

Supplementary Table S1. Study characteristics.

Study	Country	Data source	Study duration	N participants
Cacciapaglia 2023 (1)	Italy	Four Italian rheumatology units	2009 - 2020	912
Fairley 2023 (2)	Australia	Australian Scleroderma Cohort Study	2007 - Oct 2019	1,561
Liem 2023 (3)	Netherlands	Leiden Combined Care in Systemic Sclerosis cohort	NR - Jan 2022	517
Moinzadeh 2023 (4)	Germany	German Network for Systemic Sclerosis	2003 - Mar 2022*	3,257
Nevskaya 2023 (5)	Canada	Canadian Scleroderma Research Group registry	Sep 2005 - Feb 2020	208
Rosato 2023 (6)	Italy	Centre at Sapienza University	2017 - NR	101
Caetano 2022 (7)	Portugal	Patients' medical files unit and from the National Healthcare Registry Platform	2011 - 2020	95
de Oliveira Martins 2022 (8)	Brazil	Federal University of São Paulo's Medical School	1982 - 2020	380
González Garcia 2022 (9)	Spain	RESCLE (Registro de ESCLerodermia) Registry	NR - Jun 2019	1,517
Morrisroe 2022 (10)	Australia	Australian Scleroderma Cohort Study	Jan 2008 - Jun 2021	2,039
Paik 2022 (11)	USA	Johns Hopkins Scleroderma Centre Research Registry	NR - Jun 2017	272
Uddin 2022 (12)	USA	National Emergency Department Sample	2009 - 2014	180,435
Vos 2022 (13)	Netherlands	Radboud University Medical Centre and Leiden University Medical Centre	Jan 2009 - Jul 2021	100
Xiang 2022 (14)	Singapore	Systemic Sclerosis Cohort in Singapore, scleroderma clinic in Singapore General Hospital	Oct 2017 - Jan 2020*	111
Chen 2022 (15)	China	First Affiliated Hospital of Guangxi Medical University (Nanning)	Oct 2012 - Jan 2019	470
Coffey 2021 (16)	USA	Rochester Epidemiology Project (for Olmsted County residents only)	1980 - 2018	85
De Almeida Chaves 2021 (17)	France	Systemic Scleroderma Toulouse Cohort	Jan 2000 - May 2018	375
Dwivedi 2021 (18)	India	Rheumatology Unit of a University Hospital in North-India	Jan 2014 - Sep 2018	94
Fairley 2021 (19)	Australia	Australian Scleroderma Cohort Study	NR	1,728
Khadra 2021 (20)	Australia	South Australian Scleroderma Register	1985 - 2018	30
Leeuwen 2021 (21)	Netherlands	Leiden University Medical Centre	2009 - 2019	492
Allanore 2020 (22)	Europe <sup>†</sup>	European Scleroderma Trials and Research (EUSTAR)	Jan 1995 - Feb 2019	4,822
Chung 2020 (23)	USA	Kaiser Permanente Northern California	2006 - Dec 2016	609
Foocharoen 2020 (24)	Thailand	Scleroderma Clinic at Srinagarind Hospital, Khon Kaen University	Jan 2013 - Jun 2019	566
Gayle 2020 (25)	England	Clinical Practice Research Datalink linked to Hospital Episode Statistics	Jan 2005 - Mar 2016	675
Morrisroe 2020 (26)	Australia	Australian Scleroderma Cohort Study	2008 - 2015*	1,128
Noviani 2020 (27)	Singapore	Systemic Sclerosis Cohort in Singapore (SCORE), three tertiary rheumatology centres in Singapore	Jan 2008 - Oct 2016	490
Ariani 2019 (28)	Italy	NR	NR	470
Castellvi 2019 (29)	Spain	Tertiary or secondary hospitals	Sep 2012 - Jan 2013	199
Hoffmann-Vold 2019 (30)	Norway	Databases of all public hospitals in Norway, and of all private rheumatologists in the country	2000 - 2018	815
Hsu 2019 (31)	USA	Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma registry	2005 - 2014	236
Morrisroe 2019a (32)	Australia	Australian Scleroderma Cohort Study	2008 - 2015*	1,128
Morrisroe 2019b (33)	Australia	Australian Scleroderma Cohort Study	2008 - 2015*	1,085
Park 2019 (34)	South Korea	Seoul National University Hospital	Mar 2018 - Jun 2018	120
Pokeerbox 2019 (35)	France	University hospitals, Lille, Paris (two centres), Nantes, and Lyon	Jan 2000 - Jul 2016	625
Sierakowska 2019 (36)	Poland	11 rheumatology centres in Poland	NR	231
Wu 2019 (37)	Europe <sup>†</sup>	European Scleroderma Trials and Research (EUSTAR) database	Jan 2009 - Aug 2017	1,021
Yang 2019 (38)	China	Peking Union Medical College Hospital	Aug 2010 - Aug 2011*	65
Apipattarakul 2018 (39)	Thailand	Srinagarind Hospital, Khon Kaen University	2006 - 2010	350
Fischer 2018 (40)	USA	Truven Health MarketScan Commercial and Medicare Supplemental healthcare claims databases	2003 - 2014	11,752 (4,605 for mortality analyses)
Hu 2018 (41)	China	Scleroderma Trials and Research Group (EUSTAR) and Chinese Rheumatism Data Centre (CRDC) database of the Peking Union Medical College Hospital	Feb 2009 - Dec 2015*	448
Li 2018 (42)	China	Peking University People's Hospital	Sep 2002 - Sep 2014*	201
Moon 2018 (43)	South Korea	11 university hospitals representing each geographic area of Korea	1986 - 2016	751
Panopoulos 2018 (44)	Greece	NR	Jan 1997 - Jun 2014	115
Rubio-Rivas 2018 (45)	Spain	Spanish Scleroderma Registry	1955 - Dec 2015	1,625
Morrisroe 2017 (46)	Australia	Australian Scleroderma Cohort Study	2011 - 2015*	531
Morrisroe 2016 (47)	Australia	Australian Scleroderma Cohort Study	Dec 2007 - Jun 2015*	802

\* enrolment period (study duration was not reported); <sup>†</sup> exact countries not specified.

Supplementary Table S2. Patient characteristics.

Study	Population	N	dcSSc %	lcSSc %	Other SSs %	Age in years	Age timepoint	% female
Cacciapaglia 2023 (1)	All	912	20%	80%	NA	Mean (SD): 45.2 (16)	Onset	91.6%
Fairley 2023 (2)	All	1,561	25.9%	NA	NA	Median (IQR): 47.1 (36.2, 56.4)	Onset	86.4%
Liem 2023 (3)	All	517	23%	NA	NA	Mean (SD): 54 (14)	Onset	81%
Moinzadeh 2023 (4)	All	3,257	31.4%	54.2%	NA	Mean (SD): 47.94 (14.58)	Diagnosis	80.2%
Nevskaya 2023 (5)	All	208	26%	NA	NA	Mean (SD): 52.1 (11.9)	NR	82.7%
Rosato 2023 (6)	All	101	42.6%	NA	NA	Median (IQR): 55 (47, 66)	NR	85.1%
Caetano 2022 (7)	Hospitalized	53	45.3%	54.7%	NA	Mean (SD): 52.9 (16.5)	Diagnosis	81.10%
	Non-hospitalized	42	23.8%	76.2%	NA	Mean (SD): 50.7 (15.6)	Diagnosis	92.90%
de Oliveira Martins 2022 (8)	All	380	32.1%	67.9%	NA	Mean (SD): 55.5 (13.0)	Baseline	89.7%
González Garcia 2022 (9)	All	1,517	61.1%	20.1%	scSSc: 11.5%	Mean (SD): 46.4 (16.5)	Onset	88.7%
Morrisroe 2022 (10)	GAVE	216	35.3%	NA	NA	Median (IQR): 49.51 (40.04, 58.21)	Onset	87%
	No GAVE	1,823	24.1%	NA	NA	Median (IQR): 46.70 (35.97, 56.70)	Onset	85.9%
Paik 2022 (11)	Troponin positive	83	55.4%	NA	NA	Mean (SD): 45.7 (14.2)	Onset	72.3%
	Troponin negative	189	37%	NA	NA	Mean (SD): 43.9 (13.8)	Onset	81.5%
Uddin 2022 (12)	Renal crisis	771	NA	NA	NA	Mean (SD): 59.6 (15.5)	NR	75.4%
	Without renal crisis	179,669	NA	NA	NA	Mean (SD): 57.9 (16.1)	NR	85%
Vos 2022 (13)	All	100	50%	NA	NA	Median (IQR): 54 (46, 64)	Baseline	58%
Xiang 2022 (14)	All	111	34.2%	43.2%	NA	Mean (SD): 49.4 (10.5)	Questionnaire	87.4%
Coffey 2021 (16)	All	85	82%	14%	scSSc: 4%	Mean (SD): 55.4 (16.0)	Diagnosis	91%
Chen 2022 (15)	All	470	70.2%	29.7%	NA	Mean (SD): 50.44 (12.31)	NR	60.5%
De Almeida Chaves 2021 (17)	All	375	17%	74%	scSSc: 9%	Mean (SD): 55.3 (14.2)	Onset	77.9%
Dwivedi 2021 (18)	Renal crisis	15	80%	NA	NA	Mean (SD): 47.3 (9.6)	Baseline	87%
	Without renal crisis	30	63%	NA	NA	Mean (SD): 40.0 (11)	Baseline	93%
Fairley 2021 (19)	No mixed connective tissue disease	1,505	27%	73%	NA	Mean (SD): 46.8 (14.1)	Onset	85.9%
	Mixed connective tissue disease	97	15.5%	84.5%	NA	Mean (SD): 38.4 (14.4)	Onset	85.6%
	Overlap	126	16.7%	83.3%	NA	Mean (SD): 46.5 (15.2)	Onset	89.7%
Khadra 2021 (20)	Scleroderma renal crisis	30	93%	7%	NA	Mean (SD): 51.2 (15.9)	NR	NR
Leeuwen 2021 (21)	All	492	24%	NA	NA	Mean (SD): 55 (14)	Baseline	79%
Allanore 2020 (22)	No HAQ-DI score at any time	4,132	100%	NA	NA	Mean (SD): 52.2 (13.6)	Baseline	77.8%
	≥ 1 HAQ-DI score	690	100%	NA	NA	Mean (SD): 53.8 (12.9)	Baseline	77.8%
	≥ 2 HAQ-DI scores	424	100%	NA	NA	Mean (SD): 53.1 (12.7)	Baseline	75.5%
Chung 2020 (23)	All	609	19%	NA	NA	Mean (SD): 55.4 (14.8)	Diagnosis	89.3%
Foocharoen 2020 (24)	All	566	73%	27%	NA	Mean (SD): 50.0 (11.8)	Onset	62.9%
Gayle 2020 (25)	No ILD	127	NA	NA	NA	Mean (SD): 62 (17)	Diagnosis	79%
	ILD	477	NA	NA	NA	Mean (SD): 71 (13)	Diagnosis	75%
	Other organ involvement	103	NA	NA	NA	Mean (SD): 65 (18)	Diagnosis	79%
Morrisroe 2020 (26)	ILD	355	42.5%	57.5%	NA	Mean (SD): 46.2 (14.7)	Onset	80.3%
	No ILD	793	19.2%	80.8%	NA	Mean (SD): 46.2 (13.9)	Onset	83.1%
Noviani 2020 (27)	ILD	92	48.9%	31.5%	NA	Mean (SD): 46.9 (2.4)	Diagnosis	82.6%
	PAH	50	26.5%	46.9%	NA	Mean (SD): 51.1 (16.4)	Diagnosis	88.0%
	ILD-PH	43	26.2%	47.6%	NA	Mean (SD): 53.8 (15.2)	Diagnosis	88.4%
	No/mild pulmonary involvement	305	33.4%	38.5%	NA	Mean (SD): 46.4 (14.6)	Diagnosis	88.5%
Ariani 2019 (28)	All	470	NA	NA	NA	Mean (95% CIs): 59.2 (57.2, 60.5)	NR	80.85%
Castellvi 2019 (29)	All	199	31%	64%	scSSc: 2%	Mean (range): 54 (21–90)	Baseline	82%
Hoffmann-Vold 2019 (30)	All	815	18%	NA	NA	Mean (SD): 53 (14.8)	Diagnosis	84%
Hsu 2019 (31)	All	236	NA	NA	NA	NR	NA	88%
Morrisroe 2019a (32)	PAH	153	NA	75.2%	NA	Mean (SD): 49.3 (13.9)	Onset	87.6%
	Without PAH	975	NA	73.4%	NA	Mean (SD): 45.7 (13.9)	Onset	81.40%
Morrisroe 2019b (33)	Digital ulcer	527	81.8%	65%	NA	Mean (SD): 43.6 (13.9)	Onset	81.9%
	No digital ulcer	558	18.2%	34.9%	NA	Mean (SD): 48.8 (14.0)	Onset	88.5%
Park 2019 (34)	All	120	65.8%	34.2%	NA	Mean (SD): 57.2 (11.2)	Baseline	88.3%
Pokeerbux 2019 (35)	All	625	28.8%	71%	NA	Mean (SD): 50.6 (14.5)	Onset	79%
Sierakowska 2019 (36)	All	231	50.6%	49.4%	NA	Mean (SD): 55.82 (12.55)	Questionnaire	85.7%
Wu 2019 (37)	All (dcSSc)	1,021	100%	0%	NA	Mean (SD): 52.0 (13.7)	Baseline	75.7%

Study	Population	N	dcSSc %	lcSSc %	Other SSc%	Age in years	Age timepoint	% female
Yang 2019 (38)	All	65	61.5%	38.5%	NA	Mean (SD): 47.8 (13.3)	Baseline	92.3%
Apipattarakul 2018 (39)	Adult-onset SSc	297	76.1%	NA	NA	<60	First SSc symptom	65%
	Elderly-onset SSc	53	75.5%	NA	NA	≥60	First SSc symptom	60.4%
Fischer 2018 (40)	Incident SSc (newly diagnosed, no manifestations)	11,752	NA	NA	NA	Mean (SD): 54.9 (14.7)	Diagnosis	84.8%
	Newly diagnosed ILD	1,808	NA	NA	NA	Mean (SD): 57.0 (12.7)	Diagnosis	80.8%
	Newly diagnosed PAH	1,223	NA	NA	NA	Mean (SD): 59.9 (12.1)	Diagnosis	86.8%
Hu 2018 (41)	All	448	43.3%	56.7%	NA	Mean (SD): 39.0 (12.5)	At onset	90.4%
Li 2018 (42)	All	201	50%	30.3%	NA	Mean (SD): 41.6 (13.5)	At onset	91%
Moon 2018 (43)	All	751	35.2%	64.8%	NA	Mean (SD): 46.0 (14.2)	At onset	86.7%
Panopoulos 2018 (44)	All	115	47%	NA	NA	Mean (SD): 48.1 (13.5)	Diagnosis	84.3%
Rubio-Rivas 2018 (45)	All	1,625	22%	60%	scSSc: 11%	Mean (SD): 45.5 (16.4)	Onset	89%
Morrisroe 2017 (46)	Hospitalization: admitted	432	NA	70.8%	NA	Mean (SD): 46.3 (14.4)	Onset	86.6%
	Hospitalization: not admitted	99	NA	73.7%	NA	Mean (SD): 46.1 (12.9)	Onset	87.9%
	ED presentation	284	NA	70.7%	NA	Mean (SD): 46.5 (14.9)	Onset	86.4%
	No ED presentation	231	NA	72.1%	NA	Mean (SD): 45.9 (13.0)	Onset	87.5%
	Ambulatory care: utilized MBS listed service	494	NA	71.7%	NA	Mean (SD): 46.2 (14.1)	Onset	87.9%
	Ambulatory care: attended public outpatient	263	NA	70.3%	NA	Mean (SD): 47.7 (14.4)	Onset	86.3%
Morrisroe 2016 (47)	Medication use	531	NA	71.4%	NA	Mean (SD): 46.3 (14.1)	Onset	86.8%
	Employed	642	25.4%	67.8%	NA	Mean (SD): 50.4 (10.7)	Recruitment	83.80%
	Unemployed	160	38.1%	53.8%	NA	Mean (SD): 51.9 (10.4)	Recruitment	82.50%

SSc: systemic sclerosis; dcSSc: diffuse cutaneous SSc; DU: digital ulcer; ED: emergency department; sSSc: extensive SSc; GAVE: gastric antral vascular ectasia; HAQ-DI: Health Assessment Questionnaire-Disability Index; IQR: interquartile range; ILD: interstitial lung disease; lcSSc: limited cutaneous SSc; MBS: Medicare Benefits Schedule; NA: not applicable; NR: not reported; PH: pulmonary hypertension; SRC: scleroderma renal crisis; scSSc: sine cutaneous SSc; SD: standard deviation.

**Supplementary Table S3.** Kaplan-Meier survival estimates of patients with SSc and organ involvement.

Study	Manifestation description	N participants at baseline	Length of estimate	p-value for decreased survival (compared to SSc patients without manifestation)
<b>Interstitial lung disease</b>				
Cacciapaglia 2023 (19)	ILD	380	10 years	0.23
Fairley 2023 (2)	ILD	345	25 years	<0.001
	ILD and PAH (lcSSc)	229	12 years	NR
Moinzadeh 2023 (4)	ILD and PAH (dcSSc)	86	12 years	NR
	ILD	923	5 years	<0.001
de Oliveira Martins 2022 (8)	ILD	216	15 years	0.006
Foocharoen 2020 (24)	Lung fibrosis	265	30 years	NR
Ariani 2019 (28)	ILD	196	5 years	0.1
Hoffmann-Vold 2019 (30)	Lung fibrosis	61	10 years	<0.001
Fischer 2018 (40)	ILD	715	10 years	NR
Hu 2018 (41)	ILD	358	30 years	<0.001
<b>Pulmonary hypertension</b>				
Cacciapaglia 2023 (1)	Group 1 PH	36	10 years	<0.001
Fairley 2023 (2)	PAH	109	25 years	<0.001
Moinzadeh 2023 (4)	PAH	148	5 years	<0.001
Foocharoen 2020 (24)	PAH	102	30 years	NR
Fischer 2018 (40)	PAH	525	10 years	NR
Hu 2018 (41)	PAH	67	30 years	<0.001
<b>PH-ILD</b>				
Cacciapaglia 2023 (1)	Group 3 pulmonary hypertension	NR	10 years	<0.001
Fairley 2023 (2)	ILD and PAH	107	25 years	<0.001
	ILD and PAH (lcSSc)	55	12 years	NR
Moinzadeh 2023 (4)	ILD and PAH (dcSSc)	48	12 years	NR
	ILD and PH	200	5 years	<0.001
<b>Cardiac</b>				
González Garcia 2022 (9)	Left ventricular diastolic dysfunction	272	30 years	0.048
Foocharoen 2020 (24)	Impaired left ventricular function	7	30 years	NR
Moon 2018 (43)	Cardiovascular involvement	84	25 years	<0.001
Hu 2018 (41)	Arrhythmia	16	30 years	0.000
	Pericardial effusion	57	30 years	0.009
<b>Renal involvement</b>				
Dwivedi 2021 (18)	Renal crisis	15	80 months	<0.001
Khadra 2021 (20)	Renal crisis	30	60 years	0.0002
Foocharoen 2020 (24)	Renal crisis	11	30 years	NR
Hu 2018 (41)	Renal crisis	5	30 years	0.001
<b>Gastrointestinal</b>				
Morrisroe 2022 (10)	GAVE	216	30 years	0.390
Foocharoen 2020 (24)	Intestinal involvement	99	30 years	NR
Hu 2018 (41)	Gastrointestinal	NR	30 years	0.87
<b>Musculoskeletal</b>				
Hu 2018 (41)	Joint involvement	121	30 years	0.09
	Muscular involvement	44	30 years	0.315
<b>Peripheral vascular</b>				
Morrisroe 2019b (33)	Digital ulcers	505	40 years	≥0.05
Hu 2018 (41)	Vascular involvement	430	30 years	0.121
<b>Skin</b>				
Hu 2018 (41)	Modified Rodnan's score ≤15	370	20 years	0.005

GAVE: gastric antral vascular ectasia; ILD: interstitial lung disease; NR: not reported; PAH: pulmonary arterial hypertension; PH: pulmonary hypertension.

Supplementary Table S4. Healthcare resource use of patients with SSc manifestations.

Study	Country	Summary of reported impact on healthcare resource use compared to SSc patients without manifestation
<b>ILD</b>		
Caetano 2022 (7)	Portugal	No significant association with hospitalisation
Gayle 2020 (25)	England	<b>Higher inpatient stays, emergency department attendances, general practitioner visits and outpatient stays</b> , but similar SSc-related inpatient stays
Noviani 2020 (27)	Singapore	No significant association with hospitalisation
Morrisroe 2019a (32)	Australia	<b>Significantly higher hospitalisation, emergency department, and medical benefits schedule use</b>
Fischer 2018 (40)	USA	<b>A higher percentage of SSc-ILD patients required inpatient admission (53% vs 44%) or emergency room visits (74% vs 61%) over five years of follow-up</b>
Morrisroe 2017 (46)	Australia	<b>Significant association with emergency room visits</b> , but no significant association with hospitalization
<b>Pulmonary hypertension</b>		
Caetano 2022 (7)	Portugal	No significant association with hospitalization
Fischer 2018 (40)	USA	<b>A higher percentage of SSc-PAH patients required inpatient admission (64% vs 44%) or emergency room visits (72% vs 61%) over five years of follow-up</b>
Morrisroe 2017 (46)	Australia	No significant association with hospitalisation (p=0.27) or emergency room visits.
Morrisroe 2019a (32)	Australia	<b>Significantly higher hospitalisation, emergency department, and medical benefits schedule use</b>
Noviani 2020 (27)	Singapore	No significant association with hospitalisation
<b>PH-ILD</b>		
Noviani 2020 (27)	Singapore	<b>Significant association with hospitalization (p&lt;0.001) by univariate analysis</b> , however, no significant association in multivariate analysis
<b>Cardiac involvement</b>		
Caetano 2022 (7)	Portugal	<b>Significant association between diastolic dysfunction of left ventricle and hospitalisation</b> , however no significant association between right ventricle dysfunction and hospitalisation
Noviani 2020 (27)	Singapore	<b>Significant association between right heart failure and hospitalisation</b>
<b>Renal involvement</b>		
Noviani 2020 (27)	Singapore	<b>Significant association with hospitalisation</b>
Morrisroe 2017 (46)	Australia	No significant association with emergency room visits or hospitalisation
<b>Gastrointestinal involvement</b>		
Caetano 2022 (7)	Portugal	No significant association with hospitalisation
Morrisroe 2017 (46)	Australia	No significant association with hospitalisation or emergency room visits
Noviani 2020 (27)	Singapore	No significant association with higher hospitalisation
<b>Peripheral vascular involvement</b>		
Nevskaya 2023 (5)	Canada	<b>Significant increase in total number of healthcare visits, including rheumatologist visits and internal medicine specialist visits, total number of tests or diagnostic procedures performed, number of aids purchased/received</b>
Caetano 2022 (7)	Portugal	<b>Significant association with hospitalisation</b>
Noviani 2020 (27)	Singapore	<b>Significant association with hospitalisation for digital ulcer/gangrene</b> , but not for telangiectasia or Raynaud phenomenon
Morrisroe 2019b (33)	Australia	<b>Significant association with hospitalisation, emergency department visits and medical benefits schedule service utilization rate</b>
Morrisroe 2017 (46)	Australia	<b>Significant association with emergency department visits</b> , but not with hospitalisations

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