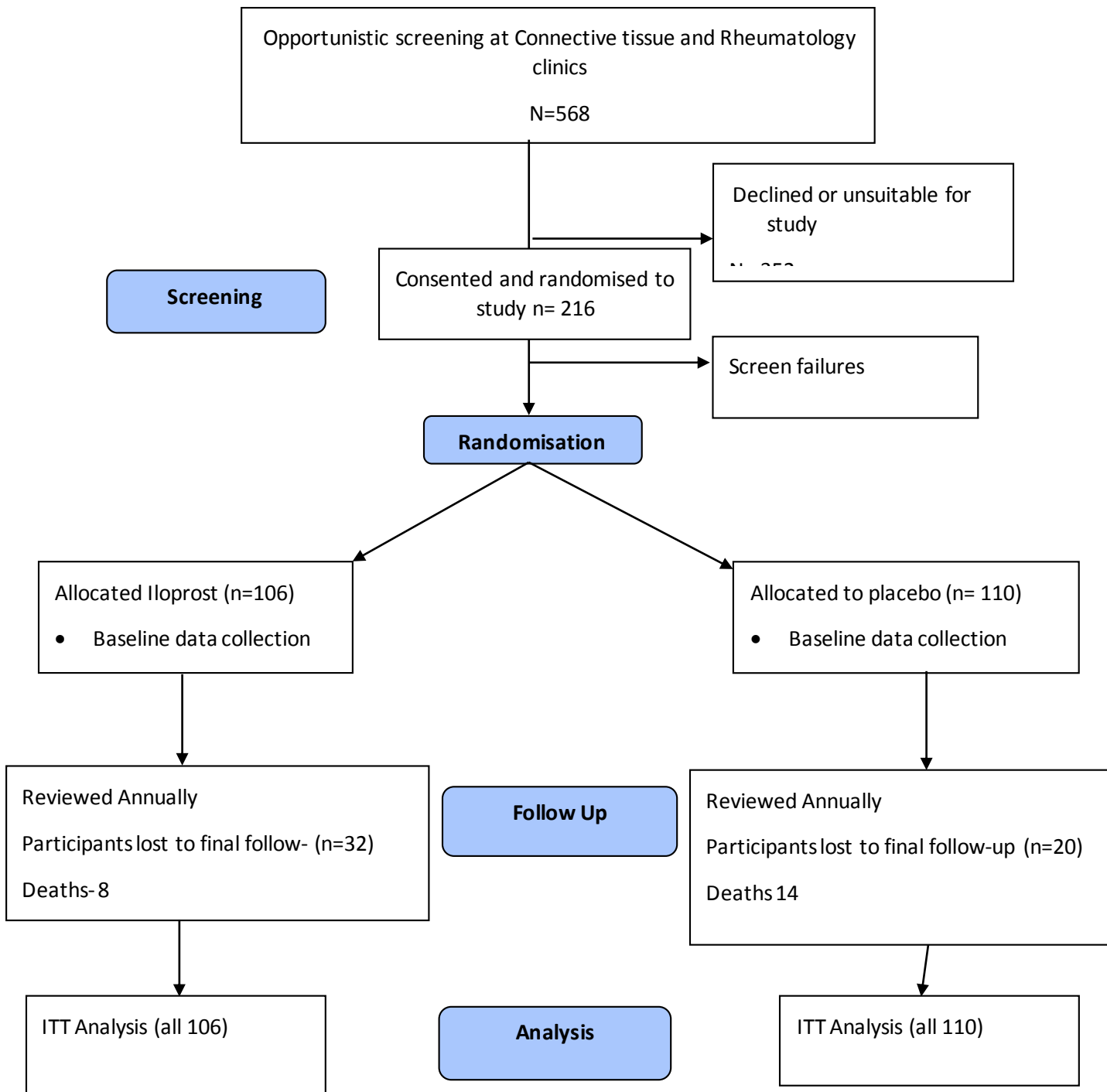


Participant Flow



Baseline characteristics

Demographics of SSTEP study participants

	Iloprost (n=106)	Placebo (n=110)	Total (216)
Age (years) mean (SD)	57.4 (8.8)	56.0 (10.0)	56.7 (9.4)
Gender : males	14 (13%)	19 (17%)	33 (15%)
: females	92 (87%)	91 (83%)	183 (85%)
Race - Caucasian	102 (96%)	106 (96%)	208 (96%)
Afro Caribbean	0	2 (2%)	2 (1%)
Asian	3 (3%)	0	3 (1%)
Other	1 (1%)	2 (2%)	3 (1%)
Age at diagnosis (years) (SD)	50.4 (10.6)	50.2 (10.8)	50.3 (10.7)
Duration of SSc disease (years) Median (IQR)	5 (2 – 9)	4 (1 – 8)	5 (2 – 9)
Duration of Raynaud's (years) – median (IQR)	15.0 (5.0 – 27.0)	14.9 (5.4 – 30.0)	15.0 (5.0 – 30.0)
Smoking: never	42 (40%)	47 (43%)	89 (41%)

ex-smoker	50 (47%)	48 (44%)	98 (46%)
current	14 (13%)	15 (14%)	29 (13%)

Disease characteristics on entry to the study

	Iloprost (n=106)	Placebo (n=110)	Total (216)
Proximal scleroderma	53 (50%)	60 (55%)	113 (50%)
Sclerodactyly	82 (77%)	90 (82%)	172 (80%)
Raynaud's Phenomenon	98 (92%)	104 (95%)	202 (94%)
Digital pitting scars or Loss of finger pulp	39 (37%)	39 (35%)	78 (36%)
Pulmonary interstitial fibrosis	17 (16%)	21 (19%)	38 (18%)
Subcutaneous calcification	35 (33%)	22 (20%)	57 (26%)
Oesophageal involvement	58 (55%)	65 (59%)	123 (57%)
Telangiectasia	60 (57%)	54 (49%)	114 (53%)
Positive antibody			
Anti-nuclear Ab	65/92 (71%)	83/96 (86%)	148/188 (79%)
Extractable Nuclear Antigen	18/68 (26%)	17/64 (27%)	35/132 (27%)

Scleroderma 70	12/80 (15%)	15/86 (17%)	27/166 (16%)
Anti-centromere Ab	46/80 (58%)	42/79 (53%)	88/159 (55%)
Anti-U1RNP	1 (1%)	0	1 (0.5%)
Anti-U3RNP	0	2 (2%)	2 (1%)

Clinical findings at screening

	Iloprost	Placebo	Total
ABI – (N)	(99)	(108)	(207)
mean (SD)	1.02 (0.13)	1.01 (0.14)	1.02 (0.14)
DLCO (%) – (N)	(96)	(95)	(191)
mean (SD)	70.8 (19.0)	74.0 (20.1)	72.4 (19.6)
Pulmonary Artery Systolic	(57)	(46)	(103)
Pressure – (N) mean (SD)	27.5 (8.4)	28.3 (7.1)	27.8 (7.8)
Skin score – (N)	(106)	(109)	(215)
median (IQR)	7 (3 – 11)	7 (4 – 12)	7 (4 – 12)
eGFR (mL/min/1.73m²)	(83)	(81)	(164)
(N) median (IQR)	75 (61-103)	74 (58-96)	75 (60-97)
Carotid duplex scan –N (%)	35 (33%)	33 (30%)	68 (31%)
Stenosis? – N (%)	4 (11%)	3 (9%)	7 (10%)

Left	0	0	0
Right	1 (3%)	3 (9%)	4 (6%)
Both	3 (9%)	0	3 (4%)
< 20%	0	0	0
≥ 20% but < 50%	1 (3%)	3 (9%)	4 (6%)
≥ 50%	3 (9%)	0	3 (4%)

Outcome measures

Potential endpoints submitted to and total confirmed by Clinical Endpoints Committee

Endpoint	Iloprost		Placebo	
	Number submitted	Number Confirmed	Number submitted	Number Confirmed
Death	8	8	14	14
Cardiovascular	15	13	13	13
Renal	41	37	38	34
Pulmonary hypertension	22	22	25	22
ILD	27	25	26	25
Skin	29	29	39	39

Summary of frequency of clinical endpoints for organ screening tests, compared per group (Iloprost v placebo)

Clinical endpoints	Event rates per assessment: Iloprost	Event rates per assessment: Placebo	Mantel-Haenszel Test		Overall test for trend in rates	
			Chi square	p value	Chi square	p value
Renal	37/163 (22.7%)	34/184 (18.5%)	0.64	0.42	0.50	0.48
Pulmonary hypertension	22/127 (17.3%)	22/123 (17.9%)	0.004	0.95	0.43	0.51

ILD	25/265 (9.4%)	25/300 (8.3%)	0.02	0.90	0.33	0.57
Skin	29/304 (9.5%)	39/335 (11.6%)	0.61	0.43	1.18	0.28

Adverse events

Breakdown of SAE's reported to DSMB (9th April 2002- 31st Jan 2009)

	Elective Admissions (organ screening & IV iloprost)	Elective Surgery	Complications of SSc	Accident	Other	SuSAR	Death	
TOTAL	135	28	72	6	96	0	22	359

Complications of SSc, breakdown of SAE reports

	<i>Iloprost</i>	<i>Placebo</i>
Infected digital ulceration requiring antibiotics +/- iv Iloprost	11	21
Critical digital ischaemia requiring IV Iloprost	9	11
Pulmonary hypertension	5	11
Pulmonary fibrosis	1	1
Assessment of SSc	0	2

Breakdown of 'Other' reported SAEs

	<i>Iloprost</i>	<i>Placebo</i>
Infections		
Respiratory Infection	6	4
Urinary Tract Infection	0	2
Cellulitis	1	0
Septicaemia	1	0
Infected ankle ulcer	0	1

GIT		
Diverticulosis/Gastroenteritis	2	7
Pseudo bowel obstruction	0	3
Diarrhoea	1	0
Gastritis	1	0
Cholecystectomy and hernia repair	1	0
Cholecystectomy	1	0
Acute Pancreatitis	1	0
Ulcerative oesophagitis	1	0
Multiple Antral angiod streaks	0	1
Blood transfusion (post GI bleed)	0	1
Dyspepsia	0	1
Stoma formation	0	1
GAVE syndrome	1	0
Gastrointestinal bleed- overdose of warfarin	1	0
Rectal bleeding, abdominal pain, diarrhoea	1	0
Cancers		
Breast Cancer or Ductal carcinoma in situ	0	2
Lung Cancer	0	2
Parotidectomy: Warthins Tumour	1	0
Rectal Cancer	0	1
Liver Cancer	0	1
Stage 4B large cell diffuse lymphoma	1	0
Chemotherapy for Lymphoma	1	0
Basal cell carcinoma	1	0

Cardiovascular		
Chest Pain	2	4
Atypical Chest Pain	1	1
Atherosclerotic coronary artery	0	1
Trans-ischaemic attack	0	1
Non ST Myocardial Infarction/ Lower Respiratory Tract Infection	1	0
Anterior MI	1	1
Carotid arterectomy	1	0
Aortic plaque	1	0
Congestive cardiac failure and UTI	1	0
Occluded superficial femoral artery	1	0
Left below knee amputation	0	1
Peripheral Oedema	0	3
Respiratory		
Dyspnoea	0	2
Exacerbation of COPD	1	0
Psychiatric		
Senility	1	0
Depression	1	0
Psychiatric Care	0	1
Neurological		
Labyrinthitis	1	0
Fit: possible ketamine overdose	0	1

Fall- Haemorrhagic Stroke	1	0
Haematological		
Thrombosis	1	2
Anaemia	1	0
Anaemia- requiring blood transfusion	1	0
Temporal arteritis	0	1
Musculoskeletal/Dermatological		
Myositis	1	0
Myalgia	0	1
Exacerbation of eczema	1	0
Skin papilloma & neutropenia	1	0
Surgical		
Back surgery	2	0
Hysterectomy	0	1
Renal		
Renal failure- dialysis	0	1
Collapse- renal failure	0	1
Endocrine		
Hyperosmolar kinetic state	0	1
Total	45	51