Clinical derivation and data simulated validation of rule-out and rule-in algorithms for the Siemens Atellica IM high-sensitivity cardiac troponin I assay

Supplemental Material

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Content

Supplemental Methods

Diagnostic definitions

Myocardial infarction (AMI, MI): defined according to the third universal definition of myocardial infarction[1]:

Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin) with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:

1. Symptoms of ischemia
2. Development of pathologic Q waves in the electrocardiogram (ECG)
3. New or presumed new significant ST-Segment-T wave (ST-T) changes or new left bundle branch block (LBBB).
4. Identification of an intracoronary thrombus by angiography or autopsy
5. Imaging evidence of new loss of viable myocardium or a new regional wall motion abnormality

Unstable angina pectoris **(**UAP): defined as symptoms suggestive of an ACS without elevation in biomarkers with or without ECG changes indicative of ischemia.[2]

Stable angina was defined as typical angina symptoms lasting >1 month without an increase in magnitude, duration or frequency of the pain and a known history of coronary artery disease.[3]

Pericarditis was diagnosed if at least two of four diagnostic criteria were present, as defined in several studies: typical pleuritic chest pain, detection of a pericardial rub on auscultation, typical ECG changes, new or increased amount of pericardial effusion on echocardiography.[4]

Myocarditis was diagnosed according to the position statement of ESC from 2013.[5]

Takotsubo cardiomyopathy was diagnosed with the modified criteria suggested by The Mayo Clinic in 2008.[6]

Heart failure was defined according to the ESC diagnostic criteria of 2016.[7]

Atrial fibrillation, atrial flutter and other supraventricular arrhythmias were diagnosed by ECG findings and the lack of symptoms and biochemical results supporting another disease.

Aortic stenosis and other valvular diseases were diagnosed in accordance with echocardiographic results and a history supporting the valve disease as cause of the symptoms.[8]

Myalgia was defined as chest pain provoked by palpation in lack of cardiac disease.

GERD was based on gastroscopic findings, also in the lack of cardiac disease.

Cholecystitis was defined by the Tokyo Guidelines of 2006 while other abdominal diseases where defined according to operative, endoscopic or radiological findings.[9]

Pneumonia was defined by typical symptoms and a chest X-ray supporting the disease, while the diagnosis of both pulmonary embolism and pneumothorax were based on radiologic results and the lack of concurrent cardiac disease.

COPD was defined in accordance with the criteria by Stephens MB from 2008.[10]

NCCP was defined as chest pain without any specific clinical, radiologic or biochemical findings.

Biochemical analysis

Hs-cTnT was measured using the Roche Diagnostics hs-cTnT assay with limit of blank (LoB) 3 ng/L, limit of detection (LoD) 5 ng/L, 99th percentile 14 ng/L, measurement range 4 - 10 000 ng/L and 10% analytical within-series coefficient of variation (CV_A) at 4.5 ng/L; CV_A was below 5% for concentrations of 10 ng/L or higher[11].

Hs-cTnI (Abbott) was measured using the Abbott Diagnostics hs-cTnI assay. The assay has a LoB 0.9 ng/L, LoD 1.7 ng/L, 99th percentile 26 ng/L and measurement range 2-50 000 ng/L, with 10% CV_A at 4.6 ng/L[11].

Hs-cTnI (Siemens) was measured using the Siemens hs-cTnI assay with limit of blank (LoB) 0.5 ng/L, limit of detection (LoD) 1.6 ng/l, measurement range 2.5-25 000 ng/L and 10% coefficient of variation at 6 ng/L. The 99th percentile is 38.6 ng/L in women and 53.5 ng/L in men.[11]

The glomerular filtration rate was estimated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration)[12] formula using an enzymatic isotope dilution mass spectrometry traceable creatinine assay (Roche Diagnostics) with a CV_A less than 3% for concentrations > 60 µmol/L.[12]

Supplemental Results

Review of missed patients

Index NSTEMI missed by single sample Siemens hs-cTnI < 5 ng/L

Patient A

66 year old male. Non-early presenter. Prior CAD

0-3 cTn: Roche 4-71, Abbott 2-80, Siemens 2-146.

Patient B

79 year old male. Non-early presenter. No known prior CAD.

0-1-3 cTn: Roche 17-117-115, Abbott 184-195-177, Siemens 3-334-331.

30 day MI (other than index) or death missed both by single sample Siemens hs-cTnI < 5 ng/L and 0-1 hs-cTnI <10 and Δ < 3 ng/L

Patient C

54 year old male. Prior CAD. Symptoms > 3 hours before first blood draw.

0-1-3 hour cTn: Roche 3-3-3, Abbott 1-2-1, Siemens 1-1-1.

New pain event 6 hours after admittance. STEMI on EKG. Subtotal occlusion on coronary angiography.

Supplemental Tables

Supplemental Table 1. Expanded baseline characteristics

Patients divided by diagnostic groups and percentage of diagnostic modalities and management.

	Total	NSTEMI	UAP	Other cardiac	Non-cardiac	NCCP
Diagnostic groups						
Patient count (%)	1896	234 (12.3)	252 (13.3)	172 (9.1)	131 (6.9)	1107 (58.4)
Echo						
Echocardiography performed	42.9%	88.0%	71.4%	49.4%	31.3%	27.2%
Echocardiography EF < 50%	5.0%	16.2%	5.6%	14.0%	3.1%	1.4%
Stress-EKG						
N/A	82.5%	99.6%	82.1%	84.9%	91.6%	77.6%
Positive	2.8%	0.4%	7.9%	3.5%	0.8%	2.3%
Normal	10.1%	N/A	3.2%	8.7%	6.1%	14.5%
Inconclusive	3.5%	N/A	6.0%	2.3%	1.5%	4.1%
CT angiography						
N/A	64.7%	93.2%	67.1%	79.1%	84.7%	53.6%
Possible stenosis	5.7%	2.6%	21.0%	4.1%	1.5%	3.6%
Non-stenotic calcification(s)	12.7%	1.7%	6.0%	7.0%	3.8%	18.5%
Patent vessels	15.6%	2.1%	2.4%	7.0%	9.2%	23.5%
High calcium score/inconclusive	1.2%	0.4%	3.2%	2.9%	0.8%	0.6%

Coronary angiography						
N/A	73.4%	11.5%	29.4%	80.2%	94.7%	92.9%
Angio. no intervention	10.1%	16.2%	19.8%	16.3%	4.6%	6.2%
Angio + PCI	14.0%	63.2%	43.7%	1.7%	0.8%	0.3%
Angio + CABG	2.1%	7.7%	5.2%	1.7%	N/A	0.5%
Angio + CTO-PCI	0.2%	N/A	1.2%	N/A	N/A	N/A
Angio + failed PCI	0.3%	1.3%	0.8%	N/A	N/A	N/A
Management						
Discharged from ED to home	6.2%	N/A	0.8%	9.3%	7.6%	8.0%
Admitted to ward	92.0%	100.0%	99.2%	90.7%	92.4%	92.0%
Planned procedure on discharge						
N/A	96.4%	91.5%	89.7%	93.0%	99.2%	99.2%
Elective angio/PCI	2.5%	4.3%	8.7%	4.7%	N/A	0.7%
Transfer for complex PCI	0.1%	0.9%	N/A	N/A	N/A	N/A
Elective/urgent CABG	0.7%	3.4%	1.6%	0.6%	N/A	N/A
Elective other cardiac surgery	0.2%	N/A	N/A	1.7%	N/A	N/A

Supplemental Table 2: Events by subgroup and types

Diagnostic group	**Patient count**	**Myocardial infarction (MI)**		**Revascularization (R)**	**Death (D)**	**MI or Death**	**MI or Death or R**
		On presentation	**Later than presentation**				
Derivation cohort							
NSTEMI	234	234 (100%) *Type 1: 204 (87%)* *Type 2: 30 (13%)*	1 (0.4%) *Type 1: 1 (100%)*	170 (72.6%)	1 (0.4%)	234 (100%)	234 (100%)
UAP	252	0	4 (1.6%) *Type 1: 4 (100%)*	138 (54.8%)	1 (0.4%)	5	139 (55.2%)
Other cardiac	172	0	0	6 (3.5%)	2 (1.2%)	2	8 (4.7%)
Non-cardiac	131	0	1 (0.8%) *Type 1: 1 (100%)*	1 (0.8%)	1 (0.8%)	2	3 (2.3%)
NCCP	1107	0	1 (0.09%) *Type 1: 1 (100%)*	11 (1.0%)	0	1	12 (1.1%)
Total	1896	234 (12.3%)	7 (0.4%) *Type 1: 7 (100%)*	325 (17.1%)	5 (0.3%)	244 (12.9%)	396 (20.9%)

Supplemental Table 3: AUC tables

Pairwise comparison of diagnostic accuracy. P-values calculated by DeLong test.

Hs-cTn assay	Endpoint	AUC	95% CI	P-values	
				Hs-cTnI (Abbott)	Hs-cTnI (Siemens)
Hs-cTnT (Roche) - Real	30-day MI or death	0.916	0.897-0.935	0.005	0.001
	Index NSTEMI	0.920	0.901-0.938	0.003	<0.001
Hs-cTnI (Abbott) - Real	30-day MI or death	0.937	0.919-0.955		0.68
	Index NSTEMI	0.942	0.925-0.960		0.45
Hs-cTnI (Siemens) - Real	30-day MI or death	0.939	0.923-0.955		
	Index NSTEMI	0.946	0.932-0.960		
Hs-cTnT (Roche) - Synthetic	30-day MI or death	0.919	0.918-0.920	<0.001	<0.001
	Index NSTEMI	0.919	0.918-0.920	<0.001	<0.001
Hs-cTnI (Abbott) - Synthetic	30-day MI or death	0.946	0.945-0.947		0.19
	Index NSTEMI	0.946	0.945-0.947		0.19
Hs-cTnI (Siemens) - Synthetic	30-day MI or death	0.946	0.945-0.946		
	Index NSTEMI	0.946	0.945-0.946		

Supplemental Table 4: Derivation of single sample rule-out 30 day MI or death algorithms

Assay	Cutoff < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
Roche	5	98.4 (95.8 - 99.5)	99.3 (98.2 - 99.8)	34.1 (31.8 - 36.4)	18.0 (16-0 - 20.2)	566	29.9	4	1,088
Abbott	4.0	95.9 (92.6 - 98)	99.0 (98.3 - 99.5)	63.2 (60.8 - 65.6)	27.8 (24.8 - 30.9)	1,052	55.6	10	606
Siemens	1.0	99.6 (97.7 - 100)	97.7 (88.0 - 99.9)	2.6 (1.9 - 3.5)	13.1 (11.6 - 14.7)	44	2.3	1	1,607
	1.5	99.6 (97.7 - 100)	99.1 (95.0 - 100)	6.6 (5.5 - 7.9)	13.6 (12.0 - 15.3)	110	5.8	1	1,541
	2.0	99.6 (97.7 - 100)	99.5 (97.2 - 100)	11.9 (10.4 - 13.5)	14.3 (12.6 - 16.0)	197	10.4	1	1,454
	2.5	99.2 (97.1 - 99.9)	99.4 (97.7 - 99.9)	18.6 (16.8 - 20.6)	15.2 (13.5 - 17.1)	309	16.3	2	1,343
	3.0	99.2 (97.1 - 99.9)	99.5 (98.3 - 99.9)	25.9 (23.8 - 28.1)	16.5 (14.6 - 18.5)	429	22.7	2	1,223
	3.5	98.8 (96.4 - 99.7)	99.5 (98.5 - 99.9)	34.5 (32.2 - 36.8)	18.2 (16.1 - 20.4)	572	30.2	3	1,081
	4.0	98.8 (96.4 - 99.7)	99.6 (98.7 - 99.9)	41.0 (38.6 - 43.4)	19.8 (17.6 - 22.1)	679	35.9	3	974
	4.5	98.8 (96.4 - 99.7)	99.6 (98.9 - 99.9)	46.8 (44.4 - 49.3)	21.5 (19.1 - 24.0)	776	41.0	3	877
	5.0	98.8 (96.4 - 99.7)	99.7 (99.0 - 99.9)	52.1 (49.6 - 54.5)	23.3 (20.7 - 26.0)	862	45.5	3	791
	5.5	98.4 (95.8 - 99.5)	99.6 (98.9 - 99.9)	55.8 (53.3 - 58.2)	24.7 (22.0 - 27.5)	924	48.8	4	730
	6.0	97.5 (94.7 - 99.1)	99.4 (98.7 - 99.8)	59.5 (57.1 - 61.9)	26.2 (23.3 - 29.2)	988	52.2	6	668
	6.5	97.1 (94.2 - 98.8)	99.3 (98.6 - 99.7)	62.3 (59.9 - 64.6)	27.5 (24.5 - 30.6)	1,035	54.7	7	622
	7.0	97.1 (94.2 - 98.8)	99.4 (98.7 - 99.7)	65.4 (63.0 - 67.7)	29.2 (26.1 - 32.5)	1,086	57.4	7	571
	7.5	96.7 (93.6 - 98.6)	99.3 (98.6 - 99.7)	67.6 (65.3 - 69.8)	30.5 (27.3 - 33.9)	1,123	59.3	8	535
	8.0	96.7 (93.6 - 98.6)	99.3 (98.6 - 99.7)	69.3 (67.0 - 71.6)	31.7 (28.4 - 35.2)	1,152	60.9	8	506
	8.5	96.3 (93.1 - 98.3)	99.2 (98.6 - 99.7)	71.0 (68.8 - 73.2)	32.9 (29.4 - 36.5)	1,181	62.4	9	478
	9.0	95.9 (92.6 - 98.0)	99.2 (98.5 - 99.6)	72.2 (70.0 - 74.4)	33.7 (30.2 - 37.4)	1,202	63.5	10	458
	9.5	94.7 (91.0 - 97.1)	98.9 (98.2 - 99.4)	73.3 (71.1 - 75.4)	34.3 (30.7 - 38.0)	1,222	64.6	13	441
	10.0	94.2 (90.5 - 96.8)	98.9 (98.1 - 99.4)	74.5 (72.4 - 76.6)	35.3 (31.6 - 39.1)	1,244	65.7	14	420

Supplemental Table 5: Validation of single sample rule-out 30 day MI or death algorithms

Assay	Cutoff < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
Roche	5	98.6 (98.5 - 98.7)	99.4 (99.4 - 99.5)	33.9 (33.8 - 34)	17.3 (17.2 - 17.4)	29.9
Abbott	4.0	96.5 (96.4 - 96.6)	99.2 (99.2 - 99.3)	63.1 (63 - 63.3)	26.8 (26.7 - 27.0)	55.8
Siemens	1.0	99.7 (99.7 - 99.8)	98.6 (98.4 - 98.7)	2.8 (2.7 - 2.8)	13.1 (13.1 - 13.2)	2.4
	1.5	99.6 (99.5 - 99.6)	99.0 (98.9 - 99.1)	6.7 (6.6 - 6.7)	13.6 (13.5 - 13.7)	5.9
	2.0	99.3 (99.3 - 99.4)	99.2 (99.1 - 99.2)	11.9 (11.8 - 12.0)	14.3 (14.2 - 14.3)	10.5
	2.5	99.0 (98.9 - 99.0)	99.2 (99.1 - 99.2)	18.7 (18.6 - 18.8)	15.2 (15.1 - 15.3)	16.4
	3.0	98.6 (98.5 - 98.6)	99.2 (99.2 - 99.2)	26.0 (25.9 - 26.0)	16.4 (16.3 - 16.5)	22.8
	3.5	98.6 (98.5 - 98.6)	99.4 (99.4 - 99.4)	34.5 (34.4 - 34.6)	18.2 (18.1 - 18.3)	30.2
	4.0	98.6 (98.5 - 98.6)	99.5 (99.5 - 99.5)	40.9 (40.8 - 41.0)	19.7 (19.6 - 19.8)	35.8
	4.5	98.6 (98.5 - 98.6)	99.5 (99.5 - 99.6)	46.7 (46.6 - 46.8)	21.4 (21.3 - 21.6)	40.9
	5.0	98.1 (98.0 - 98.2)	99.5 (99.4 - 99.5)	51.9 (51.8 - 52.0)	23.1 (23.0 - 23.2)	45.5
	5.5	97.1 (97.0 - 97.2)	99.2 (99.2 - 99.3)	55.6 (55.5 - 55.7)	24.4 (24.3 - 24.5)	48.8
	6.0	96.1 (96.0 - 96.2)	99.0 (99.0 - 99.1)	59.4 (59.2 - 59.5)	25.9 (25.7 - 26.0)	52.2
	6.5	95.5 (95.4 - 95.6)	99.0 (98.9 - 99.0)	62.3 (62.2 - 62.4)	27.2 (27.1 - 27.3)	54.9
	7.0	95.0 (94.9 - 95.1)	98.9 (98.9 - 98.9)	65.2 (65.1 - 65.3)	28.7 (28.6 - 28.9)	57.5
	7.5	94.4 (94.3 - 94.5)	98.8 (98.8 - 98.8)	67.3 (67.2 - 67.4)	29.9 (29.8 - 30.0)	59.4
	8.0	94.3 (94.1 - 94.4)	98.8 (98.8 - 98.8)	69.0 (68.9 - 69.1)	31.0 (30.8 - 31.1)	60.9
	8.5	94.1 (94.0 - 94.2)	98.8 (98.8 - 98.8)	70.8 (70.7 - 70.9)	32.2 (32.1 - 32.4)	62.4
	9.0	93.9 (93.8 - 94.0)	98.8 (98.7 - 98.8)	72.0 (71.9 - 72.1)	33.1 (32.9 - 33.3)	63.5
	9.5	93.3 (93.1 - 93.4)	98.7 (98.6 - 98.7)	73.1 (73.0 - 73.2)	33.8 (33.7 - 34.0)	64.5
	10.0	93 (92.8 - 93.1)	98.6 (98.6 - 98.7)	74.4 (74.3 - 74.5)	34.9 (34.7 - 35.0)	65.7

Supplemental Table 6: Derivation of single sample rule-out NSTEMI algorithms (all comers)

Assay	Cutoff < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
Roche	5	98.7 (96.3 - 99.7)	99.5 (98.5 - 99.9)	33.9 (31.6 - 36.2)	17.3 (15.3 - 19.4)	566	29.9	3	1,098
Abbott	4.0	96.1 (92.8 - 98.2)	99.1 (98.4 - 99.6)	62.9 (60.5 - 65.2)	26.6 (23.6 - 29.7)	1,052	55.6	9	616
Siemens	1.0	100 (98.4 - 100)	100 (92.0 - 100)	2.6 (1.9 - 3.5)	12.5 (11.1 - 14.1)	44	2.3	0	1,617
	1.5	100 (98.4 - 100)	100 (96.7 - 100)	6.6 (5.5 - 7.9)	13.0 (11.5 - 14.7)	110	5.8	0	1,551
	2.0	100 (98.4 - 100)	100 (98.1 - 100)	11.9 (10.3 - 13.5)	13.7 (12.1 - 15.4)	197	10.4	0	1,464
	2.5	99.6 (97.6 - 100)	99.7 (98.2 - 100)	18.5 (16.7 - 20.5)	14.6 (12.9 - 16.4)	309	16.3	1	1,353
	3.0	99.6 (97.6 - 100)	99.8 (98.7 - 100)	25.8 (23.7 - 27.9)	15.8 (13.9 - 17.7)	429	22.7	1	1,233
	3.5	99.1 (96.9 - 99.9)	99.7 (98.7 - 100)	34.3 (32.0 - 36.7)	17.4 (15.4 - 19.6)	572	30.2	2	1,091
	4.0	99.1 (96.9 - 99.9)	99.7 (98.9 - 100)	40.8 (38.4 - 43.2)	18.9 (16.8 - 21.3)	679	35.9	2	984
	4.5	99.1 (96.9 - 99.9)	99.7 (99.1 - 100)	46.6 (44.2 - 49.0)	20.6 (18.3 - 23.1)	776	41.0	2	887
	5.0	99.1 (96.9 - 99.9)	99.8 (99.2 - 100)	51.8 (49.3 - 54.2)	22.3 (19.8 - 25.0)	862	45.5	2	801
	5.5	98.7 (96.3 - 99.7)	99.7 (99.1 - 99.9)	55.4 (53.0 - 57.9)	23.6 (21.0 - 26.4)	924	48.8	3	740
	6.0	97.8 (95.0 - 99.3)	99.5 (98.8 - 99.8)	59.2 (56.8 - 61.6)	25.1 (22.3 - 28.0)	988	52.2	5	678
	6.5	97.8 (95.0 - 99.3)	99.5 (98.9 - 99.8)	62.0 (59.6 - 64.4)	26.5 (23.5 - 29.5)	1,035	54.7	5	631
	7.0	97.8 (95.0 - 99.3)	99.5 (98.9 - 99.9)	65.1 (62.7 - 67.4)	28.1 (25.0 - 31.4)	1,086	57.4	5	580
	7.5	97.4 (94.5 - 99.0)	99.5 (98.8 - 99.8)	67.2 (64.9 - 69.5)	29.4 (26.2 - 32.7)	1,123	59.3	6	544
	8.0	97.4 (94.5 - 99.0)	99.5 (98.9 - 99.8)	69.0 (66.7 - 71.2)	30.5 (27.2 - 34.0)	1,152	60.9	6	515
	8.5	97.4 (94.5 - 99.0)	99.5 (98.9 - 99.8)	70.7 (68.5 - 72.9)	31.7 (28.3 - 35.3)	1,181	62.4	6	486
	9.0	97 (93.9 - 98.8.0)	99.4 (98.8 - 99.8)	71.9 (69.7 - 74.1)	32.6 (29.1 - 36.2)	1,202	63.5	7	466
	9.5	96.1 (92.8 - 98.2)	99.3 (98.6 - 99.7)	73.0 (70.8 - 75.2)	33.2 (29.7 - 36.9)	1,222	64.6	9	448
	10.0	95.7 (92.2 - 97.9)	99.2 (98.5 - 99.6)	74.3 (72.1 - 76.4)	34.2 (30.6 - 38.0)	1,244	65.7	10	427

Supplemental Table 7: Validation of single sample rule-out NSTEMI algorithms (all comers)

Assay	Cutoff < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
Roche	5	98.6 (98.5 - 98.7)	99.4 (99.4 - 99.5)	33.9 (33.8 - 34.0)	17.3 (17.2 - 17.4)	29.9
Abbott	4.0	96.5 (96.4 - 96.6)	99.2 (99.2 - 99.3)	63.1 (63 - 63.3)	26.8 (26.7 - 27.0)	55.8
Siemens	1.0	100 (100 - 100)	99.8 (99.8 - 99.9)	2.6 (2.6 - 2.6)	12.6 (12.5 - 12.6)	2.3
	1.5	99.9 (99.9 - 99.9)	99.8 (99.8 - 99.9)	6.5 (6.4 - 6.5)	13.0 (12.9 - 13.1)	5.7
	2.0	99.8 (99.8 - 99.9)	99.8 (99.8 - 99.8)	11.7 (11.7 - 11.8)	13.7 (13.6 - 13.7)	10.3
	2.5	99.7 (99.6 - 99.7)	99.8 (99.7 - 99.8)	18.5 (18.4 - 18.6)	14.6 (14.5 - 14.7)	16.3
	3.0	99.5 (99.5 - 99.6)	99.7 (99.7 - 99.8)	25.8 (25.7 - 25.9)	15.8 (15.7 - 15.9)	22.7
	3.5	99.0 (99.0 - 99.1)	99.6 (99.6 - 99.6)	34.3 (34.2 - 34.4)	17.4 (17.3 - 17.5)	30.2
	4.0	98.9 (98.9 - 99.0)	99.6 (99.6 - 99.6)	40.7 (40.6 - 40.8)	18.9 (18.8 - 19.0)	35.9
	4.5	98.9 (98.8 - 98.9)	99.7 (99.6 - 99.7)	46.6 (46.5 - 46.7)	20.6 (20.5 - 20.7)	41.0
	5.0	98.8 (98.8 - 98.9)	99.7 (99.7 - 99.7)	51.7 (51.6 - 51.8)	22.3 (22.2 - 22.4)	45.5
	5.5	98.3 (98.3 - 98.4)	99.6 (99.6 - 99.6)	55.4 (55.3 - 55.5)	23.6 (23.5 - 23.7)	48.8
	6.0	97.7 (97.6 - 97.8)	99.5 (99.4 - 99.5)	59.2 (59.1 - 59.3)	25.1 (25 - 25.2.0)	52.2
	6.5	97.6 (97.5 - 97.7)	99.5 (99.4 - 99.5)	62.1 (62.0 - 62.2)	26.5 (26.4 - 26.6)	54.8
	7.0	97.3 (97.3 - 97.4)	99.4 (99.4 - 99.5)	65.1 (65.0 - 65.2)	28.1 (27.9 - 28.2)	57.4
	7.5	96.8 (96.7 - 96.9)	99.3 (99.3 - 99.4)	67.2 (67.1 - 67.3)	29.2 (29.1 - 29.4)	59.3
	8.0	96.7 (96.6 - 96.8)	99.3 (99.3 - 99.4)	68.9 (68.8 - 69.0)	30.3 (30.1 - 30.4)	60.8
	8.5	96.6 (96.5 - 96.7)	99.3 (99.3 - 99.4)	70.6 (70.5 - 70.7)	31.5 (31.4 - 31.7)	62.4
	9.0	96.5 (96.4 - 96.6)	99.3 (99.3 - 99.3)	71.9 (71.8 - 72.0)	32.4 (32.3 - 32.6)	63.5
	9.5	95.9 (95.8 - 96.0)	99.2 (99.2 - 99.2)	72.9 (72.9 - 73.0)	33.2 (33.0 - 33.3)	64.5
	10.0	95.6 (95.5 - 95.7)	99.2 (99.2 - 99.2)	74.3 (74.2 - 74.4)	34.2 (34.0 - 34.4)	65.7

Supplemental Table 8: Derivation of single sample rule-out NSTEMI algorithms (> 3 hours of symptoms)

Assay	Cutoff < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
Roche	5	98.8 (95.7 - 99.9)	99.5 (98.4 - 99.9)	32.9 (30.4 - 35.5)	15.7 (13.6 - 18.0)	437	29.4	2	886
Abbott	4.0	98.2 (94.9 - 99.6)	99.6 (98.9 - 99.9)	62.4 (59.7 - 65)	25.0 (21.7 - 28.4)	826	55.5	3	496
Siemens	1.0	100 (97.8 - 100)	100 (90.3 - 100)	2.7 (1.9 - 3.8)	11.5 (9.9 - 13.3)	36	2.4	0	1,285
	1.5	100 (97.8 - 100)	100 (95.7 - 100)	6.4 (5.1 - 7.8)	11.9 (10.2 - 13.7)	84	5.6	0	1,237
	2.0	100 (97.8 - 100)	100 (97.7 - 100)	11.8 (10.1 - 13.7)	12.5 (10.8 - 14.4)	156	10.5	0	1,165
	2.5	99.4 (96.7 - 100)	99.6 (97.7 - 100)	17.8 (15.8 - 20)	13.3 (11.4 - 15.3)	236	15.9	1	1,086
	3.0	99.4 (96.7 - 100)	99.7 (98.3 - 100)	24.8 (22.4 - 27.2)	14.3 (12.3 - 16.5)	328	22.0	1	994
	3.5	98.8 (95.7 - 99.9)	99.5 (98.4 - 99.9)	33.2 (30.7 - 35.8)	15.8 (13.6 - 18.1)	441	29.6	2	882
	4.0	98.8 (95.7 - 99.9)	99.6 (98.6 - 100)	39.6 (36.9 - 42.3)	17.1 (14.8 - 19.7)	525	35.3	2	798
	4.5	98.8 (95.7 - 99.9)	99.7 (98.8 - 100)	45.4 (42.7 - 48.2)	18.6 (16.1 - 21.3)	602	40.5	2	721
	5.0	98.8 (95.7 - 99.9)	99.7 (98.9 - 100)	50.9 (48.1 - 53.6)	20.3 (17.6 - 23.2)	674	45.3	2	649
	5.5	98.8 (95.7 - 99.9)	99.7 (99.0 - 100)	55.0 (52.3 - 57.7)	21.7 (18.9 - 24.8)	729	49.0	2	594
	6.0	98.2 (94.8 - 99.6)	99.6 (98.9 - 99.9)	58.7 (56.0 - 61.3)	23.1 (20.0 - 26.4)	778	52.3	3	546
	6.5	98.2 (94.8 - 99.6)	99.6 (98.9 - 99.9)	61.4 (58.7 - 64.0)	24.3 (21.1 - 27.8)	814	54.7	3	510
	7.0	98.2 (94.8 - 99.6)	99.6 (99.0 - 99.9)	64.4 (61.8 - 67.0)	25.9 (22.5 - 29.5)	854	57.4	3	470
	7.5	97.6 (94.0 - 99.3)	99.5 (98.8 - 99.9)	66.7 (64.1 - 69.2)	27.0 (23.5 - 30.8)	885	59.5	4	440
	8.0	97.6 (94.0 - 99.3)	99.6 (98.9 - 99.9)	68.6 (66.0 - 71.1)	28.2 (24.6 - 32.1)	910	61.2	4	415
	8.5	97.6 (94.0 - 99.3)	99.6 (98.9 - 99.9)	70.7 (68.2 - 73.1)	29.6 (25.8 - 33.6)	938	63.0	4	387
	9.0	97.6 (94.0 - 99.3)	99.6 (98.9 - 99.9)	71.8 (69.3 - 74.3)	30.5 (26.6 - 34.6)	953	64.0	4	372
	9.5	97.0 (93.2 - 99.0)	99.5 (98.8 - 99.8)	72.7 (70.3 - 75.1)	31.0 (27.1 - 35.2)	966	64.9	5	360
	10.0	96.4 (92.3 - 98.7)	99.4 (98.7 - 99.8)	73.8 (71.3 - 76.2)	31.8 (27.7 - 36.0)	981	65.9	6	346

Supplemental Table 9: Validation of single sample rule-out NSTEMI algorithms (> 3 hours of symptoms)

Assay	Cutoff < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
Roche	5	98.5 (98.4 - 98.5)	99.4 (99.4 - 99.5)	33.4 (33.3 - 33.6)	15.8 (15.7 - 15.9)	29.8
Abbott	4.0	98.3 (98.2 - 98.4)	99.7 (99.6 - 99.7)	62.5 (62.4 - 62.6)	25.0 (24.8 - 25.1)	55.7
Siemens	1.0	100 (99.9 - 100)	99.8 (99.8 - 99.9)	2.7 (2.7 - 2.7)	11.5 (11.4 - 11.6)	2.4
	1.5	99.9 (99.9 - 99.9)	99.8 (99.7 - 99.8)	6.3 (6.2 - 6.3)	11.9 (11.8 - 12.0)	5.6
	2.0	99.8 (99.8 - 99.8)	99.8 (99.7 - 99.8)	11.7 (11.6 - 11.8)	12.5 (12.5 - 12.6)	10.4
	2.5	99.7 (99.7 - 99.8)	99.8 (99.8 - 99.8)	17.8 (17.7 - 17.9)	13.3 (13.2 - 13.4)	15.8
	3.0	99.5 (99.4 - 99.5)	99.7 (99.7 - 99.8)	24.7 (24.6 - 24.8)	14.4 (14.3 - 14.4)	22.0
	3.5	98.7 (98.6 - 98.8)	99.5 (99.5 - 99.5)	33.2 (33.1 - 33.3)	15.8 (15.7 - 15.9)	29.6
	4.0	98.5 (98.4 - 98.5)	99.5 (99.5 - 99.5)	39.6 (39.4 - 39.7)	17.1 (17.0 - 17.2)	35.3
	4.5	98.2 (98.1 - 98.3)	99.5 (99.5 - 99.5)	45.3 (45.2 - 45.4)	18.5 (18.4 - 18.7)	40.4
	5.0	98.1 (98 - 98.2)	99.5 (99.5 - 99.5)	50.8 (50.7 - 50.9)	20.2 (20.1 - 20.3)	45.3
	5.5	98.0 (97.9 - 98.1)	99.5 (99.5 - 99.6)	55.1 (55.0 - 55.2)	21.7 (21.6 - 21.8)	49.1
	6.0	97.9 (97.8 - 98.0)	99.5 (99.5 - 99.6)	58.8 (58.7 - 58.9)	23.1 (23.0 - 23.3)	52.4
	6.5	97.6 (97.5 - 97.7)	99.5 (99.5 - 99.5)	61.5 (61.4 - 61.7)	24.3 (24.2 - 24.5)	54.9
	7.0	97.4 (97.3 - 97.5)	99.5 (99.5 - 99.5)	64.4 (64.3 - 64.5)	25.7 (25.6 - 25.9)	57.4
	7.5	97.3 (97.2 - 97.4)	99.5 (99.5 - 99.5)	66.7 (66.6 - 66.8)	27.0 (26.9 - 27.2)	59.5
	8.0	97.1 (97.0 - 97.2)	99.5 (99.4 - 99.5)	68.6 (68.5 - 68.7)	28.2 (28.0 - 28.3)	61.2
	8.5	97.0 (96.9 - 97.1)	99.5 (99.4 - 99.5)	70.7 (70.6 - 70.8)	29.6 (29.4 - 29.7)	63.1
	9.0	96.8 (96.6 - 96.9)	99.4 (99.4 - 99.5)	71.8 (71.7 - 71.9)	30.3 (30.1 - 30.5)	64.1
	9.5	96.5 (96.4 - 96.6)	99.4 (99.4 - 99.4)	72.7 (72.6 - 72.8)	30.9 (30.8 - 31.1)	64.9
	10.0	96.2 (96.0 - 96.3)	99.3 (99.3 - 99.4)	73.7 (73.6 - 73.8)	31.7 (31.5 - 31.9)	65.9

Supplemental Table 10: Derivation of 0-1 hour delta rule-out 30 day MI or death algorithms

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
Roche	12	3	98.5 (94.7 - 99.8)	99.7 (99.0 - 100)	75.4 (72.6 - 78.1)	35.3 (30.4 - 40.4)	738	66.5	2	240
Abbott	5	2	99.2 (95.9 - 100)	99.9 (99.2 - 100)	69.9 (66.9 - 72.8)	31.1 (26.8 - 35.8)	679	61.6	1	292
Siemens	1	1	99.3 (95.9 - 100)	95.8 (78.9 - 99.9)	2.3 (1.5 - 3.5)	12.2 (10.3 - 14.3)	24	2.2	1	959
		2	99.3 (95.9 - 100)	96.8 (83.3 - 99.9)	3.1 (2.1 - 4.3)	12.3 (10.4 - 14.4)	31	2.8	1	952
		3	99.3 (95.9 - 100)	96.8 (83.3 - 99.9)	3.1 (2.1 - 4.3)	12.3 (10.4 - 14.4)	31	2.8	1	952
		4	99.3 (95.9 - 100)	96.8 (83.3 - 99.9)	3.1 (2.1 - 4.3)	12.3 (10.4 - 14.4)	31	2.8	1	952
		5	99.3 (95.9 - 100)	96.8 (83.3 - 99.9)	3.1 (2.1 - 4.3)	12.3 (10.4 - 14.4)	31	2.8	1	952
	2	1	99.3 (95.9 - 100)	98.8 (93.6 - 100)	8.6 (6.9 - 10.5)	12.9 (10.9 - 15.1)	85	7.6	1	898
		2	99.3 (95.9 - 100)	99.2 (95.4 - 100)	12.1 (10.1 - 14.3)	13.4 (11.3 - 15.6)	120	10.8	1	863
		3	99.3 (95.9 - 100)	99.2 (95.6 - 100)	12.4 (10.4 - 14.7)	13.4 (11.3 - 15.7)	123	11.0	1	860
		4	99.3 (95.9 - 100)	99.2 (95.6 - 100)	12.5 (10.5 - 14.8)	13.4 (11.3 - 15.7)	124	11.1	1	859
		5	99.3 (95.9 - 100)	99.2 (95.6 - 100)	12.5 (10.5 - 14.8)	13.4 (11.3 - 15.7)	124	11.1	1	859
	3	1	99.3 (95.9 - 100)	99.5 (97.0 - 100)	18.7 (16.3 - 21.3)	14.3 (12.1 - 16.7)	185	16.6	1	798
		2	99.3 (95.9 - 100)	99.6 (97.9 - 100)	26.6 (23.8 - 29.5)	15.6 (13.2 - 18.2)	262	23.5	1	721
		3	99.3 (95.9 - 100)	99.6 (98.0 - 100)	27.7 (24.9 - 30.6)	15.8 (13.4 - 18.4)	273	24.5	1	710
		4	99.3 (95.9 - 100)	99.6 (98.0 - 100)	28.0 (25.2 - 30.9)	15.8 (13.4 - 18.5)	276	24.7	1	707
		5	99.3 (95.9 - 100)	99.6 (98.0 - 100)	28.0 (25.2 - 30.9)	15.8 (13.4 - 18.5)	276	24.7	1	707
	4	1	99.3 (95.9 - 100)	99.6 (98 - 100)	28.1 (25.3 - 31.0)	15.9 (13.4 - 18.5)	277	24.8	1	706
		2	99.3 (95.9 - 100)	99.8 (98.6 - 100)	40.7 (37.6 - 43.9)	18.6 (15.8 - 21.7)	401	35.9	1	582

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
		3	99.3 (95.9 - 100)	99.8 (98.7 - 100)	43.0 (39.9 - 46.1)	19.2 (16.3 - 22.3)	423	37.9	1	560
		4	99.3 (95.9 - 100)	99.8 (98.7 - 100)	43.3 (40.2 - 46.4)	19.3 (16.4 - 22.4)	426	38.2	1	557
		5	99.3 (95.9 - 100)	99.8 (98.7 - 100)	43.4 (40.3 - 46.5)	19.3 (16.4 - 22.5)	427	38.3	1	556
	5	1	99.3 (95.9 - 100)	99.7 (98.4 - 100)	34.5 (31.5 - 37.6)	17.1 (14.6 - 20.0)	340	30.5	1	643
		2	99.3 (95.9 - 100)	99.8 (98.9 - 100)	51.8 (48.7 - 55.0)	21.9 (18.7 - 25.5)	510	45.7	1	473
		3	99.3 (95.9 - 100)	99.8 (99.0 - 100)	54.6 (51.4 - 57.7)	23.0 (19.6 - 26.6)	537	48.1	1	446
		4	99.3 (95.9 - 100)	99.8 (99.0 - 100)	55.0 (51.8 - 58.1)	23.1 (19.7 - 26.8)	541	48.5	1	442
		5	99.3 (95.9 - 100)	99.8 (99.0 - 100)	55.1 (51.9 - 58.2)	23.2 (19.8 - 26.8)	542	48.6	1	441
	6	1	99.3 (95.9 - 100)	99.7 (98.5 - 100)	38.3 (35.2 - 41.4)	18.0 (15.3 - 21.0)	377	33.8	1	606
		2	99.3 (95.9 - 100)	99.8 (99.0 - 100)	58.5 (55.3 - 61.6)	24.6 (21.0 - 28.4)	575	51.5	1	408
		3	99.3 (95.9 - 100)	99.8 (99.1 - 100)	61.6 (58.5 - 64.7)	26.1 (22.3 - 30.1)	606	54.3	1	377
		4	99.3 (95.9 - 100)	99.8 (99.1 - 100)	62.0 (58.9 - 65.1)	26.3 (22.5 - 30.4)	610	54.7	1	373
		5	99.3 (95.9 - 100)	99.8 (99.1 - 100)	62.1 (59.0 - 65.2)	26.3 (22.5 - 30.4)	611	54.7	1	372
	7	1	99.3 (95.9 - 100)	99.8 (98.6 - 100)	40.9 (37.8 - 44.1)	18.7 (15.9 - 21.7)	403	36.1	1	580
		2	99.3 (95.9 - 100)	99.8 (99.1 - 100)	62.7 (59.6 - 65.8)	26.7 (22.8 - 30.8)	617	55.3	1	366
		3	99.3 (95.9 - 100)	99.8 (99.2 - 100)	66.6 (63.6 - 69.5)	28.9 (24.8 - 33.2)	655	58.7	1	328
		4	99.3 (95.9 - 100)	99.8 (99.2 - 100)	67.2 (64.2 - 70.1)	29.2 (25.1 - 33.6)	661	59.2	1	322
		5	99.3 (95.9 - 100)	99.8 (99.2 - 100)	67.3 (64.3 - 70.2)	29.3 (25.1 - 33.7)	662	59.3	1	321
	8	1	99.3 (95.9 - 100)	99.8 (98.7 - 100)	42.2 (39.0 - 45.3)	19.0 (16.1 - 22.1)	415	37.2	1	568
		2	99.3 (95.9 - 100)	99.8 (99.1 - 100)	65.1 (62.0 - 68.1)	27.9 (24.0 - 32.2)	640	57.3	1	343
		3	99.3 (95.9 - 100)	99.9 (99.2 - 100)	69.5 (66.5 - 72.3)	30.7 (26.4 - 35.3)	683	61.2	1	300

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
		4	99.3 (95.9 - 100)	99.9 (99.2 - 100)	70.2 (67.2 - 73.0)	31.2 (26.8 - 35.9)	690	61.8	1	293
		5	99.3 (95.9 - 100)	99.9 (99.2 - 100)	70.4 (67.4 - 73.2)	31.4 (27.0 - 36.0)	692	62.0	1	291
	9	1	99.3 (95.9 - 100)	99.8 (98.7 - 100)	43.1 (40.0 - 46.2)	19.2 (16.3 - 22.4)	424	38.0	1	559
		2	99.3 (95.9 - 100)	99.8 (99.2 - 100)	67.1 (64.1 - 70.0)	29.2 (25.0 - 33.6)	660	59.1	1	323
		3	99.3 (95.9 - 100)	99.9 (99.2 - 100)	72.1 (69.2 - 74.9)	32.7 (28.1 - 37.5)	709	63.5	1	274
		4	99.3 (95.9 - 100)	99.9 (99.2 - 100)	72.9 (70.0 - 75.7)	33.3 (28.7 - 38.2)	717	64.2	1	266
		5	99.3 (95.9 - 100)	99.9 (99.2 - 100)	73.2 (70.3 - 76.0)	33.6 (28.9 - 38.5)	720	64.5	1	263
	10	1	99.3 (95.9 - 100)	99.8 (98.7 - 100)	43.8 (40.7 - 47.0)	19.4 (16.5 - 22.6)	431	38.6	1	552
		2	99.3 (95.9 - 100)	99.9 (99.2 - 100)	68.6 (65.6 - 71.5)	30.2 (25.9 - 34.7)	675	60.5	1	308
		3	99.3 (95.9 - 100)	99.9 (99.2 - 100)	74.1 (71.3 - 76.8)	34.4 (29.6 - 39.3)	729	65.3	1	254
		4	99.3 (95.9 - 100)	99.9 (99.2 - 100)	75.1 (72.2 - 77.7)	35.2 (30.4 - 40.2)	738	66.1	1	245
		5	99.3 (95.9 - 100)	99.9 (99.3 - 100)	75.5 (72.6 - 78.1)	35.6 (30.7 - 40.6)	742	66.5	1	241

Supplemental Table 11: Validation of 0-1 hour delta rule-out 30 day MI or death algorithms

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
Roche	12	3	95.5 (95.3 - 95.7)	99.2 (99.2 - 99.2)	75.7 (75.6 - 75.9)	34.6 (34.4 - 34.8)	67.3
Abbott	5	2	97.6 (97.5 - 97.7)	99.5 (99.5 - 99.6)	69.2 (69.0 - 69.3)	29.9 (29.7 - 30.1)	61.2
Siemens	1	1	99.9 (99.9 - 100)	99.6 (99.4 - 99.7)	1.9 (1.9 - 2.0)	12.1 (12.0 - 12.2)	1.7
		2	99.9 (99.9 - 99.9)	99.5 (99.4 - 99.7)	2.9 (2.8 - 2.9)	12.2 (12.1 - 12.3)	2.5
		3	99.9 (99.9 - 99.9)	99.6 (99.4 - 99.7)	3 (2.9 - 3.0)	12.2 (12.1 - 12.3)	2.6
		4	99.9 (99.9 - 99.9)	99.6 (99.4 - 99.7)	3 (2.9 - 3.0)	12.2 (12.1 - 12.3)	2.6
		5	99.9 (99.9 - 99.9)	99.5 (99.4 - 99.6)	3 (2.9 - 3.0)	12.2 (12.1 - 12.3)	2.6
	2	1	99.7 (99.7 - 99.8)	99.6 (99.5 - 99.6)	7.8 (7.8 - 7.9)	12.7 (12.6 - 12.8)	6.9
		2	99.6 (99.6 - 99.7)	99.6 (99.5 - 99.6)	11.8 (11.7 - 11.9)	13.2 (13.1 - 13.3)	10.4
		3	99.6 (99.5 - 99.6)	99.6 (99.5 - 99.6)	12.2 (12.2 - 12.3)	13.3 (13.2 - 13.4)	10.8
		4	99.6 (99.5 - 99.6)	99.6 (99.5 - 99.6)	12.3 (12.2 - 12.4)	13.3 (13.2 - 13.4)	10.9
		5	99.6 (99.5 - 99.6)	99.5 (99.5 - 99.6)	12.3 (12.2 - 12.4)	13.3 (13.2 - 13.4)	10.9
	3	1	99.4 (99.4 - 99.5)	99.6 (99.5 - 99.6)	17.5 (17.4 - 17.6)	14.0 (13.9 - 14.1)	15.5
		2	99.1 (99.1 - 99.2)	99.6 (99.5 - 99.6)	26.1 (25.9 - 26.2)	15.3 (15.2 - 15.4)	23.1
		3	99.1 (99.0 - 99.2)	99.6 (99.5 - 99.6)	27.2 (27.1 - 27.3)	15.5 (15.4 - 15.6)	24.1
		4	99.1 (99.0 - 99.2)	99.6 (99.5 - 99.6)	27.4 (27.3 - 27.5)	15.5 (15.4 - 15.7)	24.2
		5	99.1 (99.0 - 99.1)	99.5 (99.5 - 99.6)	27.4 (27.3 - 27.5)	15.5 (15.4 - 15.7)	24.3
	4	1	99.1 (99.0 - 99.1)	99.5 (99.5 - 99.6)	27.0 (26.9 - 27.1)	15.5 (15.4 - 15.6)	23.9
		2	98.6 (98.5 - 98.7)	99.5 (99.5 - 99.6)	40.1 (40.0 - 40.3)	18.2 (18.1 - 18.3)	35.5
		3	98.5 (98.4 - 98.6)	99.5 (99.5 - 99.6)	42.2 (42.0 - 42.3)	18.7 (18.6 - 18.8)	37.3
		4	98.5 (98.4 - 98.6)	99.5 (99.5 - 99.5)	42.6 (42.4 - 42.7)	18.8 (18.7 - 18.9)	37.7
		5	98.4 (98.3 - 98.5)	99.5 (99.5 - 99.5)	42.6 (42.5 - 42.8)	18.8 (18.7 - 18.9)	37.8
	5	1	98.8 (98.8 - 98.9)	99.5 (99.5 - 99.6)	33.8 (33.7 - 34.0)	16.8 (16.7 - 16.9)	29.9
		2	98.2 (98.1 - 98.3)	99.5 (99.5 - 99.6)	50.9 (50.7 - 51.0)	21.2 (21.1 - 21.4)	45.0
		3	98.1 (98.0 - 98.2)	99.5 (99.5 - 99.5)	53.7 (53.6 - 53.9)	22.2 (22.1 - 22.4)	47.6

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
		4	98.0 (97.9 - 98.2)	99.5 (99.5 - 99.5)	54.2 (54.1 - 54.4)	22.4 (22.3 - 22.6)	48.0
		5	97.9 (97.8 - 98.0)	99.5 (99.5 - 99.5)	54.3 (54.2 - 54.5)	22.4 (22.3 - 22.6)	48.1
	6	1	98.7 (98.6 - 98.8)	99.5 (99.5 - 99.6)	37.4 (37.2 - 37.5)	17.5 (17.4 - 17.7)	33.1
		2	98.0 (97.9 - 98.1)	99.5 (99.5 - 99.6)	57.1 (57.0 - 57.2)	23.6 (23.4 - 23.7)	50.5
		3	97.8 (97.7 - 97.9)	99.5 (99.5 - 99.5)	60.8 (60.7 - 61.0)	25.2 (25.0 - 25.4)	53.9
		4	97.8 (97.6 - 97.9)	99.5 (99.5 - 99.5)	61.5 (61.4 - 61.7)	25.5 (25.4 - 25.7)	54.5
		5	97.5 (97.4 - 97.7)	99.5 (99.4 - 99.5)	61.6 (61.5 - 61.8)	25.5 (25.4 - 25.7)	54.6
	7	1	98.6 (98.5 - 98.7)	99.5 (99.5 - 99.6)	39.3 (39.2 - 39.5)	18.0 (17.9 - 18.1)	34.8
		2	97.9 (97.8 - 98.0)	99.5 (99.5 - 99.6)	61.1 (60.9 - 61.2)	25.3 (25.2 - 25.5)	54.1
		3	97.6 (97.5 - 97.7)	99.5 (99.5 - 99.5)	65.5 (65.4 - 65.7)	27.6 (27.5 - 27.8)	58.0
		4	97.6 (97.5 - 97.7)	99.5 (99.5 - 99.5)	66.3 (66.2 - 66.5)	28.1 (27.9 - 28.3)	58.8
		5	97.3 (97.2 - 97.4)	99.5 (99.4 - 99.5)	66.5 (66.4 - 66.7)	28.2 (28.0 - 28.4)	58.9
	8	1	98.6 (98.5 - 98.7)	99.5 (99.5 - 99.6)	40.5 (40.4 - 40.6)	18.3 (18.1 - 18.4)	35.8
		2	97.8 (97.6 - 97.9)	99.5 (99.5 - 99.5)	63.5 (63.4 - 63.7)	26.6 (26.4 - 26.7)	56.3
		3	97.5 (97.4 - 97.6)	99.5 (99.5 - 99.5)	68.5 (68.4 - 68.6)	29.5 (29.3 - 29.7)	60.7
		4	97.4 (97.3 - 97.6)	99.5 (99.5 - 99.5)	69.4 (69.3 - 69.5)	30.1 (29.9 - 30.3)	61.5
		5	97.1 (97.0 - 97.3)	99.4 (99.4 - 99.5)	69.6 (69.5 - 69.8)	30.1 (29.9 - 30.3)	61.7
	9	1	98.5 (98.4 - 98.6)	99.5 (99.5 - 99.6)	41.6 (41.5 - 41.8)	18.5 (18.4 - 18.7)	36.8
		2	97.7 (97.6 - 97.8)	99.5 (99.5 - 99.6)	65.8 (65.6 - 65.9)	27.8 (27.6 - 28.0)	58.2
		3	97.4 (97.3 - 97.5)	99.5 (99.5 - 99.5)	71.3 (71.1 - 71.4)	31.4 (31.2 - 31.6)	63.1
		4	97.4 (97.2 - 97.5)	99.5 (99.5 - 99.5)	72.3 (72.1 - 72.4)	32.1 (31.9 - 32.3)	64.0
		5	97.0 (96.9 - 97.2)	99.5 (99.4 - 99.5)	72.5 (72.4 - 72.6)	32.2 (32.0 - 32.5)	64.2
	10	1	98.5 (98.4 - 98.6)	99.5 (99.5 - 99.6)	42.4 (42.3 - 42.6)	18.7 (18.6 - 18.9)	37.6
		2	97.6 (97.5 - 97.7)	99.5 (99.5 - 99.5)	67.4 (67.3 - 67.5)	28.8 (28.6 - 29.0)	59.7
		3	97.3 (97.2 - 97.4)	99.5 (99.5 - 99.5)	73.4 (73.3 - 73.5)	33.1 (32.8 - 33.3)	65.0
		4	97.3 (97.1 - 97.4)	99.5 (99.5 - 99.5)	74.5 (74.4 - 74.6)	34.0 (33.8 - 34.2)	66.0
		5	96.9 (96.7 - 97.0)	99.4 (99.4 - 99.5)	74.8 (74.7 - 74.9)	34.1 (33.9 - 34.4)	66.3

Supplemental Table 12: Derivation of 0-1 hour delta rule-out NSTEMI algorithms

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
Roche	12	3	99.2 (95.7 - 100)	99.9 (99.2 - 100)	75.1 (72.3 - 77.8)	34.2 (29.4 - 39.3)	738	66.5	1	244
Abbott	5	2	100 (97.2 - 100)	100 (99.5 - 100)	69.6 (66.6 - 72.5)	30.2 (25.9 - 34.8)	679	61.6	0	296
Siemens	1	1	100 (97.2 - 100)	100 (85.8 - 100)	2.4 (1.6 - 3.6)	11.8 (10.0 - 13.9)	24	2.2	0	963
		2	100 (97.2 - 100)	100 (88.8 - 100)	3.1 (2.1 - 4.4)	11.9 (10.0 - 14.0)	31	2.8	0	956
		3	100 (97.2 - 100)	100 (88.8 - 100)	3.1 (2.1 - 4.4)	11.9 (10.0 - 14.0)	31	2.8	0	956
		4	100 (97.2 - 100)	100 (88.8 - 100)	3.1 (2.1 - 4.4)	11.9 (10.0 - 14.0)	31	2.8	0	956
		5	100 (97.2 - 100)	100 (88.8 - 100)	3.1 (2.1 - 4.4)	11.9 (10.0 - 14.0)	31	2.8	0	956
	2	1	100 (97.2 - 100)	100 (95.8 - 100)	8.6 (6.9 - 10.5)	12.5 (10.6 - 14.7)	85	7.6	0	902
		2	100 (97.2 - 100)	100 (97.0 - 100)	12.2 (10.2 - 14.4)	13.0 (10.9 - 15.2)	120	10.8	0	867
		3	100 (97.2 - 100)	100 (97.0 - 100)	12.5 (10.5 - 14.7)	13.0 (11.0 - 15.2)	123	11.0	0	864
		4	100 (97.2 - 100)	100 (97.1 - 100)	12.6 (10.6 - 14.8)	13.0 (11.0 - 15.3)	124	11.1	0	863
		5	100 (97.2 - 100)	100 (97.1 - 100)	12.6 (10.6 - 14.8)	13.0 (11.0 - 15.3)	124	11.1	0	863
	3	1	100 (97.2 - 100)	100 (98.0 - 100)	18.7 (16.4 - 21.3)	13.9 (11.7 - 16.2)	185	16.6	0	802
		2	100 (97.2 - 100)	100 (98.6 - 100)	26.5 (23.8 - 29.4)	15.1 (12.8 - 17.7)	262	23.5	0	725
		3	100 (97.2 - 100)	100 (98.7 - 100)	27.7 (24.9 - 30.6)	15.3 (12.9 - 17.9)	273	24.5	0	714
		4	100 (97.2 - 100)	100 (98.7 - 100)	28.0 (25.2 - 30.9)	15.4 (13.0 - 18.0)	276	24.7	0	711
		5	100 (97.2 - 100)	100 (98.7 - 100)	28.0 (25.2 - 30.9)	15.4 (13.0 - 18.0)	276	24.7	0	711
	4	1	100 (97.2 - 100)	100 (98.7 - 100)	28.1 (25.3 - 31.0)	15.4 (13.0 - 18.0)	277	24.8	0	710
		2	100 (97.2 - 100)	100 (99.1 - 100)	40.6 (37.5 - 43.8)	18.0 (15.3 - 21.1)	401	35.9	0	586

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
		3	100 (97.2 - 100)	100 (99.1 - 100)	42.9 (39.7 - 46.0)	18.6 (15.8 - 21.7)	423	37.9	0	564
		4	100 (97.2 - 100)	100 (99.1 - 100)	43.2 (40.0 - 46.3)	18.7 (15.9 - 21.8)	426	38.2	0	561
		5	100 (97.2 - 100)	100 (99.1 - 100)	43.3 (40.1 - 46.4)	18.7 (15.9 - 21.8)	427	38.3	0	560
	5	1	100 (97.2 - 100)	100 (98.9 - 100)	34.4 (31.5 - 37.5)	16.6 (14.1 - 19.4)	340	30.5	0	647
		2	100 (97.2 - 100)	100 (99.3 - 100)	51.7 (48.5 - 54.8)	21.3 (18.1 - 24.8)	510	45.7	0	477
		3	100 (97.2 - 100)	100 (99.3 - 100)	54.4 (51.2 - 57.5)	22.3 (19.0 - 25.9)	537	48.1	0	450
		4	100 (97.2 - 100)	100 (99.3 - 100)	54.8 (51.6 - 57.9)	22.4 (19.1 - 26.1)	541	48.5	0	446
		5	100 (97.2 - 100)	100 (99.3 - 100)	54.9 (51.7 - 58.1)	22.5 (19.1 - 26.1)	542	48.6	0	445
	6	1	100 (97.2 - 100)	100 (99.0 - 100)	38.2 (35.2 - 41.3)	17.5 (14.8 - 20.4)	377	33.8	0	610
		2	100 (97.2 - 100)	100 (99.4 - 100)	58.3 (55.1 - 61.4)	23.8 (20.3 - 27.7)	575	51.5	0	412
		3	100 (97.2 - 100)	100 (99.4 - 100)	61.4 (58.3 - 64.4)	25.3 (21.6 - 29.3)	606	54.3	0	381
		4	100 (97.2 - 100)	100 (99.4 - 100)	61.8 (58.7 - 64.8)	25.5 (21.8 - 29.5)	610	54.7	0	377
		5	100 (97.2 - 100)	100 (99.4 - 100)	61.9 (58.8 - 64.9)	25.5 (21.8 - 29.6)	611	54.7	0	376
	7	1	100 (97.2 - 100)	100 (99.1 - 100)	40.8 (37.7 - 44.0)	18.1 (15.3 - 21.1)	403	36.1	0	584
		2	100 (97.2 - 100)	100 (99.4 - 100)	62.5 (59.4 - 65.5)	25.9 (22.1 - 29.9)	617	55.3	0	370
		3	100 (97.2 - 100)	100 (99.4 - 100)	66.4 (63.3 - 69.3)	28.0 (23.9 - 32.3)	655	58.7	0	332
		4	100 (97.2 - 100)	100 (99.4 - 100)	67.0 (63.9 - 69.9)	28.4 (24.3 - 32.7)	661	59.2	0	326
		5	100 (97.2 - 100)	100 (99.4 - 100)	67.1 (64.0 - 70.0)	28.4 (24.3 - 32.8)	662	59.3	0	325
	8	1	100 (97.2 - 100)	100 (99.1 - 100)	42.0 (38.9 - 45.2)	18.4 (15.6 - 21.5)	415	37.2	0	572
		2	100 (97.2 - 100)	100 (99.4 - 100)	64.8 (61.8 - 67.8)	27.1 (23.2 - 31.3)	640	57.3	0	347
		3	100 (97.2 - 100)	100 (99.5 - 100)	69.2 (66.2 - 72.1)	29.8 (25.5 - 34.3)	683	61.2	0	304

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	Ruled out	% ruled out	False negatives	False positives
		4	100 (97.2 - 100)	100 (99.5 - 100)	69.9 (66.9 - 72.8)	30.3 (26.0 - 34.9)	690	61.8	0	297
		5	100 (97.2 - 100)	100 (99.5 - 100)	70.1 (67.1 - 73.0)	30.4 (26.1 - 35.0)	692	62.0	0	295
	9	1	100 (97.2 - 100)	100 (99.1 - 100)	43.0 (39.8 - 46.1)	18.6 (15.8 - 21.7)	424	38.0	0	563
		2	100 (97.2 - 100)	100 (99.4 - 100)	66.9 (63.8 - 69.8)	28.3 (24.2 - 32.7)	660	59.1	0	327
		3	100 (97.2 - 100)	100 (99.5 - 100)	71.8 (68.9 - 74.6)	31.7 (27.2 - 36.5)	709	63.5	0	278
		4	100 (97.2 - 100)	100 (99.5 - 100)	72.6 (69.7 - 75.4)	32.3 (27.8 - 37.2)	717	64.2	0	270
		5	100 (97.2 - 100)	100 (99.5 - 100)	72.9 (70.1 - 75.7)	32.6 (28.0 - 37.4)	720	64.5	0	267
	10	1	100 (97.2 - 100)	100 (99.1 - 100)	43.7 (40.5 - 46.8)	18.8 (16.0 - 22.0)	431	38.6	0	556
		2	100 (97.2 - 100)	100 (99.5 - 100)	68.4 (65.4 - 71.3)	29.3 (25.0 - 33.7)	675	60.5	0	312
		3	100 (97.2 - 100)	100 (99.5 - 100)	73.9 (71.0 - 76.6)	33.3 (28.7 - 38.3)	729	65.3	0	258
		4	100 (97.2 - 100)	100 (99.5 - 100)	74.8 (71.9 - 77.5)	34.1 (29.4 - 39.1)	738	66.1	0	249
		5	100 (97.2 - 100)	100 (99.5 - 100)	75.2 (72.4 - 77.8)	34.5 (29.7 - 39.6)	742	66.5	0	245

Supplemental Table 13: Validation of 0-1 hour delta rule-out NSTEMI algorithms

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
Roche	12	3	97.7 (97.6 - 97.9)	99.6 (99.6 - 99.6)	75.7 (75.5 - 75.8)	34.1 (33.8 - 34.3)	67.3
Abbott	5	2	99.7 (99.7 - 99.7)	99.9 (99.9 - 100)	69.1 (68.9 - 69.2)	29.4 (29.2 - 29.6)	61.2
Siemens	1	1	100 (100 - 100)	99.9 (99.9 - 100)	1.9 (1.9 - 2.0)	11.6 (11.5 - 11.7)	1.7
		2	100 (100 - 100)	100 (99.9 - 100)	2.9 (2.8 - 2.9)	11.7 (11.6 - 11.8)	2.5
		3	100 (100 - 100)	100 (99.9 - 100)	3.0 (2.9 - 3.0)	11.7 (11.6 - 11.8)	2.6
		4	100 (100 - 100)	100 (99.9 - 100)	3.0 (2.9 - 3.0)	11.7 (11.7 - 11.8)	2.6
		5	100 (100 - 100)	99.9 (99.8 - 100)	3.0 (2.9 - 3.0)	11.7 (11.7 - 11.8)	2.6
	2	1	100 (100 - 100)	100 (100 - 100)	7.8 (7.8 - 7.9)	12.3 (12.2 - 12.4)	6.9
		2	100 (100 - 100)	100 (100 - 100)	11.8 (11.7 - 11.9)	12.8 (12.7 - 12.8)	10.4
		3	100 (100 - 100)	100 (100 - 100)	12.2 (12.1 - 12.3)	12.8 (12.7 - 12.9)	10.8
		4	100 (100 - 100)	100 (100 - 100)	12.3 (12.2 - 12.4)	12.8 (12.7 - 12.9)	10.9
		5	100 (99.9 - 100)	100 (99.9 - 100)	12.3 (12.2 - 12.4)	12.8 (12.7 - 12.9)	10.9
	3	1	100 (99.9 - 100)	100 (100 - 100)	17.5 (17.3 - 17.6)	13.5 (13.4 - 13.6)	15.5
		2	99.9 (99.9 - 99.9)	100 (100 - 100)	26.0 (25.9 - 26.2)	14.8 (14.7 - 15.0)	23.1
		3	99.9 (99.9 - 99.9)	100 (100 - 100)	27.2 (27.1 - 27.3)	15.0 (14.9 - 15.1)	24.1
		4	99.9 (99.9 - 99.9)	100 (100 - 100)	27.4 (27.2 - 27.5)	15.1 (15.0 - 15.2)	24.2
		5	99.9 (99.9 - 99.9)	99.9 (99.9 - 100)	27.4 (27.3 - 27.5)	15.1 (15.0 - 15.2)	24.3
	4	1	99.9 (99.9 - 99.9)	99.9 (99.9 - 100)	26.9 (26.8 - 27.1)	15.0 (14.9 - 15.1)	23.9
		2	99.8 (99.8 - 99.9)	99.9 (99.9 - 100)	40.1 (40.0 - 40.2)	17.7 (17.6 - 17.8)	35.5
		3	99.8 (99.8 - 99.8)	99.9 (99.9 - 99.9)	42.1 (42.0 - 42.3)	18.2 (18.1 - 18.3)	37.3
		4	99.8 (99.7 - 99.8)	99.9 (99.9 - 99.9)	42.5 (42.4 - 42.7)	18.3 (18.2 - 18.4)	37.7
		5	99.7 (99.6 - 99.7)	99.9 (99.9 - 99.9)	42.6 (42.5 - 42.7)	18.3 (18.2 - 18.4)	37.8
	5	1	99.9 (99.8 - 99.9)	100 (99.9 - 100)	33.8 (33.7 - 33.9)	16.3 (16.2 - 16.4)	29.9
		2	99.8 (99.7 - 99.8)	99.9 (99.9 - 100)	50.8 (50.7 - 50.9)	20.7 (20.6 - 20.9)	45.0
		3	99.7 (99.7 - 99.7)	99.9 (99.9 - 99.9)	53.7 (53.5 - 53.8)	21.7 (21.6 - 21.9)	47.6

Assay	0 hour cutoff < ng/L	1-hour Δ < ng/L	Sensitivity	NPV	Specificity	PPV	% ruled out
		4	99.7 (99.6 - 99.7)	99.9 (99.9 - 99.9)	54.2 (54.0 - 54.3)	21.9 (21.8 - 22.1)	48.0
		5	99.5 (99.5 - 99.6)	99.9 (99.9 - 99.9)	54.3 (54.1 - 54.4)	21.9 (21.8 - 22.1)	48.1
	6	1	99.8 (99.8 - 99.9)	99.9 (99.9 - 100)	37.3 (37.2 - 37.5)	17.1 (16.9 - 17.2)	33.1
		2	99.7 (99.7 - 99.7)	99.9 (99.9 - 99.9)	57.0 (56.9 - 57.2)	23.0 (22.9 - 23.2)	50.5
		3	99.6 (99.6 - 99.7)	99.9 (99.9 - 99.9)	60.8 (60.6 - 60.9)	24.7 (24.5 - 24.8)	53.9
		4	99.6 (99.6 - 99.7)	99.9 (99.9 - 99.9)	61.5 (61.3 - 61.6)	25.0 (24.8 - 25.2)	54.5
		5	99.4 (99.3 - 99.4)	99.9 (99.9 - 99.9)	61.6 (61.4 - 61.7)	25.0 (24.9 - 25.2)	54.6
	7	1	99.8 (99.8 - 99.8)	99.9 (99.9 - 100)	39.3 (39.1 - 39.4)	17.5 (17.4 - 17.6)	34.8
		2	99.7 (99.6 - 99.7)	99.9 (99.9 - 99.9)	61.0 (60.9 - 61.1)	24.8 (24.6 - 25.0)	54.1
		3	99.6 (99.5 - 99.6)	99.9 (99.9 - 99.9)	65.5 (65.3 - 65.6)	27.1 (26.9 - 27.3)	58.0
		4	99.5 (99.5 - 99.6)	99.9 (99.9 - 99.9)	66.3 (66.1 - 66.4)	27.6 (27.4 - 27.8)	58.8
		5	99.3 (99.2 - 99.4)	99.9 (99.9 - 99.9)	66.4 (66.3 - 66.6)	27.6 (27.4 - 27.8)	58.9
	8	1	99.8 (99.8 - 99.8)	99.9 (99.9 - 99.9)	40.4 (40.3 - 40.6)	17.8 (17.7 - 17.9)	35.8
		2	99.6 (99.6 - 99.7)	99.9 (99.9 - 99.9)	63.5 (63.3 - 63.6)	26.0 (25.9 - 26.2)	56.3
		3	99.5 (99.5 - 99.6)	99.9 (99.9 - 99.9)	68.4 (68.3 - 68.6)	28.9 (28.7 - 29.1)	60.7
		4	99.5 (99.4 - 99.6)	99.9 (99.9 - 99.9)	69.3 (69.2 - 69.5)	29.5 (29.3 - 29.7)	61.5
		5	99.2 (99.1 - 99.3)	99.9 (99.8 - 99.9)	69.6 (69.4 - 69.7)	29.6 (29.4 - 29.8)	61.7
	9	1	99.8 (99.8 - 99.8)	99.9 (99.9 - 99.9)	41.6 (41.4 - 41.7)	18.1 (17.9 - 18.2)	36.8
		2	99.6 (99.6 - 99.7)	99.9 (99.9 - 99.9)	65.7 (65.6 - 65.8)	27.3 (27.1 - 27.4)	58.2
		3	99.5 (99.5 - 99.6)	99.9 (99.9 - 99.9)	71.2 (71.0 - 71.3)	30.8 (30.6 - 31.0)	63.1
		4	99.5 (99.4 - 99.6)	99.9 (99.9 - 99.9)	72.2 (72.0 - 72.3)	31.6 (31.4 - 31.8)	64.0
		5	99.2 (99.1 - 99.3)	99.9 (99.8 - 99.9)	72.4 (72.3 - 72.5)	31.7 (31.5 - 31.9)	64.2
	10	1	99.8 (99.7 - 99.8)	99.9 (99.9 - 99.9)	42.4 (42.2 - 42.5)	18.3 (18.1 - 18.4)	37.6
		2	99.6 (99.6 - 99.7)	99.9 (99.9 - 99.9)	67.3 (67.2 - 67.5)	28.2 (28.1 - 28.4)	59.7
		3	99.5 (99.5 - 99.6)	99.9 (99.9 - 99.9)	73.3 (73.2 - 73.5)	32.5 (32.3 - 32.7)	65.0
		4	99.5 (99.4 - 99.5)	99.9 (99.9 - 99.9)	74.4 (74.3 - 74.5)	33.4 (33.2 - 33.6)	66.0
		5	99.1 (99.0 - 99.2)	99.8 (99.8 - 99.9)	74.7 (74.6 - 74.8)	33.6 (33.4 - 33.8)	66.3

Supplemental Table 14: Derivation of single sample rule-in 30 day MI or death algorithms

Assay	Cutoff ≥ ng/L	Specificity	PPV	Ruled in	% ruled in	False negatives	False positives
Roche	52	98.0 (97.2 - 98.6)	77.6 (69.9 - 84.0)	147	7.8	129	33
Abbott	64	97.5 (96.6 - 98.2)	77.1 (70.2 - 83.0)	179	9.5	105	41
Siemens	115	97.3 (96.4 - 98.1)	74.6 (67.4 - 80.9)	173	9.1	114	44
	116	97.3 (96.4 - 98.1)	74.6 (67.4 - 80.9)	173	9.1	114	44
	117	97.3 (96.4 - 98.1)	74.6 (67.4 - 80.9)	173	9.1	114	44
	118	97.3 (96.4 - 98.1)	74.6 (67.4 - 80.9)	173	9.1	114	44
	119	97.3 (96.4 - 98.1)	74.4 (67.2 - 80.8)	172	9.1	115	44
	120	97.3 (96.4 - 98.1)	74.4 (67.2 - 80.8)	172	9.1	115	44
	121	97.3 (96.4 - 98.1)	74.3 (67.0 - 80.6)	171	9.0	116	44
	122	97.3 (96.4 - 98.1)	74.3 (67.0 - 80.6)	171	9.0	116	44
	123	97.4 (96.5 - 98.1)	74.7 (67.5 - 81.0)	170	9.0	116	43
	124	97.4 (96.5 - 98.1)	74.6 (67.3 - 80.9)	169	8.9	117	43
	125	97.4 (96.5 - 98.1)	74.6 (67.3 - 80.9)	169	8.9	117	43

Supplemental Table 15: Validation of single sample rule-in 30 day MI or death algorithms

Assay	Cutoff ≥ ng/L	Specificity	PPV	% ruled in
Roche	52	97.6 (97.5 - 97.6)	73.2 (72.9 - 73.5)	8.0
Abbott	64	97.4 (97.4 - 97.4)	76.5 (76.2 - 76.7)	9.6
Siemens	115	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	116	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	117	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	118	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	119	97.3 (97.3 - 97.4)	74.9 (74.6 - 75.2)	9.3
	120	97.3 (97.3 - 97.4)	74.9 (74.6 - 75.2)	9.3
	121	97.4 (97.3 - 97.4)	75.0 (74.7 - 75.3)	9.3
	122	97.4 (97.3 - 97.4)	75.0 (74.7 - 75.3)	9.3
	123	97.4 (97.3 - 97.4)	75.1 (74.8 - 75.4)	9.3
	124	97.4 (97.4 - 97.4)	75.3 (75.0 - 75.6)	9.2
	125	97.4 (97.4 - 97.4)	75.3 (75.0 - 75.6)	9.2

Supplemental Table 16: Derivation of single sample rule-in NSTEMI algorithms

Assay	Cutoff ≥ ng/L	Specificity	PPV	Ruled in	% ruled in	False negatives	False positives
Roche	52	97.8 (97.0 - 98.5)	75.5 (67.7 - 82.2)	147	7.8	121	36
Abbott	64	97.4 (96.5 - 98.1)	76.0 (69.0 - 82.0)	179	9.5	96	43
Siemens	115	97.2 (96.3 - 98)	73.4 (66.2 - 79.8)	173	9.1	105	46
	116	97.2 (96.3 - 98)	73.4 (66.2 - 79.8)	173	9.1	105	46
	117	97.2 (96.3 - 98)	73.4 (66.2 - 79.8)	173	9.1	105	46
	118	97.2 (96.3 - 98)	73.4 (66.2 - 79.8)	173	9.1	105	46
	119	97.2 (96.3 - 98)	73.3 (66.0 - 79.7)	172	9.1	106	46
	120	97.2 (96.3 - 98)	73.3 (66.0 - 79.7)	172	9.1	106	46
	121	97.2 (96.3 - 98)	73.1 (65.8 - 79.6)	171	9.0	107	46
	122	97.2 (96.3 - 98)	73.1 (65.8 - 79.6)	171	9.0	107	46
	123	97.3 (96.4 - 98)	73.5 (66.2 - 80.0)	170	9.0	107	45
	124	97.3 (96.4 - 98)	73.4 (66.0 - 79.9)	169	8.9	108	45
	125	97.3 (96.4 - 98)	73.4 (66.0 - 79.9)	169	8.9	108	45

Supplemental Table 17: Validation of single sample rule-in NSTEMI algorithms

Assay	Cutoff ≥ ng/L	Specificity	PPV	% ruled in
Roche	52	97.6 (97.5 - 97.6)	73.2 (72.9 - 73.5)	8.0
Abbott	64	97.4 (97.4 - 97.4)	76.5 (76.2 - 76.7)	9.6
Siemens	115	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	116	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	117	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	118	97.3 (97.3 - 97.3)	74.9 (74.6 - 75.2)	9.4
	119	97.3 (97.3 - 97.4)	74.9 (74.6 - 75.2)	9.3
	120	97.3 (97.3 - 97.4)	74.9 (74.6 - 75.2)	9.3
	121	97.4 (97.3 - 97.4)	75.0 (74.7 - 75.3)	9.3
	122	97.4 (97.3 - 97.4)	75.0 (74.7 - 75.3)	9.3
	123	97.4 (97.3 - 97.4)	75.1 (74.8 - 75.4)	9.3
	124	97.4 (97.4 - 97.4)	75.3 (75.0 - 75.6)	9.2
	125	97.4 (97.4 - 97.4)	75.3 (75.0 - 75.6)	9.2

Supplemental Table 18: Derivation of 0-1 hour delta rule-in 30 day MI or death algorithms

Assay	0-1 h Δ ≥ Cutoff	Specificity	PPV	Ruled in	% ruled in	False negatives	False positives
Roche	5	97.5 (96.4 - 98.4)	79.1 (70.6 - 86.1)	115	10.4	42	24
Abbott	6	96.5 (95.1 - 97.6)	76.9 (69.2 - 83.4)	147	13.3	20	34
Siemens	5	91.4 (89.5 - 93.1)	59.2 (52.2 - 66.0)	206	18.5	12	84
	6	92.7 (90.9 - 94.2)	62.5 (55.2 - 69.4)	192	17.2	14	72
	7	93.5 (91.8 - 94.9)	65.0 (57.6 - 71.9)	183	16.4	15	64
	8	94.5 (92.9 - 95.8)	68.4 (60.9 - 75.3)	171	15.3	17	54
	9	94.9 (93.3 - 96.2)	69.9 (62.3 - 76.7)	166	14.9	18	50
	10	95.4 (93.9 - 96.6)	71.5 (63.8 - 78.4)	158	14.2	21	45
	11	96.2 (94.8 - 97.3)	75.0 (67.2 - 81.7)	148	13.3	23	37
	12	96.2 (94.8 - 97.3)	74.5 (66.6 - 81.4)	145	13.0	26	37
	13	96.2 (94.8 - 97.3)	74.5 (66.6 - 81.4)	145	13.0	26	37
	14	96.4 (95.1 - 97.5)	75.2 (67.2 - 82.1)	141	12.6	28	35
	15	96.5 (95.2 - 97.6)	75.7 (67.8 - 82.6)	140	12.5	28	34

Supplemental Table 19: Validation of 0-1 hour delta rule-in 30 day MI or death algorithms

Assay	0-1 h Δ ≥ Cutoff	Specificity	PPV	% ruled in
Roche	5	97.1 (97.1 - 97.1)	75.3 (74.9 - 75.6)	10.3
Abbott	6	96.4 (96.4 - 96.5)	76.2 (75.9 - 76.5)	13.2
Siemens	5	91.1 (91.0 - 91.2)	57.3 (57.0 - 57.6)	18.3
	6	92.4 (92.3 - 92.5)	60.8 (60.5 - 61.1)	17.1
	7	93.2 (93.1 - 93.2)	63.0 (62.7 - 63.3)	16.3
	8	94.2 (94.2 - 94.3)	66.4 (66.1 - 66.7)	15.2
	9	94.5 (94.5 - 94.6)	67.5 (67.2 - 67.8)	14.8
	10	95.0 (95.0 - 95.1)	69.2 (68.9 - 69.5)	14.2
	11	95.8 (95.7 - 95.8)	72.0 (71.7 - 72.3)	13.4
	12	95.9 (95.9 - 96.0)	72.7 (72.4 - 73.0)	13.1
	13	95.9 (95.9 - 96.0)	72.7 (72.4 - 73.0)	13.1
	14	96.2 (96.1 - 96.2)	73.7 (73.4 - 74.0)	12.8
	15	96.3 (96.2 - 96.3)	74.0 (73.7 - 74.3)	12.6

Supplemental Table 20: Derivation of 0-1 hour delta rule-in NSTEMI algorithms

Assay	0-1 h Δ ≥ Cutoff	Specificity	PPV	Ruled in	% ruled in	False negatives	False positives
Roche	5	97.5 (96.3 - 98.3)	78.3 (69.6 - 85.4)	115	10.4	38	25
Abbott	6	96.4 (95.0 - 97.5)	76.2 (68.5 - 82.8)	147	13.3	16	35
Siemens	5	91.3 (89.4 - 93.0)	58.3 (51.2 - 65.1)	206	18.5	9	86
	6	92.5 (90.7 - 94.1)	61.5 (54.2 - 68.4)	192	17.2	11	74
	7	93.3 (91.6 - 94.8)	63.9 (56.5 - 70.9)	183	16.4	12	66
	8	94.3 (92.7 - 95.7)	67.3 (59.7 - 74.2)	171	15.3	14	56
	9	94.7 (93.1 - 96.0)	68.7 (61.0 - 75.6)	166	14.9	15	52
	10	95.2 (93.7 - 96.5)	70.3 (62.5 - 77.3)	158	14.2	18	47
	11	96.0 (94.6 - 97.2)	73.6 (65.8 - 80.5)	148	13.3	20	39
	12	96.0 (94.6 - 97.2)	73.1 (65.1 - 80.1)	145	13.0	23	39
	13	96.0 (94.6 - 97.2)	73.1 (65.1 - 80.1)	145	13.0	23	39
	14	96.3 (94.9 - 97.3)	73.8 (65.7 - 80.8)	141	12.6	25	37
	15	96.4 (95.0 - 97.4)	74.3 (66.2 - 81.3)	140	12.5	25	36

Supplemental Table 21: Validation of 0-1 hour delta rule-in NSTEMI algorithms

Assay	0-1 h Δ ≥ Cutoff	Specificity	PPV	% ruled in
Roche	5	97.0 (97.0 - 97.1)	74.6 (74.2 - 74.9)	10.3
Abbott	6	96.3 (96.3 - 96.4)	75.5 (75.2 - 75.8)	13.2
Siemens	5	91.0 (91.0 - 91.1)	56.7 (56.4 - 57.0)	18.3
	6	92.3 (92.2 - 92.4)	60.1 (59.8 - 60.4)	17.1
	7	93.1 (93.0 - 93.2)	62.3 (62.0 - 62.7)	16.3
	8	94.1 (94.1 - 94.2)	65.8 (65.4 - 66.1)	15.2
	9	94.5 (94.4 - 94.5)	66.8 (66.5 - 67.2)	14.8
	10	95.0 (94.9 - 95.0)	68.5 (68.2 - 68.9)	14.2
	11	95.7 (95.6 - 95.7)	71.3 (71.0 - 71.6)	13.4
	12	95.9 (95.8 - 95.9)	72.0 (71.7 - 72.3)	13.1
	13	95.9 (95.8 - 95.9)	72.0 (71.7 - 72.3)	13.1
	14	96.1 (96.1 - 96.2)	73.0 (72.7 - 73.3)	12.8
	15	96.2 (96.1 - 96.2)	73.3 (73.0 - 73.6)	12.6

Supplemental Table 22: Siemens Atellica IM algorithms from prior studies

Diagnostic performance of proposed algorithms in prior studies. The results given are the published data from the original papers and their supplements.

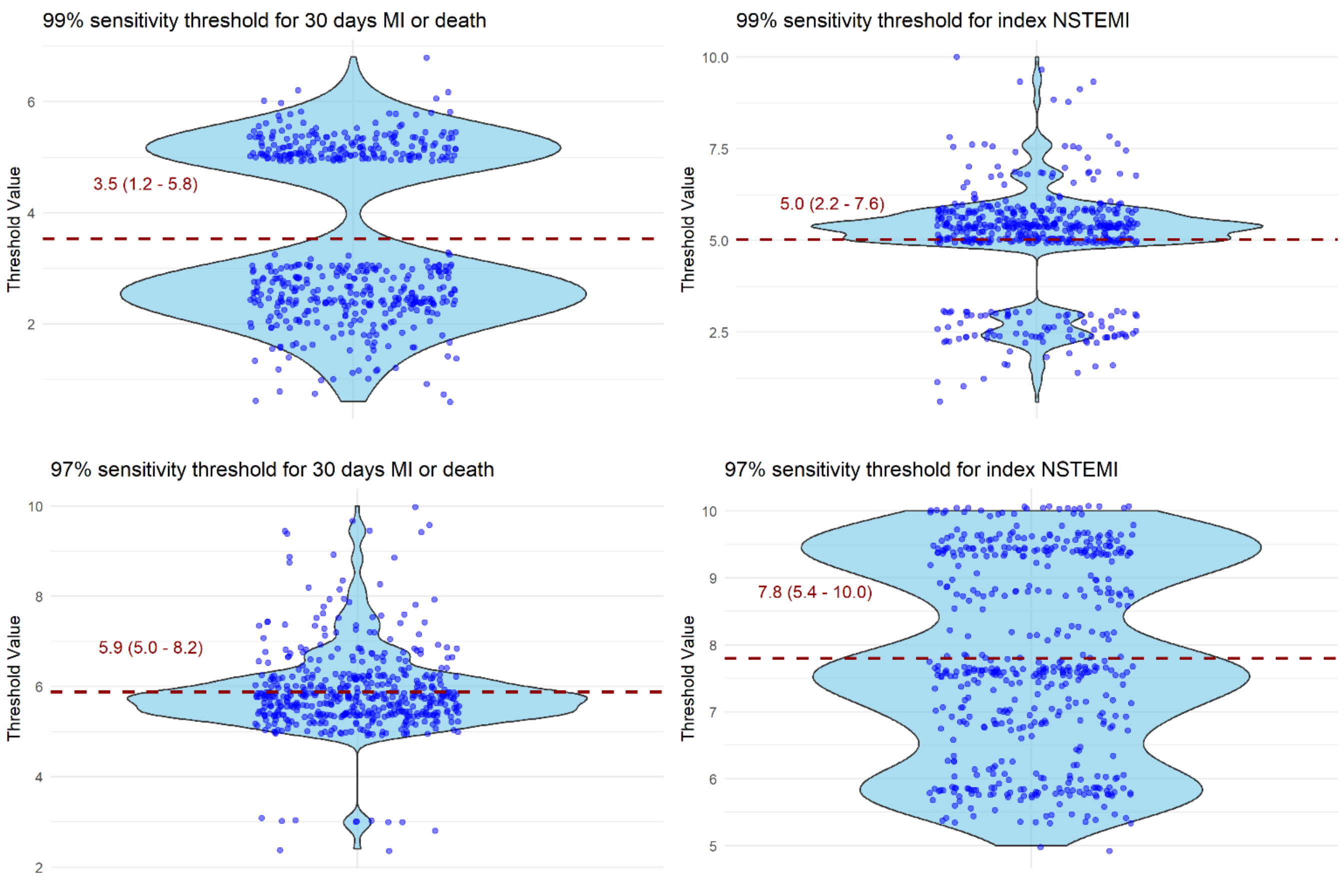
Rule-out						
0 hour cTn-concentration	**Delta 0-1 hour**	**Sensitivity**	**NPV**	**Specificity**	**PPV**	**% of patients ruled out**
Boeddinghaus et al (2018) - Centaur						
Hs-cTnI (Siemens) < 3 ng/L	N/A	Derivation: 99.2 (95.6 - 100.0) Validation: 99.1 (95.3 - 100.0)	Derivation: 99.7 (97.7 - 100.0) Validation: 99.7 (97.8 - 100.0)	-	-	Derivation: 45 Validation: 46
Hs-cTnI (Siemens) < 6 ng/L	< 3 ng/L					
Sörensen et al (2021)						
Hs-cTnI (Siemens) < 3 ng/L	N/A	Derivation: 98.3 (93.8 - 100.0) Validation: 100.0 (95.1 - 100.0)	Derivation: 99.4 (96.9 - 100.9) Validation: 100.0 (97.5-100.0)	Derivation: 34.1 (30.0 - 38.4) Validation: 29.5 (25.5 - 33.8)	-	Derivation: 29.3 Validation: 29.5
Hs-cTnI (Siemens) < 5 ng/L	N/A	Derivation: 97.7 (92.0 - 99.7)	Derivation: 99.6 (97.6 - 100.0)	Derivation: 51.0 (46.6 - 55.4)	-	Derivation: 43.9
Hs-cTnI (Siemens) < 6 ng/L	< 3 ng/L	Derivation: 97.9 (93.9 - 99.6) Validation: 99.1 (95.1 - 100.0)	Derivation: 99.3 (98.1 - 99.9) Validation: 99.8 (98.6 - 100.0)	Derivation: 60.7 (57.1 - 64.2) Validation: 55.5 (51.8 - 59.1)	-	Derivation: 51.4 Validation: 48.3
Chapman et al (2018)						
Hs-cTnI (Siemens) < 5 ng/L	N/A	98.0 (96.4 - 99.5)	99.5 (99.1 - 99.8)	-	-	29.7
Hs-cTnI (Siemens) < 3 ng/L	N/A	92.2 (83.0 - 99.4)	99.0 (97.6 - 99.8)	-	-	23.9
Hs-cTnI (Siemens) < 6 ng/L	< 3 ng/L			-	-	40.6
Nowak et al (2019)						
Hs-cTnI (Siemens) < 3 ng/L	N/A	99.1 (96.9 - 99.9)	99.7 (99.0 - 100.0)	-	-	33.8
Hs-cTnI (Siemens) < 6 ng/L	< 3 ng/L	99.6 (97.6 - 100.9)	99.7 (98.4 - 100.9)	-	-	16.6
Sandoval et al (2019)						
Hs-cTnI (Siemens) < 3 ng/L	N/A	98.8 (97.5 - 100.0)	99.6 (99.1 - 100.0)	-	-	33.0
Hs-cTnI (Siemens) < 5 ng/L	N/A	98.8 (97.5 - 100.9)	99.7 (99.4 - 100.0)	-	-	47.0
Rule-in						
0 hour cTn-concentration	**Delta 0-1 hour**	**Sensitivity**	**NPV**	**Specificity**	**PPV**	**% of patients ruled in**
Boeddinghaus et al (2018) - Centaur						
Hs-cTnI (Siemens) ≥120 ng/L	N/A	-	-	Derivation: 95.3 (93.1-96.9) Validation:	Derivation: 78.5 (70.1-85.5) Validation: 72.5 (63.6-80.3)	Derivation: 18 Validation: 18
N/A	≥ 12 ng/L					
Sörensen et al (2021)						

Hs-cTnI (Siemens) ≥120 ng/L	N/A	Derivation: 78.7 (71.0 - 85.2) Validation: 78.4 (69.6-85.6)	-	Derivation: 94.0 (92.0 - 95.6) Validation: 94.4 (92.5 - 96.0)	Derivation: 71.2 (63.4 - 78.1) Validation: 68.0 (59.1 - 75.9)	Derivation: 17.6 Validation: 15.1
N/A	≥ 12 ng/L					
N/A	≥ 15 ng/L	Derivation: 78.7 (71.0 - 85.2)	-	Derivation: 94.1 (92.2 - 95.7)	Derivation: 71.6 (63.8 - 78.6)	Derivation: 17.5
Chapman et al (2018)						
Hs-cTnI (Siemens) ≥120 ng/L	N/A	-	-	98.2 (96.8 - 99.4)	77.6 (61.1 - 90.5)	4.7
N/A	≥ 12 ng/L	-	-			2.2
Nowak et al (2019)						
Hs-cTnI (Siemens) ≥120 ng/L	N/A	-	-	96.8 (95.9 - 97.5)	71.0 (64.3 - 77.0)	9.9
N/A	≥ 12 ng/L	-	-	98.9 (98.4 - 99.3)	63.6 (49.6 - 76.2)	2.6
Sandoval et al (2019)						
Hs-cTnI (Siemens) ≥120 ng/L	N/A	-	-	96.5 (95.7 - 97.3)	71.1 (65.4 - 76.9)	11.0

Supplemental figures

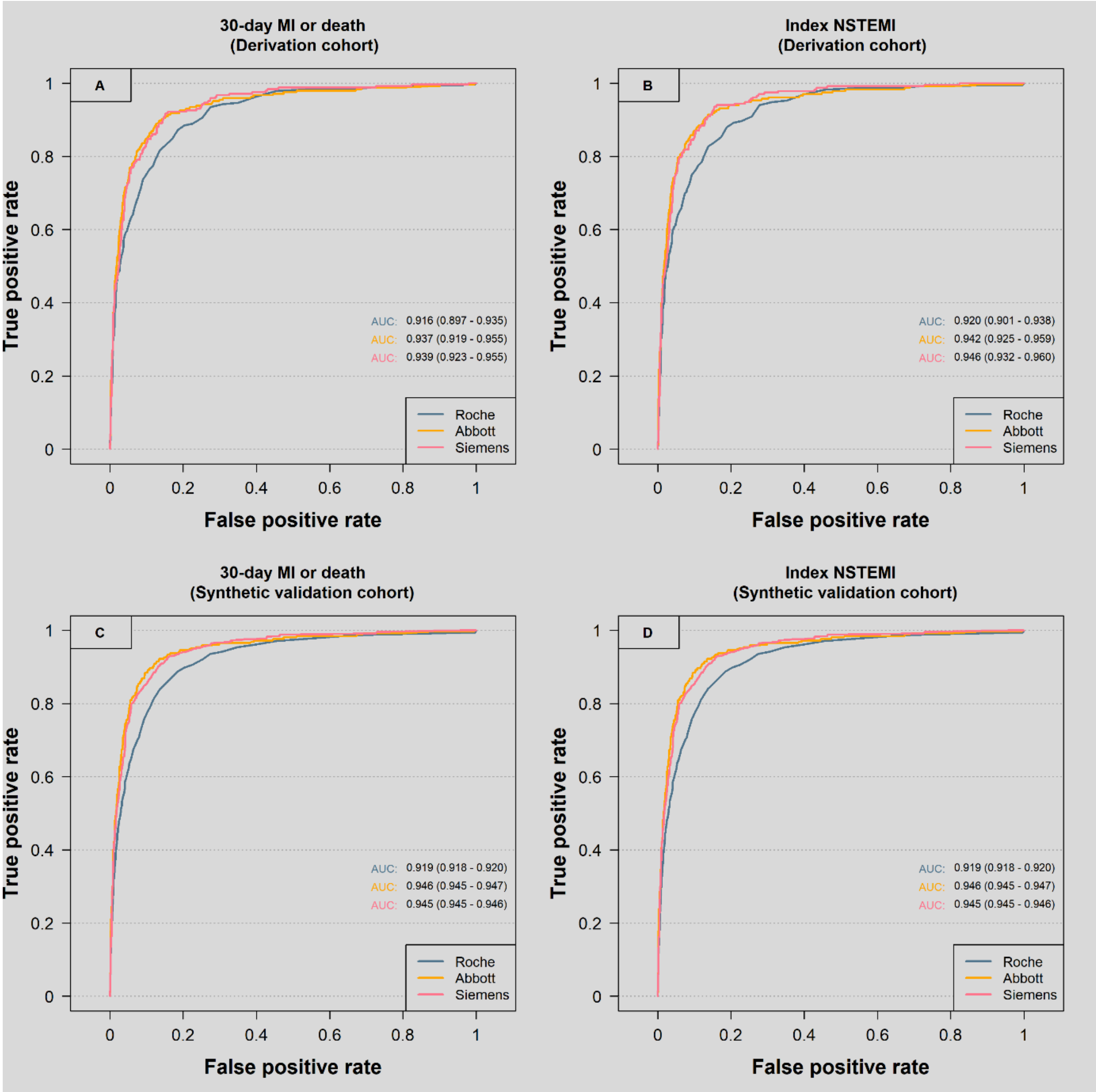
Supplemental Figure 1: 99% and 97% sensitivity Siemens hs-cTnI thresholds

Violin plots of 500 draws of 1896 random data sets from the synthetic validation cohort with estimated mean hs-cTnI thresholds and 95% CI to achieve either 99% or 97% sensitivity for the primary and secondary endpoint.

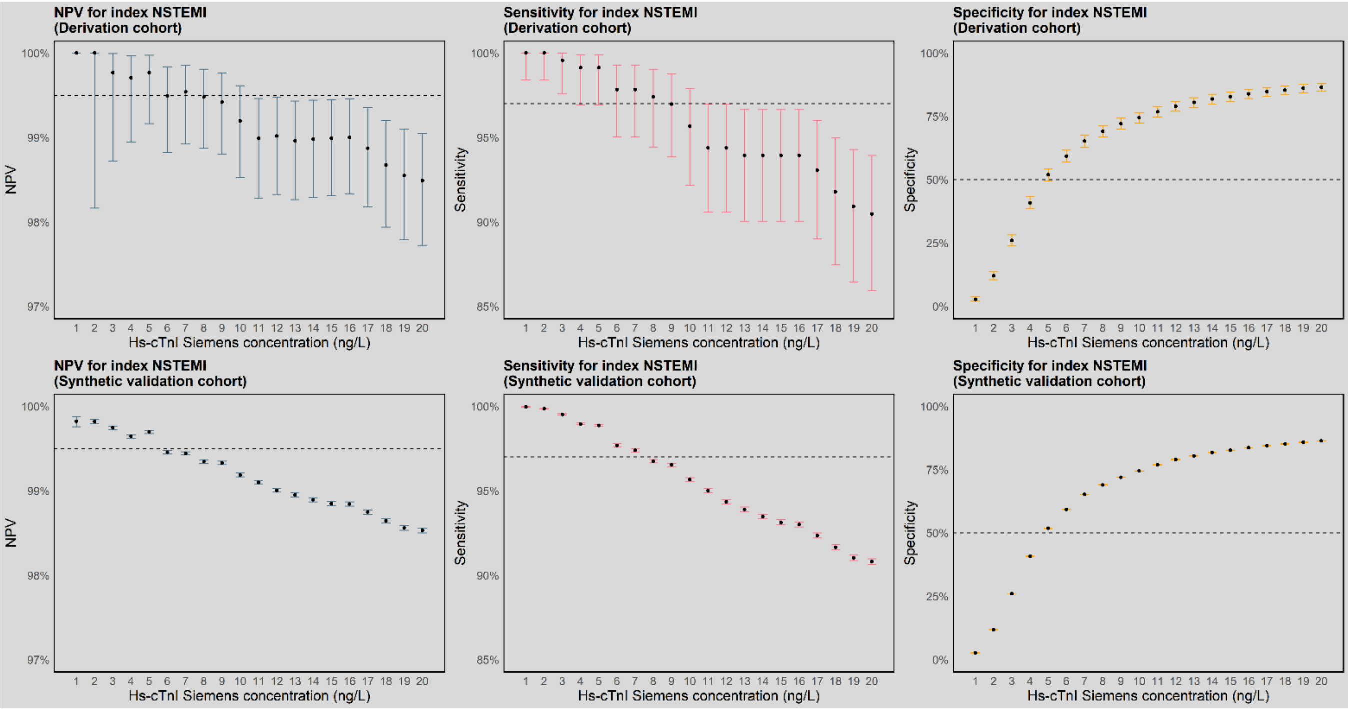


Supplemental Figure 2: ROC curves

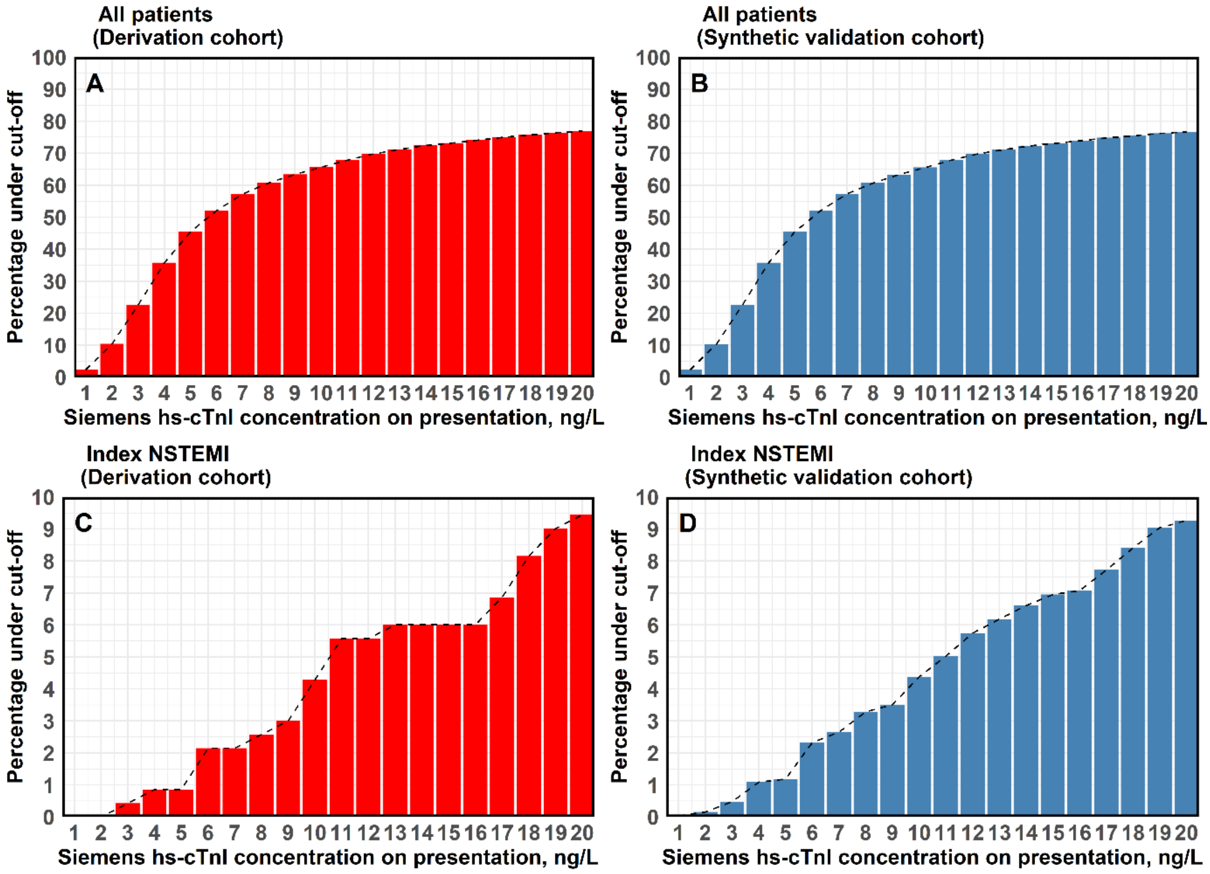
ROC curves for the three different hs-cTn assays for both cohorts (A-D).



Supplemental figure 3: NPV, sensitivity, specificity for NSTEMI



Supplemental figure 4: Cumulative percentage of patients with NSTEMI with first TNI < cutoff.



Supplemental references

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