Supplemental Digital Content 5. Clinical Utility

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SDC 5: Table 1. Performance metrics for the simulated children's hospital with varying percentage of ICU patients.

Metric	6 to 12 Hours	12 to 18 Hours	18 to 24 Hours	24 to 30 Hours
Simulated Hospital with 30% of the Patients Admitted to ICU				
AUROC	0.958 (0.958, 0.958)	0.956 (0.955, 0.956)	0.953 (0.952, 0.953)	0.951 (0.951, 0.951)
AUPRC	0.873 (0.870, 0.876)	0.859 (0.856, 0.862)	0.846 (0.843, 0.849)	0.831 (0.828, 0.835)
Sensitivity	0.827 (0.824, 0.830)	0.818 (0.814, 0.821)	0.795 (0.791, 0.798)	0.783 (0.779, 0.787)
Specificity	0.933 (0.932, 0.934)	0.934 (0.933, 0.935)	0.936 (0.935, 0.938)	0.937 (0.936, 0.938)
Precision (Positive Predictive Value)	0.774 (0.770, 0.778)	0.768 (0.764, 0.771)	0.759 (0.756, 0.763)	0.749 (0.745, 0.753)
Negative Predictive Value	0.951 (0.950, 0.952)	0.951 (0.950, 0.952)	0.948 (0.946, 0.949)	0.947 (0.946, 0.948)
Accuracy	0.910 (0.909, 0.911)	0.910 (0.909, 0.911)	0.908 (0.907, 0.909)	0.907 (0.906, 0.908)
F1 score	0.800 (0.797, 0.802)	0.792 (0.789, 0.794)	0.777 (0.774, 0.779)	0.765 (0.763, 0.768)
False Discovery Rate (False Detection Rate)	0.226 (0.222, 0.230)	0.232 (0.229, 0.236)	0.241 (0.237, 0.244)	0.251 (0.247, 0.255)
Simulated Hospital with 15% of the Patients Admitted to ICU				
AUROC	0.970 (0.969, 0.970)	0.968 (0.966, 0.968)	0.969 (0.968, 0.969)	0.968 (0.967, 0.968)
AUPRC	0.853 (0.849, 0.858)	0.835 (0.829, 0.839)	0.831 (0.826, 0.836)	0.819 (0.814, 0.825)
Sensitivity	0.828 (0.823, 0.833)	0.809 (0.803, 0.814)	0.792 (0.786, 0.797)	0.780 (0.774, 0.785)
Specificity	0.960 (0.959, 0.960)	0.958 (0.957, 0.959)	0.964 (0.963, 0.965)	0.965 (0.964, 0.966)
Precision (Positive Predictive Value)	0.735 (0.729, 0.740)	0.715 (0.709, 0.721)	0.732 (0.726, 0.738)	0.728 (0.722, 0.734)
Negative Predictive Value	0.976 (0.975, 0.977)	0.975 (0.974, 0.975)	0.974 (0.973, 0.974)	0.973 (0.972, 0.974)
Accuracy	0.944 (0.943, 0.945)	0.941 (0.940, 0.942)	0.944 (0.943, 0.945)	0.945 (0.944, 0.946)
F1 score	0.779 (0.775, 0.782)	0.759 (0.755, 0.763)	0.761 (0.757, 0.765)	0.753 (0.749, 0.757)
False Discovery Rate (False Detection Rate)	0.265 (0.260, 0.271)	0.285 (0.279, 0.291)	0.268 (0.262, 0.274)	0.272 (0.266, 0.278)
Simulated Hospital with 10% of the Patients Admitted to ICU				
AUROC	0.975 (0.974, 0.975)	0.975 (0.974, 0.975)	0.974 (0.973, 0.974)	0.975 (0.973, 0.975)

AUPRC	0.821 (0.814, 0.828)	0.803 (0.796, 0.810)	0.801 (0.794, 0.809)	0.781 (0.773, 0.789)
Sensitivity	0.816 (0.809, 0.823)	0.809 (0.801, 0.816)	0.792 (0.784, 0.799)	0.781 (0.773, 0.789)
Specificity	0.969 (0.968, 0.970)	0.968 (0.967, 0.969)	0.974 (0.973, 0.974)	0.973 (0.972, 0.974)
Precision (Positive Predictive Value)	0.676 (0.668, 0.683)	0.655 (0.647, 0.662)	0.685 (0.677, 0.693)	0.669 (0.660, 0.677)
Negative Predictive Value	0.985 (0.985, 0.986)	0.985 (0.985, 0.986)	0.985 (0.984, 0.985)	0.985 (0.984, 0.985)
Accuracy	0.958 (0.957, 0.959)	0.957 (0.956, 0.958)	0.961 (0.960, 0.962)	0.961 (0.960, 0.962)
F1 score	0.739 (0.734, 0.744)	0.724 (0.718, 0.729)	0.735 (0.729, 0.740)	0.720 (0.715, 0.726)
False Discovery Rate (False Detection Rate)	0.324 (0.317, 0.332)	0.345 (0.338, 0.353)	0.315 (0.307, 0.323)	0.331 (0.323, 0.340)

Legend: The metrics for a prevalence of 20% for ICU patients is shown in Table 2. Metrics are shown for a decision threshold of 0.5 for prediction of ICU care during the future time period. The following components of the confusion matrix are not shown since they can be computed from other data: False Negative Rate = [1 – Sensitivity]; False Positive Rate = [1 – Specificity]; False Omission Rate = [1 – Negative Predictive Value]; Number Needed to Evaluate = 1/Precision.

Abbreviations: AUROC = area under the receiver operating characteristic curve; AUPRC = area under the precision recall curve.

SDC 5: Table 2. Percentage of correct predictions of transfer from non-ICU to ICU if one or more of the prediction models made a transfer prediction prior to transfer.

Test Sample: Percentage Correct Prediction: Non-ICU to ICU Transfers (95% CI)[a]				
Sensitivity	First 6-hour time period	Second 6-hour time period	Third 6- hour time period	Fourth 6-hour time period
0.85	74.2 (71.7, 76.7)	74.7 (72.1, 77.2)	72.3 (69.4, 75.1)	67.0 (63.9, 70.1)
0.90	83.5 (81.3, 85.6)	84.2 (82.00, 86.3)	83.5 (81.1, 85.8)	79.4 (76.6, 81.9)
0.95	92.7 (91.1, 94.1)	92.3 (90.5, 93.7)	92.0 (90.2, 93.6)	89.7 (87.6, 91.6)
0.99	99.2 (98.5, 99.6)	99.4 (98.7, 99.8)	99.3 (98.6, 99.7)	98.8 (97.9, 99.4)
Independent Cohort: Percentage Correct Prediction: Non-ICU to ICU Transfers (95% CI)[a]				
0.85	75.6 (69.2, 81.2)	84.5 (82.8, 86.0)	85.1 (83.4, 86.6)	85.3 (83.7, 86.8)
0.90	80.3 (74.3, 85.4)	89.0 (87.6, 90.3)	89.3 (87.8, 90.6)	89.5 (88.1, 90.8)
0.95	88.7 (83.7, 92.6)	95.8 (94.8, 96.6)	95.8 (94.8, 96.6)	95.4 (94.4, 96.3)
0.99	99.1 (96.6, 99.9)	99.9 (99.6, 100.0)	99.9 (99.6, 100.0)	99.7 (99.4, 99.9)

    a. Times are referenced to the prediction time interval.

Legend: The accuracy was assessed for the first, second, third and fourth 6-hour time periods after transfer but only when the prediction was done prior to the transfer. The first 6-hour time period after transfer into the ICU had predictions from all four models, the second 6-hour period had predictions from 3 models, the third 6-hour period had predictions from 2 models, and the fourth period had predictions from only one model. For the test sample, the positive predictive value of these patients needing vasoactive agent infusions or mechanical ventilation if correctly predicted was 37%-38%. The decision thresholds are based on the lower 95% confidence interval (CI) of the sensitivity or specificity. Data is the percentage (95% confidence interval). Demographic data for these samples are shown in Table 1.

SDC 5: Table 3. Percentage of correct predictions in the 2017-2018 cohort sample transferred from non-ICU to ICU care.

A. Test Sample

Prediction Model	Sensitivity	Percentage Correct ICU Care Prediction (%) (95% CI)[1]			
		First 6-hour time period	Second 6-hour time period	Third 6- hour time period	Fourth 6-hour time period
6 -12 Hours	0.85	61.2 (58.4,64.0)			
6 -12 Hours	0.90	73.2 (70.6,75.7)			
6 -12 Hours	0.95	87.9 (85.9,89.7)			
6 -12 Hours	0.99	98.5 (97.6,99.1)			
12 - 18 Hours	0.85	62.8 (59.5,66.1)	65.6 (62.7,68.3)		
12 - 18 Hours	0.90	75.9 (72.9,78.7)	76.3 (73.7,78.8)		
12 - 18 Hours	0.95	88.7 (86.4,90.8)	88.8 (86.8,90.6)		
12 - 18 Hours	0.99	98.7 (97.7,99.3)	98.8 (97.9,99.3)		
18 – 24 Hours	0.85	61.7 (57.8,65.5)	62.6 (59.2,66)	65.9 (62.9,68.9)	
18 – 24 Hours	0.90	75.0 (71.4,78.3)	77.4 (74.3,80.2)	78.6 (75.9,81.1)	
18 – 24 Hours	0.95	88.3 (85.6,90.7)	89.6 (87.3,91.7)	90.7 (88.7,92.4)	
18 – 24 Hours	0.99	98.6 (97.3,99.3)	98.4 (97.2,99.1)	99.1 (98.3,99.6)	
24 - 30 Hours	0.85	58.4 (53.9,62.8)	62.4 (58.4,66.3)	64.9 (61.2,68.4)	67 (63.9,70.0)
24 - 30 Hours	0.90	71.8 (67.6,75.7)	76.4 (72.8,79.7)	78 (74.8,81)	79.4 (76.6,81.9)
24 - 30 Hours	0.95	85.0 (81.5,88.0)	87.7 (84.8,90.2)	89.0 (86.5,91.2)	89.7 (87.6,91.6)
24 - 30 Hours	0.99	98.2 (96.6,99.2)	98.5 (97.2,99.3)	98.3 (97.0,99.1)	98.8 (97.9,99.4)

1. Times are referenced to the prediction time interval.

Legend: The time periods are referenced to the admission to the ICU. For example, the first 6-hour time period is the first 6 hours in the ICU and the correct predictions are reference to the 4 prediction models. The decision thresholds are based on the lower 95% confidence interval (CI) of the indicated sensitivity. Times are referenced to the prediction time interval. Data are the percentage (95% CI).

B. 2017-2018 Cohort

Prediction Model	Sensitivity	Percentage Correct ICU Care Prediction (%) (95% CI)[1]			
		First 6-hour time period	Second 6-hour time period	Third 6- hour time period	Fourth 6-hour time period
6-12 Hours	0.85	75.4 (69.0, 81.0)			
6-12 Hours	0.90	80.1 (74.1, 85.3)			
6-12 Hours	0.95	84.8 (79.3, 89.4)			
6-12 Hours	0.99	98.6 (95.9, 99.7)			
12-18 Hours	0.85	78.6 (72.2, 84.2)	84.2 (82.5, 85.7)		
12-18 Hours	0.90	80.2 (73.9, 85.6)	88.7 (87.2, 90.0)		
12-18 Hours	0.95	89.6 (84.4, 93.5)	95.0 (93.9, 95.9)		
12-18 Hours	0.99	99.0 (96.3, 99.9)	99.8 (99.4, 99.9)		
18-24 Hours	0.85	77.2 (70.4, 83.0)	88.4 (86.6, 90.0)	84.7 (83.1, 86.2)	
18-24 Hours	0.90	81.5 (75.1, 86.9)	91.8 (90.3, 93.2)	89.2 (87.8, 90.5)	
18-24 Hours	0.95	88.6 (83.1, 92.8)	96.3 (95.2, 97.2)	95.4 (94.4, 96.3)	
18-24 Hours	0.99	99.5 (97.0, 100)	99.6 (99.2, 99.9)	99.8 (99.4, 99.9)	
24-30 Hours	0.85	56.5 (46.6, 66.0)	84.6 (82.0, 86.9)	87.8 (86.0, 89.5)	85.3 (83.7, 86.8)
24-30 Hours	0.90	64.8 (55.0, 73.8)	89.0 (86.7, 91.0)	91.3 (89.7, 92.7)	89.5 (88.1, 90.8)
24-30 Hours	0.95	74.1 (64.8, 82.0)	93.5 (91.6, 95.0)	95.7 (94.5, 96.7)	95.4 (94.4, 96.3)
24-30 Hours	0.99	97.2 (92.1, 99.4)	99.1 (98.2, 99.6)	99.7 (99.3, 99.9)	99.7 (99.4, 99.9)

1. Times are referenced to the prediction time interval.

Legend: The time periods are referenced to the admission to the ICU. For example, the first 6-hour time period is the first 6 hours in the ICU and the correct predictions are reference to the 4 prediction models. The decision thresholds are based on the lower 95% confidence interval (CI) of the indicated sensitivity. Times are referenced to the prediction time interval. Data are the percentage (95% CI).

Table 4. Performance characteristics in the test sample by hospital size, geographic location, and teaching status.

A. Patient and hospital numbers for each characteristic

Characteristic	Future Prediction Time Period	Patients (n)	Hospitals (n)
Hospital Bed Numbers (n)			
<99	6 - 12 Hours	2534	4
<99	12 - 18 Hours	2534	4
<99	18 - 24 Hours	2534	4
<99	24 - 30 Hours	2534	4
100-299	6 - 12 Hours	2291	14
100-299	12 - 18 Hours	2292	14
100-299	18 - 24 Hours	2291	14
100-299	24 - 30 Hours	2292	14
300-499	6 - 12 Hours	3354	14
300-499	12 - 18 Hours	3356	14
300-499	18 - 24 Hours	3354	14
300-499	24 - 30 Hours	3356	14
500+	6 - 12 Hours	3014	12
500+	12 - 18 Hours	3016	12
500+	18 - 24 Hours	3016	12
500+	24 - 30 Hours	3016	12
Geographic Location of Hospital			
Midwest	6 - 12 Hours	1292	8
Midwest	12 - 18 Hours	1293	8
Midwest	18 - 24 Hours	1292	8
Midwest	24 - 30 Hours	1293	8
Northeast	6 - 12 Hours	2818	10
Northeast	12 - 18 Hours	2820	10
Northeast	18 - 24 Hours	2818	10
Northeast	24 - 30 Hours	2820	10
South	6 - 12 Hours	3685	10
South	12 - 18 Hours	3687	10
South	18 - 24 Hours	3687	10
South	24 - 30 Hours	3687	10
West	6 - 12 Hours	3398	7
West	12 - 18 Hours	3398	7
West	>18 - 24 Hours	3398	7
West	24 - 30 Hours	3398	7

Teaching Status			
Non-Teaching	6 - 12 Hours	3416	11
Non-Teaching	12 - 18 Hours	3416	11
Non-Teaching	18 - 24 Hours	3416	11
Non-Teaching	24 - 30 Hours	3416	11
Teaching	6 - 12 Hours	7536	25
Teaching	12 - 18 Hours	7541	25
Teaching	18 - 24 Hours	7538	25
Teaching	24 - 30 Hours	7541	25

B.   Performance matrices for each characteristic at a decision cutpoint of 0.5

Characteristic	Future Prediction Time Period	AUROC	Sensitivity	Specificity	Precision	Accuracy
Hospital Bed Numbers (n)						
<99	6 - 12 Hours	0.982 (0.981, 0.982)	0.886 (0.880, 0.892)	0.963 (0.961, 0.964)	0.797 (0.790, 0.805)	0.952 (0.950, 0.953)
<99	12 - 18 Hours	0.980 (0.978, 0.980)	0.895 (0.889, 0.901)	0.966 (0.964, 0.967)	0.808 (0.800, 0.815)	0.956 (0.954, 0.957)
<99	18 - 24 Hours	0.979 (0.977, 0.979)	0.851 (0.844, 0.858)	0.970 (0.969, 0.971)	0.817 (0.809, 0.824)	0.954 (0.952, 0.955)
<99	24 - 30 Hours	0.977 (0.975, 0.977)	0.842 (0.835, 0.850)	0.968 (0.967, 0.970)	0.803 (0.795, 0.811)	0.952 (0.950, 0.953)
100-299	6 - 12 Hours	0.923 (0.921, 0.923)	0.791 (0.785, 0.797)	0.900 (0.897, 0.903)	0.748 (0.742, 0.753)	0.870 (0.868, 0.873)
100-299	12 - 18 Hours	0.919 (0.917, 0.919)	0.780 (0.775, 0.786)	0.899 (0.896, 0.901)	0.735 (0.729, 0.741)	0.867 (0.865, 0.870)
100-299	18 - 24 Hours	0.919 (0.916, 0.919)	0.774 (0.768, 0.780)	0.898 (0.895, 0.900)	0.725 (0.718, 0.731)	0.866 (0.863, 0.868)
100-299	24 - 30 Hours	0.913 (0.911, 0.913)	0.752 (0.746, 0.759)	0.900 (0.897, 0.902)	0.715 (0.709, 0.722)	0.863 (0.861, 0.865)

300-499	6 - 12 Hours	0.926 (0.925, 0.926)	0.823 (0.819, 0.826)	0.863 (0.860, 0.866)	0.814 (0.810, 0.818)	0.846 (0.844, 0.848)
300-499	12 - 18 Hours	0.921 (0.920, 0.921)	0.797 (0.793, 0.801)	0.874 (0.871, 0.877)	0.812 (0.808, 0.816)	0.843 (0.840, 0.845)
300-499	18 - 24 Hours	0.917 (0.915, 0.917)	0.781 (0.777, 0.785)	0.875 (0.873, 0.878)	0.800 (0.796, 0.804)	0.839 (0.836, 0.841)
300-499	24 - 30 Hours	0.914 (0.912, 0.914)	0.773 (0.769, 0.778)	0.871 (0.869, 0.874)	0.782 (0.778, 0.786)	0.835 (0.832, 0.837)
500+	6 - 12 Hours	0.863 (0.861, 0.863)	0.772 (0.767, 0.776)	0.788 (0.785, 0.792)	0.754 (0.749, 0.758)	0.781 (0.778, 0.784)
500+	12 - 18 Hours	0.862 (0.860, 0.862)	0.773 (0.769, 0.778)	0.789 (0.785, 0.793)	0.740 (0.736, 0.745)	0.782 (0.779, 0.785)
500+	18 - 24 Hours	0.851 (0.849, 0.851)	0.736 (0.732, 0.741)	0.799 (0.795, 0.802)	0.725 (0.720, 0.729)	0.773 (0.770, 0.776)
500+	24 - 30 Hours	0.850 (0.848, 0.850)	0.720 (0.715, 0.725)	0.816 (0.812, 0.819)	0.722 (0.717, 0.727)	0.778 (0.775, 0.781)
Geographic Location of Hospital						
Midwest	6 - 12 Hours	0.946 (0.944, 0.946)	0.778 (0.770, 0.787)	0.922 (0.919, 0.925)	0.773 (0.764, 0.781)	0.886 (0.883, 0.889)
Midwest	12 - 18 Hours	0.943 (0.941, 0.943)	0.781 (0.772, 0.789)	0.917 (0.913, 0.920)	0.750 (0.741, 0.759)	0.884 (0.880, 0.887)
Midwest	18 - 24 Hours	0.943 (0.941, 0.943)	0.739 (0.729, 0.748)	0.927 (0.924, 0.930)	0.754 (0.745, 0.763)	0.884 (0.880, 0.887)
Midwest	24 - 30 Hours	0.939 (0.936, 0.939)	0.736 (0.726, 0.746)	0.928 (0.925, 0.931)	0.744 (0.734, 0.754)	0.886 (0.882, 0.889)
Northeast	6 - 12 Hours	0.880 (0.877, 0.880)	0.738 (0.732, 0.743)	0.849 (0.846, 0.853)	0.767 (0.761, 0.772)	0.804 (0.801, 0.807)

Northeast	12 - 18 Hours	0.871 (0.868, 0.871)	0.741 (0.736, 0.747)	0.835 (0.831, 0.838)	0.738 (0.732, 0.743)	0.799 (0.796, 0.802)
Northeast	18 - 24 Hours	0.868 (0.865, 0.868)	0.716 (0.711, 0.722)	0.852 (0.849, 0.856)	0.739 (0.733, 0.744)	0.802 (0.799, 0.805)
Northeast	24 - 30 Hours	0.861 (0.858, 0.861)	0.687 (0.681, 0.693)	0.860 (0.857, 0.863)	0.727 (0.721, 0.733)	0.799 (0.796, 0.802)
South	6 - 12 Hours	0.898 (0.896, 0.898)	0.820 (0.817, 0.824)	0.821 (0.818, 0.824)	0.805 (0.801, 0.808)	0.821 (0.819, 0.823)
South	12 - 18 Hours	0.896 (0.894, 0.896)	0.804 (0.801, 0.808)	0.833 (0.830, 0.836)	0.801 (0.798, 0.805)	0.820 (0.817, 0.822)
South	18 - 24 Hours	0.890 (0.888, 0.890)	0.788 (0.784, 0.791)	0.829 (0.826, 0.832)	0.783 (0.780, 0.787)	0.811 (0.808, 0.813)
South	24 - 30 Hours	0.886 (0.884, 0.886)	0.781 (0.777, 0.784)	0.827 (0.824, 0.830)	0.769 (0.765, 0.773)	0.807 (0.805, 0.810)
West	6 - 12 Hours	0.969 (0.968, 0.969)	0.871 (0.866, 0.875)	0.931 (0.930, 0.933)	0.741 (0.735, 0.747)	0.920 (0.919, 0.922)
West	12 - 18 Hours	0.968 (0.967, 0.968)	0.850 (0.845, 0.855)	0.941 (0.939, 0.942)	0.757 (0.751, 0.763)	0.924 (0.923, 0.926)
West	18 - 24 Hours	0.963 (0.962, 0.963)	0.817 (0.811, 0.822)	0.940 (0.938, 0.941)	0.740 (0.734, 0.746)	0.918 (0.917, 0.920)
West	24 - 30 Hours	0.963 (0.962, 0.963)	0.804 (0.799, 0.810)	0.943 (0.941, 0.944)	0.740 (0.734, 0.746)	0.920 (0.918, 0.921)
Teaching Status						
Non-Teaching	6 - 12 Hours	0.970 (0.969, 0.970)	0.802 (0.796, 0.808)	0.957 (0.956, 0.959)	0.809 (0.803, 0.815)	0.929 (0.927, 0.930)
Non-Teaching	12 - 18 Hours	0.968 (0.967, 0.968)	0.811 (0.805, 0.816)	0.959 (0.958, 0.961)	0.813 (0.807, 0.818)	0.933 (0.931, 0.934)

Non-Teaching	18 - 24 Hours	0.966 (0.964, 0.966)	0.753 (0.747, 0.759)	0.964 (0.963, 0.966)	0.816 (0.810, 0.822)	0.928 (0.926, 0.929)
Non-Teaching	24 - 30 Hours	0.965 (0.963, 0.965)	0.759 (0.753, 0.766)	0.962 (0.961, 0.963)	0.802 (0.795, 0.808)	0.928 (0.926, 0.930)
Teaching	6 - 12 Hours	0.904 (0.903, 0.904)	0.808 (0.806, 0.811)	0.837 (0.834, 0.839)	0.775 (0.772, 0.777)	0.825 (0.823, 0.827)
Teaching	12 - 18 Hours	0.900 (0.899, 0.900)	0.794 (0.791, 0.797)	0.840 (0.838, 0.842)	0.765 (0.762, 0.768)	0.822 (0.820, 0.824)
Teaching	18 - 24 Hours	0.896 (0.894, 0.896)	0.778 (0.775, 0.781)	0.843 (0.841, 0.845)	0.752 (0.749, 0.755)	0.818 (0.816, 0.820)
Teaching	24 - 30 Hours	0.891 (0.890, 0.891)	0.760 (0.757, 0.763)	0.849 (0.847, 0.850)	0.743 (0.740, 0.746)	0.816 (0.815, 0.818)

AUROC = area under the receiver characteristic curve.