Pulmonary Function Tests as Outcomes for Systemic Sclerosis Interstitial Lung Disease

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Supplemental Material

e-APPENDIX 1: Detailed MEDLINE (PubMed) Search Strategy

AND AND

OR

Systemic Sclerosis	Interstitial Lung Disease	Pulmonary Function Test
"scleroderma, systemic" [mesh]	"lung diseases, interstitial"[mesh:noexp]	"lung volume measurements"[mesh]
CREST syndrome[tw]	"pulmonary fibrosis"[mesh:noexp]	"pulmonary gas exchange"[mesh]
scleroderma[tw]	fibrosing alveolitis[tw]	"pulmonary ventilation"[mesh]
SSc[tw]	ILD[tw]	"spirometry"[mesh]
systemic sclerosis[tw]	interstitial lung disease[tw]	alveolar volume[tw]
	interstitial pneumon*[tw]	diffusi*[tw]
	lung fibrosis[tw]	DLCO[tw]
	NSIP[tw]	expiratory flow[tw]
	pulmonary fibrosis[tw]	expiratory volume[tw]
	restrictive lung disease[tw]	FEF*[tw]
	UIP[tw]	FEV1[tw]
		FRC[tw]
		functional residual capacity[tw]
		FVC[tw]
		gas exchange[tw]
		KCO[tw]
		lung capacity[tw]
		lung function[tw]
		lung test[tw]
		lung volume[tw]
		PEF[tw]
		PFT[tw]
		pulmonary function[tw]
		pulmonary test[tw]
		respiratory function[tw]
		respiratory test[tw]
		spirometry[tw]
		TLC[tw]
		TLCO[tw]
		transfer capacity[tw]
		VC[tw]
		vital capacity[tw]

Screens: 1949 – Present

e-APPENDIX 2: Reasons for Study Exclusion by Screening Stage

Primary Screen: Titles and Abstracts (1,415 Excluded Records)		**Secondary Screen: Full-Text Assessment (384 Excluded Records)**	
-Duplicate	25	-Duplicate	4
-Not in English or in French	87	-Not in English or in French	6
-Not Original Research	467	-Not Original Research	18
-Unrelated to SSc-ILD	654	-Unrelated to/Unclear if SSc-ILD	25
-Did Not Validate or Use PFTs as Outcomes in SSc-ILD	51	-Did Not Validate or Use PFTs as Outcomes in SSc-ILD	86
		-Unclear which PFTs Used	33
-Did Not Have a Minimum of 20 SSc Patients at Baseline	131	-Did Not Have a Minimum of 20 SSc Patients at Baseline	11
		-Did Not Focus Primarily on SSc-ILD	56
		-Other Reason	11
		-Cross-Sectional Outcome Study	134

ILD: Interstitial Lung Disease; PFT: Pulmonary Function Test; SSc: Systemic Sclerosis.

e-APPENDIX 3: Characteristics of the Outcome Studies (N = 170)

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Schneider et al. 1982[1]	United States	Cohort Study (Hospital Discharge Records)	38 (74% Female)	44 (17-65)	DLCO Absolute, FEV_1 Absolute, FEV_1/FVC, FVC Absolute	N/A	N/A
Konig et al. 1984[2]	Germany	Cohort Study	101	N/R	DLCO%, TLC%, VC%	DLCO%	Most Sensitive PFT
Peters-Golden et al. 1984[3]	United States	Cohort Study (Rheumatology Unit)	24 (92% Female)	46.1 ± 2.61 (19-67)	DLCO Absolute, FEV_1/FVC, FVC Absolute, FVC%, TLC Absolute, TLC%	N/A	N/A
Steen et al. 1985[4]	United States	Cohort Study (Hospital Records)	92 (73% Female)	N/R	DLCO%, FEV_1/FVC, FVC%	N/A	N/A
De Clerck et al. 1987[5]	Belgium	Cohort Study	23	47.6 ± 10.3 (28-63)	DLCOcorr%, DLCOcorr/LV%, FEV_1/FVC, TLC%	DLCO%	Most Sensitive PFT

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Greenwald et al. 1987[6]	United States	Cohort Study (Chlorambucil Clinical Trial)	61 (87% Female)	47 ± 12	DLCO Absolute, DLCO%, $FEF_{25-75\%}$ Absolute, $FEF_{25-75\%}$%, FEV_1 Absolute, FEV_1%, FEV_1/FVC, FRC Absolute, FRC%, FVC Absolute, FVC%, TLC Absolute, TLC%	N/A	N/A
McCarthy et al. 1988[7]	Canada	Cohort Study (Rheumatic Disease Unit)	36 (75% Female)	48.5 ± 11 (23-66)	FVC Absolute	FVC Absolute	N/R
Zarafonetis et al. 1989[8]	United States	Cohort Study (Hospital Records)	390	N/R	DLCO%, FVC%	N/A	N/A
Silver et al. 1990[9]	United States	Cohort Study (General Clinical Research Center)	43 (60% Female)	43.9 ± 11.6 (21-63.4)	DLCO Absolute, FVC Absolute	N/A	N/A
Abramson et al. 1991[10]	Australia	Cohort Study (Clinical Notes and Lung Function Records)	113 (81% Female)	50.6 ± 14 (16-81)	FEV_1 Absolute, VC Absolute	N/A	N/A

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Wells et al. 1993[11]	United Kingdom	Cohort Study (ILD Unit)	66 (76% Female)	50.1 ± 12.0	DLCO%, FVC%	N/A	N/A
Wells et al. 1993[12]	United Kingdom	Cohort Study (Hospital Records)	53 (74% Female)	49 ± 12	DLCO Absolute, FVC Absolute	N/A	N/A
Wells et al. 1993[13]	United Kingdom	Cohort Study (Hospital Records)	35	N/R	DLCO%, FVC%	N/A	N/A
Dujic et al. 1994[14]	Croatia	Cohort Study (Department of Dermatology)	29 (86% Female)	51.5 ± 12.7 (27-75)	DLCO%	DLCO%	Previous Use
Steen et al. 1994[15]	United States	Cohort Study (Division of Rheumatology and Clinical Immunology)	890 (92% Female)	42	FVC Absolute, FVC%	FVC	Previous Use
Steen et al. 1994[16]	United States	Cohort Study (Hospital Records)	122	45	DLCO%, FVC Absolute, FVC%	FVC	N/R
Tashkin et al. 1994[17]	United States	Cohort Study (Chlorambucil Clinical Trial)	90	47 ± 11	DLCO Absolute, DLCO%, FEV_1 Absolute, FVC Absolute, TLC Absolute	N/A	N/A
Behr et al. 1995[18]	Germany	Case-Control Study	43 (65% Female)	54.3 ± 3.0 (15-71)	DLCO%, TLC%, VC%	N/A	N/A

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Behr et al. 1996[19]	Germany	Cohort Study (Department of Internal Medicine)	79 (67% Female)	50.4 ± 1.2	DLCO%, VC%	N/A	N/A
Jacobsen et al. 1997[20]	Denmark	Cohort Study (Participating Clinical Centres Chart Records)	176 (85% Female)	41 (4-74)	DLCO%, DLCO/VA%, FEV_1/VC%, VC%	N/A	N/A
Greidinger et al. 1998[21]	United States	Cohort Study (Scleroderma Center)	101 (75% Female)	49.5 ± 13.5	DLCO%, FEV_1%, FVC%	N/A	N/A
Atamas et al. 1999[22]	United States	Case-Control Study (Scleroderma Center)	37 (68% Female)	44.4 ± 13.0 (18-69)	DLCO Absolute, DLCO%, FVC Absolute, FVC%	N/A	N/A
Kon et al. 1999[23]	United Kingdom	Case-Control Study	37 (89% Female)	49.6 ± 11.6 (24-79)	FVC%	FVC%	N/R
Witt et al. 1999[24]	Germany	Cohort Study (Pneumological Outpatient Clinic)	73 (78% Female)	54.4 ± 9.6 (20–80)	DLCO%, FVC%, TLC%	DLCO%	Validation
White et al. 2000[25]	United States	Cohort Study (Scleroderma Center)	103 (69% Female)	48 (30-59)	DLCO Absolute, DLCO%, FVC Absolute, FVC%	N/A	N/A
Yuhara et al. 2000[26]	Japan	Cohort Study (Hospital Records)	24 (96% Female)	36.7 ± 10.6	DLCO%, DLCO/VA%, FVC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Marie et al. 2001[27]	France	Cohort Study (Hospital Records)	43 (86% Female)	59 (33-79)	DLCO%, FEV_1%, FEV_1/VC%, FRC%, FVC%, RV%, TLC% VC%	N/A	N/A
Scorza et al. 2001[28]	Italy	Experimental Study (Outpatient Clinic)	46 (85% Female)	53 (25-75)	DLCO%, FEV_1%, VC%	N/A	N/A
Bouros et al. 2002[29]	United Kingdom	Cohort Study (Hospital Records)	80	N/R	DLCO%, FVC%	N/A	N/A
Giacomelli et al. 2002[30]	Italy	Cohort Study (Outpatient Clinic Centers)	23 (83% Female)	57.3 (39-67)	DLCO%, FEV_1%, FVC%	N/A	N/A
Pakas et al. 2002[31]	Greece	Experimental Study (Rheumatology Outpatient Clinic)	28 (82% Female)	48.3	DLCO%, FVC%, TLC%	N/A	N/A
Kowal-Bielecka et al. 2003[32]	Poland	Case-Control Study	30 (100% Female)	46 (24-62)	FVC%	FVC%	N/R
Yanaba et al. 2003[33]	Japan	Case-Control Study	39 (85% Female)	49 (2-72)	DLCO%, VC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Airo et al. 2004[34]	Italy, United Kingdom	Individual Patient Data Meta-Analysis	53	N/R	DLCO%, FVC%	N/A	N/A
Yanaba et al. 2004[35]	Japan	Case-Control Study	42 (86% Female)	49 ± 18	DLCO%, VC%	N/A	N/A
De Santis et al. 2005[36]	Italy	Cohort Study (Outpatient Clinic of the Division of Rheumatology)	100 (92% Female)	55.4 ± 11.9	DLCO%, FVC%	N/A	N/A
Kodera et al. 2005[37]	Japan	Case-Control Study	123 (86% Female)	51 ± 14	DLCO%, VC%	N/A	N/A
Kowal-Bielecka et al. 2005[38]	Poland	Cohort Study	21 (100% Female)	52 (25–66)	FVC%	FVC%	N/R
Hoyles et al. 2006[39]	United Kingdom	Experimental Study (Fibrosing Alveolitis in Scleroderma Trial (FAST))	45 (71% Female)	55 (18-75)	DLCO% DLCO/VA%, DLCOcorr%, FEV_1%, FVC%, TLC%	N/A	N/A
Plastiras et al. 2006[40]	Greece	Cohort Study (Outpatient University Rheumatology Clinic)	78 (85% Female)	45.9 ± 13.5	DLCO%, FVC%	FVC%	Previous Use

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Tashkin et al. 2006[41]	United States	Experimental Study (Scleroderma Lung Study I (SLS I))	158 (70% Female)	47.9 ± 1.0 (19.6-83.1)	DLCO%, DLCO/VA%, FVC%, TLC%	FVC%	Previous Use
Beretta et al. 2007[42]	Italy	Case-Control Study (Outpatient Clinical Immunology and Allergology Clinic)	204 (91% Female)	48.6 ± 13.2 (16-75)	FVC%	FVC%	N/R
Beretta et al. 2007[43]	Italy	Cohort Study (Outpatient Allergology, Clinical Immunology and Rheumatology Clinic)	33 (79% Female)	49.7 ± 10.4	DLCO Absolute, DLCO%, VC Absolute, VC%	N/A	N/A
Clements et al. 2007[44]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	158 (70% Female)	48 ± 13	DLCO%, FEV_1%, FVC%, TLC%	N/A	N/A
Goh et al. 2007[45]	United Kingdom	Cohort Study (ILD Unit)	141 (81% Female)	47.3 ± 12.2	DLCO%, FVC%	N/A	N/A

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Mittoo et al. 2007[46]	United States	Cohort Study (Scleroderma Center)	25 (64% Women)	43.5 ± 12.5 (16-67)	DLCO Absolute, DLCO%, FVC Absolute, FVC%	N/A	N/A
Tashkin et al. 2007[47]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	145 (70% Female)	47.9 ± 1.0	DLCO%, DLCO/VA%, FVC%, TLC%	FVC%	Previous Use
Tzelepis et al. 2007[48]	Greece	Cohort Study (University Rheumatology Clinic)	59 (81% Female)	47.5 ± 13.9	FVC%	FVC%	Previous Use
Berezne et al. 2008[49]	France	Cohort Study (National Reference Centers for Systemic Sclerosis)	27 (74% Female)	49.4 ± 15	DLCO%, FVC%, TLC%	N/A	N/A
Boin et al. 2008[50]	United States	Case-Control Study (Scleroderma Center)	62 (84% Female)	51.1	FVC%	FVC%	N/R
Goh et al. 2008[51]	United Kingdom	Cohort Study (Hospital Records)	215 (81% Female)	49.1 ± 13.0	DLCO%, FVC%	N/A	N/A
Strange et al. 2008[52]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	141 (72% Female)	48.6 ± 12.0	FVC%	FVC%	Previous Use

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Assassi et al. 2009[53] (Abstract)	United States	Cohort Study	36	N/R	FVC%	FVC%	N/R
De Souza et al. 2009[54]	Brazil	Cohort Study (Hospital Records)	28 (100% Female)	44.89 ± 8.74	DLCO%, FEV_1%, FVC%	N/A	N/A
Gordon et al. 2009[55] (Abstract)	United States	Experimental Study	30	N/R	DLCO%, FVC%	N/A	N/A
Khanna et al. 2009[56]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	158 (71% Female)	48.5 ± 12.3	FVC%	FVC%	Previous Use
Ottewell et al. 2009[57] (Abstract)	United Kingdom	Cohort Study	22 (91% Female)	56 (31-79)	DLCO%, VC%	N/A	N/A
Schmidt et al. 2009[58]	Germany	Case-Control Study	32 (72% Female)	58.5 (30-72)	DLCO%, FVC%, TLC%	N/A	N/A
Wanchu et al. 2009[59]	India	Cohort Study (Rheumatology Clinic)	36 (94% Female)	37.5 ± 10.5	DLCO%, FVC Absolute, FVC%	N/A	N/A
Assassi et al. 2010[60]	United States	Cohort Study (Genetics versus Environment in Scleroderma Outcome Study (GENISOS))	266 (80% Female)	48.63 ± 13.5	FVC%	FVC%	Validation

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Boin et al. 2010[61] (Abstract)	United States	Cohort Study	22	N/R	FVC%	FVC%	N/R
Colaci et al. 2010[62]	Italy	Cohort Study (Rheumatology Unit)	26 (77% Female)	47.8 ± 10.5	DLCOcorr%, FVC%	N/A	N/A
Cuomo et al. 2010[63] (Abstract)	Italy	Cohort Study	20 (90% Female)	46 (18-57)	DLCO%, FVC%	N/A	N/A
Gilson et al. 2010[64]	France	Cohort Study (Department of Rheumatology)	105 (86% Female)	52.7 ± 11.8	DLCO%, FVC%	FVC%	Previous Use
Mittoo et al. 2010[65] (Abstract)	Canada	Cohort Study (Canadian Scleroderma Research Group (CSRG))	67 (88% Female)	54.5 ± 12.1	DLCO%, FVC%	FVC%	N/R
Schorr et al. 2010[66] (Abstract)	United States	Cohort Study (Scleroderma Specialty Center Database)	91	N/R	FVC%	FVC%	N/R
Seibold et al. 2010[67]	United States	Experimental Study	152 (74% Female)	52.5 (15-80)	DLCO%, FVC%	N/A	N/A
Shahane et al. 2010[68] (Abstract)	United States	Cohort Study (Clinic Scleroderma Database)	133	N/R	DLCO, FVC	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Steen et al. 2010[69] (Abstract)	United States	Cohort Study	1,029	N/R	DLCO%, FVC%	N/A	N/A
Theodore et al. 2010[70]	United States	Cohort Study	24	N/R	FVC	FVC	Previous Use
Abhishek et al. 2011[71]	United Kingdom	Cohort Study (Rheumatology Day-Case Unit Databases)	36 (75% Female)	54.26 ± 14.03	DLCO Absolute, FVC Absolute	N/A	N/A
De Santis et al. 2011[72]	Italy	Case-Control Study (Outpatient Clinic of Rheumatology Division)	46 (78% Female)	55.1 ± 14	DLCO%, FVC%	N/A	N/A
Espinosa et al. 2011[73]	Spain	Cohort Study (Autoimmune Disease and Internal Medicine Departments)	37 (81% Female)	43.0 ± 12.4	DLCO%, FVC%	N/A	N/A
Goh et al. 2011[74]	United Kingdom	Cohort Study	168 (82% Female)	49.5 ± 13.2	DLCO Absolute, DLCO%, FVC Absolute, FVC%	N/A	N/A
Hasegawa et al. 2011[75]	Japan	Case-Control Study	92 (87% Female)	52.3 ± 13.5	DLCO%, VC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Hoshino et al. 2011[76]	Japan	Case-Control Study (Hospital Records)	314 (88% Female)	44.9	FVC%	FVC%	N/R
Jayaweera et al. 2011[77] (Abstract)	Australia	Cohort Study (Australia Scleroderma Interest Group (ASIG))	43	N/R	DLCO%, FVC%	N/A	N/A
Khanna et al. 2011[78]	United States	Experimental Study	20 (65% Female)	46.1 ± 14.2	DLCO%, FVC%, TLC%	N/A	N/A
Khanna et al. 2011[79]	United States	Cohort Study (Scleroderma Lung Study I (SLS I) Placebo Group)	77 (62% Female)	48.3 ± 12.5	DLCO%, FVC%	N/A	N/A
Mittoo et al. 2011[80]	United States	Cohort Study (Scleroderma Center Database)	38 (68% Female)	44.3 ± 11.4 (21-74)	DLCO%, FVC%	N/A	N/A
Poormoghim et al. 2011[81]	Iran	Cohort Study (Rheumatology Clinic)	91 (93% Female)	44.10 ± 14.88	DLCO%, FVC%	N/A	N/A
Rosato et al. 2011[82]	Italy	Cohort Study (Clinical Immunology Unit-Scleroderma Center)	41 (90% Female)	47.5 (23-70)	DLCOcorr%, FEV_1%, TLC%, VC%	DLCOcorr%	N/R

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Roth et al. 2011[83]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	112 (71% Female)	46.9 ± 0.9	FVC%	FVC%	Previous Use
Tiev et al. 2011[84]	France	Cohort Study	83 (88% Female)	53.5 ± 12.2	FVC%, TLC%	N/A	N/A
Volpinari et al. 2011[85]	Italy	Cohort Study	79 (90% Female)	55 ± 13	DLCO%, FVC%	N/A	N/A
Abignano et al. 2012[86] (Abstract)	United Kingdom	Cohort Study (Medical Records)	45	N/R	DLCO%, FVC%	N/A	N/A
De Santis et al. 2012[87]	Italy	Cohort Study (Outpatient Clinic of Rheumatology Division)	110 (87% Female)	54.9 ± 12.6	DLCO%, FVC%	N/A	N/A
Hesselstrand et al. 2012[88]	Sweden	Cohort Study (SSc Cohort)	244	N/R	VC%	VC%	N/R
Kishore Babu et al. 2012[89] (Abstract)	India	Cohort Study (Discharge Summaries)	23 (78% Female)	35.9 ± 4.5	FVC%	FVC%	N/R
Kuwana et al. 2012[90] (Abstract)	Japan	Cohort Study (Institutional SSc Database)	50	N/R	FVC%	FVC%	N/R

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Kuwana et al. 2012[91] (Abstract)	Japan	Cohort Study (Institutional SSc Database)	50	N/R	FVC%	FVC%	N/R
Le Gouellec et al. 2012[92] (Abstract)	France	Cohort Study	75	N/R	DLCO%, FVC%	N/A	N/A
Schupp et al. 2012[93] (Abstract)	Germany	Cohort Study	126	N/R	FVC%	FVC%	N/R
Sfriso et al. 2012[94]	Italy	Case-Control Study (Rheumatology Unit)	32 (100% Female)	55.1 ± 9.2 (45.6-67.4)	DLCO%, FVC%	N/A	N/A
Soriano et al. 2012[95] (Abstract)	Italy	Cohort Study	31	N/R	FEV_1%, TLC%	N/A	N/A
Tiev et al. 2012[96]	France	Cohort Study (Department of Internal Medicine)	105 (88% Female)	54.8 ± 12.9	FVC%, TLC%	N/A	N/A
Ananyeva et al. 2013[97] (Abstract)	Russia	Cohort Study	27 (96% Female)	45	DLCO%, FVC%	N/A	N/A

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Ando et al. 2013[98]	Japan	Cohort Study (Department of Respiratory Medicine at Tertiary Care Center)	71 (82% Female)	58.2 ± 13.9	FVC%	FVC%	Previous Use
Burt et al. 2013[99]	Brazil, United States	Cohort Study (Previous Study or Compassionate Basis)	90 (81% Female)	42 (16-71)	DLCOcorr%, FVC%, TLC%	N/A	N/A
Celeste et al. 2013[100]	Italy	Cohort Study (Outpatient Clinic Referral Center for Systemic Autoimmune Diseases)	221 (90% Female)	45.5	DLCO%, FVC%	N/A	N/A
De Lauretis et al. 2013[101]	United Kingdom	Case-Control Study (Interstitial Lung Disease Unit)	286 (78% Female)	51.0	DLCO%, FVC%	N/A	N/A
Elhaj et al. 2013[102]	United States	Case-Control Study (Genetics versus Environment in Scleroderma Outcome Study (GENISOS))	266 (83% Female)	48.6 ± 13.5	DLCOcorr%, FVC%	FVC%	Validation

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Enghelmayer et al. 2013[103] (Abstract)	Argentina	Cohort Study	24	N/R	DLCO Absolute, FVC Absolute, FVC%	N/A	N/A
Koneva et al. 2013[104] (Abstract)	Russia	Cohort Study (Institute of Rheumatology)	44 (93% Female)	49 ± 13	DLCO%, FVC%	N/A	N/A
Liu et al. 2013[105]	United States	Case-Control Study (Genetics versus Environment in Scleroderma Outcome Study (GENISOS))	266 (83% Female)	48.6 ± 13.5	FVC%	FVC%	Validation
Panopoulos et al. 2013[106]	Greece	Case-Control Study (Department of Therapeutics)	26 (92% Female)	47.1	DLCO%, FVC%, TLC%	N/A	N/A
Radic et al. 2013[107] (Abstract)	Germany	Cohort Study	153	N/R	DLCO%, FVC%	N/A	N/A
Stock et al. 2013[108]	United Kingdom	Case-Control Study (Tertiary Referral Centre Clinics)	440 (81% Female)	52.8 (15-83)	DLCO%, FVC%	N/A	N/A
Vacca et al. 2013[109] (Abstract)	Italy	Cohort Study (Rheumatology Unit)	22	N/R	DLCO%, FVC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Wu et al. 2013[110] (Abstract)	United States	Cohort Study (Genetics versus Environment in Scleroderma Outcome Study (GENISOS))	266	N/R	FVC%	FVC%	N/R
Zhang et al. 2013[111]	Canada	Cohort Study (Canadian Scleroderma Research Group (CSRG))	1,043 (86% Female)	55.74 ± 11.88	FVC%	FVC%	Previous Use
Ananyeva et al. 2014[112] (Abstract)	Russia	Cohort Study (Rheumatology Clinic Lung Study Program)	77 (94% Female)	38	DLCO%, FVC%, FVC%/DLCO%	N/A	N/A
Chakr et al. 2014[113] (Abstract)	Brazil	Cohort Study (SSc Clinic)	28 (86% Female)	49.7 ± 14.2	DLCO%, FEV_1%, FVC%	N/A	N/A
Christmann et al. 2014[114]	Brazil, United States	Cohort Study	28	N/R	FVC%	FVC%	N/R
Cottrell et al. 2014[115]	United States	Cohort Study (Scleroderma Center)	2,205 (83% Female)	46.2 ± 13.6	FVC%	FVC%	N/R
Fraticelli et al. 2014[116]	Italy	Experimental Study	30 (70% Female)	51 (41.75 - 62)	DLCO Absolute, FVC Absolute	N/A	N/A

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Guillen-Del Castillo et al. 2014[117]	Spain	Cohort Study (Hospital Records)	63 (86% Female)	43.0 (33.0-54.0)	DLCO/VA%, FVC%	FVC%	N/A
Hoffmann-Vold et al. 2014[118] (Abstract)	Norway	Cohort Study (Norwegian Systemic Connective Tissue Disease and Vasculitis Registry (NOSVAR))	305 (79% Female)	48.0	DLCO%, FVC%	N/A	N/A
Kumanovics et al. 2014[119]	Hungary	Cohort Study (Tertiary Care Centre)	173 (89% Female)	57.6 ± 11.3	DLCO%, FVC%	FVC%	Most Specific PFT
Kwon et al. 2014[120] (Abstract)	South Korea	Cohort Study (Rheumatology Clinic)	32 (84% Female)	47.5 ± 9.4	FVC%	FVC%	N/R
Lambrecht et al. 2014[121]	Belgium	Case-Control Study (Scleroderma Clinic)	119	N/R	DLCO%	DLCO%	N/R
Le Gouellec et al. 2014[122] (Abstract)	France	Cohort Study	75 (76% Female)	N/R	DLCO%, FVC%	N/A	N/A
Narvaez et al. 2014[123] (Abstract)	Spain	Cohort Study (Hospital Recruitment)	30 (87% Female)	54	DLCO%, FVC%, TLC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Nihtyanova et al. 2014[124]	United Kingdom	Cohort Study (Tertiary Referral Center)	398 (86% Female)	41	DLCO%, FVC%	N/A	N/A
Parida et al. 2014[125] (Abstract)	India	Experimental Study	30	N/R	DLCO%, FVC%, TLC%	FVC%	N/R
Pham et al. 2014[126] (Abstract)	United States	Cohort Study	20	N/R	DLCO%, FVC%	N/A	N/A
Poormoghim et al. 2014[127]	Iran	Cohort Study (Hospital SSc Database)	36 (83% Female)	N/R Azathioprine Group: 35.0 (30.1–45.0); Cyclophospa-mide Group: 33.0 (29.0–40.5)	DLCOcorr%, FVC%	N/A	N/A
Rotondo et al. 2014[128] (Abstract)	Italy	Cohort Study	70 (90% Female)	59.7 ± 4.5	DLCO%, FVC%, RV%, TLC%	RV%	N/R
Ariani et al. 2015[129] (Abstract)	Italy	Cohort Study (Multi-Centre Study)	149	N/R	FVC%	FVC%	N/R

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Balbir-Gurman et al. 2015[130]	Israel	Cohort Study (Tertiary Care Rheumatology Unit)	26 (77% Female)	50.7 ± 12.7	DLCO%, FVC%	N/A	N/A
Bosello et al. 2015[131]	Italy	Experimental Study	20 (85% Female)	41.4 ± 13.1	DLCO%, FEV_1%, FVC%, TLC%	N/A	N/A
De Luca et al. 2015[132]	Italy	Case-Control Study (Rheumatology Inpatient Clinic)	120	N/R	DLCO%, FEV_1% FVC%	N/A	N/A
Hoffmann-Vold et al. 2015[133]	Norway	Cohort Study (Norwegian Systemic Connective Tissue Disease and Vasculitis Registry (NOSVAR))	305 (79% Female)	48 ± 15.0	DLCO%, FVC%	FVC%	Previous Use
Iudici et al. 2015[134]	Italy	Cohort Study (Rheumatology Unit)	45 (91% Female)	49.86 ± 13.33	DLCOcorr%, FVC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Jordan et al. 2015[135]	Switzerland	Case-Control Study (European Scleroderma Trial and Research (EUSTAR) Centres)	63 (71% Female)	50.9 ± 1.6	DLCO%, FVC%	FVC%	Previous Use
Khanna et al. 2015[136] (Abstract)	United States	Experimental Study (LOTUSS Study)	63 (83% Female)	50.6 ± 12.3	DLCO%, FVC%	N/A	N/A
Khanna et al. 2015[137]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	93 (73% Female)	47.19 ± 11.72	DLCO%, FVC%	N/A	N/A
Koneva et al. 2015[138] (Abstract)	Russia	Cohort Study	54 (81% Female)	48.5 ± 12.9	DLCO%, FVC%	N/A	N/A
Lepri et al. 2015[139] (Abstract)	Australia, France, Italy, Spain, Switzerland	Cohort Study (Multi-Centre Study)	23	N/R	DLCO%, FVC%	FVC%	N/R
Man et al. 2015[140]	United States	Cohort Study (SSc Referral Centre)	254 (80% Female)	49 ± 13	FVC%	FVC%	Validation

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Mani et al. 2015[141] (Abstract)	India	Experimental Study (Tertiary Care Hospital)	62	N/R	FVC%	FVC%	N/R
Mateos-Toledo et al. 2015[142] (Abstract)	Mexico	Cohort Study	46	N/R	DLCO%, FVC Absolute, FVC%	N/A	N/A
Narvaez et al. 2015[143] (Abstract)	Spain	Cohort Study	31	59	DLCO%, FVC%, TLC%	N/A	N/A
Ninaber et al. 2015[144]	The Netherlands	Cohort Study (Referrals to Tertiary Outpatient Targeted Multidisciplinary Healthcare Program)	41 (76% Female)	50.9	DLCO%, FVC%	DLCO%	N/R
Radic et al. 2015[145] (Abstract)	Croatia, Germany, Switzerland	Cohort Study (European Scleroderma Trial and Research (EUSTAR) Database)	124	N/R	DLCO%, FVC%	N/A	N/A

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Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Sakamoto et al. 2015[146]	Japan	Case-Control Study (Hospital Records)	33 (70% Female)	63 (54-70)	VC Absolute	VC Absolute	Previous Use
Saketkoo et al. 2015[147] (Abstract)	United States	Cohort Study (Pulmonary Hypertension Recognition and Outcomes in Scleroderma (PHAROS) Registry)	256	N/R	FVC%	FVC%	N/R
Schulam et al. 2015[148] (Abstract)	United States	Cohort Study	672	N/R	FVC%	FVC%	N/R
Shirai et al. 2015[149] (Abstract)	Japan	Cohort Study (SSc Database)	58	N/R	FVC%	FVC%	N/R
Suliman et al. 2015[150]	Switzerland	Cohort Study (Division of Rheumatology)	102 (77% Female)	58.5 (28-90)	FVC%	FVC%	Previous Use
Tanaseanu et al. 2015[151]	Romania	Cohort Study	40 (95% Female)	34 ± 12	DLCO%, FEV_1%	N/A	N/A

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Tashkin et al. 2015[152] (Abstract)	United States	Experimental Study (Scleroderma Lung Study II (SLS II))	142	N/R	DLCO%, FVC%	FVC%	N/R
Volkmann et al. 2015[153]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	82 (73% Female)	47.2	FVC%, TLC%	N/A	N/A
Volkmann et al. 2015[154] (Abstract)	United States	Cohort Study (Scleroderma Lung Study II (SLS II))	136	N/R	DLCO%	DLCO%	Previous Use
Wallace et al. 2015[155]	United States	Cohort Study (Combined Response Index in Systemic Sclerosis (CRISS) Database)	177 (75% Female)	50.5 ± 11.7	DLCO%, FVC%, TLC%	N/A	N/A
Fava et al. 2016[156]	United States	Cohort Study (Scleroderma Center)	27 (78% Female)	51.3 ± 9.6	FVC%	FVC%	N/R

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
Hoffmann-Vold et al. 2016[157]	Norway	Case-Control Study (Norwegian Systemic Connective Tissue Disease and Vasculitis Registry (NOSVAR))	298 (82% Female)	48 ± 15.4	DLCO%, FVC%	FVC%	N/R
Kloth et al. 2016[158]	Germany	Cohort Study (Radiology Department Database)	26 (54% Female)	37.45 ± 9.83 (11-51)	DLCO Absolute, DLCO%, FEV_1 Absolute, FEV_1%, FVC Absolute, FVC%, TLC Absolute, TLC% VC Absolute, VC%	N/A	N/A
Owen et al. 2016[159]	Australia	Cohort Study (Australia Scleroderma Cohort Study (ASCS))	47 (79% Female)	54.6	DLCO Absolute, FVC Absolute	FVC Absolute	Previous Use
Shenoy et al. 2016[160]	India	Cohort Study (Rheumatology Outpatient Department)	57 (86% Female)	45.55	FVC%	FVC%	Most Specific PFT

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
ClinicalTrials.gov ID: NCT00319033[161] (Registration)	Canada, France, Germany, Israel, Italy, Republic of Korea, The Netherlands, Sweden, Switzerland, United Kingdom, United States	Experimental Study (BUILD 2 OL)	132	N/A	DLCO, FVC	N/A	N/A
EudraCT #: 2008-000224-27[162] (Registration)	United Kingdom	Cohort Study	20 (Anticipated)	N/A	DLCO%, FVC%	N/A	N/A
ClinicalTrials.gov ID: NCT01570764 [163] (Registration)	France	Experimental Study (SCLEROCYC)	50 (Anticipated)	N/A	DLCO%, FVC%	FVC%	N/R

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
ClinicalTrials.gov ID: NCT01559129[164] (Registration)	Australia, France, Germany, Italy, Poland, Russia. Spain, Switzerland, United Kingdom, United States	Experimental Study	23	N/A	FVC Absolute	FVC Absolute	N/R
ClinicalTrials.gov ID: NCT01858259 [165] (Registration)	France, Germany, Hungary, Italy, Switzerland, United Kingdom	Cohort Study (DeSScipher)	1,372	N/A	DLCO%, FVC%	FVC%	N/R

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
ClinicalTrials.gov ID: NCT02597933[166] (Registration)	Australia, Belgium, Canada, China, Denmark, France, Germany, Greece, India, Ireland, Israel, Italy, Japan, The Netherlands, Poland, Portugal, Spain, Switzerland, United Kingdom, United States	Experimental Study	520 (Anticipated)	N/A	DLCO%, FVC Absolute, FVC%	FVC Absolute	Previous Use
ClinicalTrials.gov ID: NCT02588625[167] (Registration)	Canada, Poland, United Kingdom, United States	Experimental Study	N/R	N/A	FVC%	FVC%	N/R

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

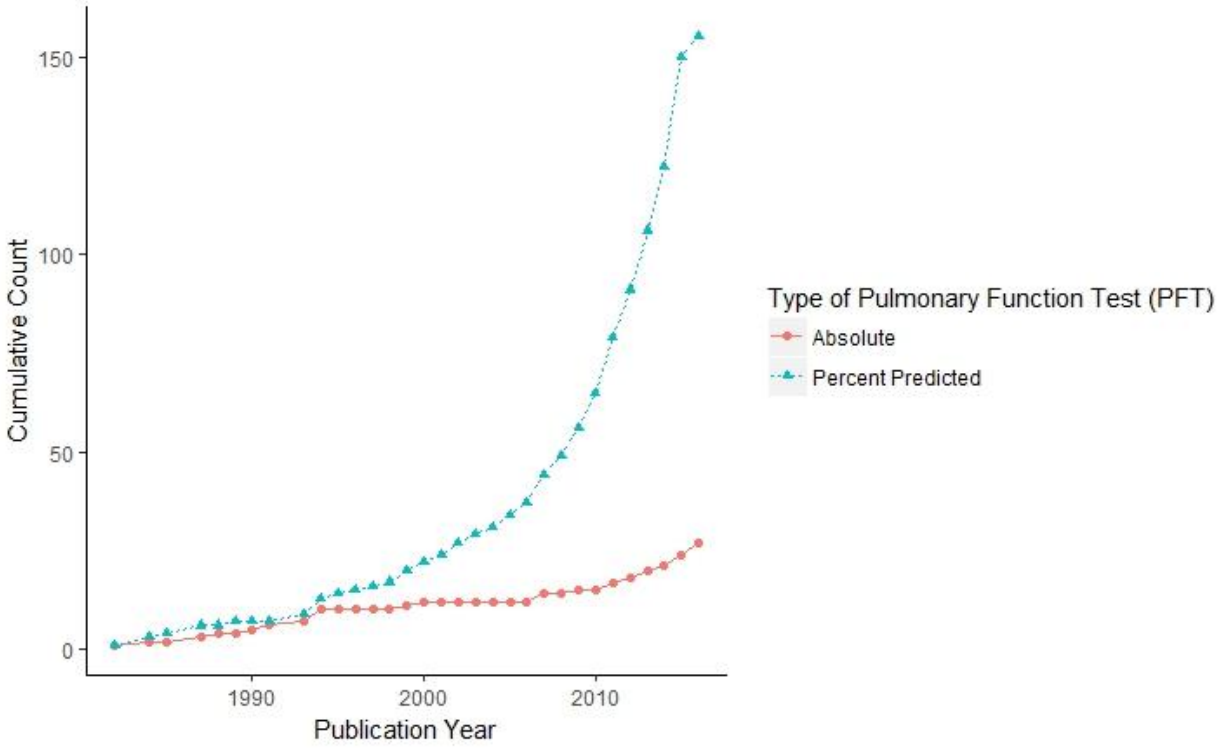
Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	PFT Measure(s) Used	Main PFT Measure	Reason for Using Main PFT
ClinicalTrials.gov ID: NCT02370693[168] (Registration)	United States	Experimental Study	30 (Anticipated)	N/A	FVC	FVC	N/R
ClinicalTrials.gov ID: NCT02745145[169] (Registration)	Argentina, Australia, Canada, Israel, Italy, Poland, Spain, United Kingdom, United States	Experimental Study	175 (Anticipated)	N/A	DLCO%, DLCO/VA, FVC Absolute, FVC%, TLC%	FVC Absolute	N/R

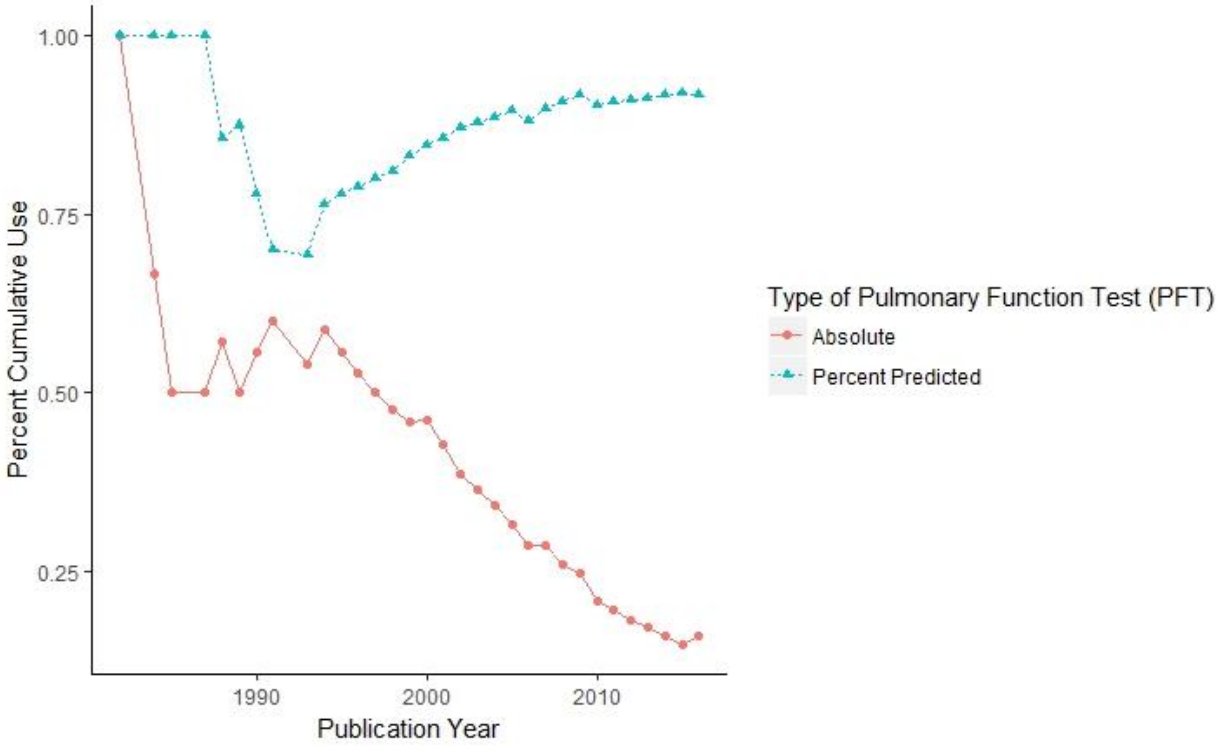
Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/LV% = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin and Lung Volume; $FEF_{25-75\%}$ = Forced Expiratory Flow over Mid-Half of FVC; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FVC = Forced Vital Capacity; ILD = Interstitial Lung Disease; N/A = Not Applicable; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; SSc = Systemic Sclerosis; TLC = Total Lung Capacity; VC = Vital Capacity

e-APPENDIX 4: Cumulative Use and Percent Cumulative Use of Absolute and Percent Predicted Values

Percent predicted PFT values were cumulatively more commonly used than absolute measures as outcomes for SSc-ILD progression throughout the study period. However, their use was similar to that of absolute PFT values until the mid- 1990's, at which point the cumulative use of percent predicted values skyrocketed (e-Figure 1a). By the end of the study period, PFTs were expressed as percent predicted values in 155 (93.9%) of the 169 outcome studies, while they were reported as absolute values in 27 (16.4%) of studies. This is further depicted in e-Figure 1b which illustrates the percent cumulative use of absolute and percent predicted PFT values. Indeed, while the cumulative percent use of percent predicted PFT values increased steadily as of the mid-1990's, the cumulative percent use of absolute PFT values plummeted in a consistent manner.

A probable explanation for the increasing popularity of percent predicted values throughout the study period is the proposal of new PFT standardization and interpretative guidelines. In fact, in a 1987 report, the American Thoracic Society (ATS) focused mainly on absolute values, while also discussing the new development of standardizing PFTs using reference values.[170] Following a 1991 ATS statement on the selection and interpretation of PFT reference values,[171] the ATS's subsequent guideline on the standardization of PFTs in 1995 placed emphasis solely on percent predicted values.[172] It is perhaps this report that can explain the decrease in percent cumulative use of absolute values in favour of percent predicted values in the mid-1990s.


150
100
50
0
Cumulative Count
1990
2000
2010
Publication Year
Type of Pulmonary Function Test (PFT)
Absolute
Percent Predicted


1.00
0.75
0.50
0.25
Percent Cumulative Use
1990
2000
2010
Publication Year
Type of Pulmonary Function Test (PFT)
Absolute
Percent Predicted

e-Figure 1: a) Cumulative Use and b) Percent Cumulative Use of Absolute and Percent Predicted Pulmonary Function Test (PFT) Measures as Longitudinal Outcomes for Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) Progression.

For each year, percent cumulative use was calculated by dividing the cumulative use of both absolute and percent predicted PFT measures by the cumulative number of published articles.

e-APPENDIX 5: Characteristics of the Validation Studies (N = 50)

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Harrison et al. 1991[173]	United Kingdom	Case-Control Study (Hospital Records)	34 (76% Female)	45 (22-67)	Lung Biopsy (Four-Point Scoring System for Interstitial Fibrosis, Four-Point Scoring System for Loss of Lung Architecture)	Cross-Sectional	DLCO%
Wells et al. 1997[174]	United Kingdom	Cross-Sectional Study (Interstitial Lung Disease Unit)	64 (80% Female)	48.8 ± 11.6	HRCT (Nearest 5% - Overall Lung Involvement)	Cross-Sectional	DLCO%, DLCO/VA%, FEV_1%, FVC%, TLC%
Wells et al. 1997[175]	United Kingdom	Cross-Sectional Study (Interstitial Lung Disease Unit)	57 (82% Female)	48 ± 12	HRCT (Nearest 5% - Overall Lung Involvement)	Cross-Sectional	DLCO%
Diot et al. 1998[176]	France	Cross-Sectional Study (Hospital Referrals)	52 (98% Female)	53.71 ± 14.12 (23-79)	HRCT (Warrick Total Score (0-30))	Cross-Sectional	DLCO%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Kim et al. 2001[177]	South Korea	Cohort Study (Tertiary Hospital Clinical Records)	40 (85% Female)	54 (27-76)	HRCT (Nearest 5% - Ground-Glass Opacity, Nearest 5% - Honeycombing, Nearest 5% - Irregular Linear Opacity, Nearest 5% - Overall Lung Involvement)	Longitudinal	DLCO%, FEV_1 Absolute, FEV_1/FVC%, FVC Absolute
Shahin et al. 2001[178]	Egypt	Case-Control Study (Department of Rheumatology and Rehabilitation)	22 (95% Female)	37.6 ± 14.3	HRCT (Total Score (0-At Least 21))	Cross-Sectional	DLCO%
Han et al. 2003[179] (Abstract)	South Korea	Cross-Sectional Study	43	46.8 ± 11.9	HRCT (Absence/Presence of Pulmonary Fibrosis)	Cross-Sectional	DLCO%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Ooi et al. 2003[180]	China	Cross-Sectional Study (Division of Rheumatology)	45 (89% Female)	48.5 ± 13.4	HRCT (Fibrosis Index (0-48), Inflammatory Index (0-48), Total Score (0-96))	Cross-Sectional	DLCO%, FEV_1%, FVC%, TLC%
De Santis et al. 2005[36]	Italy	Cohort Study (Outpatient Clinic of the Division of Rheumatology)	100 (92% Female)	55.4 ± 11.9	HRCT (Kazerooni Alveolar Score (0-5), Kazerooni Interstitial Score (0-5))	Cross-Sectional	DLCO%, FVC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Orlandi et al. 2006[181]	Italy	Cross-Sectional Study (SSc Outpatients)	39 (87% Female)	58 ± 13 (18-80)	HRCT (Inspiratory Volume/Body Surface Area, Low-Dose Volumetric Kurtosis, Low-Dose Volumetric Mean Lung Attenuation, Low-Dose Volumetric Total Lung Skewness, Total Mean Lung Attenuation, Total Lung Kurtosis, Total Lung Skewness, Warrick Total Score (0-30))	Cross-Sectional	DLCO%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Beretta et al. 2007[182]	Italy	Cross-Sectional Study (Centre of Expertise for Systemic Autoimmune Diseases Outpatient Clinic)	28 (82% Female)	52.2 ± 10.6	HRCT (Warrick Total Score (0-30))	Cross-Sectional	DLCOcorr%, FVC%, TLC%
Camiciottoli et al. 2007[183]	Italy	Cross-Sectional Study	48 (88% Female)	57 ± 13 (18-80)	HRCT (Total Lung Kurtosis, Total Lung Skewness, Total Mean Lung Attenuation, Warrick Total Score (0-30))	Cross-Sectional	DLCO%, FEV_1%, FRC%, FVC%
Goldin et al. 2008[184]	United States	Cross-Sectional Study (Scleroderma Lung Study I (SLS I))	162 (70% Female)	51 ± 12.3	HRCT (Global Fibrosis Score (0-4), Global Ground-Glass Opacity Score (0-4), Global Honeycombing Score (0-4))	Cross-Sectional	DLCO%, FEV_1%, FEV_1/FVC%, FVC%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Bellia et al. 2009[185]	Italy	Cross-Sectional Study (Department of Rheumatology)	31 (97% Female)	54 ± 10.4	HRCT (Warrick Alveolitis Index (0-4), Warrick Extent Score (1-3), Warrick Fibrosis Index (0-26), Warrick Severity Score (1-5), Warrick Total Score (0-30))	Cross-Sectional	DLCO%, FEV_1%, TLC%
Goldin et al. 2009[186]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	98 (74% Female)	46.6	HRCT (Global Fibrosis Score (0-4))	Longitudinal	DLCO%, FVC%, TLC%
Vonk et al. 2009[187]	The Netherlands	Cross-Sectional Study (Pulmonary Hypertension Screening, a Multidisciplinary Approach in Scleroderma (POEMAS) and Nationwide Survey)	1,000	N/R	HRCT (Scoring Not Reported)	Cross-Sectional	TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Ananyeva et al. 2010[188] (Abstract)	Russia	Cross-Sectional Study	138 (90% Female)	47 ± 13	HRCT (Extent of Lung Involvement – Scoring Not Reported)	Cross-Sectional	DLCO%, FVC%
Gilson et al. 2010[64]	France	Cohort Study (Department of Rheumatology)	105 (86% Female)	52.7 ± 11.8	HRCT (Wells Total Score (0-3))	Longitudinal	FVC%
Peng et al. 2010[189] (Abstract)	China	Cross-Sectional Study (Scleroderma Study of Peking Union Medical College Hospital (PUMCH))	68	N/R	HRCT (Extent of Lung Involvement – Scoring Not Reported)	Cross-Sectional	DLCO%, FVC%, TLC%
Kim et al. 2011[190] (Abstract)	United States	Cross-Sectional Study (Anonymized Research Database)	119	48 ± 10.6	HRCT (Quantitative Percentage with Fibrosis in Whole Lung)	Cross-Sectional	DLCO%, FEV_1%, FVC%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Kim et al. 2011[191]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	83	N/R	HRCT (Quantitative Percentage with Fibrosis in Highest Score Zone at Baseline, Quantitative Percentage with Fibrosis in Whole Lung)	Longitudinal	FVC%, TLC%
Moghadam et al. 2011[192]	Iran	Cross-Sectional Study (Rheumatology Research Center)	55 (91% Female)	38.4 ± 1.3 (17–63)	HRCT (Wells Total Score (0-4))	Cross-Sectional	DLCO Absolute, DLCO%, FVC Absolute, FVC%, TLC Absolute, TLC%
Parra et al. 2011[193] (Abstract)	Brazil	Cross-Sectional Study	30 (77% Female)	N/R	HRCT (Extent of Lung Involvement – Scoring Not Reported)	Cross-Sectional	DLCO%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Assayag et al. 2012[194] (Abstract)	Canada	Cross-Sectional Study (Canadian Scleroderma Research Group (CSRG))	54 (89% Female)	58.5	HRCT (Global Fibrosis Score (0-4), Global Ground-Glass Opacity Score (0-4), Global Honeycombing Score (0-4), Global Severity Score (0-12))	Cross-Sectional	DLCO%, FVC%
Mantero et al. 2012[195] (Abstract)	Italy	Case-Control Study	32 (84% Female)	62.5 (59-73)	HRCT (Extent of Lung Involvement – Scoring Not Reported)	Cross-Sectional	FVC%
Mittal et al. 2012[196] (Abstract)	India	Cross-Sectional Study	23 (91% Female)	35.3 ± 9.9	HRCT (Total Score (0-24))	Cross-Sectional	FVC%
Pernot et al. 2012[197]	France	Case-Control Study (Department of Dermatology, Department of Internal Medicine)	35 (83% Female)	60.1	HRCT (Absence/Presence of ILD)	Cross-Sectional	DLCO%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Perrin et al. 2012[198] (Abstract)	France	Cross-Sectional Study	72	N/R	HRCT (Absence/Presence of ILD)	Cross-Sectional	DLCO%
Wilsher et al. 2012[199]	New Zealand	Cross-Sectional Study (Rheumatology Clinics)	30 (80% Female)	47 ± 12 (18-70)	HRCT (Total Extent of Ground-Glass Opacity (0-24), Total Extent of Reticular Pattern (0-24))	Cross-Sectional	DLCO%, FEV_1%, VC%
Zimmermann et al. 2012[200] (Abstract)	Brazil	Cross-Sectional Study	45	N/R	HRCT (Tomographic Index)	Cross-Sectional	DLCO, Final Expiratory Volume, FVC, RV, TLC
Celeste et al. 2013[100]	Italy	Cohort Study (Outpatient Clinic Referral Center for Systemic Autoimmune Diseases)	221 (90% Female)	45.5	HRCT (Nearest 5% - Overall Lung Involvement)	Cross-Sectional	DLCO%, FVC%
Gatta et al. 2013[201]	Italy	Cross-Sectional Study (Hospital Information System)	42 (14% Female)	48 (27-66)	HRCT (Modified Warrick Total Score (0-115))	Cross-Sectional	DLCO%, DLCO/VA%, FVC%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Nguyen-Kim et al. 2013[202] (Abstract)	Switzerland	Cross-Sectional Study	37 (95% Female)	57 ± 12.5	HRCT (Total Lung Kurtosis, Total Lung Skewness)	Cross-Sectional	DLCO, FEV_1, FVC, TLC
Piorunek et al. 2013[203]	Poland	Cross-Sectional Study	37 (84% Female)	43.2 ± 13.9	HRCT (Warrick Total Score (0-30))	Cross-Sectional	DLCO%
Zamora et al. 2013[204] (Abstract)	United States	Cross-Sectional Study (Pulmonary Hypertension Recognition and Outcomes in Scleroderma (PHAROS) Registry)	336	N/R	HRCT (Total Extent of Fibrosis – Scoring Not Reported, Total Extent of Ground-Glass Opacity – Scoring Not Reported, Total Extent of Honeycombing – Scoring Not Reported)	Cross-Sectional	DLCO%, FVC%, TLC%
Colaci et al. 2014[205]	Italy	Cross-Sectional Study (Rheumatology Centre)	107 (81% Female)	52.1 ± 12.3	HRCT (Modified Schurawitzki Total Score (0-18))	Cross-Sectional	DLCOcorr/VA%, FEV_1%, FVC%, TLC%, VC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Ariani et al. 2015[206]	Italy	Cross-Sectional Study (Units of Rheumatology)	257 (91% Female)	60.0 ± 13.4	HRCT (Fibrosis Ratio, Parenchymal Kurtosis, Parenchymal Mean Lung Attenuation, Parenchymal Skewness, Parenchymal Standard Deviation, Total Lung Kurtosis, Total Lung Skewness, Total Mean Lung Attenuation, Total Lung Standard Deviation)	Cross-Sectional	DLCO%, DLCO/VA%, FVC%, TLC%
Bernstein et al. 2015[207] (Abstract)	United States	Cross-Sectional Study (Prospective Registry of Early Systemic Sclerosis (PRESS))	91 (68% Female)	52.0 ± 15.3	HRCT (Absence/Presence of ILD)	Cross-Sectional	DLCO%, FVC%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Ghandour et al. 2015[208] (Abstract)	Egypt	Cross-Sectional Study (Outpatient Clinic of Rheumatology & Rehabilitation Department)	40 (100% Female)	(17-57)	HRCT (Extent of Lung Involvement – Scoring Not Reported)	Cross-Sectional	FEV_1/FVC%, FVC%
Guarnieri et al. 2015[209]	Italy	Case-Control Study (Outpatient Clinic of Rheumatology Unit)	37 (81% Female)	54	HRCT (Global Severity Score (0-12))	Cross-Sectional	DLCO%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Khanna et al. 2015[137]	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	93 (73% Female)	47.19 ± 11.72	HRCT (Maximum Fibrosis Score in Zone of Maximal Involvement (0-4), Nearest 5% - Overall Lung Involvement, Quantitative Percentage with Fibrosis in Whole Lung, Quantitative Percentage with Fibrosis in Zone of Maximal Involvement, Quantitative Total Extent of Interstitial Lung Disease in Whole Lung, Quantitative Total Extent of Interstitial Lung Disease in Zone of Maximal Involvement)	Cross-Sectional	DLCO%, FVC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Kim et al. 2015[210] (Abstract)	United States	Cohort Study (Scleroderma Lung Study I (SLS I))	76	N/R	HRCT (Quantitative Percentage with Fibrosis in Whole Lung, Total Lung Kurtosis)	Cross-Sectional, Longitudinal	DLCO%, FVC%
Ninaber et al. 2015[144]	The Netherlands	Cohort Study (Referrals to Tertiary Outpatient Targeted Multidisciplinary Healthcare Program)	41 (76% Female)	50.9	HRCT (% High Attenuation Areas, 85th Percentile Density Score)	Cross-Sectional	DLCO%, FVC%
Salaffi et al. 2015[211]	Italy	Cross-Sectional Study	79 (85% Female)	59 ± 9.7	HRCT (Computer-Aided Method Pulmonary Fibrosis Fraction (%))	Cross-Sectional	DLCO%, FEV_1%, FVC%
Suliman et al. 2015[150]	Switzerland	Cohort Study (Division of Rheumatology)	102 (77% Female)	58.5 (28-90)	HRCT (Absence/Presence of ILD)	Cross-Sectional	DLCOcorr%, FVC%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
Antoniou et al. 2016[212]	United Kingdom	Cross-Sectional Study (Hospital Records, Centre for Rheumatology and Pulmonary Hypertension)	333 (78% Female)	54.4 ± 13.1	HRCT (Nearest 5% - Overall Lung Involvement)	Cross-Sectional	DLCO%, FEV_1%, FVC%, FVC/DLCO Absolute
Cetincakmak et al. 2016[213]	Turkey	Cross-Sectional Study (Referrals to Department of Radiology Clinic)	38 (95% Female)	41	HRCT (Left Percentage of Lower Lobe Volume, Right Percentage of Lower Lobe Volume, Total Percentage of Lower Lobe Volume)	Cross-Sectional	DLCOcorr%, FEV_1/FVC%, FVC%
Kloth et al. 2016[158]	Germany	Cohort Study (Radiology Department Database)	26 (54% Female)	37.45 ± 9.83 (11-51)	HRCT (Mean Lung Density)	Longitudinal	FEV_1
Salaffi et al. 2016[214]	Italy	Cross-Sectional Study (Department of Rheumatology)	126 (84% Female)	60.68 ± 10.74 (22-78)	HRCT (Computer-Aided Method Pulmonary Fibrosis Fraction (%))	Cross-Sectional	DLCO%, FVC%
Tashkin et al.	United	Cross-Sectional	300	50.3	HRCT	Cross-	DLCOcorr%,

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
2016[215]	States	Study (Scleroderma Lung Study I (SLS I), Scleroderma Lung Study II (SLS II))	(72% Female)		(Quantitative Ground-Glass Opacity in Whole Lung, Quantitative Ground-Glass Opacity in Zone of Maximal Involvement, Quantitative Percentage with Fibrosis in Whole Lung, Quantitative Percentage with Fibrosis in Zone of Maximal Involvement, Quantitative Total Extent of Interstitial Lung Disease in Whole Lung, Quantitative Total Extent of Interstitial Lung Disease in Zone of	Sectional	FEV_1/FVC%, FVC%, TLC%

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

Record	Country	Study Design (SSc Recruitment Method/Site)	SSc Subjects in Study (% Female)	Age, Years (Range)	Gold Standard (Scoring Method)	Type of Validation	PFT Measures Considered
					Maximal Involvement)		

Abbreviations: % = Percent Predicted; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FEV_1 = Forced Expiratory Volume in the 1^{st} Second of Forced Exhalation; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; N/R = Not Reported; PFT = Pulmonary Function Test; RV = Residual Volume; TLC = Total Lung Capacity; VC = Vital Capacity

e-APPENDIX 6: Results of the Validation Studies whose Aim was Other than to Validate Pulmonary Function Tests (N = 45). The measures of validity are grouped alphabetically by scoring system used.

HRCT: % High Attenuation Areas	
Ninaber et al. 2015[144]	DLCO%: r = -0.48 (p = 0.002) FVC%: r = -0.62 (p < 0.001)
HRCT: 85th Percentile Density Score	
Ninaber et al. 2015[144]	DLCO%: r = -0.49 (p = 0.001) FVC%: r = -0.64 (p < 0.001)
HRCT: Absence/Presence of Pulmonary Fibrosis/ILD	
Han et al. 2003[179] (Abstract)	DLCO% = 68%: AUC = 0.814
Pernot et al. 2012[197]	DLCO% = 67%: AUC = 0.75 (p = 0.005) Se = 54% Sp = 91%
Perrin et al. 2012[198] (Abstract)	DLCO% = Unclear: AUC = 0.67

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Bernstein et al. 2015[207] (Abstract)	DLCO% < 80%: Se = 86.4% Sp = 60.0% PPV = 70.4% NPV = 80.0% FVC% < 80%: Se = 56.0% Sp = 55.0% PPV = 60.9% NPV = 50.0% TLC% < 80%: Se = 52.9% Sp = 70.6% PPV = 64.3% NPV = 60.0% DLCO% & FVC% < 80%: Se = 90.9% Sp = 45.0% PPV = 64.5% NPV = 81.8% DLCO% & FVC & TLC% < 80%: Se = 88.2% Sp = 47.1% PPV = 62.5% NPV = 80.0%

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Suliman et al. 2015[150]	FVC% < 80%: FNR = 62.5% FPR = 7.9% Se = 37.5% (0.3-0.5) Sp = 92% (0.8-1.0) LR+ = 4.7 (1.5-4.7) LR- = 0.7 (0.5-0.8) DLCOcorr <70% or FVC% < 80%: FNR = 41.0% FPR = 34.3% Se = 59.0% (0.4-0.7) Sp = 65.8% (0.5-0.7) LR+ = 1.7 (1.0-2.8) LR- = 0.6 (0.4-0.9) FVC% or TLC% < 80%: FNR = 55.0% FPR = 13.2% Se = 45.0% (0.3-0.5) Sp = 86.0% (0.7-0.9) LR+ = 3.4 (1.4-8.1) LR- = 0.6 (0.4-0.8) DLCOcorr% < 70% or FVC% or TLC% < 80%: FNR = 37.0% FPR = 37.0% Se = 62.0% (0.5-0.7) Sp = 63.0% (0.4-0.7) LR+ = 1.7 (1.0-2.6) LR- = 0.6 (0.4-0.8)
HRCT: Computer-Aided Method Pulmonary Fibrosis Fraction (%)	
Salaffi et al. 2015[211]	DLCO%: r = -0.490 (p < 0.0001) FEV_1%: r = -0.675 (p < 0.0001) FVC%: r = -0.653 (p < 0.0001)
Salaffi et al. 2016[214]	DLCO%: r = -0.556 (p < 0.0001) FVC%: r = -0.670 (p < 0.0001)
HRCT: Extent of Lung Involvement – Scoring Not Reported	
Ananyeva et al. 2010[188] (Abstract)	DLCO%: r = -0.42 (p = 0.00) FVC%: r = -0.31 (p = 0.0002)
Peng et al. 2010[189] (Abstract)	DLCO%: r = -0.496 (p = 0.000) FVC%: r = -0.324 (p = 0.009) TLC%: r = -0.465 (p = 0.000)
Parra et al. 2011[193] (Abstract)	DLCO%: r = -0.601 (p = 0.01)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Mantero et al. 2012[195] (Abstract)	FVC%: r = -0.77 (p < 0.0001)
Ghandour et al. 2015[208] (Abstract)	FEV_1/FVC%: r = 0.593 (p = 0.000) FVC%: r = 0.373 (p = 0.018)
HRCT: Fibrosis Index (0-48)	
Ooi et al. 2003[180]	FVC%: r = -0.31 (p = 0.05) TLC%: r = -0.38 (p = 0.02)
HRCT: Fibrosis Ratio	
Ariani et al. 2015[206]	DLCO%: r = -0.10 (NS) DLCO/VA%: r = 0.06 (NS) FVC%: r = -0.18 (p = 0.0038) TLC%: r = -0.04 (NS)
HRCT: Global Fibrosis Score (0-4)	
Goldin et al. 2008[184]	DLCO%: r = -0.44 (p = 0.0001) FEV_1%: r = -0.05 (p = 0.54) FEV_1/FVC%: r = 0.31 (p = 0.0002) FVC%: r = -0.22 (p = 0.007) TLC%: r = -0.36 (p = 0.0001)
Goldin et al. 2009[186]	**Longitudinal Validation:** DLCO%: Kendall τ = 0.199 (p = 0.053) FVC%: Kendall τ = 0.21 (p = 0.041) TLC%: Kendall τ = 0.22 (p = 0.035)
Assayag et al. 2012[194] (Abstract)	DLCO%: r = -0.587 (p < 0.005) FVC%: r = -0.535 (p < 0.005)
HRCT: Global Ground-Glass Opacity Score (0-4)	
Goldin et al. 2008[184]	DLCO%: r = 0.05 (p = 0.52) FEV_1%: r = 0.19 (p = 0.02) FEV_1/FVC%: r = 0.02 (p = 0.76) FVC%: r = 0.14 (p = 0.08) TLC%: r = -0.03 (p = 0.7)
Assayag et al. 2012[194] (Abstract)	DLCO%: r = -0.521 (p < 0.005) FVC%: r = -0.450 (p < 0.005)
HRCT: Global Honeycombing Score (0-4)	
Goldin et al. 2008[184]	DLCO%: r = -0.25 (p = 0.002) FEV_1%: r = -0.07 (p = 0.41) FEV_1/FVC%: r = -0.005 (p = 0.59) FVC%: r = -0.04 (p = 0.61) TLC%: r = -0.19 (p = 0.02)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Assayag et al. 2012[194] (Abstract)	DLCO%: r = -0.398 ($p < 0.005$) FVC%: r = -0.458 ($p < 0.005$)
HRCT: Global Severity Score (0-12)	
Assayag et al. 2012[194] (Abstract)	DLCO%: r = -0.617 ($p < 0.0001$) FVC%: r = -0.580 ($p < 0.0001$)
Guarnieri et al. 2015[209]	DLCO%: r = 0.45 ($p = 0.01$)
HRCT: Inflammatory Index (0-48)	
Ooi et al. 2003[180]	DLCO%: r = -0.43 ($p = 0.008$)
HRCT: Inspiratory Volume/Body Surface Area	
Orlandi et al. 2006[181]	DLCO%: r = 0.56 ($p < 0.01$) TLC%: r = 0.69 ($p < 0.01$)
HRCT: Kazerooni Alveolar Score (0-5)	
De Santis et al. 2005[36]	DLCO%: r = -0.53 ($p < 0.0001$) FVC%: r = -0.51 ($p < 0.0001$)
HRCT: Kazerooni Interstitial Score (0-5)	
De Santis et al. 2005[36]	DLCO%: r = -0.35 ($p = 0.0006$) FVC%: r = -0.32 ($p = 0.0016$)
HRCT: Left Percentage of Lower Lobe Volume	
Cetincakm et al. 2016[213]	DLCOcorr%: r = 0.076 ($p = 0.750$) FEV_1/FVC%: r = -0.037 ($p = 0.873$) FVC%: r = 0.579 ($p = 0.006$)
HRCT: Low-Dose Volumetric Kurtosis	
Orlandi et al. 2006[181]	DLCO%: r = 0.72 ($p < 0.01$) TLC%: r = 0.75 ($p < 0.01$)
HRCT: Low-Dose Volumetric Mean Lung Attenuation	
Orlandi et al. 2006[181]	DLCO%: r = -0.68 ($p < 0.01$) TLC%: r = -0.74 ($p < 0.01$)
HRCT: Low-Dose Volumetric Total Lung Skewness	
Orlandi et al. 2006[181]	DLCO%: r = 0.72 ($p < 0.01$) TLC%: r = 0.71 ($p < 0.01$)
HRCT: Maximum Fibrosis Score in Zone of Maximal Involvement (0-4)	
Khanna et al. 2015[137]	<u>Placebo Group:</u> DLCO%: r = -0.46 ($p = 0.001$) FVC%: r = -0.21 ($p = 0.15$) <u>Cyclophosphamide Group:</u> DLCO%: r = -0.44 ($p = 0.003$) FVC%: r = -0.16 ($p = 0.29$)
HRCT: Mean Lung Density	

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Kloth et al. 2016[158]	**Longitudinal Validation:** FEV_1: r = 0.733 (p = 0.016)
HRCT: Modified Schurawitzki Total Score (0-18)	
Colaci et al. 2014[205]	DLCOcorr/VA%: r = -0.124 (NS) TLC%: r = -0.206 (p = 0.033) VC%: r = -0.310 (p < 0.001)
HRCT: Modified Warrick Total Score (0-115)	
Gatta et al. 2013[201]	DLCO%: r = -0.741 (p = 2.02E-08) DLCO/VA%: r = -0.687 (p = 0.0000005) FVC%: r = -0.509 (p = 0.000575) TLC%: r = -0.654 (p = 0.00000264)
HRCT: Nearest 5% - Ground-Glass Opacity	
Kim et al. 2001[177]	**Longitudinal Validation:** DLCO%: Kendall τ = 0.57 (NS) FEV_1 Absolute: Kendall τ = -0.221 (NS) FEV_1/FVC%: Kendall τ = -0.134 (NS) FVC Absolute: Kendall τ = -0.125 (NS)
HRCT: Nearest 5% - Honeycombing	
Kim et al. 2001[177]	**Longitudinal Validation:** DLCO%: Kendall τ = -0.411 (p = 0.049) FEV_1 Absolute: Kendall τ = -0.295 (p > 0.05) FEV_1/FVC%: Kendall τ = -0.276 or -0.020 (p > 0.05) FVC Absolute: Kendall τ = -0.272 (p > 0.05)
HRCT: Nearest 5% - Irregular Linear Opacity	
Kim et al. 2001[177]	**Longitudinal Validation:** DLCO%: Kendall τ = -0.172 (NS) FEV_1 Absolute: Kendall τ = 0.0 (NS) FEV_1/FVC%: Kendall τ = 0.256 (NS) FVC Absolute: Kendall τ = 0.20 (NS)
HRCT: Nearest 5% – Overall Lung Involvement	

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Wells et al. 1997[174]	<u>All Patients:</u> DLCO%: r = -0.70 ($p < 0.0005$) DLCO/VA%: r = -0.38 ($p < 0.003$) FEV_1%: r = -0.43 ($p < 0.001$) FVC%: r = -0.46 ($p < 0.0005$) TLC%: r = -0.51 ($p < 0.0005$) <u>Patients Undergoing Maximal Exercise Tests:</u> DLCO%: $R^2 = 0.52$ DLCO%: r = -0.69 ($p < 0.0005$) DLCO/VA%: r = -0.33 ($p < 0.02$) FEV_1%: r = -0.41 ($p = 0.003$) FVC%: r = -0.43 ($p < 0.002$) TLC%: r = -0.51 ($p < 0.0005$)
Wells et al. 1997[175]	<u>Patients with Predominant Ground-Glass Attenuation (HRCT Grade 1):</u> DLCO%: r = -0.68 <u>Patients with Mixed Appearances (HRCT Grade 2):</u> DLCO%: r = -0.78 <u>Patients with Predominance of a Reticular Pattern (HRCT Grade 3):</u> DLCO%: r = -0.76 <u>Patients with Reversible Disease on Serial HRCT:</u> DLCO%: r = -0.79 <u>Patients with No Regression of Disease at Follow-Up HRCT:</u> DLCO%: r = -0.72
Kim et al. 2001[177]	**<u>Longitudinal Validation:</u>** DLCO%: Kendall $\tau = -0.124$ (NS) FEV_1 Absolute: Kendall $\tau = -0.249$ (NS) FEV_1/FVC%: Kendall $\tau = -0.168$ (NS) FVC Absolute: Kendall $\tau = -0.172$ (NS)
Celeste et al. 2013[100]	DLCO%: r = -0.52 ($p < 0.0001$) (95% CI: -0.64, -0.38) FVC%: r = -0.456 ($p < 0.0001$) (95% CI: -0.599, -0.29)
Khanna et al. 2015[137]	<u>Placebo Group:</u> DLCO%: r = -0.48 ($p = 0.001$) FVC%: r = -0.05 ($p = 0.75$) <u>Cyclophosphamide Group:</u> DLCO%: r = -0.51 ($p = 0.001$) FVC%: r = -0.25 ($p = 0.09$)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Antoniou et al. 2016[212]	DLCO%: r = -0.56 FEV_1%: r = -0.28 FVC%: r = -0.35 FVC/DLCO Absolute: r = 0.36 ($p < 0.0005$)
HRCT: Parenchymal Kurtosis	
Ariani et al. 2015[206]	DLCO%: r = 0.42 ($p < 0.0001$) DLCO/VA%: r = 0.13 (NS) FVC%: r = 0.51 ($p < 0.0001$) TLC%: r = 0.50 ($p < 0.0001$)
HRCT: Parenchymal Mean Lung Attenuation	
Ariani et al. 2015[206]	DLCO%: r = -0.41 ($p < 0.0001$) DLCO/VA%: r = -0.09 (NS) FVC%: r = -0.52 ($p < 0.0001$) TLC%: r = -0.52 ($p < 0.0001$)
HRCT: Parenchymal Skewness	
Ariani et al. 2015[206]	DLCO%: r = 0.41 ($p < 0.0001$) DLCO/VA%: r = 0.13 (NS) FVC%: r = 0.49 ($p < 0.0001$) TLC%: r = 0.46 ($p < 0.0001$)
HRCT: Parenchymal Standard Deviation	
Ariani et al. 2015[206]	DLCO%: r = -0.33 ($p < 0.0001$) DLCO/VA%: r = -0.12 (NS) FVC%: r = -0.4 ($p < 0.0001$) TLC%: r = -0.43 ($p < 0.0001$)
HRCT: Quantitative Ground-Glass Opacity in Whole Lung	
Tashkin et al. 2016[215]	DLCOcorr%: r = -0.28 ($p < 0.0001$) FEV_1/FVC%: r = 0.15 ($p < 0.01$) FVC%: r = -0.10 ($p \geq 0.01$) TLC%: r = -0.21 ($p < 0.0001$)
HRCT: Quantitative Ground-Glass Opacity in Zone of Maximal Involvement	
Tashkin et al. 2016[215]	DLCOcorr%: r = 0.03 ($p \geq 0.01$) FEV_1/FVC%: r = -0.02 ($p \geq 0.01$) FVC%: r = -0.11 ($p \geq 0.01$) TLC%: r = 0.08 ($p \geq 0.01$)
HRCT: Quantitative Percentage with Fibrosis in Highest Zone at Baseline	
Kim et al. 2011[191]	**<u>Longitudinal Validation:</u>** FVC%: r = -0.40 ($p = 0.0003$) TLC%: r = -0.18 ($p = 0.12$)
HRCT: Quantitative Percentage with Fibrosis in Whole Lung	

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Kim et al. 2011[190] (Abstract)	Evaluation Set: DLCO%: r = -0.35 ($p < 0.0001$) FEV_1%: r = -0.23 ($p < 0.0001$) FVC%: r = -0.31 ($p < 0.0001$) New Cohort: DLCO%: r = -0.35 ($p < 0.0001$) FEV_1%: r = -0.45 ($p < 0.0001$) FVC%: r = -0.53 ($p < 0.0001$)
Kim et al. 2011[191]	**Longitudinal Validation:** FVC%: r = -0.33 ($p = 0.003$) TLC%: r = -0.16 ($p = 0.17$)
Khanna et al. 2015[137]	Placebo Group: DLCO%: r = -0.22 ($p = 0.13$) FVC%: r = -0.17 ($p = 0.26$) Cyclophosphamide Group: DLCO%: r = -0.20 ($p = 0.20$) FVC%: r = -0.25 ($p = 0.11$)
Kim et al. 2015[210] (Abstract)	DLCO%: r = -0.50 FVC%: r = -0.49 **Longitudinal Validation:** FVC%: r = -0.39 ($p = 0.0007$)
Tashkin et al. 2016[215]	DLCOcorr%: r = -0.42 ($p < 0.0001$) FEV_1/FVC%: r = 0.15 ($p \geq 0.01$) FVC%: r = -0.27 ($p < 0.0001$) TLC%: r = -0.37 ($p < 0.0001$) Scleroderma Lung Study I (SLS I): DLCOcorr%: $R^2 = 0.46$ ($p < 0.0001$) Scleroderma Lung Study II (SLS II): DLCOcorr%: $R^2 = 0.39$ ($p < 0.0001$)
HRCT: Quantitative Percentage with Fibrosis in Zone of Maximal Involvement	
Khanna et al. 2015[137]	Placebo Group: DLCO%: r = -0.43 ($p = 0.002$) FVC%: r = -0.45 ($p = 0.002$) Cyclophosphamide Group: DLCO%: r = -0.41 ($p = 0.005$) FVC%: r = -0.39 ($p = 0.02$)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Tashkin et al. 2016[215]	DLCOcorr%: r = -0.49 ($p < 0.0001$) FEV_1/FVC%: r = 0.14 ($p \geq 0.01$) FVC%: r = -0.34 ($p < 0.0001$) TLC%: r = -0.44 ($p < 0.0001$) <u>Scleroderma Lung Study I (SLS I):</u> DLCOcorr%: R^2 = 0.48 ($p < 0.0001$) <u>Scleroderma Lung Study II (SLS II):</u> DLCOcorr%: R^2 = 0.44 ($p < 0.0001$)
HRCT: Quantitative Total Extent of ILD in Whole Lung	
Khanna et al. 2015[137]	<u>Placebo Group</u>: DLCO%: r = -0.35 ($p = 0.01$) FVC%: r = -0.38 ($p = 0.008$) <u>Cyclophosphamide Group</u>: DLCO%: r = -0.07 ($p = 0.63$) FVC%: r = -0.08 ($p = 0.61$)
Tashkin et al. 2016[215]	DLCOcorr%: r = -0.43 ($p < 0.0001$) FEV_1/FVC%: r = 0.20 ($p < 0.01$) FVC%: r = -0.22 ($p < 0.0001$) TLC%: r = -0.32 ($p < 0.0001$) <u>Scleroderma Lung Study I (SLS I):</u> DLCOcorr%: R^2 = 0.44 ($p < 0.0001$) <u>Scleroderma Lung Study II (SLS II):</u> DLCOcorr%: R^2 = 0.37 ($p < 0.0001$)
HRCT: Quantitative Total Extent of ILD in Zone of Maximal Involvement	
Khanna et al. 2015[137]	<u>Placebo Group</u>: DLCO%: r = -0.41 ($p = 0.005$) FVC%: r = -0.27 ($p = 0.07$) <u>Cyclophosphamide Group</u>: DLCO%: r = -0.24 ($p = 0.12$) FVC%: r = -0.19 ($p = 0.23$)
Tashkin et al. 2016[215]	DLCOcorr%: r = -0.44 ($p < 0.0001$) FEV_1/FVC%: r = 0.17 ($p \geq 0.01$) FVC%: r = -0.32 ($p < 0.0001$) TLC%: r = -0.47 ($p < 0.0001$) <u>Scleroderma Lung Study I (SLS I):</u> DLCOcorr%: R^2 = 0.55 ($p < 0.0001$) <u>Scleroderma Lung Study II (SLS II):</u> DLCOcorr%: R^2 = 0.44 ($p < 0.0001$)
HRCT: Right Percentage of Lower Lobe Volume	

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Cetincakm et al. 2016[213]	DLCOcorr%: r = 0.115 (p = 0.628) FEV_1/FVC%: r = -0.041 (p = 0.860) FVC%: r = 0.536 (p = 0.012)
HRCT: Scoring Not Reported	
Vonk et al. 2009[187]	TLC%: r = 0.527 (p < 0.01)
HRCT: Tomographic Index	
Zimmermann et al. 2012[200] (Abstract)	DLCO: r = 0.31 (p = 0.04) Final Expiratory Volume: r = 0.31 (p = 0.03) FVC: r = 0.40 (p = 0.005) RV: r = 0.33 (p = 0.02) TLC: r = 0.55 (p < 0.001)
HRCT: Total Extent of Fibrosis – Scoring Not Reported	
Zamora et al. 2013[204] (Abstract)	DLCO%: r = -0.37 (p < 0.0001) FVC%: r = -0.44 (p < 0.0001) TLC%: r = -0.41 (p < 0.0001)
HRCT: Total Extent of Ground-Glass Opacity – Scoring Not Reported	
Zamora et al. 2013[204] (Abstract)	DLCO%: r = -0.10 (p = 0.11) FVC%: r = -0.17 (p = 0.005) TLC%: r = -0.066 (p = 0.34)
HRCT: Total Extent of Ground-Glass Opacity (0-24)	
Wilsher et al. 2012[199]	DLCO%: r = -0.57 (p = 0.01) FEV_1%: r = -0.38 (p = 0.05) VC%: r = -0.36 (p = 0.07)
HRCT: Total Extent of Honeycombing – Scoring Not Reported	
Zamora et al. 2013[204] (Abstract)	DLCO%: r = -0.32 (p < 0.0001) FVC%: r = -0.38 (p < 0.0001) TLC%: r = -0.34 (p < 0.0001)
HRCT: Total Extent of Reticular Pattern (0-24)	
Wilsher et al. 2012[199]	DLCO%: r = -0.53 (p = 0.01) FEV_1%: r = -0.19 (p = 0.33) VC%: r = -0.13 (p = 0.51)
HRCT: Total Lung Kurtosis	
Orlandi et al. 2006[181]	DLCO%: r = 0.75 (p < 0.01) TLC%: r = 0.78 (p < 0.01)
Camiciottoli et al. 2007[183]	DLCO%: r = 0.58 (p < 0.0001) FEV_1%: r = 0.56 (p < 0.0001) FRC%: r = 0.57 (p < 0.0001) FVC%: r = 0.71 (p < 0.0001)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Nguyen-Kim et al. 2013[202] (Abstract)	DLCO: r = 0.29 (p = 0.1) FEV_1: r = 0.45 (p = 0.01) FVC: r = 0.39 (p = 0.03) TLC: r = 0.29 (p = 0.1)
Ariani et al. 2015[206]	DLCO%: r = 0.38 (p < 0.0001) DLCO/VA%: r = 0.07 (NS) FVC%: r = 0.51 (p < 0.0001) TLC%: r = 0.49 (p < 0.0001)
Kim et al. 2015[210] (Abstract)	DLCO%: r = 0.45 FVC%: r = 0.42 **Longitudinal Validation:** FVC%: r = 0.14 (p = 0.24)
HRCT: Total Lung Skewness	
Orlandi et al. 2006[181]	DLCO%: r = 0.73 (p < 0.01) TLC%: r = 0.77 (p < 0.01)
Camiciottoli et al. 2007[183]	DLCO%: r = 0.62 (p < 0.0001) FEV_1%: r = 0.52 (p < 0.0005) FRC%: r = 0.58 (p < 0.0001) FVC%: r = 0.67 (p < 0.0001)
Nguyen-Kim et al. 2013[202] (Abstract)	DLCO: r = 0.34 (p = 0.056) FEV_1: r = 0.38 (p = 0.03) FVC: r = 0.47 (p = 0.006) TLC: r = 0.34 (p = 0.056)
Ariani et al. 2015[206]	DLCO%: r = 0.41 (p < 0.0001) DLCO/VA%: r = 0.11 (NS) FVC%: r = 0.52 (p < 0.0001) TLC%: r = 0.51 (p < 0.0001)
HRCT: Total Lung Standard Deviation	
Ariani et al. 2015[206]	DLCO%: r = -0.15 (p = 0.0226) DLCO/VA%: r = 0.05 (NS) FVC%: r = -0.23 (p = 0.0005) TLC%: r = -0.11 (NS)
HRCT: Total Mean Lung Attenuation	
Orlandi et al. 2006[181]	DLCO%: r = -0.66 (p < 0.01) TLC%: r = -0.77 (p < 0.01)
Camiciottoli et al. 2007[183]	DLCO%: r = -0.55 (p < 0.0001) FEV_1%: r = -0.58 (p < 0.001) FRC%: r = -0.59 (p < 0.0001) FVC%: r = -0.66 (p < 0.0001)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Ariani et al. 2015[206]	DLCO%: r = -0.41 ($p < 0.0001$) DLCO/VA%: r = -0.07 (NS) FVC%: r = -0.54 ($p < 0.0001$) TLC%: r = -0.52 ($p < 0.0001$)
HRCT: Total Percentage of Lower Lobe Volume	
Cetincakm et al. 2016[213]	DLCOcorr%: r = 0.121 ($p = 0.61$) FEV_1/FVC%: r = -0.062 ($p = 0.792$) FVC%: r = 0.539 ($p = 0.012$)
HRCT: Total Score (0-At Least 21)	
Shahin et al. 2001[178]	DLCO%: r = 0.64 ($p < 0.01$)
HRCT: Total Score (0-24)	
Mittal et al. 2012[196] (Abstract)	FVC%: r = -0.48
HRCT: Total Score (0-96)	
Ooi et al. 2003[180]	DLCO%: r = -0.43 ($p = 0.008$) FEV_1%: r = -0.37 ($p = 0.03$) FVC%: r = -0.43 ($p = 0.008$) TLC%: r = -0.47 ($p = 0.003$ or 0.008)
HRCT: Warrick Alveolitis Index (0-4)	
Bellia et al. 2009[185]	DLCO%: r = -0.46 ($p = 0.01$) TLC%: r = -0.28 ($p = 0.13$)
HRCT: Warrick Extent Score (1-3)	
Bellia et al. 2009[185]	DLCO%: r = -0.41 ($p = 0.02$) FEV_1%: r = -0.33 ($p = 0.06$) TLC%: r = -0.37 ($p = 0.04$)
HRCT: Warrick Fibrosis Index (0-26)	
Bellia et al. 2009[185]	DLCO%: r = -0.38 ($p = 0.04$) TLC%: r = -0.35 ($p = 0.05$)
HRCT: Warrick Severity Score (1-5)	
Bellia et al. 2009[185]	DLCO%: r = -0.39 ($p = 0.03$) FEV_1%: r = -0.33 ($p = 0.07$) TLC%: r = -0.34 ($p = 0.06$)
HRCT: Warrick Total Score (0-30)	
Diot et al. 1998[176]	DLCO%: r = -0.50 ($p < 0.0002$) TLC%: r = -0.39 ($p < 0.005$)
Orlandi et al. 2006[181]	DLCO%: r = -0.45 ($p < 0.01$) TLC%: r = -0.69 ($p < 0.01$)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

Beretta et al. 2007[182]	DLCOcorr%: r = -0.18 ($p \geq 0.05$) FVC%: r = -0.25 ($p \geq 0.05$) TLC%: r = -0.42 ($p < 0.05$)
Camiciottoli et al. 2007[183]	DLCO%: r = -0.39 ($p < 0.01$) FEV_1%: r = -0.53 ($p < 0.005$) FRC%: r = -0.51 ($p < 0.001$) FVC%: r = -0.56 ($p < 0.0001$)
Bellia et al. 2009[185]	DLCO%: r = -0.43 ($p = 0.02$) FEV_1%: r = -0.36 ($p = 0.05$) TLC%: r = -0.38 ($p = 0.04$)
Piorunek et al. 2013[203]	DLCO%: r = -0.36 ($p < 0.05$)
HRCT: Wells Total Score (0-3)	
Gilson et al. 2010[64]	**Longitudinal Validation:** FVC%: Concordance $\kappa = 0.6$
HRCT: Wells Total Score (0-4)	
Moghadam et al. 2011[192]	DLCO Absolute: r = -0.513 ($p < 0.001$) DLCO%: r = -0.657 ($p < 0.001$) FVC Absolute: r = -0.429 ($p = 0.001$) FVC%: r = -0.523 ($p < 0.001$) TLC Absolute: r = -0.375 ($p = 0.005$) TLC%: r = -0.549 ($p < 0.001$)
Lung Biopsy: Four-Point Scoring System for Interstitial Fibrosis	
Harrison et al. 1991[173]	DLCO%: r = -0.46 ($p < 0.01$)
Lung Biopsy: Four-Point Scoring System for Loss of Lung Architecture	
Harrison et al. 1991[173]	DLCO%: r = -0.4 ($p < 0.05$)

Abbreviations: % = Percent Predicted; AUC = Area Under the Curve; CI = Confidence Interval; DLCO = Diffusing Capacity for Carbon Monoxide; DLCO/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume; DLCOcorr = Diffusing Capacity for Carbon Monoxide Corrected for Haemoglobin; DLCOcorr/VA = Diffusing Capacity for Carbon Monoxide Corrected for Alveolar Volume and Haemoglobin; FRC = Functional Residual Capacity; FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the 1st Second of Forced Exhalation; FNR = False Negative Rate; FPR = False Positive Rate; HRCT = High-Resolution Computed Tomography; ILD = Interstitial Lung Disease; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; NPV = Negative Predictive Value; NS = Not Significant; p = p-value; PPV = Positive Predictive Value; R^2 = Coefficient of Determination; RV = Residual Volume; Se = Sensitivity; Sp = Specificity; TLC = Total Lung Capacity; VC = Vital Capacity

e-APPENDIX 7: Quality of the Five Validation Studies Evaluating the Performance of Pulmonary Function Tests (PFTs) Against High-Resolution Computed Tomography (HRCT). Study quality assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool.

Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standards
Wells 1997[174]	Low Risk	Unclear Risk	Unclear Risk	High Risk	Unclear Risk	Low Risk	Low Risk
Zamora 2013[204] (Abstract)	Low Risk	Unclear Risk	Unclear Risk	High Risk	Unclear Risk	Low Risk	Low Risk
Bernstein 2015[207] (Abstract)	Low Risk	Unclear Risk	Unclear Risk	High Risk	Low Risk	Low Risk	Low Risk
Suliman 2015[150]	Low Risk	Unclear Risk	Low Risk	Unclear Risk	Unclear Risk	Low Risk	Low Risk
Tashkin 2016[215]	Low Risk	Unclear Risk	Low Risk	High Risk	Unclear Risk	Low Risk	Low Risk

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