SUPPLEMENTARY MATERIAL

WAITING LIST DYNAMICS AND LUNG TRANSPLANTATION OUTCOMES AFTER INTRODUCTION OF THE LUNG ALLOCATION SCORE IN THE NETHERLANDS

T.W. Hoffman[1], A.C. Hemke[2], P. Zanen,[1,3] B. Luijk[3], R.A.S. Hoek[4], E.A.M. Verschuuren[5]. D.A. van Kessel[1,3]

1. Department of Pulmonology, St. Antonius Hospital, Nieuwegein, The Netherlands

2. Dutch Transplant Foundation, Leiden, The Netherlands

3. Department of Pulmonology, Division of Heart and Lungs, University Medical Center Utrecht, Utrecht, The Netherlands

4. Department of Pulmonology, Erasmus University Medical Center, Rotterdam, The Netherlands

5. Department of Pulmonology, University Medical Center Groningen, Groningen, The Netherlands

Corresponding author: Dr. D.A. van Kessel, Department of Pulmonology, St. Antonius Hospital, Koekoekslaan 1, 3435CM, Nieuwegein, The Netherlands. Telephone: +31 88 320 1471; email: d.kessel@antoniusziekenhuis.nl

Figure S1: study flow chart

Candidates who were not transplanted, removed from the waiting list, or died on the waiting list, were still on the waiting list on 31 December 2019.
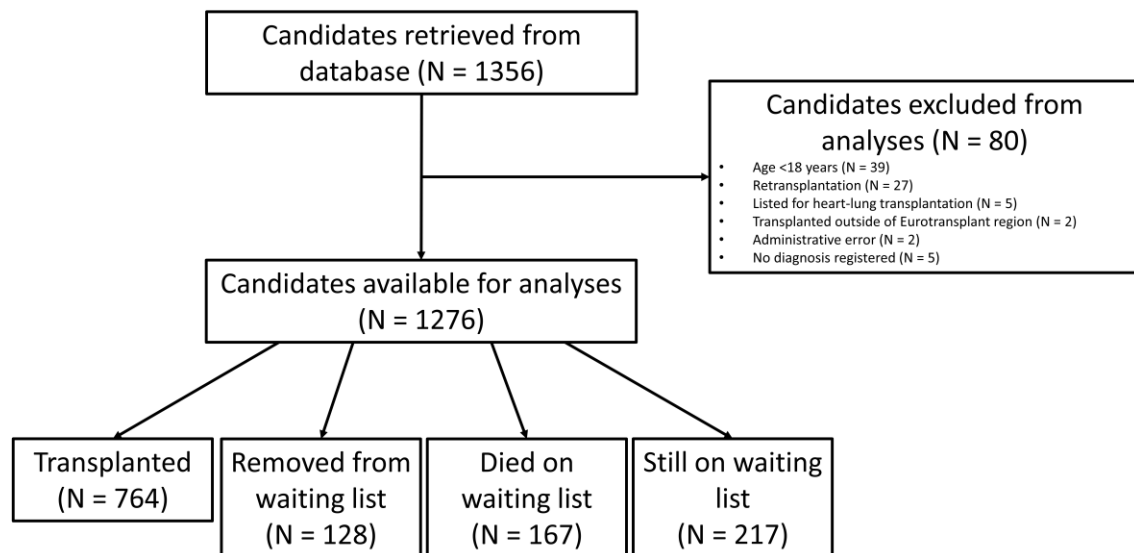
Figure S2: patients removed from waiting list

The annual number of patients removed from the waiting list did not significantly change after introduction of the LAS (p=1.00; Wilcoxon Signed Ranks test; 2014 excluded).
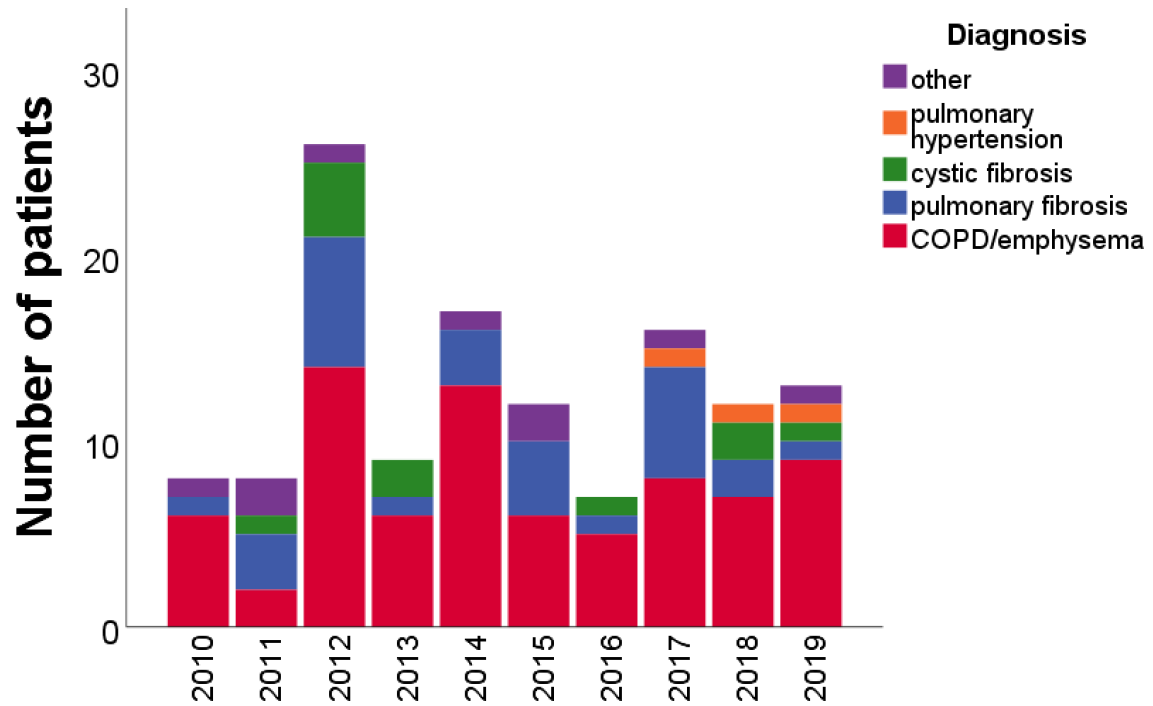
Table S1: diagnosis categories for the included patients, subdivided into five groups Bronchiolitis obliterans did not include patients listed for re-transplantation.

Chronic obstructive pulmonary disease or emphysema	- Chronic obstructive pulmonary disease - Alpha-1 antitrypsin deficiency
Pulmonary fibrosis	- Idiopathic pulmonary fibrosis - Other pulmonary fibrosis - Connective-tissue disease associated interstitial lung disease - Sarcoidosis
Cystic fibrosis	Cystic fibrosis
Pulmonary hypertension	- Pulmonary arterial hypertension - Chronic thrombo-embolic pulmonary hypertension
Other	- Bronchiolitis obliterans - Lymphangioleiomyomatosis - Pulmonary vascular disease, not specified - Pulmonary Langerhans' cell histiocytosis - Bronchiectasis - Inhalation burns - Eisenmenger syndrome - Other lung disease

Table S2: hazard ratios for waiting list mortality, dependent on diagnosis category

Hazard ratios were calculated using time-dependent Cox-regression. The overall risk for waiting list mortality was not different prior to and after the introduction of the LAS. COPD/emphysema was used as the reference diagnosis category. 95% CI = 95 % confidence interval

Variable	Hazard-ratio (95% CI)	p-value
LAS versus pre-LAS	1.624 (0.969-2.728)	0.067
Center 2 versus center 1	0.476 (0.318-0.714)	<0.001
Center 3 versus center 1	0.497 (0.331-0.745)	0.001
Diagnosis (compared to COPD)		
• Pulmonary fibrosis	3.596 (2.126-6.083)	<0.001
• Cystic fibrosis	1.360 (0.631-2.931)	0.432
• Pulmonary hypertension	5.438 (1.844-16.036)	0.002
• Other	1.670 (0.636-4.381)	0.297
LAS versus pre-LAS * diagnosis (compared to COPD)		
• Pulmonary fibrosis	0.580 (0.288-1.169)	0.128
• Cystic fibrosis	1.007 (0.348-2.910)	0.990

• Pulmonary hypertension	0.338(0.085-1.334)	0.121
• Other	0.402 (0.072-2.242)	0.299

Table S3: hazard ratios for waiting list mortality or removal from waiting list because patients were unfit for transplantation, dependent on diagnosis category

Hazard ratios were calculated using time-dependent Cox-regression. The overall chance of waiting list mortality or removal from waiting list because a patient was unfit for transplantation was significantly higher after the introduction of the LAS. The chance of waiting list mortality or removal from the waiting list because a patient was unfit for transplantation was significantly higher for patients with pulmonary fibrosis compared to patients with COPD/emphysema. COPD/emphysema was used as the reference diagnosis category. 95% CI = 95 % confidence interval

Variable	Hazard-ratio (95% CI)	p-value
LAS versus pre-LAS	1.522 (1.003-2.308)	0.048
Center 2 versus center 1	0.602 (0.376-0.963)	0.034
Center 3 versus center 1	1.030 (0.690-1.539)	0.883
Diagnosis (compared to COPD)		
• Pulmonary fibrosis	2.483 (1.686-3.657)	<0.001
• Cystic fibrosis	1.041 (0.596-1.815)	0.889
• Pulmonary hypertension	1.808 (0.643-5.083)	0.262
• Other	1.378 (0.703-2.702)	0.350
LAS versus pre-LAS * diagnosis (compared to COPD)		

• Pulmonary fibrosis	0.653 (0.384-1.110)	0.115
• Cystic fibrosis	0.956 (0.425-2.151)	0.913
• Pulmonary hypertension	0.676 (0.194-2.358)	0.539
• Other	0.766 (0.263-2.232)	0.625

Table S4: hazard ratios for transplantation, dependent on diagnosis category

Hazard ratios were calculated using Cox-regression. Overall, patients with a pulmonary fibrosis, cystic fibrosis, or other diagnoses had a higher chance of transplantation compared to patients with COPD. COPD/emphysema was used as the reference diagnosis category. 95% CI = 95 % confidence interval

Variable	Hazard-ratio (95% CI)	p-value
Diagnosis (compared to COPD)		
• Pulmonary fibrosis	1.477 (1.104-1.978)	0.009
• Cystic fibrosis	1.890 (1.418-2.519)	<0.001
• Pulmonary hypertension	1.675 (0.924-3.035)	0.089
• Other	1.576 (1.049-2.367)	0.026

Table S5: hazard ratios for transplantation, dependent on diagnosis category

Hazard ratios were calculated using a Fine-Gray analysis. Overall, patients with a pulmonary fibrosis, cystic fibrosis, or other diagnoses had a higher chance of transplantation compared to patients with COPD. The interaction between center and period (pre-LAS or LAS) was not significant, and was removed from the model. COPD/emphysema was used as the reference diagnosis category. 95% CI = 95 % confidence interval

Variable	Hazard-ratio (95% CI)	p-value
LAS versus pre-LAS	0.972 (0.764-1.187)	0.784
Center 2 versus center 1	1.273 (1.070-1.513)	0.006
Center 3 versus center 1	1.519 (1.342-1.887)	<0.001
Diagnosis (compared to COPD)		
• Pulmonary fibrosis	1.966 (1.573-2.534)	<0.001
• Cystic fibrosis	2.118 (1.517-2.956)	<0.001
• Pulmonary hypertension	0.931 (0.547-1.580)	0.792
• Other	2.046 (1.361-3.076)	<0.001
LAS versus pre-LAS * diagnosis (compared to COPD)		
• Pulmonary fibrosis	1.632 (1.170-2.276)	0.004

• Cystic fibrosis	1.164 (0.769-1.761)	0.473
• Pulmonary hypertension	0.897(0.413-1.948)	0.748
• Other	1.586 (0.913-2.754)	0.102

Table S6: mean LAS at outcome, stratified by diagnosis category and outcome

ANCOVA was used with LAS at outcome as the dependent variable, LAS at waiting list placement as covariate and diagnosis category and outcome as fixed effects. These analyses only include patients in whom the outcome happened after the introduction of the LAS.

Diagnosis	Outcome	Mean LAS at outcome (95% CI)
COPD/emphysema	Died on waiting list (n=37)	38.35 (33.48-43.23)
	Transplanted (n=201)	39.79 (36.76-42.82)
	Removed from waiting list (n=31)	37.84 (32.52-43.16)
Pulmonary fibrosis	Died on waiting list (n=38)	57.30 (53.18-61.42)
	Transplanted (n=207)	48.34 (46.55-50.13)
	Removed from waiting list (n=11)	39.18 (31.65-46.72)
Cystic fibrosis	Died on waiting list (n=9)	56.59 (48.23-64.95)
	Transplanted (n=92)	45.60 (42.99-48.21)
	Removed from waiting list (n=4)	68.19 (55.55-80.83)
Pulmonary hypertension	Died on waiting list (n=7)	49.83 (40.25-59.42)
	Transplanted (n=27)	41.01 (36.20-45.82)

	Removed from waiting list (n=1)	40.98 (15.90-66.05)
Other	Died on waiting list (n=2)	47.46 (25.40-69.53)
	Transplanted (n=40)	45.72 (41.73-49.71)
	Removed from waiting list (n=4)	36.41 (23.89-48.94)