OVLIVNĚNÍ MORTALITY U PACIENTŮ S PLICNÍ ARTERIÁLNÍ HYPERTENZÍ

PAVEL JANSA

pavel.jansa@vfn.cz

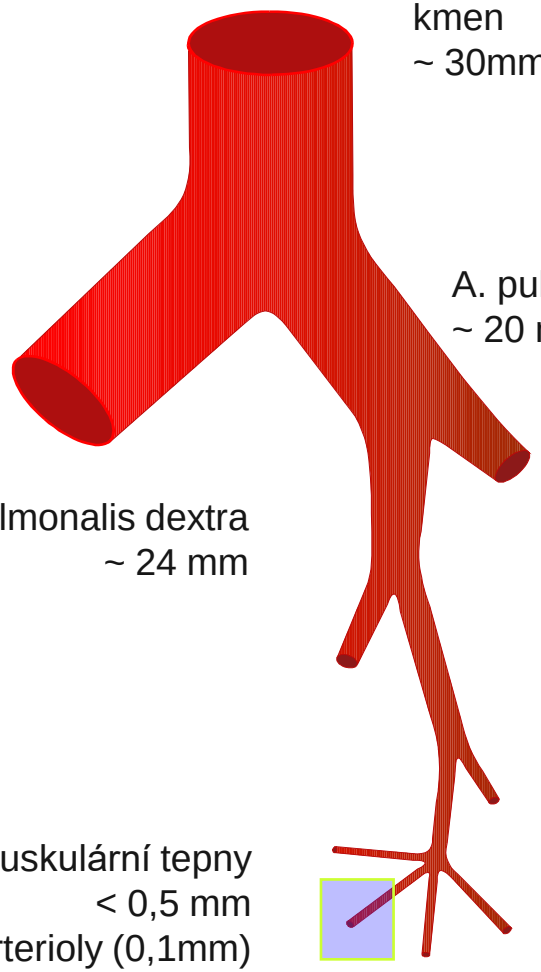
KOMPLEXNÍ KARDIO VASKULÁRNÍ CENTRUM VFN Praha

European Reference Network for rare or low prevalence complex diseases

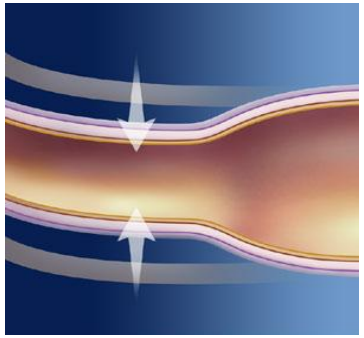
Network Respiratory Diseases (ERN-LUNG)

Member General University Hospital in Prague — Czechia

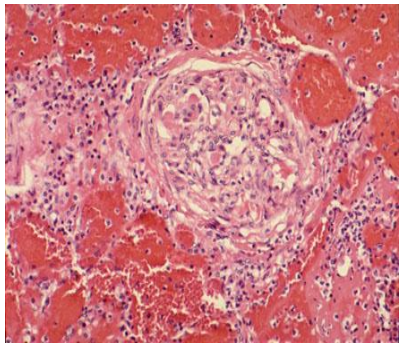
PODSTATA PLICNÍ ARTERIÁLNÍ HYPERTENZE (PAH)

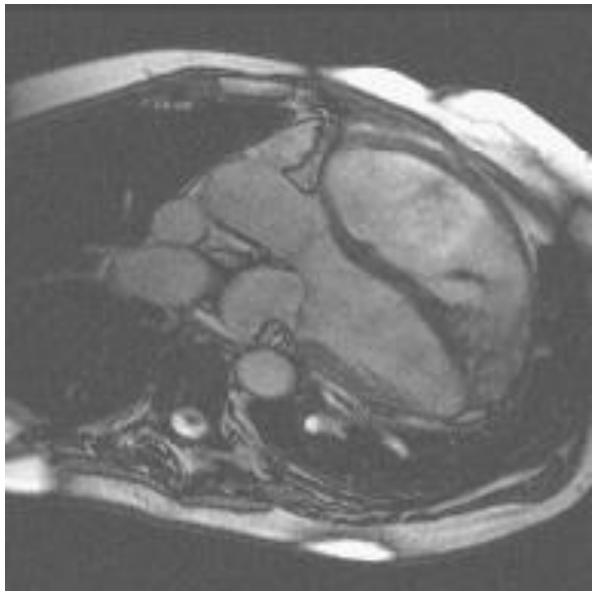


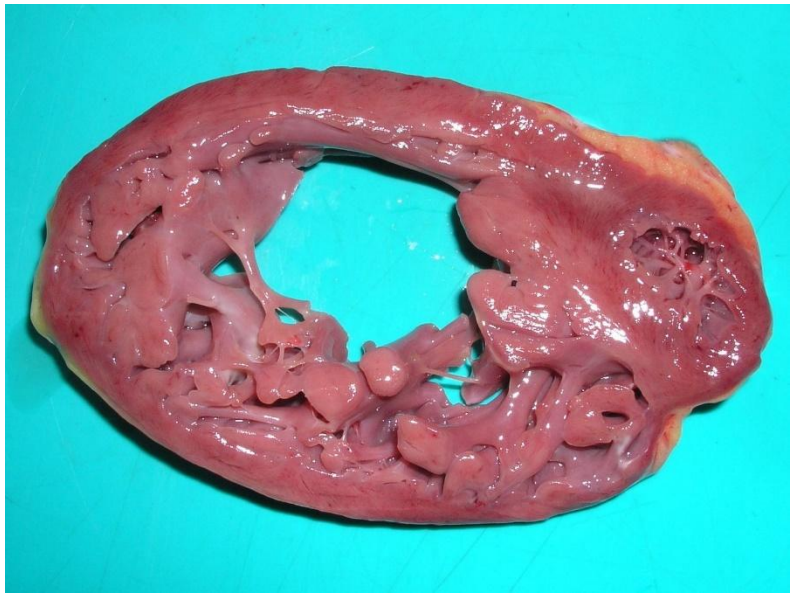
Vazokonstrikce



Remodelace

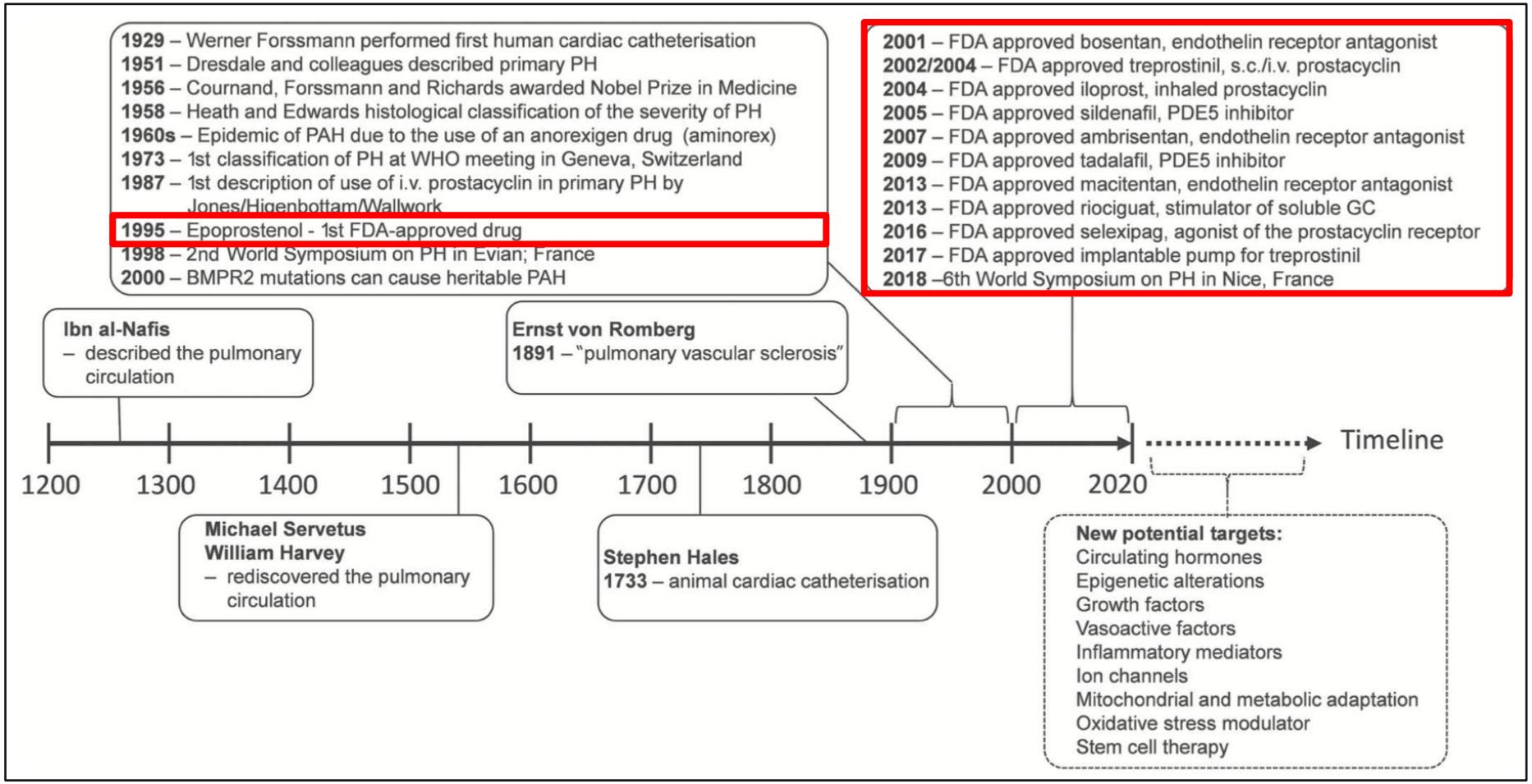






Zdroj: VFN, archiv autora

EVOLUCE LÉČBY PLICNÍ ARTERIÁLNÍ HYPERTENZE



Sommer N et al. Current and future treatments of pulmonary arterial hypertension. *Br J Pharmacol.* 2020;1–25

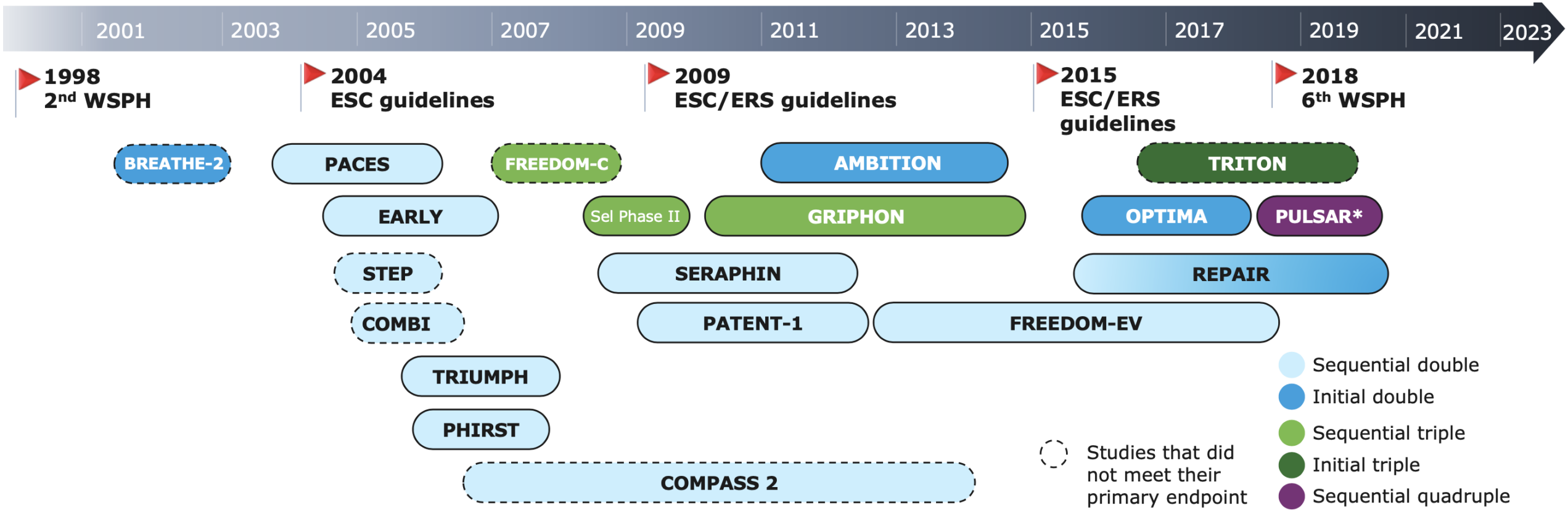
VÝVOJ TAKTIKY TERAPIE PAH

Kombinační léčba nedoporučována

Kombinační léčba u pokročilého onemocnění při zhoršení

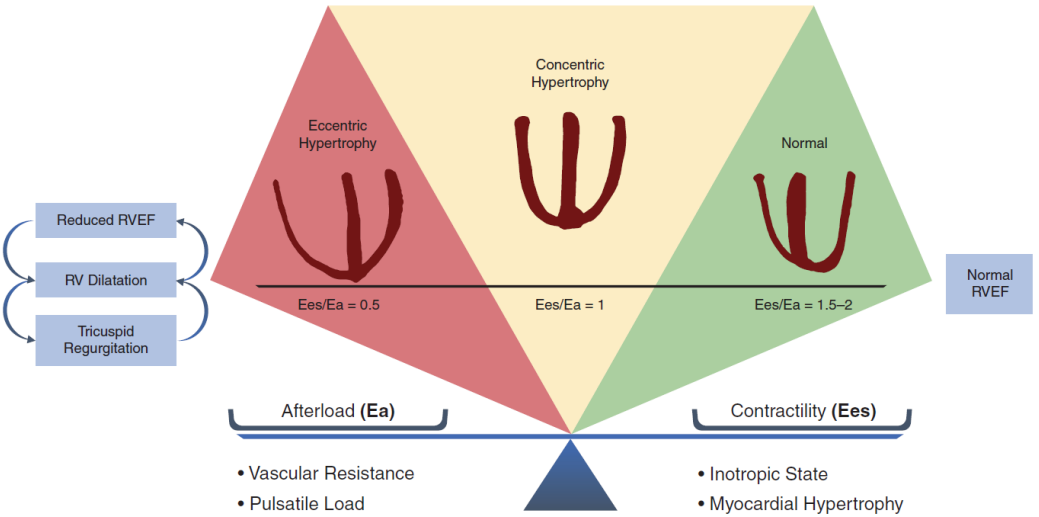
Kombinační léčba při nedostatečném efektu iniciální terapie

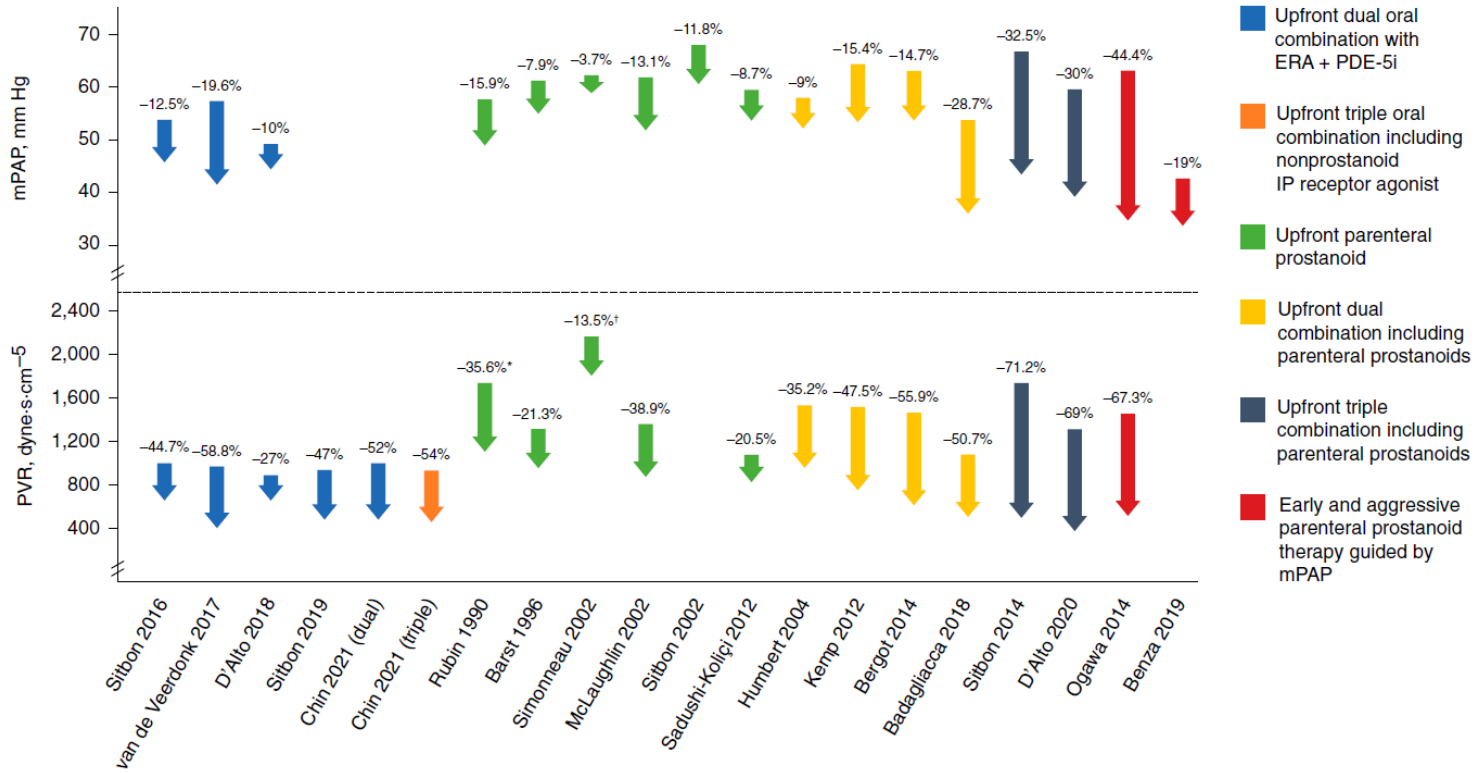
Kombinační léčba iniciálně pro většinu pacientů



VÝVOJ TAKTIKY TERAPIE PAH

Aggressive Afterload Lowering to Improve the Right Ventricle
A New Target for Medical Therapy in Pulmonary Arterial Hypertension?





Vizza CD et al. *Am J Respir Crit Care Med* Vol 205, Iss 7, pp 751–760, Apr 1, 2022

PACIENTSKÉ REGISTRY

Definice Evropské lékové agentury (EMA):

- Organizované systémy používající observační metody pro sběr dat o populacích pacientů se stejnou základní charakteristikou

- Charakteristiky relevantní pro definici populace pacientů
  - onemocnění (registry onemocnění)
  - specifické expozice (lékové registry)

www.ema.europa.eu

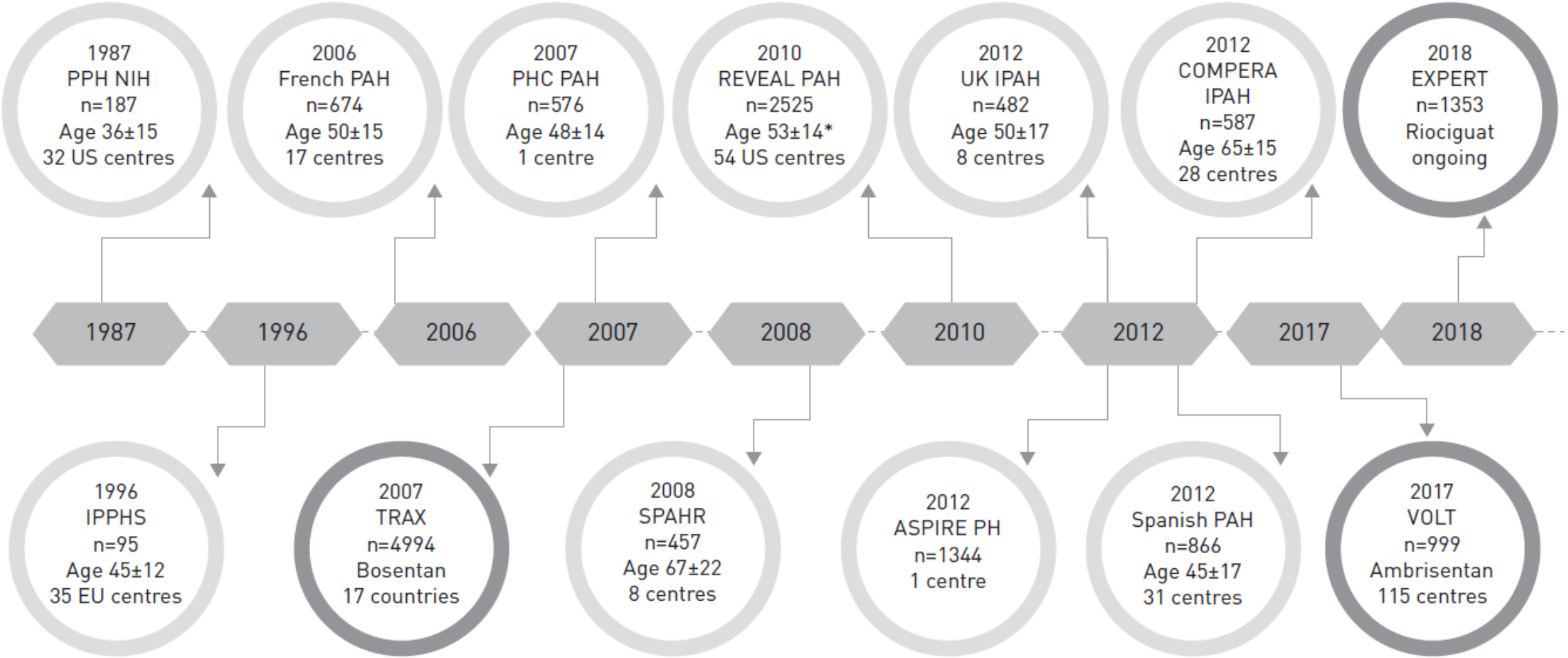
PACIENTSKÉ REGISTRY U VZÁCNÝCH ONEMOCNĚNÍ

- Charakteristika populace pacientů v běžné klinické praxi (vs pacienti klinických studií)
- Incidence, prevalence
- Dlouhodobé přežití
- Prediktory prognózy

PACIENTSKÉ REGISTRY U PAH

- Epidemiologie PAH
- Characteristika podskupin PAH
- Demogragie, symptom, doba do správné diagnózy, komorbidity
- Léčebné přístupy, prediktory prognózy, riziková stratifikace

REGISTRY U PLICNÍ ARTERIÁLNÍ HYPERTENZE



Swinnen K et al. *Eur Respir Rev* 2019; 28: 190050

REGISTRY U PLICNÍ ARTERIÁLNÍ HYPERTENZE

	NIH 1987	French 2006	Swedish 2007	PHC 2007	Scottish 2007	REVEAL 2010	ASPIRE 2012	UK 2012	Spanish 2012	COMPERA 2012
Incidence/ prevalence	-	x	x	-	x	x	-	x	x	-
PH (sub)groups	-	x	-	-	x	x	x	-	x	-
Demographics	x	x	x	x	-	x	x	x	x	x
Symptoms	x	x	-	-	-	x	-	x	x	-
Diagnostic delay	x	x	-	-	-	x	-	x	x	-
PFT	x	x	x	x	-	x	x	x	-	-
Haemodynamic parameters	x	x	x	x	-	x	x	x	x	x
Treatment practices	-	x	x	x	-	x	x	x	-	x
Outcome and predictors	x	x	x	x	-	x	x	x	x	x
Oral anticoagulation	-	-	-	x	-	x	-	-	-	x
Risk stratification	-	x	-	-	-	x	-	x	x	x

NIH: National Institutes of Health; PHC: Pulmonary Hypertension Connection; REVEAL: Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension; ASPIRE: Assessing the Spectrum of Pulmonary Hypertension Identified at a Referral Centre; COMPERA: Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; PFT: pulmonary function test.

Swinnen K et al. *Eur Respir Rev* 2019; 28: 190050

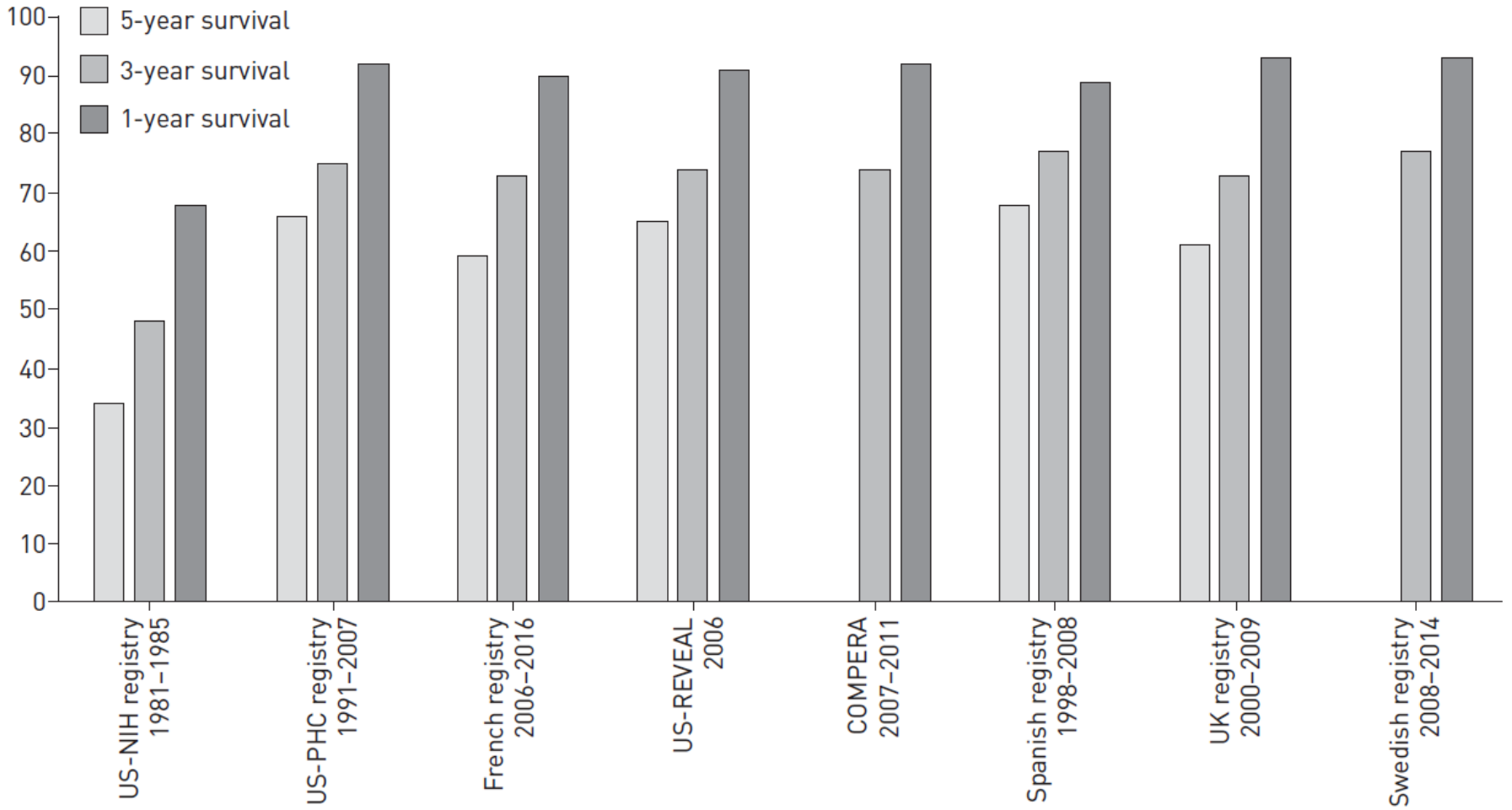
REGISTRY U PLICNÍ ARTERIÁLNÍ HYPERTENZE

	NIH 1987	French 2006	Swedish 2007	PHC 2007	Scottish 2007	REVEAL 2010	ASPIRE 2012	UK 2012	Spanish 2012	COMPERA 2012
Incidence/ prevalence	-	x	x	-	x	x	-	x	x	-
PH (sub)groups	-	x	-	-	x	x	x	-	x	-
Demographics	x	x	x	x	-	x	x	x	x	x
Symptoms	x	x	-	-	-	x	-	x	x	-
Diagnostic delay	x	x	-	-	-	x	-	x	x	-
PFT	x	x	x	x	-	x	x	x	-	-
Haemodynamic parameters	x	x	x	x	-	x	x	x	x	x
Treatment practices	-	x	x	x	-	x	x	x	-	x
Outcome and predictors	x	x	x	x	-	x	x	x	x	x
Oral anticoagulation	-	-	-	x	-	x	-	-	-	x
Risk stratification	-	x	-	-	-	x	-	x	x	x

NIH: National Institutes of Health; PHC: Pulmonary Hypertension Connection; REVEAL: Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension; ASPIRE: Assessing the Spectrum of Pulmonary Hypertension Identified at a Referral Centre; COMPERA: Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; PFT: pulmonary function test.

Swinnen K et al. *Eur Respir Rev* 2019; 28: 190050

REGISTRY U PLICNÍ ARTERIÁLNÍ HYPERTENZE



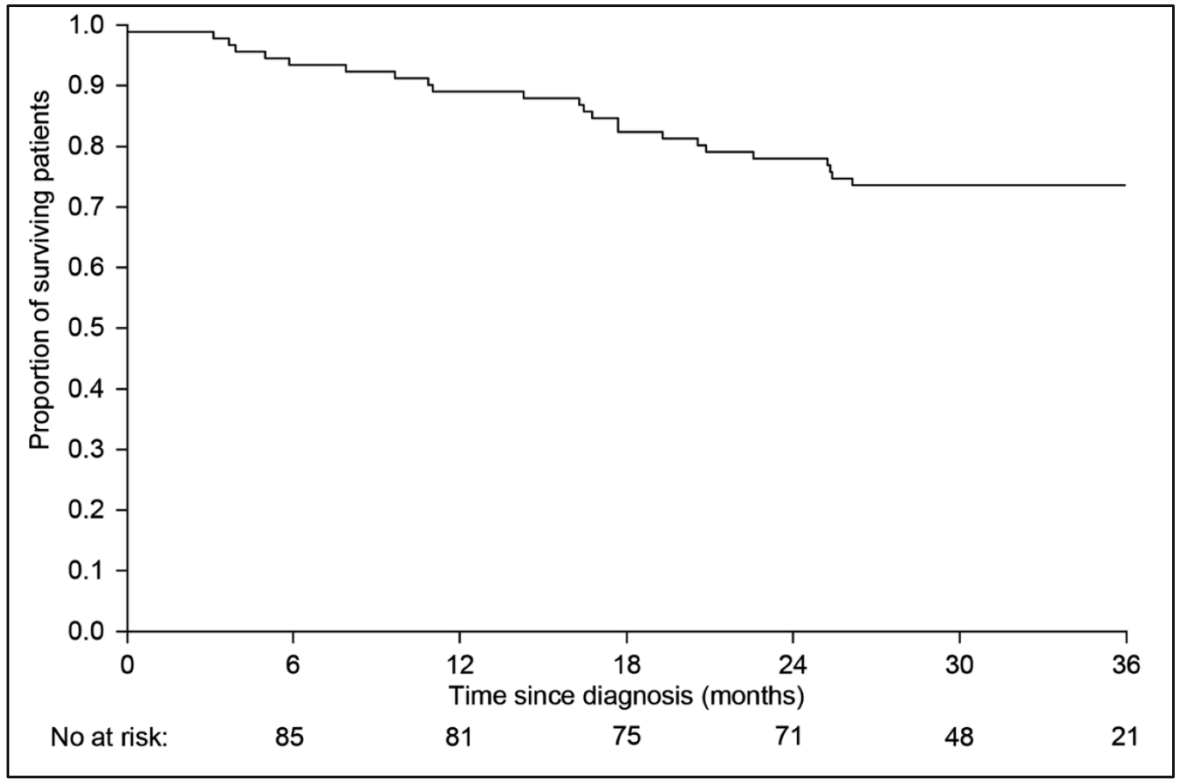
Swinnen K et al. *Eur Respir Rev* 2019; 28: 190050

Epidemiology and long-term survival of pulmonary arterial hypertension in the Czech Republic: a retrospective analysis of a nationwide registry

N=191, diagnostikovaní 2000-2007 (100 prevalentní, 91 incidentní)
IPAH 60.7%, CHD-PAH 20.4%, CTD-PAH 11.4%

Table 3 Treatment of incident and prevalent patients following diagnosis

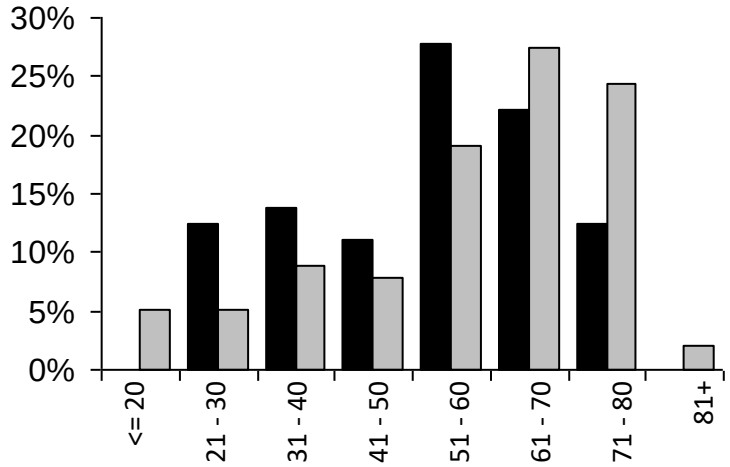
Treatment, n	Incident (n = 91)	Prevalent (n = 100)
Calcium channel blockers	3	2
Bosentan	27	25
Sildenafil	35	31
Treprostinil	4	5
Epoprostenol	-	1
Combination therapy	11	26
Bosentan + sildenafil	3	14
Bosentan + iloprost	2	-
Sildenafil + iloprost	2	2
Sildenafil + treprostinil	2	4
Sildenafil + epoprostenol	2	4
Epoprostenol + sildenafil + bosentan	-	2
Investigational drugs	7	5
No specific therapy	4	5



Jansa et al. *BMC Pulmonary Medicine* 2014, 14:45

NOVĚ DIAGNOSTIKOVANÍ PACIENTI S PAH

Všeobecná fakultní nemocnice v Praze, 2002-2006 vs 2007-2010

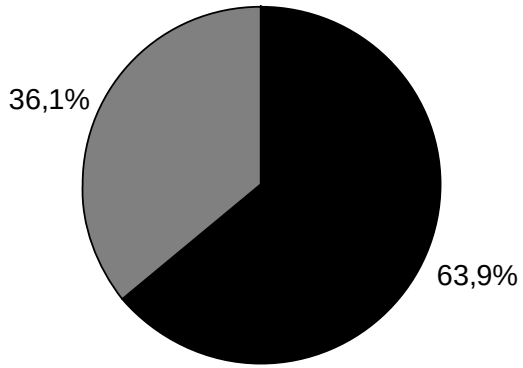


Věk v době diagnózy

	Median (5-95%)	
2002-2006 (N=72)	55 (26-75)	p=0.008
2007-2010 (N=194]	63 (18-78)	

Komorbidity: 2007-2010:
ICHS 25 %, arteriální hypertenze 41 %, CHOPN 17 %

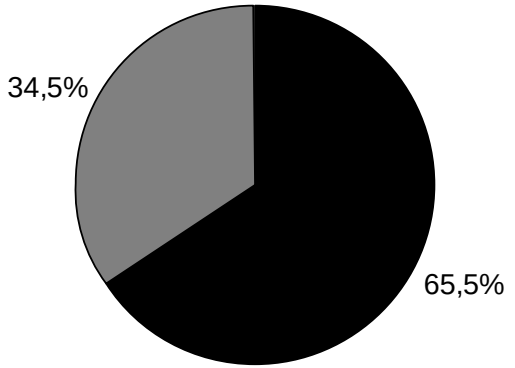
2002-2006 (N=72]



Muži
Ženy

p=0.885

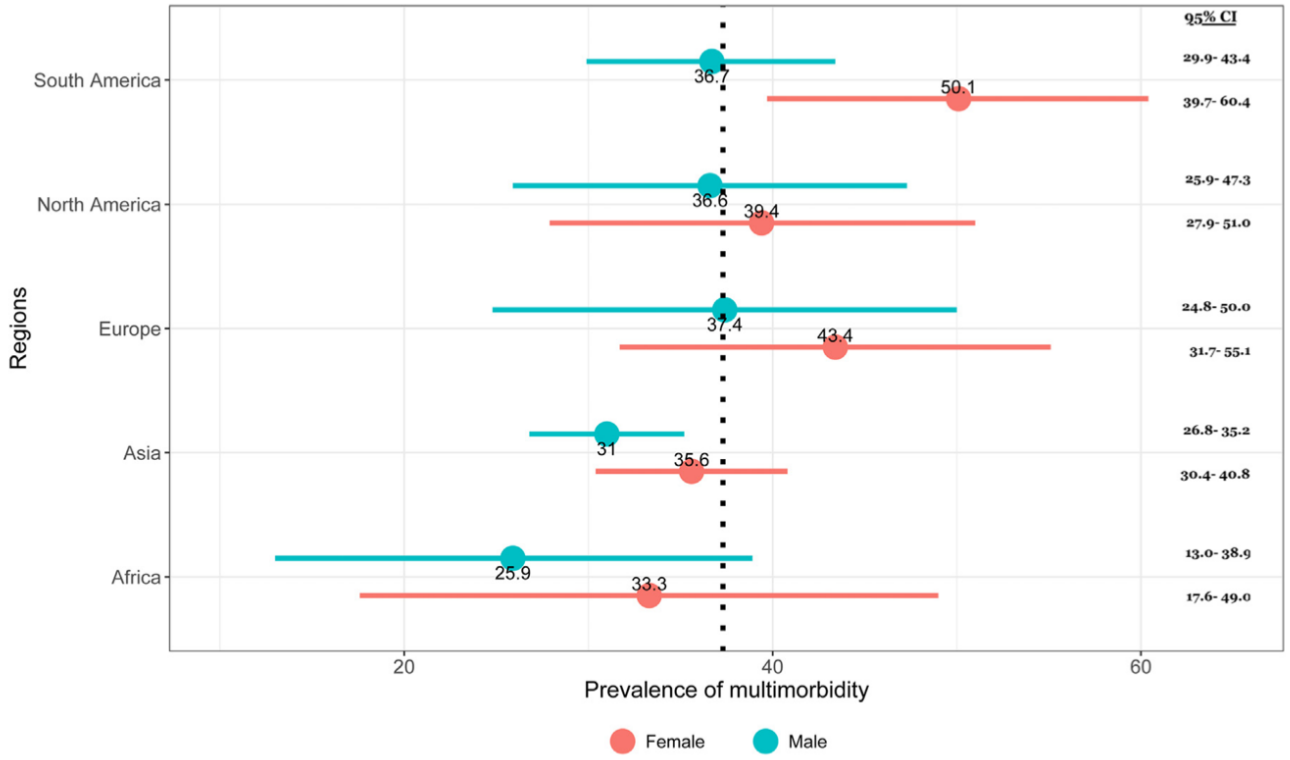
2007-2010 (N=194)

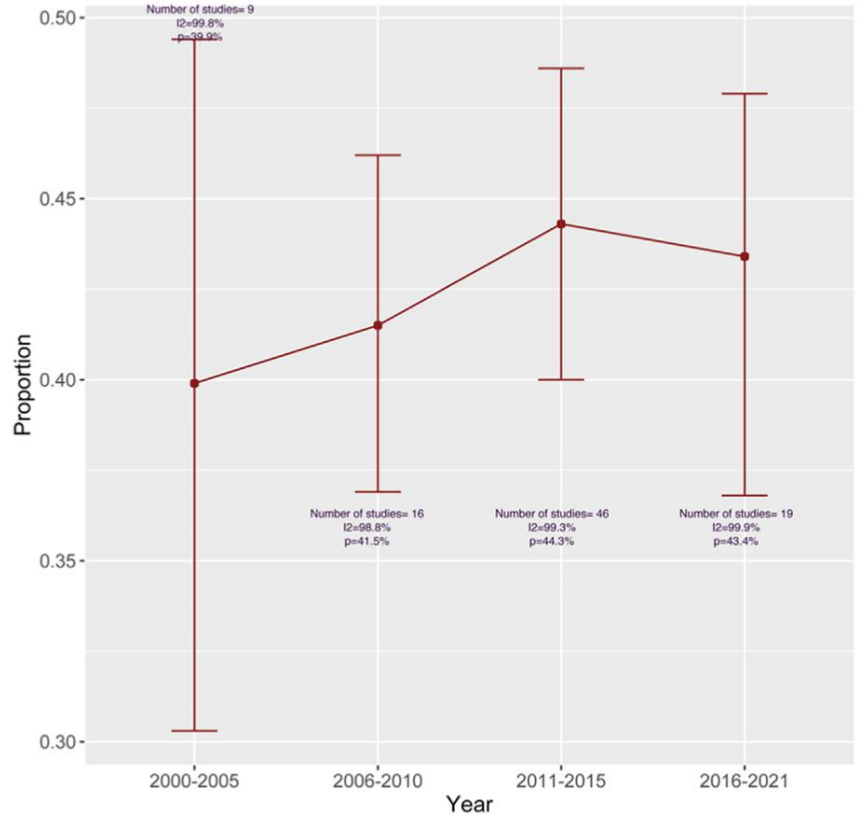


Jansa et al. *BMC Pulmonary Medicine* 2014, 14:45

Global and regional prevalence of multimorbidity in the adult population in community settings: a systematic review and meta-analysis

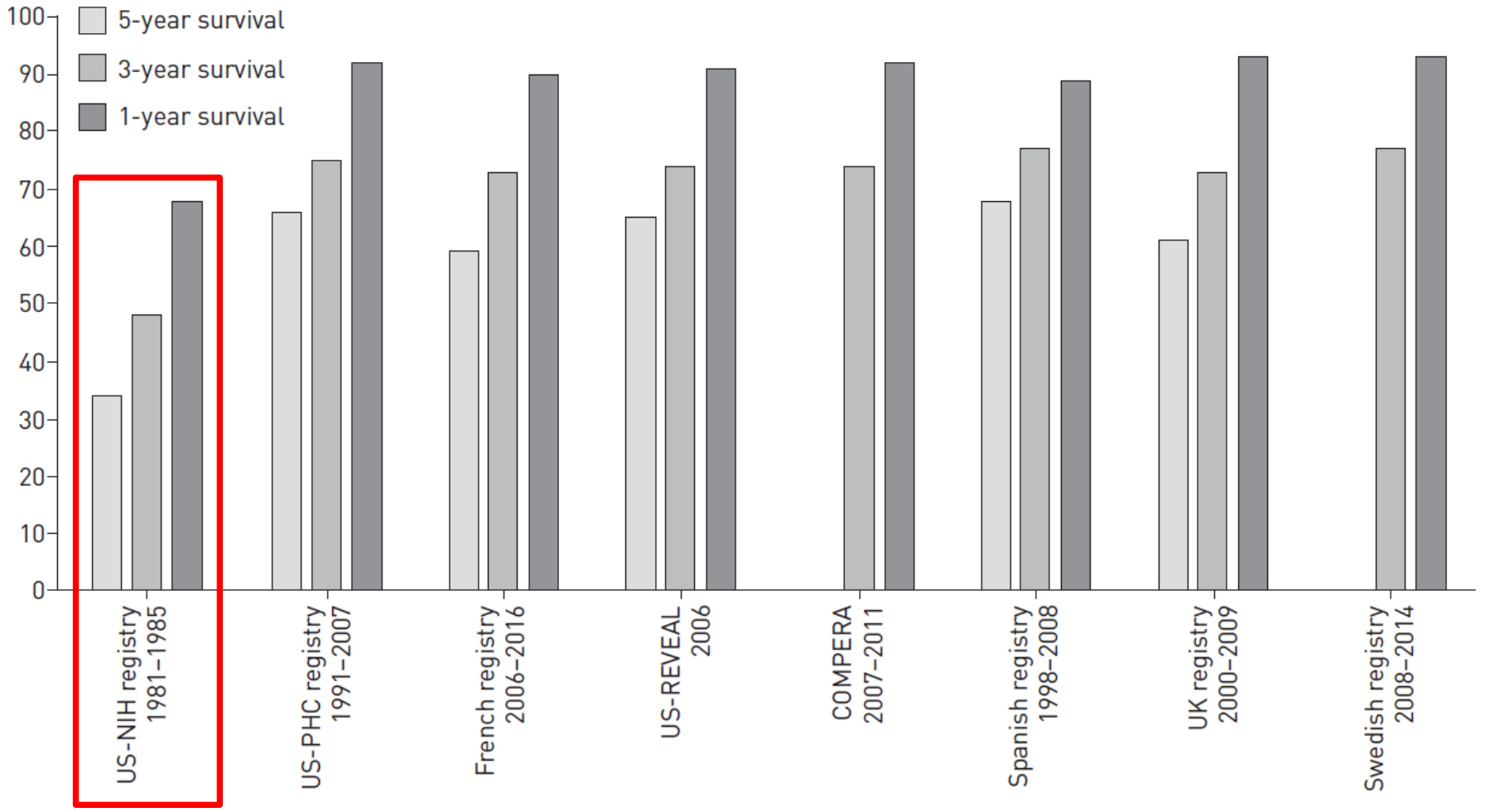
126 studií, 15.4 milionů osob z 54 zemí (32.1% mužů, průměrný věk 56.94 ± 10.84 roku)
Definice multimorbidity: více než jedna komorbidita





Chawdhury SR et al. *EClinicalMedicine* 2023, Feb 16;57:101860

REGISTRY U PLICNÍ ARTERIÁLNÍ HYPERTENZE



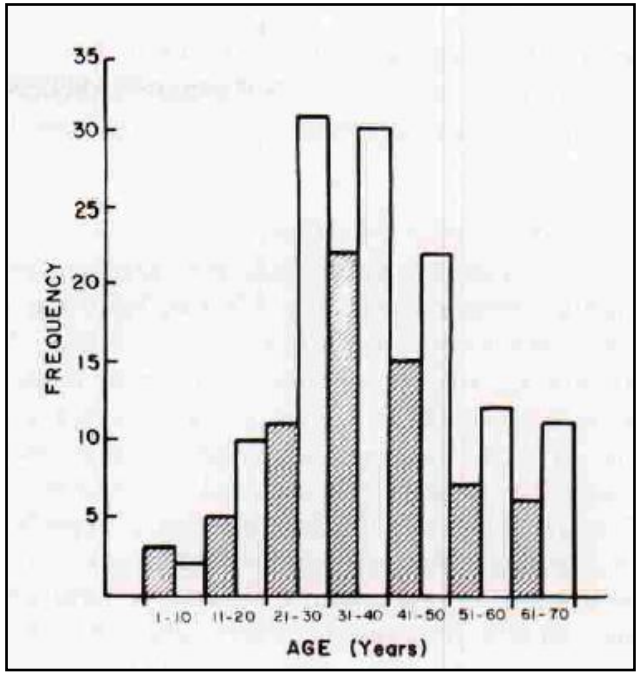
Swinnen K et al. *Eur Respir Rev* 2019; 28: 190050

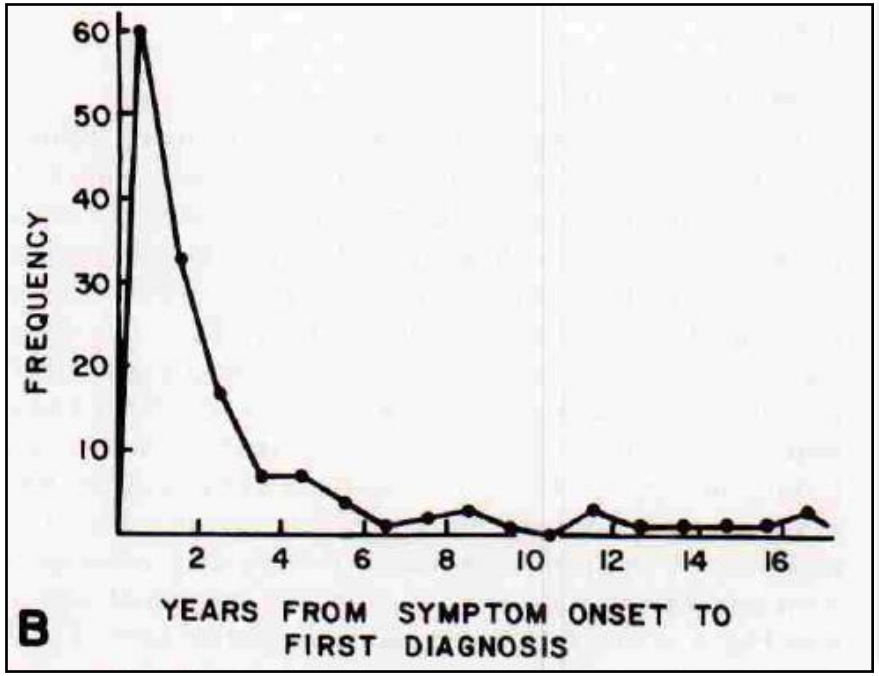
Primary Pulmonary Hypertension

A National Prospective Study

STUART RICH, M.D.; DAVID R. DANTZKER, M.D.; STEPHEN M. AYRES, M.D.; EDWARD H. BERGOFSKY, M.D.; BRUCE H. BRUNDAGE, M.D.; KATHERINE M. DETRE, M.D., Dr.P.H.; ALFRED P. FISHMAN, M.D.; ROBERTA M. GOLDRING, M.D.; BERTRON M. GROVES, M.D.; SPENCER K. KOERNER, M.D.; PAUL C. LEVY, Sc.D.; LYNNE M. REID, M.D.; CAROL E. VREIM, Ph.D.; and GEORGE W. WILLIAMS, Ph.D.; Bethesda, Maryland

32 center v USA, 187 pacientů diagnostikovaných v letech 1981 až 1985, FU do 1988 (106 úmrtí)
Průměrný věk 36±15 roku, M:F 1:1.7
Medián přežití 2.8 roku, pravděpodobnost přežití 1, 3, 5 let: 68 %, 48 %, 34%





MEDICAL AND FAMILY HISTORY

Forty-five percent of the patients were previous or current cigarette smokers, and only 5% had histories of appetite suppressant drug use. Fifty-four percent of the female patients had taken oral contraceptives at some time. There were 2.3 live births per female patient in the registry. None of these frequencies appear to differ dramatically from those found in the general population. There were 12 cases (6%) of familial pulmonary hypertension (disease affecting a first-order blood relative), 7 in men and 5 in women. Patients who had positive family histories were usually diagnosed sooner after the onset of symptoms than were the other registry patients (0.68 compared with 2.56 years; $p = 0.0002$). There were no differences, however, in their ages or hemodynamic findings.

Annals of Internal Medicine 1987, 107, 216-223

Continuous Subcutaneous Infusion of Treprostinil, a Prostacyclin Analogue, in Patients with Pulmonary Arterial Hypertension

A Double-blind, Randomized, Placebo-controlled Trial

GERALD SIMONNEAU, ROBYN J. BARST, NAZZARENO GALIE, ROBERT NAEIJE, STUART RICH, ROBERT C. BOURGE, ANNE KEOGH, RONALD OUDIZ, ADAANI FROST, SHELMER D. BLACKBURN, JAMES W. CROW, and LEWIS J. RUBIN, for the Treprostinil Study Group

470 pacientů s PAH (IPAH, CTD-PAH, CHD-PAH), průměrný věk 44.5 roku

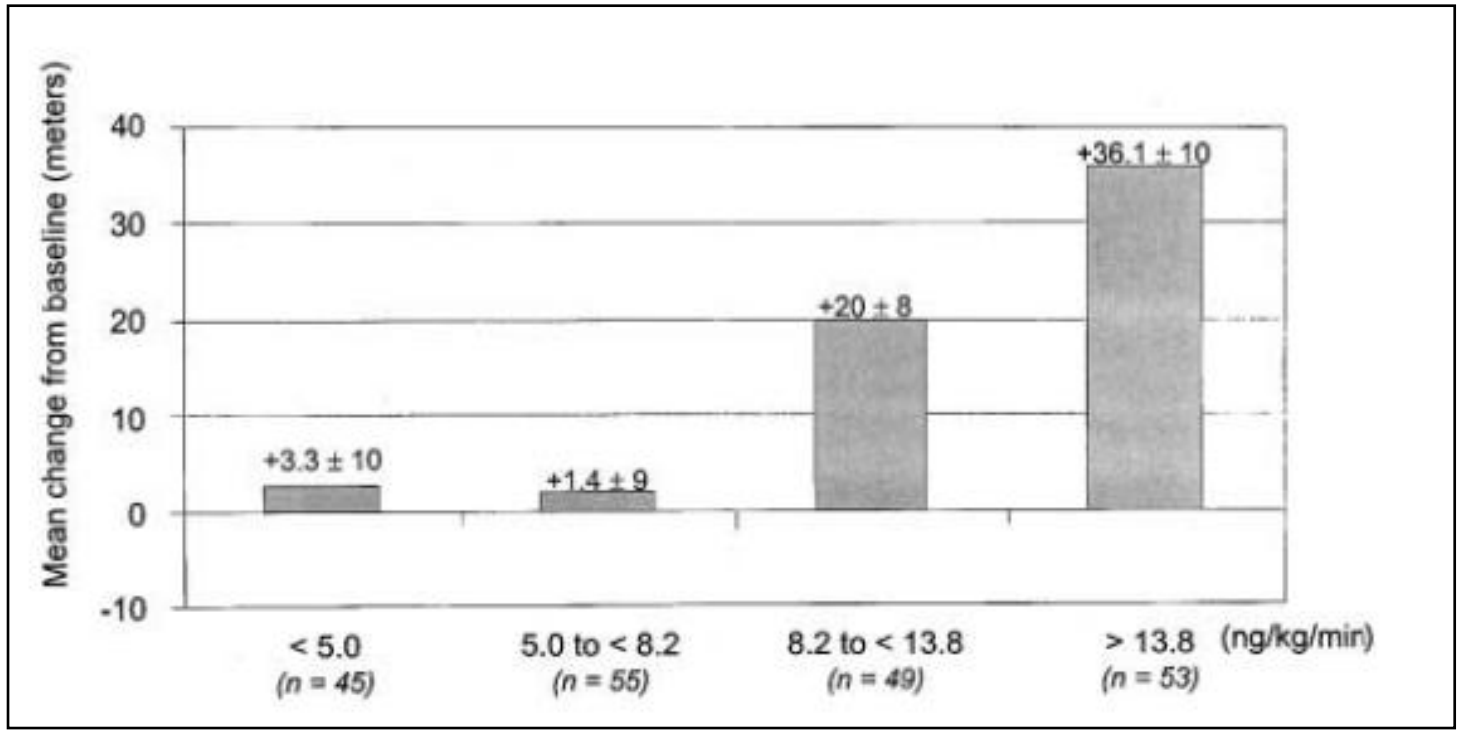


TABLE 1. MAIN INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria
- Primary pulmonary hypertension or pulmonary hypertension associated with connective tissue diseases or associated with congenital systemic to pulmonary shunts
- Age between 8 and 75 yr
- New York Heart Association (NYHA) functional class II, III, or IV
- Significant pulmonary hypertension defined by
  - Mean pulmonary arterial pressure ≥ 25 mm Hg at rest
  - Mean pulmonary capillary wedge pressure ≤ 15 mm Hg
  - Pulmonary vascular resistance > 3 mm Hg/L/min
- Ventilation perfusion lung scan or pulmonary angiography not indicative of thromboembolic disease

Exclusion criteria
- Significant parenchymal pulmonary disease as evidenced by pulmonary function tests or high resolution CT scan
- Porto pulmonary hypertension or HIV-associated pulmonary hypertension
- Uncontrolled sleep apnea
- History of left side heart disease
- Other diseases associated with pulmonary hypertension (e.g., sickle cell anemia, shistosomiasis)
- Baseline exercise capacity of less than 50 m or greater than 450 m walked in 6 min
- Any new type of chronic therapy for pulmonary hypertension added within the last month
- Any pulmonary hypertension medication discontinued within the last week except anticoagulants
- Any use of prostaglandin derivatives within the past 30 d

Definition of abbreviations: CT = computed tomography; HIV = human immunodeficiency virus.

Am J Respir Crit Care Med 2002 165: 800-804

Comorbid Conditions and Outcomes in Patients With Pulmonary Arterial Hypertension

A REVEAL Registry Analysis

2959 pacientů s PAH, 78.9 % žen, průměrný věk 52.7 roku v době zařazení
45.9% idiopatická PAH, 51.1%+7% NYHA III+IV
Vznik databáze: 2006 (incidentní a prevalentní pacienti s PAH)

Characteristic	All Patients (N = 2,959)	Hypertension (n = 1,021)	Obesity[a] (n = 956)	Type 2 Diabetes (n = 324)	COPD (n = 498)	Sleep Apnea (n = 599)	Depression (n = 408)	Thyroid Disease[b] (n = 667)	None of the Analyzed Comorbidities[c] (n = 786)
Age at enrollment, mean ± SD, y	52.7 ± 14.7	58.9 ± 12.9	53.3 ± 13.3	58.6 ± 12.3	59.7 ± 12.8	56.3 ± 12.4	53.0 ± 13.4	56.4 ± 13.9	46.3 ± 14.9
Female sex	2,334 (78.9)	802 (78.6)	784 (82.0)	241 (74.4)	364 (73.1)	439 (73.3)	348 (85.3)	606 (90.9)	601 (76.5)
White	2,138 (72.3)	734 (71.9)	710 (74.3)	218 (67.3)	378 (75.9)	469 (78.3)	326 (79.9)	532 (79.8)	528 (67.2)
Etiology									
Idiopathic	1,358 (45.9)	515 (50.4)	505 (52.8)	184 (56.8)	249 (50.0)	353 (58.9)	187 (45.8)	285 (42.7)	330 (42.0)
APAH									
CTD	787 (26.6)	302 (29.6)	201 (21.0)	46 (14.2)	141 (28.3)	104 (17.4)	111 (27.2)	237 (35.5)	187 (23.8)
CHD	285 (9.6)	46 (4.5)	57 (6.0)	19 (5.9)	53 (10.6)	37 (6.2)	29 (7.1)	49 (7.3)	126 (16.0)
PoPH	175 (5.9)	43 (4.2)	54 (5.6)	37 (11.4)	23 (4.6)	31 (5.2)	23 (5.6)	28 (4.2)	45 (5.7)

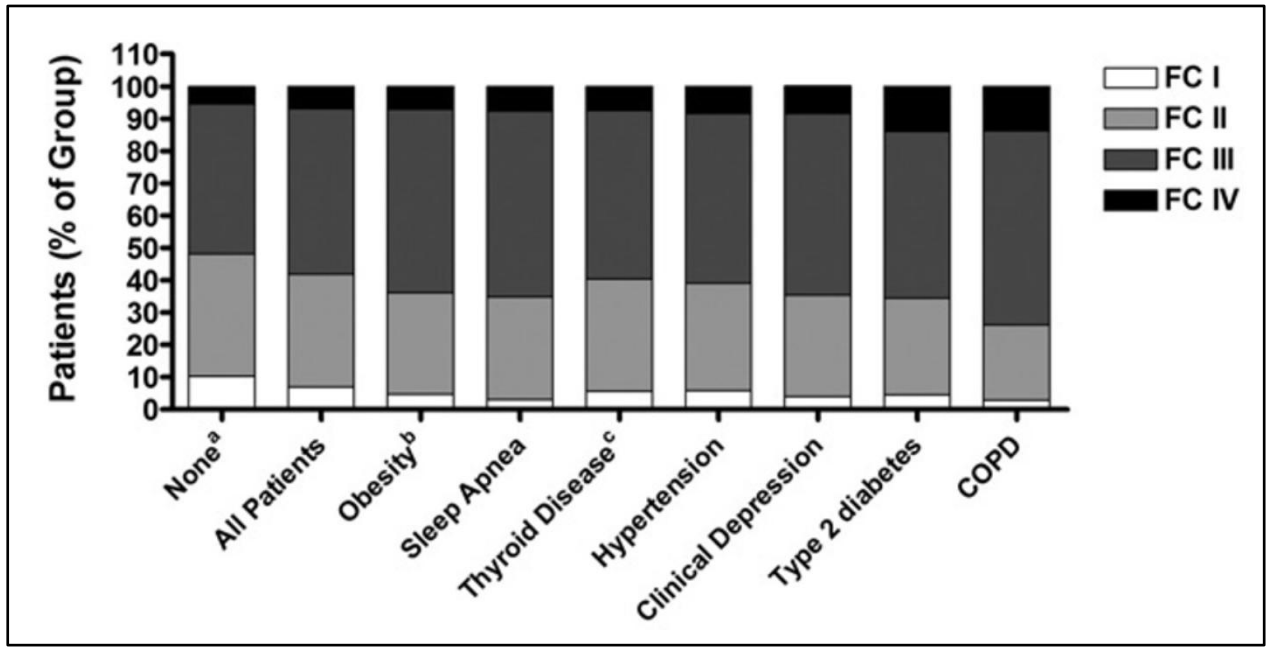
Obesity was defined as BMI ≥ 30 kg/m^2
Thyroid disease was defined as patients with hyperthyroidism or hypothyroidism and/or patients having taken synthetic thyroid replacement for hypothyroidism.

Poms AD et al. *CHEST* 2013; 144(1):169–176

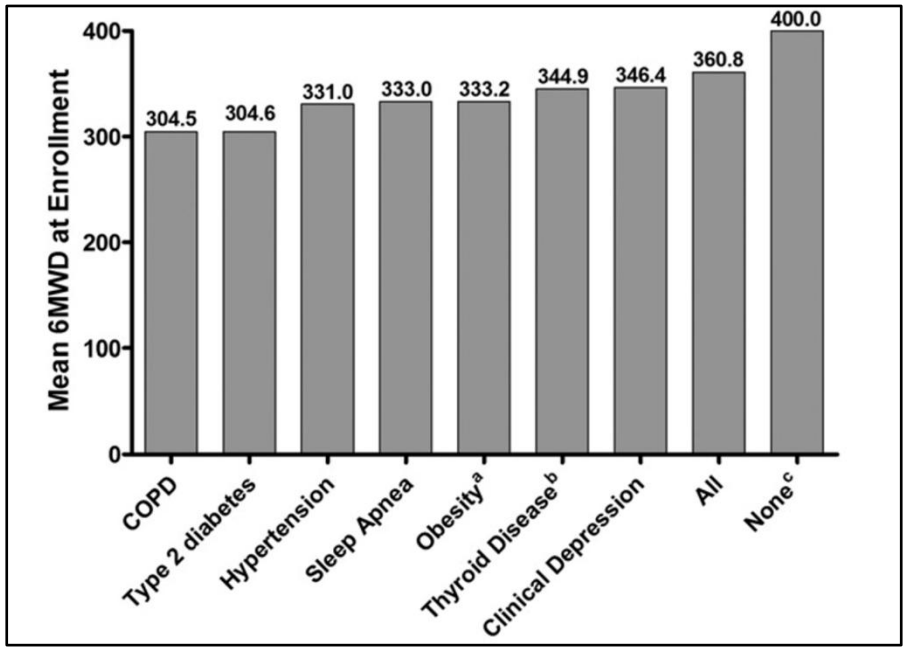
Comorbid Conditions and Outcomes in Patients With Pulmonary Arterial Hypertension

A REVEAL Registry Analysis

2959 pacientů s PAH, 78.9 % žen, průměrný věk 52.7 roku v době zařazení
45.9% idiopatická PAH, 51.1%+7% NYHA III+IV



NYHA při zařazení



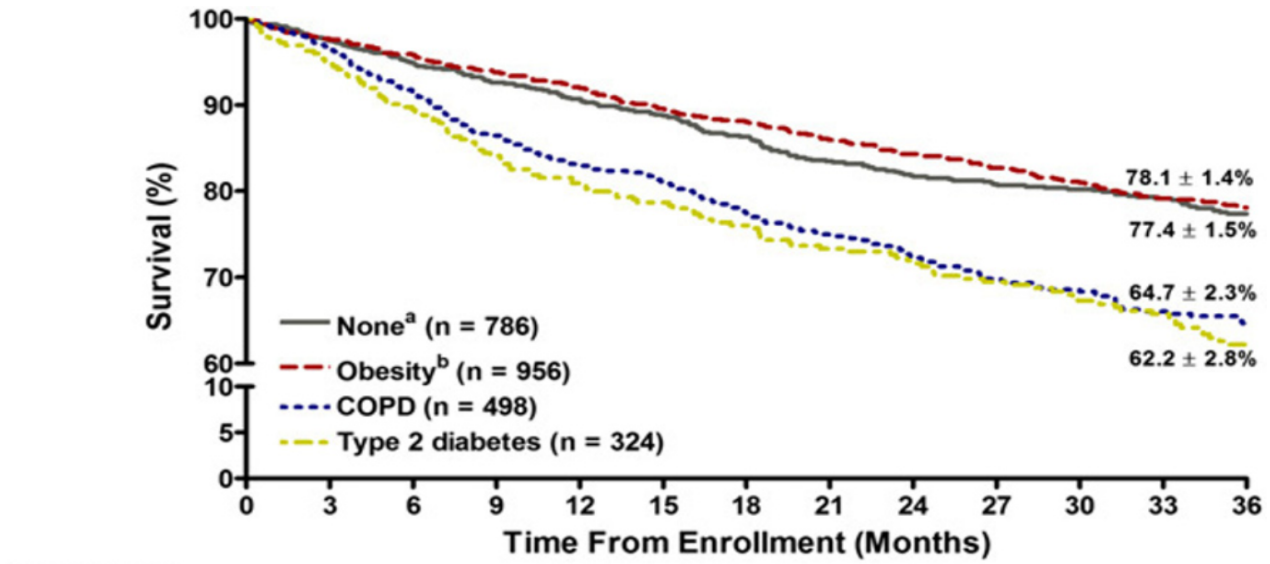
6MWD při zařazení

Poms AD et al. *CHEST* 2013; 144(1):169–176

Comorbid Conditions and Outcomes in Patients With Pulmonary Arterial Hypertension

A REVEAL Registry Analysis

2959 pacientů s PAH, 78.9 % žen, průměrný věk 52.7 roku v době zařazení
45.9% idiopatická PAH, 51.1%+7% NYHA III+IV



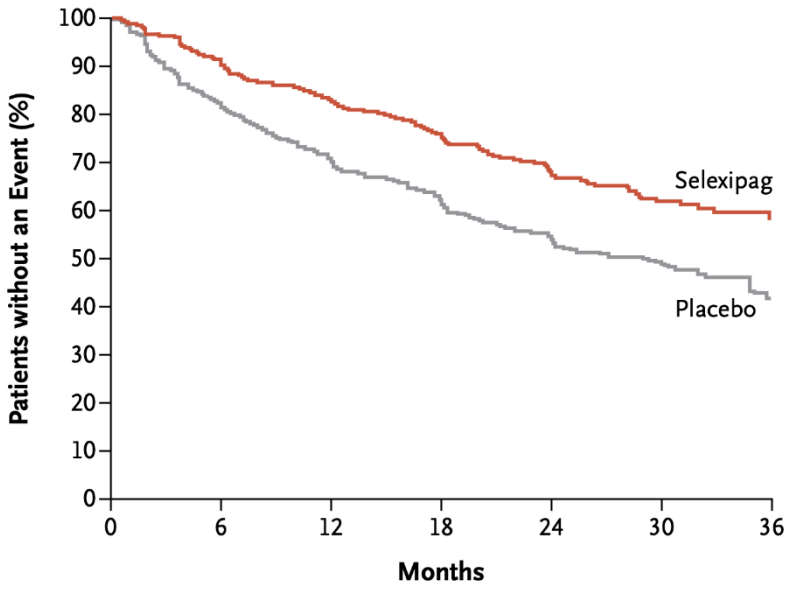
Number at risk:													
None	786	764	744	723	705	681	644	609	593	562	525	512	483
Obesity	956	929	910	882	858	823	790	736	713	677	626	610	589
COPD	498	480	452	423	406	392	358	330	314	289	267	256	239
Type 2 diabetes	324	305	287	268	254	243	230	216	210	195	179	173	158

přežití

Poms AD et al. *CHEST* 2013; 144(1):169–176

Selexipag for the Treatment of Pulmonary Arterial Hypertension

1156 pacientů s PAH, pbo vs selexipag (maximální dávka 2x1600 µg) 79.8% žen, průměrný věk 48.1
NYHA FC I/II 46.6 %, kombinační léčba 79.6 %, komorbidity 50.5 %
Zahájení studie: 2009



No. at Risk							
Placebo	582	433	347	220	149	88	28
Selexipag	574	455	361	246	171	101	40

Primární cílový ukazatel

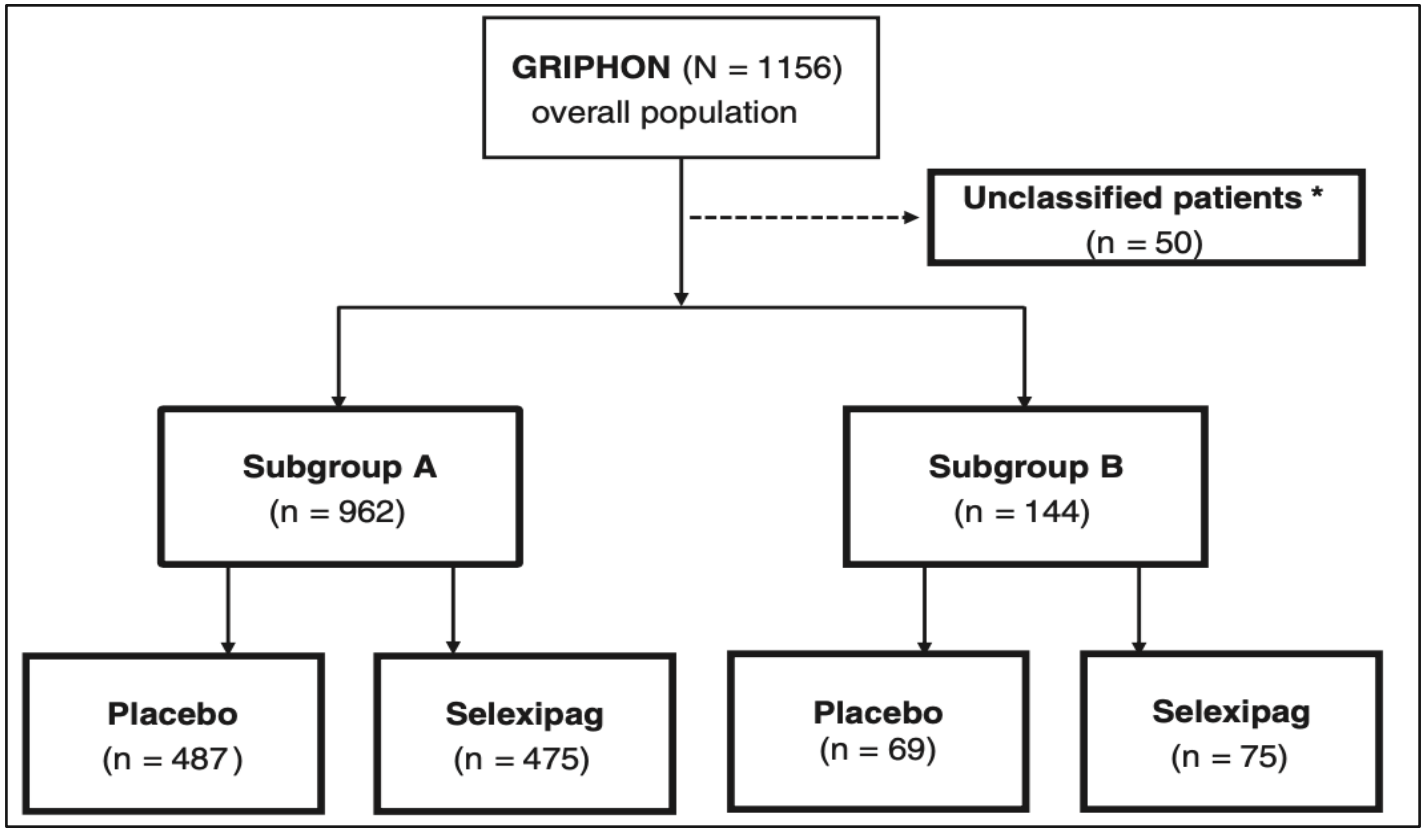
Patients will not be entered into the study if they meet any of the following criteria:

1. Patients with pulmonary hypertension (PH) in the updated Dana Point Clinical Classification Groups 2–5, and PAH Group 1 subgroups that are not covered by the inclusion criteria.
2. Patients who have received prostacyclin (epoprostenol) or prostacyclin analogs[7] (i.e., treprostinil, iloprost, beraprost) within one month before Baseline Visit, or are scheduled to receive any of these compounds during the trial.
3. Patients with moderate or severe obstructive lung disease: $FEV_1/FVC < 70\%$ and $FEV_1 < 65\%$ of predicted value after bronchodilator administration.
4. Patients with moderate or severe restrictive lung disease: Total Lung Capacity < 70% of predicted value.
5. Patients with moderate or severe hepatic impairment (Child-Pugh B and C).
6. Patients with documented left ventricular dysfunction (i.e., ejection fraction < 45%)
7. Patients with severe renal insufficiency (estimated creatinine clearance < 30 mL/min, or serum creatinine > 2.5 mg/dL).
8. Patients with BMI < 18.5 kg/m^2.
9. Patients who are receiving or have been receiving any investigational drugs within 1 month before the Baseline Visit.
10. Acute or chronic impairment (other than dyspnea), limiting the ability to comply with study requirements, in particular with 6MWT (e.g., angina pectoris, claudication, musculoskeletal disorder, need for walking aids).

Vylučující kritéria

Sitbon O et al. *N Engl J Med* 2015;373:2522-33

The impact of comorbidities on selexipag treatment effect in patients with pulmonary arterial hypertension: insights from the GRIPHON study



Komorbidity: BMI ≥30kg/m^2,arteriální hypertenze, diabetes,ICHS, fibrilace síní
Skupina A: <3 komorbidity a restriktivní hemodynamická kritéria (≤12 mmHg u PVR <6.25 WU)
Subgroup B: ≥3 komorbidity a/nebo nesplněna restriktivní hemodynamická kritéria

Rosenkranz S et al. *European Journal of Heart Failure* (2022) 24, 205–214

The impact of comorbidities on selexipag treatment effect in patients with pulmonary arterial hypertension: insights from the GRIPHON study

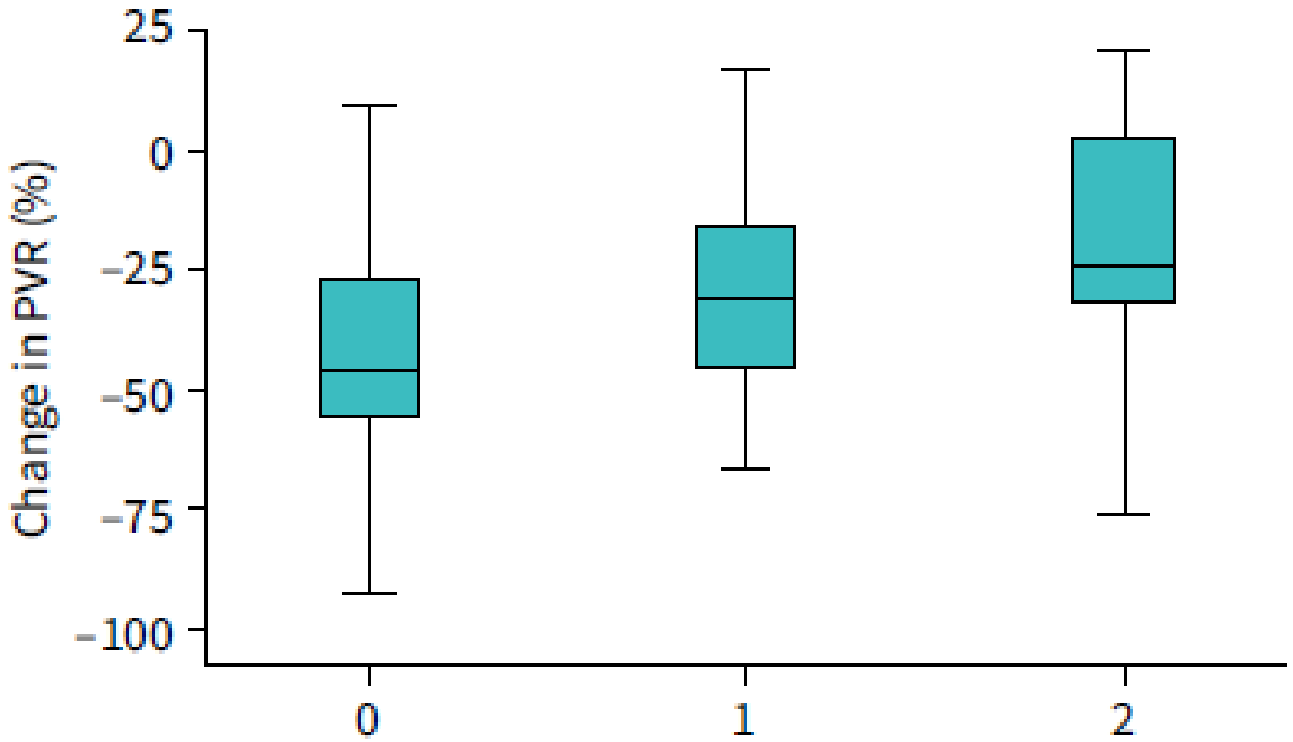
	Subgroup A		Subgroup B	
	Placebo (n = 483)	Selexipag (n = 476)	Placebo (n = 68)	Selexipag (n = 75)
Patients with ≥1 AE, *n* (%)	468 (96.9)	466 (97.9)	67 (98.5)	75 (100)
Patients with ≥1 serious AE, *n* (%)	227 (47.0)	213 (44.7)	37 (54.4)	34 (45.3)
Patients with ≥1 AE leading to discontinuation of study drug[a], *n* (%)	29 (6.0)	63 (13.2)	9 (13.2)	16 (21.3)
Patients with ≥1 PGI_2-like AE during titration phase, *n* (%)	252 (52.2)	417 (87.6)	43 (63.2)	64 (85.3)
Patients with ≥1 PGI_2-like AE during maintenance phase[b], *n* (%)	206 (47.9)	302 (71.7)	26 (45.6)	53 (80.3)

Bezpečnost

Rosenkranz S et al. *European Journal of Heart Failure* (2022) 24, 205–214

Relevance of comorbidities on initial combination therapy in pulmonary arterial hypertension

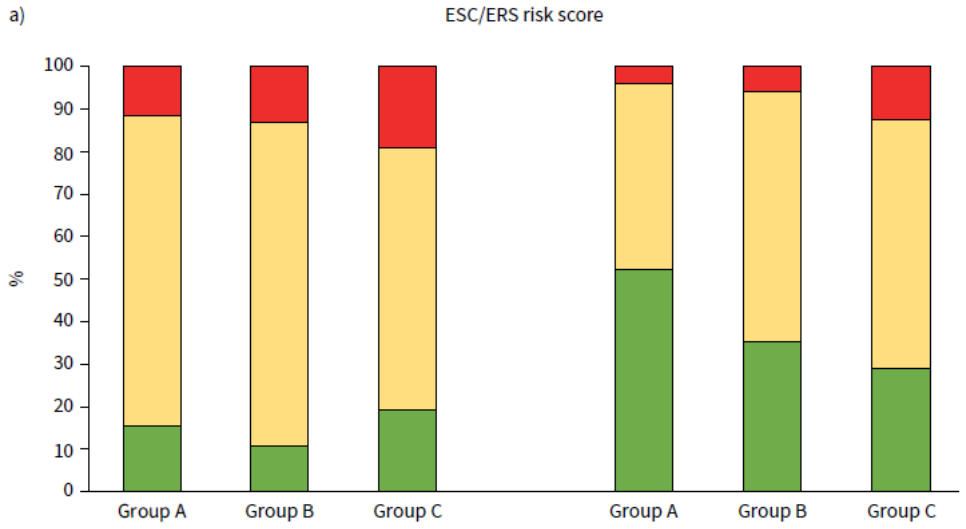
181 pacientů s idiopatickou PAH, 1/2013-12/2018. 11 center, medián FU 180 dní
Kardiovaskulární komorbidity: hypertenze, HLP, obezita (BMI ⩾30 kg·m^{-2}), diabetes,ICHDK, ICHS
Skupina A (bez komorbidit, 53 %), **Skupina B** (1 komorbidita, 29.8 %), **Skupina C** (≥ 2 komorbidity, 17.1 %)



Badagliacca R et al. ERJ Open Res 2022; 8: 00298-2022

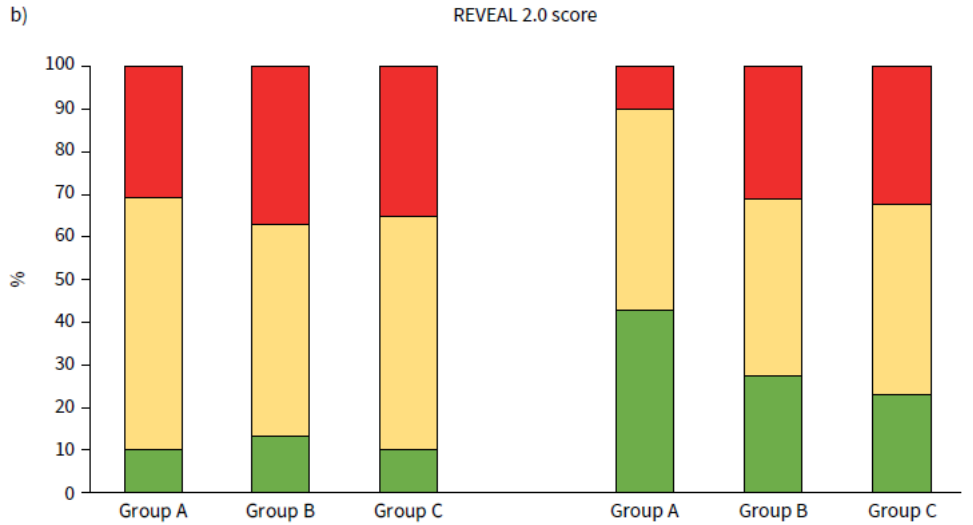
Relevance of comorbidities on initial combination therapy in pulmonary arterial hypertension

181 pacientů s idiopatickou PAH, 1/2013-12/2018. 11 center, medián FU 180 dní
Kardiovaskulární komorbidity: hypertenze, HLP, obezita (BMI ⩾30 kg·m^{-2}), diabetes,ICHDK, ICHS
Skupina A (bez komorbidit, 53 %), **Skupina B** (1 komorbidita, 29.8 %), **Skupina C** (≥ 2 komorbidity, 17.1 %)



Diagnóza

Poslední kontrola



Diagnóza

Poslední kontrola

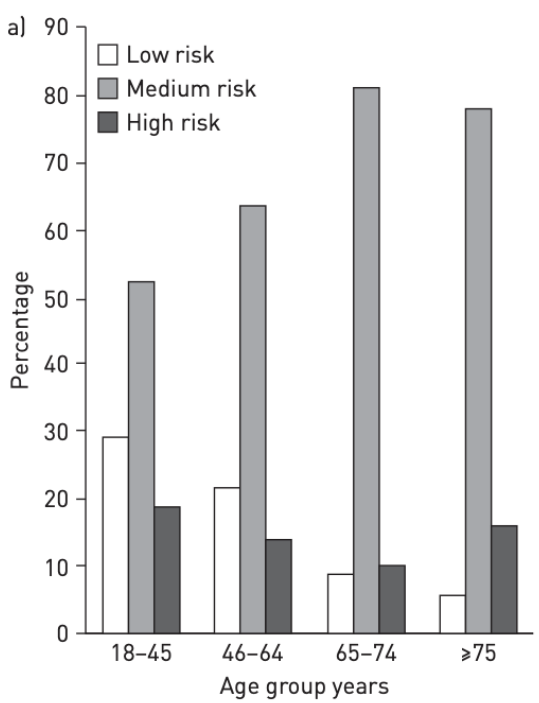
Badagliacca R et al. ERJ Open Res 2022; 8: 00298-2022

Impact of age and comorbidity on risk stratification in idiopathic pulmonary arterial hypertension

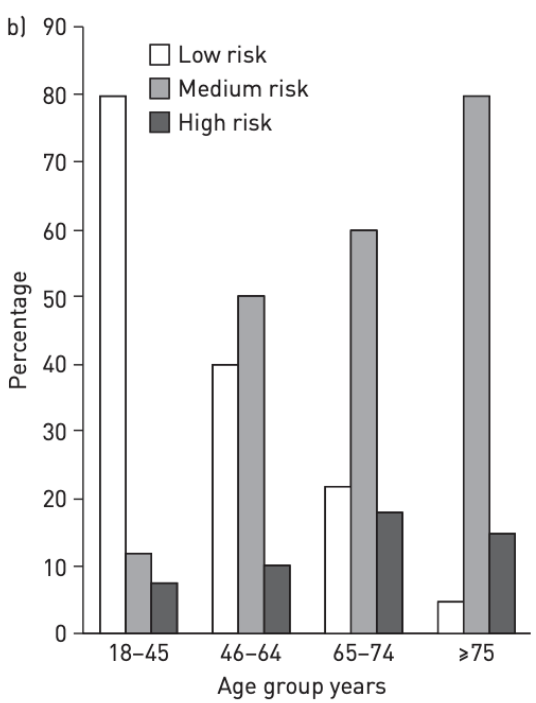
264 pacientů s nově diagnostikovanou idiopatickou PAH

Věkové kategorie: 18–45, 46–64, 65–74, ⩾75 roku. Riziková stratifikace podle ESC/ERS guidelines

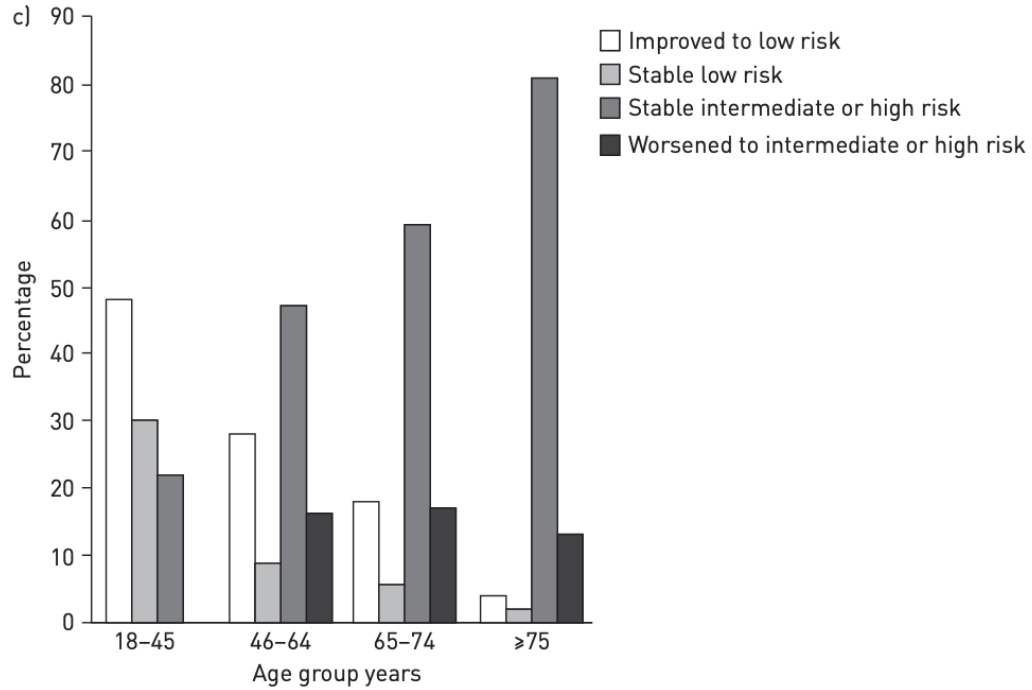
Komorbidity: arteriální hypertenze, diabetes, CMP, ICHS, fibrilace síní, obezita, renální insuficience



Diagnóza



Follow-up



Změna rizikové kategorie

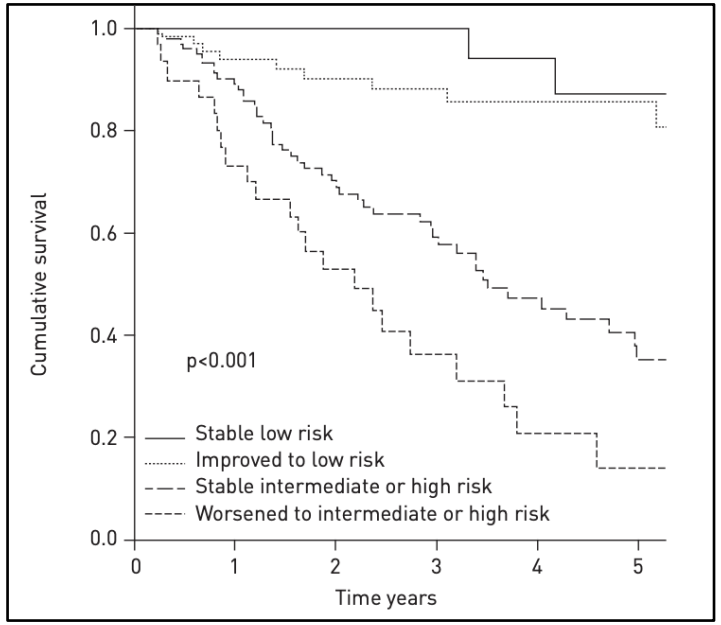
Hjalmarsson C et al. *Eur Respir J* 2018; 51: 1702310

Impact of age and comorbidity on risk stratification in idiopathic pulmonary arterial hypertension

264 pacientů s nově diagnostikovanou idiopatickou PAH

Věkové kategorie: 18–45, 46–64, 65–74, ⩾75 roku. Riziková stratifikace podle ESC/ERS guidelines

Komorbidity: arteriální hypertenze, diabetes, CMP, ICHS, fibrilace síní, obezita, renální insuficience



Přežití

Explanatory variable	HR (95% CI)	p-value
Sex	0.82 (0.48–1.41)	0.473
Worsening of risk group from baseline	1.75 (1.14–2.69)	**0.011**
Hypertension	0.89 (0.51–1.56)	0.685
Diabetes mellitus type 2	1.01 (0.56–1.82)	0.973
Atrial fibrillation	1.00 (0.48–2.10)	1.000
Ischaemic heart disease	2.14 (1.21–3.78)	**0.009**
Stroke	2.00 (0.85–4.74)	0.114
Obesity	1.44 (0.78–2.66)	0.245
Kidney dysfunction	1.85 (1.09–3.14)	**0.022**

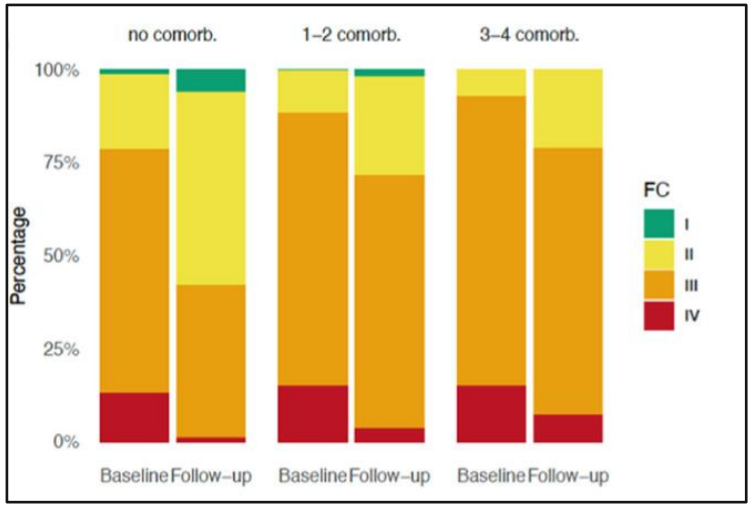
Worsening of risk group from baseline, ischaemic heart disease and kidney dysfunction were independent predictors of survival. Bold indicates statistical significance at p<0.05. HR: hazard ratio.

Prediktory přežití

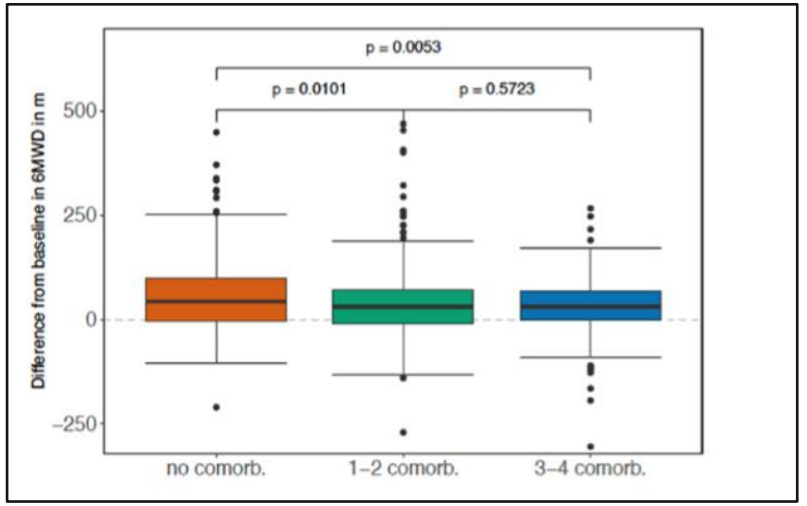
Hjalmarsson C et al. *Eur Respir J* 2018; 51: 1702310

Risk stratification and response to therapy in patients with pulmonary arterial hypertension and comorbidities: A COMPERA analysis

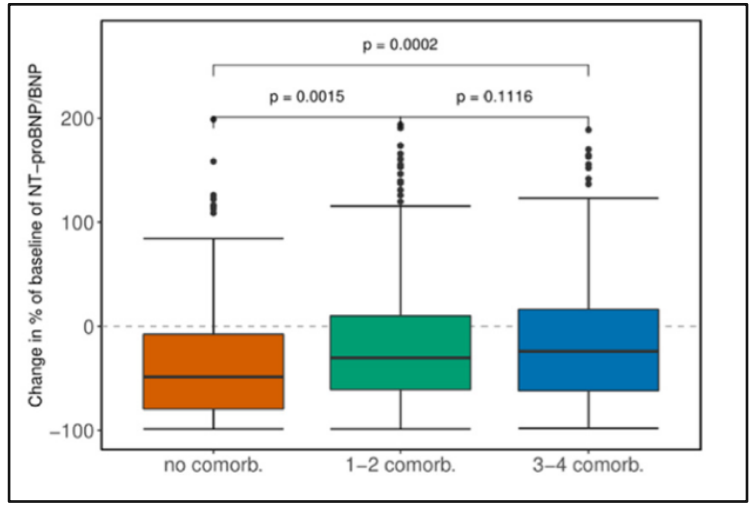
N=1120, nově diagnostikovaná idiopatická, ESC/ERS riziková stratifikace (4 strata)
(208 [19%]bez komorbidit, 641 [57%]1-2 komorbidity, 271 [24%]3-4 komorbidity)
Komorbidity: arteriální hypertenze, diabetes,ICHS, obezita (BMI >30 kg/m^2)
Kombinační léčba po roce léčby: 62.6% bez komorbidit, 37.3% s 1-2 komorbiditami, 34.7% se 3-4 komorbiditami
Ukončení léčby během 1. roku léčby:
PDE5i 7-11%, ERAs in 4% bez komorbidit, 12.7% s 1-2 komorbiditami, 17.3% s 3-4 komorbiditami



NYHA FC



6MWD

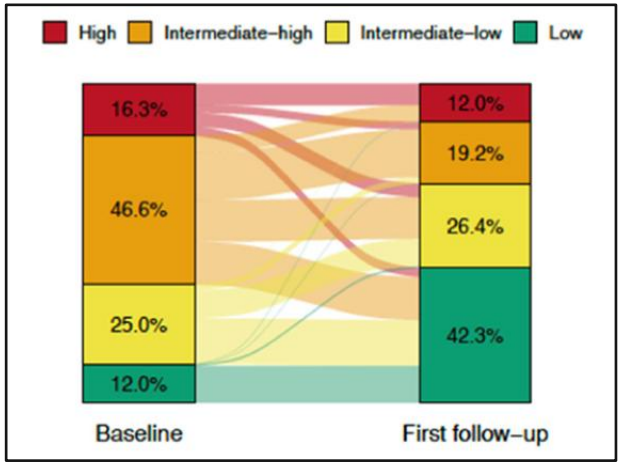


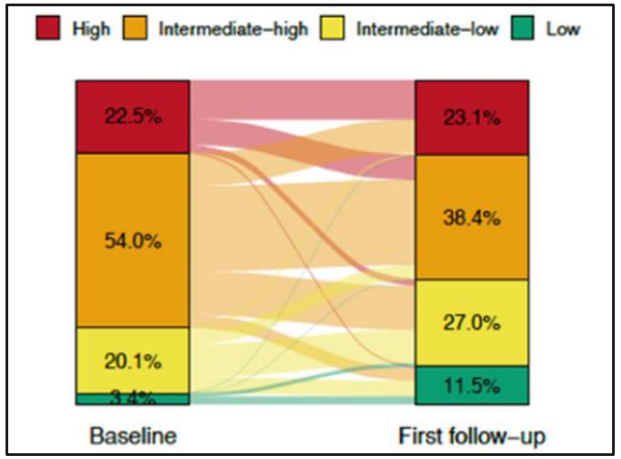
proBNP

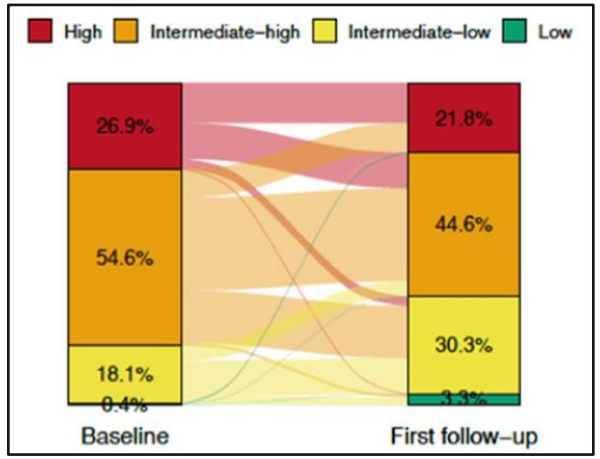
Rosenkranz S et al. *J Heart Lung Transplant* 2023;42:102−114

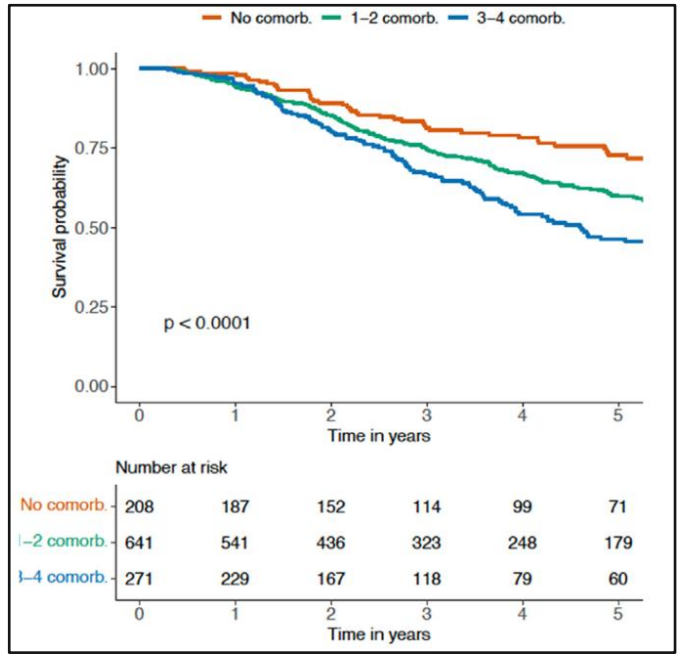
Risk stratification and response to therapy in patients with pulmonary arterial hypertension and comorbidities: A COMPERA analysis

N=1120, nově diagnostikovaná idiopatická, ESC/ERS riziková stratifikace (4 strata)
(208 [19%]bez komorbidit, 641 [57%]1-2 komorbidity, 271 [24%]3-4 komorbidity)
Komorbidity: arteriální hypertenze, diabetes,ICHS, obezita (BMI >30 kg/m^2)









Bez komorbidit

1-2 komorbidity

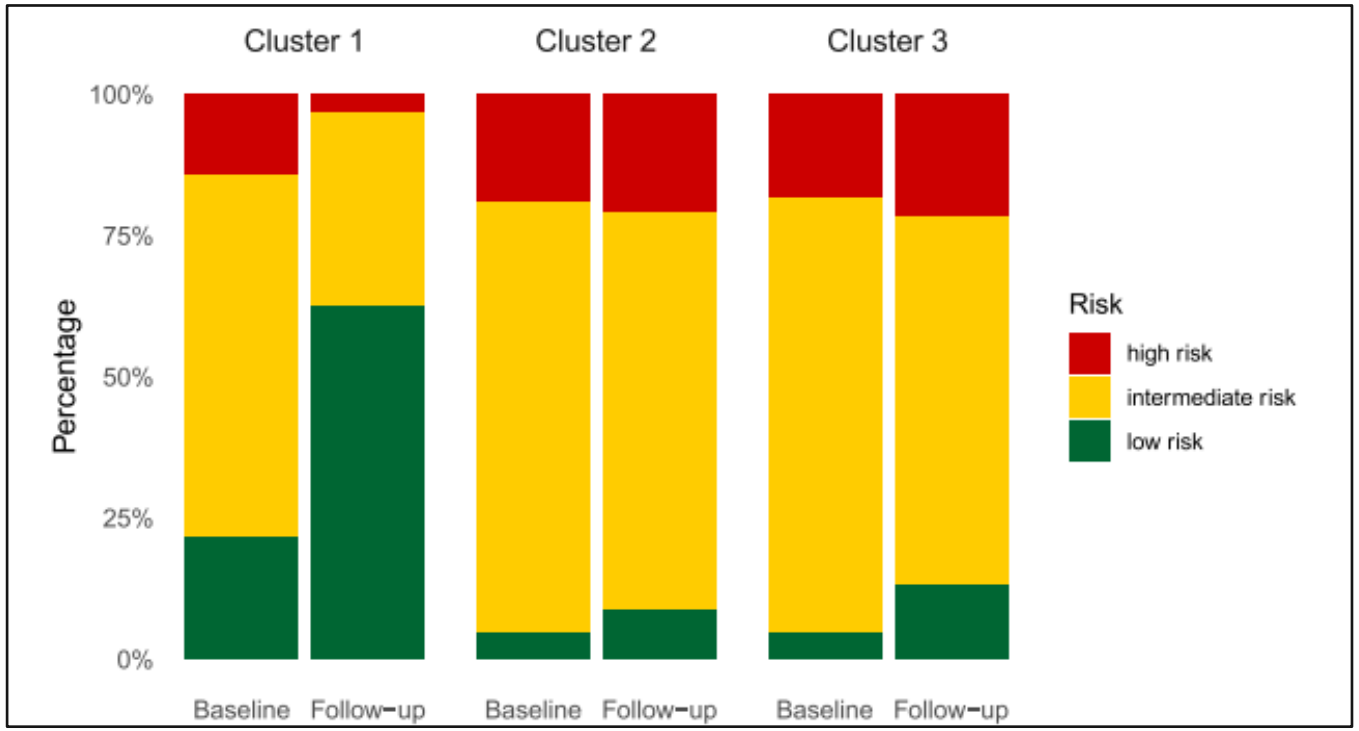
3-4komorbidity

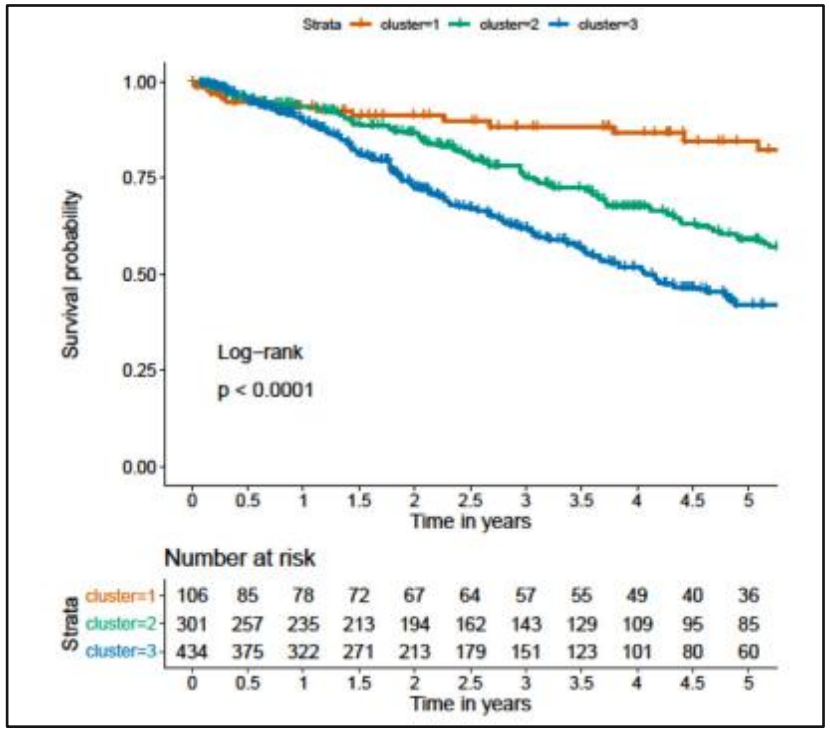
Přežití – celá populace

Rosenkranz S et al. *J Heart Lung Transplant* 2023;42:102−114

Idiopathic pulmonary arterial hypertension phenotypes determined by cluster analysis from the COMPERA registry

N=841. Komorbidity: obezita, ICHS, arteriální hypertenze, DM
Cluster 1 (n = 106; 12.6%): věk 45, 76% ženy, bez komorbidit, nekuřáci, DLCO ≥45%
Cluster 2 (n = 301; 35.8%): věk 75, 98% ženy, časté komorbidity, nekuřáci, DLCO ≥45%
Cluster 3 (n = 434; 51.6%): věk 72, 72% muži, časté komorbidity, kuřáci, DLCO <45%



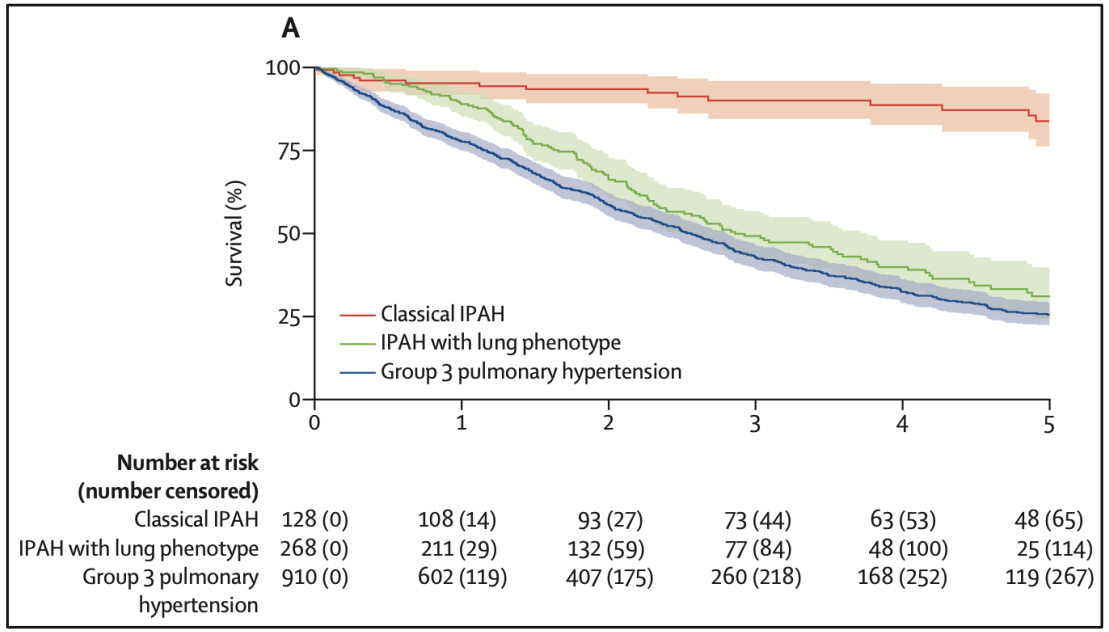


Hoeper MM et al. *J Heart Lung Transplant* 2020;39:1435−1444

Phenotyping of idiopathic pulmonary arterial hypertension: a registry analysis

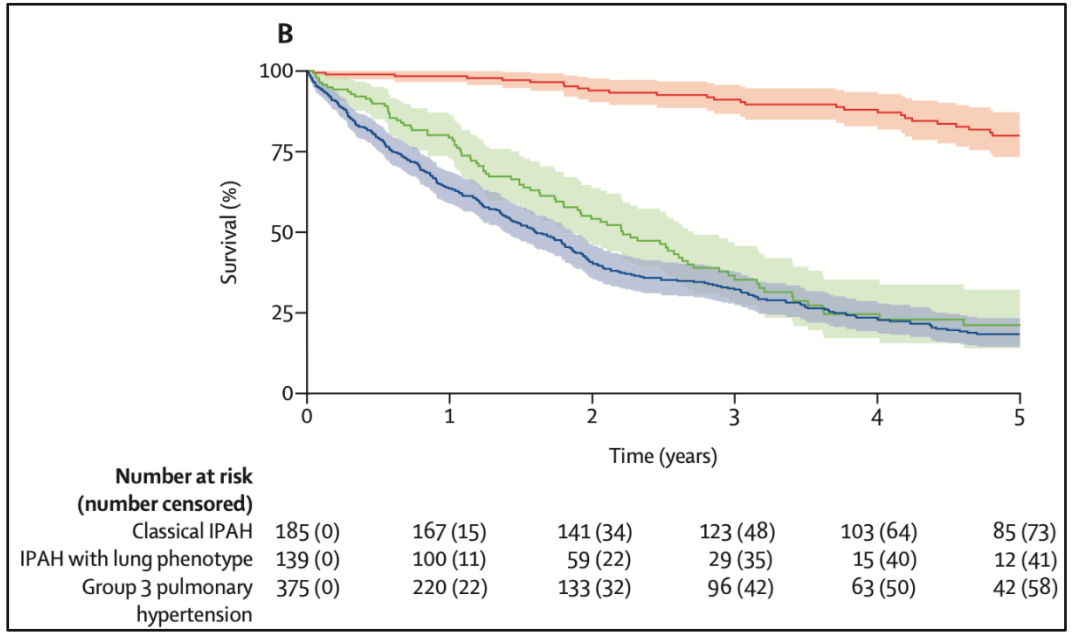
COMPERA (n=1306) and **ASPIRE** (699) registries, patient characteristics, response to therapy, survival

- classical IPAH (DLCO ≥ 45%, absence of cardiopulmonary comorbidities)
- IPAH + lung phenotype (DLCO < 45%, smoking history)
- PH due to lung disease (group 3 pulmonary hypertension)



Number at risk (number censored)						
Classical IPAH	128 (0)	108 (14)	93 (27)	73 (44)	63 (53)	48 (65)
IPAH with lung phenotype	268 (0)	211 (29)	132 (59)	77 (84)	48 (100)	25 (114)
Group 3 pulmonary hypertension	910 (0)	602 (119)	407 (175)	260 (218)	168 (252)	119 (267)

COMPERA registry



Number at risk (number censored)						
Classical IPAH	185 (0)	167 (15)	141 (34)	123 (48)	103 (64)	85 (73)
IPAH with lung phenotype	139 (0)	100 (11)	59 (22)	29 (35)	15 (40)	12 (41)
Group 3 pulmonary hypertension	375 (0)	220 (22)	133 (32)	96 (42)	63 (50)	42 (58)

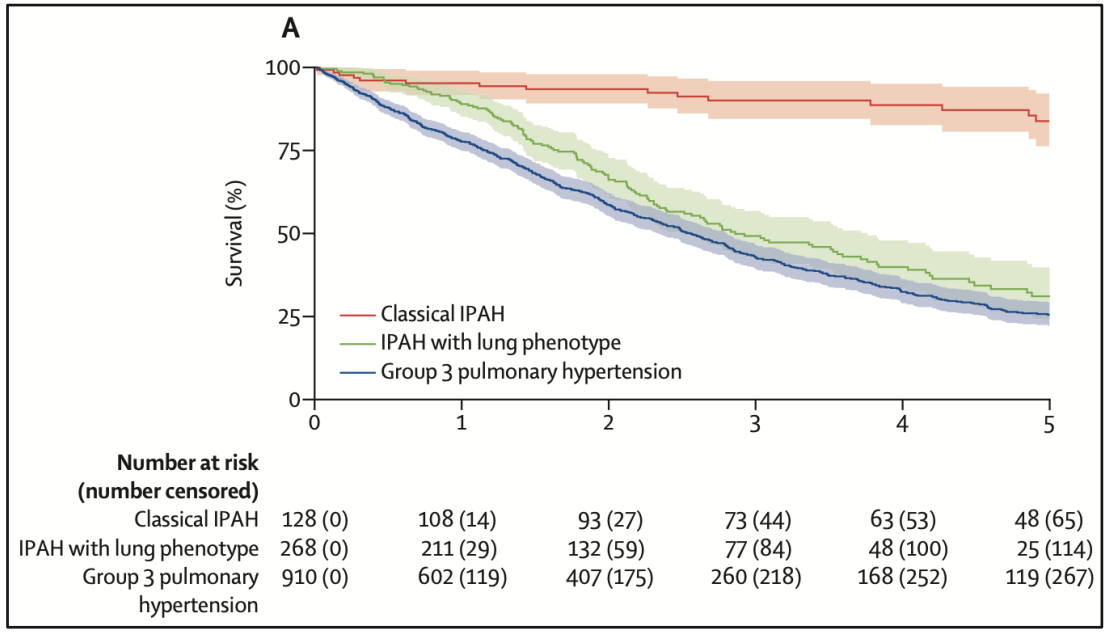
ASPIRE registry

Hoeper MM et al. *Lancet Respir Med* 2022 Oct;10(10):937-948

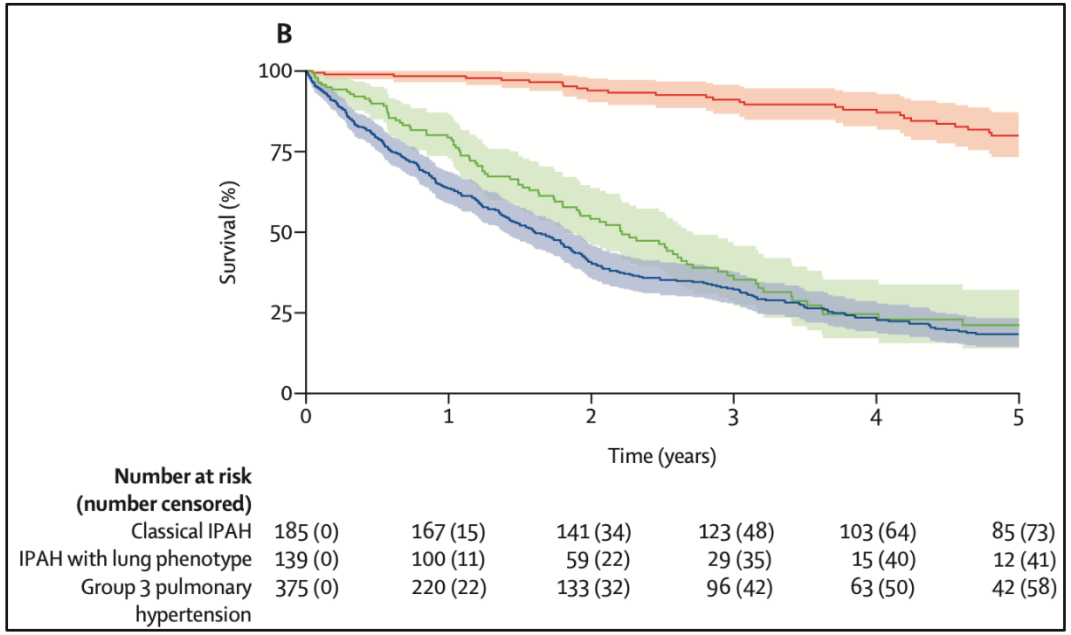
Phenotyping of idiopathic pulmonary arterial hypertension: a registry analysis

COMPERA (n=1306) and ASPIRE (699) registries, patient characteristics, response to therapy, survival

- classical IPAH (DLCO ≥ 45%, absence of cardiopulmonary comorbidities)
- IPAH + lung phenotype (DLCO < 45%, smoking history)
- PH due to lung disease (group 3 pulmonary hypertension)



COMPERA registry



ASPIRE registry

Hoeper MM et al. *Lancet Respir Med* 2022 Oct;10(10):937-948

Kazuistika ♀ J.Š., *1948

Anamnéza

- CHOPN
- FVC 1,45l (83%). VC 1,41l (77%), FEV1 0,71l (51%), FEV1/VCmax 48, TLCO 35%, KCO 44%
- Permanentní fibrilace síní
- ICHS, PCI v 2007
- Arteriální hypertenze

Leden 2023, Všeobecná fakultní nemocnice v Praze

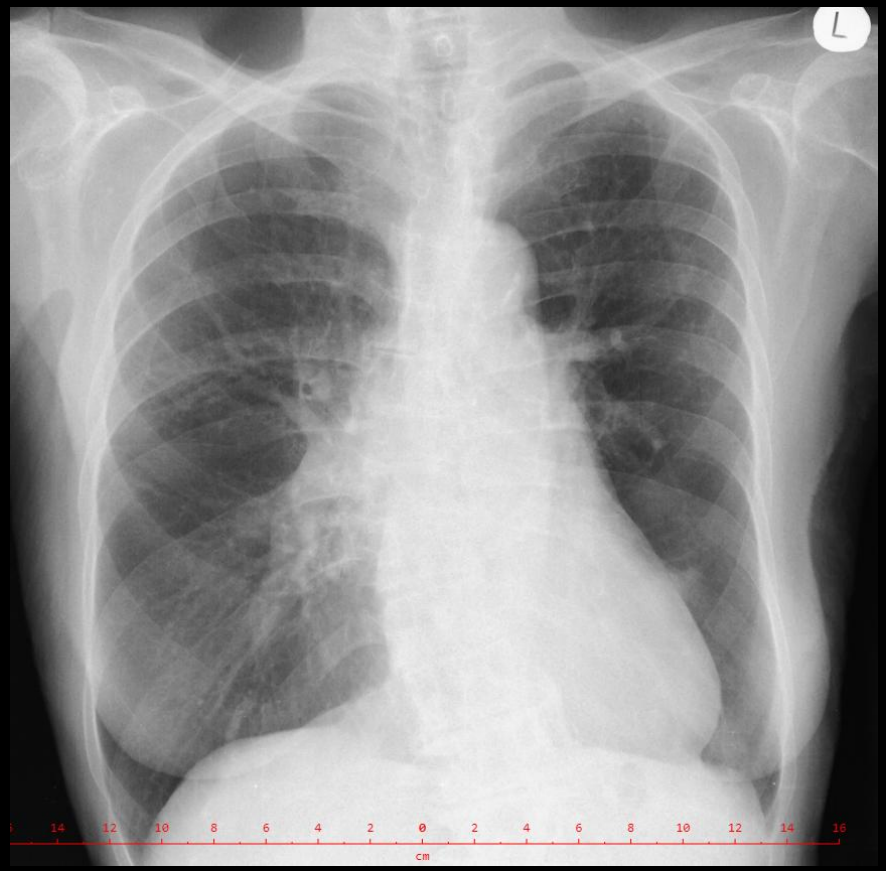
NYHA III, váha 42 kg, váha154 cm, TK 190/110

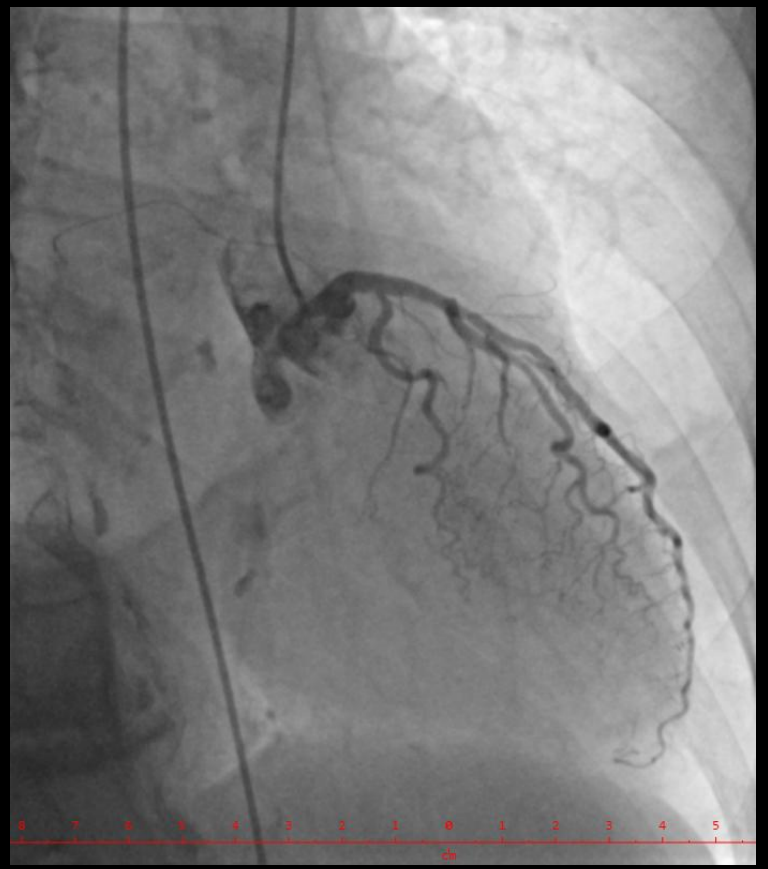
ECHO: EFLK 68 %, LAVi 54 mL/m^2, PASP 78 mmHg
V/Q scintigrafie: souhlasné defekty
6MWT 225 m

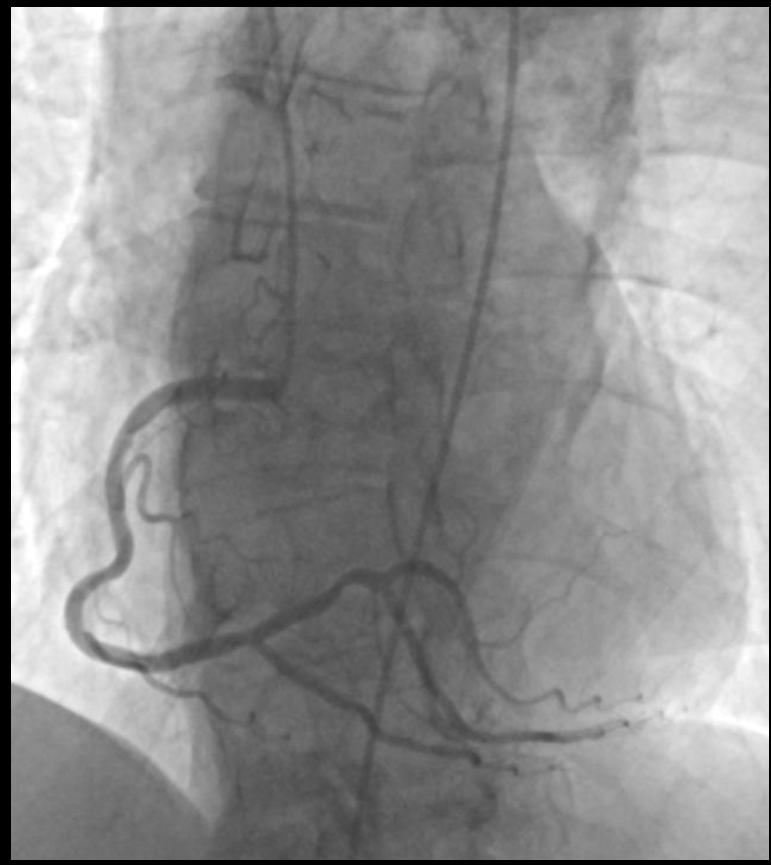
Pro BNP 4377 pg/mL

Hemodynamika:
RA 10 PA 83/42/55, PCW 18, CO 2.70 L/min, CI 1.97 L/min/m^2, PVR 13.7 WU, HR 81/min

Kazuistika ♀ J.Š., *1948







Kazuistika ♀ J.Š., *1948

Klinický závěr:

PAH s kardiopulmonálními komorbiditami

x

PH skupiny 2+3 s těžkou prekapilární komponentou

Léčba PH: Sildenafil 20 mg 3x1 tbl

	NYHA	6MWD (m)	proBNP (pg/mL)	PAMP (mmHg)	PCWP (mmHg)	CO (L/min)	CI (L/min/m^2)	PVR (WU)	SaO_2 (%)	SvO_2 (%)	BP (mmHg)
PH diagnóza (1/2023)	III	225	4377	55	18	2.7	1.97	13.7	95	63	145/94

Kazuistika ♀ J.Š., *1948

Klinický závěr:

PAH s kardiopulmonálními komorbiditami

x

PH skupiny 2+3 s těžkou prekapilární komponentou

Léčba PH: Sildenafil 20 mg 3x1 tbl

	NYHA	6MWD (m)	proBNP (pg/mL)	PAMP (mmHg)	PCWP (mmHg)	CO (L/min)	CI (L/min/m^2)	PVR (WU)	SaO_2 (%)	SvO_2 (%)	BP (mmHg)
PH diagnóza (1/2023)	III	225	4377	55	18	2.7	1.97	13.7	95	63	145/94
PH Reevaluace (6/2023)	III	229	2348	39	15	3.97	2.39	6.0	97	66	138/89

SHRNUTÍ

- Neléčená PAH je progredující a potenciálně fatální onemocnění
- Současné terapeutické možnosti PAH vyvinuté v posledních 30 letech (>10 přípravků, 3 signální cesty) zlepšují symptomy
- Ovlivnění prognózy je limitováno absencí přímého vlivu léčby na pravou komoru, komorbiditami a pozdní diagnózou
- Pacienti s četnějšími a významnějšími komorbiditami jsou vylučováni z klinických studií


European Reference Network
for rare or low prevalence complex diseases
Network
Respiratory Diseases (ERN-LUNG)
Member
General University Hospital in Prague — Czechia
www.pph.cz
www.cteph.cz