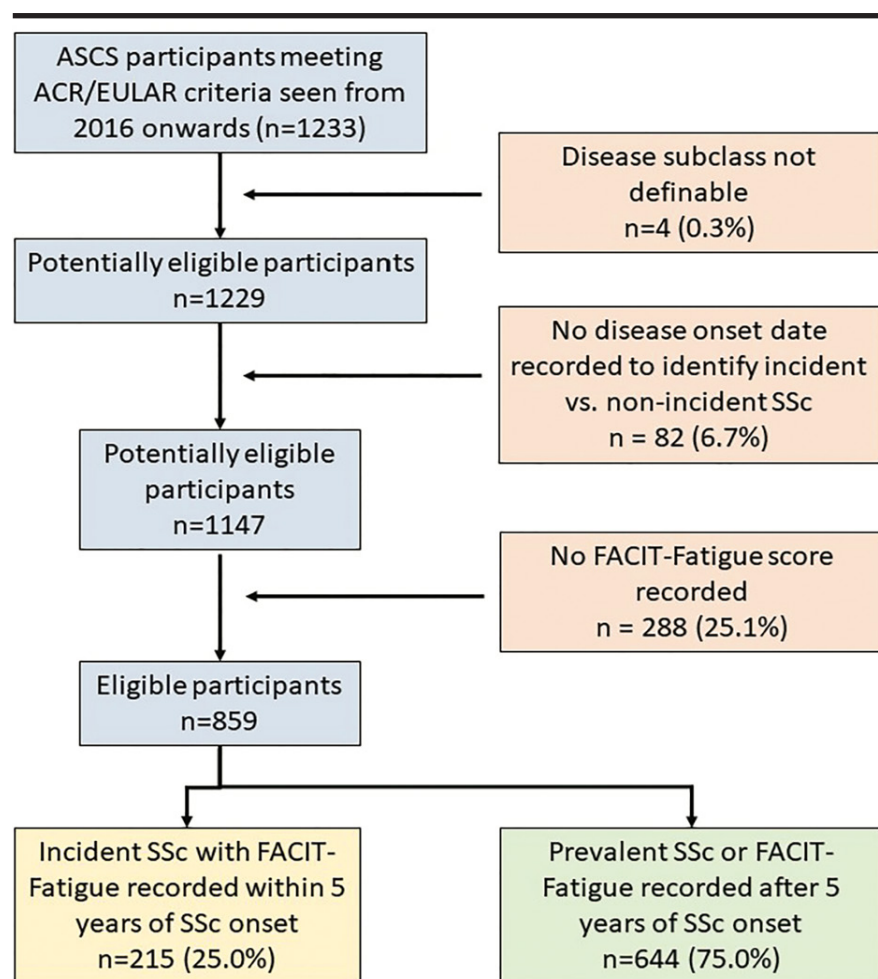


Appendix 1.**Collection of clinical data**

At each visit participants were asked to report gastrointestinal symptoms (including reflux, vomiting, sicca symptoms, diarrhoea/constipation) and clinical examination features were recorded (including modified Rodnan Skin Score (MRSS), tendon friction rubs, muscle atrophy, proximal weakness and synovitis). All participants underwent annual transthoracic echocardiography (TTE) and pulmonary function testing (PFT) as screening for pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD). PAH was confirmed by right heart catheterisation, according to the revised (15) or previous (16) PAH classification criteria. ILD was diagnosed by high-resolution computed tomography (HRCT), which was performed if abnormalities

were detected on screening investigations. ILD severity was defined by the extent of radiological involvement and percent-predicted forced vital capacity (FVC) (limited: <20% HRCT involvement or 20-30% with FVC \geq 70%, or extensive: >30% HRCT involvement or 20-30% with FVC<70%) (17). Anaemia was defined as haemoglobin levels <120g/L. Serological testing was performed according to local laboratory protocols. To measure multimorbidity, we calculated a modified Charlson Comorbidity Index (CCI) score (18) (included items provided in Supplementary Table S3). Hemiplegia, HIV/AIDS and dementia were excluded from the calculation of the CCI as these data are not collected in the ASCS. A maximum possible CCI score in our cohort was 19. Scores of ≥ 4 were defined as multimorbidity (19).



Supplementary Fig. S1. Flowchart of included participants.

ACR/EULAR: American College of Rheumatology/European Alliance of Associations for Rheumatology; ASCS: Australian Scleroderma Cohort Study; n: number; SSc: systemic sclerosis.

Supplementary Table S1. Included vs. excluded participants.

Variable	Included Participants (n=859, 74.9%)	Excluded Participants (n=288, 25.1%)	p-value
Age at SSc onset (years)	47.2 (35.6-56.6)	46.9 (37.3-57.7)	0.46
Female sex	735 (85.6%)	239 (83.0%)	0.29
Caucasian	731 (89.0%)	244 (88.4%)	0.43
Baseline MSS Score	5 (3-7)	5 (3-7)	0.60
Diffuse SSc	209 (24.3%)	87 (30.2%)	0.05
ANA Centromere	380 (45.1%)	131 (47.0%)	0.60
Sci70	138 (16.5%)	42 (15.4%)	0.66
RNA Polymerase-3	109 (14.8%)	25 (14.2%)	0.85
PAH*	65 (7.6%)	29 (10.1%)	0.18
ILD* [^]	276 (32.1%)	77 (26.7%)	0.09
Multimorbidity (CCI Scores ≥ 4)*	211 (24.6%)	50 (17.4%)	0.01

*Denotes ever from SSc onset. [^]ILD defined on HRCT.

ANA: antinuclear antibody; CCI: Charlson Comorbidity Index; HRCT: high resolution computed tomography; ILD: interstitial lung disease; MSS: Medsger Severity Score; n: number; PAH: pulmonary arterial hypertension; SSc: systemic sclerosis.

Supplementary Table S2. Univariable GEE regression modelling.

Variable	N ¹	Regression coefficient	95% CI	p-value
Within incident only				
Age at SSc onset	662	-0.1 units	-0.2 to 0.0	<0.01
Male sex	662	-3.2 units	-6.6 to 0.1	0.06
Modified Rodnan Skin Score	569	-0.3 units	-0.5 to -0.2	<0.01
SF-36 MCS lower than cohort median	602	-10.0 units	-12.3 to -7.7	<0.01
SF-36 PCS lower than cohort median	662	-12.2 units	-14.4 to -10.1	<0.01
Pulmonary arterial hypertension	662	-9.7 units	-16.9 to -2.5	<0.01
FVC 10% reduction	370	-3.3 units	-6.7 to 0.2	0.06
DLCO 10% reduction	292	0.8 units	-3.2 to 4.7	0.71
Any ILD on HRCT	662	-1.3 units	-4.3 to 1.7	0.39
Extensive ILD	662	-1.5 units	-7.0 to 3.9	0.58
Left ventricular ejection fraction<50%	596	-13.0 units	-20.7 to -5.2	<0.01
Gastrointestinal symptoms ²	645	-1.1 units	-4.0 to 1.9	0.48
Hypoalbuminaemia (Albumin <35g/L)	618	-4.3 units	-7.8 to -0.8	0.02
Anaemia (haemoglobin<120g/L)	628	-4.2 units	-7.3 to -1.1	<0.01
BMI<18.5kg/m ²	574	-4.1 units	-9.4 to 1.3	0.14
CRP>5IU/L	613	-3.3 units	-6.0 to -0.6	0.02
Prednisolone at each visit	662	-6.0 units	-9.3 to -2.7	<0.01
Non-corticosteroid immunosuppression ³	662	-5.7 units	-8.1 to -3.2	<0.01
Within prevalent only				
Age at SSc onset	2161	-0.1 units	-0.2 to 0.0	0.01
Male sex	2161	0.7 units	-1.8 to 3.3	0.57
Modified Rodnan Skin Score	1856	-0.2 units	-0.3 to -0.1	<0.01
SF-36 MCS lower than cohort median	1975	-10.1 units	-11.3 to -9.0	<0.01
SF-36 PCS lower than cohort median	2161	-9.5 units	-10.7 to -8.4	<0.01
Pulmonary arterial hypertension	2161	-3.0 units	-6.0 to 0.0	0.05
FVC 10% reduction	1599	-0.3 units	-1.7 to 1.2	0.73
DLCO 10% reduction	1358	0.1 units	-1.4 to 1.6	0.89
Any ILD on HRCT	2161	-2.4 units	-4.1 to -0.7	<0.01
Extensive ILD	2160	-2.5 units	-5.2 to 0.1	0.06
Gastrointestinal symptoms ²	2127	-5.2 units	-7.3 to -3.2	<0.01
Hypoalbuminaemia (Albumin <35g/L)	2005	-3.7 units	-5.5 to -1.8	<0.01
Anaemia (haemoglobin<120g/L)	2021	-2.7 units	-4.3 to -1.2	<0.01
BMI<18.5kg/m ²	1891	-5.4 units	-8.8 to -2.0	<0.01
CRP>5IU/L	1955	-3.3 units	-4.7 to -1.9	<0.01
Prednisolone at each visit	2160	-1.8 units	-3.7 to 0.1	0.07
Non-corticosteroid immunosuppression ³	2160	-0.7 units	-2.3 to 0.8	0.34

CRP: C-reactive protein; DLCO: diffusing capacity for carbon monoxide; FVC: forced vital capacity; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; IU/L: international units per litre; MCS: mental component summary; n: number; PCS: physical component summary; SF-36: short form-36; SSc: systemic sclerosis.

¹Number of observations available for analysis. ²Gastrointestinal symptoms defined as reflux, dysphagia, vomiting, constipation, diarrhoea, bloating or faecal incontinence at each study visit. ³Missing information

Supplementary Table S3. Charlson comorbidity index score calculation.

Original Charlson Comorbidity Index		ASCS Adaptation	
Item	Score	Item	Score
Cerebrovascular disease	1	Patient-reported CVA/TIA*	1
Congestive heart failure	1	LVEF≤50%*	1
COPD/Asthma	1	Patient-reported COPD or asthma	1
Dementia	1	Not recorded; excluded	N/A
Depression	1	Not recorded; excluded	N/A
Hypertension	1	Patient-reported hypertension*	1
Diabetes without end organ dysfunction	1	Patient-reported diabetes*	1
Diabetes with end organ damage	2	Not recorded; excluded	N/A
Liver disease - Mild	1	Not recorded; excluded	N/A
Liver disease – moderate or severe	3	Not recorded; excluded	N/A
Myocardial infarction	1	Patient-reported angina or AMI*	1
PVD	1	Patient-reported PVD or PVD treatments*	1
Rheumatic disease	1	Applicable to all patients with SSc	1
Peptic ulcer disease	1	Excluded; not recorded independently of other GI manifestations of SSc	N/A
Hemiplegia	2	Not recorded; excluded	N/A
Moderate to severe renal disease	2	Creatinine>265umol/L ever, or previous dialysis or renal transplantation*	2
Any tumour	2	Patient-reported malignancy (excluding NMSC)	2
Metastatic solid tumour	6	Not recorded; excluded	N/A
Skin ulcers or cellulitis	2	Patient-reported non-hand skin ulcers*	2
Takes warfarin	1	Warfarin or other anticoagulation	1
Leukaemia	2	Patient-reported leukaemia	2
Lymphoma	2	Patient-reported lymphoma	2
HIV/AIDS	6	Not recorded; excluded	N/A
Maximum score	38	Maximum Score	19

AMI: acute myocardial infarction; ASCS: Australian Scleroderma Cohort study; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome; GI: gastrointestinal; LVEF: left ventricular ejection fraction; NMSC: non-melanoma skin cancer; PVD: peripheral vascular disease; SSc: systemic sclerosis; TIA: transient ischaemic attack; umol/L: micromoles per litre.