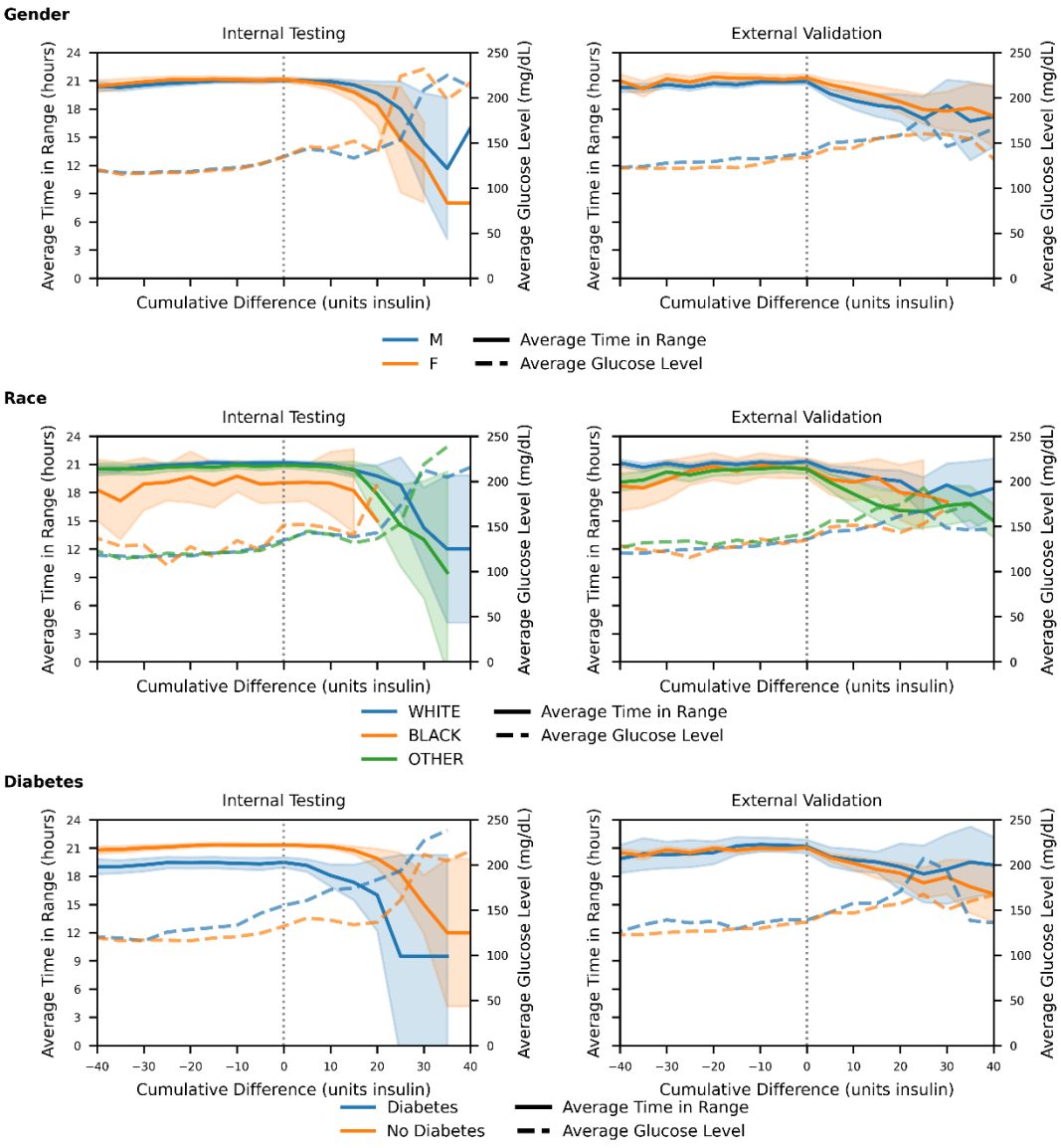
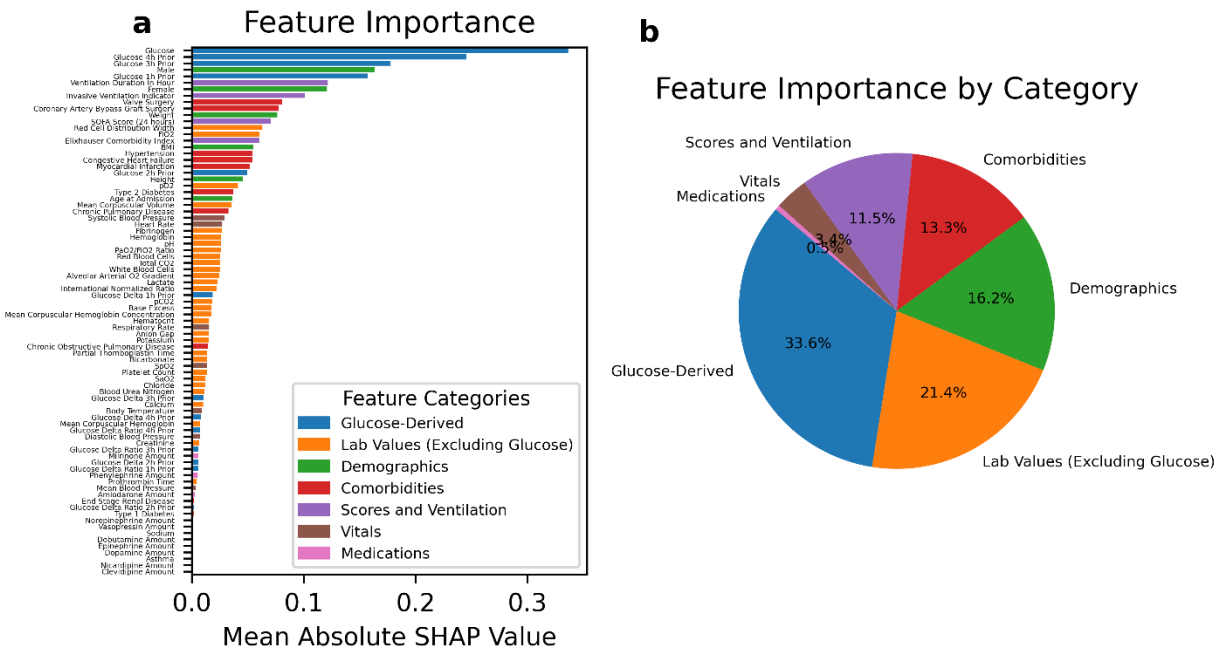
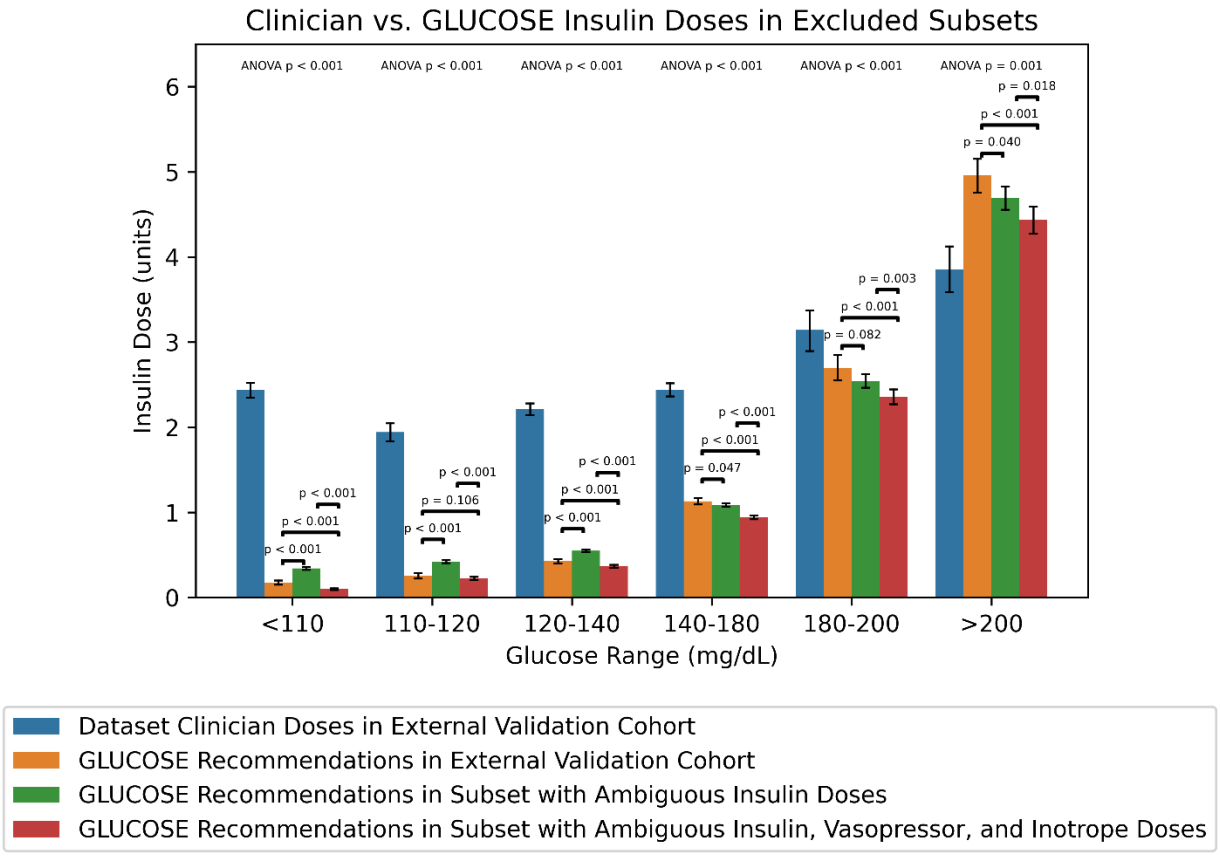


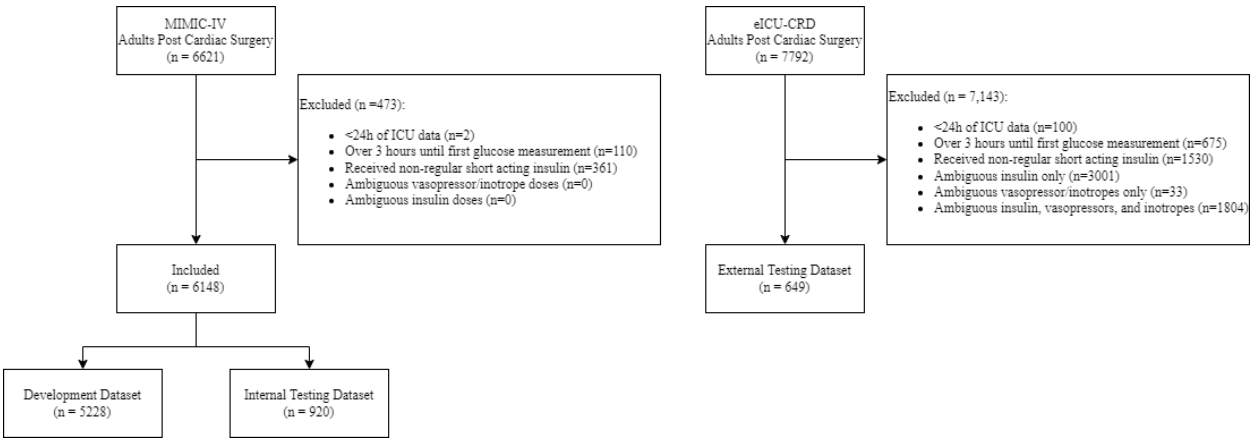
Supplementary Figure 1. Time in range analysis stratified by subgroup. Average time in range ± the standard error of the mean shown via solid lines. Dashed lines indicate the average glucose level corresponding to that subgroup.



Supplementary Figure 2. Feature importances for GLUOCSE. **a)** Ranked feature importances by mean absolute SHAP value. **b)** Relative contributions of varying categorizations of features.



Supplementary Figure 3. Analysis of GLUCOSE predictions in excluded subsets. Average insulin values in varying clinically relevant ranges are shown in each of the subsets. 95% confidence intervals are shown for each bar.



Supplementary Figure 4. CONSORT diagram. Inclusion/exclusion criteria applied during data preprocessing.

Supplementary Table 1. Baseline population characteristics. Characteristics of all patients used in the primary analysis across demographic information, vitals, laboratory data, scores, and medications.

		Development Cohort	External Validation Cohort	P-Value
Admission Age, median [Q1, Q3]		68.0 [61.0,76.0]	67.0 [60.0,75.0]	0.093
	Female	1746 (28.4)	213 (32.8)	0.02
Gender, n (%)	**Male**	4402 (71.6)	436 (67.2)	
	Asian	136 (2.2)	15 (2.3)	<0.001
	Black	222 (3.6)	51 (7.9)	
	Hispanic	175 (2.8)	79 (12.2)	
	Native American	11 (0.2)		
	Other	219 (3.6)		
	Unknown	841 (13.7)	72 (11.1)	
Race, n (%)	**White**	4544 (73.9)	432 (66.6)	
Height, median [Q1,Q3]		173.0 [165.0,178.0]	170.2 [162.6,177.8]	0.059
Weight, median [Q1,Q3]		83.2 [72.0,96.0]	85.6 [72.6,99.7]	0.005
BMI, median [Q1,Q3]		28.2 [25.1,32.1]	29.2 [25.8,33.9]	<0.001
Type 1 Diabetes, n (%)		33 (0.5)	2 (0.3)	0.77
Type 2 Diabetes, n (%)		868 (14.1)	59 (9.1)	<0.001
Hypertension, n (%)		3814 (62.0)	177 (27.3)	<0.001
End Stage Renal Disease, n (%)		131 (2.1)	17 (2.6)	0.503
Chronic Obstructive Pulmonary Disease, n (%)		297 (4.8)	65 (10.0)	<0.001
Chronic Pulmonary Disease, n (%)		1036 (16.9)	40 (6.2)	<0.001
Asthma, n (%)		1 (0.0)	29 (4.5)	<0.001
History of Myocardial Infarct, n (%)		1782 (29.0)	56 (8.6)	<0.001
Congestive Heart Failure, n (%)		1665 (27.1)	52 (8.0)	<0.001
SaO2, median [Q1,Q3]		97.0 [96.0,98.0]	98.0 [96.0,99.0]	<0.001
pO2, median [Q1,Q3]		174.0 [113.0,300.0]	111.0 [86.0,153.0]	<0.001
pCO2, median [Q1,Q3]		40.0 [36.0,44.0]	40.4 [36.4,44.8]	0.527
FIO2, median [Q1,Q3]		50.0 [50.0,80.0]	50.0 [40.0,60.0]	<0.001
AaDO2, median [Q1,Q3]		200.8 [133.5,323.0]	168.8 [125.2,269.2]	<0.001
paO2 FIO2 ratio, median [Q1,Q3]		244.1 [180.0,322.5]	230.2 [171.0,304.1]	<0.001
pH, median [Q1,Q3]		7.4 [7.3,7.4]	7.4 [7.4,7.4]	<0.001
Base Excess, median [Q1,Q3]		-1.0 [-3.0,0.0]	-2.0 [-4.0,0.0]	<0.001
Bicarbonate, median [Q1,Q3]		23.0 [22.0,25.0]	24.0 [22.0,25.0]	<0.001
Total CO2, median [Q1,Q3]		25.0 [23.0,26.0]	24.2 [22.0,26.0]	0.265
Hematocrit, median [Q1,Q3]		29.8 [26.8,32.9]	29.3 [26.0,33.0]	0.013
Hemoglobin, median [Q1,Q3]		10.0 [8.9,11.1]	9.9 [8.8,11.1]	0.094
Chloride, median [Q1,Q3]		107.0 [105.0,110.0]	109.0 [107.0,112.0]	<0.001
Calcium, median [Q1,Q3]		8.2 [7.9,8.5]	8.1 [7.7,8.5]	<0.001
Temperature, median [Q1,Q3]		36.8 [36.3,37.2]	37.1 [36.7,37.5]	<0.001
Potassium, median [Q1,Q3]		4.4 [4.1,4.7]	4.2 [3.9,4.5]	<0.001

Sodium, median [Q1,Q3]		138.0 [137.0,140.0]	141.0 [138.0,143.0]	<0.001
Lactate, median [Q1,Q3]		2.0 [1.6,2.7]	2.1 [1.7,2.6]	<0.001
Glucose, median [Q1,Q3]		124.0 [108.0,145.0]	130.0 [113.0,150.0]	<0.001
WBC, median [Q1,Q3]		13.1 [10.4,16.9]	13.1 [10.7,16.7]	0.071
MCH, median [Q1,Q3]		30.5 [29.3,31.6]	30.0 [28.9,31.1]	<0.001
MCHC, median [Q1,Q3]		33.7 [32.8,34.6]	33.6 [32.9,34.1]	<0.001
MCV, median [Q1,Q3]		90.0 [87.0,93.0]	89.4 [86.1,92.7]	<0.001
Platelets, median [Q1,Q3]		144.0 [116.0,179.0]	144.0 [113.0,181.0]	0.668
RBC, median [Q1,Q3]		3.3 [2.9,3.7]	3.3 [3.0,3.8]	<0.001
RDW, median [Q1,Q3]		13.7 [13.0,14.7]	14.2 [13.5,15.4]	<0.001
Anion Gap, median [Q1,Q3]		11.0 [10.0,13.0]	8.0 [6.0,10.0]	<0.001
BUN, median [Q1,Q3]		16.0 [13.0,20.0]	17.0 [13.0,22.0]	<0.001
Creatinine, median [Q1,Q3]		0.9 [0.7,1.1]	1.0 [0.8,1.2]	<0.001
Fibrinogen, median [Q1,Q3]		201.0 [167.0,246.0]	210.0 [173.0,270.0]	0.109
INR, median [Q1,Q3]		1.3 [1.2,1.4]	1.2 [1.1,1.4]	<0.001
PT, median [Q1,Q3]		14.2 [13.1,15.7]	13.4 [12.1,16.1]	<0.001
PTT, median [Q1,Q3]		30.3 [27.4,34.9]	31.7 [28.4,35.3]	0.001
Heart Rate, median [Q1,Q3]		81.0 [75.0,89.0]	86.0 [77.0,93.0]	<0.001
SBP, median [Q1,Q3]		111.0 [101.0,121.0]	115.0 [104.0,128.0]	<0.001
DBP, median [Q1,Q3]		56.0 [50.0,62.7]	55.0 [49.0,62.0]	<0.001
MBP, median [Q1,Q3]		73.0 [66.0,80.0]	74.0 [67.0,81.0]	<0.001
Respiratory Rate, median [Q1,Q3]		17.0 [14.0,20.0]	18.0 [14.0,22.0]	<0.001
SpO2, median [Q1,Q3]		99.0 [96.0,100.0]	98.0 [96.0,100.0]	<0.001
24h SOFA Score, median [Q1,Q3]		5.0 [3.0,7.0]	6.0 [4.0,8.0]	<0.001
Elixhauser, median [Q1,Q3]		4.0 [3.0,6.0]	0.0 [0.0,2.0]	<0.001
Invasive Ventilation in Hour	**0**	79626 (57.2)	1039 (7.0)	<0.001
	1	59623 (42.8)	13769 (93.0)	
Minutes on Ventilator in Hour, median [Q1,Q3]		0.0 [0.0,60.0]	60.0 [60.0,60.0]	<0.001
Dopamine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Epinephrine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.052
Norepinephrine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.4 [0.0,3.5]	<0.001
Phenylephrine Amount, median [Q1,Q3]		3.7 [0.0,22.2]	0.0 [0.0,0.0]	<0.001
Vasopressin Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.199
Amiodarone Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Clevidipine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.329
Dobutamine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Milrinone Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.001
Nicardipine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001

Supplementary Table 2. Population characteristics of excluded external validation patients. Characteristics of all patients excluded from external validation due to ambiguous medication information. Information across demographic information, vitals, laboratory data, scores, and medications shown.

		Subset with Ambiguous Insulin Doses	Subset with Ambiguous Insulin, Vasopressor, and Inotrope Doses	Primary External Validation Cohort	P-Value
n		3001	1804	649	
Admission Age, mean (SD)		67.0 (12.4)	67.6 (11.5)	67.0 (11.1)	0.27
Gender, n (%)	**Female**	992 (33.1)	584 (32.4)	213 (32.8)	0.888
	Male	2009 (66.9)	1220 (67.6)	436 (67.2)	
Race, n (%)	**Asian**	97 (3.2)	9 (0.5)	15 (2.3)	<0.001
	Black	235 (7.8)	43 (2.4)	51 (7.9)	
	Hispanic	79 (2.6)	50 (2.8)	79 (12.2)	
	Unkown	156 (5.2)	84 (4.7)	72 (11.1)	
	White	2434 (81.1)	1618 (89.7)	432 (66.6)	
Height, mean (SD)		171.2 (11.6)	171.7 (10.9)	170.3 (10.2)	0.029
Weight, mean (SD)		86.4 (22.4)	87.0 (20.4)	87.8 (21.4)	0.262
BMI, mean (SD)		29.2 (6.4)	29.5 (6.4)	30.1 (6.3)	0.005
Type 1 Diabetes, n (%)		8 (0.3)	5 (0.3)	2 (0.3)	0.983
Type 2 Diabetes, n (%)		93 (3.1)	22 (1.2)	59 (9.1)	<0.001
Hypertension, n (%)		750 (25.0)	121 (6.7)	177 (27.3)	<0.001
End Stage Renal Disease, n (%)		58 (1.9)	25 (1.4)	17 (2.6)	0.111
Chronic Obstructive Pulmonary Disease, n (%)		290 (9.7)	176 (9.8)	65 (10.0)	0.962
Chronic Pulmonary Disease, n (%)		212 (7.1)	45 (2.5)	40 (6.2)	<0.001
Asthma, n (%)		146 (4.9)	108 (6.0)	29 (4.5)	0.161
History of Myocardial Infarct, n (%)		148 (4.9)	98 (5.4)	56 (8.6)	0.001
Congestive Heart Failure, n (%)		236 (7.9)	97 (5.4)	52 (8.0)	0.003
Glucose, mean (SD)		132.2 (30.7)	130.6 (30.5)	134.5 (33.0)	<0.001
Hyperglycemia Step Count, n (%)	**Non-hyperglycemic**	64715 (94.6)	38877 (94.2)	13597 (91.8)	<0.001
	Hyperglycemic	3699 (5.4)	2401 (5.8)	1211 (8.2)	
Hypoglycemia Step Count, n (%)	**Non-hypoglycemic**	68221 (99.7)	41123 (99.6)	14739 (99.5)	<0.001
	Hypoglycemic	193 (0.3)	155 (0.4)	69 (0.5)	
Glucose During Hyperglycemia, mean (SD)		210.5 (47.4)	206.7 (28.4)	209.7 (28.8)	0.001
Glucose During Hypoglycemia, mean (SD)		60.0 (12.2)	64.0 (5.2)	60.9 (11.1)	0.001
SaO2, median [Q1,Q3]		97.0 [96.0,99.0]	97.0 [95.0,99.0]	98.0 [96.0,99.0]	<0.001
pO2, median [Q1,Q3]		109.0 [85.0,149.0]	105.0 [81.0,145.0]	111.0 [86.0,153.0]	<0.001
pCO2, median [Q1,Q3]		41.0 [37.0,45.0]	40.0 [36.0,44.0]	40.4 [36.4,44.8]	<0.001
FIO2, median [Q1,Q3]		40.0 [36.0,52.0]	45.0 [40.0,70.0]	50.0 [40.0,60.0]	<0.001

AaDO2, median [Q1,Q3]		143.0 [83.5,220.0]	161.7 [112.2,252.7]	168.8 [125.2,269.2]	<0.001
paO2 FIO2 ratio, median [Q1,Q3]		262.0 [190.0,367.5]	234.0 [172.5,316.1]	230.2 [171.0,304.1]	<0.001
pH, median [Q1,Q3]		7.4 [7.4,7.4]	7.4 [7.4,7.4]	7.4 [7.4,7.4]	<0.001
Base Excess, median [Q1,Q3]		-1.1 [-3.7,1.0]	-2.1 [-4.0,0.0]	-2.0 [-4.0,0.0]	<0.001
Bicarbonate, median [Q1,Q3]		24.0 [22.0,25.0]	23.0 [21.0,25.0]	24.0 [22.0,25.0]	<0.001
Total CO2, median [Q1,Q3]		24.0 [22.0,26.0]	24.0 [22.0,26.0]	24.2 [22.0,26.0]	<0.001
Hematocrit, median [Q1,Q3]		31.0 [27.3,34.6]	29.7 [26.5,33.2]	29.3 [26.0,33.0]	<0.001
Hemoglobin, median [Q1,Q3]		10.3 [9.1,11.6]	9.9 [8.8,11.1]	9.9 [8.8,11.1]	<0.001
Chloride, median [Q1,Q3]		108.0 [106.0,111.0]	109.0 [107.0,112.0]	109.0 [107.0,112.0]	<0.001
Calcium, median [Q1,Q3]		8.2 [7.8,8.6]	8.1 [7.7,8.6]	8.1 [7.7,8.5]	0.002
Temperature, median [Q1,Q3]		37.2 [36.7,37.6]	37.2 [36.7,37.6]	37.1 [36.7,37.5]	<0.001
Potassium, median [Q1,Q3]		4.2 [3.9,4.5]	4.2 [3.9,4.5]	4.2 [3.9,4.5]	<0.001
Sodium, median [Q1,Q3]		139.0 [137.0,142.0]	141.0 [139.0,143.0]	141.0 [138.0,143.0]	<0.001
Lactate, median [Q1,Q3]		2.0 [1.6,2.4]	2.0 [1.7,2.4]	2.1 [1.7,2.6]	<0.001
Glucose, median [Q1,Q3]		129.0 [114.0,146.0]	127.0 [110.0,147.0]	130.0 [113.0,150.0]	<0.001
WBC, median [Q1,Q3]		12.5 [9.5,16.2]	13.1 [10.1,16.6]	13.1 [10.4,16.7]	<0.001
MCH, median [Q1,Q3]		30.1 [28.9,31.3]	30.1 [29.1,31.2]	30.0 [28.9,31.1]	0.425
MCHC, median [Q1,Q3]		33.5 [32.8,34.2]	33.6 [32.8,34.3]	33.6 [32.9,34.1]	0.385
MCV, median [Q1,Q3]		89.7 [86.2,93.0]	89.6 [86.6,92.9]	89.4 [86.1,92.7]	0.17
Platelets, median [Q1,Q3]		138.0 [110.0,172.0]	135.0 [107.0,169.0]	144.0 [113.0,181.0]	<0.001
RBC, median [Q1,Q3]		3.5 [3.1,3.9]	3.4 [3.0,3.8]	3.3 [3.0,3.8]	<0.001
RDW, median [Q1,Q3]		14.2 [13.4,15.2]	14.3 [13.5,15.3]	14.2 [13.5,15.4]	<0.001
Anion Gap, median [Q1,Q3]		8.0 [6.0,11.5]	10.3 [8.0,13.0]	8.0 [6.0,10.0]	<0.001
BUN, median [Q1,Q3]		16.0 [13.0,22.0]	17.0 [13.0,22.0]	17.0 [13.0,22.0]	0.002
Creatinine, median [Q1,Q3]		1.0 [0.8,1.3]	1.0 [0.8,1.2]	1.0 [0.8,1.2]	0.294
Fibrinogen, median [Q1,Q3]		241.0 [193.0,306.2]	241.0 [197.8,299.2]	210.0 [173.0,270.0]	<0.001
INR, median [Q1,Q3]		1.2 [1.1,1.3]	1.4 [1.2,1.5]	1.2 [1.1,1.4]	<0.001
PT, median [Q1,Q3]		13.5 [11.9,15.8]	16.5 [15.2,17.9]	13.4 [12.1,16.1]	<0.001
PTT, median [Q1,Q3]		30.5 [27.4,34.9]	34.9 [31.0,40.0]	31.7 [28.4,35.3]	<0.001
Heart Rate, median [Q1,Q3]		80.0 [73.0,90.0]	81.0 [73.0,91.0]	86.0 [77.0,93.0]	<0.001
SBP, median [Q1,Q3]		116.0 [104.0,130.0]	114.0 [103.0,127.0]	115.0 [104.0,128.0]	<0.001
DBP, median [Q1,Q3]		55.0 [48.0,62.0]	54.0 [48.0,61.0]	55.0 [49.0,62.0]	<0.001
MBP, median [Q1,Q3]		74.0 [67.0,82.0]	73.0 [66.0,80.0]	74.0 [67.0,81.0]	<0.001
Respiratory Rate, median [Q1,Q3]		17.0 [14.0,21.0]	17.0 [14.0,21.0]	18.0 [14.0,22.0]	<0.001
SpO2, median [Q1,Q3]		98.0 [96.0,100.0]	98.0 [96.0,100.0]	98.0 [96.0,100.0]	<0.001
24h SOFA Score, median [Q1,Q3]		3.0 [1.0,5.0]	4.0 [1.0,5.0]	6.0 [4.0,8.0]	<0.001
Elixhauser, median [Q1,Q3]		1.0 [0.0,2.0]	0.0 [0.0,1.0]	0.0 [0.0,2.0]	<0.001
Invasive Ventilation in Hour, median [Q1,Q3]	**0**	19056 (27.9)	4507 (10.9)	1039 (7.0)	<0.001
	1	49358 (72.1)	36771 (89.1)	13769 (93.0)	
Minutes on Ventilator Within Hour, median [Q1,Q3]		60.0 [0.0,60.0]	60.0 [60.0,60.0]	60.0 [60.0,60.0]	<0.001

Dopamine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Epinephrine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Norepinephrine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.4 [0.0,3.5]	<0.001
Phenylephrine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Vasopressin Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Amiodarone Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Clevidipine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Dobutamine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Milrinone Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001
Nicardipine Amount, median [Q1,Q3]		0.0 [0.0,0.0]	0.0 [0.0,0.0]	0.0 [0.0,0.0]	<0.001

Supplemental Table 3. ICD-9-PCS and ICD-10-PCS codes. Table of codes used to identify CABG, valve repair, and valve replacement procedures.

Category	Code	Translation
CABG	361X	Aortocoronary Bypass for Heart Revascularization
	2100X	Coronary Artery, One Artery
	2110X	Coronary Artery, Two Arteries
	2120X	Coronary Artery, Three Arteries
	2130X	Coronary Artery, Four or More Arteries
Valve Repair/Replacement	352X	Open and other replacement of unspecified heart valve
	3511	Open heart valvuloplasty of aortic valve without replacement
	3512	Open heart valvuloplasty of mitral valve without replacement
	3513	Open heart valvuloplasty of pulmonary valve without replacement
	3514	Open heart valvuloplasty of tricuspid valve without replacement
	02RF0X	Replacement, Aortic Valve
	02RG0X	Replacement, Tricuspid Valve
	02RH0X	Replacement, Pulmonary Valve
	02RJ0X	Replacement, Tricuspid Valve
	02QF0X	Repair, Aortic Valve
	02QG0X	Repair, Mitral Valve
	02QH0X	Repair, Pulmonary Valve
	02QJ0X	Repair, Tricuspid Valve

Supplementary Table 4. Admission diagnosis reasons. Admission diagnosis reasons used in eICU-CRD in the absence of available ICD-9-PCS and ICD-10-PCS to identify post-cardiac surgery patient.

Category	String
CABG	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG, minimally invasive; mid-CABG
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG alone, coronary artery bypass grafting
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG alone, redo
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG redo with other operation
Valve	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|Pulmonary valve surgery
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|Aortic valve replacement (isolated)
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|Mitral valve repair
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|Aortic and Mitral valve replacement
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|Mitral valve replacement
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|Tricuspid valve surgery
Both	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG redo with valve repair/replacement
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG with pulmonic or tricuspid valve repair or replacement ONLY
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG with double valve repair/replacement
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG with mitral valve replacement
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG with aortic valve replacement
	admission diagnosis|All Diagnosis|Operative|Diagnosis|Cardiovascular|CABG with mitral valve repair