

Online supplement

Hoeper et al.:

Temporal trends in pulmonary arterial hypertension:
Results from the COMPERA registry

Figure S1: Selected baseline variables per year of PAH diagnosis

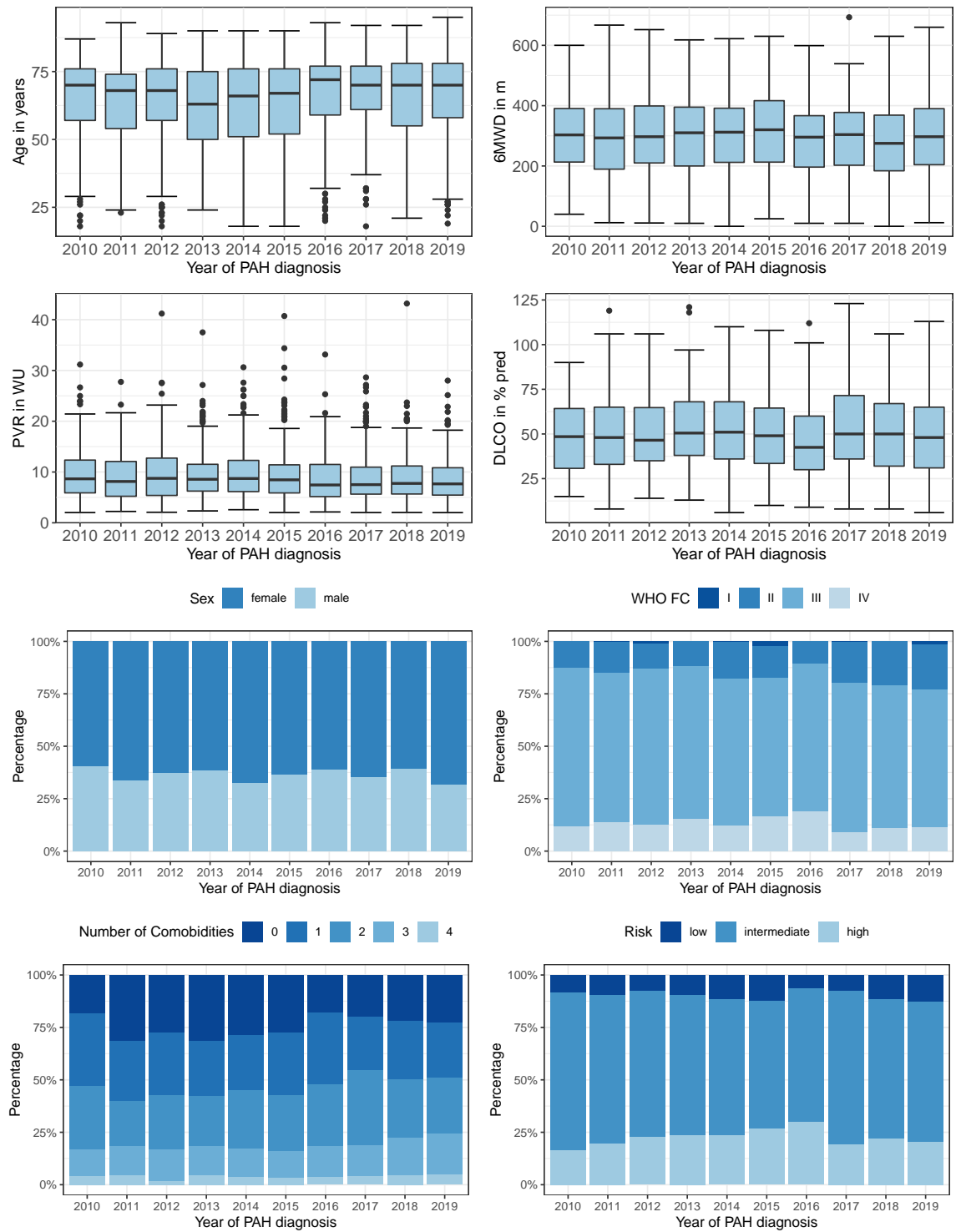


Figure S2a: Kaplan-Meier survival estimates in PAH for patients <65 years at baseline

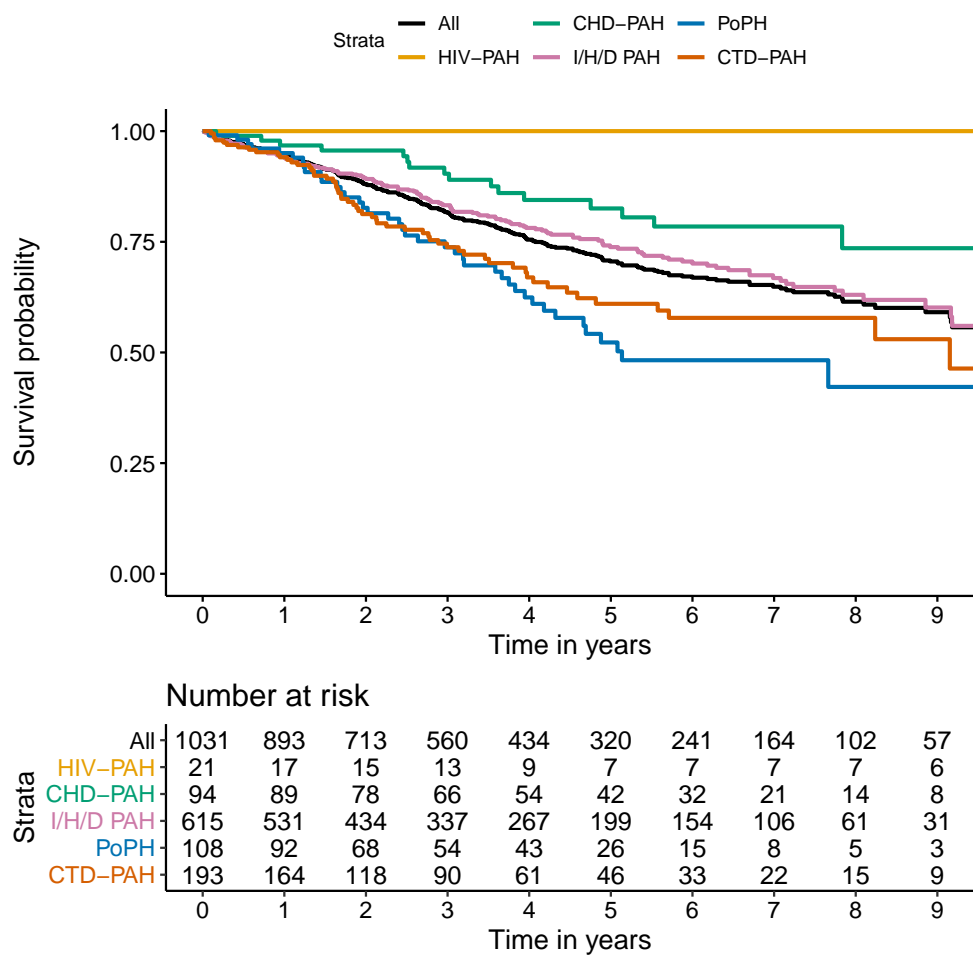


Figure S2b: Kaplan-Meier survival estimates in PAH for patients ≥ 65 years at baseline, HIV-PAH patients (n=3) omitted

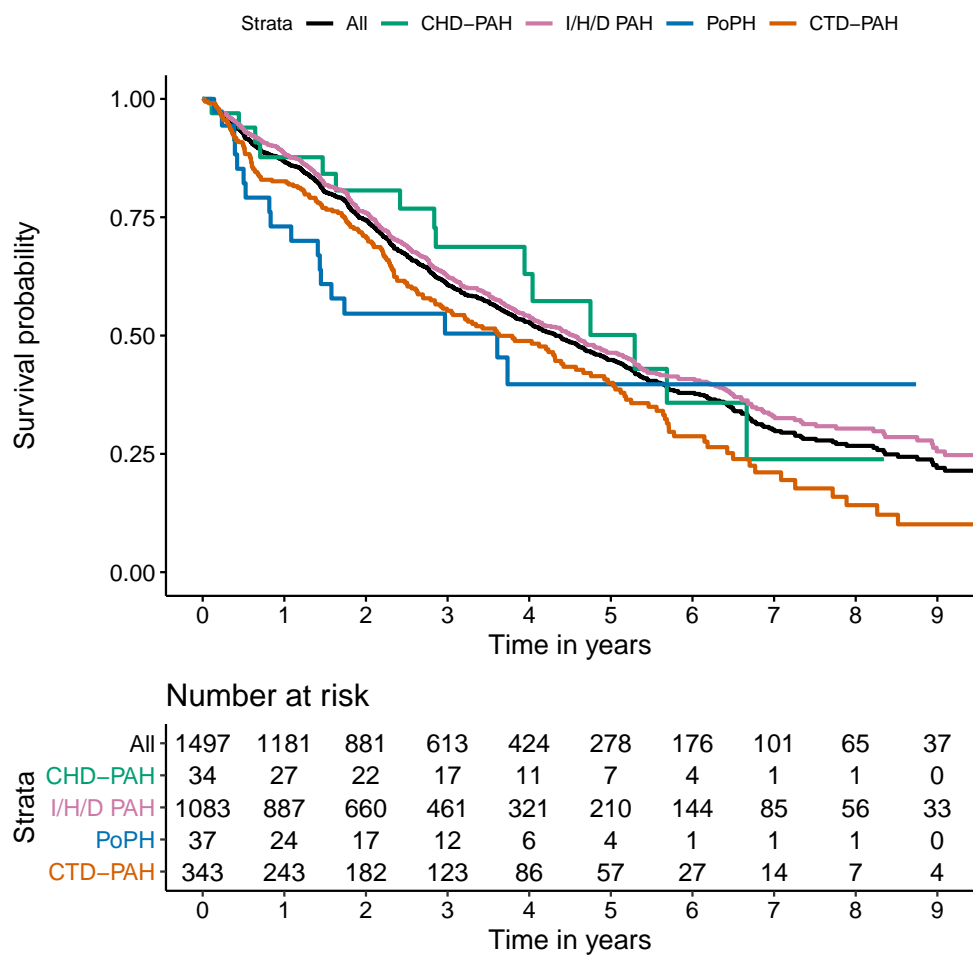


Figure S2c: Kaplan-Meier survival estimates for patients with I/H/D-PAH, no comorbidities and DLCO > 45%

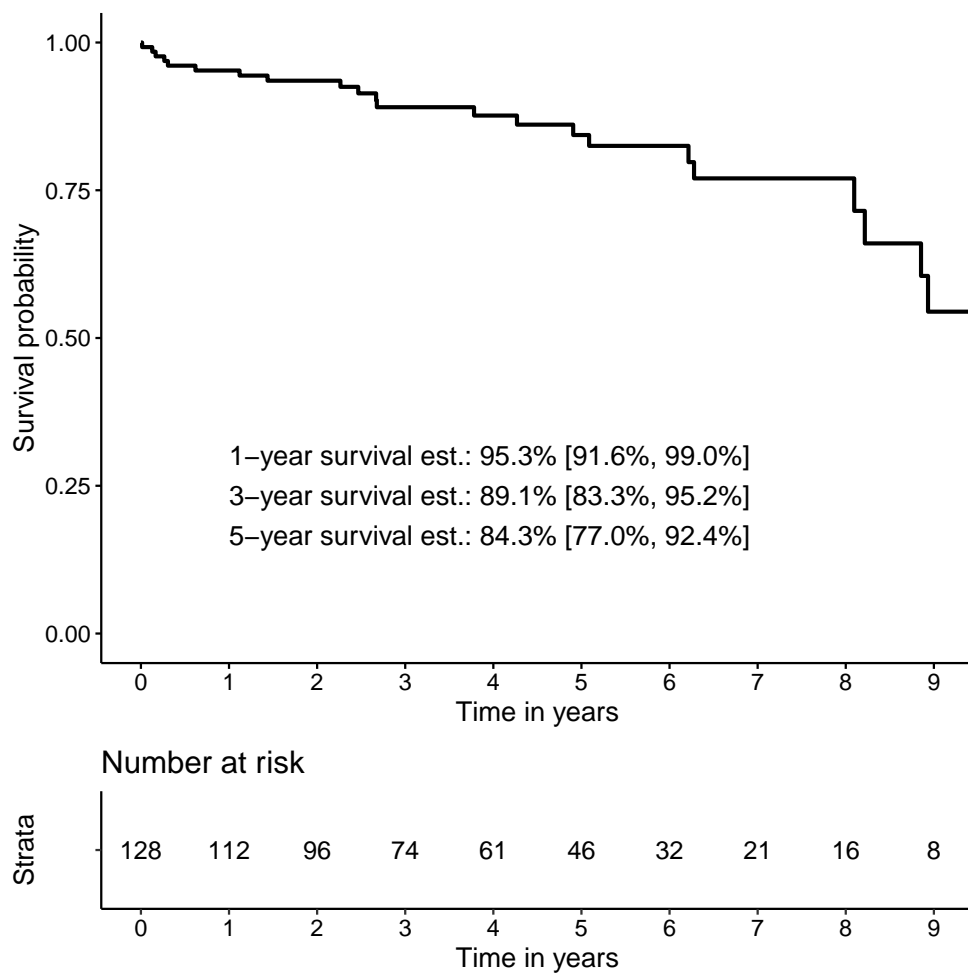


Table S1a: Baseline characteristics of adult patients newly diagnosed with PAH between 2010 and 2019: No. (%), mean (SD) or median [Q1 - Q3]. Subgroup of 1031 patients <65 years old at baseline.

	All PAH n=1031 (100 %)	I/H/D PAH n=615 (59.7%)	CTD-PAH n=193 (18.7%)	CHD-PAH n=94 (9.1%)	HIV-PAH n=21 (2.0%)	PoPH n=108 (10.5%)
Age, years	49.0 (12.3)	48.6 (12.8)	52.5 (10.8)	42.2 (12.9)	42.4 (8.4)	52.5 (7.9)
Female	669 (64.9%)	395 (64.2%)	153 (79.3%)	66 (70.2%)	11 (52.4%)	44 (40.7%)
BMI, kg/m ²	28.1 (6.9)	28.4 (7.0)	27.5 (6.3)	26.0 (6.7)	27.9 (8.7)	30.0 (6.6)
WHO FC						
I	12 (1.3%)	6 (1.1%)	0 (0.0%)	4 (4.9%)	1 (4.8%)	1 (1.0%)
II	214 (22.6%)	136 (24.1%)	37 (20.4%)	22 (27.2%)	6 (28.6%)	13 (12.9%)
III	622 (65.6%)	357 (63.3%)	128 (70.7%)	49 (60.5%)	12 (57.1%)	76 (75.2%)
IV	100 (10.5%)	65 (11.5%)	16 (8.8%)	6 (7.4%)	2 (9.5%)	11 (10.9%)
6MWD, m	347.2 (133.4)	354.9 (136.7)	325.6 (128.2)	361.3 (109.4)	398.0 (133.3)	321.5 (134.1)
Pulmonary function test						
TLC, % pred	90.8 (17.5)	93.6 (16.8)	83.0 (18.1)	85.5 (14.5)	91.4 (10.5)	95.7 (16.1)
FVC, % pred	81.2 (20.9)	82.6 (20.9)	79.0 (21.8)	72.6 (19.1)	85.0 (11.8)	83.7 (18.9)
FEV ₁ , % pred	76.2 (20.6)	76.2 (21.2)	76.9 (19.7)	67.3 (17.6)	81.8 (14.7)	79.6 (20.2)
DLCO, % pred	54.8 (22.0)	58.0 (23.1)	42.8 (16.7)	63.8 (16.9)	55.3 (6.4)	58.8 (15.4)
PaO ₂ , mmHg	67.7 (12.4)	67.7 (13.0)	67.3 (11.5)	65.5 (8.4)	75.5 (16.8)	70.0 (11.7)
PaCO ₂ , mmHg	34.1 (6.5)	34.5 (7.0)	33.3 (5.8)	35.0 (6.7)	35.0 (1.4)	32.6 (4.2)
Smoking history						
current	75 (16.2%)	56 (15.7%)	5 (10.0%)	3 (14.3%)	0 (0.0%)	11 (33.3%)
former	190 (40.9%)	144 (40.3%)	21 (42.0%)	8 (38.1%)	2 (66.7%)	15 (45.5%)
never	199 (42.9%)	157 (44.0%)	24 (48.0%)	10 (47.6%)	1 (33.3%)	7 (21.2%)
if current or former: Pack years	25.0 [15.0, 40.0]	25.0 [15.0, 40.0]	29.0 [20.0, 39.2]	10.0 [10.0, 25.0]	NA [NA, NA]	20.0 [17.5, 32.5]
Comorbid conditions						
Obesity (BMI > 30)	344 (34.2%)	211 (35.0%)	52 (28.1%)	26 (27.7%)	6 (33.3%)	49 (45.8%)
Hypertension	345 (40.0%)	236 (44.2%)	55 (38.2%)	17 (20.5%)	6 (46.2%)	31 (34.8%)
Coronary heart disease	103 (12.4%)	70 (13.7%)	16 (11.6%)	4 (5.0%)	1 (7.7%)	12 (13.6%)
Diabetes mellitus	128 (14.9%)	103 (19.4%)	9 (6.4%)	5 (6.1%)	0 (0.0%)	11 (12.1%)
Haemodynamics						
RAP, mmHg	8.7 (5.2)	8.8 (5.4)	8.2 (5.1)	7.9 (4.8)	8.4 (3.7)	9.6 (5.2)
PAPm, mmHg	49.1 (14.5)	50.3 (14.2)	43.5 (13.1)	53.3 (20.1)	47.4 (11.2)	48.8 (10.7)
PAWP, mmHg	8.9 (3.3)	8.8 (3.3)	9.1 (3.3)	9.1 (3.6)	7.6 (2.9)	9.5 (3.5)
CI, L/min/m ²	2.4 (0.9)	2.3 (0.8)	2.6 (0.9)	2.8 (1.3)	2.2 (0.7)	2.7 (1.1)
PVR, dyn·s·cm ⁻⁵	826.6 (449.7)	889.6 (463.7)	677.6 (370.4)	858.8 (547.0)	851.1 (319.5)	693.7 (339.9)
PVR, WU	10.3 (5.6)	11.1 (5.8)	8.5 (4.6)	10.7 (6.8)	10.6 (4.0)	8.7 (4.2)
SvO ₂ , %	63.1 (9.4)	62.0 (9.7)	65.1 (8.1)	65.1 (10.4)	57.1 (8.2)	65.2 (7.4)
Laboratory findings						
Creatinine, μmol/L	90.0 (53.1)	94.3 (60.9)	85.0 (33.2)	82.0 (53.5)	78.7 (20.6)	83.2 (29.3)
Uric acid, μmol/L	419.3 (156.1)	428.6 (149.1)	422.4 (148.1)	385.3 (199.6)	345.7 (119.4)	406.7 (155.4)
Bilirubin, μmol/L	17.5 (16.2)	16.2 (14.3)	12.9 (10.2)	15.5 (20.5)	25.7 (27.0)	30.5 (19.7)
NT-proBNP, pg/mL	903 [257, 2442]	1044 [308, 2799]	941 [254, 2740]	424 [196, 980]	1166 [204, 1959]	727 [170, 1802]
BNP, pg/mL	169 [77, 398]	187 [77, 397]	228 [70, 530]	130 [36, 172]	175 [150, 201]	153 [133, 331]
Risk						
Low	182 (17.8%)	113 (18.5%)	29 (15.2%)	20 (21.7%)	6 (28.6%)	14 (13.0%)
Intermediate	687 (67.1%)	405 (66.2%)	128 (67.0%)	66 (71.7%)	13 (61.9%)	75 (69.4%)
High	155 (15.1%)	94 (15.4%)	34 (17.8%)	6 (6.5%)	2 (9.5%)	19 (17.6%)

Table S1b: Baseline characteristics of adult patients newly diagnosed with PAH between 2010 and 2019: No. (%), mean (SD) or median [Q1 - Q3]. Subgroup of 1500 patients ≥ 65 years old at baseline.

	All PAH n=1500 (100 %)	I/H/D PAH n=1083 (72.2%)	CTD-PAH n=343 (22.9%)	CHD-PAH n=34 (2.3%)	HIV-PAH n=3 (0.2%)	PoPH n=37 (2.5%)
Age, years	75.3 (5.8)	75.8 (5.8)	74.1 (5.8)	73.8 (5.2)	69.7 (1.2)	73.4 (5.2)
Female	940 (62.7%)	621 (57.3%)	281 (81.9%)	18 (52.9%)	0 (0.0%)	20 (54.1%)
BMI, kg/m ²	28.0 (5.5)	28.5 (5.6)	26.3 (4.8)	27.3 (6.0)	25.9 (4.1)	28.5 (4.7)
WHO FC						
I	3 (0.2%)	1 (0.1%)	2 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
II	159 (11.1%)	108 (10.5%)	41 (12.7%)	4 (12.1%)	0 (0.0%)	6 (16.2%)
III	1053 (73.6%)	760 (73.6%)	241 (74.4%)	24 (72.7%)	2 (66.7%)	26 (70.3%)
IV	215 (15.0%)	164 (15.9%)	40 (12.3%)	5 (15.2%)	1 (33.3%)	5 (13.5%)
6MWD, m	262.5 (110.1)	264.8 (109.0)	250.1 (112.8)	303.0 (113.0)	195.3 (92.1)	277.0 (107.2)
Pulmonary function test						
TLC, % pred	89.0 (17.2)	90.7 (16.1)	84.5 (19.2)	80.6 (16.9)	75.0 (NA)	92.5 (18.8)
FVC, % pred	79.3 (19.9)	79.2 (19.4)	80.5 (21.4)	65.2 (16.5)	88.0 (NA)	80.0 (19.6)
FEV ₁ , % pred	76.5 (19.3)	76.7 (19.3)	76.9 (19.5)	63.3 (15.5)	101.0 (NA)	76.8 (18.3)
DLCO, % pred	48.0 (21.2)	49.1 (21.8)	42.5 (17.2)	70.2 (23.0)	22.0 (NA)	55.9 (22.5)
PaO ₂ , mmHg	63.4 (12.0)	62.9 (12.0)	64.1 (12.1)	67.1 (13.0)	47.0 (NA)	66.4 (8.1)
PaCO ₂ , mmHg	35.8 (6.4)	36.1 (6.0)	34.8 (7.2)	37.8 (3.8)	36.0 (NA)	34.0 (8.7)
Smoking history						
current	21 (2.3%)	20 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
former	404 (44.0%)	346 (43.6%)	45 (44.6%)	5 (55.6%)	0 (0.0%)	8 (57.1%)
never	494 (53.8%)	428 (53.9%)	56 (55.4%)	4 (44.4%)	1 (100.0%)	5 (35.7%)
if current or former: Pack years	30.0 [15.0, 45.0]	30.0 [15.0, 50.0]	20.0 [10.0, 30.0]	20.0 [13.8, 27.5]	NA [NA, NA]	25.0 [20.0, 42.5]
Comorbid conditions						
Obesity (BMI > 30)	466 (31.7%)	378 (35.2%)	68 (21.1%)	8 (23.5%)	0 (0.0%)	12 (32.4%)
Hypertension	984 (74.3%)	771 (77.0%)	170 (65.9%)	19 (67.9%)	1 (50.0%)	23 (63.9%)
Coronary heart disease	451 (34.9%)	365 (37.0%)	73 (29.7%)	6 (21.4%)	0 (0.0%)	7 (21.9%)
Diabetes mellitus	462 (35.3%)	386 (38.9%)	52 (20.6%)	13 (44.8%)	0 (0.0%)	11 (31.4%)
Haemodynamics						
RAP, mmHg	8.0 (4.5)	8.0 (4.3)	7.5 (4.7)	10.8 (7.0)	7.7 (7.2)	10.7 (5.5)
PAPm, mmHg	40.8 (10.4)	40.8 (10.2)	40.1 (10.4)	44.1 (14.3)	44.3 (15.4)	43.4 (10.2)
PAWP, mmHg	9.9 (3.3)	9.9 (3.3)	9.5 (3.4)	11.0 (3.3)	10.0 (3.5)	10.5 (3.3)
CI, L/min/m ²	2.2 (0.8)	2.2 (0.7)	2.4 (0.7)	2.7 (0.8)	2.6 (2.4)	2.4 (1.1)
PVR, dyn·s·cm ⁻⁵	687.3 (357.4)	695.6 (363.4)	674.4 (345.3)	599.3 (336.0)	1005.3 (577.6)	598.3 (250.8)
PVR, WU	8.6 (4.5)	8.7 (4.5)	8.4 (4.3)	7.5 (4.2)	12.6 (7.2)	7.5 (3.1)
SvO ₂ , %	62.6 (8.0)	62.5 (7.7)	62.6 (9.0)	66.4 (9.2)	58.0 (4.0)	62.5 (7.7)
Laboratory findings						
Creatinine, μ mol/L	109.2 (55.4)	112.3 (58.9)	100.7 (44.9)	98.9 (41.2)	105.7 (36.7)	104.7 (40.3)
Uric acid, μ mol/L	446.3 (148.2)	449.7 (144.9)	433.8 (157.0)	417.3 (153.8)	496.1 (29.0)	459.6 (169.8)
Bilirubin, μ mol/L	14.4 (12.5)	14.0 (10.3)	12.9 (13.1)	19.1 (24.4)	59.1 (56.9)	26.8 (20.9)
NT-proBNP, pg/mL	1819 [722, 4122]	1848 [762, 4120]	1828 [660, 4286]	1160 [641, 2310]	4499 [2332, 4775]	1235 [626, 3164]
BNP, pg/mL	244 [110, 553]	214 [110, 509]	310 [82, 704]	315 [142, 484]	NA [NA, NA]	310 [278, 603]
Risk						
Low	64 (4.3%)	40 (3.7%)	20 (5.9%)	2 (6.1%)	0 (0.0%)	2 (5.4%)
Intermediate	1011 (67.9%)	739 (68.7%)	221 (65.2%)	25 (75.8%)	2 (66.7%)	24 (64.9%)
High	413 (27.8%)	297 (27.6%)	98 (28.9%)	6 (18.2%)	1 (33.3%)	11 (29.7%)

Table S1c: Baseline characteristics of adult patients newly diagnosed with PAH between 2010 and 2019: No. (%), mean (SD) or median [Q1 - Q3]. Subgroup of 128 patients with I/H/D-PAH, no comorbidities and DLCO > 45%.

	I/H/D-PAH without comorbidities and DLCO > 45%
Age, years	46.7 (18.2)
Female	96 (75.0%)
BMI, kg/m ²	24.1 (3.3)
WHO FC	
I	2 (1.6%)
II	30 (24.6%)
III	80 (65.6%)
IV	10 (8.2%)
6MWD, m	388.3 (133.4)
Pulmonary function test	
TLC, % pred	97.0 (15.2)
FVC, % pred	89.9 (17.7)
FEV ₁ , % pred	85.4 (17.2)
DLCO, % pred	69.2 (14.2)
PaO ₂ , mmHg	76.9 (10.2)
PaCO ₂ , mmHg	32.5 (3.7)
Smoking history	
current	10 (8.7%)
former	33 (28.7%)
never	72 (62.6%)
if current or former: Pack years	16.0 [10.0, 29.0]
Comorbid conditions	
Obesity (BMI > 30)	0 (0.0%)
Hypertension	0 (0.0%)
Coronary heart disease	0 (0.0%)
Diabetes mellitus	0 (0.0%)
Haemodynamics	
RAP, mmHg	6.9 (4.3)
PAPm, mmHg	48.1 (14.5)
PAWP, mmHg	8.0 (3.3)
CI, L/min/m ²	2.1 (0.7)
PVR, dyn·s·cm ⁻⁵	954.3 (468.6)
PVR, WU	11.9 (5.9)
SvO ₂ , %	63.4 (9.9)
Laboratory findings	
Creatinine, μmol/L	85.6 (32.4)
Uric acid, μmol/L	358.0 (132.3)
Bilirubin, μmol/L	13.2 (9.9)
NT-proBNP, pg/mL	1108 [370, 1932]
BNP, pg/mL	127 [68, 268]
Risk	
Low	24 (18.8%)
Intermediate	93 (72.7%)
High	11 (8.6%)

Table S2: Baseline characteristics of adult patients newly diagnosed with PAH per year of diagnosis: No. (%), mean (SD) or median [Q1 - Q3]

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
	n=242 (9.6%)	n=199 (7.9%)	n=204 (8.1%)	n=237 (9.4%)	n=241 (9.5%)	n=282 (11.1%)	n=301 (11.9%)	n=271 (10.7%)	n=268 (10.6%)	n=286 (11.3%)
Diagnosis										
I/H/D PAH	171 (70.7%)	122 (61.3%)	127 (62.3%)	145 (61.2%)	147 (61.0%)	178 (63.1%)	212 (70.4%)	181 (66.8%)	200 (74.6%)	215 (75.2%)
CTD-PAH	42 (17.4%)	48 (24.1%)	53 (26.0%)	51 (21.5%)	65 (27.0%)	65 (23.0%)	63 (20.9%)	63 (23.2%)	38 (14.2%)	48 (16.8%)
CHD-PAH	14 (5.8%)	11 (5.5%)	12 (5.9%)	12 (5.1%)	16 (6.6%)	21 (7.4%)	10 (3.3%)	10 (3.7%)	15 (5.6%)	7 (2.4%)
HIV-PAH	8 (3.3%)	4 (2.0%)	2 (1.0%)	4 (1.7%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	2 (0.7%)	1 (0.4%)	2 (0.7%)
PoPH	7 (2.9%)	14 (7.0%)	10 (4.9%)	25 (10.5%)	13 (5.4%)	18 (6.4%)	15 (5.0%)	15 (5.5%)	14 (5.2%)	14 (4.9%)
Age, years	65 (15)	62 (17)	64 (16)	61 (16)	62 (17)	63 (17)	67 (15)	67 (13)	66 (16)	66 (15)
Female	144 (59.5%)	132 (66.3%)	128 (62.7%)	146 (61.6%)	163 (67.6%)	179 (63.5%)	184 (61.1%)	175 (64.6%)	163 (60.8%)	195 (68.2%)
BMI, kg/m ²	27.6 (6.0)	27.7 (6.1)	27.7 (5.8)	27.3 (5.8)	28.1 (6.2)	27.4 (5.9)	28.3 (6.1)	29.0 (5.9)	28.3 (6.3)	28.5 (6.5)
WHO FC										
I	3.0 (0.5)	3.0 (0.6)	3.0 (0.5)	3.0 (0.5)	2.9 (0.6)	3.0 (0.6)	3.1 (0.5)	2.9 (0.5)	2.9 (0.6)	2.9 (0.6)
II	0 (0.0%)	1 (0.5%)	2 (1.0%)	0 (0.0%)	1 (0.4%)	6 (2.3%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	4 (1.5%)
III	30 (12.4%)	28 (14.4%)	23 (12.0%)	27 (11.8%)	39 (17.2%)	39 (15.1%)	28 (10.5%)	49 (19.5%)	52 (20.9%)	58 (21.5%)
IV	183 (75.9%)	138 (71.1%)	143 (74.5%)	167 (72.9%)	159 (70.0%)	171 (66.0%)	188 (70.7%)	179 (71.3%)	170 (68.3%)	177 (65.6%)
6MWD, m	302.7 (118.2)	293.9 (135.1)	299.3 (131.8)	294.8 (132.6)	302.7 (125.6)	313.4 (137.6)	285.8 (118.2)	293.3 (120.4)	284.0 (125.6)	302.9 (128.0)
Pulmonary function test										
DLCO, % pred	47.5 (19.6)	51.3 (23.3)	50.5 (21.5)	52.9 (22.1)	52.8 (21.4)	50.7 (21.6)	46.1 (20.0)	54.0 (22.9)	50.6 (21.8)	49.8 (22.3)

Variables with high proportion of missing data were omitted.

Table S2: Baseline characteristics of adult patients newly diagnosed with PAH per year of diagnosis: No. (%), mean (SD) or median [Q1 - Q3], continued

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
	n=242 (9.6%)	n=199 (7.9%)	n=204 (8.1%)	n=237 (9.4%)	n=241 (9.5%)	n=282 (11.1%)	n=301 (11.9%)	n=271 (10.7%)	n=268 (10.6%)	n=286 (11.3%)
Comorbid conditions										
Obesity (BMI > 30)	1.5 (1.1) 60 (28.0%)	1.3 (1.2) 54 (30.5%)	1.3 (1.1) 67 (32.8%)	1.3 (1.2) 69 (29.2%)	1.4 (1.1) 77 (32.0%)	1.3 (1.1) 89 (31.6%)	1.5 (1.1) 108 (35.9%)	1.6 (1.1) 100 (37.3%)	1.6 (1.2) 84 (31.3%)	1.6 (1.2) 102 (35.8%)
Hypertension	108 (67.9%)	50 (44.6%)	64 (50.0%)	115 (55.6%)	124 (56.4%)	165 (59.1%)	190 (64.4%)	172 (66.4%)	161 (63.6%)	180 (65.2%)
Coronary heart disease	37 (24.8%)	26 (23.4%)	33 (25.2%)	47 (23.5%)	55 (25.6%)	56 (21.1%)	71 (24.5%)	66 (26.7%)	79 (31.3%)	84 (31.8%)
Diabetes mellitus	47 (31.1%)	37 (32.7%)	33 (24.6%)	49 (23.2%)	51 (22.9%)	58 (20.9%)	77 (26.6%)	76 (30.2%)	81 (32.9%)	81 (30.0%)
Haemodynamics										
RAP, mmHg	8.4 (4.6)	8.8 (5.1)	9.0 (5.0)	9.2 (5.7)	7.7 (5.2)	7.8 (4.9)	7.8 (4.3)	8.7 (4.7)	8.0 (4.2)	7.7 (4.5)
PAPm, mmHg	44.2 (13.1)	45.2 (13.1)	45.8 (14.9)	46.4 (12.8)	46.3 (14.3)	44.0 (12.6)	41.6 (11.8)	44.6 (11.8)	42.8 (12.5)	42.5 (12.1)
PAWP, mmHg	9.5 (3.5)	9.7 (3.6)	9.5 (3.3)	9.6 (3.2)	9.1 (3.6)	9.1 (3.2)	9.4 (3.3)	10.3 (3.2)	9.4 (3.2)	9.3 (3.5)
CI, L/min/m ²	2.2 (0.8)	2.4 (0.9)	2.4 (0.8)	2.4 (0.8)	2.4 (0.8)	2.3 (0.9)	2.2 (0.7)	2.3 (0.7)	2.4 (1.0)	2.3 (0.8)
PVR, dyn·s·cm ⁻⁵	773.7 (409.9)	743.3 (379.3)	763.3 (443.7)	782.8 (414.3)	793.4 (429.6)	772.0 (454.6)	696.4 (364.4)	718.6 (393.2)	708.8 (376.1)	696.5 (350.3)
PVR, WU	9.7 (5.1)	9.3 (4.7)	9.5 (5.5)	9.8 (5.2)	9.9 (5.4)	9.7 (5.7)	8.7 (4.6)	9.0 (4.9)	8.9 (4.7)	8.7 (4.4)
SvO ₂ , %	62.5 (8.0)	62.7 (8.6)	62.8 (8.5)	63.1 (9.2)	63.0 (9.2)	63.0 (9.4)	62.6 (8.9)	62.8 (8.6)	62.3 (7.9)	63.0 (7.3)
Laboratory findings										
Creatinine, μmol/L	103.6 (59.6)	96.1 (50.5)	96.8 (44.3)	102.6 (65.4)	93.3 (35.5)	99.1 (39.7)	110.8 (70.1)	110.4 (78.8)	101.0 (46.0)	98.5 (38.5)
NT-proBNP, pg/mL	1804 [767, 4582]	1358 [433, 3562]	1497 [505, 3492]	1405 [447, 3035]	1239 [365, 3091]	1246 [390, 3446]	1808 [729, 3305]	1424 [471, 3562]	1504 [541, 2826]	1097 [458, 3482]
Risk										
Low	20 (8.3%)	19 (9.6%)	15 (7.4%)	23 (9.7%)	28 (11.7%)	34 (12.2%)	19 (6.4%)	21 (7.8%)	31 (11.6%)	36 (12.7%)
Intermediate	182 (75.2%)	140 (70.7%)	142 (70.0%)	157 (66.5%)	155 (64.9%)	170 (61.2%)	189 (63.9%)	197 (73.0%)	177 (66.3%)	189 (66.8%)
High	40 (16.5%)	39 (19.7%)	46 (22.7%)	56 (23.7%)	56 (23.4%)	74 (26.6%)	88 (29.7%)	52 (19.3%)	59 (22.1%)	58 (20.5%)

Variables with high proportion of missing data were omitted.

Table S3a: Use of PAH drugs within 3 months and within 1, 2 and 3 (± 6 months) years after diagnosis, n (%). Percentages refer to subgroups only, if applicable. Subgroup of patients <65 years old at baseline.

	3 months (n=963)	1 year (n=899)	2 years (n=751)	3 years (n=590)
No therapy	6 (0.6%)	23 (2.6%)	16 (2.1%)	18 (3.1%)
Monotherapy	674 (70.0%)	374 (41.6%)	268 (35.7%)	199 (33.7%)
ERA	168 (24.9%)	99 (26.5%)	68 (25.4%)	54 (27.1%)
PDE5i	434 (64.4%)	237 (63.4%)	173 (64.6%)	129 (64.8%)
sGCs	27 (4.0%)	11 (2.9%)	7 (2.6%)	4 (2.0%)
PCA	4 (0.6%)	2 (0.5%)	0 (0.0%)	1 (0.5%)
PCA oral or inhaled ¹	0 (0.0%)	1 (50.0%)	0 (NaN%)	0 (0.0%)
PCA SC or IV ²	4 (100.0%)	1 (50.0%)	0 (NaN%)	1 (100.0%)
CCB	41 (6.1%)	25 (6.7%)	20 (7.5%)	11 (5.5%)
Other PAH treatment	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Combination therapy	283 (29.4%)	502 (55.8%)	467 (62.2%)	373 (63.2%)
ERA+PDE5i	193 (68.2%)	322 (64.1%)	290 (62.1%)	221 (59.2%)
Other than ERA+PDE5i	90 (31.8%)	180 (35.9%)	177 (37.9%)	152 (40.8%)
ERA+PDE-5+PCA	29 (32.2%)	68 (37.8%)	70 (39.5%)	71 (46.7%)
Triple combination therapy incl. IV/SC PCA ³	20 (22.2%)	35 (19.4%)	39 (22.0%)	42 (27.6%)

¹ Selexipag, Iloprost inhaled, Treprostinil inhaled, Beraprost

² Epoprostenol, Iloprost intravenously, Treprostinil intravenously/subcutaneously

³ All triple combination therapies that include IV or SC PCA therapy

Table S3b: Use of PAH drugs within 3 months and within 1, 2 and 3 (± 6 months) years after diagnosis, n (%). Percentages refer to subgroups only, if applicable. Subgroup of patients ≥ 65 years old at baseline.

	3 months (n=1412)	1 year (n=1237)	2 years (n=976)	3 years (n=709)
No therapy	2 (0.1%)	50 (4.0%)	45 (4.6%)	30 (4.2%)
Monotherapy	1227 (86.9%)	772 (62.4%)	573 (58.7%)	405 (57.1%)
ERA	233 (19.0%)	124 (16.1%)	77 (13.4%)	45 (11.1%)
PDE5i	941 (76.7%)	614 (79.5%)	469 (81.8%)	338 (83.5%)
sGCs	36 (2.9%)	29 (3.8%)	24 (4.2%)	19 (4.7%)
PCA	2 (0.2%)	1 (0.1%)	1 (0.2%)	0 (0.0%)
PCA oral or inhaled ¹	1 (50.0%)	1 (100.0%)	1 (100.0%)	0 (NaN%)
PCA SC or IV ²	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (NaN%)
CCB	10 (0.8%)	4 (0.5%)	2 (0.3%)	3 (0.7%)
Other PAH treatment	5 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Combination therapy	183 (13.0%)	415 (33.5%)	358 (36.7%)	274 (38.6%)
ERA+PDE5i	127 (69.4%)	297 (71.6%)	249 (69.6%)	179 (65.3%)
Other than ERA+PDE5i	56 (30.6%)	118 (28.4%)	109 (30.4%)	95 (34.7%)
ERA+PDE-5+PCA	4 (7.1%)	38 (32.2%)	40 (36.7%)	33 (34.7%)
Triple combination therapy incl. IV/SC PCA ³	1 (1.8%)	9 (7.6%)	8 (7.3%)	3 (3.2%)

¹ Selexipag, Iloprost inhaled, Treprostinil inhaled, Beraprost

² Epoprostenol, Iloprost intravenously, Treprostinil intravenously/subcutaneously

³ All triple combination therapies that include IV or SC PCA therapy

Table S3c: Use of PAH drugs within 3 months and within 1, 2 and 3 (± 6 months) years after diagnosis, n (%). Percentages refer to subgroups only, if applicable. Subgroup of patients with I/H/D-PAH.

	3 months (n=1593)	1 year (n=1457)	2 years (n=1192)	3 years (n=891)
No therapy	0 (0.0%)	47 (3.2%)	40 (3.4%)	36 (4.0%)
Monotherapy	1285 (80.7%)	810 (55.6%)	603 (50.6%)	426 (47.8%)
ERA	200 (15.6%)	122 (15.1%)	80 (13.3%)	47 (11.0%)
PDE5i	985 (76.7%)	629 (77.7%)	479 (79.4%)	348 (81.7%)
sGCs	43 (3.3%)	30 (3.7%)	22 (3.6%)	16 (3.8%)
PCA	6 (0.5%)	1 (0.1%)	0 (0.0%)	1 (0.2%)
PCA oral or inhaled ¹	1 (16.7%)	0 (0.0%)	0 (NaN%)	0 (0.0%)
PCA SC or IV ²	5 (83.3%)	1 (100.0%)	0 (NaN%)	1 (100.0%)
CCB	48 (3.7%)	28 (3.5%)	22 (3.6%)	14 (3.3%)
Other PAH treatment	3 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Combination therapy	308 (19.3%)	600 (41.2%)	549 (46.1%)	429 (48.1%)
ERA+PDE5i	198 (64.3%)	383 (63.8%)	330 (60.1%)	243 (56.6%)
Other than ERA+PDE5i	110 (35.7%)	217 (36.2%)	219 (39.9%)	186 (43.4%)
ERA+PDE-5+PCA	24 (21.8%)	72 (38.5%)	74 (39.4%)	78 (45.6%)
Triple combination therapy incl. IV/SC PCA ³	16 (14.5%)	33 (15.2%)	32 (14.6%)	35 (18.8%)

¹ Selexipag, Iloprost inhaled, Treprostinil inhaled, Beraprost

² Epoprostenol, Iloprost intravenously, Treprostinil intravenously/subcutaneously

³ All triple combination therapies that include IV or SC PCA therapy

Table S3d: Use of PAH drugs within 3 months and within 1, 2 and 3 (± 6 months) years after diagnosis, n (%). Percentages refer to subgroups only, if applicable. Subgroup of patients with CTD-PAH.

	3 months (n=501)	1 year (n=431)	2 years (n=328)	3 years (n=242)
No therapy	0 (0.0%)	19 (4.4%)	11 (3.4%)	7 (2.9%)
Monotherapy	391 (78.0%)	203 (47.1%)	140 (42.7%)	101 (41.7%)
ERA	137 (35.0%)	65 (32.0%)	40 (28.6%)	27 (26.7%)
PDE5i	239 (61.1%)	130 (64.0%)	91 (65.0%)	68 (67.3%)
sGCs	12 (3.1%)	7 (3.4%)	8 (5.7%)	6 (5.9%)
PCA	0 (0.0%)	1 (0.5%)	1 (0.7%)	0 (0.0%)
PCA oral or inhaled ¹	0 (NaN%)	1 (100.0%)	1 (100.0%)	0 (NaN%)
PCA SC or IV ²	0 (NaN%)	0 (0.0%)	0 (0.0%)	0 (NaN%)
CCB	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other PAH treatment	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Combination therapy	110 (22.0%)	209 (48.5%)	177 (54.0%)	134 (55.4%)
ERA+PDE5i	85 (77.3%)	159 (76.1%)	135 (76.3%)	96 (71.6%)
Other than ERA+PDE5i	25 (22.7%)	50 (23.9%)	42 (23.7%)	38 (28.4%)
ERA+PDE-5+PCA	6 (24.0%)	25 (32.5%)	23 (39.0%)	14 (34.1%)
Triple combination therapy incl. IV/SC PCA ³	3 (12.0%)	7 (14.0%)	12 (28.6%)	5 (13.2%)

¹ Selexipag, Iloprost inhaled, Treprostinil inhaled, Beraprost

² Epoprostenol, Iloprost intravenously, Treprostinil intravenously/subcutaneously

³ All triple combination therapies that include IV or SC PCA therapy

Table S3e: Use of PAH drugs within 3 months and within 1, 2 and 3 (± 6 months) years after diagnosis, n (%). Percentages refer to subgroups only, if applicable. Subgroup of patients with I/H/D-PAH, no comorbidities and DLCO > 45%.

	3 months (n=121)	1 year (n=112)	2 years (n=108)	3 years (n=79)
No therapy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Monotherapy	72 (59.5%)	41 (36.6%)	36 (33.3%)	27 (34.2%)
ERA	9 (12.5%)	9 (22.0%)	8 (22.2%)	5 (18.5%)
PDE5i	42 (58.3%)	22 (53.7%)	18 (50.0%)	15 (55.6%)
sGCs	2 (2.8%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
PCA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PCA oral or inhaled ¹	0 (NaN%)	0 (NaN%)	0 (NaN%)	0 (NaN%)
PCA SC or IV ²	0 (NaN%)	0 (NaN%)	0 (NaN%)	0 (NaN%)
CCB	19 (26.4%)	10 (24.4%)	10 (27.8%)	6 (22.2%)
Other PAH treatment	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Combination therapy	49 (40.5%)	71 (63.4%)	72 (66.7%)	52 (65.8%)
ERA+PDE5i	29 (59.2%)	31 (43.7%)	30 (41.7%)	20 (38.5%)
Other than ERA+PDE5i	20 (40.8%)	40 (56.3%)	42 (58.3%)	32 (61.5%)
ERA+PDE-5+PCA	8 (40.0%)	11 (47.8%)	3 (21.4%)	6 (42.9%)
Triple combination therapy incl. IV/SC PCA ³	6 (30.0%)	10 (25.0%)	7 (16.7%)	5 (15.6%)

¹ Selexipag, Iloprost inhaled, Treprostinil inhaled, Beraprost

² Epoprostenol, Iloprost intravenously, Treprostinil intravenously/subcutaneously

³ All triple combination therapies that include IV or SC PCA therapy

Table S4: Median doses of PAH drugs within 3 months and within 1 (± 6 months) year after diagnosis and number of patients with available data.

	3 months		1 year	
	Median dose	n	Median dose	n
ERA				
Ambrisentan [mg/day]	5.0	197	5.0	268
Bosentan [mg/day]	125.0	212	250.0	239
Macitentan [mg/day]	10.0	365	10.0	557
PDE5i				
Sildenafil [mg/day]	60.0	1037	60.0	834
Tadalafil [mg/day]	20.0	727	40.0	819
PCA				
Epoprostenol [ng/kg/min]	7.5	9	12.0	11
Iloprost inhaled [μ g/day]	15.0	27	30.0	62
Selexipag [μ g/day]	800.0	8	1600.0	57
Treprostinil intravenously [ng/kg/min]	10.0	7	32.0	22
Treprostinil subcutaneously [ng/kg/min]	17.0	11	24.0	22
sGC				
Riociguat [mg/day]	3.0	90	6.0	121

Figure S3: Treatment type at inclusion (within 3 months after diagnosis) and 1 year (± 6 months) after diagnosis for the years 2010 to 2019, for I/H/D-PAH (a) and CTD-PAH (b) patients, as well as for the years 2010 to 2014 and 2015 to 2019 for patients with I/H/D-PAH, no comorbidities and DLCO $> 45\%$ (c).

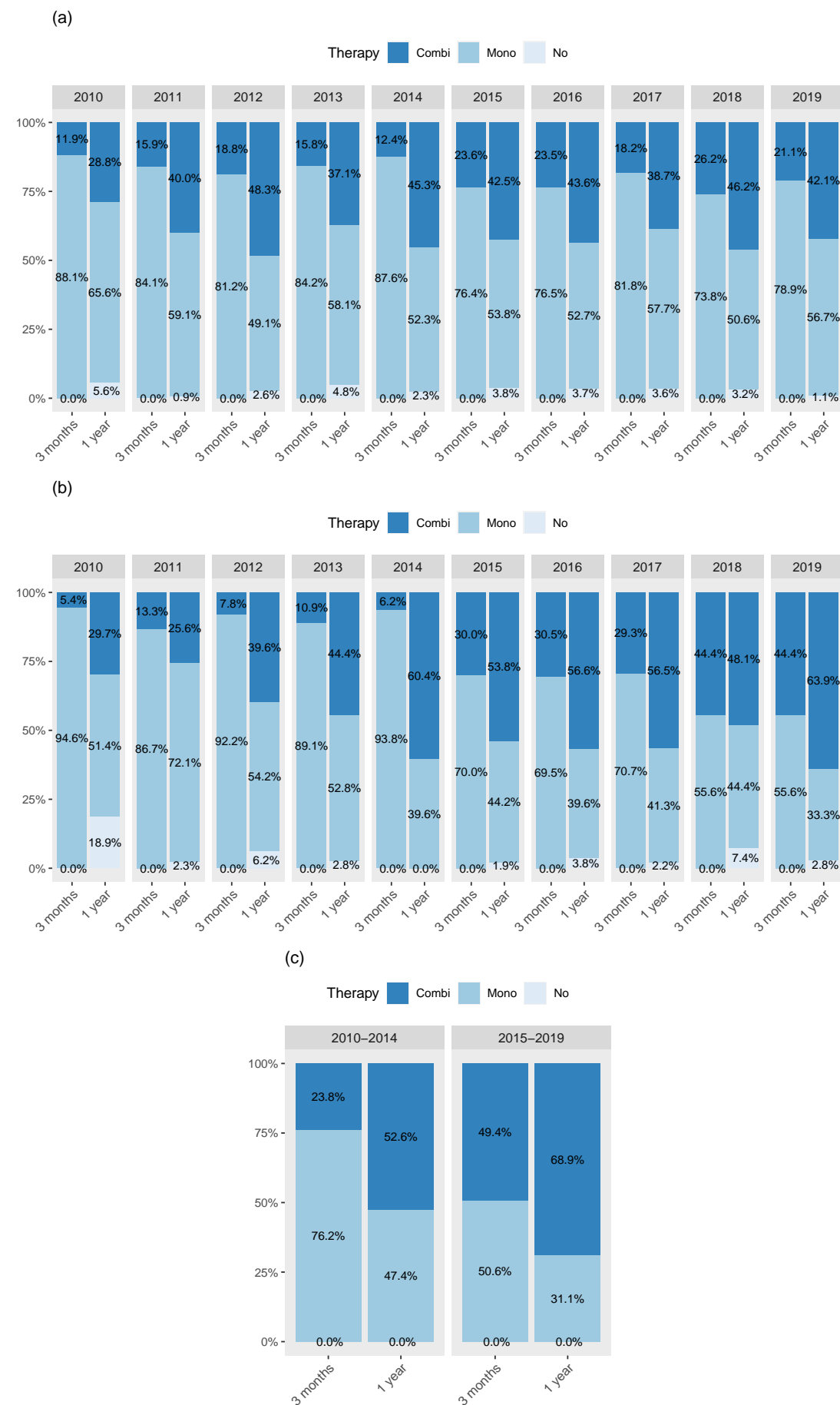


Figure S4: Estimated survival probability at 1 year (black) and 3 years (red) after inclusion with 95% confidence interval and number of patients at risk, for I/H/D-PAH patients (a) and CTD-PAH patients (b).

