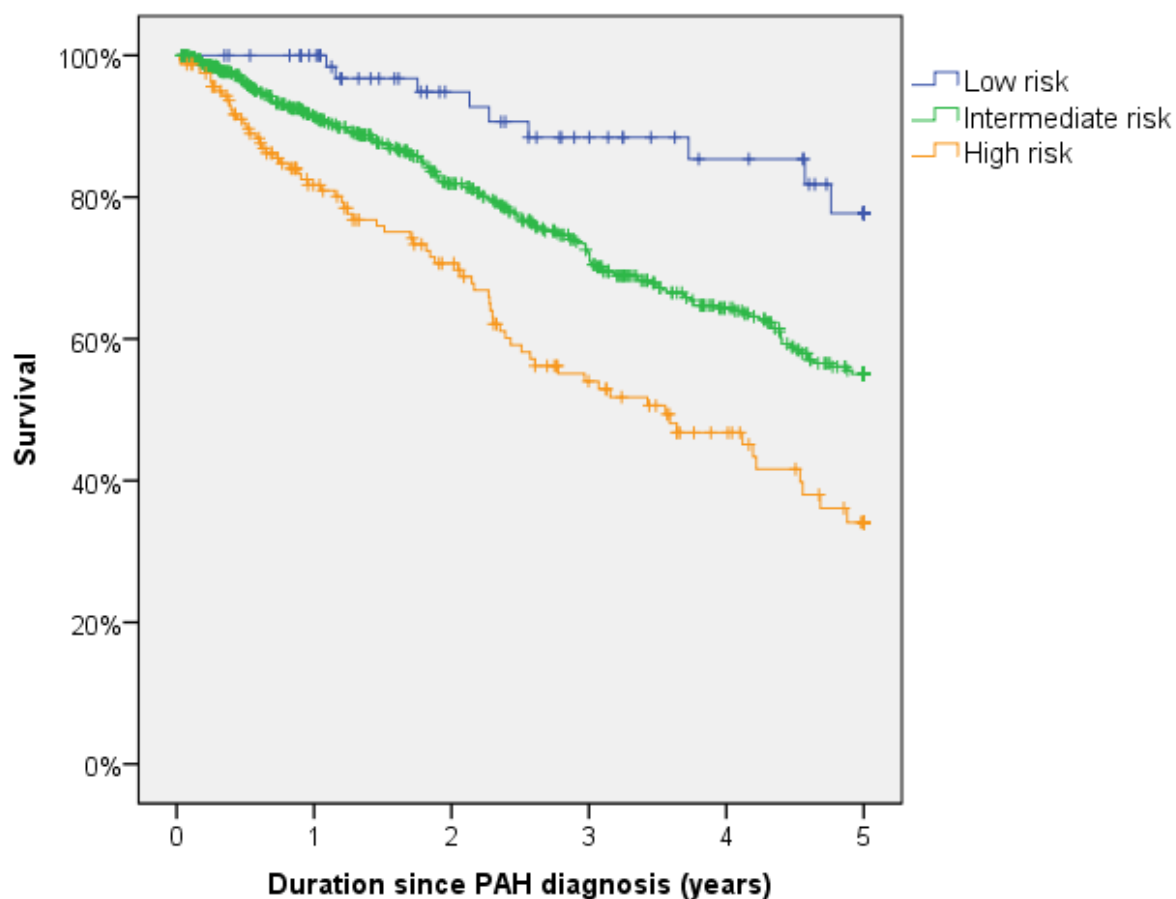


Online Supplement

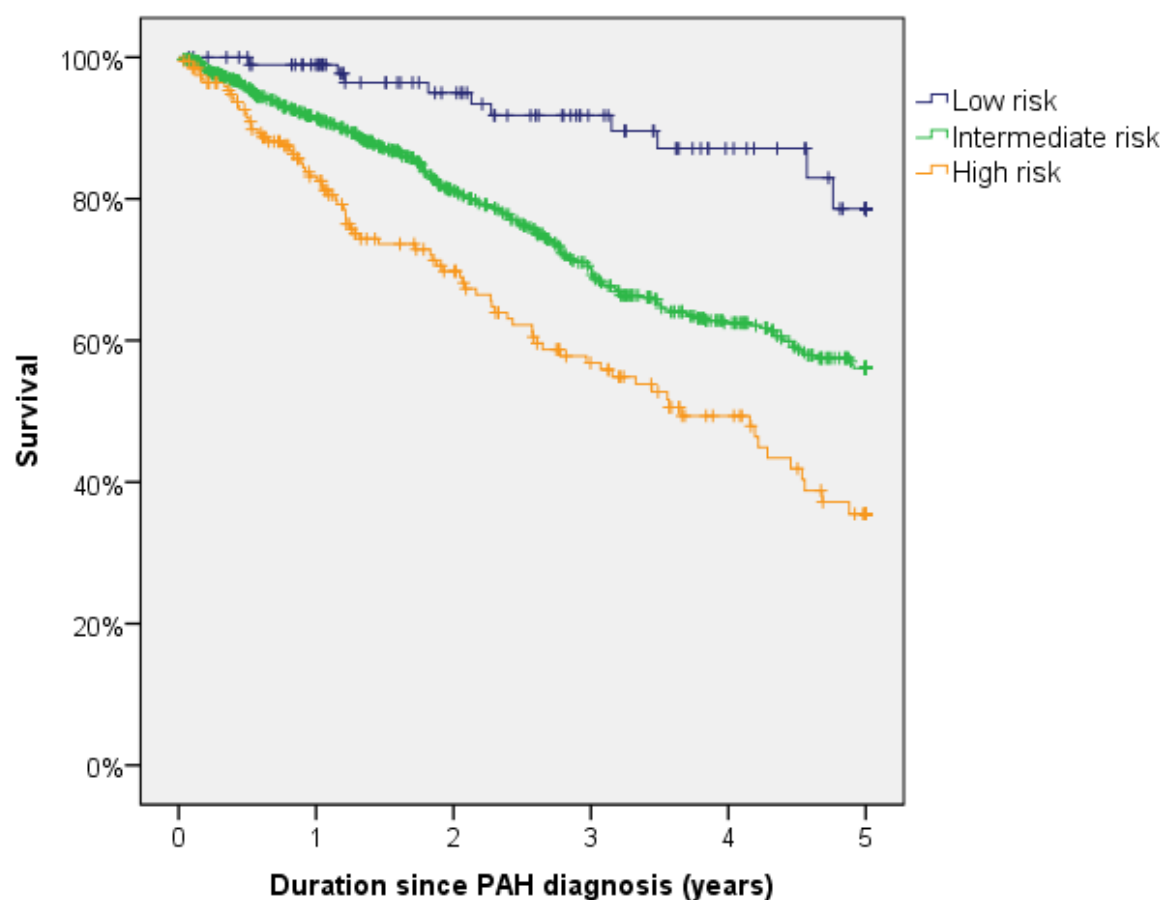
Mortality in Pulmonary Arterial Hypertension: Prediction by the 2015 European Pulmonary Hypertension Guidelines Risk Stratification Model

Supplementary Figure S1 Kaplan-Meier survival estimates of patients with all forms of PAH combined per individual risk stratification at baseline (analysis included only patients for whom all selected variables were available).



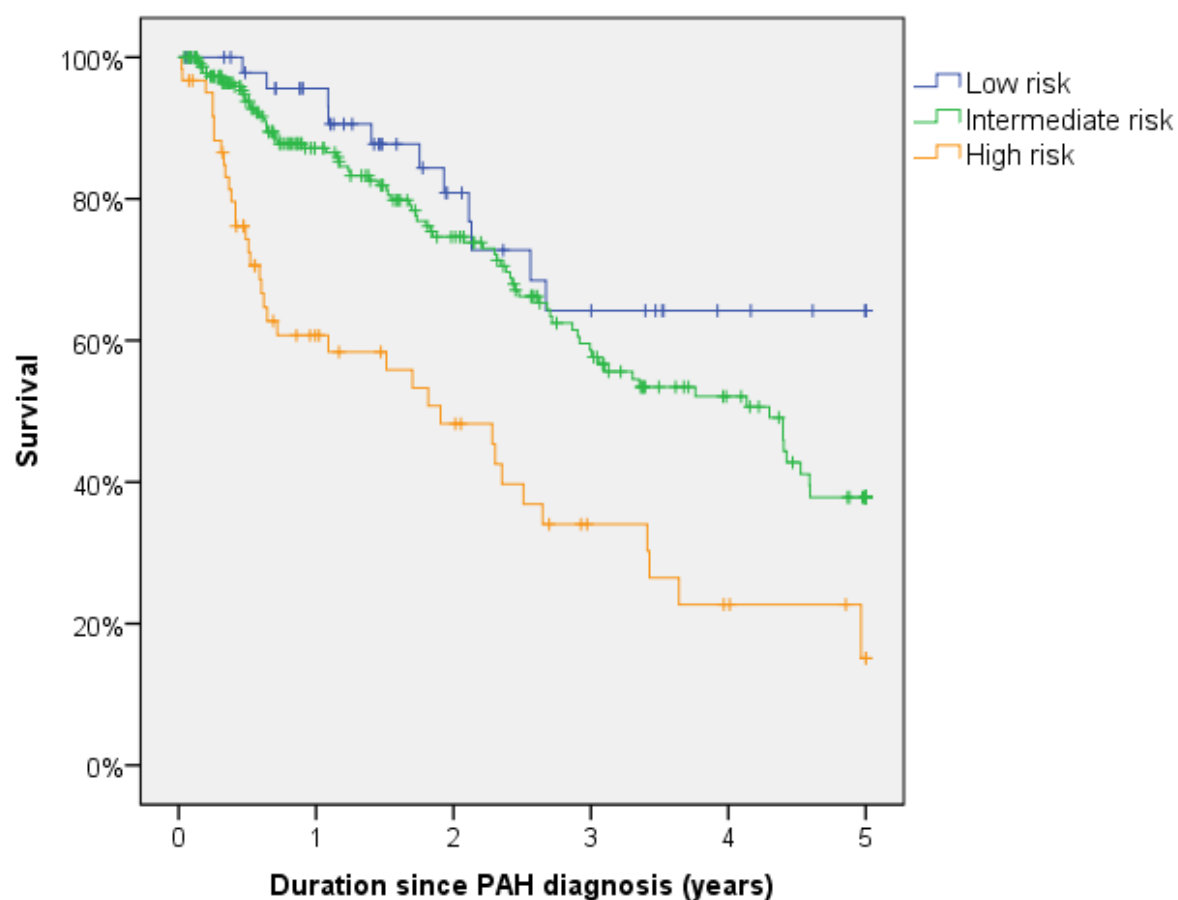
Years after enrolment	Survival			Number at risk		
	Low risk	Intermediate risk	High risk	Low risk	Intermediate risk	High risk
0	100.0%	100.0%	100.0%	75	642	162
1	100.0%	91.3%	81.7%	65	445	103
2	94.9%	81.9%	70.7%	45	328	77
3	88.4%	72.0%	54.0%	35	239	49
4	85.4%	64.4%	46.8%	27	166	31
5	77.7%	55.0%	34.1%	19	106	16

Supplementary Figure S2 Kaplan-Meier survival estimates of patients with idiopathic, drug-associated or hereditary PAH per individual risk stratification at baseline.



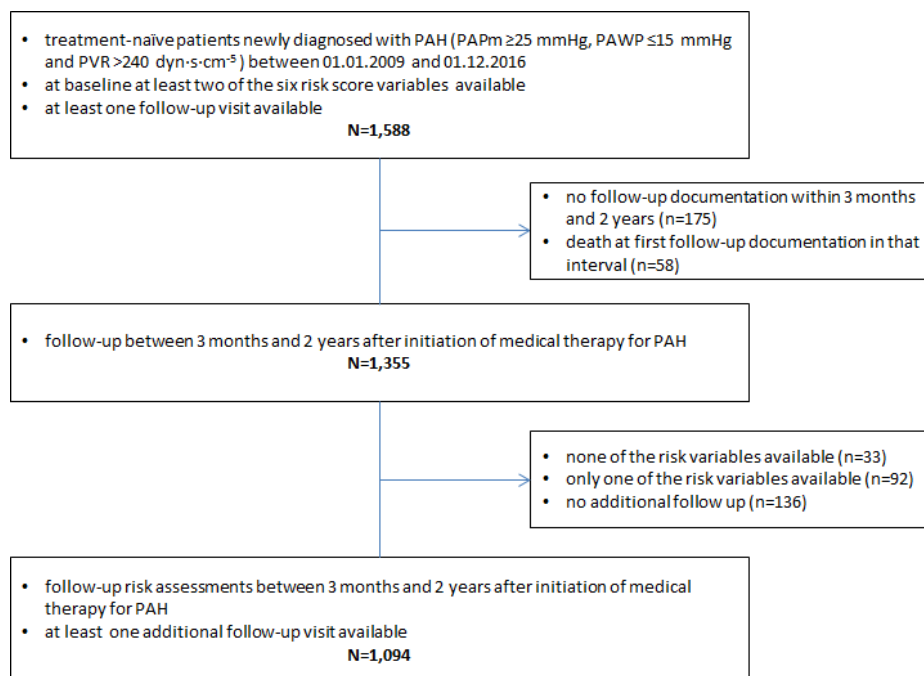
Years after enrolment	Survival			Number at risk		
	Low risk	Intermediate risk	High risk	Low risk	Intermediate risk	High risk
0	100.0%	100.0%	100.0%	101	760	199
1	98.9%	91.4%	83.2%	86	545	130
2	95.0%	81.3%	69.8%	64	381	88
3	91.8%	70.0%	56.8%	44	272	59
4	87.1%	62.5%	49.3%	27	186	37
5	78.6%	56.1%	35.5%	16	118	19

Supplementary Figure S3 Kaplan-Meier survival estimates of patients with connective tissue disease-associated PAH per individual risk stratification at baseline.

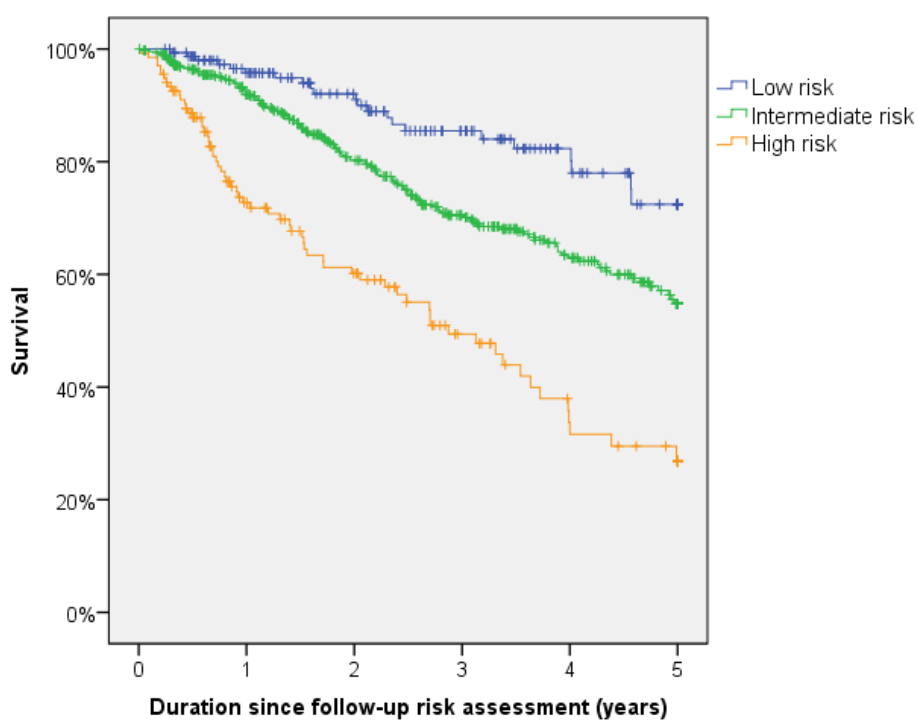


Years after enrolment	Survival			Number at risk		
	Low risk	Intermediate risk	High risk	Low risk	Intermediate risk	High risk
0	100.0%	100.0%	100.0%	52	234	61
1	95.6%	87.2%	60.7%	38	138	27
2	80.9%	74.6%	48.2%	21	97	19
3	64.2%	58.6%	34.0%	15	61	9
4	64.2%	52.1%	22.7%	9	37	5
5	64.2%	37.8%	15.1%	7	19	2

Supplementary Figure S4 Flow chart showing the number of patients lost between baseline and follow-up

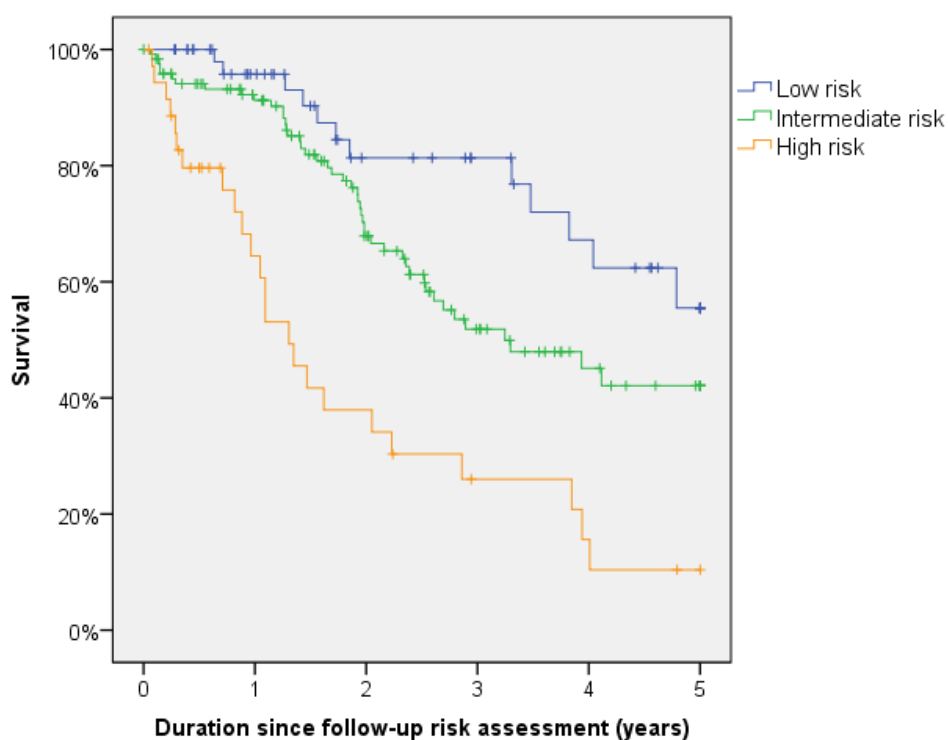


Supplementary Figure S5 Kaplan-Meier survival estimates of patients with idiopathic, drug-associated or hereditary PAH per individual risk stratification at follow-up.



Years after enrolment	Survival			Number of cases left		
	Low risk	Intermediate risk	High risk	Low risk	Intermediate risk	High risk
0	100.0%	100.0%	100.0%	158	460	138
1	95.7%	91.9%	72.8%	124	358	76
2	92.1%	80.2%	60.2%	90	259	55
3	85.5%	70.5%	49.4%	62	180	30
4	82.3%	62.9%	31.6%	38	117	15
5	72.4%	54.8%	26.8%	22	65	10

Supplementary Figure S6 Kaplan-Meier survival estimates of patients with connective tissue disease-associated PAH per individual risk stratification at follow-up.



Years after enrolment	Survival			Number of cases left		
	Low risk	Intermediate risk	High risk	Low risk	Intermediate risk	High risk
0	100.0%	100.0%	100.0%	55	122	36
1	95.7%	91.2%	64.4%	40	93	17
2	81.3%	67.9%	37.9%	24	56	10
3	81.3%	51.9%	26.0%	19	30	5
4	67.2%	45.1%	15.6%	14	16	3
5	55.5%	42.1%	10.4%	8	10	1

Supplementary Table S1 Characteristics of the patients included into the baseline risk stratification group (analysis included only patients for whom all selected variables were available)

	Low risk n=75	Intermediate risk n=642	High risk n=162	All n=879
Age (years)	51 ± 18	67 ± 14	66 ± 16	65 ± 15
Female	60%	65%	65%	65%
BMI (kg/m ²)	26 ± 6	28 ± 7	28 ± 7	28 ± 7
PAH Aetiology (n; %)				
I/D/H-PAH	39 (52%)	455 (71%)	119 (73%)	613 (70%)
CTD-PAH	22 (29%)	128 (20%)	34 (21%)	184 (21%)
HIV-PAH	3 (4%)	4 (1%)	1 (0%)	8 (1%)
PoPH	5 (7%)	30 (5%)	7 (4%)	42 (5%)
CHD-PAH	6 (8%)	25 (4%)	1 (0%)	32 (4%)
WHO FC Class I/II/III/IV	1%, 55%, 44%, 0%	0%, 7%, 81%, 12%	0%, 1%, 58%, 41%	0%, 10%, 74%, 16%
6MWD (m)	470 ± 85	299 ± 107	187 ± 103	293 ± 126
NT-pro BNP (ng/L), median (Q1; Q3)	178 (75; 351)	1,351 (614; 2,825)	3,923 (2,488; 6,103)	1,510 (560; 3,381)
BNP (ng/L), median (Q1; Q3)	34 (9; 99)	182 (96; 334)	518 (380; 736)	223 (101; 438)
Haemodynamics				
RA pressure (mmHg)	5 ± 3	8 ± 5	13 ± 5	8 ± 5

PAPm (mmHg)	41 ± 14	42 ± 12	49 ± 12	43 ± 12
PAWP (mmHg)	8 ± 3	9 ± 4	10 ± 3	9 ± 3
CI (l/min/m ²)	3.0 ± 0.8	2.2 ± 0.7	1.6 ± 0.4	2.2 ± 0.8
PVR (dyn·s·cm ⁻⁵)	515 ± 272	714 ± 374	1,156 ± 560	779 ± 448
SvO ₂	72 ± 4	65 ± 7	54 ± 7	63 ± 9
Initial therapy (within 3 months after diagnosis)				
ERA	51%	34%	40%	36%
PDE5i/sGCs	59%	73%	74%	72%
SC/IV PCA	1%	0%	1%	4%
Monotherapy	81%	90%		88%
Combination therapy	19%	11%	18%	12%
Anticoagulation	27%	49%	54%	48%

Categorical data are shown as n and % of the respective population. Continuous data are depicted as mean ± SD unless stated otherwise.

Abbreviations: BMI, body mass index; PAH, pulmonary arterial hypertension; I/D/H-PAH, idiopathic, drug-associated or hereditary PAH; CTD, connective tissue disease; HIV, human immunodeficiency virus; PoPH, portopulmonary hypertension; CHD, congenital heart disease; WHO FC, World Health Organization Functional Class; 6MWD, 6-minute walking distance; BNP, brain natriuretic peptide; NT-proBNP, N-terminal fragment of pro-brain natriuretic peptide; RA, right atrial; PAPm, mean pulmonary arterial pressure; PAWP, pulmonary arterial wedge pressure; CI, cardiac index; PVR, pulmonary vascular resistance; SvO₂, mixed-venous oxygen saturation; ERA endothelin receptor antagonists; PDE5i, phosphodiesterase-5 inhibitors; sGCs, stimulator of soluble guanylate cyclase; PCA, prostacyclin analogues

Supplementary Table S2 Characteristics of the patients with idiopathic, drug-associated or hereditary PAH included into the baseline risk stratification group

	Low risk n=101	Intermediate risk n=760	High risk n=199	All n=1,060
Age (years)	50 ± 20	67 ± 14	66 ± 17	65 ± 16
Female	70%	60%	64%	61%
BMI (kg/m ²)	26 ± 6	29 ± 7	28 ± 7	28 ± 7
WHO FC Class I/II/III/IV N=1,021	2%, 54%, 37%, 0% (unknown, 8%)	0%, 7%, 78%, 11% (unknown, 3%)	0%, 1%, 53%, 43% (unknown, 3%)	0%, 10%, 70%, 16% (unknown, 4%)
6MWD (m) N=846	459 ± 99	304 ± 104	187 ± 101	299 ± 123
NT-pro BNP (ng/L); median (Q1; Q3) N=685	148 (92; 341)	1,401 (614; 2,924)	3,982 (2,453; 6,188)	1,629 (573; 3,581)
BNP (ng/L); median (Q1; Q3); N=189	54 (28; 99)	175 (90; 348)	523 (380; 784)	232 (102; 489)
Haemodynamics				
RA pressure (mmHg) N=1,008	5 ± 3	8 ± 4	13 ± 5	8 ± 5
PAPm (mmHg) N=1,060	44 ± 14	43 ± 12	50 ± 12	45 ± 13
PAWP (mmHg)	8 ± 3	9 ± 4	10 ± 3	9 ± 3

N=1,060				
CI (l/min/m ²) N=1,001	3.0 ± 0.6	2.2 ± 0.7	1.6 ± 0.4	2.2 ± 0.7
PVR (dyn·s·cm ⁻⁵) N=1,060	590 ± 314	744 ± 381	1,140 ± 472	804 ± 428
SvO ₂ N=951	72 ± 5	64 ± 8	53 ± 8	62 ± 9
Initial therapy (within 3 months after diagnosis)				
ERA	42%	31%	41%	34%
PDE5i/sGCs	66%	76%	82%	76%
SC/IV PCA	1%	2%	8%	3%
Monotherapy	80%	89%	71%	85%
Combination therapy	20%	11%	29%	15%
Anticoagulation	45%	54%	60%	54%

Categorical data are shown as n and % of the respective population. Continuous data are depicted as mean ± SD unless stated otherwise.

Abbreviations: BMI, body mass index; PAH, pulmonary arterial hypertension; WHO FC, World Health Organization Functional Class; 6MWD, 6-minute walk distance; BNP, brain natriuretic peptide; NT-proBNP, N-terminal fragment of pro-brain natriuretic peptide; RA, right atrial; PAPm, mean pulmonary arterial pressure; PAWP, pulmonary arterial wedge pressure; CI, cardiac index; PVR, pulmonary vascular resistance; SvO₂, mixed-venous oxygen saturation; ERA endothelin receptor antagonists; PDE5i, phosphodiesterase-5 inhibitors; sGCs, stimulator of soluble guanylate cyclase; PCA, prostacyclin analogues

Supplementary Table S3 Characteristics of the patients with connective tissue disease-associated PAH included into the baseline risk stratification group

	Low risk n=52	Intermediate risk n=234	High risk n=61	All n=347
Age (years)	62 ± 12	67 ± 13	67 ± 16	66 ± 13
Female	75%	79%	77%	78%
BMI (kg/m ²)	26 ± 5	27 ± 5	26 ± 6	26 ± 5
Aetiology (n)				
SSc	41	139	36	216
SLE	2	17	2	21
MCTD	2	14	5	21
Others	7	64	18	89
WHO FC Class I/II/III/IV N=334	0%, 42%, 50%, 0% (unknown, 8%)	0%, 6%, 81%, 9% (unknown, 3%)	0%, 2%, 51%, 44%, (unknown 3%)	0%, 11%, 71%, 14% (unknown, 4%)
6MWD (m) N=273	408 ± 100	267 ± 116	173 ± 107	273 ± 130
NT-pro BNP (ng/L); median (Q1; Q3) N=217	195 (104; 410)	1,952 (747; 3,766)	4,420 (3,046; 10,070)	1,958 (563; 3,994)
BNP (ng/L); median (Q1; Q3) N=37	58 (23; 92)	330 (78; 560)	642 (432; 926)	437 (100; 637)

Haemodynamics				
RA pressure (mmHg) N=326	5 ± 3	7 ± 5	13 ± 4	8 ± 5
PAPm (mmHg) N=347	35 ± 11	43 ± 11	48 ± 10	42 ± 11
PAWP (mmHg) N=347	8 ± 3	9 ± 3	10 ± 3	9 ± 3
CI (l/min/m ²) N=325	3.1 ± 0.8	2.4 ± 0.6	1.7 ± 0.4	2.4 ± 0.7
PVR (dyn·s·cm ⁻⁵) N=347	454 ± 201	686 ± 318	1,067 ± 365	718 ± 360
SvO ₂ N=309	72 ± 4	64 ± 7	53 ± 7	63 ± 9
Initial therapy (within 3 months after diagnosis)				
ERA	50%	47%	56%	49%
PDE5i/sGCs	54%	64%	63%	62%
SC/IV PCA	0%	2%	3%	2%
Monotherapy	92%	85%	79%	85%
Combination therapy	8%	15%	21%	15%
Anticoagulation	15%	35%	31%	31%

Categorical data are shown as n and % of the respective population. Continuous data are depicted as mean ± SD unless stated otherwise.

Abbreviations: BMI, body mass index; PAH, pulmonary arterial hypertension; SSc, systemic sclerosis; SLE, systemic lupus erythematosus; MCTD; mixed connective tissue disease; WHO FC, World Health Organization Functional Class; 6MWD, 6-minute walk distance; BNP, brain natriuretic peptide; NT-proBNP, N-terminal fragment of pro-brain natriuretic peptide; RA, right atrial; PAPm, mean pulmonary arterial pressure; PAWP, pulmonary arterial wedge pressure; CI, cardiac index; PVR, pulmonary vascular resistance; SvO₂, mixed-venous oxygen saturation; ERA endothelin receptor antagonists; PDE5i, phosphodiesterase-5 inhibitors; sGCs, stimulator of soluble guanylate cyclase; PCA, prostacyclin analogues