

Supplementary Table 1. Survival according to the different PAH aetiologies

Survival (95% CI)	I/H/D-PAH	CTD-PAH	CHD-PAH
1 year	93 (90-95)	83 (77-87)	97 (93-99)
3 years	81 (76-84)	67 (60-73)	89 (83-93)
5 years	72 (67-76)	51 (43-57)	82 (75-88)
10 years	54 (49-59)	20 (14-27)	65 (55-72)

Legend: CHD, congenital heart disease; CI, confidence interval; CTD, connective tissue disease; I/H/D, idiopathic/heritable/drug-induced; PAH, pulmonary arterial hypertension

Supplementary Table 2. Multivariable Cox proportional hazards regression at baseline including BNP/NT-proBNP

	HR (95% CI)	p-value
Age, years	1.04 (1.02-1.05)	<0.001
Male gender	2.00 (1.42-2.81)	<0.001
CTD aetiology	1.66 (1.19-2.31)	0.003
6MWD, m	0.997 (0.995-0.998)	<0.001
BNP/NT-proBNP, vs <50/<300 ng/l		
- 50-200/300-650 ng/l	1.36 (0.84-2.21)	0.211
- 200-800/650-1100 ng/l	1.96 (1.19-3.21)	0.008
- >800/>1100 ng/l	2.29 (1.49-3.51)	<0.001

Legend: 6MWD, 6-minute walk distance; BNP, brain natriuretic peptide; CTD, connective tissue disease; NT-proBNP, N-terminal pro-hormone BNP

Supplementary Table 3. Correlation matrix of hemodynamic variables at 1st follow-up

Pearson Correlation	RAP	mPAP	sPAP	Ea	CE	RV power	RVSWI	RC product	CI	SVI	PVR	PAC	SvO2
RAP	1.000	0.338	0.333	0.317	-0.346	0.038	-0.105	0.089	-0.309	-0.279	0.312	-0.288	-0.413
mPAP	0.338	1.000	0.963	0.741	-0.723	0.601	0.580	0.410	-0.311	-0.362	0.812	-0.637	-0.211
sPAP	0.333	0.963	1.000	0.724	-0.726	0.593	0.585	0.260	-0.305	-0.337	0.770	-0.711	-0.234
Ea	0.317	0.741	0.724	1.000	-0.638	0.114	0.042	0.177	-0.509	-0.590	0.960	-0.583	-0.421
CE	-0.346	-0.723	-0.726	-0.638	1.000	-0.196	-0.142	-0.247	0.622	0.759	-0.663	0.878	0.441
RV power	0.038	0.601	0.593	0.114	-0.196	1.000	0.896	0.107	0.514	0.354	0.135	-0.180	0.373
RVSWI	-0.105	0.580	0.585	0.042	-0.142	0.896	1.000	0.287	0.393	0.447	0.136	-0.151	0.355
RC product	0.089	0.410	0.260	0.177	-0.247	0.107	0.287	1.000	-0.296	-0.102	0.369	0.054	-0.124
CI	-0.309	-0.311	-0.305	-0.509	0.622	0.514	0.393	-0.296	1.000	0.839	-0.562	0.547	0.680
SVI	-0.279	-0.362	-0.337	-0.590	0.759	0.354	0.447	-0.102	0.839	1.000	-0.570	0.636	0.606
PVR	0.312	0.812	0.770	0.960	-0.663	0.135	0.136	0.369	-0.562	-0.570	1.000	-0.589	-0.433
PAC	-0.288	-0.637	-0.711	-0.583	0.878	-0.180	-0.151	0.054	0.547	0.636	-0.589	1.000	0.420
SvO2	-0.413	-0.211	-0.234	-0.421	0.441	0.373	0.355	-0.124	0.680	0.606	-0.433	0.420	1.000

Legend: CE, cardiac efficiency; CI, cardiac index; Ea, pulmonary artery elastance; mPAP, mean pulmonary artery pressure; PAC, pulmonary arterial compliance; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RC, resistance-compliance; RV, right ventricle; RVSWI, RV stroke work index; sPAP, systolic pulmonary artery pressure; SVI, stroke volume index; SvO2, mixed venous oxygen saturation.

All correlations significant at the 0.02 level (2-tailed) but RC product*PAC, RV power*RAP, and Ea*RVSWI whose correlations were not statistically significant.

Supplementary Table 4. Comparison of multivariable cox regression models for hemodynamic variables at 1st follow-up excluding patients with uncorrected CHD and responder to CCBs treatment

	Baseline		1st F-UP Model 1		1st F-UP Model 2		1st F-UP Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age, y	1.03 (1.02-1.03)	<0.001	1.03 (1.02-1.04)	<0.001	1.03 (1.02-1.04)	<0.001	1.03 (1.02-1.04)	<0.001
Male gender	2.37 (1.83-3.07)	<0.001	2.07 (1.55-2.77)	<0.001	2.08 (1.55-2.79)	<0.001	1.84 (1.38-2.46)	<0.001
CTD aetiology	1.69 (1.31-2.19)	<0.001	1.90 (1.43-2.53)	<0.001	1.93 (1.44-2.57)	<0.001	1.87 (1.41-2.48)	<0.001
6MWD, 10 m	0.96 (0.95-0.97)	<0.001	0.9997 (0.9995-0.9999)*	0.002	0.9997 (0.9995-0.9999)*	0.001	0.9997 (0.9995-0.9999)*	0.003
WHO-FC			1.38 (1.08-1.77)	0.010	1.35 (1.05-1.73)	0.019	1.39 (1.09-1.78)	0.008
eGFR, ml/min	0.994 (0.988-0.9998)	0.043						
RAP, mmHg	1.04 (1.01-1.06)	0.003	1.07 (1.05-1.10)	<0.001	1.07 (1.04-1.10)	<0.001	1.07 (1.04-1.10)	<0.001
PAC, ml/mmHg			0.77 (0.64-0.92)	0.005				
Ea, mmHg/ml					1.34 (1.13-1.59)	0.001		
SvO ₂ , %							0.98 (0.96-0.99)	0.002
Log likelihood			-1373.09		-1373.47		-1374.00	
AIC			2760.18		2760.94		2762.00	
BIC			2789.69		2790.48		2791.54	
	1st F-UP Model 4		1st F-UP Model 5		1st F-UP Model 6		1st F-UP Model 7	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age, y	1.03 (1.02-1.04)	<0.001	1.03 (1.02-1.04)	<0.001	1.03 (1.02-1.04)	<0.001	1.03 (1.02-1.04)	<0.001
Male gender	2.06 (1.53-2.76)	<0.001	2.03 (1.52-2.72)	<0.001	1.84 (1.37-2.46)	<0.001	1.88 (1.40-2.51)	<0.001
CTD aetiology	1.96 (1.46-2.62)	<0.001	1.92 (1.44-2.56)	<0.001	1.87 (1.41-2.50)	<0.001	1.83 (1.38-2.43)	<0.001
6MWD, 10 m*	0.9997 (0.9996-0.9999)	0.001	0.9997 (0.9995-0.9999)	0.002	0.9997 (0.9995-0.9999)	0.001	0.9997 (0.9995-0.9999)	0.003
WHO-FC	1.36 (1.06-1.75)	0.015	1.38 (1.07-1.77)	0.012	1.44 (1.12-1.84)	0.001	1.42 (1.10-1.82)	0.006
RAP, mmHg	1.07 (1.04-1.10)	<0.001	1.07 (1.04-1.10)	<0.001	1.08 (1.05-1.11)	<0.001	1.08 (1.05-1.11)	<0.001
PVR, WU	1.04 (1.01-1.07)	0.002						
CE, ml/mmHg			0.76 (0.62-0.94) CE	0.010				
CI, l/min/m ²					0.84 (0.70-0.996)	0.045		
SVI, ml/m ²							0.99 (0.97-1.00)	0.063

Log likelihood	-1374.20	-1375.06	-1376.55	-1376.86
AIC	2762.41	2764.12	2767.09	2767.72
BIC	2791.95	2793.67	2796.64	2797.26

Legend: 6MWD, 6-minute walk distance; AIC, Akaike's information criterion; BIC, Bayesian information criterion; CE, cardiac efficiency; CI, cardiac index; CTD, connective tissue disease; Ea, pulmonary artery elastance; F-UP, follow-up; HR, hazard ratio; PAC, pulmonary arterial compliance; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SVI, stroke volume index; SvO₂, mixed venous oxygen saturation; WHO-FC, world health organization functional class

*Time varying covariate

>38 ml/m ²	ref		ref		ref		ref	
31-38 ml/m ²	1.00 (0.75-1.34)	0.999	1.00 (0.74-1.33)	0.980	0.94 (0.70-1.26)	0.671	0.92 (0.68-1.23)	0.557
<31 ml/m ²	1.18 (0.89-1.56)	0.246	1.25 (0.94-1.66)	0.123	1.28 (0.97-1.68)	0.078	1.52 (0.18-1.96)	0.001

Legend: CE, cardiac efficiency; CI, cardiac index; COMPERA, Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; Ea, pulmonary artery elastance; FPHR, French pulmonary hypertension registry; PAC, pulmonary arterial compliance; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SVI, stroke volume index; SvO₂, mixed venous oxygen saturation.

>38 ml/m ²	ref		ref		ref		ref	
31-38 ml/m ²	1.53 (1.22-1.91)	<0.001	1.48 (1.18-1.85)	0.001	1.42 (1.13-1.78)	0.002	1.44 (1.15-1.80)	0.002
<31 ml/m ²	2.01 (1.60-2.53)	<0.001	2.01 (1.60-2.53)	<0.001	2.03 (1.62-2.55)	<0.001	2.31 (1.87-2.85)	<0.001

Legend: CE, cardiac efficiency; CI, cardiac index; COMPERA, Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; Ea, pulmonary artery elastance; FPHR, French pulmonary hypertension registry; PAC, pulmonary arterial compliance; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SVI, stroke volume index; SvO₂, mixed venous oxygen saturation.

Supplementary Table 7. Risk discrimination characteristics of the proposed RHC risk tool 3-strata vs COMPERA 1.0, FPHR and Bologna simplified risk table strategies and of the proposed RHC risk tool 4-strata vs COMPERA 2.0 risk tool for the combined endpoint (all cause death + all-cause non-elective hospitalization + need of treatment escalation) in patients with available BNP/NT-proBNP at 1st follow-up (n= 151)

	All cause death + PAH-related non-elective hospitalization + need of treatment escalation			
	RHC risk tool 3-strata	COMPERA 1.0	FPHR	Bologna
C-statistic (95% CI)	0.636 (0.582-0.689)	0.600 (0.542-0.657)	0.594 (0.534-0.653)	0.574 (0.524-0.624)
AIC	791.01	787.87	787.46	794.37
BIC	794.06	790.92	790.51	797.42
1-y event-free survival (%)				
- Low	89.6 (79.4-94.9)	84.6 (73.3-91.5)	82.9 (70.5-90.4)	89.5 (74.3-95.9)
- Intermediate	57.2 (44.7-67.9)	61.8 (50.1-71.6)	69.5 (57.7-78.6)	65.2 (55.2-73.6)
- High	37.5 (8.7-67.4)	NA	23.1 (4.3-50.5)	66.7 (19.5-90.4)
p-value	p >0.05 for all pairwise comparisons.			
	RHC risk tool 4-strata		COMPERA 2.0	
C-statistic (95% CI)	0.684 (0.626-0.741)		0.609 (0.544-0.673)	
AIC	778.52		786.47	
BIC	781.57		789.52	
1-y event-free survival (%)				
- Low	92.8 (82.0-97.2)		84.1 (70.6-91.7)	
- Intermediate-low	72.1 (58.1-82.2)		77.8 (64.2-86.7)	
- Intermediate-high	37.8 (21.2-54.3)		54.3 (37.0-68.7)	
- High	25.0 (0.9-66.5)		28.6 (0.4-61.1)	
p-value	0.060			

Legend: AIC, Akaike's information criterion; BIC, Bayesian information criterion; COMPERA, Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; FPHR, French Pulmonary Hypertension Registry; RHC, right heart catheterization.

Supplementary Table 8. Risk discrimination characteristics of the proposed RHC risk tool 3-strata vs COMPERA 1.0, FPHR and Bologna simplified risk table strategies and of the proposed RHC risk tool 4-strata vs COMPERA 2.0 risk tool for the combined endpoint (all cause death + PAH-related non-elective hospitalization + need of treatment escalation)

	All cause death + PAH-related non-elective hospitalization + need of treatment escalation			
	RHC risk tool 3-strata	COMPERA 1.0	FPHR	Bologna
C-statistic (95% CI)	0.666* (0.644-0.689)	0.647 (0.625-0.668)	0.646 (0.623-0.669)	0.640* (0.618-0.663)
AIC	5906.79	5920.80	5927.45	5933.45
BIC	5911.35	5925.36	5932.01	5938.01
1-y event-free survival (%)				
- Low	91.6 (87.4-94.4)	86.7 (83.0-89.7)	86.6 (82.6-89.7)	87.8 (83.6-91.0)
- Intermediate	69.4 (64.0-74.2)	59.4 (53.2-64.9)	68.2 (62.1-73.5)	66.2 (61.0-70.9)
- High	46.1 (36.8-54.9)	28.0 (12.4-46.0)	33.3 (22.9-44.0)	37.1 (22.7-51.6)
	RHC risk tool 4-strata		COMPERA 2.0	
C-statistic (95% CI)	0.682 (0.658-0.705)		0.659 (0.636-0.682)	
AIC	5884.35		5894.95	
BIC	5888.91		5899.50	
1-y event-free survival (%)				
- Low	92.4 (88.0-95.2)		88.7 (84.7-91.7)	
- Intermediate-low	81.4 (75.2-86.2)		76.3 (68.9-82.2)	
- Intermediate-high	59.8 (52.6-66.2)		52.9 (45.6-59.6)	
- High	37.3 (26.5-48.1)		31.8 (14.2-51.1)	

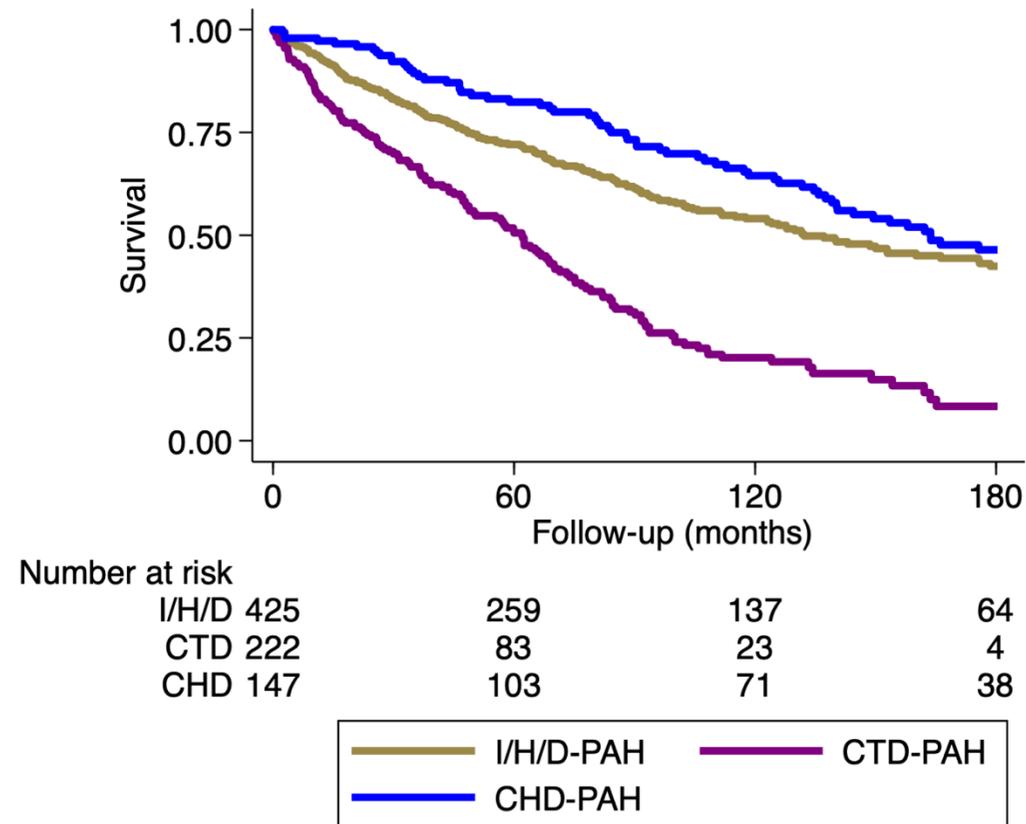
Legend: AIC, Akaike's information criterion; BIC, Bayesian information criterion; COMPERA, Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; FPHR, French Pulmonary Hypertension Registry; RHC, right heart catheterization. *= p<0.05 for the comparison

Supplementary Table 9. Risk discrimination characteristics of the COMPERA-RHC 4-strata risk tool vs COMPERA 2.0 risk tool for the combined endpoint (all cause death + all cause non-elective hospitalization + need of treatment escalation)

All patients (n= 706)	All cause death + all cause non-elective hospitalization + need of treatment escalation	
	COMPERA 2.0	COMPERA-RHC 4-strata
C-statistic (95% CI)	0.655 (0.632-0.678)	0.683 (0.661-0.705)
AIC	6075.77	6038.37
BIC	6080.33	6042.93
1-y event-free survival (%)		
- Low	86.5 (82.2-89.8)	91.1 (86.3-94.2)
- Intermediate-low	73.2 (65.6-79.3)	77.5 (72.1-82.0)
- Intermediate-high	48.7 (41.5-55.5)	42.9 (35.7-50.0)
- High	31.8 (14.2-51.1)	30.4 (13.5-49.3)
	p-value= 0.005	
Only patients with BNP (n= 151)	All cause death + all cause non-elective hospitalization + need of treatment escalation	
	COMPERA 2.0	COMPERA-RHC 4-strata
C-statistic (95% CI)	0.609 (0.544-0.673)	0.670 (0.618-0.721)
AIC	786.47	776.56
BIC	789.52	779.61
1-y event-free survival (%)		
- Low	84.1 (70.6-91.7)	100 (NA)
- Intermediate-low	77.8 (64.2-86.7)	76.9 (65.8-84.8)
- Intermediate-high	54.3 (37.0-68.7)	37.1 (22.0-52.1)
- High	28.6 (0.4-61.1)	NA
	p-value= 0.023	

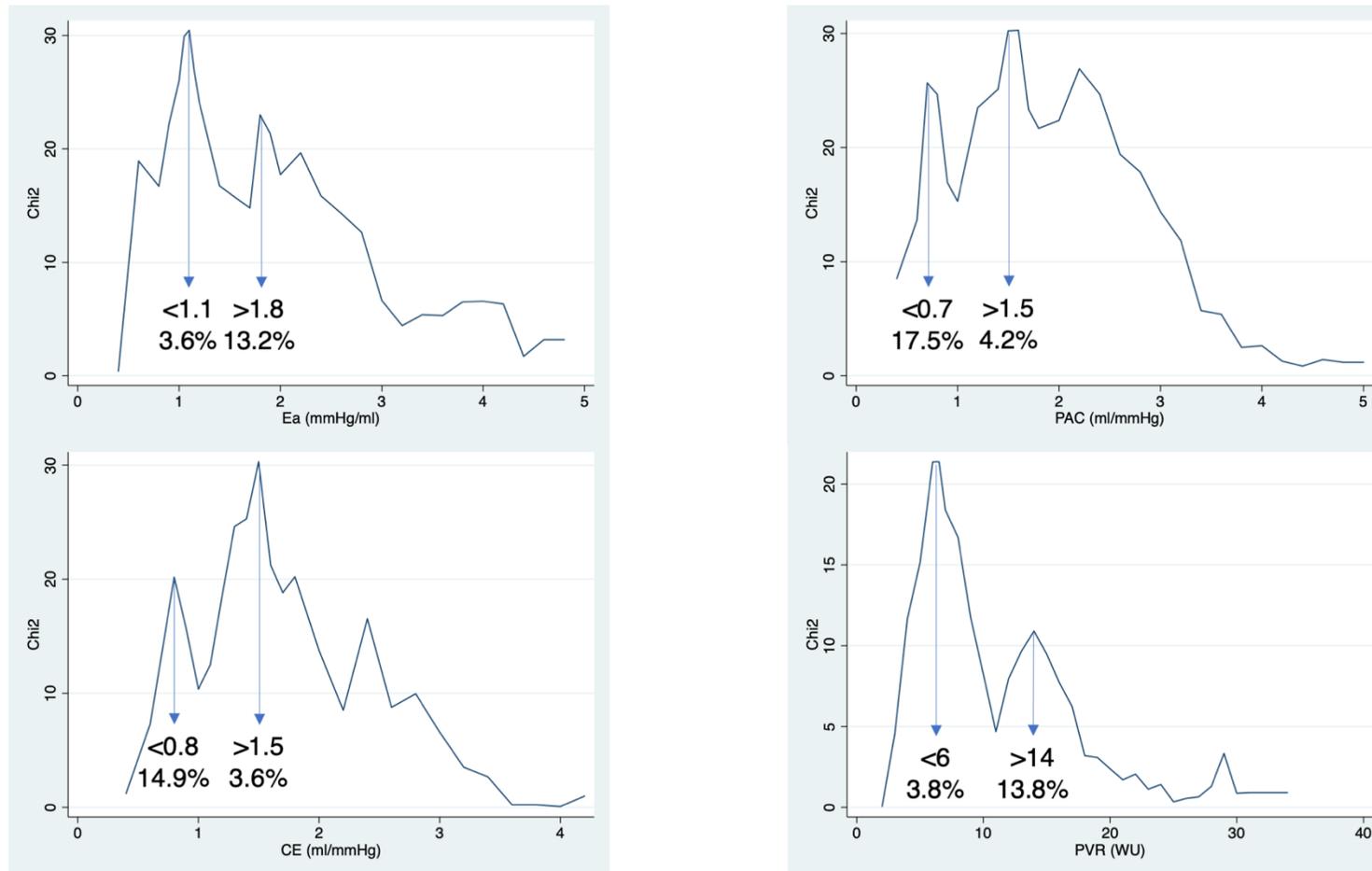
Legend: AIC, Akaike's information criterion; BIC, Bayesian information criterion; COMPERA, Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; RHC, right heart catheterization.

Supplementary Figure 1. Survival according to the different PAH aetiologies from baseline evaluation.



Legend: CHD, congenital heart disease; CTD, connective tissue disease; I/H/D, idiopathic/heritable/drug induced; PAH, pulmonary arterial hypertension. Log-rank test p-value I/H/D vs CHD= 0.095; I/H/D vs CTD <0.001; CHD vs CTD <0.001

Supplementary Figure 2. Line graph of different cut-off values and the corresponding chi2 of the long-rank test for the relative hemodynamic variables at 1st follow-up. Arrows indicate the cut-offs with the highest chi2 and the corresponding 1-y mortality.



Legend: CE, cardiac efficiency; Ea, pulmonary artery elastance; PAC, pulmonary arterial compliance; PVR, pulmonary vascular resistance.