

## **Online Data Supplement**

### **CT Honeycombing Identifies a Progressive Fibrotic Phenotype with Increased Mortality Across Diverse Interstitial Lung Diseases**

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**Table E1.** Summary of CT scanners, image acquisition and reconstruction techniques used for assessment of CT Honeycombing

CT machine	Image Acquisition	Reconstruction protocols
<b>University of Chicago</b>		
Philips Brilliance 16 and 64-slice scanners Philips Brilliance iCT 256-slice scanners (Philips Medical System, Cleveland Inc, United States)	Supine helical CT acquisition was performed during end-inspiration at 120 kVp, 220 mAs. End-expiratory phase helical CT images (120 kVp, 60 mA) and end-inspiration 1 mm prone series (axial 1.2mm thick x 10mm) were also obtained.	Inspiratory supine: CT images were reconstructed using a 512 x 512-pixel image matrix. Axial images were reconstructed contiguously at 1 mm and 3 mm slice thickness using a lung reconstruction algorithm. Coronal and sagittal images were created at 2.5 mm thickness. Expiratory: 3 mm axial contiguous reconstruction Prone: Axial 1.2mm thick x 10mm
<b>Evanston Hospital</b>		
SIEMENS Somatom Definition Flash 128 Slices (Siemens Healthcare GmbH)	Unenhanced Scan Scan: Spiral CAREkV: 120kV CAREDose4D: 150 Qual Ref mAs Detector Configuration: 128 x 0.6 mm Pitch Factor: 0.6 Rotation Time: 0.5 sec	Recon 1 - Kernel: I41f, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: SAFIRE 1 Recon 2 - Kernel: I41f, Plane: Coronal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: SAFIRE 1 Recon 3 - Kernel: I41f, Plane: Sagittal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: SAFIRE 1 Recon 4 - Kernel: I70f, Plane: Axial, Slice Thickness: 2 mm Slice Interval: 2 mm IR: SAFIRE 1 Recon 5 - Kernel: I70f, Plane: Axial MIP Slice Thickness:8 mm Slice Interval: 4 mm IR: SAFIRE 1
SIEMENS Somatom Definition AS 64 Slices (Siemens Healthcare GmbH)	Unenhanced Scan Scan: Spiral CAREkV: 120kV CAREDose4D: 180 Qual Ref mAs Detector Configuration: 64 x 0.6 mm Pitch Factor: 0.7 Rotation Time: 0.5 sec	Recon 1 - Kernel: B31f, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: NA Recon 2 - Kernel: B31f, Plane: Coronal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: NA Recon 3 - Kernel: B31f, Plane: Sagittal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: NA Recon 4 - Kernel: B75f, Plane: Axial, Slice Thickness: 2 mm Slice Interval: 2 mm IR: NA Recon 5 - Kernel: B75f, Plane: Axial MIP Slice Thickness:8 mm Slice Interval: 4 mm IR: NA
GE LightSpeed VCT 64 Slices (GE Healthcare)	Unenhanced Scan Scan: Helical kV: 120kV Auto mA: 100 - 500 mA Range Ref Noise Index: 12 Detector Configuration: 64 x 0.625 mm Pitch Factor: 0.984 Rotation Time: 0.5 sec	Recon 1 - Algorithm: Standard Plus, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: No Recon 2 - Algorithm: Lung, Full, Plane: Axial, Slice Thickness: 2.5 mm Slice Interval: 2.5 mm IR: No Recon 3 - Algorithm: Standard, Plus, Plane: Axial, Slice Thickness: 0.625 mm Slice Interval: 0.625 mm IR: No Recon 4 - Algorithm: Standard Plus, Plane: Coronal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: No Recon 5 - Algorithm: Standard Plus, Plane: Sagittal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: No
<b>Glenbrook Hospital</b>		
SIEMENS Somatom Definition AS 64 Slices (Siemens Healthcare GmbH)	Unenhanced Scan Scan: Spiral CAREkV: 120kV CAREDose4D: 180 Qual Ref mAs Detector Configuration: 64 x 0.6 mm Pitch Factor: 0.7 Rotation Time: 0.5 sec	Recon 1 - Kernel: I41f, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: SAFIRE 1 Recon 2 - Kernel: I41f, Plane: Coronal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: SAFIRE 1 Recon 3 - Kernel: I41f, Plane: Sagittal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: SAFIRE 1 Recon 4 - Kernel: I70f, Plane: Axial, Slice Thickness: 2 mm Slice Interval: 2 mm IR: SAFIRE 1 Recon 5 - Kernel: I70f, Plane: Axial MIP, Slice Thickness: 8 mm Slice Interval: 4 mm IR: SAFIRE 1
GE LightSpeed VCT 64 Slices (GE Healthcare)	Unenhanced Scan Scan: Helical kV: 120kV Auto mA: 200 - 300 mA Range Ref Noise Index: 11.57 Detector Configuration: 64 x 0.625 mm Pitch Factor: 1.375 Rotation Time: 0.6 sec	Recon 1 - Algorithm: Standard Plus, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: No Recon 2 - Algorithm: Lung, Full, Plane: Axial, Slice Thickness: 2.5 mm Slice Interval: 2.5 mm IR: No Recon 3 - Algorithm: Standard, Plus, Plane: Axial, Slice Thickness: 0.625 mm Slice Interval: 0.625 mm IR: No Recon 4 - Algorithm: Lung, Plus, Plane: Axial MIP, Slice Thickness: 8 mm Slice Interval: 4 mm IR: No Recon 5 - Algorithm: Standard Plus, Plane: Sagittal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: No

**Table E1(cont'd).** Summary of CT scanners, image acquisition and reconstruction techniques used for assessment of CT Honeycombing

CT machine	Image Acquisition	Reconstruction protocols
<b>Highland Park Hospital</b>		
SIEMENS Somatom Sensation 64 Slices (Siemens Healthcare GmbH)	Unenhanced Scan Scan: Spiral kV: 120kV CAREdose4D: 240 Qual Ref mAs Detector Configuration: 64 x 0.6 mm Pitch Factor: 0.7 Rotation Time: 0.5 sec	Recon 1 - Kernel: B31f, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: NA Recon 2 - Kernel: B31f, Plane: Coronal, Slice Thickness: 3 mm Slice Interval: 3 mm IR: NA Recon 3 - Kernel: B31f, Plane: Sagittal, Slice Thickness: 3 mm Slice Interval: 3 mm IR: NA Recon 4 - Kernel: B80f, Plane: Axial, Slice Thickness: 3 mm Slice Interval: 3 mm IR: NA Recon 5 - Kernel: B80f, Plane: Axial MIP Slice Thickness:8 mm Slice Interval: 4 mm IR: NA
<b>Skokie Hospital</b>		
SIEMENS Somatom Definition AS 64 Slices (Siemens Healthcare GmbH)	Unenhanced Scan Scan: Spiral CAREKV: 120kV CAREdose4D: 150 Qual Ref mAs Detector Configuration: 64 x 0.6 mm Pitch Factor: 0.8 Rotation Time: 0.5 sec	Recon 1 - Kernel: I41f, Plane: Axial, Slice Thickness: 5 mm Slice Interval: 5 mm IR: SAFIRE 1 Recon 2 - Kernel: I41f, Plane: Coronal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: SAFIRE 1 Recon 3 - Kernel: I41f, Plane: Sagittal, Slice Thickness: 4 mm Slice Interval: 4 mm IR: SAFIRE 1 Recon 4 - Kernel: I70f, Plane: Axial, Slice Thickness: 2 mm Slice Interval: 2 mm IR: SAFIRE 1 Recon 5 - Kernel: I70f, Plane: Axial MIP, Slice Thickness: 8 mm Slice Interval: 4 mm IR: SAFIRE 1

**Table E2.** Baseline Characteristics of Study Population at Tertiary and Non-Tertiary Medical Centers Stratified by CT Honeycombing depicting *P*-values for Subgroup Comparisons

Characteristics	Tertiary Center (n=852)			Non-tertiary Centers (n=478)		
	CT Honeycombing Absent (n=517)	CT Honeycombing Present (n=335)	<i>P</i> -value	CT Honeycombing Absent (n=321)	CT Honeycombing Present (n=157)	<i>P</i> -value
Age, years	62.8 (12.8)	65.8 (11.5)	<0.001	71.5 (12.2)	73.0 (10.9)	0.21
Male	249 (48.2)	192 (57.3)	0.009	141 (43.9)	78 (49.7)	0.24
<i>Race/Ethnicity</i>						
White	382 (73.9)	241 (71.9)	0.53	254 (79.1)	132 (84.1)	0.20
Black	89 (17.2)	60 (17.9)	0.79	21 (6.5)	5 (3.2)	0.13
Hispanic	30 (5.8)	25 (7.5)	0.36	7 (2.2)	2 (1.3)	0.49
Asian	16 (3.1)	9 (2.7)	0.73	24 (7.5)	11 (7.0)	0.85
Ever Smoker	285 (55.1)	218 (65.1)	0.004	44 (13.7)	27 (17.2)	0.31
Body mass index, kg.m <sup>2</sup>	30.7 (6.9)	28.8 (6.1)	<0.001	28.5 (6.7)	27.2 (4.6)	0.02
<i>Clinical features</i>						
Crackles	408 (80.6)	287 (86.2)	0.04	111 (64.9)	65 (75.6)	0.08
Clubbing	53 (10.3)	72 (21.5)	<0.001	21 (6.6)	15 (9.6)	0.25
<i>Lung Function</i>						
FVC (% predicted)	67.2 (19.4)	62.2 (17.2)	<0.001	71.6 (19.0)	74.0 (19.5)	0.20
DL <sub>CO</sub> (% predicted)	55.1 (22.7)	45.8 (19.3)	<0.001	47.3 (19.0)	46.9 (20.5)	0.82
Oxygen therapy	133 (25.7)	132 (39.4)	<0.001	95 (29.7)	40 (25.5)	0.34
Immunosuppressive therapy	183 (36.5)	163 (50.5)	<0.001	226 (70.4)	96 (61.2)	0.04
<i>HRCT fibrosis</i>						
Reticulation	392 (75.8)	256 (76.4)	0.84	140 (43.6)	72 (45.9)	0.64
Traction bronchiectasis	73 (14.1)	166 (49.6)	<0.001	84 (26.2)	76 (48.4)	<0.001
Antifibrotic therapy	29 (5.6)	12 (3.6)	0.18	34 (10.6)	26 (16.7)	0.06
Time from CT to ILD diagnosis, months	6.2 (21.7)	5.4 (22.7)	0.62	0.7 (24.6)	3.3 (25.7)	0.29
<i>ILD sub-category</i>						
Idiopathic pulmonary fibrosis	213 (41.2)	128 (38.2)	0.38	186 (57.9)	112 (71.3)	0.005
Connective tissue disease -ILD	148 (28.6)	104 (31.0)	0.45	6 (1.9)	7 (4.5)	0.10
Unclassifiable/Others	80 (15.5)	45 (13.4)	0.41	122 (38.0)	36 (22.9)	0.001
Chronic hypersensitivity pneumonitis	76 (14.7)	58 (17.3)	0.001	7 (2.2)	2 (1.3)	0.49

Total sample size, n=1,330. \*Categorical variables presented as n (%); continuous variables presented as means (SD). Exception for participants; Body mass index, n=1247; crackles, n=1096; clubbing, n=1329; FVC=forced vital capacity, n=1265; DL<sub>CO</sub> = diffusing capacity of the lungs, n=1191; immunosuppressive therapy, n=1302. ILD=interstitial lung disease; IPF=idiopathic pulmonary fibrosis, n=639; CTD-ILD=connective tissue disease associated-ILD, n=265; CHP=chronic hypersensitivity pneumonitis, n=143; Unclassifiable/Other ILD, n=283.

**Table E3.** Agreement between Original Documentation and Imaging Re-read of CT Honeycombing

<b>Variable measured</b>	<b>Agreement</b>	<b>Expected Agreement</b>	<b>Kappa (95% CI)</b>	<b>Std. Error</b>	<b>P - Value</b>
CT Honeycombing present	68.1%	50.2%	0.36 (0.26 – 0.46)	0.0523	<0.001

*Inter-observer agreement calculated using kappa statistics in subset of participants with imaging re-read scored for CT honeycombing. Imaging re-read was performed only in CTs from study participants at the tertiary center. On original documentation, CT honeycombing n=154 (107 confirmed, 47 refuted), no CT honeycombing n=207 (139 confirmed, 68 refuted); On imaging re-read, CT honeycombing n=175 (107 confirmed, 68 refuted), no CT honeycombing n=186 (139 confirmed, 47 refuted). Abbreviations: CT=computerized tomography; Std=standard.*

**Table E4.** Association between CT Honeycombing and Mortality with Multiple Imputation for Missing Data

<b>ILD Category</b>	<b>Adjusted Mortality Hazard*</b>	
	<b>HR (95% CI)</b>	<b>P-value</b>
All ILD (n=1330)	1.58 (1.26 - 1.97)	<0.001
<i>ILD Subtype</i>		
IPF	1.03 (0.75 - 1.40)	0.87
CHP	1.90 (0.89 - 4.08)	0.10
CTD-ILD	2.74 (1.48 - 5.05)	0.001
Unclassifiable <sup>+</sup>	1.88 (1.16 - 3.05)	0.01

*Multiple imputation for missing data (n=88) performed iteratively by using chained equations. ILD=interstitial lung disease; IPF=idiopathic pulmonary fibrosis, n=639; CTD-ILD=connective tissue disease associated-ILD, n=265; CHP=chronic hypersensitivity pneumonitis, n=143; <sup>+</sup>subgroup includes unclassifiable ILD, n=192, and other ILD, n=91; Adjusted=adjusted for hospital center, gender, age, forced vital capacity, diffusing capacity of the lungs for carbon monoxide, and immunosuppressive therapy; \*computed using Cox proportional hazard models.*

**Table E5.** Mortality Hazard in ILD with CT Honeycombing (n=1,330)

<b>Models evaluated</b>	<b>Adjusted Mortality Hazard</b>	
	<b>HR (95% CI)</b>	<b>P-value</b>
CT-Honeycombing	1.62 (1.29-2.02)	<0.001
CT-Honeycombing adjusted for reticulation only	1.55 (1.24-1.95)	<0.001
CT-Honeycombing adjusted for traction bronchiectasis only	1.58 (1.24-2.02)	<0.001
CT-Honeycombing adjusted for reticulation and traction bronchiectasis	1.60 (1.25-2.04)	<0.001

*ILD=interstitial lung disease; Adjusted=adjusted for hospital center, gender, age, forced vital capacity, diffusing capacity of the lungs for carbon monoxide, and immunosuppressive therapy*

**Table E6.** Association between CT Honeycombing and Mortality in ILD cohort with imaging re-read (n=361)

Characteristics	CT Honeycombing Present	CT Honeycombing Absent	P-value
Participants	n=175	n=186	
Mean survival time, months (95% CI)	62 (52-72)	110 (94-126)	<0.001
Mortality, n (%)	74 (42.3)	43 (23.1)	<0.001
Absolute mortality rate (events per person-year)	0.15	0.07	<0.001
Hazard ratio (unadjusted, 95% CI)	2.21 (1.51-3.23)	-	<0.001
Hazard ratio (adjusted <sup>+</sup> , 95% CI)	1.44 (0.97-2.14)	-	0.07
Extent of CT Honeycombing (% involvement) <sup>*</sup>			
Hazard ratio (unadjusted)	1.50 (1.25-1.80)	-	<0.001
Hazard ratio (adjusted <sup>+</sup> )	1.40 (1.13-1.74)	-	0.002
Lung transplantation, n (%)	12 (6.9)	11 (5.9)	0.71

*Hazard ratios computed using Cox proportional hazard models; <sup>+</sup>adjusted=adjusted for hospital center, gender, age, forced vital capacity, diffusing capacity of the lungs, ILD subtype, and immunosuppressive therapy. Imaging re-read was performed only in CTs from study participants at the tertiary center. <sup>\*</sup>Percent involvement of CT Honeycombing scored incrementally with 5% intervals; ILD=interstitial lung disease. Distribution of ILD subtypes, IPF=idiopathic pulmonary fibrosis, n=234; CTD-ILD=connective tissue disease associated-ILD, n=5; Unclassifiable ILD, n=4, CHP=chronic hypersensitivity pneumonitis, n=118.*



**Table E7.** \*Diagnostic confidence of UIP stratified by CT Honeycombing in cohort# with imaging re-read (n=361)

Characteristics	CT Honeycombing Present n=175	CT Honeycombing Absent n=186
UIP, n (%)	75 (62.0)	56 (35.9)
Probable UIP, n (%)	7 (5.8)	32 (20.5)
Indeterminate, n (%)	4 (3.3)	3 (1.92)
Alternative diagnosis, n (%)	35 (28.9)	65 (41.7)

\*Diagnostic confidence per ATS 2018 guidelines (*Am J Respir Crit Care Med.* 2018 Sep 1;198(5):e44-e68). #Baseline CT scan images from 84 subjects could not be optimally re-scored for UIP diagnostic confidence. Patients designated as Probable UIP were categorized previously as possible UIP. Distribution of ILD subtypes, IPF=idiopathic pulmonary fibrosis, n=234; CTD-ILD=connective tissue disease associated-ILD, n=5; Unclassifiable ILD, n=4, CHP=chronic hypersensitivity pneumonitis, n=118.

**Table E8.** Radiologist scoresheets with scores for dichotomous presence/absence of honeycombing and extent in cohort with imaging re-read (n=361)

CT chest Re-read				Original CT Report			
Subject	Honeycombing	Extent	Honeycombing	Subject	Honeycombing	Extent	Honeycombing
Subj001	Absent	< 5%	Absent	Subj061	Absent	N/A	Present
Subj002	Present	< 5%	Absent	Subj062	Absent	N/A	Present
Subj003	Absent	< 5%	Absent	Subj063	Present	10%	Present
Subj004	Absent	< 5%	Absent	Subj064	Present	< 5%	Present
Subj005	Absent	< 5%	Absent	Subj065	Present	< 5%	Present
Subj006	Present	< 5%	Present	Subj066	Present	5%	Present
Subj007	Absent	< 5%	Absent	Subj067	Present	< 5%	Present
Subj008	Present	< 5%	Present	Subj068	Present	5%	Present
Subj009	Absent	< 5%	Absent	Subj069	Present	< 5%	Present
Subj010	Absent	< 5%	Absent	Subj070	Present	15%	Present
Subj011	Absent	< 5%	Absent	Subj071	Absent	N/A	Absent
Subj012	Absent	< 5%	Absent	Subj072	Present	5%	Present
Subj013	Absent	< 5%	Absent	Subj073	Absent	N/A	Present
Subj014	Absent	< 5%	Present	Subj074	Absent	N/A	Present
Subj015	Absent	N/A	Present	Subj075	Absent	N/A	Present
Subj016	Absent	N/A	Present	Subj076	Present	10%	Present
Subj017	Absent	< 5%	Present	Subj077	Absent	N/A	Present
Subj018	Absent	N/A	Absent	Subj078	Present	< 5%	Present
Subj019	Absent	< 5%	Absent	Subj079	Absent	N/A	Present
Subj020	Absent	< 5%	Present	Subj080	Present	5%	Present
Subj021	Absent	N/A	Absent	Subj081	Present	< 5%	Present
Subj022	Absent	< 5%	Absent	Subj082	Absent	< 5%	Present
Subj023	Absent	N/A	Present	Subj083	Present	< 5%	Present
Subj024	Absent	N/A	Present	Subj084	Present	5%	Present
Subj025	Absent	N/A	Present	Subj085	Absent	N/A	Present
Subj026	Absent	< 5%	Absent	Subj086	Present	< 5%	Present
Subj027	Absent	N/A	Absent	Subj087	Present	< 5%	Present
Subj028	Present	10%	Present	Subj088	Present	< 5%	Present
Subj029	Present	5%	Present	Subj089	Absent	N/A	Present
Subj030	Present	< 5%	Present	Subj090	Present	< 5%	Present
Subj031	Present	10%	Present	Subj091	Present	< 5%	Present
Subj032	Present	< 5%	Present	Subj092	Present	5%	Present
Subj033	Present	20%	Present	Subj093	Absent	N/A	Present
Subj034	Present	< 5%	Present	Subj094	Present	5%	Present
Subj035	Absent	N/A	Present	Subj095	Present	10%	Present
Subj036	Present	5%	Present	Subj096	Present	10%	Present
Subj037	Absent	N/A	Present	Subj097	Absent	N/A	Present
Subj038	Absent	N/A	Present	Subj098	Present	5%	Present
Subj039	Present	5%	Present	Subj099	Present	5%	Present
Subj040	Present	< 5%	Present	Subj100	Present	5%	Present
Subj041	Present	5%	Present	Subj101	Absent	N/A	Present
Subj042	Present	< 5%	Present	Subj102	Absent	N/A	Present
Subj043	Present	< 5%	Present	Subj103	Present	10%	Present
Subj044	Absent	N/A	Present	Subj104	Present	10%	Present
Subj045	Present	5%	Present	Subj105	Absent	N/A	Present
Subj046	Present	< 5%	Present	Subj106	Absent	N/A	Present
Subj047	Absent	N/A	Present	Subj107	Absent	N/A	Present
Subj048	Present	15%	Present	Subj108	Present	< 5%	Present
Subj049	Present	5%	Present	Subj109	Present	< 5%	Present
Subj050	Present	5%	Present	Subj110	Present	10%	Present
Subj051	Present	N/A	Present	Subj111	Absent	N/A	Present
Subj052	Absent	N/A	Present	Subj112	Present	10%	Present
Subj053	Present	< 5%	Present	Subj113	Absent	N/A	Present
Subj054	Absent	N/A	Present	Subj114	Absent	N/A	Present
Subj055	Present	5%	Present	Subj115	Absent	N/A	Present
Subj056	Present	< 5%	Present	Subj116	Present	5%	Present
Subj057	Present	15%	Present	Subj117	Present	5%	Present
Subj058	Present	5%	Present	Subj118	Present	< 5%	Present
Subj059	Absent	N/A	Present	Subj119	Present	< 5%	Present
Subj060	Present	< 5%	Present	Subj120	Present	< 5%	Present

**Table E8.** (contd') Radiologist scoresheets with scores for dichotomous presence/absence of honeycombing and extent in cohort with imaging re-read (n=361)

CT chest Re-read				Original CT Report			
Subject	Honeycombing	Extent	Honeycombing	Subject	Honeycombing	Extent	Honeycombing
Subj121	Present	< 5%	Present	Subj181	Absent	N/A	Absent
Subj122	Present	5%	Absent	Subj182	Present	< 5%	Absent
Subj123	Absent	< 5%	Absent	Subj183	Absent	< 5%	Absent
Subj124	Present	< 5%	Absent	Subj184	Present	< 5%	Absent
Subj125	Present	< 5%	Absent	Subj185	Absent	N/A	Absent
Subj126	Absent	N/A	Absent	Subj186	Absent	N/A	Absent
Subj127	Present	5%	Absent	Subj187	Absent	N/A	Absent
Subj128	Present	5%	Absent	Subj188	Absent	N/A	Absent
Subj129	Absent	< 5%	Absent	Subj189	Absent	< 5%	Absent
Subj130	Absent	N/A	Absent	Subj190	Absent	N/A	Absent
Subj131	Absent	N/A	Absent	Subj191	Absent	< 5%	Absent
Subj132	Absent	N/A	Absent	Subj192	Present	< 5%	Absent
Subj133	Absent	N/A	Absent	Subj193	Present	< 5%	Absent
Subj134	Present	< 5%	Absent	Subj194	Present	5%	Absent
Subj135	Present	5%	Absent	Subj195	Present	< 5%	Absent
Subj136	Present	5%	Absent	Subj196	Present	5%	Absent
Subj137	Absent	< 5%	Absent	Subj197	Present	< 5%	Absent
Subj138	Absent	N/A	Absent	Subj198	Present	< 5%	Absent
Subj139	Present	15%	Absent	Subj199	Present	5%	Absent
Subj140	Present	5%	Absent	Subj200	Present	< 5%	Absent
Subj141	Absent	N/A	Absent	Subj201	Absent	< 5%	Absent
Subj142	Absent	N/A	Absent	Subj202	Absent	N/A	Absent
Subj143	Absent	N/A	Absent	Subj203	Present	< 5%	Absent
Subj144	Absent	< 5%	Absent	Subj204	Absent	N/A	Absent
Subj145	Absent	< 5%	Absent	Subj205	Present	< 5%	Absent
Subj146	Absent	N/A	Absent	Subj206	Absent	N/A	Absent
Subj147	Present	< 5%	Absent	Subj207	Absent	< 5%	Absent
Subj148	Present	< 5%	Absent	Subj208	Absent	< 5%	Absent
Subj149	Present	< 5%	Absent	Subj209	Absent	< 5%	Absent
Subj150	Present	5%	Absent	Subj210	Absent	N/A	Absent
Subj151	Present	5%	Absent	Subj211	Present	5%	Absent
Subj152	Present	5%	Absent	Subj212	Absent	N/A	Absent
Subj153	Present	< 5%	Absent	Subj213	Present	5%	Absent
Subj154	Present	< 5%	Absent	Subj214	Absent	N/A	Absent
Subj155	Present	< 5%	Absent	Subj215	Present	10%	Absent
Subj156	Present	< 5%	Absent	Subj216	Absent	< 5%	Absent
Subj157	Absent	N/A	Absent	Subj217	Present	< 5%	Absent
Subj158	Absent	N/A	Absent	Subj218	Present	10%	Absent
Subj159	Present	15%	Absent	Subj219	Present	5%	Absent
Subj160	Absent	< 5%	Absent	Subj220	Present	5%	Absent
Subj161	Absent	N/A	Absent	Subj221	Present	5%	Absent
Subj162	Present	< 5%	Absent	Subj222	Present	< 5%	Absent
Subj163	Absent	N/A	Absent	Subj223	Present	5%	Absent
Subj164	Absent	< 5%	Absent	Subj224	Absent	< 5%	Absent
Subj165	Absent	N/A	Absent	Subj225	Present	< 5%	Absent
Subj166	Present	< 5%	Absent	Subj226	Present	10%	Absent
Subj167	Absent	N/A	Absent	Subj227	Present	< 5%	Absent
Subj168	Present	< 5%	Absent	Subj228	Absent	N/A	Absent
Subj169	Absent	< 5%	Absent	Subj229	Present	< 5%	Absent
Subj170	Present	< 5%	Absent	Subj230	Present	5%	Absent
Subj171	Absent	N/A	Absent	Subj231	Absent	N/A	Absent
Subj172	Absent	< 5%	Absent	Subj232	Absent	N/A	Absent
Subj173	Absent	N/A	Absent	Subj233	Present	< 5%	Absent
Subj174	Absent	N/A	Absent	Subj234	Absent	N/A	Absent
Subj175	Absent	< 5%	Absent	Subj235	Absent	N/A	Absent
Subj176	Present	5%	Absent	Subj236	Absent	N/A	Absent
Subj177	Absent	N/A	Absent	Subj237	Present	5%	Absent
Subj178	Absent	N/A	Absent	Subj238	Absent	N/A	Absent
Subj179	Absent	N/A	Absent	Subj239	Absent	N/A	Absent
Subj180	Absent	N/A	Absent	Subj240	Absent	N/A	Absent

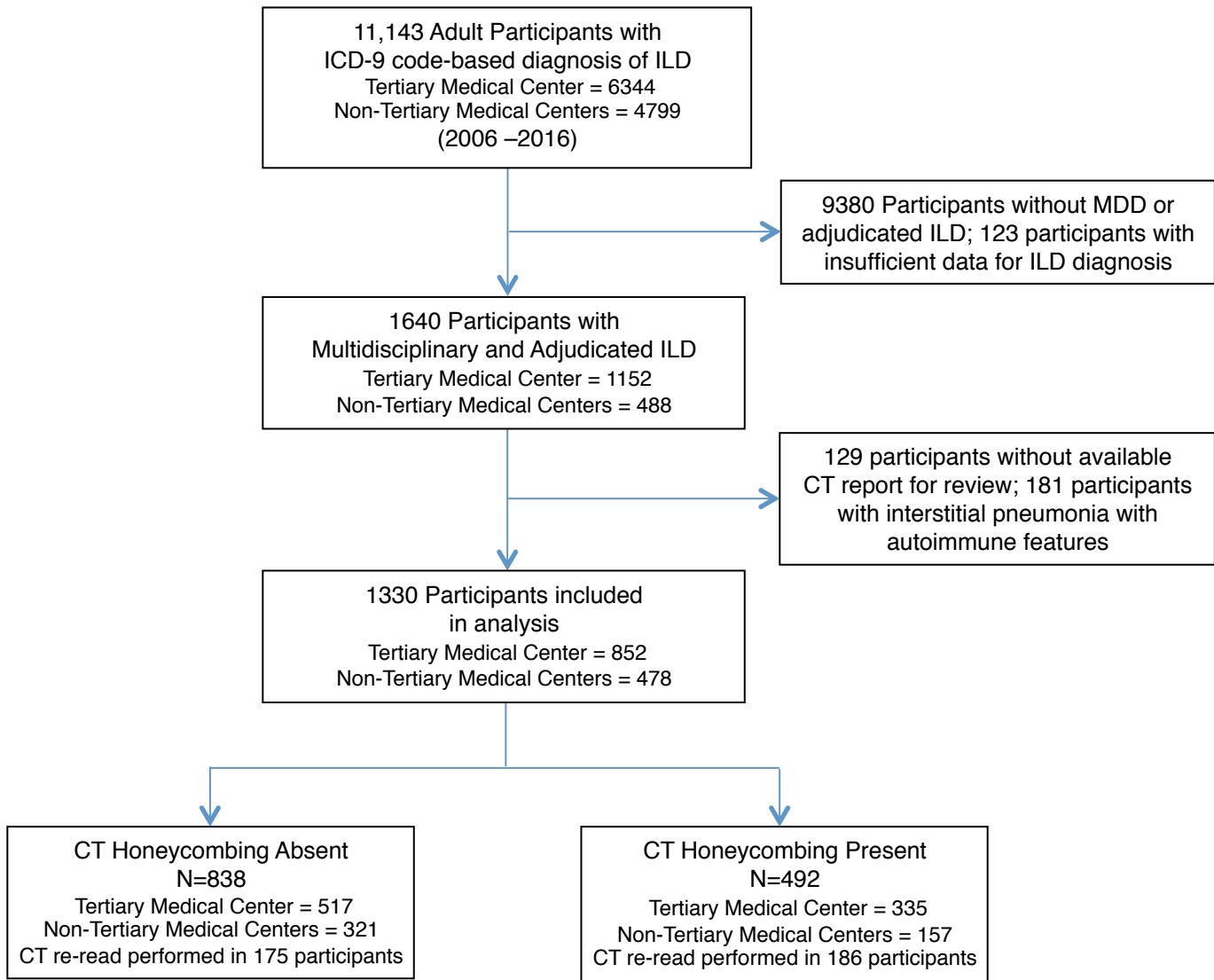
**Table E8.** (contd') Radiologist scoresheets with scores for dichotomous presence/absence of honeycombing and extent in cohort with imaging re-read (n=361)

CT chest Re-read		Original CT Report		CT chest Re-read		Original CT Report	
Subject	Honeycombing	Extent	Honeycombing	Subject	Honeycombing	Extent	Honeycombing
Subj241	Absent	< 5%	Absent	Subj302	Present	5%	Present
Subj242	Absent	< 5%	Absent	Subj303	Absent	< 5%	Absent
Subj243	Present	5%	Present	Subj304	Present	5%	Absent
Subj244	Absent	< 5%	Absent	Subj305	Absent	< 5%	Absent
Subj245	Absent	< 5%	Absent	Subj306	Present	< 5%	Present
Subj246	Present	< 5%	Present	Subj307	Absent	< 5%	Present
Subj247	Present	< 5%	Present	Subj308	Present	5%	Absent
Subj248	Absent	< 5%	Absent	Subj309	Absent	< 5%	Absent
Subj249	Present	5%	Present	Subj310	Present	< 5%	Present
Subj250	Present	< 5%	Absent	Subj311	Absent	N/A	Absent
Subj251	Present	5%	Present	Subj312	Absent	< 5%	Absent
Subj252	Absent	< 5%	Present	Subj313	Absent	< 5%	Absent
Subj253	Present	10%	Present	Subj314	Absent	< 5%	Absent
Subj254	Present	< 5%	Absent	Subj315	Present	5%	Present
Subj255	Present	5%	Present	Subj316	Absent	< 5%	Present
Subj256	Present	5%	Present	Subj317	Present	5%	Present
Subj257	Present	< 5%	Present	Subj318	Present	< 5%	Present
Subj258	Present	< 5%	Present	Subj319	Absent	< 5%	Absent
Subj259	Absent	< 5%	Absent	Subj320	Present	5%	Absent
Subj260	Present	5%	Present	Subj321	Absent	< 5%	Absent
Subj261	Absent	< 5%	Absent	Subj322	Absent	< 5%	Absent
Subj262	Present	10%	Present	Subj323	Absent	< 5%	Present
Subj263	Present	10%	Present	Subj324	Absent	< 5%	Absent
Subj264	Present	5%	Present	Subj325	Absent	< 5%	Absent
Subj265	Absent	< 5%	Absent	Subj326	Absent	< 5%	Absent
Subj266	Absent	< 5%	Absent	Subj327	Absent	< 5%	Absent
Subj267	Present	< 5%	Present	Subj328	Absent	< 5%	Absent
Subj268	Present	5%	Present	Subj329	Present	5%	Present
Subj269	Absent	< 5%	Absent	Subj330	Absent	< 5%	Absent
Subj270	Present	< 5%	Absent	Subj331	Present	5%	Present
Subj271	Absent	< 5%	Absent	Subj332	Present	< 5%	Absent
Subj272	Absent	< 5%	Absent	Subj333	Present	< 5%	Present
Subj273	Present	5%	Present	Subj334	Present	< 5%	Present
Subj274	Absent	< 5%	Absent	Subj335	Absent	< 5%	Absent
Subj275	Present	5%	Present	Subj336	Absent	< 5%	Absent
Subj276	Absent	< 5%	Absent	Subj337	Absent	< 5%	Absent
Subj277	Present	10%	Present	Subj338	Present	10%	Present
Subj278	Absent	< 5%	Absent	Subj339	Absent	< 5%	Absent
Subj279	Present	< 5%	Absent	Subj340	Absent	< 5%	Present
Subj280	Absent	< 5%	Present	Subj341	Present	5%	Present
Subj281	Absent	< 5%	Absent	Subj342	Present	< 5%	Present
Subj282	Present	< 5%	Present	Subj343	Absent	< 5%	Absent
Subj283	Absent	< 5%	Absent	Subj344	Present	5%	Present
Subj284	Absent	< 5%	Absent	Subj345	Absent	< 5%	Absent
Subj285	Absent	< 5%	Absent	Subj346	Absent	< 5%	Absent
Subj286	Present	20%	Absent	Subj347	Absent	< 5%	Present
Subj287	Absent	< 5%	Absent	Subj348	Present	10%	Present
Subj288	Absent	< 5%	Present	Subj349	Absent	< 5%	Absent
Subj289	Present	15%	Present	Subj350	Absent	< 5%	Absent
Subj290	Present	< 5%	Absent	Subj351	Absent	< 5%	Absent
Subj291	Absent	< 5%	Absent	Subj352	Absent	< 5%	Absent
Subj292	Absent	< 5%	Absent	Subj353	Absent	< 5%	Absent
Subj293	Absent	< 5%	Present	Subj354	Absent	< 5%	Absent
Subj294	Absent	< 5%	Absent	Subj355	Present	< 5%	Present
Subj295	Absent	< 5%	Absent	Subj356	Absent	< 5%	Absent
Subj296	Absent	< 5%	Absent	Subj357	Absent	< 5%	Absent
Subj297	Absent	< 5%	Absent	Subj358	Present	5%	Present
Subj298	Present	< 5%	Present	Subj359	Absent	< 5%	Absent
Subj299	Absent	< 5%	Absent	Subj360	Present	< 5%	Present
Subj300	Present	< 5%	Present	Subj361	Present	5%	Absent
Subj301	Absent	< 5%	Present				

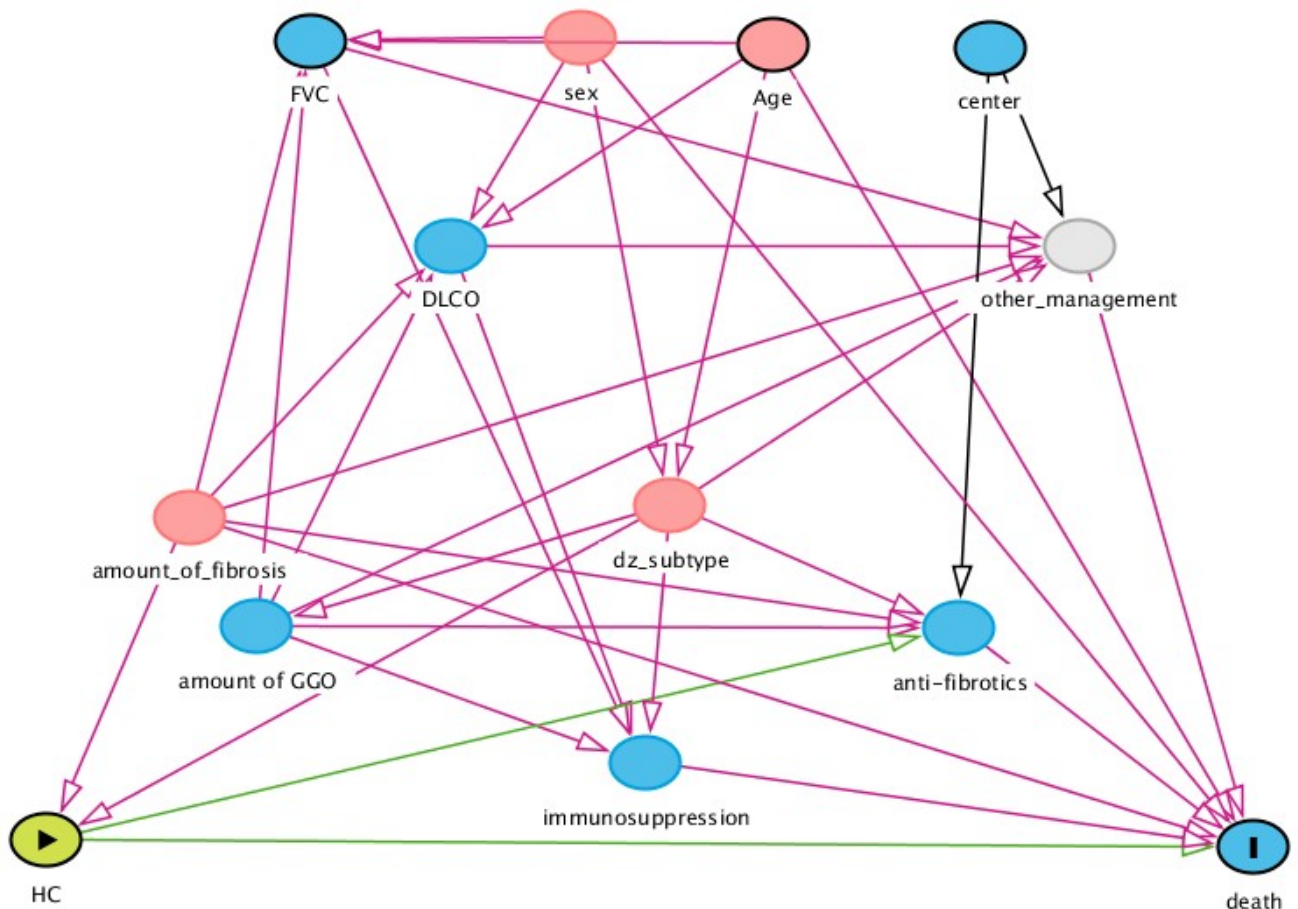
**Table E9.** Mortality Hazard in ILD stratified by Tertiary vs. Non-tertiary medical center

Characteristics	Tertiary Medical Center (n=852)		Non-Tertiary Medical Centers (n=478)	
	HR (95% CI)	P-value	HR (95% CI)	P-value
CT Honeycombing	1.85 (1.43-2.38)	<0.001	1.29 (0.90-1.86)	0.17
CT Honeycombing( <i>adj.</i> )	1.49 (1.14-1.94)	0.003	1.44 (0.99-2.09)	0.06

*adj.*=adjusted for hospital center, gender, age, forced vital capacity, diffusing capacity of the lungs, ILD subtype, and immunosuppressive therapy. ILD=interstitial lung disease



**Figure E1.** STROBE diagram. ILD= interstitial lung disease



**Figure E2.** Directed Acyclic Graph (DAG) specifying variables considered in analytic models for CT Honeycombing and mortality in ILD. HC=CT honeycombing; FVC=forced vital capacity; DLCO=diffusing capacity of the lungs; dz\_subtype= ILD subtype; amount of fibrosis = composite measure of the extent of fibrosis including reticulation and traction bronchiectasis; GGO=ground glass opacities; ILD= interstitial lung disease