### Appendix A. Differences between Recalibration, Reweighting and Rescoring

In this appendix, we clarify the distinctions between three similar terms: **recalibration**, **reweighting**, and **rescoring** in the context of clinical scoring tables.

**Recalibration** refers to updating the risk estimates associated with a given score, without modifying the structure, components, or weightings of the score itself. The primary goal of recalibration is to ensure that risk predictions align with clinical data. The numerical score remains unchanged but the estimated probability of an outcome per score group is adjusted.

Reweighting involves altering the contribution of individual variables within a scoring system. This is typically done when new evidence suggests that certain variables have more or less impact on the outcome than originally assumed. The components of the score remain the same but the assigned weight (point value or coefficient) of each component is modified.

**Rescoring** refers to modifying the overall scoring algorithm, which may include changes to the weightings, cutoff thresholds, or the inclusion or exclusion of specific variables.

Table 9 summarizes the key differences between recalibration, reweighting, and rescoring.

Aspect	Recalibration	Reweighting	Rescoring
Risk estimates updated	Yes	Yes	Yes
Weighting of components changed	No	Yes	Yes
Score cutoffs modified	No	No	Yes
Variables added or removed	No	No	Yes

Table 9: Comparison of recalibration, reweighting, and rescoring.

## Appendix B. Performance of Extended Scoring Tables

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Table 10: Discrimination, calibration and reclassification metrics performance between original score and SET fine-tuned score on the 40% test set. For all metrics except  $c^*$ , Brier and ECE, the higher the better. For Brier and ECE, the lower the better. Best performances are bolded.

		Discrimination					Calibrati	on	Reclas	sification		
	AUC	$c^*$	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	$\mathrm{HL}\ p ext{-value}$	NRI	IDI
Child-Pugh												
Original	0.615	9	0.193	0.500	0.693	0.127	0.940	0.0750	0.00628	1.00	0.00%	0.00%
SET (Extended)	0.645	10	0.238	0.667	0.571	0.122	0.950	0.0750	0.0112	0.998	-9.46%	+0.0488%
LACE												
Original	0.676	10	0.221	1.00	0.221	0.0946	1.00	0.0730	0.0693	0.115	0.00%	0.00%
SET (Extended)	0.654	16	0.255	0.714	0.541	0.112	0.959	0.0716	0.0290	0.964	+27.0%	+2.38%
NEWS												
Original	0.536	9	0.0151	0.187	0.828	0.446	0.579	0.248	0.0537	0.0510	0.00%	0.00%
SET (Extended)	0.560	10	0.0635	0.312	0.751	0.481	0.596	0.242	0.00403	1.00	+15.3%	+1.56%

## 935 Appendix C. Fine-tuned Tables

Clinical variable	Addition to score
Bilirubin (mg/dL)	
<2	1
2-3	2
>3	3
Albumin (g/dL)	
> 3.5	1
2.8 - 3.5	2
< 2.8	3
INR	
< 1.7	1
1.7 - 2.3	2
> 2.3	3
Ascites	
Absent	1
$\operatorname{Slight}$	2
Moderate	3
Encephalopathy	
None	1
Grade 1-2	2
Grade 3-4	3

Clinical variable	Addition to score
Bilirubin (mg/dL)	
< 0.5	1
0.5-3	2
>3	3
Albumin (g/dL)	
>5.1	1
3.0 - 5.1	2
< 3.0	3
INR	
<1.1	1
1.1 - 2.5	2
> 2.5	3
Ascites	
Absent	1
$\operatorname{Slight}$	2
Moderate	3
Encephalopathy	
None	1
Grade 1-2	2
Grade 3-4	4

Table 11: **Before -** The Child-Pugh Score.

Table 12: After - Tuned Child-Pugh Score by SET.

Clinical variable	$egin{array}{c} {f Addition} \ {f to\ score} \end{array}$	Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$
Sex		Sex	
Male	6	Male	6
Age (years)		Age (years)	
45-57	9	45-57	9
58-68	20	58-68	20
69-102	24	69-102	24
Hypoxemia		Hypoxemia	
Yes	7	Yes	7
Glucose (mg/dL)		Glucose (mg/dL)	
<70	14	<70	14
>140	5	>140	6
AST to ALT ratio		AST to ALT ratio	
>1	9	>1	9
C-reactive protein (mg/dL)		C-reactive protein (mg/dL)	
>10	8	>15	8
Arterial pH		Arterial pH	
< 7.35	7	< 7.35	7
>7.45	2	>7.45	1
White blood cell count per $\mu$ L	•	White blood cell count per $\mu L$	
$>10 \times 10^{3}$	9	$>10 \times 10^{3}$	13

Table 13: **Before -** CIMS.

Table 14:  ${\bf After}$  - Tuned CIMS by SET.

Clinical variable	Addition to score	Clinical variable	Addition to score
Confusion		Confusion	
Yes	1	Yes	1
Urea (mmol/L)		Urea (mmol/L)	
>7	1	>7	1
Respiratory rate (breaths/min)		Respiratory rate (breaths/min)	
≥30	1	≥30	1
Blood pressure (mmHg)		Blood pressure (mmHg)	
SBP $<90$ or DBP $\le 60$	1	SBP < 90 or DBP $\leq 59$	1
Age (years)		Age (years)	
$\geq 65$	1	≥65	1

Table 15: **Before -** CURB-65 Score. Table 16: **After -** Tuned CURB-65 Score by SET

Clinical variable	$\begin{array}{c} {\bf Addition} \\ {\bf to} \ {\bf score} \end{array}$	Clinical variable	Addition to score
Killip class		Killip class	
IĪ	20	IĪ	20
III	39	III	44
IV	59	IV	59
Systolic blood pressure (mmHg)		Systolic blood pressure (mmHg)	
≤80	58	≤80	61
80-99	53	80-99	56
100-119	43	100-119	48
120-139	34	120-139	37
140-159	24	140-159	27
160-199	10	160-282	12
Heart rate (beats/min)		Heart rate (beats/min)	
50-69	3	50-69	3
70-89	9	70-89	9
90-109	15	90-109	15
110-149	24	110-149	24
150-199	38	150-199	38
$\geq$ 200	46	$\geq 200$	46
Age (years)		Age (years)	
30-39	8	30-39	9
40-49	25	40-49	26
50-59	41	50-59	42
60-69	58	60-69	51
70-79	75	70-79	68
80-89	91	80- <mark>122</mark>	84
≥90	100	≥123	93
Creatinine (mg/dL)		Creatinine (mg/dL)	
0-0.39	1	0-0.39	1
0.40  0.79	4	0.40 - 0.79	2
0.80-1.19	7	0.80-1.19	5
1.20-1.59	10	1.20 - 1.59	8
1.60-1.99	13	1.60-1.99	10
2.00-3.99	21	2.00-3.99	18
>4.0	28	>4.0	25
Other Risk Factors		Other Risk Factors	
Cardiac Arrest at Admission	39	Cardiac Arrest at Admission	18
ST-Segment Deviation	28	ST-Segment Deviation	3
Elevated Cardiac Enzyme Levels	14	Elevated Cardiac Enzyme Levels	14

Table 17: **Before -** GRACE Score.

Table 18: After - Tuned GRACE Score by SET.

Clinical variable	Addition to score
Hypertension Yes	1
Renal disease Yes	1
Liver disease Yes	1
Stroke history Yes	1
Prior major bleeding or predisposition to bleeding Yes	1
Labile INR Yes	1
Age (years) >65	1
Medication usage predisposing to bleeding Yes	1
Alcohol use Yes	1

Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$
Hypertension	
Yes	1
Renal disease	
Yes	1
Liver disease	
Yes	1
Stroke history	
Yes	1
Prior major bleeding or	
predisposition to bleeding	
Yes	1
Labile INR	
Yes	1
Age (years)	
>43	1
Medication usage	
predisposing to bleeding	
Yes	1
Alcohol use	
Yes	1

Table 19: **Before -** HAS-BLED Score.

Table 20: After - Tuned HAS-BLED Score by SET.

Clinical variable	$\begin{array}{c} \textbf{Addition} \\ \textbf{to score} \end{array}$	Clinical variable	$\begin{array}{c} {\bf Addition} \\ {\bf to} \ {\bf score} \end{array}$
Length of stay (days)		Length of stay (days)	
1	1	1	1
2	2	2	2
3	3	3 <b>-5</b>	3
4-6	4	6-7	4
7-13	5	8-16	5
$\geq 14$	7	≥17	6
Acute (emergent) admission		Acute (emergent) admission	
Yes	3	Yes	2
Charlson Comorbidity Index		Charlson Comorbidity Index	
1	1	1	1
2	2	2 <mark>-3</mark>	2
3	3	4-5	3
$\geq 4$	5	$\geq 6$	6
Number of ED visits within 6 mor	nths	Number of ED visits within (	6 months
1	1	1-2	1
2	2	3	2
3	3	4-5	3
$\geq 4$	4	$\geq 6$	4

Table 21: **Before -** LACE Score.

Table 22:  ${\bf After}$  - Tuned LACE Score by SET.

Clinical variable	Addition to score	Clinical variable	$egin{array}{c} { m Addition} \ { m to \ score} \end{array}$
Respiratory rate (breaths/min)		Respiratory rate (breaths/min)	
≤8	3	<u>≤4</u>	3
9-11	1	<b>5-</b> 11	1
21-24	2	21-24	2
$\geq \! 25$	3	$\geq 25$	3
Oxygen saturations (%)		Oxygen saturations (%)	
≤91	3	≤ <u>44</u>	3
92-93	2	<b>45</b> -93	2
94-95	1	94-95	1
Any supplemental oxygen		Any supplemental oxygen	
Yes	2	Yes	3
Temperature (°C)		Temperature (°C)	
<35.0	3	<35.0	3
35.1-36.0	1	35.1-36.0	1
38.1-39.0	1	38.1-39.0	1
$\geq 39.1$	2	$\geq 39.1$	2
Systolic blood pressure (mmHg)		Systolic blood pressure (mmHg)	
≤90	3	≤90	3
91-100	2	91-100	2
101-110	1	101-110	1
$\geq$ 220	3	$\geq$ 220	1
Heart rate (beats/min)		Heart rate (beats/min)	
≤40	3	≤40	3
41-50	1	41-50	1
91-110	1	91-110	1
111-130	2	111-130	2
≥131	3	$\geq$ 131	3
AVPU score		AVPU score	
Voice, Pain, or Unresponsive (V, P, U)	3	Voice, Pain, or Unresponsive (V, P, U)	3

Table 23: **Before -** NEWS.

Table 24: After - Tuned NEWS by SET.

Clinical variable	$\begin{array}{c} {\bf Addition} \\ {\bf to} \ {\bf score} \end{array}$
Age (years)	Age Value
Sex Female	-10
Nursing home resident Yes	10
Neoplastic disease Yes	30
Liver disease history Yes	20
CHF history Yes	10
Cerebrovascular disease history Yes	10
Renal disease history Yes	10
Altered mental status Yes	20
Respiratory rate (breaths/min) $\geq 30$	20
Systolic blood pressure (mmHg) <90	20
Temperature (°C) <35 or >39.9	15
Pulse (beats/min) $\geq 125$	10
pH <7.35	30
BUN (mg/dL) ≥30	20
Sodium (mmol/L) <130	20
Glucose (mg/dL) ≥250	10
Hematocrit (%) <30	10
Partial pressure of oxygen (mmHg) <60	10
Pleural effusion on x-ray Yes	10

Table 25: **Before -** PSI Score.

Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$
Age (years)	Age Value
Sex	
Female	-10
Nursing home resident Yes	10
Neoplastic disease Yes	30
Liver disease history Yes	20
CHF history Yes	10
Cerebrovascular disease history Yes	10
Renal disease history Yes	10
Altered mental status Yes	20
Respiratory rate (breaths/min) $\geq 30$	20
Systolic blood pressure (mmHg) <90	20
Temperature (°C) <35 or >39.9	15
Pulse (beats/min) $\geq 125$	11
pH <7.35	30
BUN (mg/dL) ≥30	16
Sodium (mmol/L) <130	20
Glucose (mg/dL) $\geq 250$	10
Hematocrit (%) <30	10
Partial pressure of oxygen (mmHg) <60	9
Pleural effusion on x-ray Yes	10

Table 26: After - Tuned PSI Score by SET.

# 936 Appendix D. Simplified Tables

Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$	Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$
Sex		Sex	
Male	6	Male	8
Age (years)		Age (years)	
45-57	9	45-57	6
58-68	20	58-68	17
69-102	24	69-102	21
Hypoxemia		Hypoxemia	
Yes	7	Yes	7
Glucose (mg/dL)		Glucose (mg/dL)	
<70	14	<70	14
>140	5	>140	5
AST to ALT ratio		AST to ALT ratio	
>1	9	>1	9
C-reactive protein (mg/dL)		C-reactive protein (mg/dL)	
>10	8	>5	8
Arterial pH		White blood cell count per $\mu \mathbf{L}$	
<7.35	7	$>10 \times 10^{3}$	9
>7.45	2		
White blood cell count per $\mu L$		Table 28: After - Simplified CIMS with	thout Arteria
$>10 \times 10^{3}$	9	pH by SET.	

Table 27: **Before -** CIMS.

Clinical variable	Addition to score
Confusion Yes	1
Urea (mmol/L) >7	1
Respiratory rate (breaths/min) $\geq 30$	1
Blood pressure (mmHg) SBP <90 or DBP ≤60	1
Age (years) ≥65	1

Table 29: **Before -** CURB-65 Score.

•	A 1 1*/*
Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$
Confusion	
Yes	1
Respiratory rate (breaths/min)	
$\geq$ 27	1
Blood pressure (mmHg)	
$SBP < 87 \text{ or } DBP \leq 37$	1
Age (years)	
≥43	1

Table 30:  ${\bf After}$  - Simplified CURB-65 Score without Urea by SET.

Clinical variable	Addition to score	Clinical variable	Addition to score
Killip class		Killip class	
ΙΪ	20	ΙΪ	20
III	39	III	44
IV	59	IV	59
Systolic blood pressure (mmHg)		Systolic blood pressure (mmHg)	
≤80	58	≤80	61
80-99	53	80-99	56
100-119	43	100-119	48
120-139	34	120-139	37
140-159	24	140-159	27
160-199	10	160-282	12
Heart rate (beats/min)		Heart rate (beats/min)	
50-69	3	50-69	3
70-89	9	70-89	9
90-109	15	90-109	15
110-149	24	110-149	24
150-199	38	150-199	38
≥200	46	$\geq$ 200	46
Age (years)		Age (years)	
30-39	8	30-39	9
40-49	25	40-49	26
50-59	41	50-59	42
60-69	58	60-69	51
70-79	75	70-79	68
80-89	91	80-122	84
≥90	100	$\geq$ 123	93
Creatinine (mg/dL)		Other Risk Factors	
0-0.39	1	Cardiac Arrest at Admission	18
0.40-0.79	4	ST-Segment Deviation	3
0.80-1.19	7	Elevated Cardiac Enzyme Levels	14
1.20-1.59	10	·	
1.60-1.99	13	TILL 00 AC C: 1:0 1 CD 1 CD 1	N
2.00-3.99	21	Table 32: After - Simplified GRACE S	score without
>4.0	28	Creatinine level by SET.	
Other Risk Factors			
Cardiac Arrest at Admission	39		
8 m 8	20		

Table 31: **Before -** GRACE Score.

ST-Segment Deviation

Elevated Cardiac Enzyme Levels

28

Clinical variable	Addition to score
Hypertension Yes	1
Renal disease Yes	1
Liver disease Yes	1
Stroke history Yes	1
Prior major bleeding or predisposition to bleeding Yes	1
Labile INR Yes	1
Age (years) >65	1
Medication usage predisposing to bleeding Yes	1
Alcohol use Yes	1

Table 33: **Before -** HAS-BLED Score.

Clinical variable	Addition to score
Hypertension	
Yes	1
Renal disease	
Yes	1
Liver disease	
Yes	1
Stroke history	
Yes	1
Prior major bleeding or	
predisposition to bleeding	
Yes	1
Age (years)	
>59	1
Medication usage	
predisposing to bleeding	
Yes	1
Alcohol use	
Yes	1

Table 34: **After -** Simplified HAS-BLED Score without Labile INR by SET.

Clinical variable	$egin{array}{c} \mathbf{A} \mathbf{d} \mathbf{d} \mathbf{i} \mathbf{t} \mathbf{i} \mathbf{o} \mathbf{n} \\ \mathbf{t} \mathbf{o} \ \mathbf{s} \mathbf{c} \mathbf{o} \mathbf{r} \mathbf{e} \end{array}$
Age (years)	Age Value
Sex Female	-10
Nursing home resident Yes	10
Neoplastic disease Yes	30
Liver disease history Yes	20
CHF history Yes	10
Cerebrovascular disease history Yes	10
Renal disease history Yes	10
Altered mental status Yes	20
Respiratory rate (breaths/min) $\geq 30$	20
Systolic blood pressure (mmHg) <90	20
Temperature (°C) <35 or >39.9	15
$\begin{array}{c} \textbf{Pulse (beats/min)} \\ \geq 125 \end{array}$	10
pH <7.35	30
BUN (mg/dL) ≥30	20
Sodium (mmol/L) <130	20
Glucose (mg/dL) ≥250	10
Hematocrit (%) <30	10
Partial pressure of oxygen (mmHg) <60	10
Pleural effusion on x-ray Yes	10

Table 35: **Before -** PSI Score.

Clinical variable	Addition
Offical variable	${ m to\ score}$
Age (years)	Age Value
Sex	
Female	-15
Nursing home resident	
Yes	8
Neoplastic disease	
Yes	9
Altered mental status	
Yes	11
Respiratory rate (breaths/min)	0.0
≥30	23
Systolic blood pressure (mmHg) <90	2
	<u>Z</u>
Temperature (°C) <35 or >39.9	8
$\begin{array}{c} \textbf{Pulse (beats/min)} \\ \geq 125 \end{array}$	4
pH	
<7.35	32
$\mathrm{BUN}\;(\mathrm{mg/dL})$	
<u>≥</u> 30	8
$\operatorname{Sodium} \ (\operatorname{mmol}/\operatorname{L})$	
<130	8
m Glucose~(mg/dL)	
≥250	6
Hematocrit (%)	
<30	15
Partial pressure of oxygen (mmHg)	10
<60	12
Pleural effusion on x-ray	10
Yes	13

Table 36: **After -** Simplified PSI Score without patient history by SET.

## 937 Appendix E. Extended Scoring Tables

Clinical variable	Addition to score
Bilirubin (mg/dL)	
<2	1
2-3	2
>3	3
Albumin (g/dL)	
> 3.5	1
2.8 - 3.5	2
< 2.8	3
INR	
< 1.7	1
1.7 - 2.3	2
> 2.3	3
Ascites	
Absent	1
$\operatorname{Slight}$	2
Moderate	3
Encephalopathy	
None	1
Grade 1-2	2
Grade 3-4	3

Table 37: **Before -** Child-Pugh Score.

Clinical variable	$egin{array}{c} \mathbf{Addition} \ \mathbf{to} \ \mathbf{score} \end{array}$
Bilirubin (mg/dL)	
<1.2	1
1.2 - 3.4	2
>3.4	3
Albumin (g/dL)	
>4.6	1
3.1 - 4.6	2
<3.1	3
INR	
< 0.2	1
0.2 - 3.3	2
>3.3	3
Ascites	
Absent	1
$\operatorname{Slight}$	2
Moderate	3
Encephalopathy	
None	1
Grade $1-2$	2
Grade 3-4	4
Age (years)	
90-95	1
$\geq 96$	2

Table 38:  ${\bf After}$  - Extended Child-Pugh Score with Age by SET.

Clinical variable	$\begin{array}{c} \textbf{Addition} \\ \textbf{to score} \end{array}$	Clinical variable	$\begin{array}{c} \mathbf{Addition} \\ \mathbf{to} \ \mathbf{score} \end{array}$
Length of stay (days)		Length of stay (days)	
1	1	1	1
2	2	2	2
3	3	3	3
4-6	4	4-6	4
7-13	5	7-13	5
$\geq 14$	7	$\geq 14$	7
Acute (emergent) admission		Acute (emergent) admission	
Yes	3	Yes	3
Charlson Comorbidity Index		Charlson Comorbidity Index	
1	1	1	1
2	2	2	2
3	3	3	3
$\geq 4$	5	$\geq 4$	5
Number of ED visits within 6 mont	hs	Number of ED visits within 6	months
1	1	1	1
2	2	2	2
3	3	3	3
$\geq 4$	4	$\geq 4$	4
		Age (years)	
Table 39: <b>Before -</b> LACE Score.		20-39	1
		40-59	2
		≥60	3
		Sex	
		Male	1

Table 40: After - Extended LACE Score with Age and Sex by SET.

Clinical variable	Addition to score	Clinical variable	$\begin{array}{c} \textbf{Addition} \\ \textbf{to score} \end{array}$
Respiratory rate (breaths/min)		Respiratory rate (breaths/min)	
<u>≤</u> 8	3	≤8	4
9-11	1	9- <mark>10</mark>	1
21-24	2	21- <mark>27</mark>	2
$\geq 25$	3	$\geq$ 28	3
Oxygen saturations (%)		Oxygen saturations (%)	
≤91	3	≤91	3
92-93	2	92-93	2
94-95	1	94-95	1
Any supplemental oxygen		Any supplemental oxygen	
Yes	2	Yes	3
Temperature (°C)		$ \overline{ \text{Temperature } (^{\circ}\text{C}) } $	
$\leq 35.0$	3	$\leq 25.4$	3
35.1-36.0	1	<b>25.5</b> -36.0	1
38.1-39.0	1	38.1- <mark>41.7</mark>	1
$\geq 39.1$	2	$\geq$ 41.8	2
Systolic blood pressure (mmHg)		Systolic blood pressure (mmHg)	
$\leq 90$	3	$\leq 90$	3
91-100	2	91-100	2
101-110	1	101-110	1
$\geq$ 220	3	$\geq$ 220	1
Heart rate (beats/min)		Heart rate (beats/min)	
$\leq 40$	3	$\leq 40$	2
41-50	1	41-50	1
91-110	1	83-94	1
111-130	2	95-107	2
≥131	3	$\geq$ 107	3
AVPU score		AVPU score	
Voice, Pain, or Unresponsive (V, P, U)	3	Voice, Pain, or Unresponsive (V, P, U)	3
		Age (years)	<u> </u>
Table 41: <b>Before -</b> NEWS.		38-80	1
Table II. Deloie III WD.		≥81	3

Table 42:  ${\bf After}\,$  - Extended NEWS with Age by SET.

## Appendix F. Confidence Intervals and Statistical Significance Tests

Table 43: 95% confidence intervals via bootstrapping and bootstrap statistical significance test.

			Discriminati	on (95% CI)			Calibratio	on (95% CI)	Reclassifica	tion (95% CI)
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
Child-Pugh										
Original	0.583 - 0.647	0.137 - 0.254	0.445 - 0.559	$0.678 - 0.708^{\circ}$	0.109 - 0.147	0.93 - 0.949	0.068 - 0.0826	$0.00156 0.0155^*$	0.00%	0.00%
SET	$0.624 - 0.684^*$	0.195 – 0.306*	0.649-0.753*	0.534 - 0.567	0.107-0.139	0.945-0.963*	0.0674-0.0817*	0.0069-0.0248	+23.3%- $+43.3%$ *	+0.525%- $+1.15%$ *
CIMS										
Original	0.812 - 0.826	0.473 - 0.503	0.778 - 0.803	0.690 - 0.704*	$0.427 - 0.449^*$	0.912 - 0.923	0.136 - 0.142	0.016 - 0.0258	0.00%	0.00%
SET	$0.816 - 0.83^{\circ}$	$0.489 - 0.516^*$	$0.822 - 0.845^*$	0.661 - 0.676	0.419 - 0.44	$0.926 - 0.936^*$	0.136 - 0.142	0.0149 - 0.0252	+11.4% - +18%*	+0.357%- $+0.864%$ *
CURB-65										
Original	0.677 - 0.741	0.304 - 0.418	0.716 - 0.821	0.573 - 0.612	0.153 - 0.195	0.947 - 0.969	0.0754 - 0.0921	0.0188 - 0.0389	0.00%	0.00%
SET	0.683 - 0.744	$0.331 - 0.443^{\circ}$	0.716 - 0.821	0.599 - 0.638*	$0.162 - 0.207^{\circ}$	0.95 - 0.971	0.0757 - 0.0919	0.0198 - 0.0381	$+27.9\%-+45.8\%^*$	-0.393% - +1.7%*
GRACE										
Original	0.742 - 0.829	0.175 - 0.413	0.386 - 0.617	$0.763 - 0.823^{\circ}$	0.16 - 0.283	0.911 - 0.951	0.1 - 0.144	0.0908 - 0.133	0.00%	0.00%
SET	$0.81 - 0.872^{\circ}$	$0.429 - 0.63^{*}$	$0.657 - 0.847^*$	0.748 - 0.809	$0.222 - 0.345^{\circ}$	0.948 – 0.978*	0.0793 - 0.118*	$0.073 - 0.111^*$	$+17.3\%{-}{+}36.4\%^*$	$+8.53\%{-+}18.3\%^*$
HAS-BLED										
Original	0.67 - 0.705	0.259 - 0.327	0.735 - 0.8	$0.513 - 0.538^{\circ}$	0.16 - 0.185	0.937 - 0.954	0.094 - 0.106	0.00322 - 0.0146	0.00%	0.00%
SET	$0.685 - 0.717^{*}$	$0.365 - 0.412^*$	0.897 - 0.938*	0.457 - 0.483	$0.171 - 0.196^{\circ}$	$0.972 - 0.983^{\circ}$	0.0933 – 0.104	0.011 - 0.0249	$-3.35\%-+12\%^*$	$+1.58\% - +2.5\%^*$
LACE										
Original	0.645 - 0.708	0.201 - 0.241	1-1	0.201 - 0.241	0.0809 - 0.11	1-1	0.0636 - 0.0839	0.0583 - 0.0813	0.00%	0.00%
SET	$0.655 - 0.72^*$	$0.327 - 0.37^*$	1-1	$0.327 - 0.37^{\circ}$	$0.0955 - 0.129^*$	1-1	$0.0601 - 0.0793^{\circ}$	$0.0132 - 0.0353^{*}$	+32.4% - +59%*	+2.18% $-+4.34%$ *
NEWS										
Original	0.524 - 0.548	-0.00168-0.0322	0.174 - 0.2	0.818 - 0.839*	0.421 - 0.472	0.568 - 0.59	0.246 - 0.25	0.0435 - 0.064	0.00%	0.00%
SET	$0.528 - 0.552^*$	$0.0232 - 0.0598^{*}$	$0.258 - 0.287^{\circ}$	0.759 - 0.78	$0.444 - 0.487^{\circ}$	$0.577 - 0.6^*$	$0.245 - 0.249^*$	$0.0238 - 0.0435^{\circ}$	$+10.2\%-+18.2\%^*$	$+0.413\% - +0.92\%^*$
PSI										
Original	0.81 - 0.84	0.443 - 0.514	0.692 - 0.759	0.739 - 0.766*	$0.333 - 0.382^{\circ}$	0.926 - 0.944	0.136 - 0.153	0.0804 - 0.0993	0.00%	0.00%
SET	$0.813 - 0.842^*$	0.453 - 0.512	$0.852 - 0.9^{\circ}$	0.591 - 0.621	0.278 - 0.317	$0.955 - 0.97^{\circ}$	$0.128 - 0.145^{*}$	0.0785 - 0.0975	$+1.25\%{-}{+}13.7\%^*$	$+3.9\%-+8.48\%^{*}$

<sup>\*</sup> indicates p < 0.05 for the bootstrap test, with the null hypothesis being that there is no significant difference between SET and Origina

Table 44: Mean performance difference (and Wilcoxon signed-rank test) between SET and Original score (i.e., SET – Original) across different data splits. Improvement in metrics due to SET are bolded.

			$\Delta \mathbf{Discrin}$	nination			$\Delta  ext{Calib}$	oration	$\Delta \mathbf{Reclass}$	sification
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
Child-Pugh Difference	$+0.0425^\dagger$	$+0.0481^{\dagger}$	$+0.173^{\dagger}$	$-0.125^{\dagger}$	-0.000781	$+0.00974^\dagger$	$\textbf{-0.000543}^\dagger$	$+0.00143^{\dagger}$	$+16.6\%^\dagger$	$+0.589\%^\dagger$
CIMS Difference	$+0.00494^\dagger$	$+0.0098^{\dagger}$	$+0.0407^\dagger$	$-0.0309^{\dagger}$	$-0.0123^{\dagger}$	$+0.0115^{\dagger}$	$\textbf{-0.000665}^\dagger$	$\textbf{-0.00107}^\dagger$	$+17.5\%^\dagger$	$+0.571\%^\dagger$
CURB-65 Difference	$+0.00725^\dagger$	$+0.0198^\dagger$	+0.000118	$+0.0198^{\dagger}$	$+0.00777^\dagger$	$+0.000665^\dagger$	+0.000178	-0.00052	$+54.9\%^\dagger$	-0.0338%
GRACE Difference	$+0.0314^\dagger$	$+0.121^{\dagger}$	$+0.111^{\dagger}$	$+0.00985^\dagger$	$+0.0321^\dagger$	$+0.0156^{\dagger}$	$\textbf{-0.0171}^\dagger$	$\textbf{-0.0182}^\dagger$	$+25.9\%^\dagger$	$+14.1\%^\dagger$
HAS-BLED Difference	$+0.0157^{\dagger}$	$+0.117^{\dagger}$	$+0.168^{\dagger}$	$-0.0511^{\dagger}$	$+0.0144^\dagger$	$+0.037^{\dagger}$	$\textbf{-0.00269}^\dagger$	$+0.00274^\dagger$	$+16.5\%^\dagger$	$+3.16\%^\dagger$
LACE Difference	$+0.0264^{\dagger}$	$+0.0649^{\dagger}$	-0.0871 <sup>†</sup>	$+0.152^{\dagger}$	$+0.00915^{\dagger}$	-0.00157	$\textbf{-0.00159}^\dagger$	-0.0107 <sup>†</sup>	$+19.2\%^{\dagger}$	$+1.26\%^\dagger$
NEWS Difference	$+0.00482^\dagger$	$+0.0218^{\dagger}$	$+0.0782^{\dagger}$	$-0.0563^{\dagger}$	$+0.0142^{\dagger}$	$+0.00761^\dagger$	$\textbf{-0.00136}^\dagger$	-0.00219	$+6.51\%^\dagger$	$+0.705\%^\dagger$
PSI Difference	$+0.00165^\dagger$	-0.00285	$+0.139^{\dagger}$	$-0.142^{\dagger}$	-0.0561 <sup>†</sup>	$+0.0236^{\dagger}$	$\textbf{-0.0056}^\dagger$	-0.00489 <sup>†</sup>	$+3.84\%^{\dagger}$	$+4.49\%^\dagger$

 $<sup>^{\</sup>dagger}$  indicates p < 0.05 for the Wilcoxon signed-rank test.

#### F.1. SET with Same Clinical Variables

We repeat the experiments performed in Table 3 via i). 1000 different bootstraps (see Table 43) and ii). 100 different data splits (see Table 44). Each table uses a different appropriate statistical significant test used in medical and machine learning literature, respectively. For all metrics the higher the better, except for Brier and ECE in which the lower the better. SET demonstrates statistically significant improved performances across most metrics across all 8 clinical scores.

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Table 45: 95% confidence intervals via bootstrapping and bootstrap statistical significance test.

			Discriminat	ion (95% CI)			Calibrati	on (95% CI)	Reclassifica	tion (95% CI)
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
CIMS										
Original	0.803 - 0.816	0.454 - 0.484	0.737 - 0.763	$0.712 - 0.727^{\circ}$	$0.434 - 0.456^{\circ}$	0.9 - 0.911	0.138 - 0.144	0.0169 - 0.0263	0.00%	0.00%
SET (Simplified)	0.804-0.818*	0.455 - 0.485	0.746-0.772*	0.702-0.717	0.428 - 0.45	0.902-0.913*	0.138 – 0.144*	0.0126-0.0223*	+7.67%- $+14.1%$ *	+0.284%-+0.761%*
$\underline{\text{CURB-65}}$										
Original	0.553 - 0.617	0.083 - 0.207	0.328 - 0.444	$0.743 - 0.777^*$	0.126 - 0.179	0.904 - 0.93	0.0788 - 0.0979	0.0145 - 0.0379	0.00%	0.00%
SET (Simplified)	0.632-0.699*	0.226-0.346*	0.599-0.712*	0.61-0.651	0.144-0.188	0.931 – 0.954*	0.0785-0.097	0.00963-0.0263*	$+17\%-+41.7\%^*$	$+0.0235\% - +3.25\%^*$
GRACE										
Original	0.724 - 0.816	0.132 - 0.37	0.386 - 0.617	0.718 - 0.781	0.136 - 0.241	0.906 - 0.949	0.116 - 0.162	0.102 - 0.145	0.00%	0.00%
SET (Simplified)	0.805-0.868*	0.292-0.521*	0.514 – 0.74*	0.748-0.809*	0.189 – 0.31*	0.928-0.966*	0.121 - 0.168	$0.0842 - 0.125^*$	$+0.708\%-+5.29\%^*$	-1.33% - +2.21%*
HAS-BLED										
Original	0.6 - 0.643	$0.169 - 0.243^{\circ}$	0.35 - 0.42	$0.811 - 0.831^{\circ}$	0.195 - 0.24	0.904 - 0.919	0.0964 - 0.109	0.00216 - 0.0125	0.00%	0.00%
SET (Simplified)	$0.609 - 0.65^*$	0.133-0.186	0.838-0.887*	0.285 - 0.308	0.127 - 0.147	0.933 – 0.954*	0.0965-0.109*	0.00155-0.0148	+18.4% - +33.5%*	+0.0147% - +2.17%*
PSI										
Original	0.812 - 0.841	0.48 - 0.539	$0.838 - 0.887^{\circ}$	0.632 - 0.663	0.296 - 0.339	0.953 - 0.968*	0.131 - 0.146	0.953 - 0.968	0.00%	0.00%
SET (Simplified)	0.818-0.846*	0.482-0.542*	0.796-0.848	0.676-0.706*	0.314-0.358*	0.946-0.96	0.14 - 0.157	0.0881-0.109	-11.1%-+2.31%	-1.99-+2.22%
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<sup>\*</sup> indicates p < 0.05 for the bootstrap test, with the null hypothesis being that there is no significant difference between SET and Original.

Table 46: Mean performance difference (and Wilcoxon signed-rank test) between SET and Original score (i.e., SET – Original) across different data splits. Improvement in metrics due to SET are bolded.

			$\Delta \mathbf{Discrim}$	ination			$\Delta \mathbf{Calib}$	ration	$\Delta \mathbf{Reclass}$	sification
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
CIMS Difference	$+0.0021^\dagger$	$+0.00202^\dagger$	$+0.0106^{\dagger}$	-0.0086 <sup>†</sup>	$-0.00427^{\dagger}$	$+0.00253^{\dagger}$	$-0.000275^{\dagger}$	-0.000871	$+7.88\%^{\dagger}$	$+0.457\%^\dagger$
CURB-65 Difference	$+0.0562^{\dagger}$	$+0.0907^{\dagger}$	$+0.234^{\dagger}$	$-0.144^{\dagger}$	-0.0108 <sup>†</sup>	$+0.022^\dagger$	$+0.000792^{\dagger}$	+0.00104	$+22.2\%^{\dagger}$	-0.01%
GRACE Difference	$+0.04^{\dagger}$	$+0.134^{\dagger}$	$+0.106^{\dagger}$	$+0.0285^\dagger$	$+0.0433^\dagger$	$+0.0155^\dagger$	-0.000589	-0.0055 $2^\dagger$	$+5.83\%^{\dagger}$	+0.896%
HAS-BLED Difference	$+0.0101^\dagger$	-0.000738	$+0.515^{\dagger}$	$-0.516^{\dagger}$	-0.0541 <sup>†</sup>	$+0.0393^\dagger$	$\textbf{-0.00062}^\dagger$	$+0.00432^{\dagger}$	$+29\%^\dagger$	$+0.778\%^\dagger$
PSI Difference	$+0.0152^\dagger$	$+0.0278^\dagger$	$-0.0228^{\dagger}$	$+0.0506^\dagger$	$+0.0272^\dagger$	$-0.00247^{\dagger}$	$+0.00218^{\dagger}$	$+0.00449^{\dagger}$	$+10.8\%^{\dagger}$	$+1.44\%^\dagger$

<sup>†</sup> indicates p < 0.05 for the Wilcoxon signed-rank test.

#### F.2. SET for Simplification of Tables

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We repeat the experiments performed in Table 8 via i). 1000 different bootstraps (see Table 45) and ii). 100 different data splits (see Table 46). Each table uses a different appropriate statistical significant test used in medical and machine learning literature, respectively. For all metrics the higher the better, except for Brier and ECE in which the lower the better. SET demonstrates statistically significant improved performances across most metrics across simplification of all 5 clinical scores.

## Appendix G. Abalation Studies

Clinical variable	Addition to score	Clinical variable	Addition to score
Respiratory rate (breaths/min)		Respiratory rate (breaths/min)	
≤8	3	≤3	4
9-11	1	4-9	1
21-24	2	12-34	2
$\geq 25$	3	$\geq$ 35	3
Oxygen saturations (%)		Oxygen saturations (%)	
≤91	3	≤ <u>60</u>	3
92-93	2	61-100	2
94-95	1	100-101	1
Any supplemental oxygen		Any supplemental oxygen	
Yes	2	Yes	2
Temperature (°C)		Temperature (°C)	
$\leq 35.0$	3	$\leq 9.6$	3
35.1-36.0	1	9.7-24.2	1
38.1-39.0	1	31.1-34.8	1
$\geq 39.1$	2	$\geq 34.9$	2
Systolic blood pressure (mmHg)		Systolic blood pressure (mmHg)	
≤90	3	$\leq 24$	3
91-100	2	25-46	2
101-110	1	47-116	1
$\geq$ 220	3	$\geq$ 274	3
Heart rate (beats/min)		Heart rate (beats/min)	
≤40	3	≤7	4
41-50	1	8-30	1
91-110	1	31-49	1
111-130	2	50-82	2
≥131	3	$\geq 83$	3
AVPU score		AVPU score	
Voice, Pain, or Unresponsive (V, P, U)	3	Voice, Pain, or Unresponsive (V, P, U)	1

Table 47: **Before -** NEWS.

#### G.1. Ablation: Separate Penalty Objective

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Separating penalty objective led to largely 'nonsensical' tables. We perform an ablation that treats the negative of the penalty term as the fourth objective. However this led to eventual fine-tuned clinical scoring tables with high penalties (see Table 48 where the numerical constants deviate strongly from the original table). As expected, these tables also do not perform well on the test set.

We found that this is because in every generation, many candidate scoring tables which incur high penalty still survive as long as they perform sufficiently well in the other 3 objectives, leading to a

Table 48: After - Tuned NEWS by SET with penalty as separate objective. As observed, the penalty term is hardly enforced.

search process that did not respect the penalty term as intended, influencing even the first generation of evolution. Through experimentation, we found subtracting the penalty to be the more effective approach by far, which led to SET's final choice of having the penalty term subtracted from the objectives instead.

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#### G.2. Ablation: Using Only One Objective

Table 49: Mean performance difference (and Wilcoxon signed-rank test) between SET (one-objective variant) and Original score across different data splits. Improvement in metrics due to SET (one-objective variant) are bolded. By only optimizing for one objective (i.e., Brier score), the other metrics demonstrate much poorer performance than multi-objective SET.

		•	$\Delta \mathbf{Discrim}$	ination			$\Delta  extbf{Calib}$	ration	$\Delta \mathbf{Reclass}$	sification
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
Child-Pugh Difference	-0.108 <sup>†</sup>	-0.0827 <sup>†</sup>	$-0.375^{\dagger}$	$+0.292^{\dagger}$	$+0.222^{\dagger}$	-0.0106 <sup>†</sup>	$\textbf{-0.00225}^{\dagger}$	$+0.00162^{\dagger}$	$+14\%^{\dagger}$	$+3.67\%^{\dagger}$
CIMS Difference	$+0.00283^{\dagger}$	$+0.0165^{\dagger}$	$+0.0306^{\dagger}$	-0.0142 <sup>†</sup>	-0.00218 <sup>†</sup>	$+0.00946^{\dagger}$	$\textbf{-0.000425}^\dagger$	+0.000109	$+3.81\%^{\dagger}$	$+0.897\%^\dagger$
CURB-65 Difference	$+0.0125^{\dagger}$	-0.000738	-0.0816 <sup>†</sup>	$+0.0809^{\dagger}$	$+0.0197^{\dagger}$	-0.00999†	$\textbf{-0.00273}^\dagger$	-0.00299 <sup>†</sup>	-31.4%†	$+4.28\%^{\dagger}$
GRACE Difference	-0.00515 <sup>†</sup>	-0.0714 <sup>†</sup>	-0.0657 <sup>†</sup>	-0.00567	-0.0194 <sup>†</sup>	-0.00911 <sup>†</sup>	$\textbf{-0.0187}^\dagger$	$\textbf{-0.014}^\dagger$	$+36.3\%^{\dagger}$	$+19.3\%^{\dagger}$
HAS-BLED Difference	$+0.0144^{\dagger}$	$+0.117^{\dagger}$	$+0.168^{\dagger}$	$-0.0518^{\dagger}$	$+0.0142^\dagger$	$+0.037^{\dagger}$	$\textbf{-0.00269}^\dagger$	$+0.00296^{\dagger}$	$+15.6\%^\dagger$	$+3.2\%^{\dagger}$
LACE Difference	$-0.0113^{\dagger}$	-0.0275 <sup>†</sup>	-0.621 <sup>†</sup>	$+0.593^{\dagger}$	$+0.0164^{\dagger}$	-0.0278 <sup>†</sup>	$\textbf{-0.00381}^\dagger$	$+0.00657^{\dagger}$	$+28.1\%^{\dagger}$	$+9.69\%^{\dagger}$
NEWS Difference	$-0.049^{\dagger}$	-0.00196	-0.0692 <sup>†</sup>	$+0.0672^{\dagger}$	$+0.0123^{\dagger}$	-0.000998	$\textbf{-0.00838}^\dagger$	$+0.0119^{\dagger}$	$+35.2\%^{\dagger}$	$+4.33\%^{\dagger}$
PSI Difference	-0.000128	-0.00575	$+0.111^{\dagger}$	$-0.116^{\dagger}$	-0.0496 <sup>†</sup>	$+0.0176^{\dagger}$	$\textbf{-0.00229}^{\dagger}$	$+0.0113^{\dagger}$	$+8.14\%^{\dagger}$	$+6.75\%^{\dagger}$

 $^{\dagger}$  indicates p<0.05 for the Wilcoxon signed-rank test.

We also performed an ablation study that optimizes for just one of the 3 objectives (i.e., Brier score), with the results of SET (one-objective variant) in Table 49. Comparing these results against Table 44, it becomes clear that optimizing for Brier Score alone led to much poorer performance, in which discrimination performance such as  $\mathbf{AUC}$  decreases to be even worse than the original score itself (i.e., difference of  $\mathbf{AUC} < 0$ ), and even Brier metric itself is lower on average on some problems. This exemplifies that finding good clinical scoring tables is inherently not a single-objective task, but rather a multi-objective task. In other words, optimizing for one objective alone will not automatically improve the performance on other objectives as well. Therefore, the multi-objective approach with SET uses is better and preferred.

#### G.3. Ablation: Replacing NSGA-II with Other Numerical Optimizers

In clinical scoring work, there exists alternative numerical solvers/optimizers to NSGA-II such as RiskSLIM-MINLP (Ustun and Rudin, 2019) and FasterRisk (Liu et al., 2022). In order to incorporate them into our work, we created 2 new variants of SET: SET-RS and SET-FR, which replaces the numerical solver in SET (i.e., NSGA-II) with RiskSLIMMINLP and FasterRisk respectively. We use the convention that if we specify SET without any dashes, it refers to using NSGA-II as the numerical solver by default. We report the results of SET-RS and SET-FR in Tables 50 and 51 respectively.

Comparing these results to SET (Table 44), SET demonstrates robustly better performance compared to the 2 variants, SET-RS and SET-FR, on most metrics across the 8 clinical tasks. This is due to several differences:

1. The thresholds on the left column of clinical scoring tables are not adjustable via SET-RS and SET-FR. Rather, the thresholds have to be preselected before the optimization (see Definition 1 in (Ustun and Rudin, 2019) and Eq. 1 in (Liu et al., 2022)). Therefore, the algorithms and theorems obtained from RiskSLIMMINLP and FasterRisk do not apply to optimizing the thresholds, whereas NSGA-II can optimize thresholds, allowing SET greater flexibility.

Table 50: Mean performance difference (and Wilcoxon signed-rank test) between SET-RS and Original score across different data splits. Improvement in metrics due to SET-RS are bolded.

			$\Delta { m Discrim}$	ination			$\Delta  ext{Calib}$	oration	$\Delta  ext{Reclass}$	sification
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
$\frac{\textbf{Child-Pugh}}{\text{Difference}}$	$-0.0141^{\dagger}$	$-0.0351^{\dagger}$	+0.0012	$-0.0351^{\dagger}$	$-0.0106^{\dagger}$	-0.00337 <sup>†</sup>	$+0.000323^{\dagger}$	$\textbf{-0.00652}^\dagger$	$-24.6\%^\dagger$	-0.606% <sup>†</sup>
CIMS Difference	$-0.00504^{\dagger}$	+0.000381	-0.00995 <sup>†</sup>	$+0.0103^{\dagger}$	$+0.0058^\dagger$	-0.00231 <sup>†</sup>	$+0.00205^\dagger$	$\textbf{-0.00541}^\dagger$	$-16.1\%^\dagger$	$\text{-}1.62\%^\dagger$
CURB-65 Difference	$+0.0245^\dagger$	$+0.0692^\dagger$	$+0.116^{\dagger}$	$-0.0468^{\dagger}$	$+0.0467^\dagger$	-0.00348 <sup>†</sup>	$\textbf{-0.00373}^\dagger$	-0.000476	$+36\%^\dagger$	$+3.52\%^\dagger$
GRACE Difference	$+0.0884^\dagger$	$+0.205^\dagger$	$+0.0714^\dagger$	$+0.133^{\dagger}$	$+0.159^{\dagger}$	$+0.0129^\dagger$	$\textbf{-0.00634}^\dagger$	-0.015 $2^\dagger$	<b>-</b> 2.63%	+1.91%
HAS-BLED Difference	$+0.0463^\dagger$	$+0.187^{\dagger}$	$+0.2^{\dagger}$	$-0.0135^{\dagger}$	$+0.0313^{\dagger}$	$+0.0463^{\dagger}$	$\textbf{-0.00602}^\dagger$	+0.00119	$+79.3\%^{\dagger}$	$+6.48\%^{\dagger}$
LACE Difference	$+0.0204^\dagger$	$-0.0595^{\dagger}$	$+0.114^{\dagger}$	<b>-</b> 0.173 <sup>†</sup>	-0.00589 <sup>†</sup>	$+0.042^{\dagger}$	$\textbf{-0.00142}^\dagger$	$\textbf{-0.0136}^\dagger$	$+19.8\%^{\dagger}$	$+0.738\%^{\dagger}$
NEWS Difference	$-0.0392^{\dagger}$	-0.0203 <sup>†</sup>	$-0.192^{\dagger}$	$+0.172^{\dagger}$	+0.0342	-0.00605 <sup>†</sup>	-0.000409 <sup>†</sup>	$\textbf{-0.0214}^\dagger$	$+2.43\%^{\dagger}$	$-0.171\%^{\dagger}$
PSI Difference	$-0.0201^{\dagger}$	$+0.0178^{\dagger}$	$+0.147^{\dagger}$	$-0.129^{\dagger}$	$-0.0476^{\dagger}$	$+0.0268^{\dagger}$	$+0.00606^{\dagger}$	$\textbf{-0.00625}^\dagger$	$-27.8\%^{\dagger}$	$-6.34\%^{\dagger}$

 $^{\dagger}$  indicates p < 0.05 for the Wilcoxon signed-rank test.

Table 51: Mean performance difference (and Wilcoxon signed-rank test) between SET-FR and Original score across different data splits. Improvement in metrics due to SET-FR are bolded.

			$\Delta { m Discrimi}$	nation			$\Delta  ext{Calib}$	ration	$\Delta \mathbf{Reclas}$	sification
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
Child-Pugh Difference	-0.0123 <sup>†</sup>	$-0.0486^{\dagger}$	-0.0277 <sup>†</sup>	-0.0209 <sup>†</sup>	-0.0127 <sup>†</sup>	-0.00515 <sup>†</sup>	$+0.000242^{\dagger}$	$\textbf{-0.00182}^{\dagger}$	$-27.4\%^{\dagger}$	$-0.482\%^{\dagger}$
CIMS Difference	$+0.00174^\dagger$	$+ 0.01^\dagger$	$+0.0481^{\dagger}$	-0.038 <sup>†</sup>	$-0.0155^{\dagger}$	$+0.0135^{\dagger}$	-5.95e-06	$\textbf{-0.00182}^\dagger$	$+2.31\%^{\dagger}$	$-0.317\%^{\dagger}$
CURB-65 Difference	$+0.0267^{\dagger}$	$+0.0692^\dagger$	$+0.116^{\dagger}$	-0.0468 <sup>†</sup>	$+0.0467^{\dagger}$	-0.00348 <sup>†</sup>	$\textbf{-0.00376}^\dagger$	+0.000528	$+39.9\%^{\dagger}$	$+4.31\%^{\dagger}$
GRACE Difference	$+0.0753^{\dagger}$	$+0.115^{\dagger}$	$+0.0714^{\dagger}$	$+0.0439^{\dagger}$	$+0.0502^\dagger$	$+0.011^{\dagger}$	$+0.0107^{\dagger}$	$+0.00726^{\dagger}$	-15.3% <sup>†</sup>	-11.2% <sup>†</sup>
HAS-BLED Difference	$+0.0116^{\dagger}$	$+0.114^{\dagger}$	$+0.168^{\dagger}$	$-0.0545^{\dagger}$	$+0.0135^\dagger$	$+0.0369^{\dagger}$	$\textbf{-0.00274}^\dagger$	$+0.00278^{\dagger}$	$+13.7\%^{\dagger}$	$+3.18\%^{\dagger}$
LACE Difference	$+0.0219^{\dagger}$	-0.0595 <sup>†</sup>	$+0.114^{\dagger}$	-0.173 <sup>†</sup>	-0.00589 <sup>†</sup>	$+0.042^{\dagger}$	$-0.000843^{\dagger}$	$\textbf{-0.0177}^\dagger$	$+10.8\%^\dagger$	$+0.354\%^{\dagger}$
NEWS Difference	-0.0111 <sup>†</sup>	$-0.0203^{\dagger}$	$-0.192^{\dagger}$	$+0.172^{\dagger}$	+0.0275	-0.00605 <sup>†</sup>	-0.0001	$\textbf{-0.0219}^\dagger$	$-6.68\%^{\dagger}$	-0.369% <sup>†</sup>
PSI Difference	$-0.0185^{\dagger}$	$+0.0198^{\dagger}$	$+0.172^{\dagger}$	$-0.153^{\dagger}$	$-0.0538^{\dagger}$	$+0.0328^{\dagger}$	$+0.00112^{\dagger}$	- $0.0169^\dagger$	$-15\%^\dagger$	$-3.43\%^\dagger$

† indicates p < 0.05 for the Wilcoxon signed-rank test.

2. While NSGA-II can optimize for discrimination, calibration and reclassification objectives concurrently, the works in RiskSLIMMINLP and FasterRisk can only optimize a single surrogate objective, the logistic loss, as specified in Definition 1 in (Ustun and Rudin, 2019) and Eq. 1 in (Liu et al., 2022). Thus, SET, which uses NSGA-II, is better poised to create fine-tuned scores that have increased performance in all 3 areas: discrimination, calibration and reclassification.

996

998

1000

1002

1003

3. NSGA-II allows for flexibility in the objectives, allowing us to create novel objectives (i.e., Active AUC, Active Brier), which quantifies improvements relative to original baseline score, whereas RiskSLIMMINLP and FasterRisk have fixed objectives. Thus, NSGA-II is better aligned to the mission of this paper to improve existing clinical scoring tables.

Table 52: Mean performance difference (and Wilcoxon signed-rank test) between AdaBoost and Original score across different data splits. Improvement in metrics due to AdaBoost are bolded.

-			Discrimin	ation			Calib	oration	Reclass	ification
	AUC	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	NRI	IDI
Child-Pugh Difference	$+0.02^{\dagger}$	+0.0154	-0.0523 <sup>†</sup>	$+0.0676^{\dagger}$	$+0.0156^{\dagger}$	-0.000653	$+0.0318^{\dagger}$	$+0.0714^{\dagger}$	$+4.02\%^{\dagger}$	-0.0935%
CIMS Difference	$+0.00977^\dagger$	$+0.0247^{\dagger}$	$-0.0143^{\dagger}$	$+0.039^{\dagger}$	$+0.0294^\dagger$	-0.000862	$+0.0964^{\dagger}$	$+0.19^{\dagger}$	-7.6% <sup>†</sup>	$-19.1\%^\dagger$
CURB-65 Difference	$-0.0435^{\dagger}$	-0.081†	$-0.348^{\dagger}$	$+0.267^{\dagger}$	$+0.0794^\dagger$	$-0.0291^{\dagger}$	$+0.0298^{\dagger}$	$+0.0704^{\dagger}$	$-5.08\%^{\dagger}$	$-12.9\%^\dagger$
GRACE Difference	+0.00984	$-0.185^{\dagger}$	-0.387 <sup>†</sup>	$+0.202^{\dagger}$	+0.236	-0.0262 <sup>†</sup>	$\textbf{-0.0166}^\dagger$	$\textbf{-0.00763}^\dagger$	$+3.16\%^\dagger$	$+2.3\%^{\dagger}$
HAS-BLED Difference	$+0.122^\dagger$	$+0.0823^{\dagger}$	$-0.092^{\dagger}$	$+0.174^{\dagger}$	$+0.0525^\dagger$	-0.00202	$+0.0159^{\dagger}$	$+0.072^{\dagger}$	$+39.2\%^\dagger$	$+8.45\%^{\dagger}$
LACE Difference	$-0.351^{\dagger}$	-0.233 <sup>†</sup>	-0.799 <sup>†</sup>	$+0.567^{\dagger}$	-0.0932 <sup>†</sup>	-0.0919 <sup>†</sup>	$+0.0286^{\dagger}$	$+0.0466^{\dagger}$	-29.8% <sup>†</sup>	$-4.32\%^{\dagger}$
NEWS Difference	$+0.0674^\dagger$	$+0.107^{\dagger}$	$+0.336^{\dagger}$	-0.229 <sup>†</sup>	$+0.0429^{\dagger}$	$+0.0505^\dagger$	$+0.0857^{\dagger}$	$+0.167^{\dagger}$	$+19.2\%^{\dagger}$	$+5.66\%^\dagger$
PSI Difference	$-0.0367^{\dagger}$	$-0.0462^{\dagger}$	$+0.0147^{\dagger}$	-0.0609 <sup>†</sup>	-0.0455 <sup>†</sup>	-0.00189	$+0.0172^{\dagger}$	$+0.0191^{\dagger}$	<b>-</b> 17.7% <sup>†</sup>	-6.37% <sup>†</sup>

<sup>†</sup> indicates p < 0.05 for the Wilcoxon signed-rank test.

## Appendix H. Comparison with AdaBoost

Tree-based machine learning models can be said to be related to clinical scoring table since both use thresholds. Typically, tree-based models utilize many thresholds sequentially which makes it incompatible and too different with scoring tables. However, **AdaBoost** (Friedman et al., 2000) in particular, is an ensemble of tree stumps, which allows it to be converted into a scoring table, albeit with scoring components that are non-integer values and with potentially many more thresholds than a typical scoring table.

Here, we fit AdaBoost to the same features as used in the original clinical scoring table, without any threshold values (e.g., Age is given as feature to AdaBoost instead of a binary feature such as Age≥ 65), in the same way data is provided to SET. We compare the performance of AdaBoost against the original clinical scores in Table 52. By comparing these improvements with the improvements by SET (see Table 44), the results show that SET still yields better test performance (across multiple metrics and multiple clinical scores) even when compared to a more complex model such at AdaBoost (which tends to overfit), suggesting that SET's novel choice of building upon domain-experts-crafted existing clinical scoring tables help to identify high-quality generalizable components and thresholds that traditional machine learning algorithms do not incoporate.

#### Appendix I. More Dataset Details

This paper works on eight scores: Child-Pugh score (Child and Turcotte, 1964) using 913 samples with 0.0832 prevalence rate of outcome from Chang et al. (2020), COVID in-hospitality mortality score (CIMS) (Dueñas-Espín et al., 2023) using 4742 samples with 0.23 prevalence rate of outcome from Dueñas-Espín et al. (2023), CURB-65 score (Lim et al., 2003) using 646 samples with 0.0991 prevalence rate of outcome from Millman et al. (2017), GRACE score (Fox et al., 2006) using 188 samples with 0.101 prevalence rate of outcome from Zhu et al. (2020), HAS-BLED score (Pisters et al., 2010) using 1588 samples with 0.115 prevalence rate of outcome from AlAmmari et al. (2021), LACE score (Van Walraven et al., 2010) using 463 samples with 0.0778 prevalence rate of outcome from Robinson and Hudali (2017), NEWS (RCoP, 2012) using 2204 samples with 0.425 prevalence rate of outcome from Mitsunaga et al. (2019), and PSI score (Fine et al., 1997) using 1138 samples with 0.16 prevalence rate of outcome from Chang et al. (2024).

Table 53: Performance metrics of original score and SET fine-tuned score, an an alternative solution on the Pareto front of NSGA-II in SET. For all metrics except  $c^*$ , Brier and ECE, the higher the better. For Brier and ECE, the lower the better.

	Discrimination								Calibrat	Reclassification		
	AUC	$c^*$	Youden Index	Sensitivity	Specificity	PPV	NPV	Brier	ECE	HL p-value	NRI	IDI
HAS-BLED												
Original	0.687	4	0.293	0.767	0.526	0.173	0.946	0.0997	0.00692	0.992	0.00%	0.00%
SET	0.700	4	0.389	0.918	0.471	0.184	0.978	0.0988	0.0179	0.963	+4.74%	+2.07%
SET (Another Solution)	0.699	4	0.387	0.918	0.469	0.183	0.978	0.0989	0.0186	0.953	+3.32%	+2.07%

## Appendix J. Exploring Other Solutions on Pareto Set

Recall each candidate score  $\mathbf{x}$  is evaluated using:

$$F(\mathbf{x}) = [\sigma(\Delta_{\text{AUC}} - P(\mathbf{x})), \sigma(\Delta_{\text{Brier}} - P(\mathbf{x})), \mathbb{I}(\text{NRI})]$$

where  $\sigma$  is the ReLU function.

Also recall that, once NSGA-II converges, the best candidate solution is selected based on its overall performance across discrimination, calibration, and reclassification metrics while adhering to the imposed constraints and eventually based on the crowding distance selection rules in NSGA-II. Suppose we want to select a score with lower  $\sigma(\Delta_{\text{AUC}} - P(\mathbf{x}))$  and higher  $\sigma(\Delta_{\text{Brier}} - P(\mathbf{x}))$  that does not follow the crowding distance selection rule, we can search for such a score on the Pareto front of the output of NSGA-II manually. In HAS-BLED for instance, such a score exists on the Pareto front. In Table 53, we label this score as 'SET (Another Solution)'. However, do note that this Pareto front is assessed based on the objectives in NSGA-II which is on the train set, the performance on the test set, as seen in Table 53, may be different, in which the alternative SET solution performs worse on both AUC and Brier when compared to SET, although the

#### Appendix K. Genetic Algorithms and NSGA-II

Brier score objective was better on the train set during optimization.

Genetic algorithms are a class of population-based optimization techniques inspired by the principles of natural selection and evolutionary biology. They work by evolving a population of candidate solutions over multiple generations. Each candidate solution, often represented as a vector or chromosome, is evaluated using a fitness function that quantifies its quality with respect to the objective. The algorithm then selects the fittest individuals to reproduce, generating new candidate solutions through recombination (crossover) and random mutation. Over time, the population converges toward better solutions, making GAs particularly effective for complex, nonlinear, or poorly understood search spaces.

NSGA-II is a widely used genetic algorithm designed specifically for multi-objective optimization problems, where two or more objectives may be in conflict. Rather than seeking a single optimal solution, NSGA-II identifies a set of Pareto-optimal solutions, each representing a trade-off between competing objectives. It improves upon earlier approaches by introducing a fast non-dominated sorting procedure, which ranks individuals based on levels of dominance in the population. It also introduces a crowding-distance metric to promote diversity along the Pareto front, ensuring that solutions are well spread out. Additionally, NSGA-II uses an elitist strategy, combining parent and offspring populations before selecting the next generation, which helps preserve the best solutions discovered so far.