SUPPLEMENTAL MATERIAL.

Supplemental methods.

All cases with at least one cTnT increase above the 99th percentile were adjudicated using the Fourth UDMI criteria by trained physicians. All available data including documentation addressing clinical presentation, 12-lead electrocardiogram, echocardiography, stress test, and angiography were reviewed. Cases with challenging adjudication were reviewed by the principal investigator (YS), and if needed also reviewed by one of the members from the Task Force for the Fourth UDMI (ASJ).

Following the Fourth UDMI, patients with at least one cTnT concentration above the sex-specific 99th percentile URL were classified as having either myocardial injury (i.e.: isolated cTnT increases) or acute MI based on the presence or absence of clinical features of acute myocardial ischemia that included at least one of the following: myocardial ischemia symptoms, new ischemic ECG changes, development of pathological Q waves, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology, and/or identification of a culprit lesion on coronary angiography. Acute MI could be classified in the presence of a cTnT rising and/or falling pattern with at least one cTnT concentration above the 99th percentile and symptoms alone as the qualifying marker of acute myocardial ischemia, only if the symptoms were thought to be unequivocally ischemic in nature. If the symptoms were considered atypical and/or not clearly ischemic and there was no other definite sign of ischemia on ECG, imaging, and/or angiography, then such cases were recommended to be classified as isolated cTnT increases (i.e.: myocardial injury).

Those with overt clinical evidence of acute myocardial ischemia were classified as having acute MI and further sub-classified into one of the five MI subtypes, with type 1 MI

representative of atherothrombotic MI and type 2 MI due non-atherothrombotic supply-demand myocardial ischemia. Type 1 MI diagnosis was established when there was detection of a rise and/or fall of cTn with at least one concentration above the 99th percentile, with at least one clinical feature of acute myocardial ischemia as noted above. Type 2 MI diagnosis was established when there was detection of a rise and/or fall of cTn with at least one concentration above the 99th percentile and evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute coronary atherothrombosis, with at least one clinical feature of acute myocardial ischemia as noted above. For cases of type 2 MI, adjudicators were required to identify the trigger/etiology of type MI, including: coronary spasm, coronary embolism, endothelial dysfunction, spontaneous coronary artery dissection/hematoma, aortic dissection with coronary involvement, anemia, respiratory failure with hypoxia, bradyarrhythmia, hypotension, tachyarrhythmia, hypertension, or other.

To assist in determining whether a significant rise and/or fall in cTnT occurred, the following guidance was provided to adjudicators:

5th Gen cTnT: a significant change (increase or decrease) was determined following Mayo Clinic hs-cTnT guidelines.

2-hour change:

- <=3 ng/L: Not changing
- 4 to 9 ng/L: Indeterminate
- >=10 ng/L: Changing

6-hour change:

- <12 ng/L: Not changing
- >=12 ng/L: Changing

Supplemental Table 1. ICD codes for myocardial infarction and chest pain.

Acute myocardial infarction ICD-10 codes		
Acute myocardial infarction diagnoses based on ICD-10 codes as per DSS Billing / Rochester Epidemiology Project (REP) Outside Source Data methodology excluding old myocardial infarction and all ST-elevation myocardial infarction codes.		
ICD-10 code	**Code description**	**Number (%) among CV Data Biomarker Cohort Coded MIs** (n=1829)
I21.4	Non-ST elevation (NSTEMI) myocardial infarction	900 (51.9%)
I21.9	Acute myocardial infarction, unspecified	285 (16.4%)
I21.A1	Myocardial infarction type 2	524 (30.2%)
I21.A9	Other myocardial infarction type	12 (0.7%)
I22.2	Subsequent non-ST elevation (NSTEMI) myocardial infarction	1 (0.1%)
I23.1	Atrial septal defect as current complication following acute myocardial infarction	6 (0.3%)
I23.2	Ventricular septal defect as current complication following acute myocardial infarction	3 (0.2%)
I23.6	Thrombosis of atrium, auricular appendage, and ventricle as current complications following acute myocardial infarction	4 (0.2%)
Total		**1735**

Codes I21.4 (non-ST elevation myocardial infarction), I21.9 (acute myocardial infarction, unspecified), and I21.A1 (myocardial infarction type 2) explained most (98.5%) coded acute myocardial infarction diagnoses in the CV Data Mart Biomarker cohort. Old myocardial infarction and ST-elevation myocardial infarction ICD-10 codes were excluded from these analyses.

Supplemental Table 2. Baseline characteristics for the CV Data Mart Biomarker cohort across major sites.

	Rochester N=20151	**Arizona** N=14421	**Florida** N=9670	**MCHS** N=41730
Age, mean (SD)	63 (18)	64 (17)	64 (17)	62 (19)
Women, n (%)	10031 (49)	7198 (50)	4877 (50)	21235 (51)
Chest pain, n (%)	6491 (32)	5068 (35)	3497 (36)	12263 (29)
Coronary artery disease, n (%)	6493 (32)	3109 (22)	2735 (28)	11559 (28)
Prior myocardial infarction, n (%)	2777 (14)	1518 (11)	1061 (11)	5356 (13)
Hypertension, n (%)	11880 (59)	6428 (45)	4994 (52)	25725 (62)
Diabetes mellitus, n (%)	8228 (41)	3592 (25)	2629 (27)	15897 (38)
Chronic kidney disease, n (%)	3846 (19)	2197 (15)	1663 (17)	9497 (23)
Dialysis, n (%)	326 (1.6)	405 (2.8)	259 (2.7)	495 (1.2)
Peripheral vascular disease, n (%)	6584 (32)	2500 (17)	1909 (20)	10565 (25)
Heart failure, n (%)	3834 (19)	1787 (12)	1381 (14)	8170 (20)
Atrial fibrillation, n (%)	3966 (20)	2221 (15)	1700 (18)	7559 (18)
Liver cirrhosis, n (%)	3001 (15)	1573 (11)	1071 (11)	4962 (12)

Supplemental Table 3. Baseline characteristics for patients with (2 or more hs-cTnT measurements) and without (1 hs-cTnT measurement) serial hs-cTnT measurements in the CV Data Mart Biomarker cohort.

	Total with and without serial hs-cTnT			**Total with baseline hs-cTnT<6 ng/L with and without serial hs-cTnT**		
	Total (n=85610)	**With serial hs-cTnT (n=59556)**	**Without serial hs-cTnT (n=26054)**	**Total with baseline hs-cTnT<6 ng/L (n=24646)**	**Baseline hs-cTnT<6 ng/L with serial hs-cTnT (n=11962)**	**Baseline hs-cTnT<6 ng/L without serial hs-cTnT (n=12684)**
Age, mean (SD)	63 (18)	67 (17)	55 (18)	47 (15)	50 (14)	45 (15)
Women, n (%)	43043 (50)	28947 (49)	14096 (54)	16143 (66)	7698 (64)	8445 (67)
Chest pain, n (%)	27198 (32)	17767 (30)	9431 (36)	11725 (48)	5840 (49)	5885 (46)
Coronary artery disease, n (%)	23636 (28)	19633 (33)	4003 (15)	1891 (7.7)	1254 (11)	637 (5.0)
Prior myocardial infarction, n (%)	9114 (11)	7730 (13)	1384 (5.3)	665 (2.7)	448 (3.7)	217 (1.7)
Hypertension, n (%)	48717 (57)	38101 (64)	10616 (41)	7088 (29)	4062 (34)	3026 (24)
Diabetes mellitus, n (%)	30213 (35)	23804 (40)	6409 (25)	4604 (19)	2608 (22)	1996 (16)
Chronic kidney disease, n (%)	17070 (20)	14538 (24)	2532 (10)	693 (2.8)	411 (3.4)	282 (2.2)
Dialysis, n (%)	1459 (1.7)	1260 (2.1)	199 (0.8)	26 (0.1)	12 (0.1)	14 (0.1)
Peripheral vascular disease, n (%)	21394 (25)	17936 (30)	3458 (13)	1483 (6.0)	926 (7.7)	557 (4.4)
Heart failure, n (%)	14986 (18)	12911 (22)	2075 (8)	625 (2.5)	427 (3.6)	198 (1.6)
Atrial fibrillation, n (%)	15298 (18)	12712 (21)	2586 (10)	851 (3.5)	522 (4.4)	329 (2.6)
Liver cirrhosis, n (%)	10547 (12)	7880 (13)	2667 (10)	2152 (8.7)	1145 (9.6)	1007 (7.9)
Index hospitalization deaths, n (%)	775 (0.9)	622 (1.0)	153 (0.6)	19 (0.1)	9 (0.1)	10 (0.1)

Supplemental Table 4. Baseline characteristics according to sex in patients with baseline hs-cTnT<6 ng/L in the CV Data Mart Biomarker cohort.

	CV Data Mart Biomarker cohort			
	All patients with baseline hs-cTnT<6 ng/L (n=24646)		Patients with baseline hs-cTnT<6 ng/L and serial measurements (n=11962)	
	Women N=16143	Men N=8503	Women N=7698	Men N=4264
Age, mean (SD)	49 (15)	44 (14)	51 (14)	47 (13)
Chest pain, n (%)	7459 (46)	4266 (50)	3621 (47)	2219 (52)
Coronary artery disease, n (%)	1156 (7.2)	735 (8.6)	765 (10)	489 (12)
Prior myocardial infarction, n (%)	381 (2.4)	284 (3.3)	267 (3.5)	181 (4.2)
Hypertension, n (%)	4916 (31)	2172 (26)	2763 (36)	1299 (31)
Diabetes mellitus, n (%)	3426 (21)	1178 (14)	1906 (25)	702 (17)
Chronic kidney disease, n (%)	502 (3.1)	191 (2.2)	293 (3.8)	118 (2.8)
Dialysis, n (%)	18 (0.1)	8 (0.1)	7 (0.1)	5 (0.1)
Peripheral vascular disease, n (%)	1080 (6.7)	403 (4.7)	650 (8.4)	276 (6.5)
Heart failure, n (%)	467 (2.9)	158 (1.9)	311 (4.0)	116 (2.7)
Atrial fibrillation, n (%)	555 (3.4)	296 (3.5)	344 (4.5)	178 (4.2)

Supplemental Table 5. Baseline characteristics for patients with baseline hs-cTnT<6 ng/L according to 2-hour hs-cTnT concentrations.

Patients with baseline hs-cTnT<6 ng/L according to 2h hs-cTnT concentrations				
	Total (n=11962)	**2h hs-cTnT <LoQ** (n=10184)	**2h hs-cTnT LoQ-99th percentile** (n=1632)	**2h hs-cTnT >99th percentile** (n=146)
Age, mean (SD)	50 (14)	49 (14)	55 (14)	58 (15)
Women, n (%)	7698 (64)	6715 (66)	866 (53)	117 (80)
Chest pain, n (%)	5840 (49)	5085 (50)	690 (42)	65 (45)
Coronary artery disease, n (%)	1254 (11)	966 (9.5)	261 (16)	27 (19)
Prior myocardial infarction, n (%)	448 (3.7)	342 (3.4)	92 (5.6)	14 (9.6)
Hypertension, n (%)	4062 (34)	3251 (32)	747 (46)	64 (44)
Diabetes mellitus, n (%)	2608 (22)	2137 (21)	433 (27)	38 (26)
Chronic kidney disease, n (%)	411 (3.4)	310 (3.0)	96 (5.9)	5 (3.4)
Dialysis, n (%)	12 (0.1)	6 (0.1)	6 (0.4)	0 (0)
Peripheral vascular disease, n (%)	926 (7.7)	714 (7.0)	198 (12)	14 (9.6)
Heart failure, n (%)	427 (3.6)	313 (3.1)	105 (6.4)	9 (6.2)
Atrial fibrillation, n (%)	522 (4.4)	412 (4.0)	99 (6.1)	11 (7.5)
Liver cirrhosis, n (%)	1145 (9.6)	966 (9.5)	165 (10)	14 (9.6)
Index presentation death, n (%)	9 (0.1)	2 (0)	4 (0.2)	3 (2.1)

Supplemental Table 6. Two by two tables for the CV Data Mart Biomarker cohort.

Overall	**Myocardial injury**	**No myocardial injury**
>6 ng/L	32059	15535
<6 ng/L	146	11816

Men	**Myocardial injury**	**No myocardial injury**
>6 ng/L	16396	9949
<6 ng/L	29	4235

Women	**Myocardial injury**	**No myocardial injury**
>6 ng/L	15663	5586
<6 ng/L	117	7581

Supplemental Table 7. Baseline characteristics for the overall adjudicated cohort and according to baseline hs-cTnT concentrations.

	Total (n=1979)	**<LoQ** (n=624)	**LoQ-99th percentile** (n=544)	**>99th percentile** (n=811)
Age, mean (SD)	62 (18)	46 (15)	62 (14)	74 (14)
Women, n (%)	1030 (52)	410 (66)	206 (38)	414 (51)
Chest discomfort, n (%)	982 (50)	436 (70)	280 (52)	266 (33)
Dyspnea, n (%)	817(41)	249(40)	190(35)	378(47)
Early presenters, n (%)	442(22)	150(24)	129(24)	163(20)
Ischemic heart disease, n (%)	435(22)	35(6)	122(22)	279(34)
Hypertension, n (%)	1142(58)	196(31)	318(59)	628(77)
Obesity, n (%)	843(43)	262(42)	229(42)	352(43)
Current or prior tobacco use, n (%)	1107(56)	311(50)	332(61)	464(57)
Cerebrovascular disease, n (%)	199 (10)	15(2)	47(9)	137(17)
History of atrial fibrillation/flutter/tachycardia, n (%)	376(19)	28(5)	91(17)	257(32)
Heart failure, n (%)	376(19)	16(3)	60(11)	300(37)
Diabetes mellitus, n (%)	479(24)	62(10)	196(20)	311(38)
Chronic kidney disease, n (%)	398 (20)	20(3)	52(10)	326(40)
Family history of CAD, n (%)	613(31)	151(24)	175(32)	287(35)
Peripheral artery disease, n (%)	201(10)	5(1)	35(6)	161(20)
Dyslipidemia, n (%)	1020(52)	192(31)	288(53)	540(67)

Supplemental Table 8. Baseline characteristics for the adjudicated cohort among all patients with and without serial testing, and among those with baseline hs-cTnT<6 ng/L.

	Total with and without serial hs-cTnT			**Total with baseline hs-cTnT<6 ng/L with and without serial hs-cTnT**		
	Total (n=1979)	**With serial testing**	**Without serial testing**	**Total with baseline hs-cTnT<6 ng/L (n=624)**	**Baseline hs-cTnT<6 ng/L with serial testing (n=206)**	**Baseline hs-cTnT<6 ng/L without serial testing (n=418)**
Age, mean (SD)	62 (18)	68 (16)	53 (19)	46 (15)	53 (12)	43 (15)
Women, n (%)	1030 (52)	579 (49)	451 (56)	410 (66)	129 (63)	281 (67)
Chest discomfort, n (%)	982 (50)	546 (47)	436 (54)	436 (70)	150 (73)	286 (68)
Dyspnea, n (%)	817(41)	517 (44)	300 (37)	249 (40)	91 (44)	158 (38)
Early presenters, n (%)	442(22)	291 (25)	151 (19)	150 (24)	79 (38)	71 (17)
Ischemic heart disease, n (%)	435(22)	336 (29)	100 (12)	35 (6)	20 (10)	15 (4)
Hypertension, n (%)	1142(58)	797 (68)	345 (43)	196 (31)	77 (37)	119 (29)
Obesity, n (%)	843(43)	519 (44)	324 (40)	262 (24)	94 (46)	168 (40)
Current or prior tobacco use, n (%)	1107(56)	674 (57)	433 (54)	311 (50)	109 (53)	202 (58)
Cerebrovascular disease, n (%)	199 (10)	154 (13)	45 (6)	15 (2)	5 (2)	10 (2)
History of atrial fibrillation/flutter/tachycardia, n (%)	376(19)	289 (25)	87 (11)	28 (5)	12 (6)	16 (4)
Heart failure, n (%)	376(19)	311 (27)	65 (8)	16 (3)	10 (5)	6 (1)
Diabetes mellitus, n (%)	479(24)	342 (29)	137 (17)	62 (10)	26 (13)	36 (9)
Chronic kidney disease, n (%)	398 (20)	318 (27)	80 (10)	20 (3)	11 (5)	9 (2)
Family history of CAD, n (%)	613(31)	417 (36)	196 (24)	151 (24)	72 (35)	79 (19)
Peripheral artery disease, n (%)	201(10)	159 (14)	42 (5)	5 (1)	3 (2)	2 (1)
Dyslipidemia, n (%)	1020(52)	696 (59)	324 (40)	192 (31)	74 (36)	118 (28)
Index hospitalization deaths, n (%)	21 (1)	13 (1)	8 (1)	0	0	0

Supplemental Table 9. Baseline characteristics for the adjudicated cohort among patients with baseline hs-cTnT<6 ng/L with serial testing with 2h hs-cTnT<6 ng/L vs. ≥6 ng/L but <99th percentile URL.

	Total with baseline hs-cTnT<6 ng/L (n = 192)	**Baseline hs-cTnT<6 ng/L with 2h hs-cTnT <6 ng/L (n=173)**	**Baseline hs-cTnT<6 ng/L with 2h hs-cTnT≥6 ng/L but <99th percentile (n=19)**
Age, mean (SD)	53 (12)	52 (12)	62 (10)
Women, n (%)	119 (62)	107 (62)	12 (63)
Chest discomfort, n (%)	140 (73)	129 (75)	11 (58)
Dyspnea, n (%)	84 (44)	77 (45)	7 (37)
Early presenters, n (%)	75 (39)	65 (38)	10 (53)
Ischemic heart disease, n (%)	17 (9)	13 (8)	4 (21)
Hypertension, n (%)	72 (38)	59 (34)	13 (68)
Obesity, n (%)	87 (45)	75 (43)	12 (63)
Current or prior tobacco use, n (%)	101 (53)	90 (52)	11 (58)
Cerebrovascular disease, n (%)	4 (2)	3 (2)	1 (5)
History of atrial fibrillation/flutter/tachycardia, n (%)	12 (6)	11 (6)	1 (5)
Heart failure, n (%)	10 (5)	8 (5)	2 (11)
Diabetes mellitus, n (%)	24 (13)	21 (12)	3 (16)
Chronic kidney disease, n (%)	11 (6)	8 (5)	3 (16)
Family history of CAD, n (%)	68 (35)	58 (34)	10 (53)
Peripheral artery disease, n (%)	2 (1)	2 (1)	0
Dyslipidemia, n (%)	70 (37)	56 (32)	14 (74)
Index hospitalization deaths, n (%)	0	0	0

Supplemental Table 10. Two by two tables addressing diagnostic performance of hs-cTnT<6 ng/L for index acute myocardial infarction diagnosis in the adjudicated cohort.

	Total cohort	
	Index MI	**No MI**
>6 ng/L	140	1215
<6 ng/L	1	623

Total cohort with nonischemic ECG	
Index MI	**No MI**
95	1144
0	610

	Men	
	Index MI	**No MI**
>6 ng/L	70	665
<6 ng/L	0	214

Men with nonischemic ECG	
Index MI	**No MI**
51	634
0	210

	Women	
	Index MI	**No MI**
>6 ng/L	70	550
<6 ng/L	1	409

Women with nonischemic ECG	
Index MI	**No MI**
44	510
0	400

Supplemental Table 11. False negatives (events among patients with baseline hs-cTnT<6 ng/L) in the adjudication cohort.

Index presentation acute myocardial infarction
57-year-old female with 30 minutes of substernal chest pain with radiation to the left arm and jaw discomfort. Symptom onset <1h prior to presentation (i.e., early presenter). Electrocardiogram with ST-depressions in V2 and V3. Initial hs-cTnT <6 ng/L and subsequent hs-cTnT increased to 36 ng/L. Coronary angiogram with normal coronaries without culprit lesion. Cardiac magnetic resonance imaging with evidence of transmural infarction of the lateral apical, posteroapical, and anteroapical left ventricle.
30-day post-discharge mortality event
29-year-old female who at index presentation had fever, nausea, vomiting. During the initial presentation her evaluation included a hs-cTnT<6 ng/L and a nonischemic electrocardiogram and was identified to have staphylococcus aureus bacteremia due to prosthetic valve endocarditis. Patient was readmitted within 30-days. Not a candidate for surgical intervention and palliative care discussions were initiated. Patient suffered a cardiac arrest and death during this hospitalization.

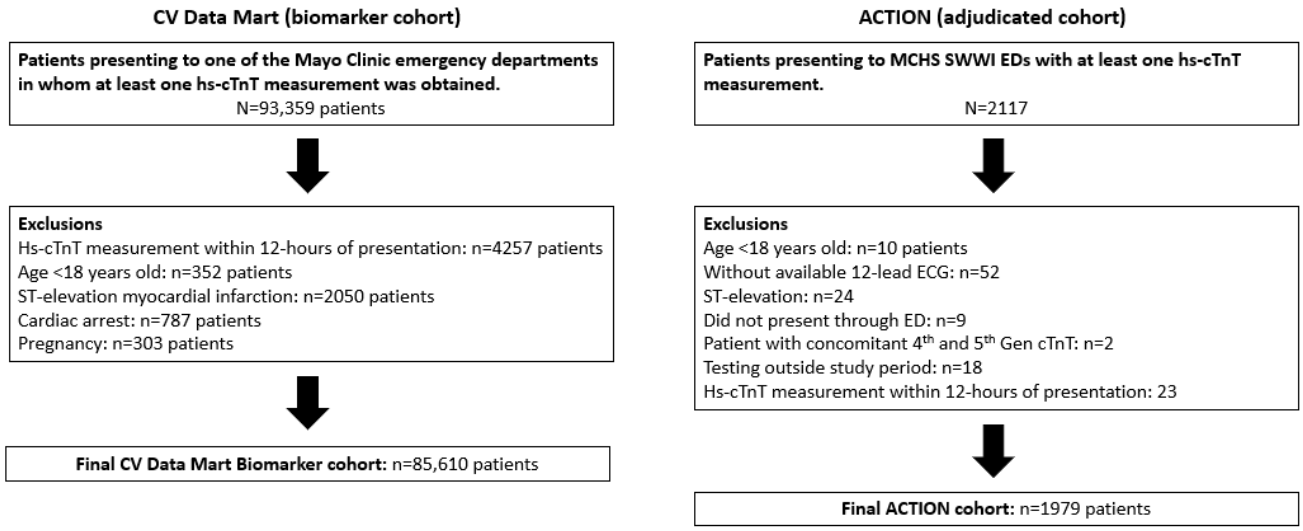
Supplemental Table 12. Adjudicated cohort: hs-cTnT<LoQ and non-ischemic ECG in early presenters.

	Hs-cTnT<LoQ AND non-ischemic ECG in early presenters		
	Total	Men	Women
Total patients, n	420	220	200
Incidence of MI, n (%)	22 (5.2)	13 (5.9)	9 (4.5)
Proportion of patients with baseline hs-cTnT <LoQ (efficacy), n (%)	145 (35)	61 (28)	84 (42)
Diagnostic performance of baseline hs-cTnT<LoQ for ruling-out index presentation acute MI			
Negative predictive value, % (95% CI)	100 (97.5, 100)	100 (94.1, 100)	100 (95.7, 100)
Sensitivity, % (95% CI)	100 (84.6, 100)	100 (75.3, 100)	100 (66.4, 100)
Missed MI rate among those with a negative test	0% 0/145	0% 0/61	0% 0/84
Safety of baseline hs-cTnT<LoQ based on acute MI or death within 30-days			
Negative predictive value, % (95% CI)	100 (97.5, 100)	100 (94.1, 100)	100 (95.7, 100)
Sensitivity, % (95% CI)	100 (87.2, 100)	100 (80.5, 100)	100 (69.2, 100)
Missed events among those with a negative test	0% 0/145	0% 0/61	0% 0/84

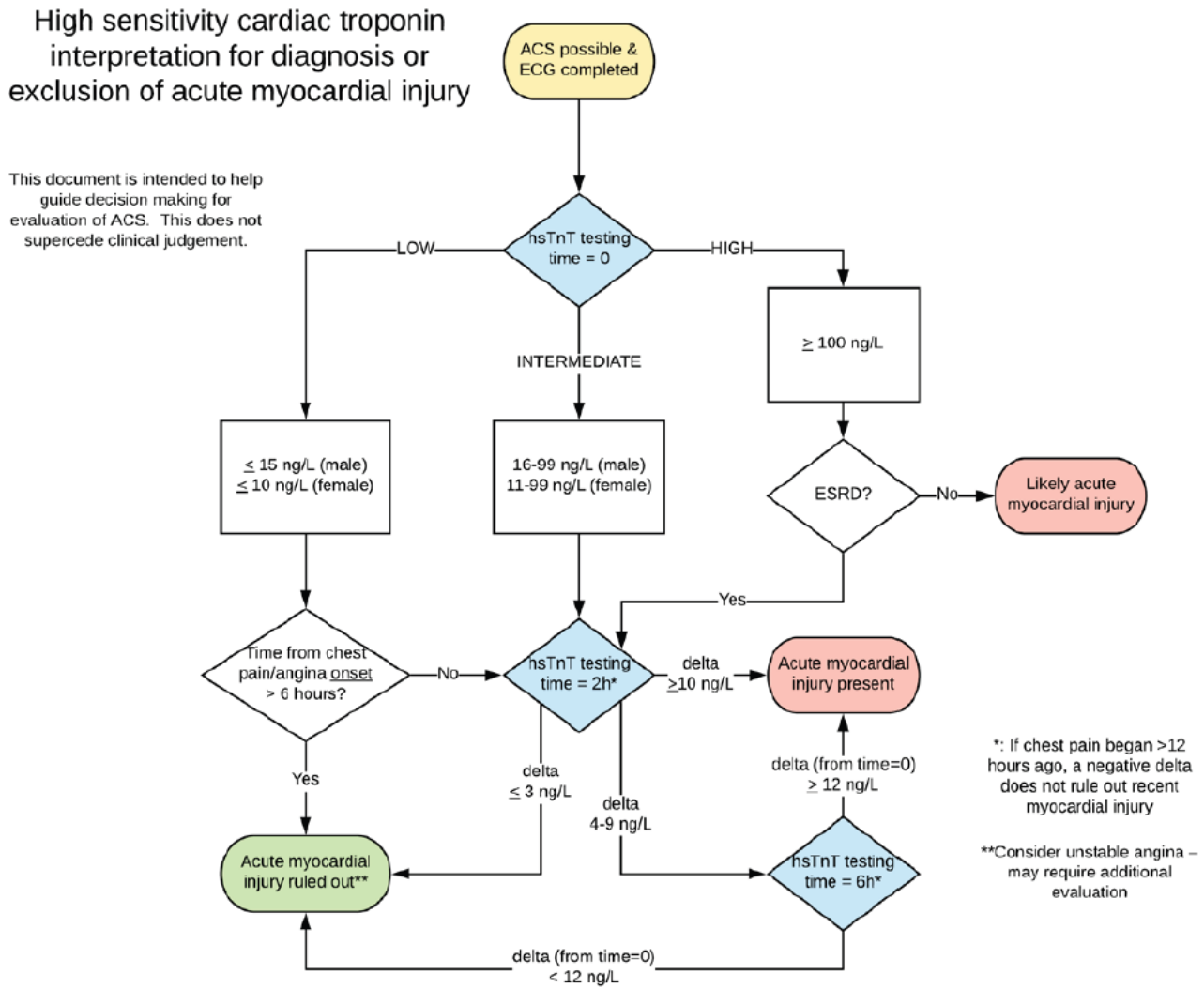
Supplemental Table 13. Diagnostic performance, efficacy, and safety of a single baseline hs-cTnT below the limit of quantitation of 6 ng/L for index acute MI rule-out in patients in the adjudicated cohort with chest pain. LoQ: limit of quantitation.

	Chest pain subset			**Chest pain with nonischemic ECG**		
	Total	Men	Women	Total	Men	Women
Population and incidence of MI						
Total chest pain patients, n	982	456	526	931	436	495
Incidence of MI, n (%)	72 (7)	37 (8)	35 (7)	50 (5)	28 (6)	22 (4)
Efficacy: proportion of patients identified as low risk						
Proportion of patients with baseline hs-cTnT <LoQ (efficacy), n (%)	436 (44)	150 (33)	286 (54)	428 (46)	147 (34)	281 (57)
Diagnostic performance of baseline hs-cTnT<LoQ for ruling-out index presentation acute MI						
Negative predictive value, % (95% CI)	99.8 (98.7, 100)	100 (97.6, 100)	99.7 (98.1, 100)	100 (99.1, 100)	100 (97.5, 100)	100 (98.7, 100)
Sensitivity, % (95% CI)	99.6 (92.5, 100)	100 (90.5, 100)	97.1 (85.1, 100)	100 (92.9, 100)	100 (87.7, 100)	100 (84.6, 100)
Missed MI rate among those with a negative test	0.2% 1/436	0% 0/150	0.4% 1/286	0% 0/428	0% 0/147	0% 0/281
Safety of baseline hs-cTnT<LoQ based on acute MI or death within 30-days						
Negative predictive value, % (95% CI)	99.7 (98.7, 100)	100 (97.6, 100)	99.6 (98.1, 99.9)	100 (99.1, 100)	100 (97.5, 100)	100 (98.7, 100)
Sensitivity, % (95% CI)	98.8 (93.4, 99.9)	100 (91.8, 100)	97.4 (86.5, 99.9)	100 (93.9, 100)	100 (89.4, 100)	100 (86.8, 100)
Missed events among those with a negative test	0.2% 1/436	0% 0/150	0.4% 1/286	0% 0/428	0% 0/147	0% 0/281

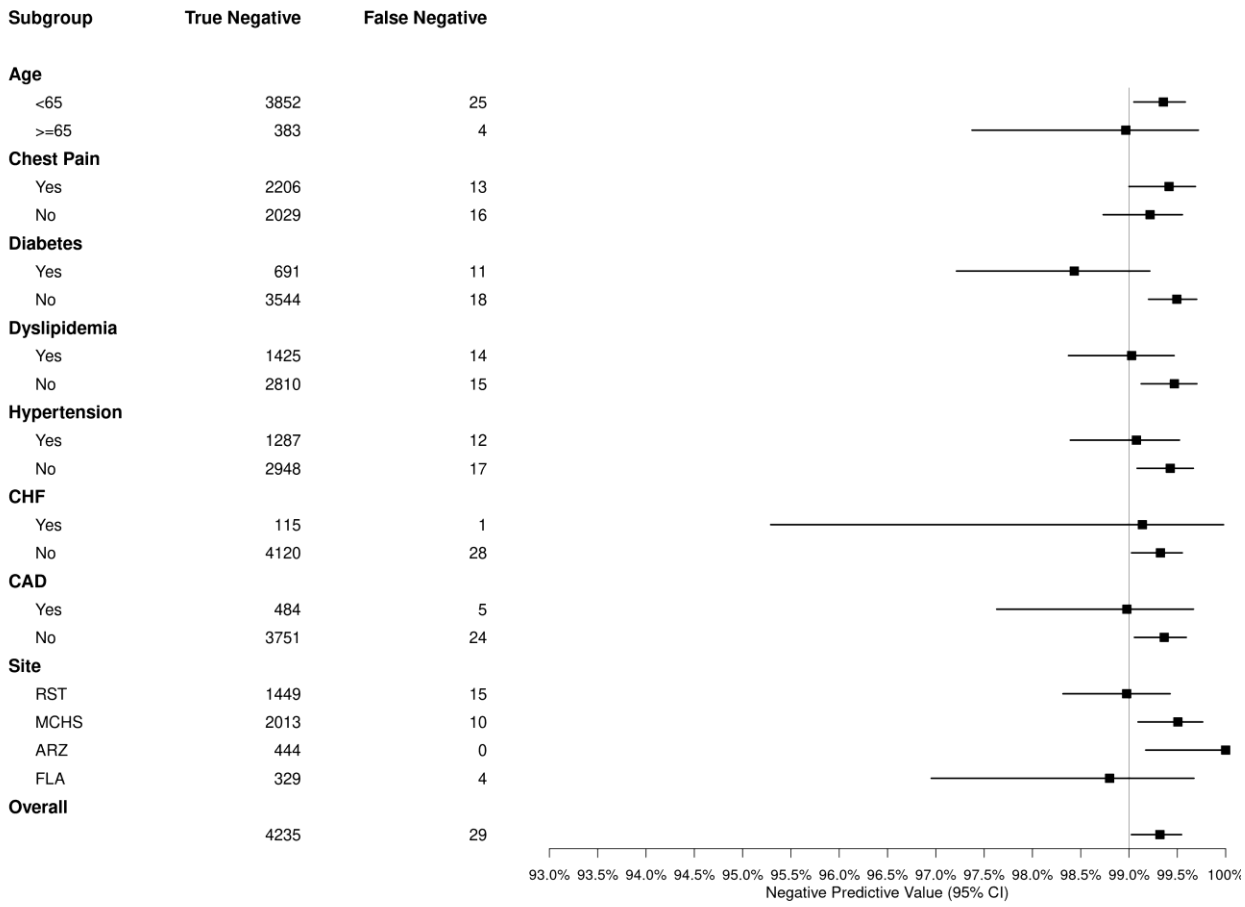
Supplemental Figure 1. Study flow for the CV Data Mart Biomarker and ACTION adjudicated cohorts.



Supplemental Figure 2. Mayo Clinic 0/2h hs-cTnT clinical protocol This algorithm summarizes the Mayo Clinic hs-cTnT protocol that was endorsed for clinical use, which differs from definitions or approaches examined in this research study.

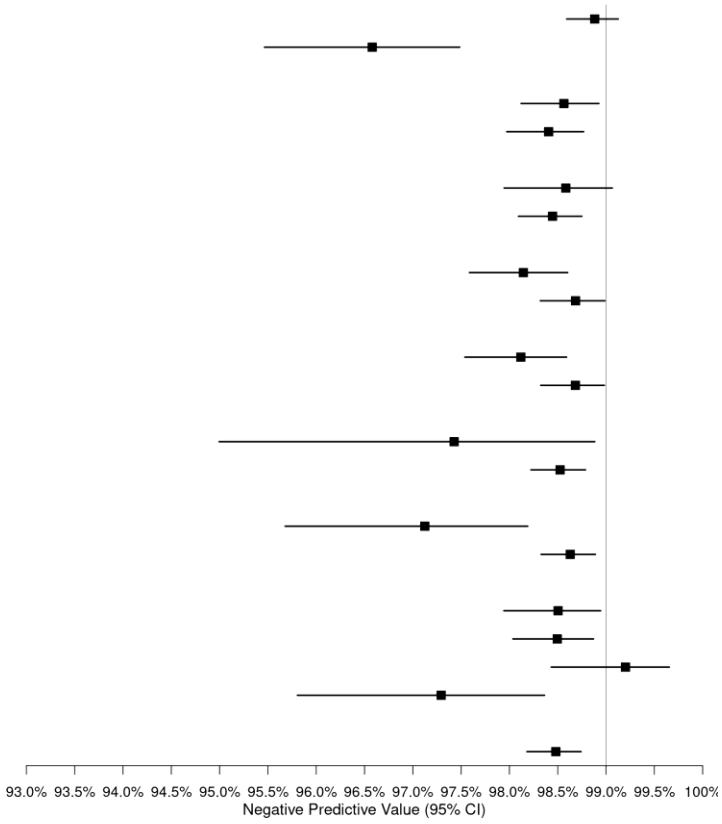


Supplemental Figure 3. Forest plot of negative predictive values for acute myocardial injury (sex-specific 99th percentile of 15 ng/L for men) among subgroups in men with baseline hs-cTnT<6 ng/L and serial measurements from the CV Data Mart Biomarker cohort.

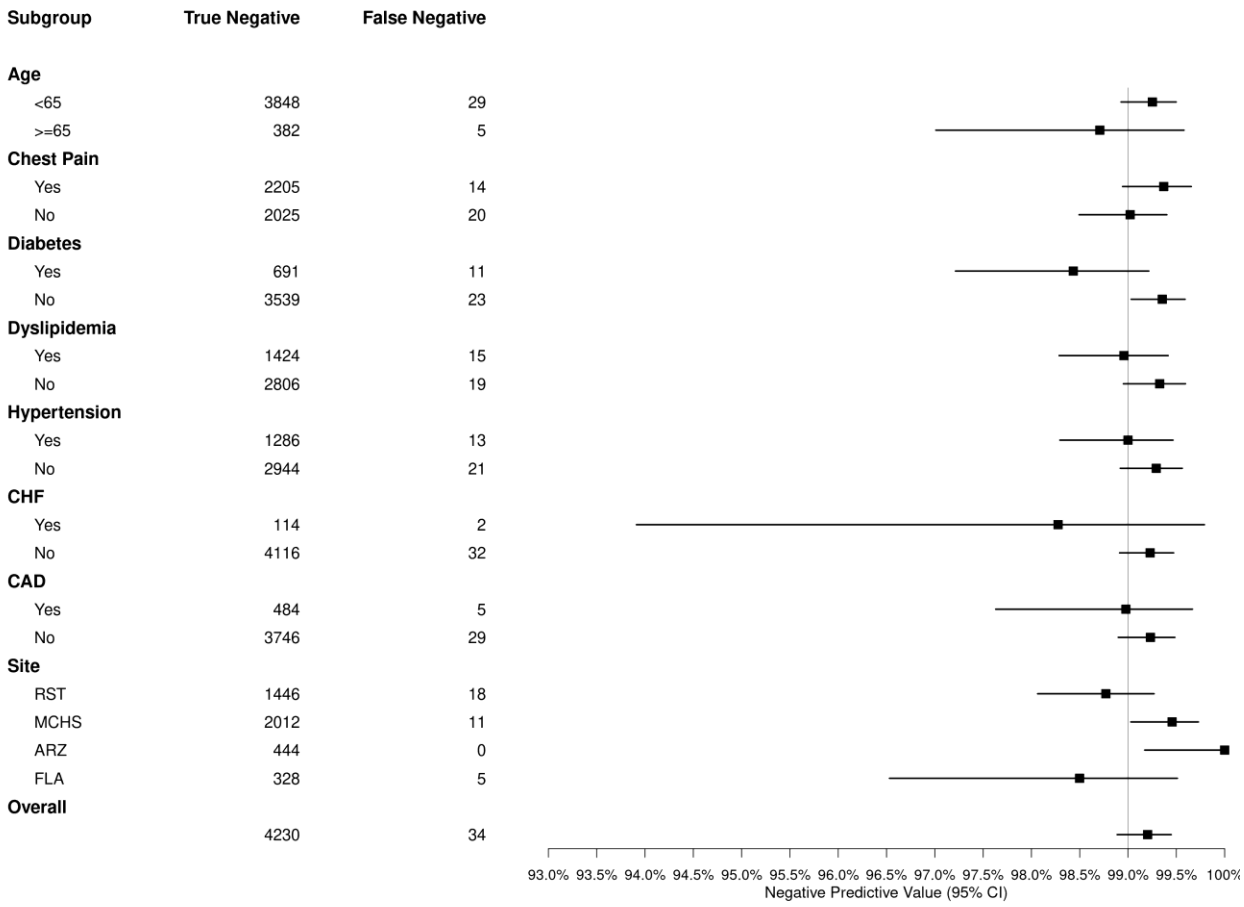


Supplemental Figure 4. Forest plot of negative predictive values for acute myocardial injury (sex-specific 99th percentile of 10 ng/L for women) among subgroups in women with baseline hs-cTnT<6 ng/L and serial measurements from the CV Data Mart Biomarker cohort.

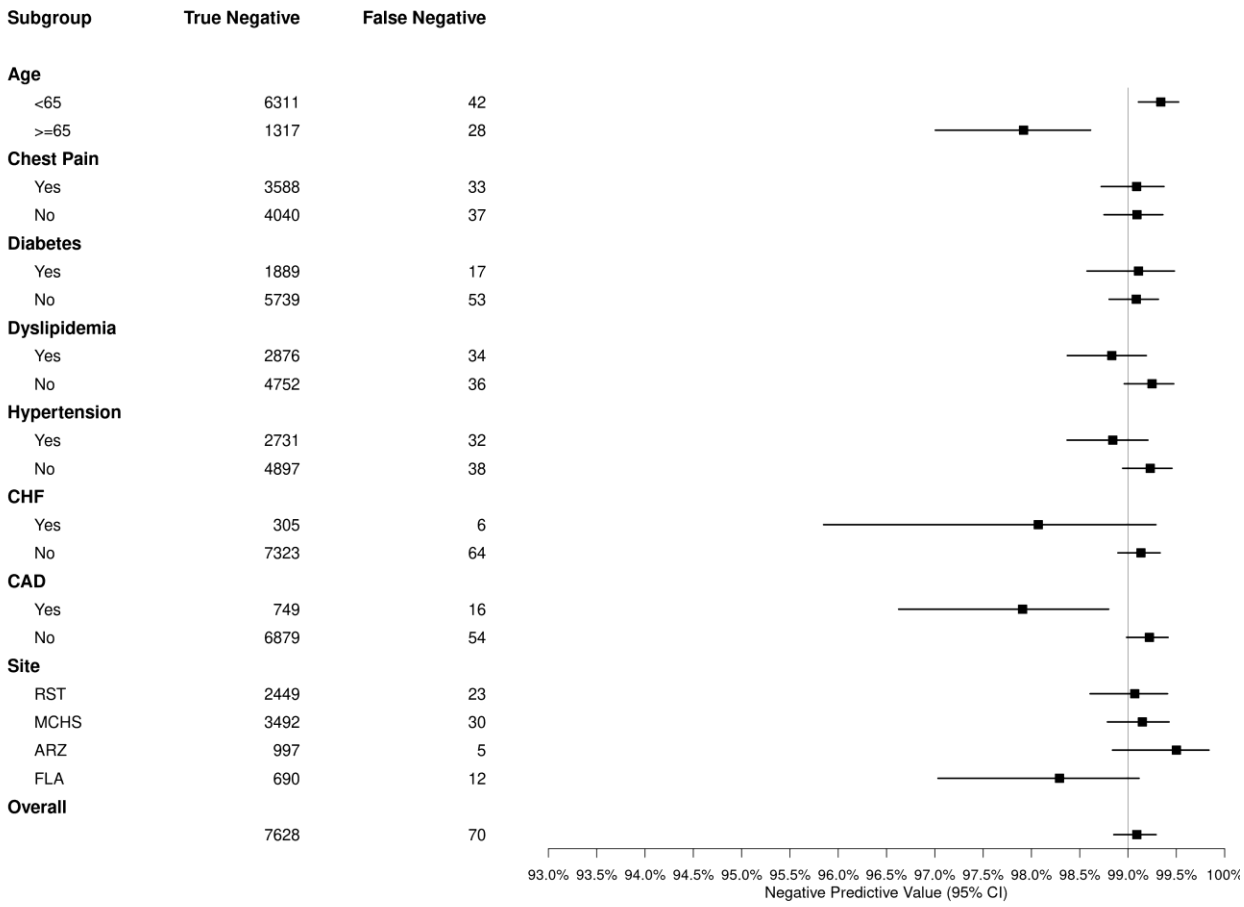
Subgroup	True Negative	False Negative
Age		
<65	6282	71
>=65	1299	46
Chest Pain		
Yes	3569	52
No	4012	65
Diabetes		
Yes	1879	27
No	5702	90
Dyslipidemia		
Yes	2856	54
No	4725	63
Hypertension		
Yes	2711	52
No	4870	65
CHF		
Yes	303	8
No	7278	109
CAD		
Yes	743	22
No	6838	95
Site		
RST	2435	37
MCHS	3469	53
ARZ	994	8
FLA	683	19
Overall		
	7581	117



Supplemental Figure 5. Forest plot of negative predictive values for acute myocardial injury (overall 99th percentile of 14 ng/L) among subgroups in men with baseline hs-cTnT<6 ng/L and serial measurements from the CV Data Mart Biomarker cohort.

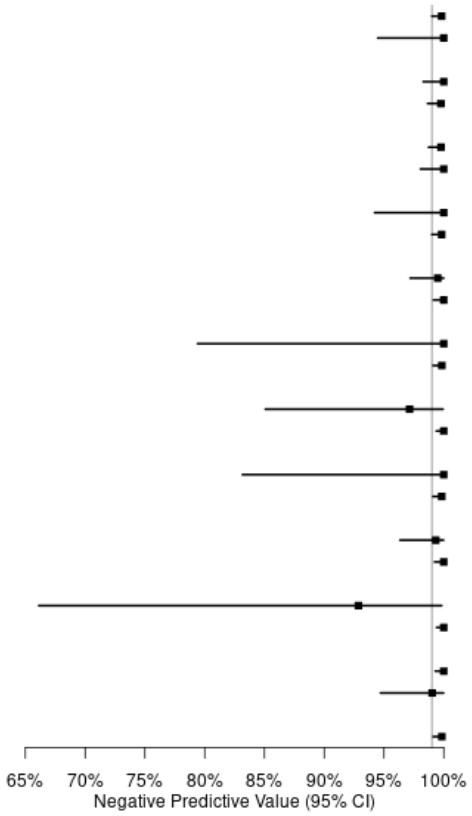


Supplemental Figure 6. Forest plot of negative predictive values for acute myocardial injury (overall 99th percentile of 14 ng/L) among subgroups in women with baseline hs-cTnT<6 ng/L and serial measurements from the CV Data Mart Biomarker cohort.

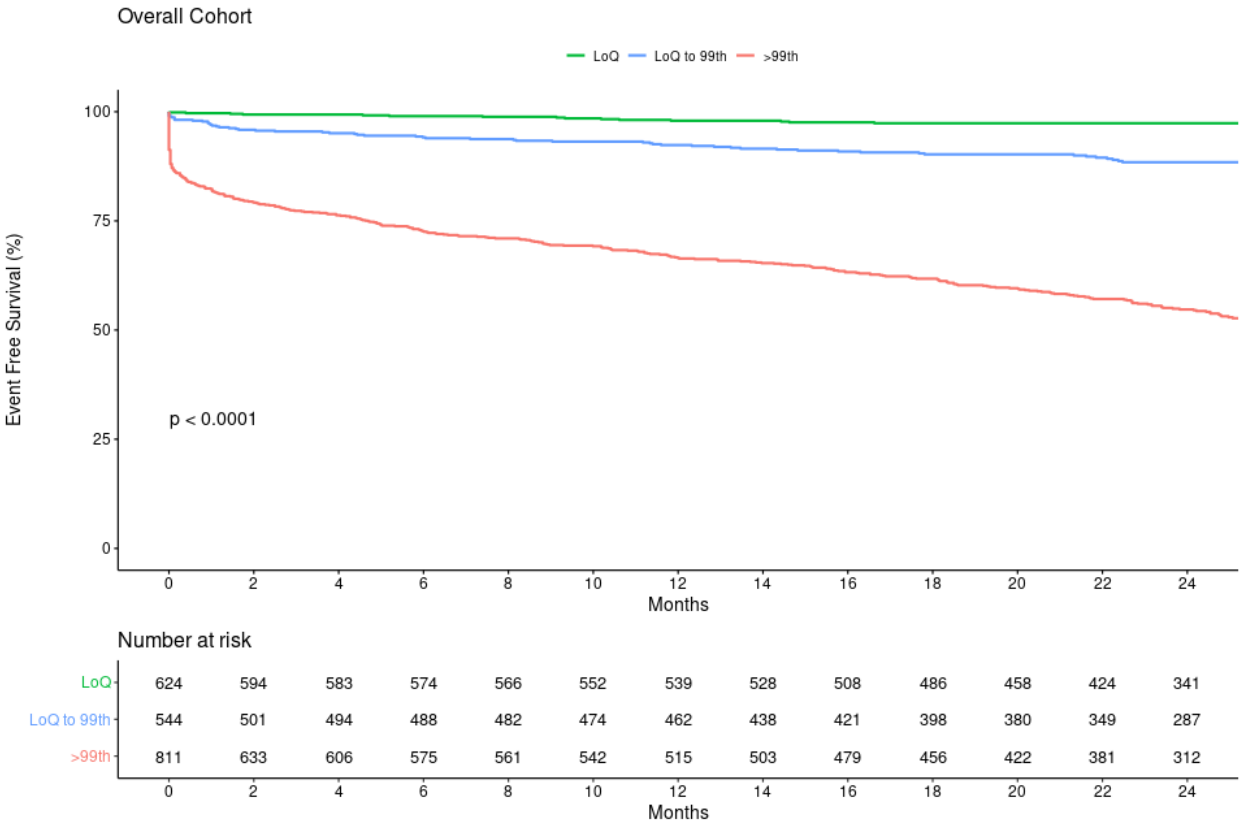


Supplemental Figure 7. Forest plot of negative predictive values for acute myocardial infarction among subgroups in the adjudicated cohort.

Subgroup	True Negative	False Negative
Age		
<65	558	1
>=65	65	0
Sex		
Male	214	0
Female	409	1
Chest Pain		
Yes	435	1
No	188	0
Diabetes		
Yes	62	0
No	561	1
Hypertension		
Yes	195	1
No	428	0
CHF		
Yes	16	0
No	607	1
CAD		
Yes	34	1
No	589	0
Chronic Kidney Disease		
Yes	20	0
No	603	1
Early Presenter (<3h)		
Yes	149	1
No	474	0
Ischemic ECG		
Yes	13	1
No	610	0
HEAR Score		
0-3	521	0
=>4	102	1
Overall	623	1



Supplemental Figure 8. Kaplan-Meier curves for survival free of myocardial infarction or death according to baseline hs-cTnT groups (biomarker alone) in the adjudicated cohort. LoQ: limit of quantitation.



Supplemental Figure 9.