026 EI Pre-launch information for the Elecsys® Troponin T hs Gen 6 Immunoassay MN-RDS-CoreLab-20250=-029

https://diagnostics.roche.com/global/en/products/lab/elecsys-troponin-t-hs-gen-6-pid00001103.html 09/06/2026

Tn T Gen 5



- **33206 results at SVUH in 2025**
  - Female approximately 42.6%
  - Male approximately 57.4%
- **Of those with results**
  - **<14 ng/L approximately 37%**
  - **14+ ng/L approximately 63%**

Troponin T: The Next Generation

- **All 3 labs in SVHG transitioned to Tn T Generation 6 on Tuesday 26/05/2026 at 14:00**
- **3 Hospitals: Public Hub, Private, Public Spoke**
  - **3 EDs**
  - **2 Acute Medical Units**
  - **1 CCU**
- **The labs do not oversee how Tn T is used**

Troponin T: The Next Generation

- A verification plan shall be in place for all changes
- A verification report shall be available
- Implementation / integration of the change in the laboratory quality system

https://www.inab.ie/media/hljin0ec/ps24.pdf 08/06/2026

Troponin T: The Next Generation

- **Lab issues before we went live**
  - **Decided to**
    - **Move from universal to sex based cut-offs unless evidence to the contrary from users**
    - **Keep the same phoning limit but happy to subsequently change based on user experience**
    - **Use new test code on LIMS**
    - **No dual reporting but happy to add generation Tn T 6 on previous samples: 2 requests**

Troponin T: The Next Generation

- **We decided to**
  - **Use previous third party IQC**
    - **Consistently higher for usual IQC**
    - **Lot to lot concentration consistency issues using separate low level**

Lot	Gen 5	Gen 6
A	15	36
B	10	22
C	7	<1.5

  - **Comparison (sample exchange) with external lab (same reagent and calibrator lots) as well as within the 3 group labs (same calibrator lots)**

Troponin T: The Next Generation

- **We decided to wait until EQA catches up**

WEQAS hsTn Distribution	261	262a	263	264	265
	BB818251Z	BB818252Q	BB818253E	BB818254H	BB818255Y
TNT6 (ng/L)	2.03	9.89	12.1	22.4	41.7
	1.97	9.71	12.3	22.2	42.3
	1.92	9.85	12	21.7	41.2
TNTX (ng/L)	3	8.06	9.21	15.9	28.8
	3	7.51	8.25	15.9	28.5
Mean TNT6 (ng/L)	**2.0**	**9.8**	**12.1**	**22.1**	**41.7**
Mean TNTX (ng/L)	**3.0**	**7.8**	**8.7**	**15.9**	**28.7**

Troponin T: The Next Generation

- **Change mentioned to Clinical Director December**
- **Grand Rounds presentation 09/04/2026 - recorded**
- **Memos 14/04/2026 and 25/05/2026**

Transition to **Generation 6 high sensitivity Troponin T assay (TNT6)**

Key changes:

- **Timeline:** Migration is scheduled for **May 2026** at SVUH, SMH, and SVPH.
- **Improved Performance:** TNT6 offers superior performance to the current assay.
- **Numerical Difference:** TNT6 results are **not directly comparable** to the current assay.
- **Reporting Limit:** The minimum reportable concentration for TNT6 will be **3 ng/L**.
- **New Sex-Specific Reference Ranges:** In a shift to align with general clinical practice, sex-specific 99th centiles will be implemented:
  - **Male:** 32 ng/L
  - **Female:** 18 ng/L

Should you have any questions in this matter then please do not hesitate to contact us.

2pm on 26th May: Transition to **Generation 6 high sensitivity Troponin T (TNT6)**

Please Note:

- **Numerical Difference:** TNT6 results are **not directly comparable** to the current assay and will not appear on the cumulative record for the previous hsTnT assay.
- **Reporting Limit:** The minimum reportable concentration for TNT6 will be **3 ng/L**.
- **New Sex-Specific Reference Ranges:** sex-specific 99th centiles will be implemented:
  - **Male:** 32 ng/L
  - **Female:** 18 ng/L

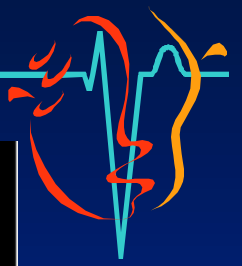
Should you have any questions in this matter please do not hesitate to contact us.

Troponin T: The Next Generation

Differences

- **Less susceptible to interference:**
  - **Biotin**
  - **Haemolysis**
  - **Icterus**

Troponin T: Haemolysis



```
Troponin T (hs)                >26    ng/L            (     0 to 14    ) Auth
  Comments :
   The haemolysis associated with this sample may reduce
   the troponin T result. The result provided is an
   estimate and should be repeated in a non-haemolysed
   sample to confirm.
```

	2025	14 days
Affected by haemolysis	1134 (3.4%)	3 (0.19%)
Haemolysis: reported as a > result	638 (1.9%)	1
Haemolysis: unable to report as <LoQ	496 (1.5%)	2

Troponin T: The Next Generation

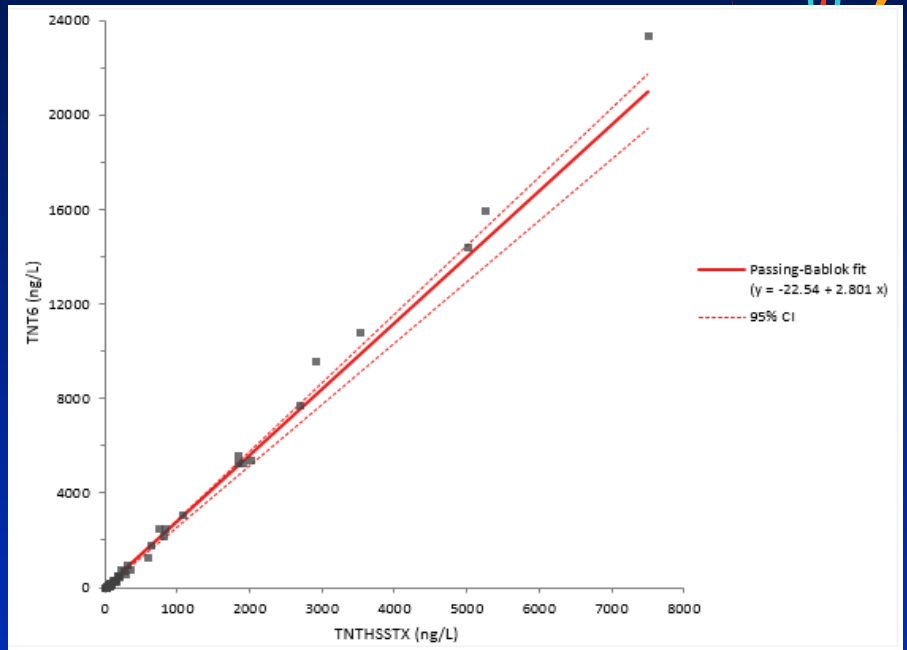
Differences

- **New Antibody that “binds to the identical epitopes as TnT hs / Gen 5”**
- **Change in calibration**
- **Higher results**
- **Some patients may change classification**

Roche Product Information Notice Information Only 11/03/2026 EI Pre-launch information for the Elecsys® Troponin T hs Gen 6 Immunoassay MN-RDS-CoreLab-20250=-029

Numerical Differences

- The numerical relationship between the assays differs especially at lower concentrations



N	91

	Minimum	Maximum
TNTHSSTX	3.000	7500.000
TNT6	2.520	23329.000

Correlation - r	0.999

Fit Y on X

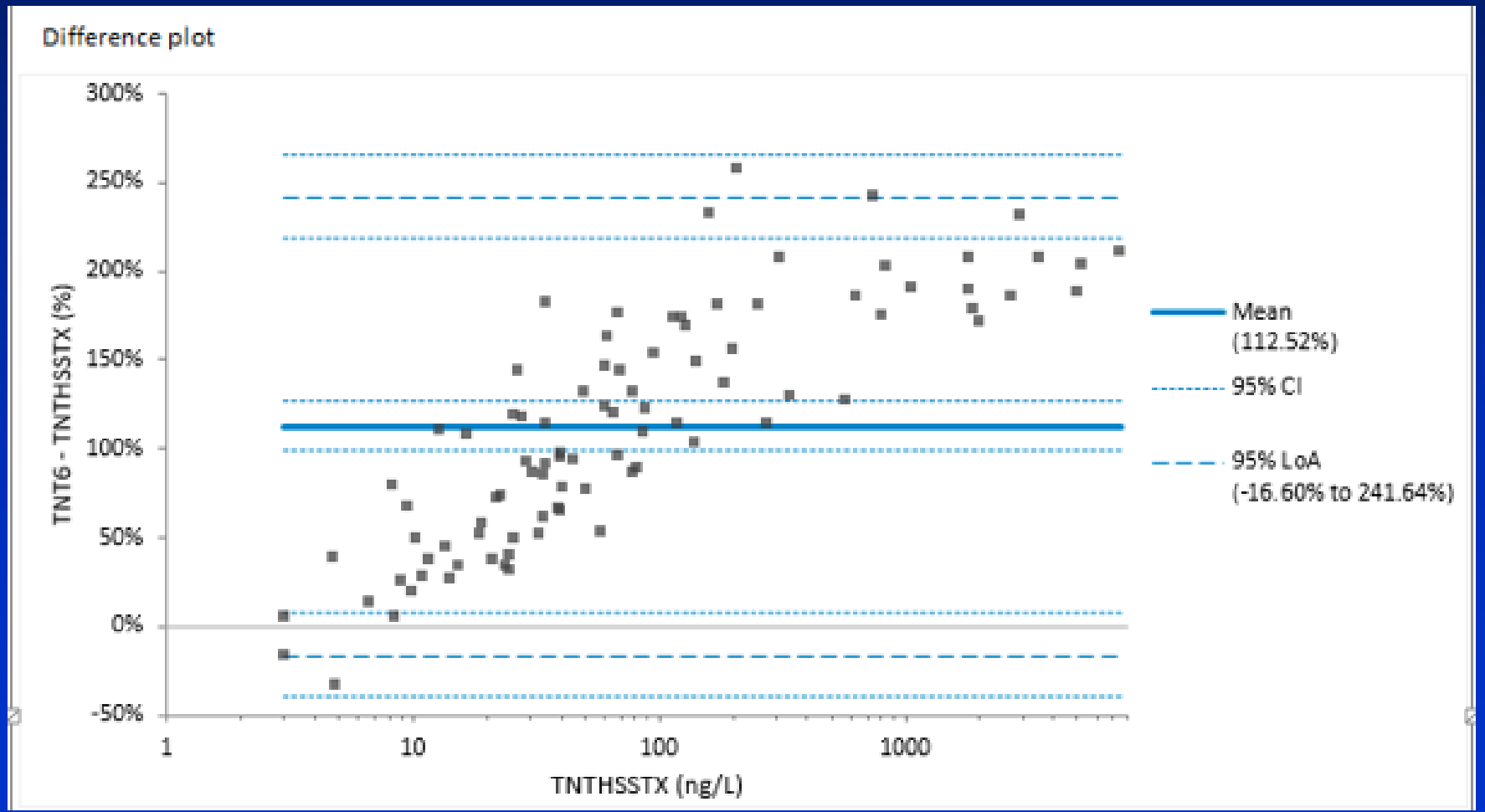
Passing-Bablok fit

Equation	TNT6 (ng/L) = -22.54 + 2.801 TNTHSSTX (ng/L)

Parameter	Estimate	Bootstrap 95% CI
Intercept	-22.54	-28.31 to -14.83
Slope	2.801	2.591 to 2.900

Numerical Differences

Percentage Differences (%)

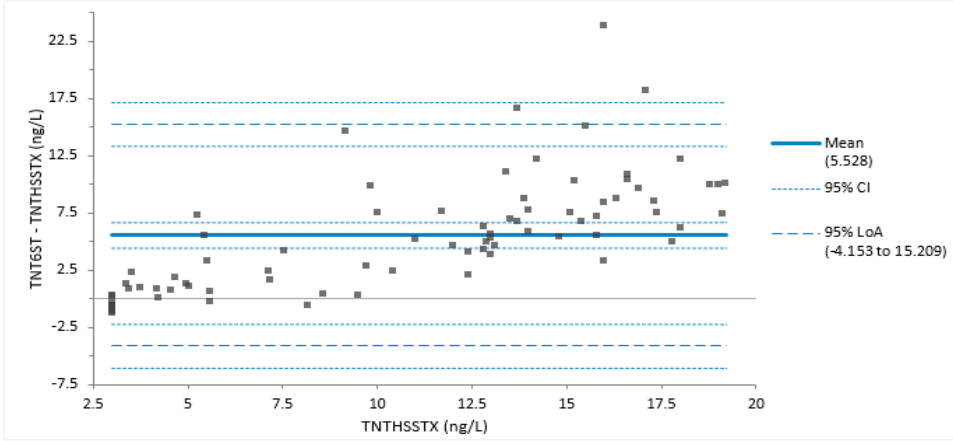


Numerical Differences

Absolute Differences (ng/L)

Descriptives

Difference plot



N	78

	Minimum	Maximum
TNTHSSTX	3.000	19.200
TNT6ST	1.690	39.900

Correlation - r	0.930

Fit Differences

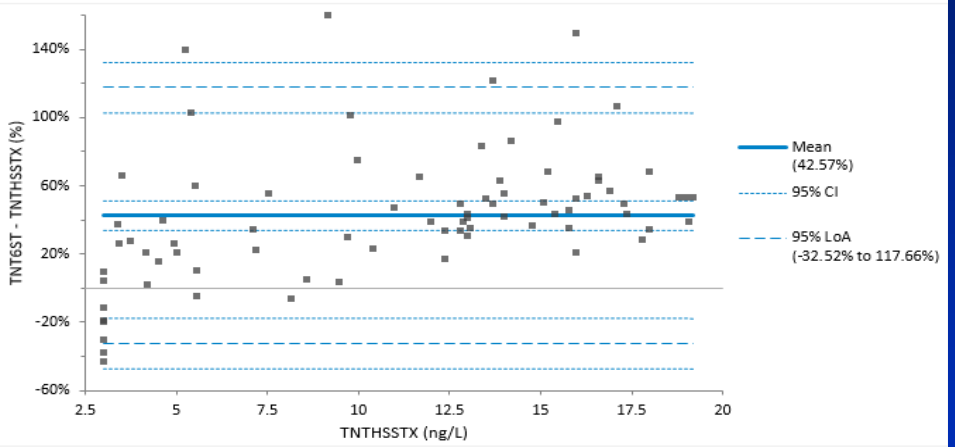
Parameter	Estimate	95% CI	SE
Mean difference	5.528	4.4148 to 6.6421	0.5593
95% Lower LoA	-4.153	-6.0639 to -2.2412	0.9599
95% Upper LoA	15.209	13.2981 to 17.1209	0.9599

SD	4.939

Percentage Differences (%)

Descriptives

Difference plot



N	78

	Minimum	Maximum
TNTHSSTX	3.000	19.200
TNT6ST	1.690	39.900

Correlation - r	0.930

Fit Differences

Parameter	Estimate	95% CI	SE
Mean difference	42.57%	33.930% to 51.206%	4.338%
95% Lower LoA	-32.52%	-47.344% to -17.694%	7.445%
95% Upper LoA	117.66%	102.830% to 132.480%	7.445%

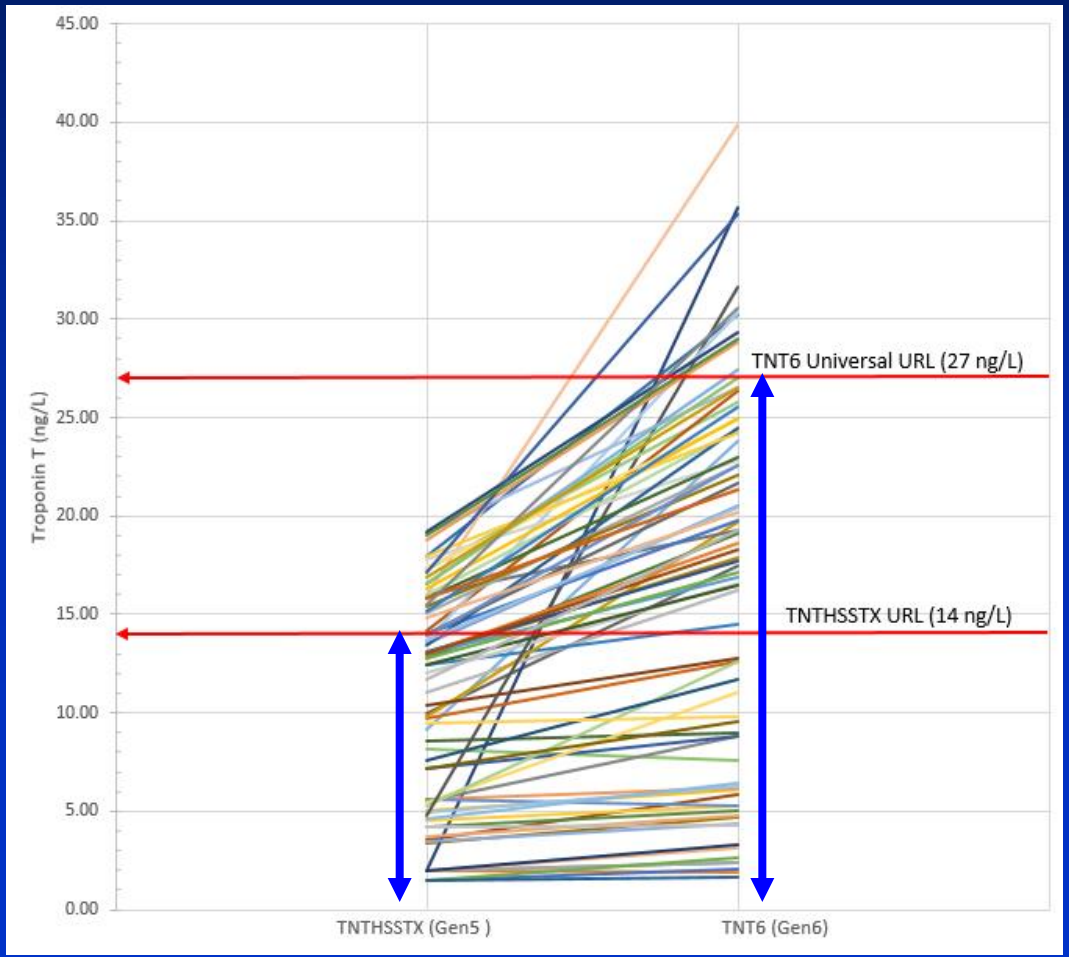
SD	38.31%

Numerical Differences

- But these are only numbers!
- We treat patients

Classification Differences

Universal 99th Percentile (20 M <14, 20 M 14-20, 20 F <14, 20 F 14-20)



Patient comparison @ 99th centile: current Gen 5 TnT hs vs proposed Gen 6 TnT hs.

Cohort: 80 patient samples (40 male, 40 female) spanning 0-20 ng/L, as measured by Gen 5 TnT hs.

Gen 5 Universal URL (>14 ng/L) vs Gen 6 Universal URL (>27 ng/L)					
		Female	*Male*	*Total (/80)*	*%*
Change	Negative → Positive	2	1	3	4
	Positive → Negative	9	8	17	21
No change	Negative → Negative	27	25	52	65
	Positive → Positive	2	6	8	10
Gen 5 Universal URL (>14 ng/L) vs Gen 6 Gender Specific URL (>18, >32 ng/L)					
		Female	*Male*	*Total (/80)*	*%*
Change	Negative → Positive	7	0	7	9
	Positive → Negative	0	13	13	16
No change	Negative → Negative	22	26	48	60
	Positive → Positive	11	1	12	15
Gen 5 Gender Specific URL (>9, >16.8 ng/L) vs Gen 6 Gender Specific URL (>18, >32 ng/L)					
		Female	*Male*	*Total (/80)*	*%*
Change	Negative → Positive	1	0	1	1
	Positive → Negative	8	5	13	16
No change	Negative → Negative	14	34	48	60
	Positive → Positive	17	1	18	23

Universal (>14) → Universal (>27)

75% unchanged

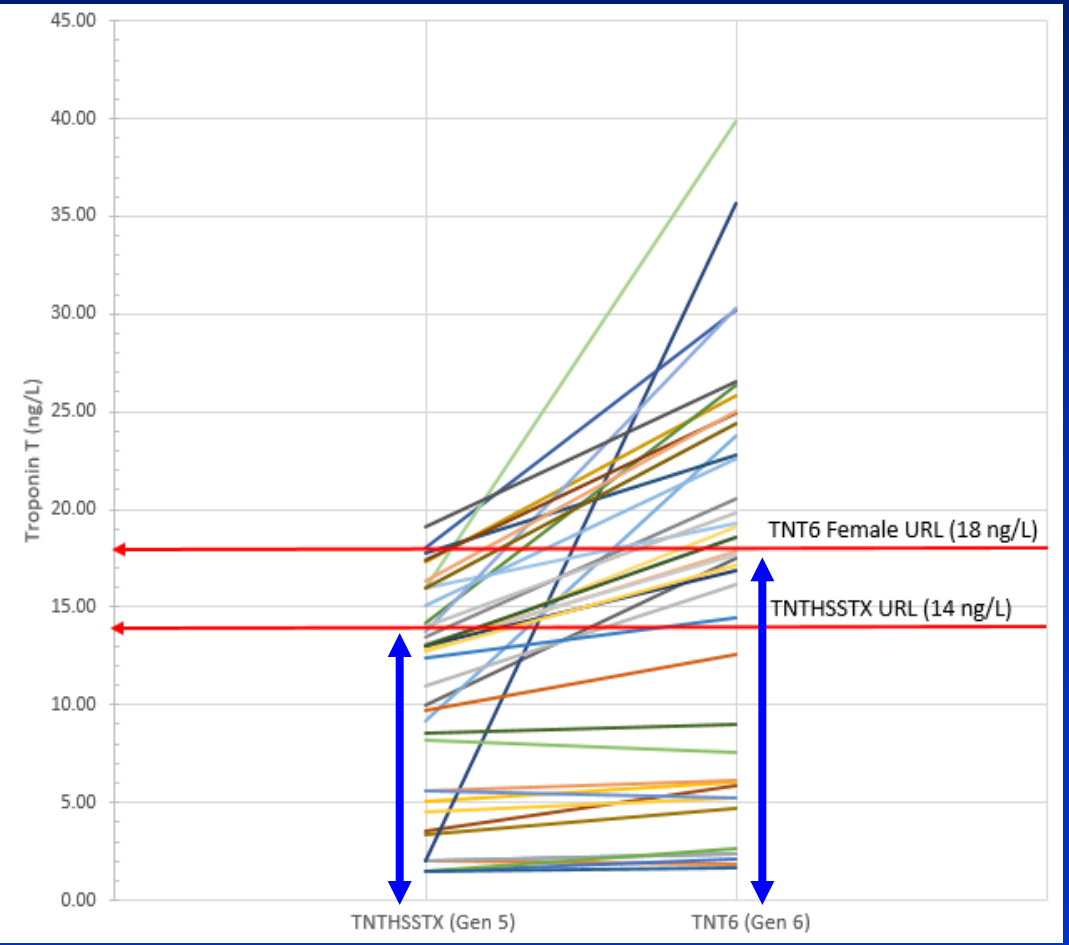
4% → +ve

21% → –ve

} 17% fewer positives overall

Classification Differences

Female 99th Percentile (20 <14, 20 14-20)



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		Female	*Male*	*Total (/80)*	*%*
Change	Negative → Positive	1	0	1	1
	Positive → Negative	8	5	13	16
No change	Negative → Negative	14	34	48	60
	Positive → Positive	17	1	18	23

Universal (>14) → Gender Specific (>18, >32)

75% unchanged

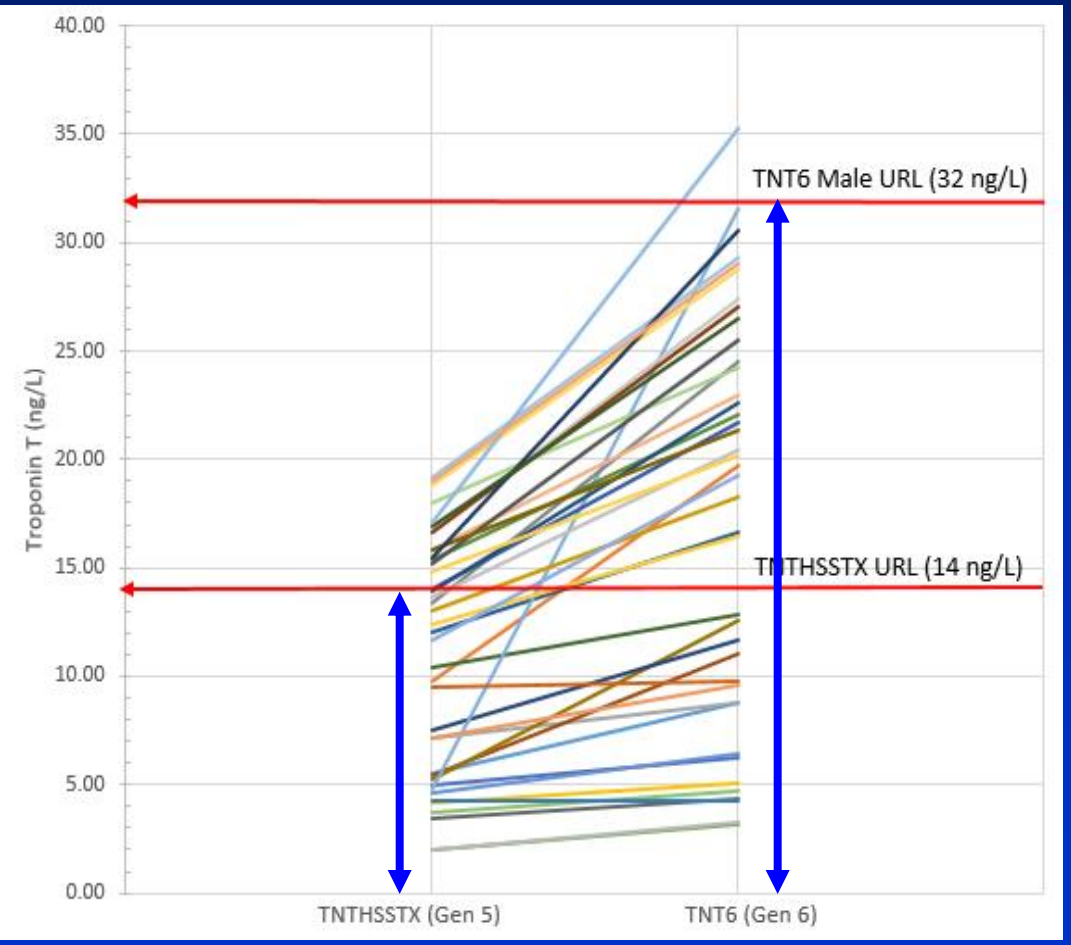
9% (all female) → +ve

16% (all male) → –ve

} 7% fewer positives overall

Classification Differences

Male 99th Percentile (20 <14, 20 14-20)



Patient comparison @ 99th centile: current Gen 5 TnT hs vs proposed Gen 6 TnT hs.

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		Female	*Male*	*Total (/80)*	*%*
Change	Negative → Positive	2	1	3	4
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Change	Negative → Positive	1	0	1	1
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Universal (>14) → Gender Specific (>18, >32)

75% unchanged

9% (all female) → +ve

16% (all male) → –ve

} 7% fewer positives overall

Result Interpretation

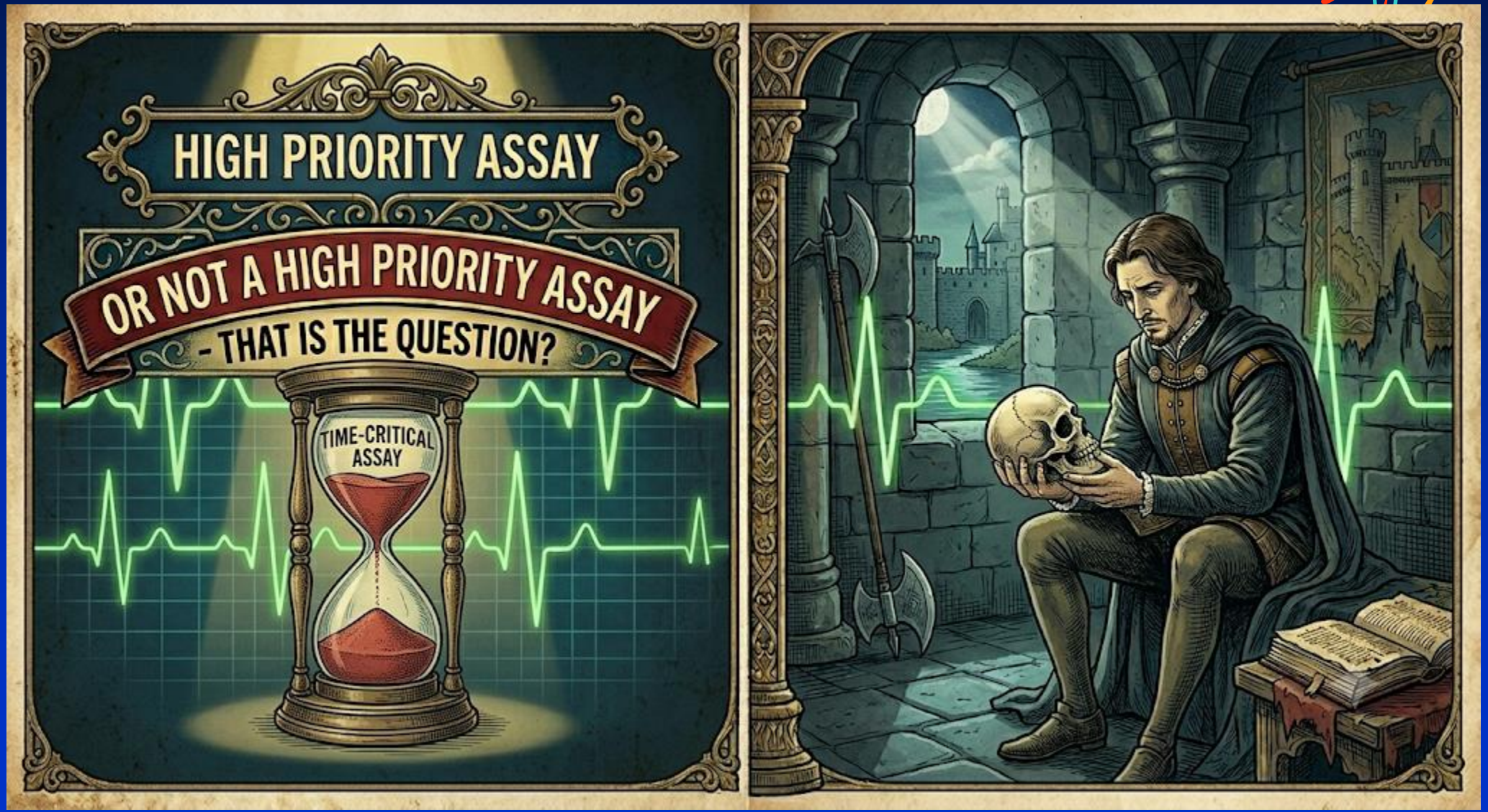
Pre-analytical	Analytical	Post-analytical
• Patient state	• Method type	• Transmission of the test result
• Biological variation	• Calibration	• Reference interval
• Patient preparation	• Lot number	• Decision points
• Collection protocol	• Operator	
• Sample processing	• Traceability	

Patient Sample

Uncertainty of measurement

Interpretation

Troponin T: The Next Generation



Troponin T: The Next Generation

VV-08883 V22
04/16/26

Roche

CustomerBulletin

☐ Reagent ☐ Software ☑ Analyzer

cobas® e 801 module (cobas 8000 modular analyzer series) and cobas e 801 analytical unit (cobas pro integrated solutions) — Handling of High Priority Tests

This Customer Bulletin has been updated to add the Elecsys® BRAHMS PCT 100-test kit. Updates are indicated by black bars in the margins.

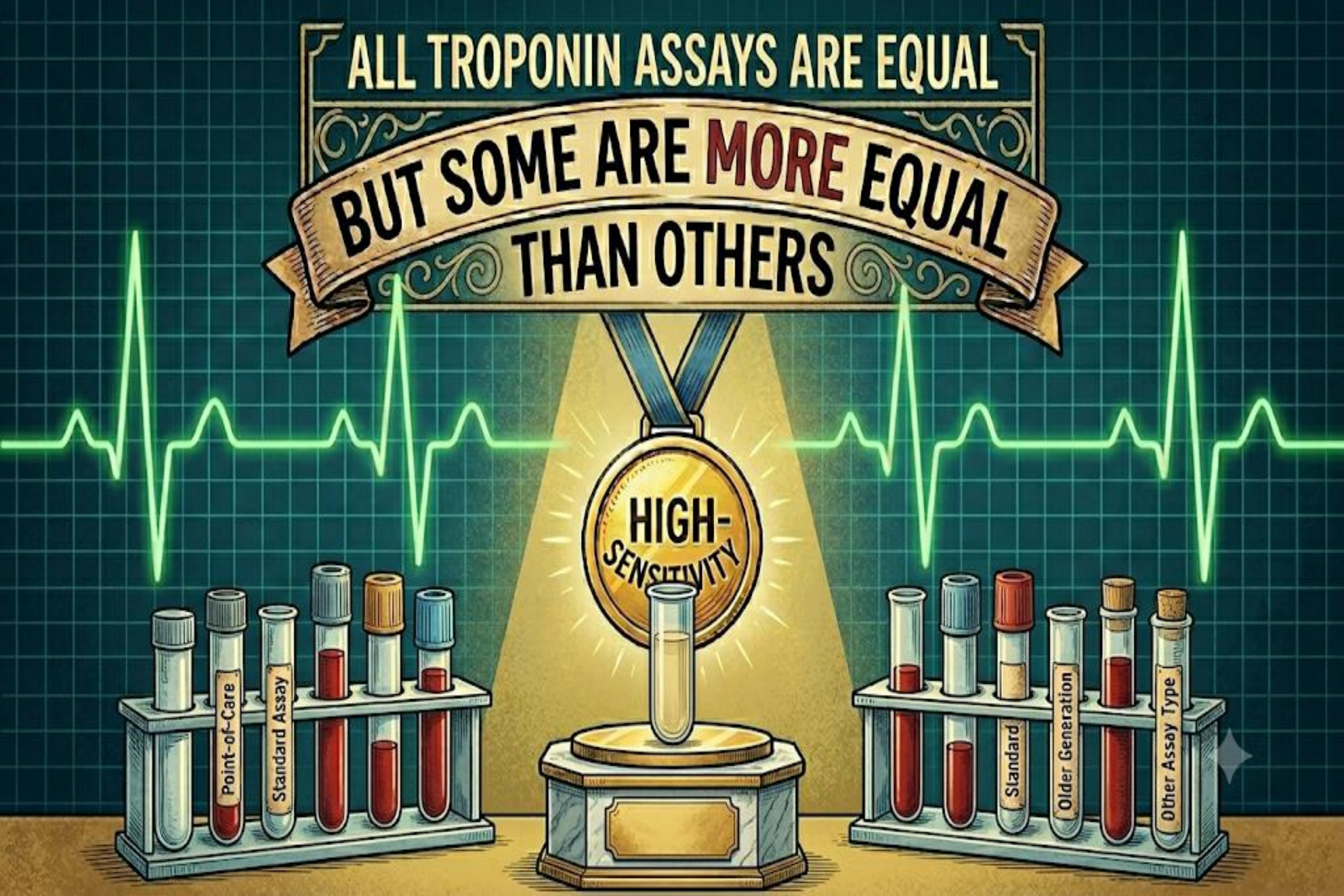
Information

The **cobas** 8000 modular analyzer series can contain combinations of the clinical chemistry analyzer (**cobas** c 502, 701, and/or 702 modules), the **cobas** 8000 ISE module, and the immunoassay analyzer (**cobas** e 602 and/or 801 modules). The **cobas pro** integrated solutions can also contain combinations of the clinical chemistry analyzer (**cobas** c 503 analytical unit), the ISE analytical unit, and the immunoassay analyzer (**cobas** e 801 analytical unit). The assays performed on these systems are assigned one of two priority levels: either normal or high. High priority levels are assigned to certain immunoassays in order to prevent potential sample carryover from the sample probes used on the clinical chemistry analyzers and the ISE module/analytical unit.

If a high priority test is run after clinical chemistry tests, a Data alarm of Samp.O will be attached to the result, and a new sample should be drawn and run. If one or more of the **cobas** e 801 analytical unit applications listed in the NAOHD - SMS - SCCS method sheet wash list is added on to a sample that has already been sampled by the **cobas** c 503 analytical unit or ISE analytical unit without a sonic wash of the sample probe prior to pipetting, a new sample should be drawn and run.

Software generates Flag 83 primary tube carryover warning (as opposed to Flag 71)

Not mentioned on IFU or VV-08883 V22 (pre-dates new assay by days)


ALL TROPONIN ASSAYS ARE EQUAL
BUT SOME ARE MORE EQUAL
THAN OTHERS
HIGH-
SENSITIVITY
Point-of-Care
Standard Assay
Standard
Older Generation
Other Assay Type

JAMA Cardiology

Brief Report

Clinical Decisions and Outcomes After Switching High-Sensitivity Cardiac Troponin Assays in Suspected ACS

An Interrupted Time-Series Study

Jasper Boeddinghaus, MD[1,2]; Ziwen Li, PhD[1]; Anda Bularga, MD[1]; Caelan Taggart, MD[1]; Ryan Wereski, MD[1]; Andrew R. Chapman, MD, PhD[1]; Kuan Ken Lee, MD, PhD[1]; Christopher Tuck, BSc[1]; Robyn Gunn, MSc[3]; Sara Jenks, MBChB[3]; Kirsty McCance, MBChB[3]; Rebecca Pattenden, MSc[4]; Jonathan Malo, MD[3]; Alexander J. F. Thurston, BMBCh[1]; Yong Yong Tew, MD[1]; Michael McDermott, MD[1]; Alasdair Gray, MD[5,6]; Nicholas L. M. Cruden, MD, PhD[7]; Atul Anand, MD, PhD[1]; Dorien M. Kimenai, PhD[1]; Nicholas L. Mills, MD, PhD[1,6]; for the TWITCH-ED Investigators

Author Affiliations | Article Information

[1]BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom

[2]Cardiovascular Research Institute Basel (CRIB) and Department of Cardiology, University Hospital Basel, University of Basel, Basel, Switzerland

[3]Department Clinical Biochemistry, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

[4]Department Clinical Biochemistry, Western General Hospital, Edinburgh, United Kingdom

[5]Department of Emergency Medicine, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

[6]Usher Institute, University of Edinburgh, Edinburgh, United Kingdom

[7]Edinburgh Heart Centre, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

JAMA Cardiol
Published Online: December 17, 2025
2026;11;(2):186-192.
doi:10.1001/jamacardio.2025.4661

Result Interpretation

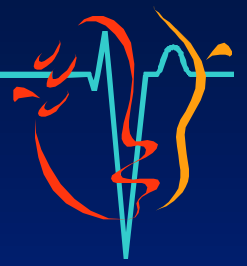
Key Points

Question What are the clinical and health system–level implications of changing high-sensitivity cardiac troponin assays?

Findings In this interrupted time-series study including 25 849 patients, switching cardiac troponin assays was associated with a doubling in the proportion of patients with suspected acute coronary syndrome identified with myocardial injury, more hospital admissions, and more serial cardiac troponin measurements without evidence of improved cardiovascular outcomes at 1 year.

Meaning High-sensitivity cardiac troponin I and T assays are not equivalent; health systems and clinicians should be aware that switching cardiac troponin assays may impact hospital admissions, testing, and resource utilization.

Potential future IVD Manufacturer claims



- **“CV risk stratification”**
- **“Tn T Gen 6 specific 0/1h and 0/2h algorithm”**
  - **Potentially shorter time to rule out a significant change in due course**

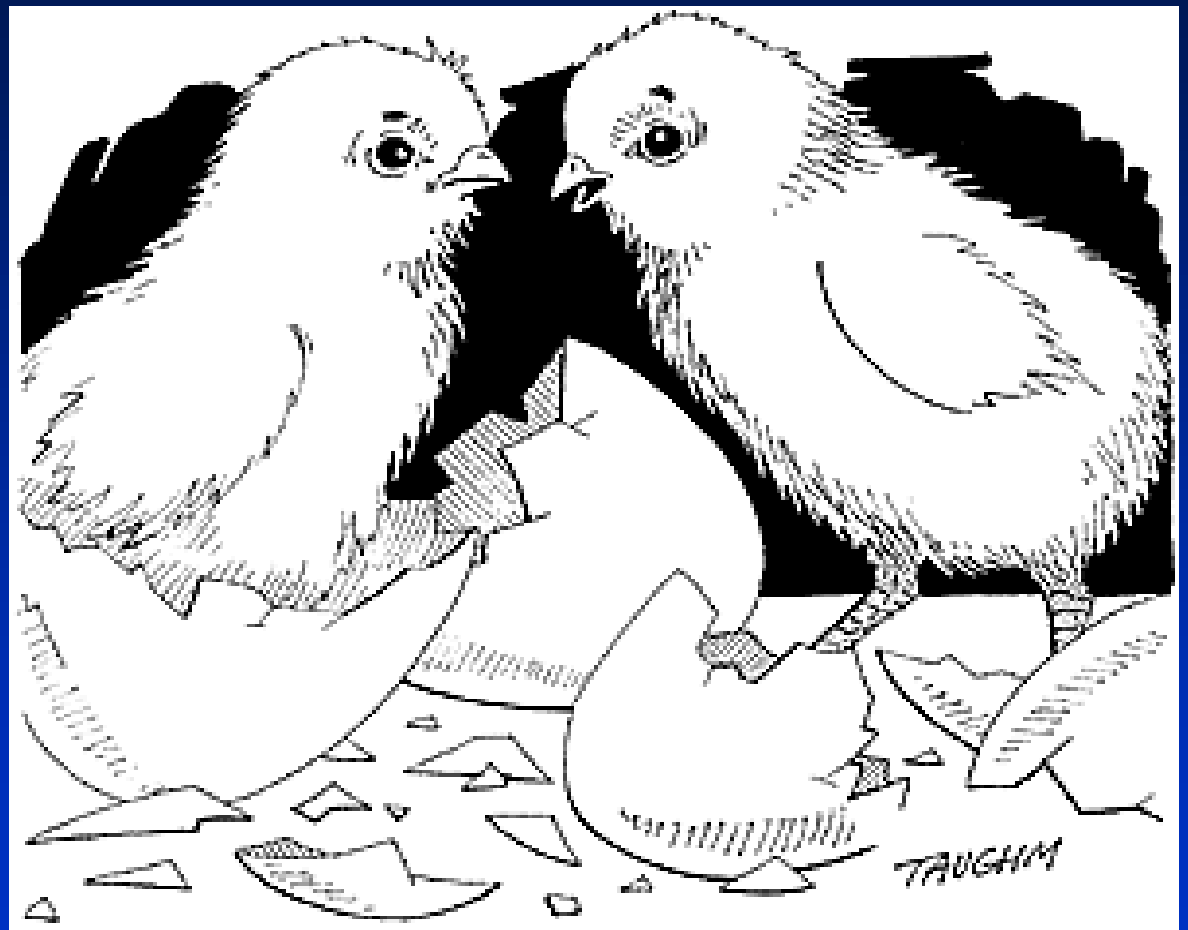
Take Home Messages

- **Results are not directly comparable to previous results**
- **More certainty when**
  - **the result is low, for example, for rule out levels**
  - **the result is below the sex-based 99th percentile**
  - **looking at result changes**
- **Watch this space for evidence based pathways**

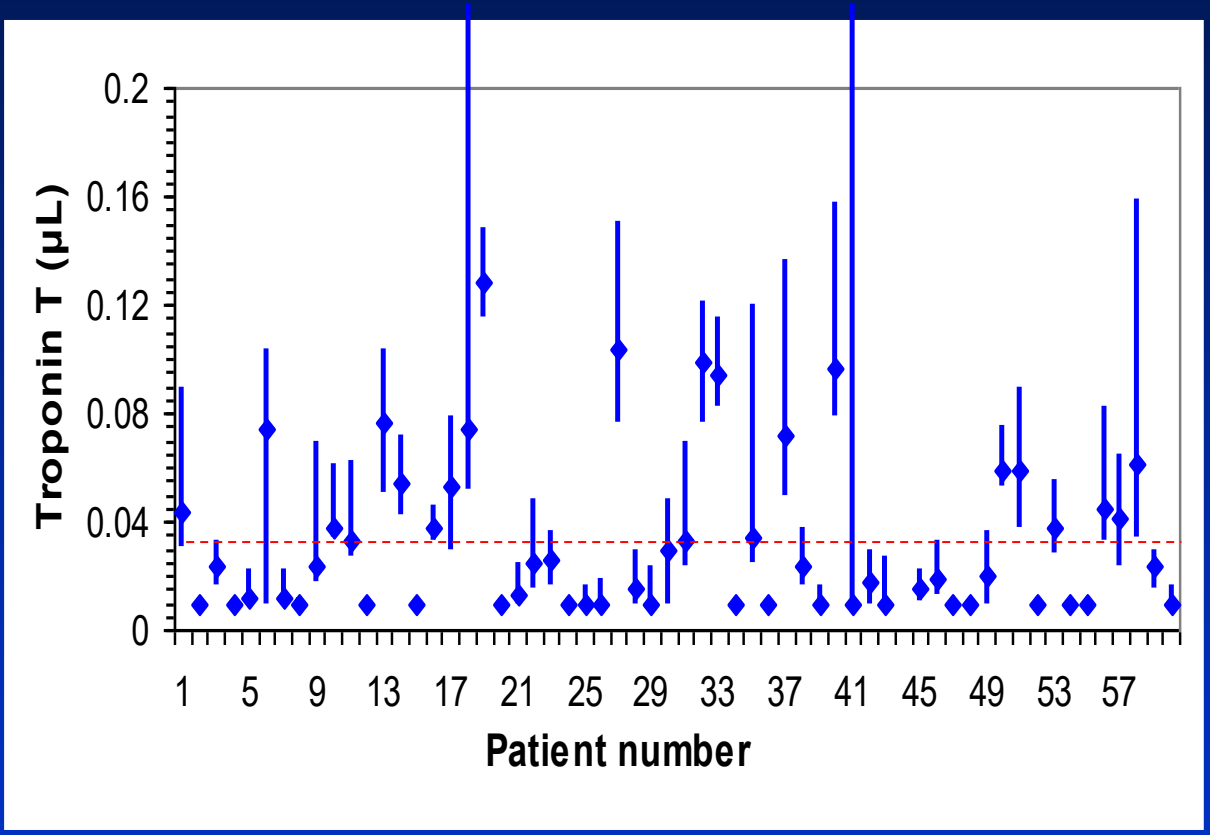
Acknowledgements

- Heloise Tarrant PhD Principal Biochemist
- Cameron Daly 4th / Final Year Medical Science
- Paraic Keane PhD Biochemist

Questions?


TAUGHM
"Whew! I'm glad that's over - all that cholesterol was killing me!"
Medscape ®
http://www.medscape.com

Tn T in dialyzed patients



TNT6 (ng/L)	TNTHSSTX (ng/L)	Sex	eGFR
236	103	Female	<15
253	77	Female	<15
491	207	Female	<15
23	14	Female	<15
373	133	Female	<15
40	21	Female	<15
67	34	Female	<15
103	49	Male	<15
219	88	Male	<15
342	119	Male	<15
517	189	Male	<15
181	55	Male	<15
135	72	Male	<15
88	42	Male	<15

Adapted from data obtained from the author. Hill SA, et al., Intra-individual variability in troponin T concentration in dialysis patients, Clin Biochem (2009), doi:10.1016/j.clinbiochem.2009.03.027.