

## Appendix E1

### Calculating the CT GAP Score

Step 1: Calculate the CT GAP score ( $S$ ):

$$S = [0.364 \cdot (M - .707) - 0.0146 \cdot (FVC - 66.763) + 0.131 \cdot (AGE1 - 67.676) - 0.0814 \cdot (AGE2) + 0.0287 \cdot (FIB - 22.147)],$$

where  $M$  is 1 if the patient is male and 0 if the patient is female; AGE1 is the patient's age in years; AGE2 is the value in Table E1 that corresponds with the patient's age. Enter the value of AGE2 that corresponds to the patient's age in years; FIB = CT fibrosis score.

Step 2: Calculate risk by using  $S$ :

$$1\text{-year risk} = 100 \cdot [1 - \exp(-\exp(S) \cdot 0.280)]$$

$$2\text{-year risk} = 100 \cdot [1 - \exp(-\exp(S) \cdot 0.555)]$$

$$3\text{-year risk} = 100 \cdot [1 - \exp(-\exp(S) \cdot 0.918)]$$

**Table E1. AGE2 Values for Calculating CT GAP Score**

Patient Age	AGE2 Value
≤50	0
51	0
52	0
53	0
54	0
55	0
56	0.002
57	0.015
58	0.051
59	0.121
60	0.236
61	0.408
62	0.648
63	0.968
64	1.378
65	1.890
66	2.516
67	3.266
68	4.153
69	5.183
70	6.345
71	7.625
72	9.009
73	10.481
74	12.027
75	13.632
76	15.280
77	16.959

Patient Age	AGE2 Value
78	18.652
79	20.348
80	22.043
81	23.739
82	25.435
83	27.130
84	28.826
85	30.522
86	32.217
87	33.913
88	35.609
89	37.304

**Table E2. Relationships between the CT Quantitative Scores and Individual GAP Predictors**

GAP Predictor	Data	<i>P</i> Value
CT fibrosis score		
Sex		
Male	22.9	.041
Female	20.2	
Age	0.18*	.001
FVC	-0.47*	<.001
DLCO	-0.37*	<.001
Able to perform DLCO?		
Yes	21.1	<.001
No	36.4	
Calculated GAP score	0.49*	<.001
CT emphysema score		
Gender		
Male	0.56	.158
Female	0.40	
Age	0.04*	.419
FVC	0.17*	.001
DLCO	-0.29*	<.001
Able to perform DLCO?		
Yes	0.52	.632
No	0.42	
Calculated GAP score	0.10*	.055

Note.—Unless otherwise indicated, data are sample means (for categorical variables).

\* Data are Spearman correlation coefficient (*r*) reported for continuous variables.

**Table E3. CT Fibrosis and Emphysema Scores and Risk of Death after Adjustment for Physiologic Variables**

Variable	Cohort 1 (n = 176)		Cohort 2 (n = 172)		Combined Cohort (n = 348)	
	Subdistribution Hazard Ratio	P Value	Subdistribution Hazard Ratio	P Value	Subdistribution Hazard Ratio	P Value
<b>Fibrosis score + FVC</b>						
FVC	0.99 (0.98, 1.00)	.137	0.99 (0.97, 1.00)	.133	0.99 (0.98, 1.00)	.028
Fibrosis score	1.03 (1.01, 1.06)	.005	1.02 (1.00, 1.04)	.065	1.03 (1.01, 1.05)	<.001
<b>Fibrosis score + DLCO</b>						
DLCO	0.98 (0.97, 1.00)	.035	0.96 (0.94, 0.99)	.002	0.98 (0.96, 0.99)	.001
Fibrosis score	1.02 (1.00, 1.05)	.077	1.00 (0.98, 1.03)	.820	1.02 (1.00, 1.03)	.059
<b>Fibrosis score + FVC + DLCO</b>						
FVC	0.99 (0.98, 1.01)	.342	1.00 (0.98, 1.01)	.766	0.99 (0.99, 1.00)	.298
DLCO	0.98 (0.97, 1.00)	.063	0.96 (0.94, 0.99)	.003	0.98 (0.96, 0.99)	.002
Fibrosis score	1.02 (1.00, 1.05)	.099	1.00 (0.98, 1.03)	.899	1.01 (1.00, 1.03)	.104
<b>Emphysema score + FVC</b>						
FVC	0.98 (0.97, 0.99)	.008	0.98 (0.97, 0.99)	.003	0.98 (0.97, 0.99)	<.001
Emphysema score	1.36 (1.09, 1.69)	.006	1.10 (0.90, 1.34)	.385	1.22 (1.05, 1.41)	.008
<b>Emphysema score + DLCO</b>						
DLCO	0.98 (0.96, 0.99)	.003	0.96 (0.94, 0.98)	<.001	0.97 (0.96, 0.98)	<.001
Emphysema score	1.13 (0.92, 1.38)	.229	0.96 (0.75, 1.23)	.742	1.05 (0.90, 1.22)	.549
<b>Emphysema score + FVC + DLCO</b>						
FVC	0.99 (0.97, 1.00)	.085	1.00 (0.98, 1.01)	.788	0.99 (0.98, 1.00)	.068
DLCO	0.98 (0.97, 1.00)	.058	0.96 (0.94, 0.98)	.001	0.98 (0.96, 0.99)	.001
Emphysema score	1.25 (0.99, 1.60)	.064	0.97 (0.75, 1.25)	.817	1.11 (0.94, 1.33)	.211

Note.—Data are subdistribution hazard ratios, with 95% CIs based on competing risks regression analysis.

**Table E4. Prognostic Value of CT Fibrosis Score and CT Emphysema Score When Added to the GAP Model**

Variables	Cohort 1 (n = 176)	Cohort 2 (n = 172)	Combined Cohort (n = 348)
<b>GAP score</b>			
C index	71.5 (65.7, 76.9)	69.5 (64.2, 76.3)	70.7 (66.4, 74.5)
<b>GAP score + fibrosis score</b>			
C index	71.4 (65.1, 76.2)	68.6 (61.3, 73.6)	70.7 (66.9, 74.4)
Change in C index	0.0 (-2.8, 1.8)	-1.0 (-2.2, -0.5)	0.0 (-1.8, 0.5)
NRI	0.0* (-9.3, 9.3)	0.0*	1.3 (-3.8, 6.4)
Clinical NRI	0.0* (-13.0, 13.0)	0.0*	1.2 (-6.1, 8.6)
<b>GAP score + emphysema score</b>			
C index	71.6 (64.7, 76.5)	68.7 (61.7, 73.4)	70.7 (66.7, 74.5)
Change in C index	0.2 (-1.1, 2.4)	-0.8 (-1.8, -0.6)	0.0 (-1.3, 0.4)
NRI	5.8 (-3.4, 14.9)	-1.1 (-5.5, 3.4)	1.8 (-1.1, 4.7)
Clinical NRI	4.7 (-9.4, 18.8)	-0.8 (-7.9, 6.3)	1.6 (-3.1, 6.4)

Note.—Data are percentages, with 95% bootstrap CIs in parentheses.

\* Symmetric reclassification occurred in cohort 1, and no reclassification occurred in cohort 2.

**Table E5. Death Risk Analysis of the GAP Score with CT Fibrosis and Emphysema Scores**

Variables	Radiologist 1		Radiologist 2		Averaged	
	Subdistribution Hazard Ratio	P Value	Subdistribution Hazard Ratio	P Value	Subdistribution Hazard Ratio	P Value
<b>Unadjusted Analysis</b>						
GAP score	3.28 (2.54, 4.23)	<.001	3.28 (2.54, 4.23)	<.001	3.28 (2.54, 4.23)	<.001
Fibrosis score	1.03 (1.01, 1.04)	<.001	1.04 (1.02, 1.05)	<.001	1.03 (1.02, 1.05)	<.001
Emphysema score	1.12 (0.98, 1.28)	.085	1.16 (1.00, 1.34)	.056	1.15 (1.00, 1.32)	.052
<b>Adjusted Analysis</b>						
<b>Model 1</b>						
GAP score	3.05 (2.30, 4.03)	<.001	2.97 (2.21, 3.98)	<.001	2.98 (2.23, 3.98)	<.001
Fibrosis score	1.01 (0.99, 1.02)	.185	1.01 (1.00, 1.03)	.143	1.01 (1.00, 1.03)	.149
<b>Model 2</b>						
GAP score	3.27 (2.53, 4.22)	<.001	3.27 (2.52, 4.23)	<.001	3.26 (2.52, 4.22)	<.001
Emphysema score	1.07 (0.93, 1.24)	.335	1.11 (0.94, 1.31)	.228	1.09 (0.93, 1.28)	.264

Note.—Unless otherwise indicated, data are subdistribution hazard ratios with 95% CIs in parentheses. Analysis restricted to subjects in the combined cohort with dual radiological readings. n = 334 of 348.

**Table E6. Performance of the GAP Score with CT Fibrosis and Emphysema Scores**

Variables	Radiologist 1	Radiologist 2	Averaged
GAP score			
C index	71.5 (68.0, 75.0)	71.5 (68.0, 75.0)	71.5 (68.0, 75.0)
GAP score + fibrosis score			
C index	71.4 (67.7, 74.8)	71.4 (67.5, 75.0)	71.4 (67.3, 74.9)
Change in C index	-0.1 (-1.6, 0.5)	-0.1 (-1.5, 0.5)	-0.1 (-1.3, 0.5)
NRI	1.3 (-3.4, 6.1)	0.3 (-5.2, 5.8)	0.4 (-5.1, 6.0)
Clinical NRI	1.3 (-5.9, 8.6)	0.7 (-7.4, 8.7)	0.9 (-7.6, 9.4)
GAP score + emphysema score			
C index	71.5 (67.6, 75.2)	71.7 (67.6, 75.1)	71.5 (67.7, 74.6)
Change in C index	0.0 (-1.1, 0.4)	0.1 (-2.2, 0.4)	0.0 (-1.2, 0.6)
NRI	-2.0 (-5.4, 1.5)	-1.9 (-4.9, 1.2)	-2.0 (-5.4, 1.5)
Clinical NRI	-2.0 (-6.3, 2.3)	-1.8 (-5.8, 2.2)	-2.0 (-6.3, 2.3)

Note.—Data are percentages, with 95% bootstrap CIs in parentheses. Analysis restricted to subjects in the combined cohort with dual radiology reads,  $n = 334$  of 348.