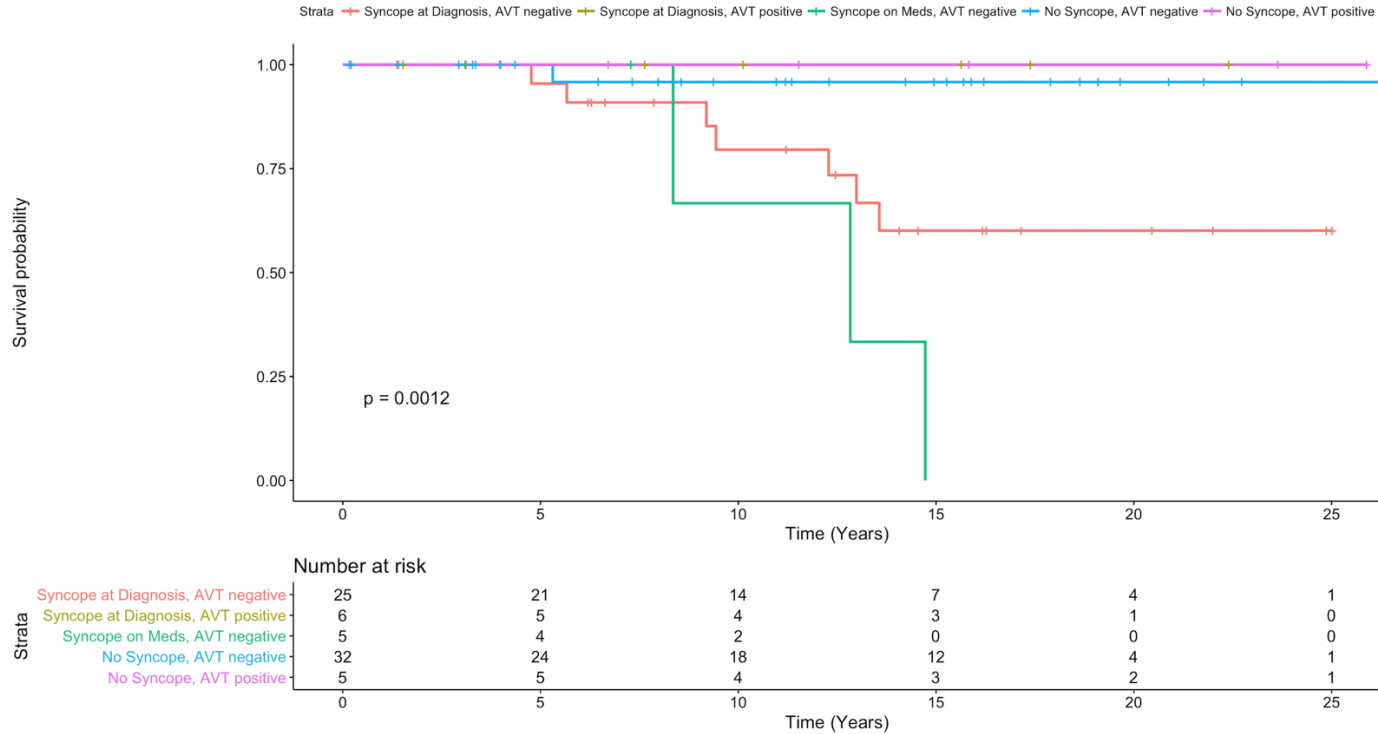


Supplemental Figure S1. Flow chart demonstrating patients included in the study and those excluded from haemodynamic analysis.



Supplemental Figure S2. Survival in IPAH patients using Sitbon criteria. Patients with positive AVT response according to Sitbon criteria had 100% survival regardless of syncope. Those with syncope and without response to acute vasodilator testing had worse survival with the worst outcomes seen in patients with syncope on medications.

Table S1. Description of Patients with Mortality/Transplant

	Death/transplant and cause	RV function- most recent echo	AVT response	Syncope	# of targeted therapies at last follow up	IV prostanoid at last follow up
1	Died due to PH (RV failure)	Severely reduced	No	No	3	Yes
2	Died due to respiratory failure	Severely reduced	No	Yes	3	Yes
3	Died due to respiratory failure and cardiac arrest	Moderately reduced	No	Yes	3	Yes
4	Lung transplant	Severely reduced	No	Yes	1	Yes
5	Underwent heart and lung transplant	Moderate-severely reduced	No	Yes	3	Yes
6	Died due to GI bleed w HHT	Moderately reduced	No	Yes	2	Yes
7	Died due to pneumothorax, respiratory and multiorgan failure requiring ECMO	Severely reduced	No	Yes	3	Yes
8	Listed for lung transplant and died awaiting transplant	Severely reduced	No	Yes	3	Yes
9	Died due to unknown cause	Mild-	No	No	2	No

		moderate				
10	Died due to respiratory and heart failure	Severely reduced	No	No	3	Yes
11	Died due to sepsis with multiorgan failure requiring ECMO	Severe	No	No	3	No (on orenitram)
12	Died due to unknown cause	Mild-moderate	No	No	3	No(on selexipag)
13	Died due to cardiac arrest requiring ECMO	Severely reduced	Cath not done	No	1	Yes
14	Died due to respiratory and heart failure	Severely reduced	Cath not done	No	2	No(on inhaled iloprost)
15	Died due to cardiac arrest during attempted atrial septostomy	Severely reduced	No	No	3	Yes
16	Died due to respiratory failure, cardiac arrest causing anoxic encephalopathy	Mildly reduced (done 2 months prior)	No	No	2	No
17	Died awaiting lung transplant	Severely reduced	No	No	2	Yes
18	Died due to hemorrhagic shock after lung transplant	Severe	No	No	3	Yes

19	Died due to unknown cause (after viral illness?)	Mild-moderate	No	Yes	2	No
20	Died due to respiratory failure, DNR	Moderate-severe	Not done	Yes	2	No
21	Died due to respiratory failure requiring ECMO	Severely reduced	No	Yes	3	Yes
22	Heart and lung transplant	Severely reduced	No	Yes	3	Yes
23	Died due to unknown cause, presumed non-compliance	Severely reduced	No	Yes	3	Yes
24	Lung transplant	Moderately reduced	No	Yes	2	Yes
25	S/p Potts shunt, w complicated post op course, sepsis and recannulation onto VA-ECMO, multiorgan failure	Severely reduced	No	No	3	Yes
26	Influenza with secondary bacterial sepsis, septic and cardiogenic shock	Low normal	No	No	2	No

Table S2: Cardiac Catheterization for Patients with Syncope at Baseline v AVT with iNO

	Baseline	AVT	p-value
RA pressure (n=31)	7 (5-9)	6 (4-8)	0.72

mPA pressure (n=44)	54 (41-69)	41.5 (28.5-62)	0.0006
sPAP/sSAP (n=43)	0.81 (0.58-1.0)	0.60 (0.4-0.9)	<0.0001
PVRI (n=42)	14.9 (9.3-22.1)	10.35 (6.0-18.0)	0.006
Rp/Rs (n=24)	0.7 (0.46-1)	0.46 (0.29-0.72)	0.006
CI (n=42)	2.9 (2.3-3.7)	3.15 (2.5-3.8)	0.027

Table S3: Cardiac Catheterization for Patients without Syncope at Baseline v AVT with iNO

	Baseline	AVT	p-value
RA pressure (n=75)	7 (6-9)	7 (6-8.5)	0.72
mPA pressure (n=99)	48.5 (36-64)	37.5 (28-56.5)	<0.00001
sPAP/sSAP (n=93)	0.75 (0.50-0.95)	0.6 (0.46-0.89)	0.0001
PVRI (n=94)	9.05 (5.3-14.5)	6.5 (3.7-11)	<0.00001
Rp/Rs (n=55)	0.6 (0.33- 0.94)	0.45 (0.21-0.83)	0.005
CI (n=85)	3.5 (2.5-4.2)	3.6 (2.6-4.6)	0.17

Table S4: Cardiac Catheterization for IPAH Patients with Syncope at Baseline v AVT with iNO

	Baseline	AVT	p-value
RA pressure (n=25)	7 (5-10)	7 (4.5-8.5)	0.56
mPA pressure (n=35)	54 (40-69)	44 (27-64)	0.006
sPAP/sSAP (n=34)	0.81 (0.58-1.00)	0.70 (0.40-0.93)	0.0004
PVRI (n=33)	16.7 (9.3-24.8)	13.2 (5.7-18.9)	0.019
Rp/Rs (n=19)	0.75 (0.6-1.0)	0.5 (0.3-0.72)	0.004
CI (n=34)	2.7 (2.0-3.4)	3.3 (2.5-3.7)	0.024

Table S5: Cardiac Catheterization for IPAH Patients without Syncope at Baseline v AVT with iNO

	Baseline	AVT	p-value
RA pressure (n=28)	6 (5-8)	6 (5-8)	0.66

mPA pressure (n=35)	52 (37-76)	41 (31-57)	0.0001
sPAP/sSAP (n=34)	0.84 (0.55-1.10)	0.70 (0.46-0.91)	0.0002
PVRI (n=34)	11.0 (5.5-20.2)	8.1 (3.6-12.2)	0.0008
Rp/Rs (n=20)	0.7 (0.4-1.10)	0.45 (0.25-0.90)	0.021
CI (n=34)	3.55 (2.8-4.6)	3.8 (2.7-5.3)	0.075

Table S6. Cardiac Catheterization, Treatment, and Outcomes for Patients with Syncope at Diagnosis only vs Recurrent Syncope on IV prostanoids

	Syncope at Diagnosis (not on medication) (n=24)	Recurrent Syncope on IV prostanoids (n=9)	P value
Baseline			
Mean RAP (mmHg)	6.5 (4.3-9.8)	8 (5-10)	0.62
Mean PAP (mmHg)	62 (42-72)	57 (44-65)	0.44
sPAP/sSAP	0.88 (0.60-1.05)	0.81 (0.72-1.00)	0.87
PVRi (WU*m2)	20.2 (8.2-31.1)	15.4 (10.7-21.2)	0.58
Rp/Rs	0.85 (0.7-1.0)	0.9 (0.7-1.0)	0.77
CI (l/min/m2)	2.5 (1.9-3.8)	3.4 (2.9-3.9)	0.18
AVT with iNO			
Mean RAP (mmHg)	6.0 (5.0-9.8)	8 (4.8-10.3)	0.78
Mean PAP (mmHg)	46.5 (26.5-74.8)	61 (38.5-70)	0.34
sPAP/sSAP	0.7 (0.4-1.0)	0.92 (0.54-1.1)	0.19
PVRi (WU*m2)	11.3 (6.0-28.9)	14.1 (8.1-18.2)	0.88
Rp/Rs	0.7 (0.3-0.9)	0.6 (0.1-1.1)	0.56
CI (l/min/m2)	2.0 (2.1-4.2)	3.7 (3.3-4.1)	0.43
AVT Responders (Barst)	8 (33%)	1 (11%)	0.20
Treatment at last follow up			
CCB	6 (25%)	0	0.15
IV prostanoids	9 (38%)	7 (78%)	0.06
Outcomes			
Death	3	2	0.45
Lung Transplant	2	1	

Data are expressed as median (interquartile range) or number (percentage). Bolded and * represents statistically significant differences.

AVT: acute vasodilator testing; CI: cardiac index; iNO: inhaled nitric oxide; PAP: pulmonary artery pressure; sPAP/sSAP: ratio of pulmonary artery/systemic arterial systolic pressure; PVRi: indexed pulmonary vascular resistance; RAP: right atrial pressure; Rp/Rs: ratio of pulmonary vascular resistance/systemic vascular resistance