Supplementary file 1.

A blood test (with serum urate level, SSc-specific antibodies and NT-proBNP) was performed. The serum urate level was expressed as milligram per decilitre. SSc-specific antibodies were detected using indirect immunofluorescence on Hep-2000 cells (Immunoconcepts, Sacramento, CA, USA) and a line-immunoasssay (INNO-LIA ANA Update, Innogenetics NV, Zwijnaarde, Belgium). Blood samples for NT-proBNP were collected into EDTA tubes, centrifuged and stored at -80°C. NT-proBNP was measured using the AlereTriage® NT-proBNP immunoassay test with the AlereTriage® MeterPro [23].

Supplementary file 2. 2009-ESC/ERS-guidelines and 2015-ESC/ERS-guidelines [5, 15].

The 2009-screening algorithm recommend referral for RHC in patients with a peak TRV >3.4 m/s, 2.8< peak TRV ≤3.4 m/s in combination with symptoms (defined as at least one of the following parameters: current dyspnoea, current syncope/near syncope, current angina, presence of peripheral oedema) or a peak TRV ≤2.8 m/s in combination with symptoms and additional echocardiographic variables suggestive for PH as used in the original DETECT-study (right atrial area [RA] >16 cm² and/or a ratio of right ventricular diameter/left ventricular end diastolic diameter >0.8) [15, 16]. When it was not possible to measure the TRV accurately, the 2009-screening algorithm was applied by the combination of symptoms and additional echocardiographic variables suggestive for PH.

According to the 2015-ESC/ERS-guidelines, RHC was recommended when patients had, based on echocardiographic findings, an intermediate or high-risk for PH defined as peak TRV >2.8 m/s or ≤2.8 m/s (or not measurable) in combination with additional echocardiographic variables suggestive for PH from at least 2 of the 3 different categories (1. the ventricles [right ventricle/left ventricle basal diameter area >1.0, flattening of the interventricular septum], 2. the pulmonary artery [right ventricular outflow doppler acceleration time <105 msec, early diastolic pulmonary regurgitation velocity >2.2 m/s when pulmonary valve insufficiency >1/4, pulmonary artery diameter >25 mm] or 3. the vena cava and right atrium [inferior vena cava diameter >21 mm with decreased inspiratory collapse, RA >18 cm²]). For 16 patients, 1 additional echocardiographic parameter was not measurable, but this did not influence the classification as low, intermediate or high-risk in all but one (for 11 patients, the pulmonary artery diameter was not measurable -7 had a right ventricular outflow doppler acceleration time <105 msec and 4 had no additional echocardiographic variables concerning the 2 other categories-, for 3 patients flattening of the interventricular septum was not interpretable -1 had additional echocardiographic parameters in the 2 other

categories and 2 in none of the other categories-, and in 2 patients, the inferior vena cava was not visible -1 patient had additional echocardiographic parameters in the 2 other categories and 1 patient only in 1 other category. The last patients was classified as low risk since the RA was not dilated. Besides the above described echocardiographic screening according to the 2015-ESC/ERS-guidelines, screening using a combination of echocardiography in all patients with the DETECT-algorithm in the high-risk subgroup (disease duration >3 years and DLCO <60% pred) was evaluated.

Supplementary file 3. Subgroup analyses for the LSSc, LcSSc and DcSSc subgroup.

1. Subgroup analysis of the LSSc subgroup

Screening, results of the RHC and cost-effectiveness

4 (19%) of the 21 LSSc patients were recommended for RHC. 3 (75%) patients were recommended by the DETECT-algorithm alone, none by the 2009-guidelines alone and 1 (25%) by both. Step 1 of the DETECT-calculator recommended echocardiography in 8 patients (38%). Step 2 of the DETECT-calculator recommended a RHC in 4 patients (19%). Following the 2009-guidelines, a RHC was recommended in 1 patient (5%) and post hoc in 2 patients (10%) by the 2015-echo-screening and in 3 patients (14%) by the 2015-combined screening.

Of the 4 LSSc patients recommended for RHC, 3 (75%) also underwent a RHC, 2 (67%) patients where RHC was recommended using the DETECT-algorithm alone, no patients using the 2009-guidelines alone, 1 (100%) using both algorithms and post hoc 2 (100%) using the 2015-echo-screening and 3 (100%) using the 2015-combined-screening.

Of the 3 LSSc patients in whom a RHC was performed, PH was diagnosed in 1 patient (1 PH secondary to LHD). No PAH was diagnosed, 2 (67%) had no PH and no patients had borderline PAP.

In our cohort, the average cost per LSSc patient for screening for PAH was 72 euro using the 2009-guidelines, 189 euro using the DETECT-algorithm, 81 euro using the 2015-echo-screening and 103 euro using the 2015-combined-screening respectively (table 2 and supplementary file 4).

2. Subgroup analysis of the LcSSc

Screening, results of the RHC, incidence and PPV and cost-effectiveness

45 (32%) of the 139 LcSSc patients were recommended for RHC. 33 (73%) patients were recommended by the DETECT-algorithm alone, 1 (2%) by the 2009-guidelines alone and 11 (24%) by both. Step 1 of the DETECT-calculator recommended echocardiography in 87 patients (63%). Step 2 of the DETECT-calculator recommended a RHC in 44 patients (32%). Following the 2009-guidelines, a RHC was recommended in 12 patients (9%) and post hoc in 23 patients (17%) by the 2015-echo-screening and in 27 patients (19%) by the 2015-combined screening.

Of the 45 LcSSc recommended for RHC, 39 (87%) also underwent a RHC, 27 (82%) of the patients where RHC was recommended using the DETECT-algorithm alone, 1 (100%) using the 2009-guidelines alone, 11 (100%) using both algorithms and post hoc 19 (83%) using the 2015-echo-screening and 21 (78%) using the 2015-combined-screening.

Of the 39 LcSSc patients in whom a RHC was performed, PH was diagnosed in 7 patients (3 PAH, 3 PH secondary to LHD and 1 PH secondary to pulmonary embolism).

23 (59%) had no PH and 9 (23%) had borderline PAP. RHC had been recommended by the DETECT-algorithm in 8 of the 9 (89%) patients diagnosed with borderline PAP, whereas the 2009-guidelines only recommended RHC in 4 (44%) of them.

Three LcSSc patients were diagnosed with PAH. RHC was recommended in the 3 patients by all screening algorithms. For 139 LcSSc patients, the PPV was 8%, 95% CI 3-21% (3/38) for the DETECT-algorithm, 25%, 95% CI 9-53% (3/12) for the 2009-guidelines, 27%, 95% CI 10-57% (3/11) for screening with both algorithms and post hoc 16%, 95% CI 6-38% (3/19) for the 2015-echo-screening and 14%, 95% CI 5-35% (3/21) for the 2015-combined-screening.

In our cohort, the average cost per LcSSc patient for screening for PAH was 79 euro using the 2009-guidelines, 229 euro using the DETECT-algorithm and post hoc 89 euro using the 2015-echo-screening and 102 euro using the 2015-combined-screening respectively (table 2 and supplementary file 4).

3. Subgroup analysis of the DcSSc

Screening, results of the RHC, Cost-effectiveness

14 (40%) of the 35 DcSSc patients were recommended for RHC. 10 (71%) patients were recommended by the DETECT-algorithm alone, 3 (21%) by the 2009-guidelines alone and 1 (7%) by both. Step 1 of the DETECT-calculator recommended echocardiography in 23 patients (66%). Step 2 of the DETECT-calculator recommended a RHC in 11 patients (31%). Following the 2009-guidelines, a RHC was recommended in 4 patients (11%) and post hoc in 9 patients (26%) by the 2015-echo-screening and in 10 patients (29%) by the 2015-combined screening.

Of the 14 DcSSc recommended for RHC, 11 (79%) also underwent a RHC, 7 (70%) of the patients where RHC was recommended using the DETECT-algorithm alone, 3 (100%) using the 2009-guidelines alone, in 1 patient (100%) using both algorithms and post hoc 7 (78%) using the 2015-echo-screening and 8 (80%) using the 2015-combined-screening.

Of the 11 in whom a RHC was performed, PH was diagnosed in 1 patients (1 PH secondary to LHD). No patients were diagnosed with PAH, 5 (45%) had no PH and 5 (45%) had borderline PAP. RHC had been recommended by the DETECT-algorithm in 5 (100%) patients diagnosed with borderline PAP, whereas the 2009-guidelines recommended RHC in no DcSSc patients.

In our cohort, the average cost per DcSSc patient for screening for PAH was 85 euro using the 2009-guidelines, 223 euro using the DETECT-algorithm and post hoc 101 euro using the 2015-echo-screening and 157 euro using the 2015-combined-screening respectively (table 2 and supplementary file 4).

Supplementary file 4. Cost per patient in the subgroups for screening following the different screening algorithms.

	price	N	LSSc cost	Cost per patient	N	LcSSc Cost	Cost per patient	N	DcSSc Cost	cost per patient
2009-guidelines										
Echocardiography *	63.21 euro	21	1327.41 euro		139	8786.19 euro		35	2212.35 euro	
RHC *	187.22 euro	1	187.22 euro		12	2246.64 euro		4	748.88 euro	
Total cost			**1514.63 euro**	**72.13 euro**		**11032.83 euro**	**79.37 euro**		**2961.23 euro**	**84.61 euro**
DETECT-algorithm										
FVC *	22 euro	21	462 euro		139	3058 euro		35	770 euro	
DLCO *	47 euro	21	987 euro		139	6533 euro		35	1645 euro	
NT-proBNP #	11 euro	21	231 euro		139	1529 euro		35	385 euro	
Serum urate *	0.48 euro	21	10.08 euro		139	66.72 euro		35	16.80 euro	
ECG *	17.77 euro	21	373.17 euro		139	2470.03 euro		35	621.95 euro	
ACA #	40 euro	21	840 euro		139	5560 euro		35	1400 euro	
Echocardiography *	63.21 euro	8	505.68 euro		87	5499.27 euro		23	1453.83 euro	
RHC *	187.22 euro	3	561.66 euro		38	7114.36 euro		8	1497.76 euro	
Total cost			**3970.59 euro**	**189.08 euro**		**31830.38 euro**	**229 euro**		**7790.34 euro**	**222.58 euro**
2015-echo-screening										
Echocardiography *	63.21 euro	21	1327.41 euro		139	8786.19 euro		35	2212.35 euro	
RHC *	187.22 euro	2	374.44 euro		19	3557.18 euro		7	1310.54 euro	
Total cost			**1701.85 euro**	**81.04 euro**		**12343.37 euro**	**88.80 euro**		**3522.89 euro**	**100.65 euro**
2015-combined-screening										
FVC *	22 euro	2	44 euro		11	242 euro		13	286 euro	
DLCO *	47 euro	2	94 euro		11	517 euro		13	611 euro	

	price	N	cost	N	cost	N	cost
NT-proBNP #	11 euro	2	22 euro	11	121 euro	13	143 euro
Serum urate *	0.48 euro	2	0.96 euro	11	5.28 euro	13	6.24 euro
ECG *	17.77 euro	2	35.54 euro	11	195.47 euro	13	231.01 euro
ACA #	40 euro	2	80 euro	11	440 euro	13	520 euro
Echocardiography *	63.21 euro	21	1327.41 euro	139	8786.19 euro	35	2212.35 euro
RHC *	187.22 euro	3	561.66 euro	21	3931.62 euro	8	1497.76 euro
Total cost			**2165.57 euro** **103.12 euro**		**14238.56 euro** **102.44 euro**		**5507.36 euro** **157.35 euro**

LSSc: limited systemic sclerosis, LcSSc: limited cutaneous systemic sclerosis, DcSSc: diffuse cutaneous systemic sclerosis, price: cost price for the investigation according to the Belgian RIZIV/INAMI (rijksdienst voor ziekte- en invaliditeitsverzekering/ l'institut national d'assurance maladie invalidité) nomenclature for * and according to the expected best local estimate of cost for # [29], N: number of patients, RHC: right heart catheterization, FVC: forced vital capacity, DLCO: diffusing capacity of the lung for carbon monoxide, NT-proBNP: N-terminal proB-type natriuretic peptide, ECG: electrocardiography, ACA: anti-centromere antibodies, 2015-echo-screening: screening following the 2015-ESC/ERS-guidelines using echocardiographic parameters, 2015-combined-screening: screening following the 2015-ESC/ERS-guidelines using the combination of echocardiographic parameters for all patients included in the cohort with the DETECT-algorithm in the high-risk subgroup (with disease duration >3 years and DLCO <60% pred).