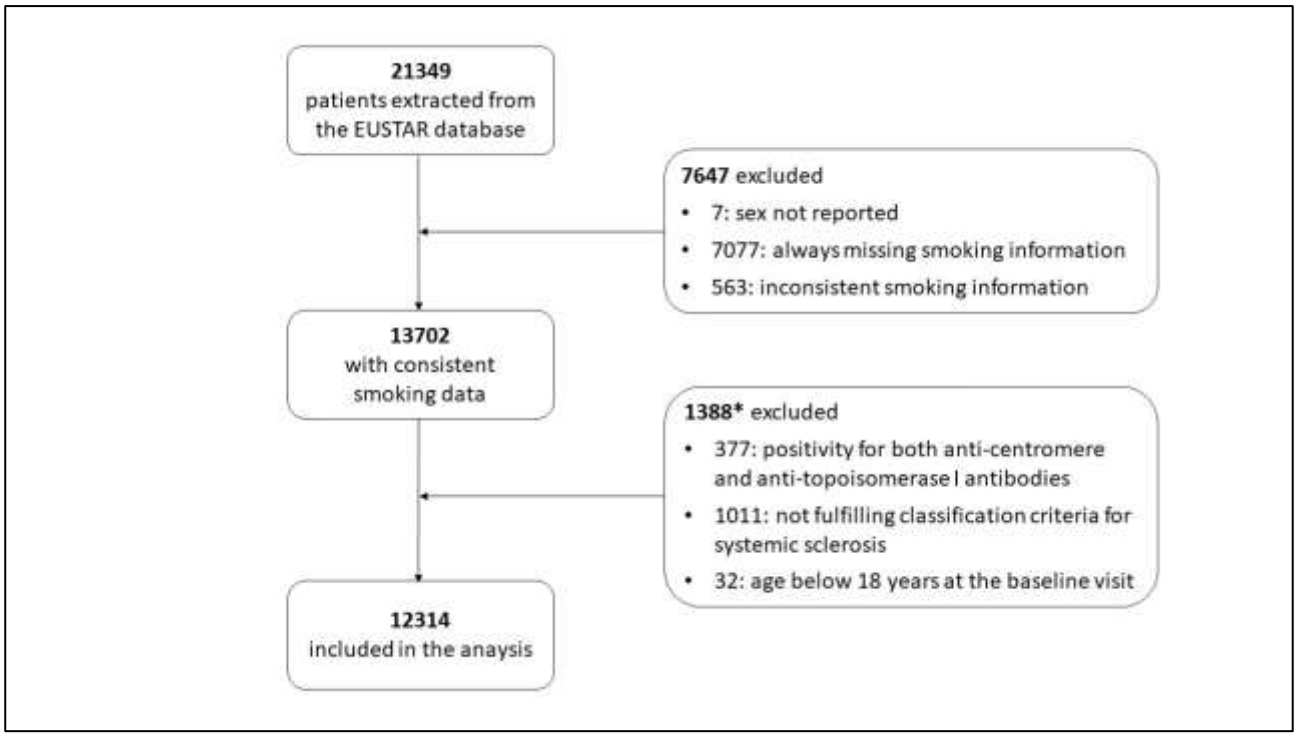
Supplementary material

Figure S1. Flowchart of the EUSTAR patients included in the analysis.



* Does not sum up as categories are not exclusive.

Figure S2. Kaplan–Meier curves of ever-smokers and never-smokers showing development of interstitial lung disease (ILD) (panel A), progression of ILD (panel B), development of cardiac involvement (panel C), progression of skin involvement (panel D), development of pulmonary hypertension (PH) (panel E), development of digital ulcers (DU) or digital ischemia (panel F), development of gastrointestinal involvement (panel G) and development of renal involvement (panel H) in the EUSTAR patients stratified by sex.

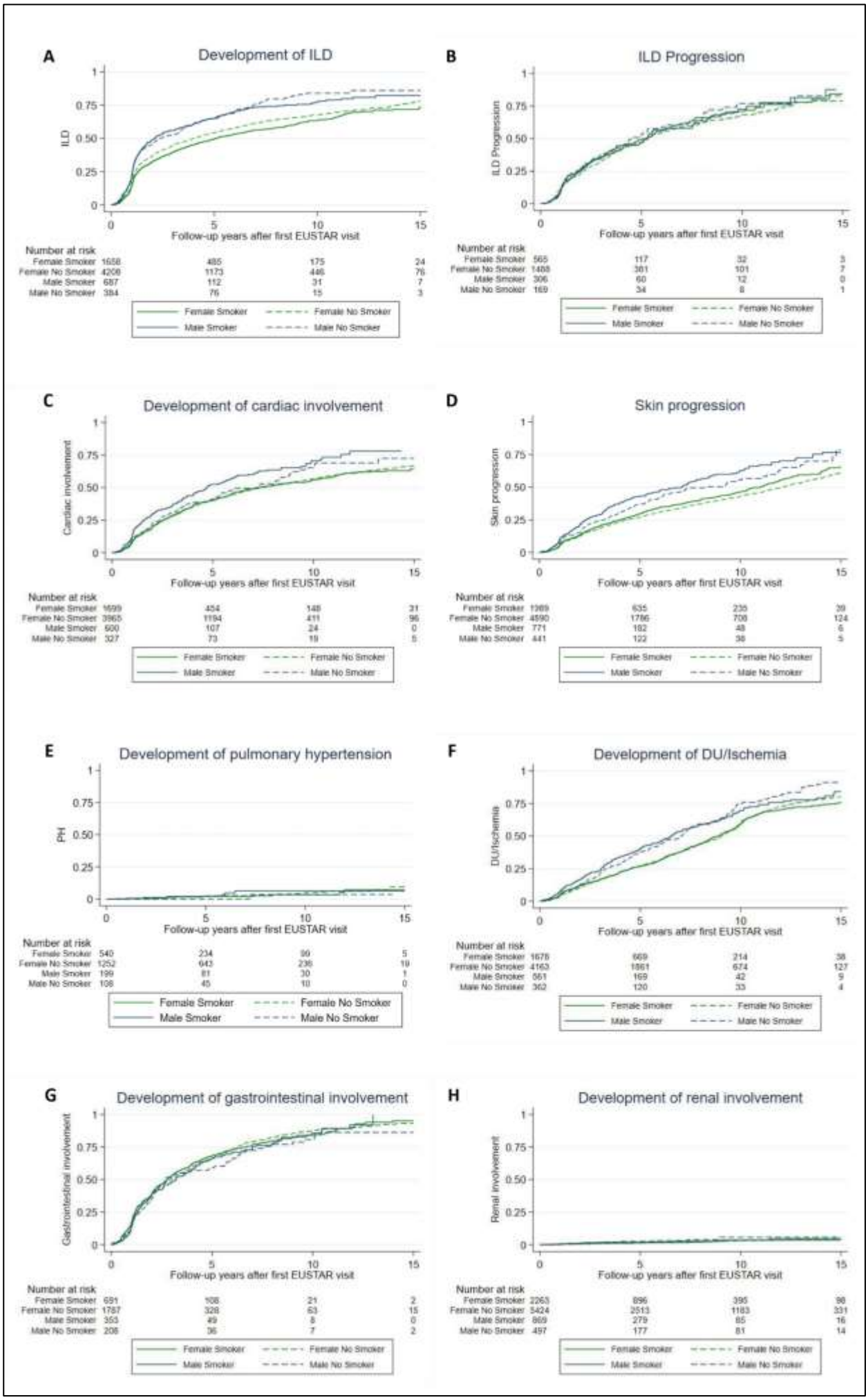

A
Development of ILD
ILD
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 1658 485 175 24
Female No Smoker 4208 1173 446 76
Male Smoker 687 112 31 7
Male No Smoker 384 76 15 3
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
B
ILD Progression
ILD Progression
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 565 117 32 3
Female No Smoker 1468 381 101 7
Male Smoker 306 60 12 0
Male No Smoker 169 34 8 1
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
C
Development of cardiac involvement
Cardiac involvement
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 1699 454 148 31
Female No Smoker 3965 1194 411 96
Male Smoker 600 107 24 0
Male No Smoker 327 73 19 5
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
D
Skin progression
Skin progression
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 1989 635 235 39
Female No Smoker 4590 1786 708 124
Male Smoker 771 182 48 6
Male No Smoker 441 122 38 5
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
E
Development of pulmonary hypertension
PH
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 540 234 99 5
Female No Smoker 1252 643 236 19
Male Smoker 199 81 30 1
Male No Smoker 108 45 10 0
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
F
Development of DU/Ischemia
DU/Ischemia
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 1676 669 214 38
Female No Smoker 4163 1861 674 127
Male Smoker 561 169 42 9
Male No Smoker 362 120 33 4
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
G
Development of gastrointestinal involvement
Gastrointestinal involvement
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 691 108 21 2
Female No Smoker 1787 328 63 15
Male Smoker 353 49 8 0
Male No Smoker 208 36 7 2
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker
H
Development of renal involvement
Renal involvement
Follow-up years after first EUSTAR visit
Number at risk
Female Smoker 2263 896 395 98
Female No Smoker 5424 2513 1183 331
Male Smoker 869 279 85 16
Male No Smoker 497 177 81 14
Female Smoker
Female No Smoker
Male Smoker
Male No Smoker

Table S3. Baseline characteristics of 9,035 patients in the EUSTAR registry excluded from the study.

Demographic and clinical variables		Number of patients with data
Male sex, n (%)*†	1,244 (14)	9,028
Age, mean ± SD, years	55.3 ± 14.5	9,017
Disease duration, median (IQR), years †	8.4 (3.3 - 16.7)	7,408
Extent of skin involvement		7,653
no skin involvement, n (%)*†	211 (3)	
only sclerodactyly, n (%)*†	883 (12)	
limited cutaneous involvement, n (%)*	4,163 (54)	
diffuse cutaneous involvement, n (%)*†	2,396 (31)	
Anti-centromere antibodies, n (%)*	3,423 (38)	9,028
Anti-topoisomerase I antibodies, n (%)*†	3,008 (33)	9,028
Anti-RNA polymerase III antibodies, n (%)*	57 (7)	864
Anti-U1RNP antibodies, n (%)*†	92 (9)	1,061
Anti-PM/Scl antibodies, n (%)*	25 (4)	624
Anti-SSA antibodies, n (%)*	43 (11)	396
Modified Rodnan Skin Score, median (IQR)	5 (2 - 12)	6,889
Digital ulcers, n (%)*†	500 (28)	1,763
Pulmonary hypertension, n (%)*	7 (3)	216
Interstitial lung disease, n (%)*†	3,095 (40)	7,744
DLCO % predicted, mean ± SD †	70.5 ± 28.8	5,960
FVC % predicted, mean ± SD	93.4 ± 21.6	3,253
Gastrointestinal symptoms, n (%)*	5,925 (67)	8,817

Legend: DLCO: diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; IQR: interquartile range; SD: standard deviation. Disease duration was defined since the date of onset of Raynaud's phenomenon; * percentage is calculated on patients with data available; † statistically significant difference with the included population.