

**Table S1. Cycling time at 2500m vs. 470m**

Dependent variable: Cycling time (min)	<b>Mixed-effect multivariable linear regression</b>		
Variables:	Coefficients	95% Confidence interval	p-value
2500m vs. 470m	-6.44	-9.47 to -3.40	<0.001
Intervention order, 470m first	-3.16	-9.95 to 3.63	0.362

Mixed linear regression model of the main outcome (Constant work-rate exercise test- time).

**Table S2a. Predictors of the difference in constant work-rate exercise test cycling time with exposure to 2500m compared to 470m**

Dependent: Change in cycling time (min) from 470m to 2500m (min) Variables:	Mixed- effect univariable linear regression		
	Coefficients	95% Confidence interval	p-value
Intervention order, 470m first	0.15	-6.08 to 6.37	0.963
Age, year	0.07	-0.14 to 0.28	0.506
Sex, male	-2.99	-8.99 to 3.00	0.328
Body mass index, kg/m <sup>2</sup>	0.32	-0.44 to 1.09	0.405
PAH (1) vs. CTEPH (2)	3.36	-2.60 to 9.33	0.270
New York Heart Association class	-0.28	-4.67 to 4.11	0.900
Maximal oxygen uptake at 470m, ml/min/kg	-9.41	-1.18 to 0.36	0.298
Constant work rate exercise test time at 470m	-0.13	-0.48 to 0.22	0.461
Maximal work rate in CPET, Watts	-0.04	-0.11 to 0.03	0.237
Total distance in 6MWT at 470m, m	-0.01	-0.04 to 0.23	0.718
SpO <sub>2</sub> at end 6MWT at 470m, %	0.06	-0.37 to 0.49	0.792
Pulmonary vascular resistance during last right heart catheterization at 470m, WU	0.32	-0.81 to 1.44	0.580
Mixed venous oxygen saturation during last right heart catheterization at 470m, %	-0.24	-0.67 to 0.19	0.280
Partial pressure of oxygen at rest at 470m, kPa	-0.42	-2.51 to 1.66	0.693

Mixed linear regression models with the change in constant work-rate exercise test time (min) as dependent variable. Negative coefficients indicate greater decrease with altitude. 6MWT = 6 minute walk test

**Table S2b. Predictors to clinically relevantly decrease the cycling time at 2500m vs. 470m**

Dependent: Change in cycling time (min) above minimal clinical relevance difference at altitude Variable	Logistic univariable linear regression		
	Odds ratio	95% Confidence interval	p-value
Intervention order, 470m first	1.05	0.22 to 5.09	0.954
Age, year	0.99	0.93 to 1.04	0.644
Sex, male	2.92	0.57 to 15.05	0.201
Body mass index, kg/m <sup>2</sup>	0.96	0.79 to 1.17	0.696
PAH (1) vs. CTEPH (2)	0.93	0.55 to 1.56	0.778
New York Heart Association class	2.46	0.71 to 8.54	0.155
Maximal oxygen uptake at 470m, ml/min/kg	0.95	0.78 to 1.16	0.595
Constant work rate exercise test time at 470m	0.92	0.82 to 1.04	0.180
Maximal work rate in CPET, Watts	1.00	0.98 to 1.02	0.981
Total distance in 6MWT at 470m, m	1.00	0.99 to 1.01	0.879
SpO <sub>2</sub> at end 6MWT at 470m, %	0.97	0.86 to 1.09	0.599
Pulmonary vascular resistance during last right heart catheterization at 470m, WU	1.07	0.79 to 1.45	0.656
Mixed venous oxygen saturation during last right heart catheterization at 470m, %	0.98	0.88 to 1.1	0.766
Partial pressure of oxygen at rest at 470m, kPa	0.67	0.36 to 1.22	0.191

Logistic linear regression models to predict the change in constant work-rate exercise test time (min) at altitude above the minimal clinically important difference of 1.75 minutes. 6MWT = 6 minute walk test, CPET = cardiopulmonary exercise test

**Table S3. Isotime at 3 and 6 minutes of constant work-rate exercise at low- (470m) and high altitude (2500m)**

Parameter	3 min exercise at		3 min exercise at		6 min exercise at			
	470m (n=27)		2500m (n=24)		6 min exercise at		2500m (n=23)	
	Mean ± SD	Mean ± SD	Mean difference (95% CI)	p-value	470m (n=27)	2500m (n=23)	Mean difference (95% CI)	p-value
<b>Non-invasive blood and tissue oxygenation</b>								
Pulse oximetry, %	91 ± 3	83 ± 6	-8 (-10 to -5)	<0.001	90 ± 4	82 ± 6	-8 (-11 to -5)	<0.001
Cerebral tissue oxygen saturation, %	61 ± 13	59 ± 9	-1 (-5 to 3)	0.670	60 ± 12	57 ± 10	-2 (-6 to 3)	0.448
Muscular tissue oxygen saturation, %	65 ± 11	62 ± 11	-3 (-7 to 0)	0.082	64 ± 11	60 ± 11	-3 (-7 to 1)	0.131
<b>Circulatory and respiratory parameters by PDX and Finapres®</b>								
Heart rate, min <sup>-1</sup>	92 ± 29	119 ± 20	27 (16 to 38)	<0.001	99 ± 28	125 ± 14	27 (15 to 38)	<0.001
Breathing rate, min <sup>-1</sup>	28 ± 5	29 ± 7	1 (-1 to 3)	0.461	29 ± 5	31 ± 6	2 (0 to 3)	0.053
Systolic arterial pressure, mmHg	133 ± 27	140 ± 30	7 (-8 to 22)	0.366	133 ± 19	153 ± 31	19 (6 to 32)	0.004
Diastolic arterial pressure, mmHg	84 ± 14	82 ± 15	-1 (-10 to 7)	0.737	84 ± 11	87 ± 19	3 (-5 to 10)	0.464
<b>Echocardiography</b>								
Tricuspid regurgitation pressure gradient (TRPG), mmHg	66 ± 23	85 ± 25	23 (13 to 33)	<0.001	76 ± 24	79 ± 21	5 (-9 to 19)	0.505
Systolic pulmonary arterial pressure (PAP); mmHg	70 ± 23	90 ± 27	23 (13 to 34)	<0.001	81 ± 25	84 ± 22	4 (-11 to 19)	0.608
Stroke volume, ml	73 ± 14	76 ± 20	3 (-8 to 14)	0.598	77 ± 19	78 ± 15	-2 (-12 to 7)	0.626
CO, l/min	6.6 ± 2.1	8.8 ± 2.2	2.2 (0.9 to 3.4)	<0.001	7.6 ± 1.7	9.6 ± 1.8	1.9 (0.8 to 2.9)	<0.001
Pulmonary vascular resistance, WU	5.9 ± 2.6	5.4 ± 2.7	-0.3 (-2.2 to 1.6)	0.782	6.4 ± 3.1	4.7 ± 1.2	-1.1 (-2.6 to 0.3)	0.123
TRPG/CO	11.0 ± 4.0	9.8 ± 4.2	-1.2 (-4.1 to 1.8)	0.435	11.6 ± 4.8	8.5 ± 2.0	-2.0 (-4.2 to 0.2)	0.072
Tricuspid annular plane systolic excursion, cm	2.2 ± 0.3	2.1 ± 0.3	-0.1 (-0.3 to 0.0)	0.101	2.4 ± 0.3	2.3 ± 0.4	-0.1 (-0.3 to 0.0)	0.164

Data shows exercise at 3 and 6 minutes of exercise under both altitudes, CI = Confidence Interval, SD = Standard deviation