A Pragmatic Lab-based Tool for Risk Assessment in Cardiac Critical Care: Data from the Critical Care Cardiology Trials Network (CCCTN) Registry

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Table S1: In-Hospital Mortality by Baseline Lab Indicators in the Derivation Cohort

Lab Indicator	Available % (n)	Median (25th-75th percentiles)	Univariable Odds Ratio per 1-SD (95% CI)	p-value	Multivariable Odds Ratio per 1-SD (95% CI)	β-coefficient per 1-SD (SE)	p-value	Wald-type Chi-square
pH	49.9 (2171)	7.40 (7.30-7.40)	2.41 (2.16-2.70)	<0.001	1.96 (1.72-2.24)	0.67 (0.07)	<0.001	98.7
Lactate (mmol/L)[a]	59.3 (2581)	1.8 (1.2-2.9)	2.28 (2.06-2.52)	<0.001	1.40 (1.22-1.62)	0.34 (0.07)	<0.001	22.0
eGFR (mL/min/1.73m^2)	99.7 (4340)	60.5 (36.1-84.3)	1.95 (1.77-2.15)	<0.001	1.26 (1.10-1.45)	0.23 (0.07)	0.001	10.7
Platelets (K/uL)[a]	99.5 (4331)	203 (155-260)	1.34 (1.24-1.44)	<0.001	1.18 (1.05-1.32)	0.16 (0.06)	0.006	7.6
Hemoglobin (mg/dL)	99.3 (4321)	11.9 (9.9-13.6)	2.00 (1.65-2.42)	<0.001	1.40 (1.06-1.85)	0.34 (0.14)	0.018	5.6
Total bilirubin (mg/dL)[a]	85.5 (3721)	0.7 (0.4-1.1)	1.34 (1.23-1.46)	<0.001	1.12 (0.98-1.28)	0.12 (0.07)	0.083	3.0
Blood glucose (mg/dL)[a]	98.7 (4297)	130 (105-176)	1.44 (1.33-1.56)	<0.001	1.07 (0.95-1.22)	0.07 (0.06)	0.265	1.2
AST (U/L)[a]	85.8 (3734)	34 (22-77)	1.80 (1.66-1.94)	<0.001	1.13 (0.89-1.43)	0.12 (0.12)	0.329	1.0
ALT (U/L)[a]	85.7 (3729)	27 (17-53)	1.70 (1.57-1.84)	<0.001	0.96 (0.76-1.20)	-0.05 (0.12)	0.699	0.1

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; SE, standard error.
[a] denotes variables which were log-transformed.

Table S2: Multivariable Analysis of In-hospital Mortality by Categorical Baseline Lab Indicators in the Derivation Cohort

Lab Indicator	In-Hospital Mortality %, (n)	Adjusted Odds Ratio (95% CI)	p-value
Hemoglobin (mg/dL)			
>12	9.9 (204)	Reference	
9-12	14.1 (231)	1.19 (0.88-1.60)	0.26
7-<9	24.8 (137)	1.70 (1.18-2.45)	<0.01
<7	26.0 (20)	1.44 (0.68-3.04)	0.35
eGFR (mL/min/1.73m^2)			
≥45	8.61 (247)	Reference	
<45	23.5 (346)	1.82 (1.40-2.37)	<0.01
Lactate (mmol/L)			
<2	11.4 (166)	Reference	
2-4	21.2 (148)	1.52 (1.11-2.08)	0.01
>4-10	43.2 (144)	2.17 (1.48-3.17)	<0.01
>10	69.8 (67)	2.51 (1.30-4.85)	0.01
ALT (U/L)			
<ULN	10.5 (284)	Reference	
1-<3 x ULN	20.0 (126)	1.40 (0.96-2.04)	0.08
3-<5 x ULN	23.0 (26)	0.70 (0.33-1.47)	0.34
5-<10 x ULN	49.0 (49)	1.32 (0.59-2.96)	0.50
>10 x ULN	41.6 (69)	0.77 (0.33-1.82)	0.55
AST (U/L)			
<ULN	9.5 (226)	Reference	
1-<3 x ULN	18.2 (147)	1.48 (1.04-2.09)	0.02
3-<5 x ULN	21.0 (37)	1.08 (0.58-2.01)	0.81
5-<10 x ULN	35.8 (54)	1.81 (0.90-3.65)	0.10
>10 x ULN	43.2 (92)	1.66 (0.74-3.77)	0.22
Total bilirubin (mg/dL)			
≤1.2	13.1 (392)	Reference	
>1.2-4	22.5 (147)	1.25 (0.91-1.72)	0.18
>4-10	28.1 (16)	0.49 (0.20-1.23)	0.13
>10	25.0 (3)	0.99 (0.19-5.21)	0.99
Platelets (K/uL)			
>200	11.3 (251)	Reference	
>100-200	14.2 (255)	1.28 (0.97-1.68)	0.08
50-100	25.3 (59)	1.42 (0.86-2.36)	0.17
<50	41.4 (29)	4.41 (2.02-9.63)	<0.01

Abbreviations: ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ULN, upper limit of normal.

Table S2: Multivariable Analysis of In-hospital Mortality by Categorical Baseline Lab Indicators in the Derivation Cohort (continued)

Lab Indicator (continued)	In-Hospital Mortality %, (n) (continued)	Adjusted Odds Ratio (95% CI) (continued)	p-value (continued)
Blood glucose (mg/dL)			
<80	15.3 (21)	Reference	
80-180	10.8 (340)	1.43 (0.68-3.02)	0.35
>180-300	20.2 (153)	1.46 (0.67-3.18)	0.34
>300	27.6 (74)	1.81 (0.78-4.21)	0.17
pH (lowest)			
>7.30	14.4 (211)	Reference	
>7.20-7.30	25.8 (106)	1.64 (1.19-2.25)	<0.01
7.00-7.20	61.2 (148)	5.60 (3.94-7.98)	<0.01
<7.00	76.8 (43)	11.21 (5.18-24.26)	<0.01

Table S3: Baseline Characteristics of the CCCTN Validation Cohort (Second Campaign)

Characteristic	Overall, % (n) (n=3888)	Alive at Discharge (n=3368)	Death in Hospital (n=520)
Demographics			
Age, median (IQR), y	66 (56, 76)	66 (55, 75)	69 (59, 78)
BMI, median (IQR), kg/m^2 (n=3845)	28.1 (24.3, 32.8)	28.1 (24.3, 32.8)	28.0 (24.1, 33.5)
Female	37.4 (1455)	37.0 (1246)	40.2 (209)
Caucasian (n=3312)	70.5 (2335)	69.5 (1985)	76.9 (350)
General Medical Problems and Risk Factors			
Smoking Status (n=3824)			
Current	16.7 (637)	17.1 (568)	13.5 (69)
Ex-smoker	35.9 (1374)	35.8 (1187)	36.5 (187)
Unknown	10.5 (402)	9.3 (307)	18.6 (95)
Hypertension	66.9 (2600)	67.0 (2256)	66.2 (344)
Diabetes mellitus	35.8 (1392)	35.4 (1191)	38.7 (201)
Chronic kidney disease	27.3 (1061)	26.3 (887)	33.5 (174)
Dialysis dependent (n=1058)	23.3 (247)	22.3 (197)	28.9 (50)
Significant pulmonary disease	17.9 (697)	16.6 (560)	26.3 (137)
Significant liver disease	3.3 (130)	2.9 (99)	6.0 (31)
Cardiovascular History			
Coronary artery disease	38.2 (1484)	37.9 (1277)	39.8 (207)
Cerebrovascular disease	10.4 (405)	9.9 (335)	13.5 (70)
Peripheral artery disease	10.4 (403)	10.6 (356)	9.0 (47)
Heart failure	40.7 (1582)	39.8 (1339)	46.7 (243)
LVEF < 40% (n=1544)	63.1 (974)	63.2 (826)	62.4 (148)
Atrial fibrillation	28.0 (1088)	27.2 (917)	32.9 (171)
Ventricular arrhythmia	7.2 (278)	7.2 (244)	6.5 (34)
Severe valvular disease	17.2 (668)	16.8 (566)	19.6 (102)
Pulmonary hypertension	6.3 (243)	6.1 (204)	7.5 (39)
Congenital heart disease	1.8 (70)	1.8 (59)	2.1 (11)

All data are reported as column % (n), unless otherwise specified.

For rows with missing baseline characteristics data, available n is specified.
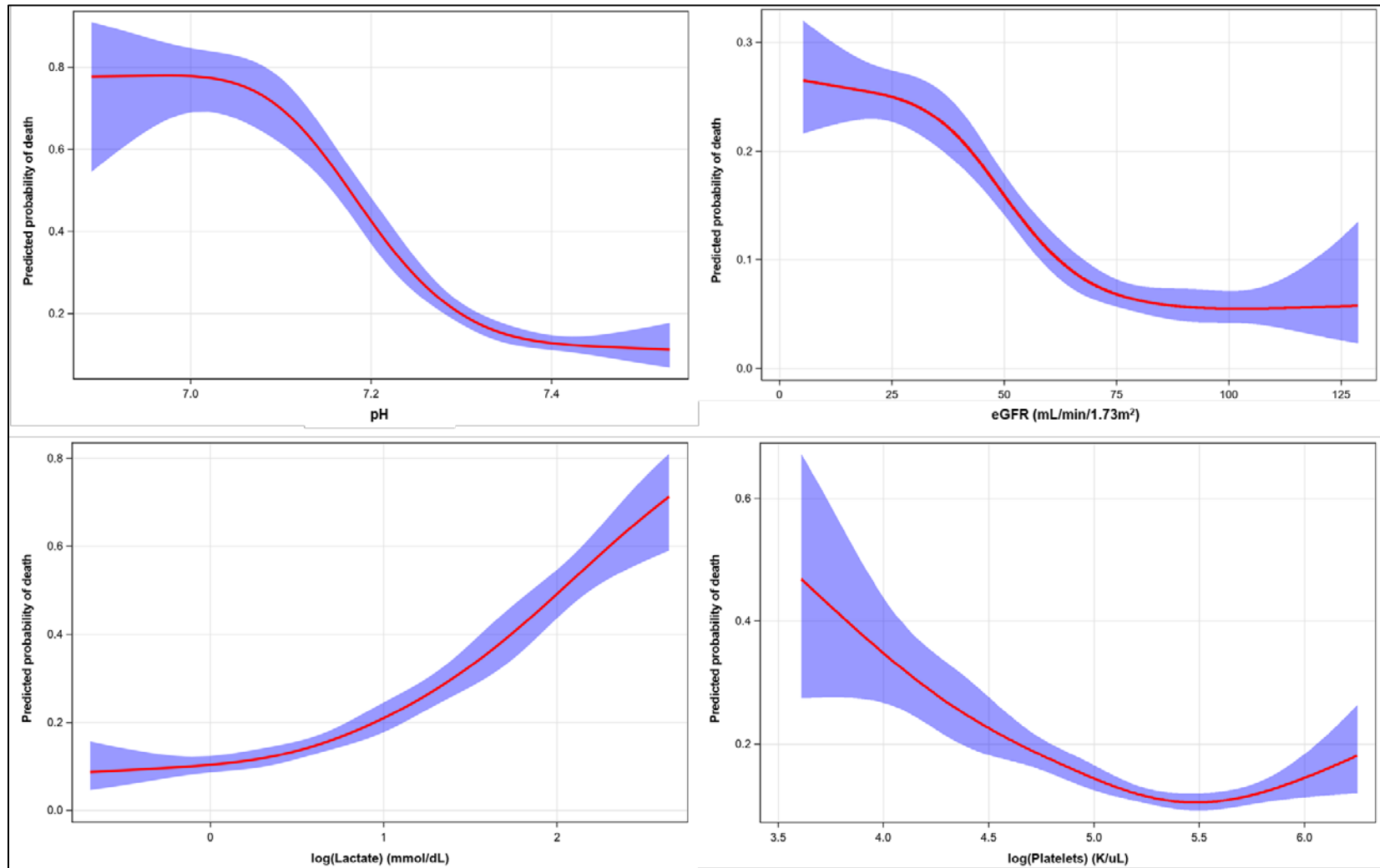
Abbreviations: BMI, body mass index; CCCTN, Critical Care Cardiology Trials Network; IQR, interquartile range; LVEF, left ventricular ejection fraction

Table S4: Comparative Performance of the CCCTN Lab-based Risk Score

	Harrell's C-index (95% CI)
CCCTN Campaign 1 (Derivation Cohort)	
Lab-Based Risk Score	0.82 (0.80-0.84)
SOFA Score	0.85 (0.83-0.87)
CCCTN Campaign 2 (Validation Cohort)	
Lab-Based Risk Score	0.82 (0.80-0.84)
SOFA Score	0.85 (0.83-0.87)
CCCTN Campaign 3	
Lab-Based Risk Score (pH = initial pH)	0.79 (0.77-0.81)
Lab-Based Risk Score (pH = worst pH)	0.83 (0.81-0.85)
SOFA Score	0.85 (0.83-0.87)
Mayo Cohort (External Validation Cohort)	
Lab-Based Risk Score (pH = initial pH)	0.79 (0.77-0.80)
SOFA Score	0.84 (0.82-0.85)

Abbreviations: CI, confidence interval; CCCTN, Critical Care Cardiology Trials Network; SOFA, Sequential Organ Failure Assessment

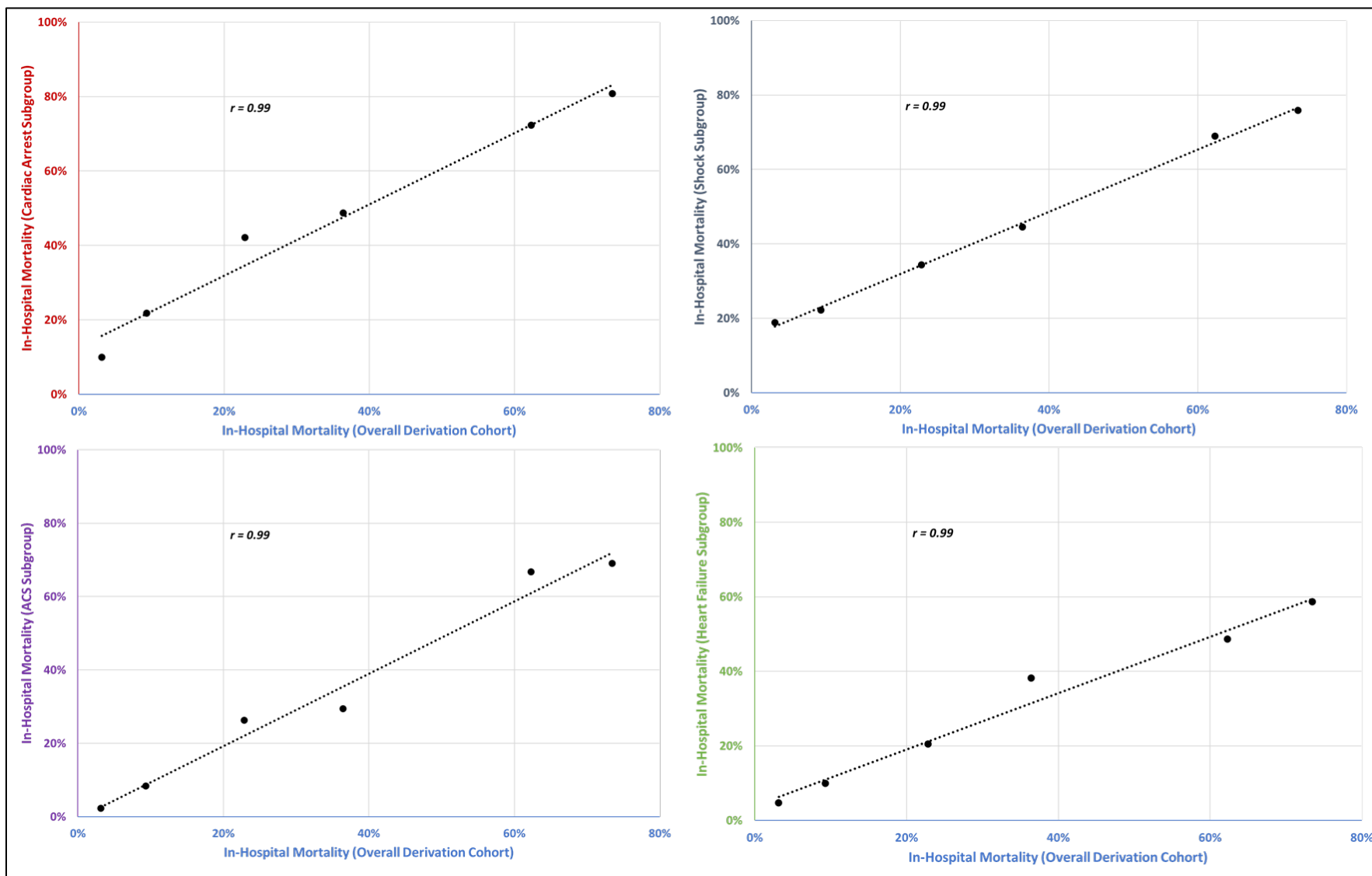**Figure S1:** Univariable Analysis Splines of In-hospital Mortality by Lab Indicator

Abbreviations: eGFR, estimated glomerular filtration rate

Figure S2: In-Hospital Mortality by CCCTN Lab-Based Risk Score in ACS and HF in the Derivation Coho
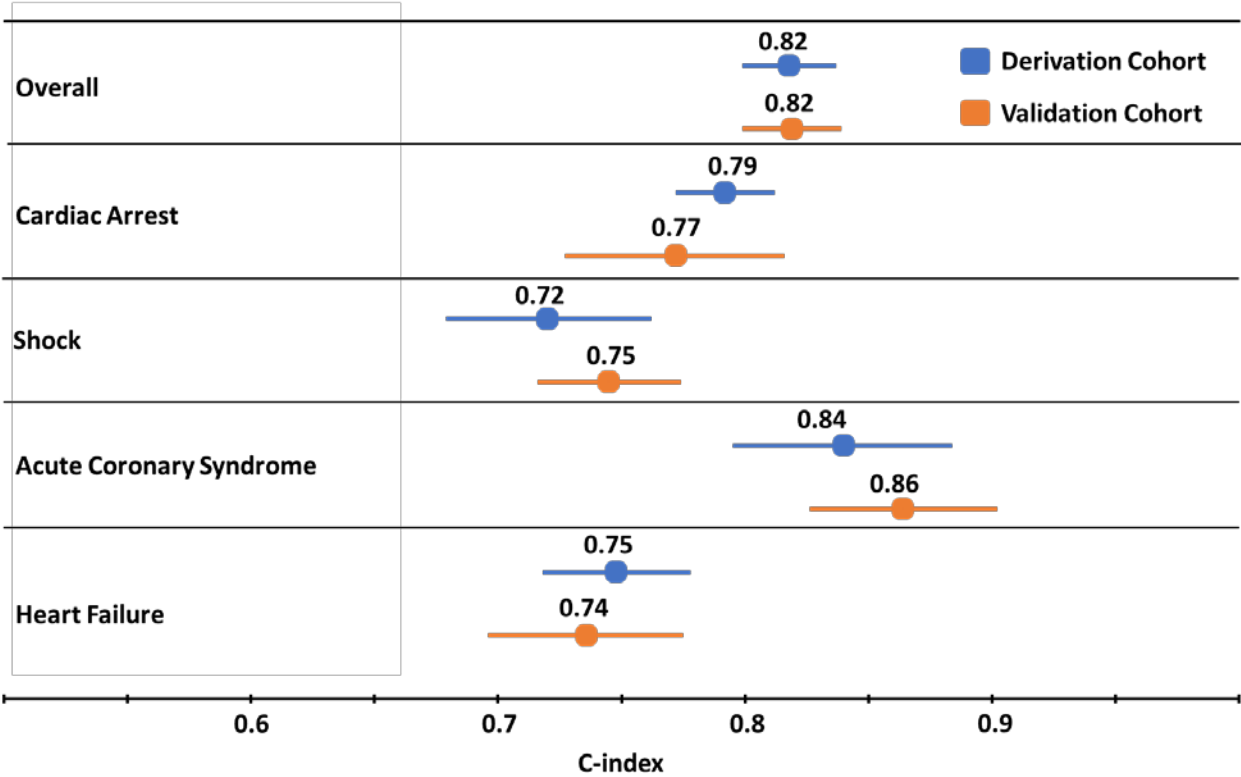

Abbreviations: CCCTN, Critical Care Cardiology Trials Network

Figure S3: Calibration Across Subgroups (Derivation Cohort) of the CCCTN Lab-Based Risk Score
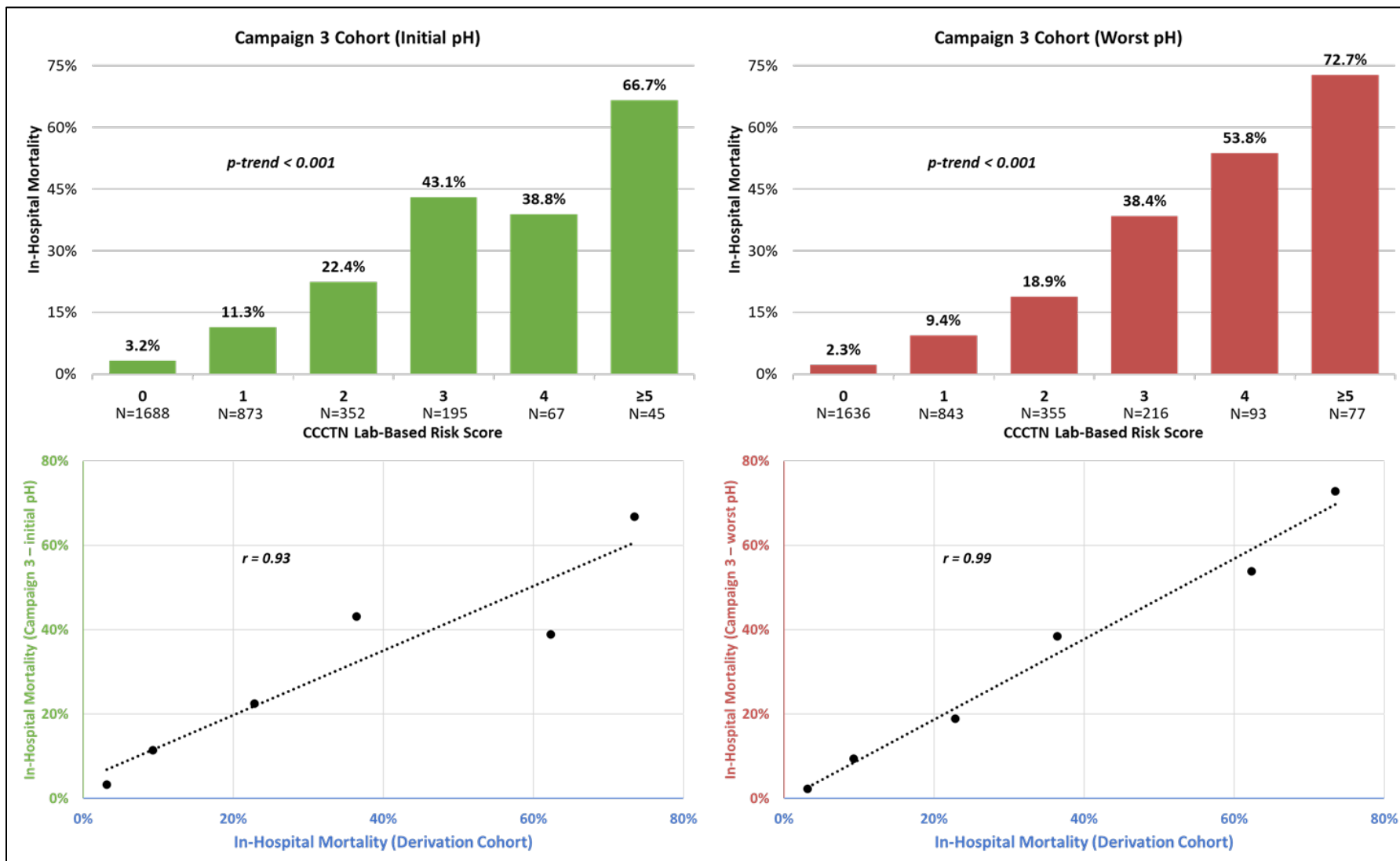

Abbreviations: ACS, acute coronary syndrome; CCCTN, Critical Care Cardiology Trials Network.

Figure S4: Discriminatory Performance of the CCCTN Lab-Based Risk Score in the Derivation Cohort and the CCCTN Validation Cohorts

Abbreviations: CCCTN, Critical Care Cardiology Trials Network

Figure S5: In-Hospital Mortality by CCCTN Lab-Based Risk Score in the Third Collection Campaign using Initial and Worst pH

Abbreviations: CCCTN, Critical Care Cardiology Trials Network