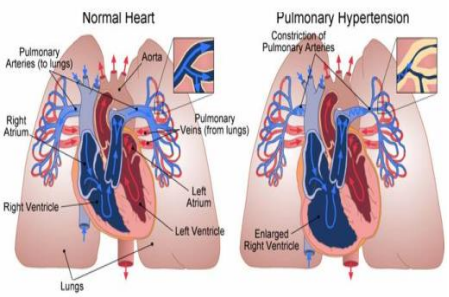

Greek Pulmonary Hypertension Registry: current data(I)

Epidemiology and Diagnosis

Nassos Manginas, MD, FACC, FESC

On behalf of the Hellenic Society for the Study of Pulmonary Hypertension (HSSPH)

Greek PAHTool Registry

Conflicts of interest

- Advisory Board
  - Astra Zeneca, Bayer, ELPEN, Actelion, MSD, NOVARTIS

Pulmonary Hypertension: Definition

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Table 3 Haemodynamic definitions of pulmonary hypertension[a]

Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg	All
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	PAPm ≥25 mmHg PAWP >15 mmHg	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms
Isolated post-capillary PH (Ipc-PH)	DPG <7 mmHg and/or PVR ≤3 WU[c]	
Combined post-capillary and pre-capillary PH (Cpc-PH)	DPG ≥7 mmHg and/or PVR >3 WU[c]	

CO = cardiac output; DPG = diastolic pressure gradient (diastolic PAP – mean PAWP); mPAP = mean pulmonary arterial pressure; PAWP = pulmonary arterial wedge pressure; PH = pulmonary hypertension; PVR = pulmonary vascular resistance; WU = Wood units.

[a]All values measured at rest; see also section 8.0.

[b]According to *Table 4*.

[c]Wood Units are preferred to dynes.s.cm^{-5}.

Pulmonary Hypertension: Classification

Table 4 Comprehensive clinical classification of pulmonary hypertension (updated from Simonneau et al.[5])

1. Pulmonary arterial hypertension
1.1 Idiopathic 1.2 Heritable 1.2.1 BMPR2 mutation 1.2.2 Other mutations 1.3 Drugs and toxins induced 1.4 Associated with: 1.4.1 Connective tissue disease 1.4.2 Human immunodeficiency virus (HIV) infection 1.4.3 Portal hypertension 1.4.4 Congenital heart disease (Table 6) 1.4.5 Schistosomiasis
1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
1'.1 Idiopathic 1'.2 Heritable 1'.2.1 EIF2AK4 mutation 1'.2.2 Other mutations 1'.3 Drugs, toxins and radiation induced 1'.4 Associated with: 1'.4.1 Connective tissue disease 1'.4.2 HIV infection
1''. Persistent pulmonary hypertension of the newborn
2. Pulmonary hypertension due to left heart disease
2.1 Left ventricular systolic dysfunction 2.2 Left ventricular diastolic dysfunction 2.3 Valvular disease 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies 2.5 Congenital /acquired pulmonary veins stenosis
3. Pulmonary hypertension due to lung diseases and/or hypoxia
3.1 Chronic obstructive pulmonary disease 3.2 Interstitial lung disease 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern 3.4 Sleep-disordered breathing 3.5 Alveolar hypoventilation disorders 3.6 Chronic exposure to high altitude 3.7 Developmental lung diseases (Web Table III)
4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions
4.1 Chronic thromboembolic pulmonary hypertension 4.2 Other pulmonary artery obstructions 4.2.1 Angiosarcoma 4.2.2 Other intravascular tumors 4.2.3 Arteritis 4.2.4 Congenital pulmonary arteries stenoses 4.2.5 Parasites (hydatidosis)
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms
5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders 5.4 Others: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

BMPR2 = bone morphogenetic protein receptor, type 2; EIF2AK4 = eukaryotic translation initiation factor 2 alpha kinase 4; HIV = human immunodeficiency virus.

European Heart Journal
doi:10.1093/eurheartj/ehv317
ESC/ERS GUIDELINES

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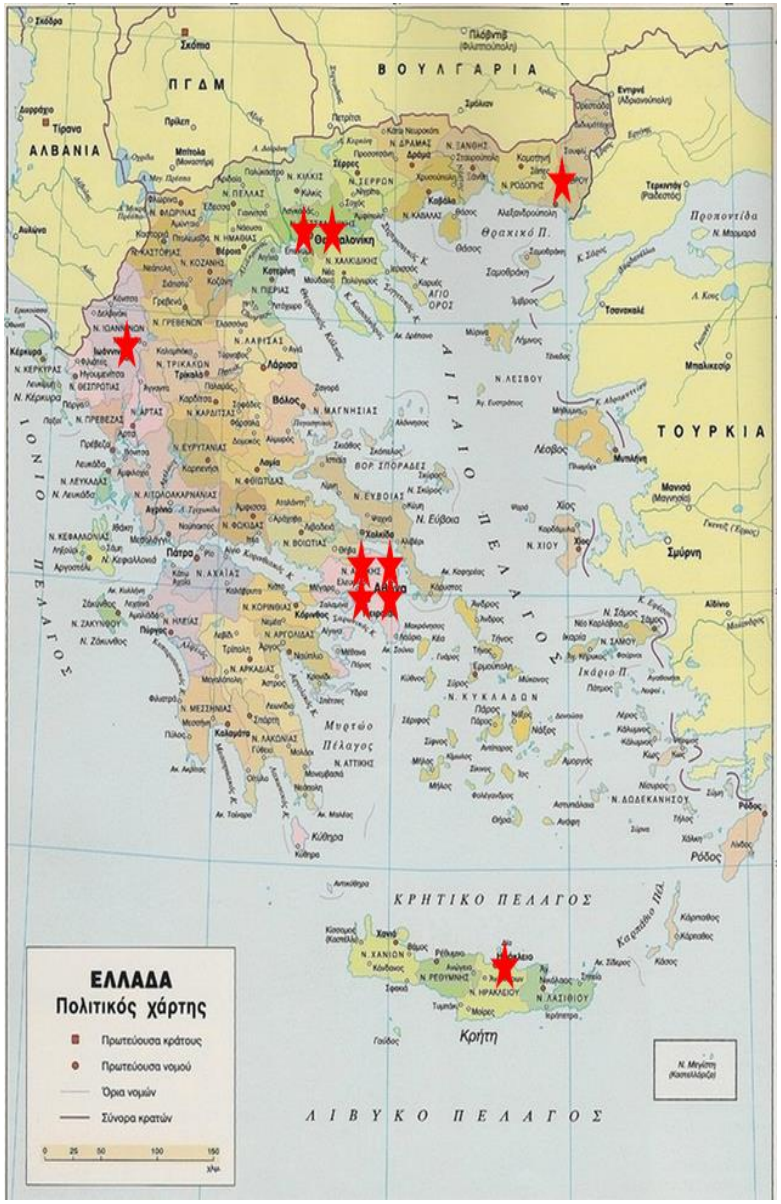
Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Greek Pulmonary Hypertension Registry Expert Centers

Greek PAHTool Registry

9 expert centers in Greece

1. Cardiolody Department, AHEPA University Hospital, Thessaloniki
2. Multidisciplinary Pulmonary Hypertension Service, Attiko General Hospital, Athens
3. Cardiology- Pediatric Cardiology Department, Onassis Cardiac Surgery Center, Athens
4. Cardiology Department, Mediterraneo Hospital, Glifada, Athens
5. Respiratory Failure Unit, Papanikolaou General Hospital, Thessaloniki
6. Pulmonary Department, PAGNI, Irakleio, Crete
7. Cardiology Department, Hippokrateio General Hospital, Athens
8. Cardiology Department, Democritus University of Thrace, Alexandroupolis
9. 2nd Cardiology Department, Ioannina University Hospital



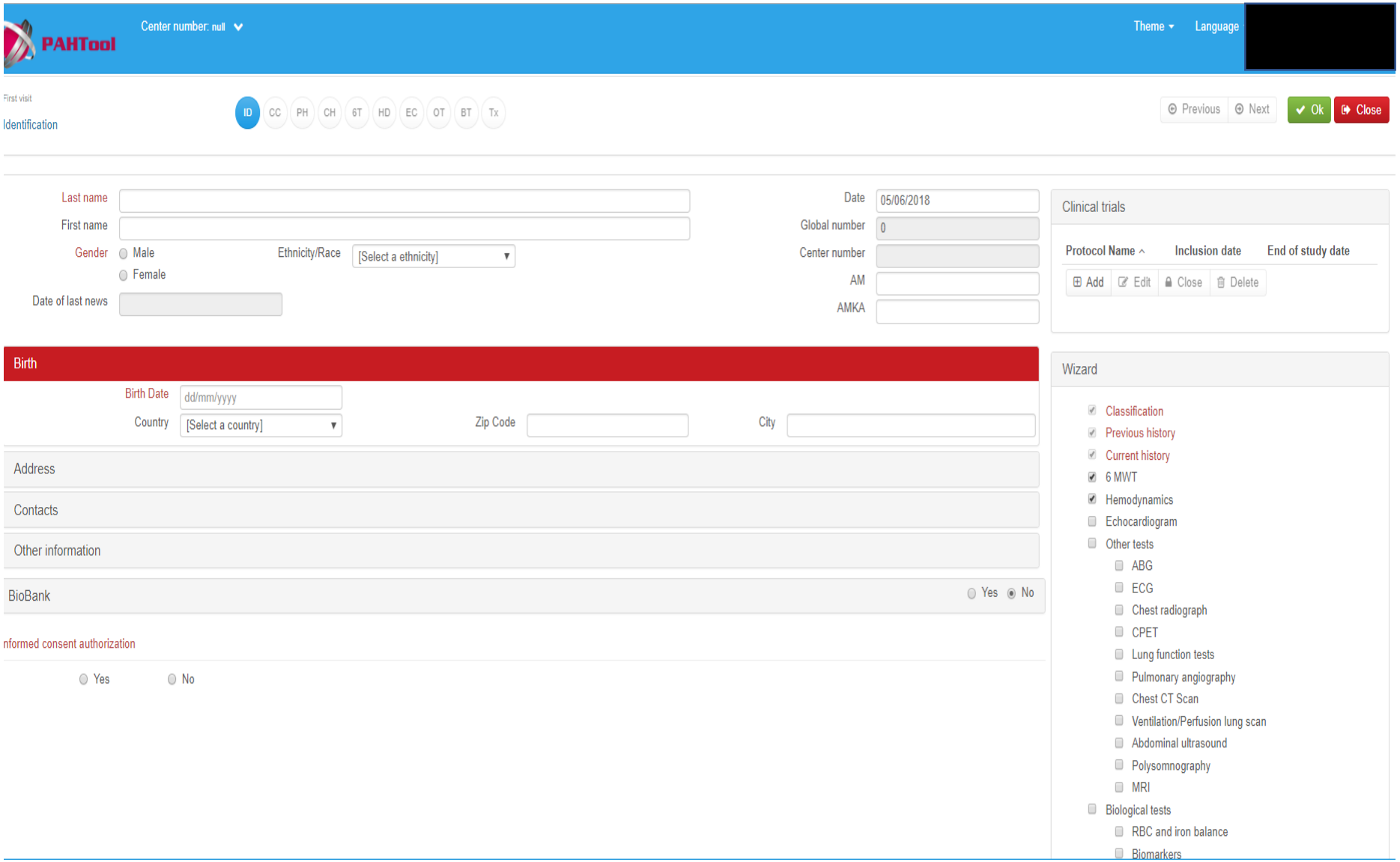
Greek Pulmonary Hypertension Registry Data Management

Greek PAHTool Registry

- ✓ **Retrospective and prospective (starting from 2015) data collection**
  - PH diagnosis, classification, symptoms, comorbidities, diagnostic procedures and treatment
  - Patients who had full work up, including an RHC
  - First visit and Follow up visits
- ✓ **PAH tool**
  - **IRB approval**
  - **Informed consent** from all participants
  - Internet based secure data entry
- ✓ **Data extraction and statistical analysis**

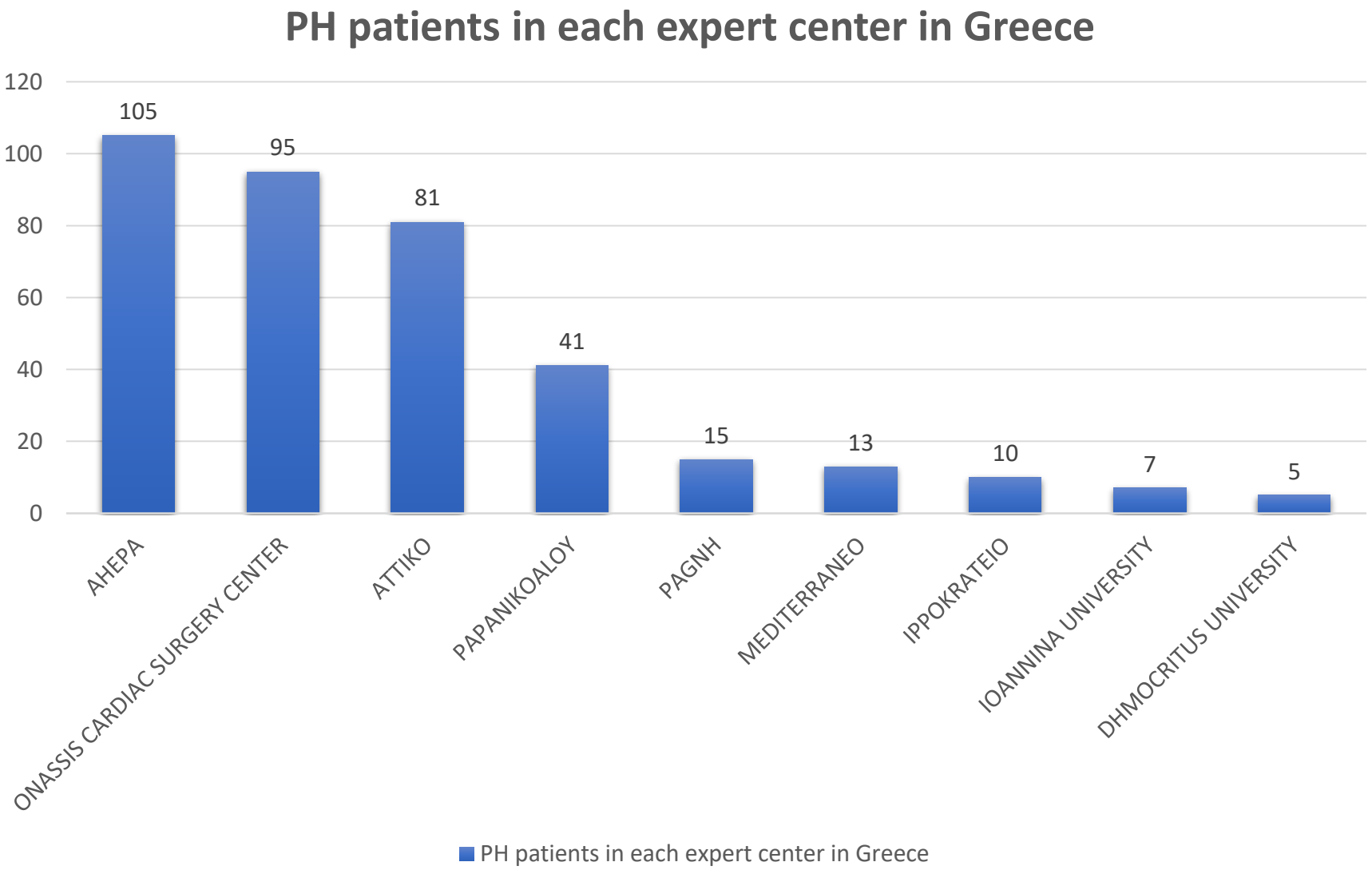
Greek Pulmonary Hypertension Registry Data Management

Greek PAHTool Registry



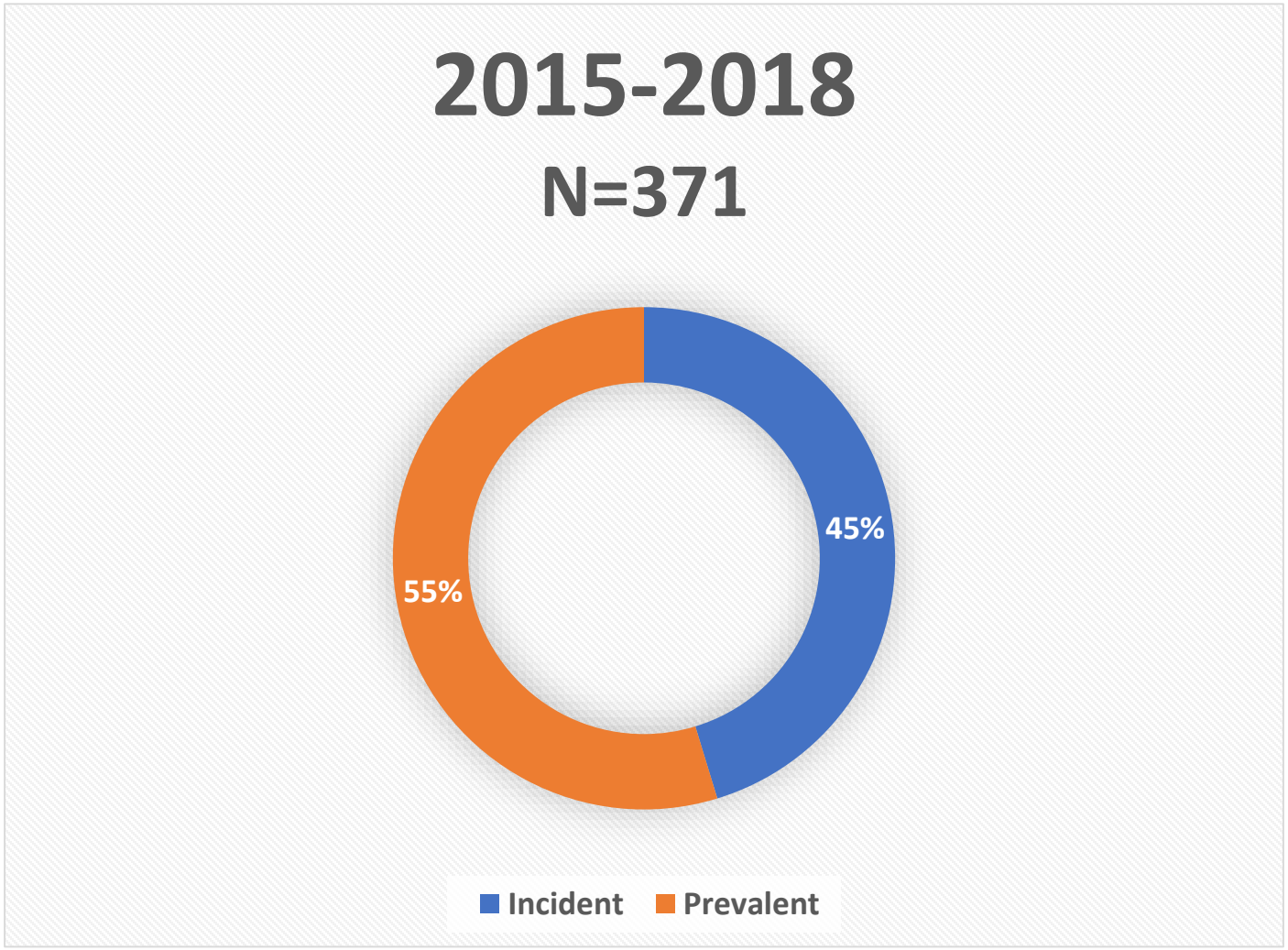
Greek Pulmonary Hypertension Registry
Center participation

Greek PAHTool Registry



Greek Pulmonary Hypertension Registry Demographics

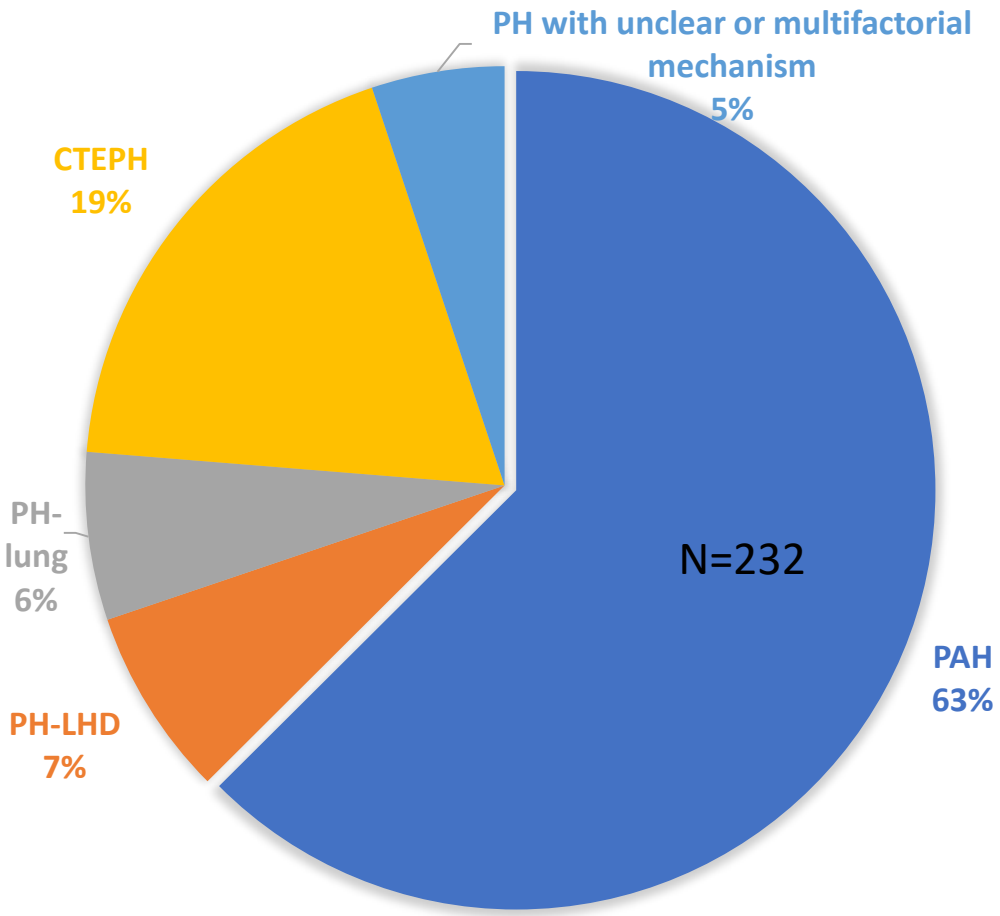
Greek PAHTool Registry



Greek Pulmonary Hypertension Registry
PH and PAH Classification

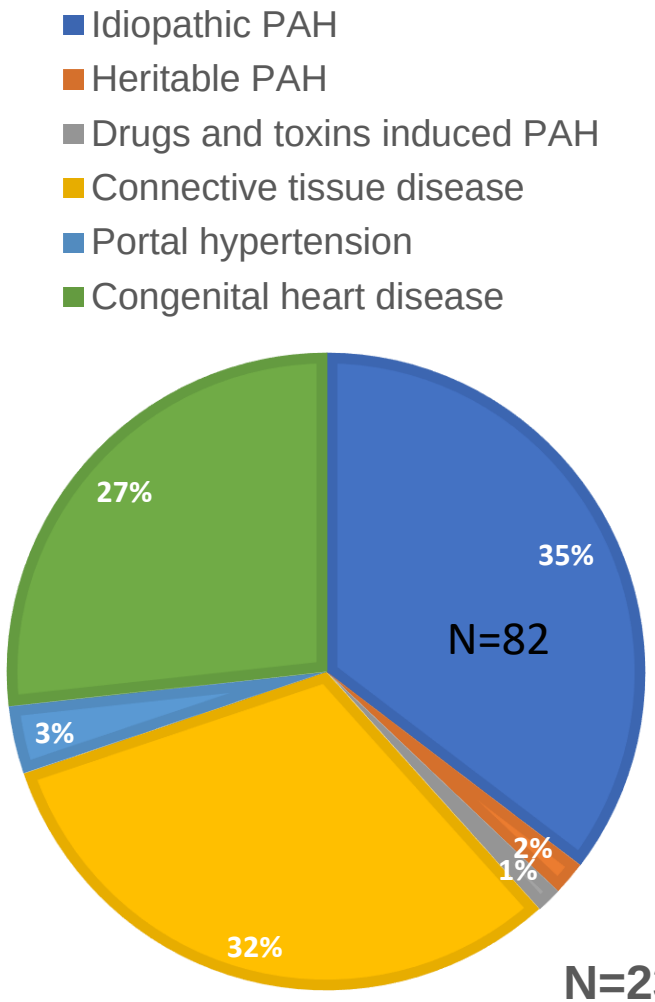
Greek PAHTool Registry

CLASSIFICATION OF PATIENTS WITH PULMONARY HYPERTENSION IN GREECE



N=371

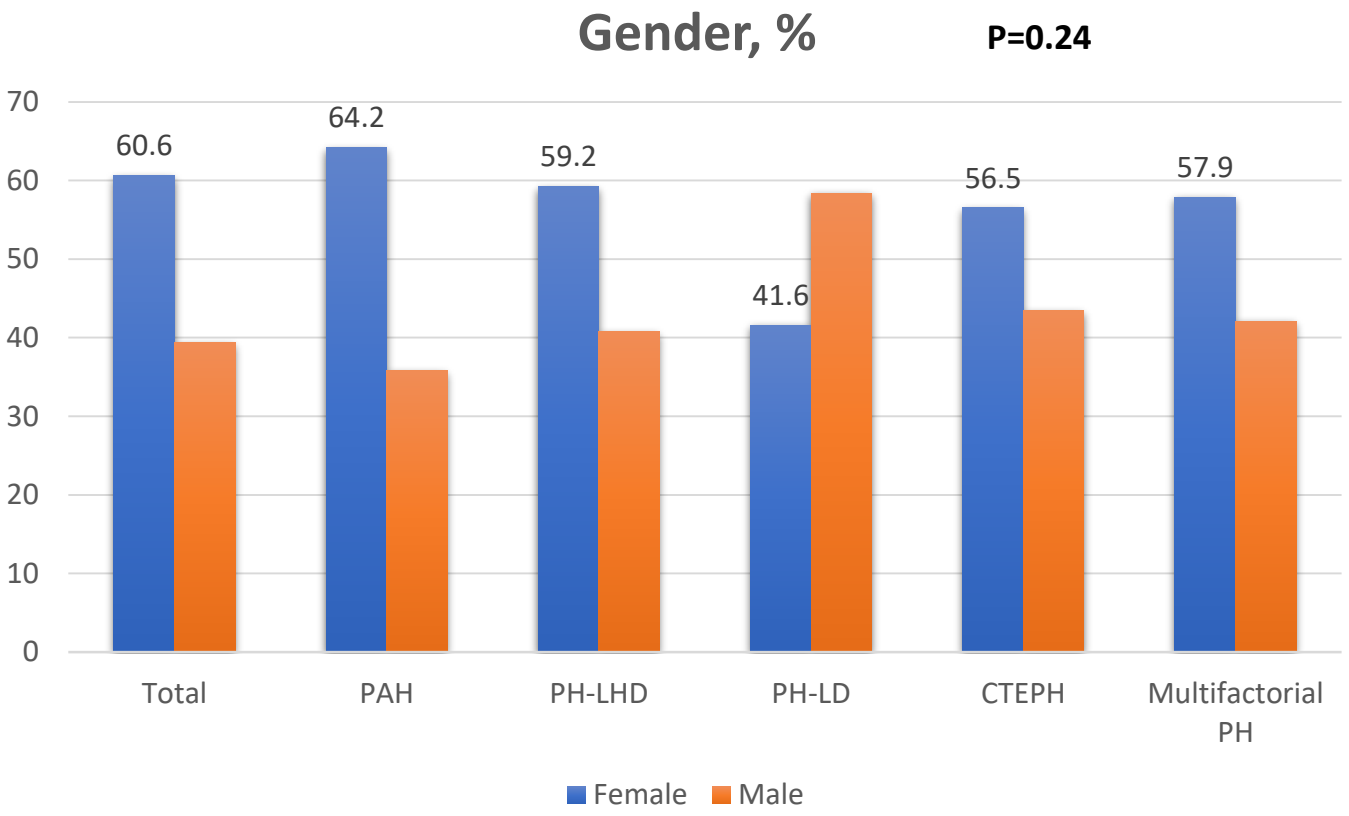
CLASSIFICATION OF PATIENTS WITH PAH IN GREECE



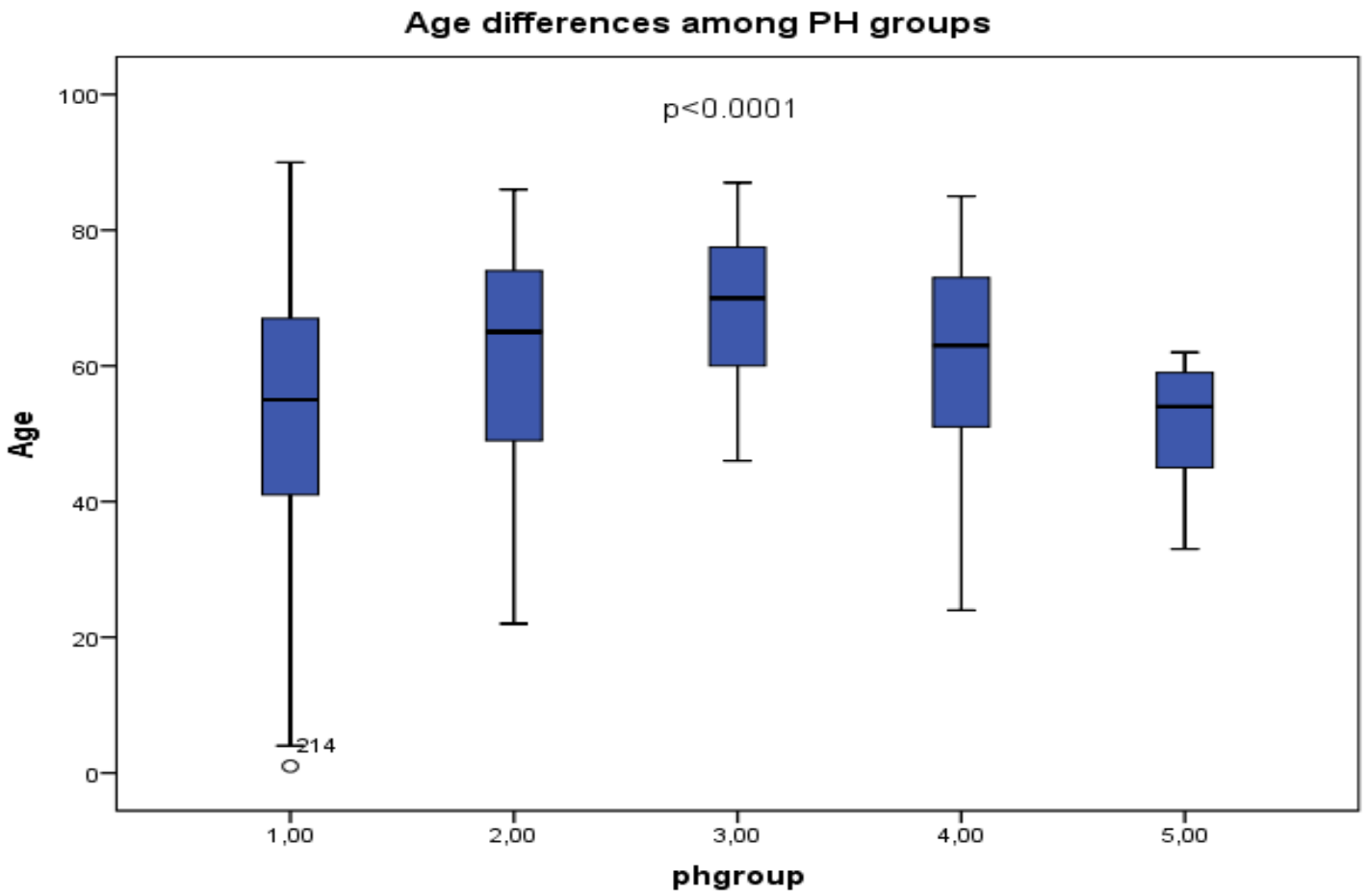
N=232

Greek Pulmonary Hypertension Registry Demographics

Greek PAHTool Registry



Greek Pulmonary Hypertension Registry Demographics



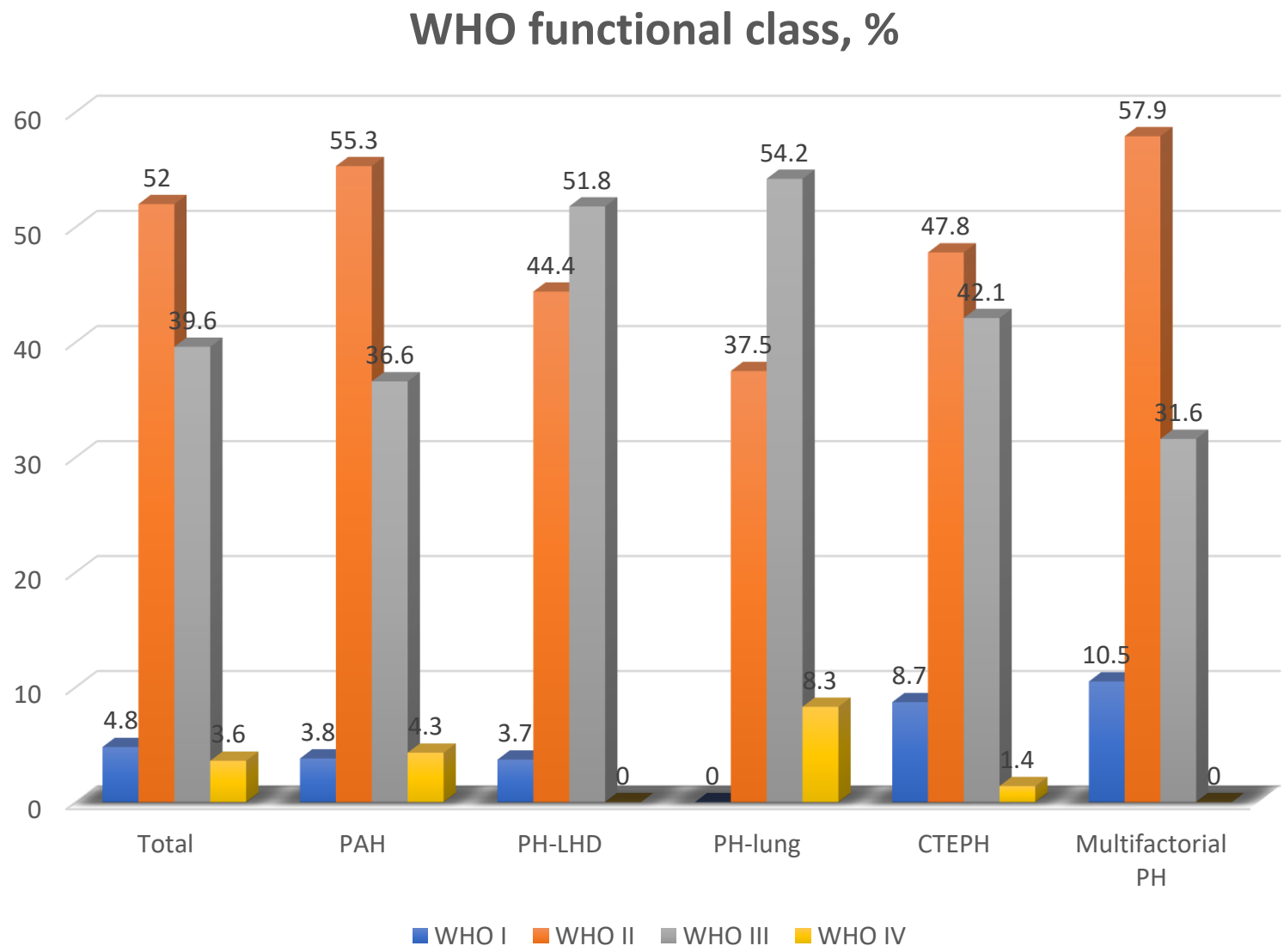
Greek Pulmonary Hypertension Registry Comorbidities

Greek PAHTool Registry

Comorbidity	Total N=371 n (%)	PAH N=232 n (%)	PH-LHD N=27 n (%)	PH-Lung N=24 n (%)	CTEPH N=69 n (%)	Multifactorial PH N=19 n (%)	P-value
AFib	14 (3.7)	8 (3.4)	4 (**14.8**)	1 (4.1)	1 (1.4)	-	0.052
Hypertension	107 (28.8)	58 (25)	8 (29.6)	10 (41.6)	26 (37.7)	5 (26.3)	0.24
Dyslipidemia	42 (11.3)	27 (11.6)	4 (14.8)	4 (16.7)	7 (10.2)	-	0.59
Diabetes	49 (13.2)	29 (12.5)	2 (7.4)	7 (29.1)	6 (8.7)	5 (26.3)	0.06
Obesity	97 (26.1)	59 (25.4)	6 (22.2)	13 (**54.2**)	18 (26)	1 (5.2)	**0.01**
CAD	30 (8)	16 (6.8)	5 (**18.5**)	5 (**20.8**)	2 (2.9)	2 (10.5)	**0.03**
COPD	48 (12.9)	20 (8.6)	5 (18.5)	12 (**50**)	9 (13)	2 (10.5)	**0.001**
Liver disease	15 (4)	12 (5)	0	1 (4.1)	1 (1.4)	1 (5.2)	0.66
Heamatological disease	36 (9.7)	10 (4.3)	3 (11.1)	1 (4.1)	14 (20.3)	8 (**42.1**)	**0.001**
Thyroid disease	55(14.8)	37 (16)	2 (7.4)	6 (25)	9 (13)	1 (5.2)	0.06
Renal disease	11 (3)	6 (2.6)	2 (7.4)	2 (8.3)	1 (1.4)	-	0.35

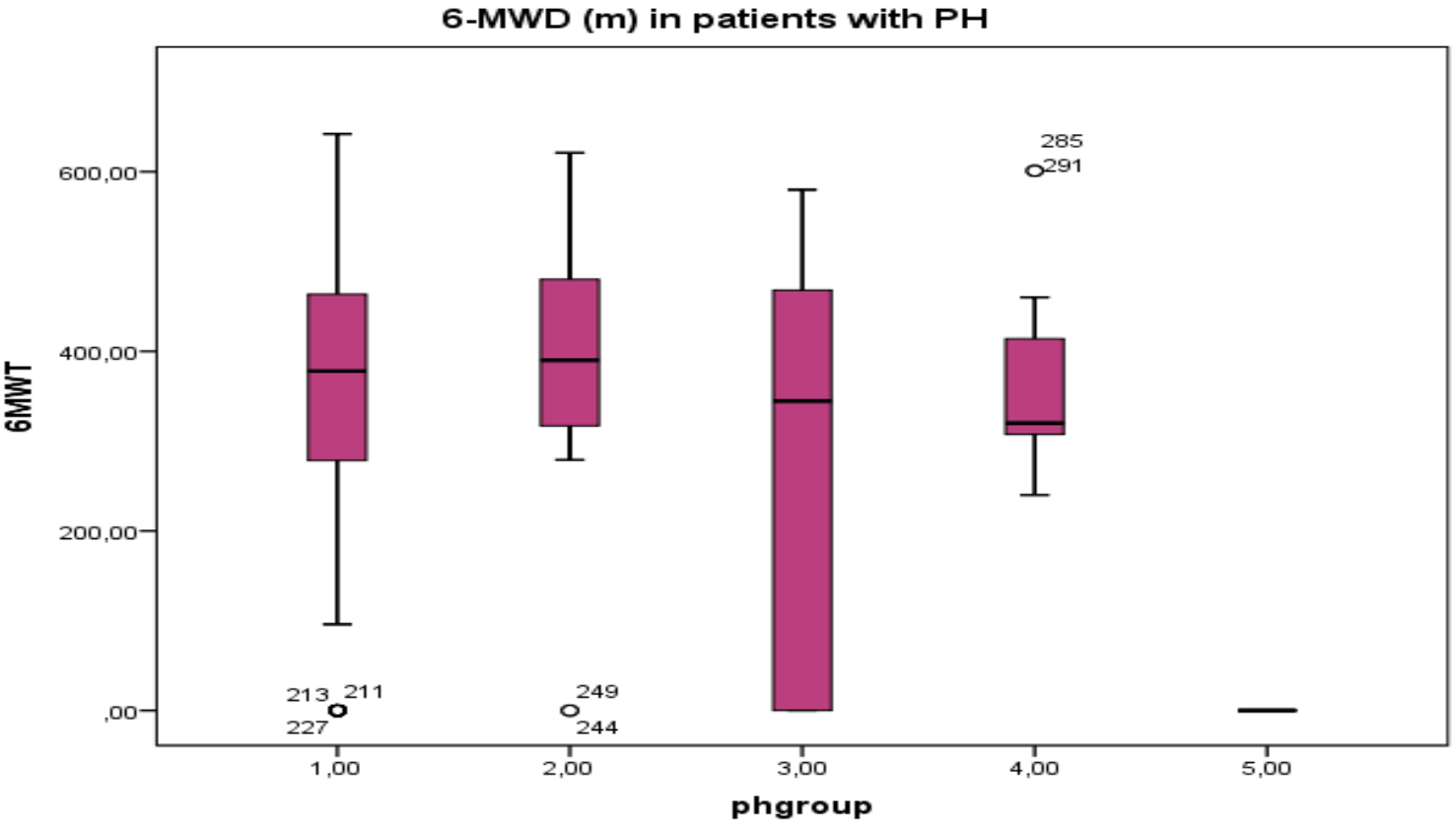
Greek Pulmonary Hypertension Registry
Initial functional status

Greek PAHTool Registry



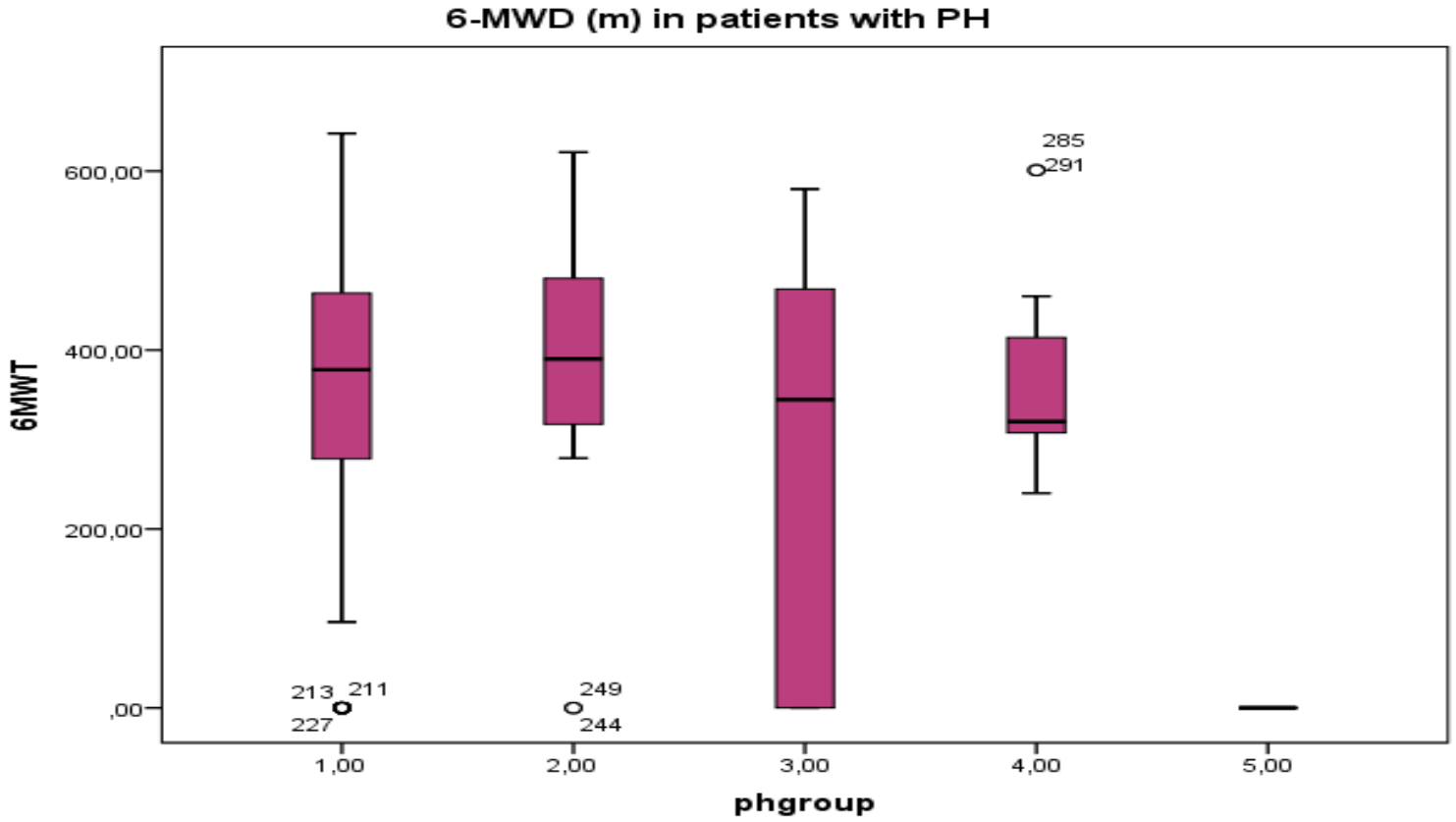
Greek Pulmonary Hypertension Registry
Initial functional status

Greek PAHTool Registry



Greek Pulmonary Hypertension Registry
Initial functional status

Greek PAHTool Registry



Functional parameters	Median (IQR)
6-MWD, (m) (n=254)	369 (176)
Nt-proBNP, (pg/mL) (n=36)	168 (333)

Greek Pulmonary Hypertension Registry
Right heart catheterization data

Greek PAHTool Registry

RHC data	Total N=371	PAH N=232	PH-LHD N=27	PH-Lung N=24	CTEPH N=69	Multifactorial PH N=19	P-value
RHC, n (%)	337 (90.8)	209 (90.1)	25 (92.6)	22 (91.7)	62 (91.3)	18 (94.7)	-
RAP, mmHg	8 (6)	8 (6)	11 (7)	8.5 (6.75)	6 (5.25)	7 (6)	**0.0001**
mPAP, mmHg	43 (18)	44 (20.5)	42 (12.5)	39 (17.5)	43 (15)	35 (13)	0.18
PAWP, mmHg	11 (5)	11 (5)	24.5 (12.8)	12 (4)	10 (4)	12 (5)	**0.0001**
CO, L/min	4.2 (1.7)	4.2 (1.7)	4.0 (2.5)	4.0 (1.1)	4.4 (1.6)	5.2 (2.5)	0.22
CI, L/min/m2	2.4 (0.9)	2.5 (0.9)	2.1 (1.1)	2.2 (0.9)	2.4 (0.9)	2.9 (0.6)	**0.02**
PVR, WU	6.8 (5.8)	8 (6.3)	4.1 (3.5)	6.5 (6.2)	6.6 (4.7)	4.9 (4.3)	**0.0001**
SVO2, %	69 (11)	70.2 (10)	64.4 (17)	69.2 (5)	67 (12)	67.7 (21)	0.01

All values are expressed as **median (IQR).**

Greek Pulmonary Hypertension Registry Echocardiography

Greek PAHTool Registry

Echocardiography	Median (IQR)
LVEF, % (n=194)	60 (5.25)
RVEDD, mm (n=74)	34 (12.2)
TAPSE, mm (n=140)	19 (7)
TR Vmax, m/s, (n=76)	3.75 (1)
RVSP, mmHg (n=173)	70 (33)

Greek Pulmonary Hypertension Registry
Differences in PAH according to WHO class

Greek PAHTool Registry

PAH (N=232)	WHO I/II N=125	WHO III/IV N=107	P-value
Female, n (%)	81(64.8)	70(65.4)	0.9
Age, y	58 (19)	64 (18)	**0.002**
BMI, kg/m2	26.8 (7.9)	29 (8.8)	0.14
6-MWD, m	430 (120)	285 (254)	**0.001**
RHC			
RAP, mmHg	7 (4)	8 (7)	0.07
mPAP, mmHg	41.5 (19.7)	44.3 (14.5)	0.11
CO, L/min	4.8 (2.3)	4.0 (1.6)	**0.01**
CI, L/min/m2	2.8 (1.1)	2.2 (1.1)	**0.001**
PVR, WU	6.2 (5.1)	7.4 (6.1)	**0.03**
SVO2, %	70.9 (9)	66.0 (10)	**0.001**
Echocardiography			
RVSP, mmHg	61.0 (34.0)	74.5 (32.9)	**0.001**

All values are expressed as **median (IQR).**

European Heart Journal
doi:10.1093/eurheartj/ehv317

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

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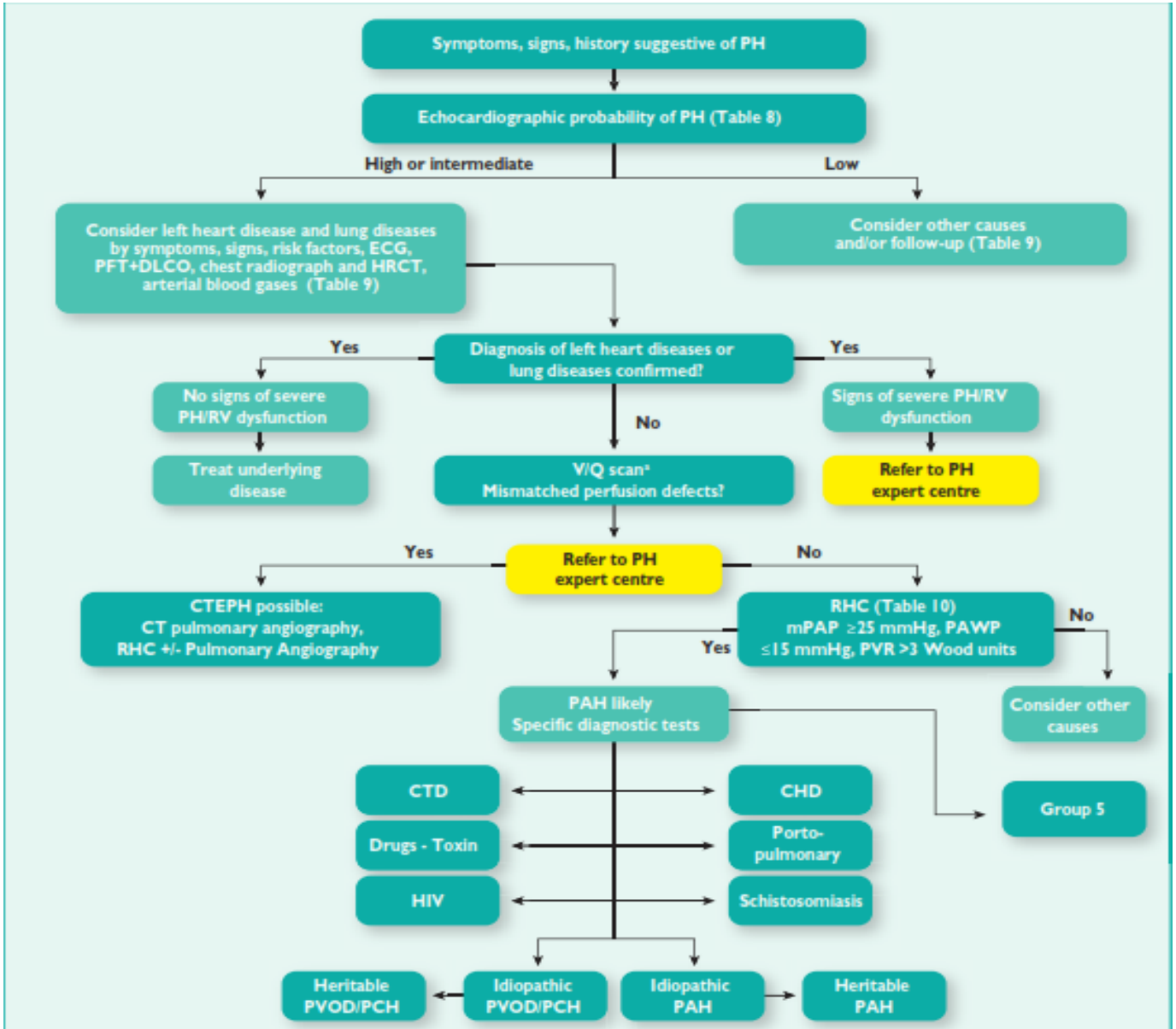


CHD = congenital heart diseases; CT = computed tomography; CTD = connective tissue disease; CTEPH = chronic thromboembolic pulmonary hypertension; DLCO = carbon monoxide diffusing capacity; ECG = electrocardiogram; HIV = Human immunodeficiency virus; HR-CT = high resolution CT; mPAP = mean pulmonary arterial pressure; PA = pulmonary angiography; PAH = pulmonary arterial hypertension; PAWP = pulmonary artery wedge pressure; PFT = pulmonary function tests; PH = pulmonary hypertension; PVOD/PCH = pulmonary veno-occlusive disease or pulmonary capillary hemangiomathosis; PVR = pulmonary vascular resistance; RHC = right heart catheterisation; RV = right ventricular; V/Q = ventilation/perfusion.

*CT pulmonary angiography alone may miss diagnosis of chronic thromboembolic pulmonary hypertension.

Pulmonary Hypertension Registries(I)

Table 1 Patient Demographics and Disease Characteristics at Enrollment

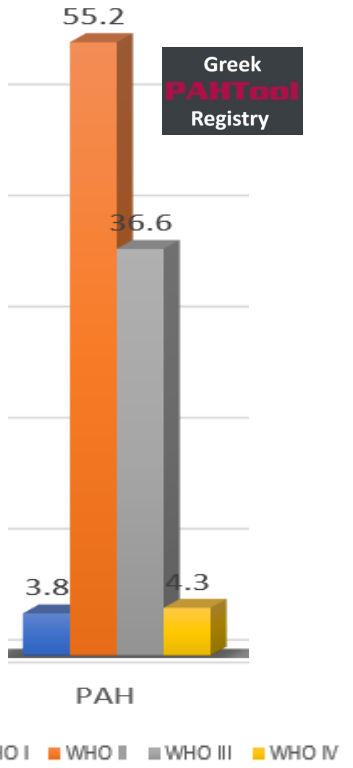
Characteristic	Serial risk assessment cohort (N = 2,529)[a]
Age, mean ± SD years	52.6 ± 14.3
Female, No. (%)	2,024 (80.0)
Newly diagnosed, No. (%)	666 (26.3)
WHO group, No. (%)	
Idiopathic PAH	1,191 (47.1)
Familial PAH	71 (2.8)
Associated PAH	
Congenital heart disease	243 (9.6)
Connective tissue disease	644 (25.5)
Portopulmonary hypertension	138 (5.5)
Other	242 (9.6)
Renal insufficiency, No. (%)	92 (3.6)
NYHA Functional Class, No. (%)	2,328 (100.0)
I	176 (7.6)
II	853 (36.6)
III	1,175 (50.5)
IV	124 (5.3)
Systolic blood pressure, mean ± SD mm Hg	(n = 2,458) 118 ± 17.4
Heart rate, mean ± SD beats/min	(n = 2,439) 82.7 ± 14.5
6-minute walk distance, mean ± SD m	(n = 2,051) 369 ± 123
BNP, mean ± SD pg/ml	(n = 1,213) 266 ± 464
Median (interquartile range) pg/ml	115 (42–299)
N-terminal pro-BNP, mean ± SD, pg/ml	(n = 261) 1,937 ± 6,753
Median (interquartile range) pg/ml	547 (148–1,620)
Pericardial effusion, No. (%)	502/1,990 (25.2)
D_{LCO}, mean ± SD % predicted	(n = 1,540) 59.6 ± 22.8
mRAP ≤1 year of enrollment, mean ± SD (mm Hg)	(n = 1,282) 9.1 ± 5.4
Pulmonary vascular resistance, mean ± SD Wood units	(n = 2,404) 10.0 ± 6.8

BNP, brain natriuretic peptide; D_{LCO}, diffusion capacity of the lung for carbon monoxide; mRAP, mean right atrial pressure; NYHA, New York Heart Association; PAH, pulmonary arterial hypertension; SD, standard deviation; WHO, World Health Organization.

[a] N = 2,529, unless otherwise noted. Information on disease characteristics may not be available for all patients at the time of enrollment.

Prognostic implications of serial risk score assessments in patients with pulmonary arterial hypertension: A Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL) analysis

Raymond L. Benza, MD,[a] Dave P. Miller, MS,[b] Aimee J. Foreman, MA,[b] Adaani E. Frost, MD,[c] David B. Badesch, MD,[d] Wade W. Benton, PharmD,[e] and Michael D. McGoon, MD[f]



Pulmonary Hypertension Registries(II)

Eur Respir J 2012; 39: 945–955
DOI: 10.1183/09031936.00078411
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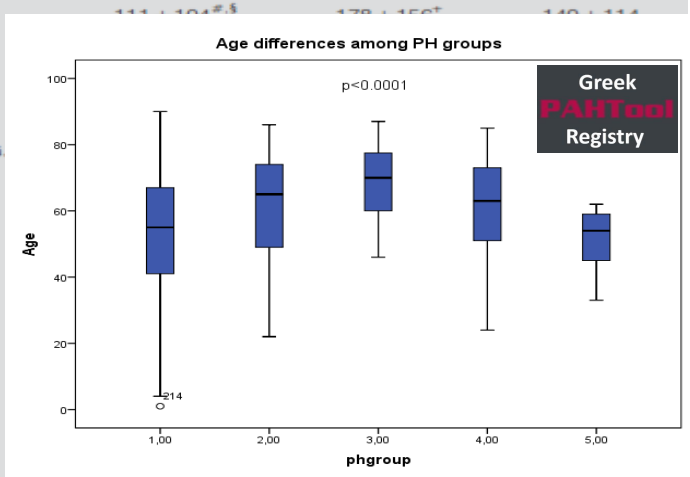
ASPIRE registry: Assessing the Spectrum of Pulmonary hypertension Identified at a REferral centre

J. Hurdman*, R. Condliffe*,#, C.A. Elliot*,#, C. Davies¶, C. Hill¶, J.M. Wild#,+, D. Capener+, P. Sephton*, N. Hamilton*, I.J. Armstrong*, C. Billings§, A. Lawrie#,/, I. Sabroe*,#,**, M. Akil##, L. O'Toole¶ and D.G. Kiely*,#

Sheffield, UK
2001-2010

TABLE 1 Baseline characteristics for the five diagnostic groups

	Overall	Group 1 PAH	Group 2 PH-LHD	Group 3 PH-lung	Group 4 CTEPH	Group 5 PH-misc
Subjects n	1344	598	157	178	242	32
Age yrs	59±17	54±18¶,+,§	69±10#,§,/	66±11#,§,/	61±15#,¶,+	57±12¶,+
Female	62	70	69	38	54	59
WHO III/IV	65/16	64/14	66/6	62/27	70/17	66/19
ISWD m	169±149	189±156+	154±144			
$\bar{P}_{ra}$ mmHg	11±6	10±6¶	15±6#,+,§,/			
$\bar{P}_{pa}$ mmHg	45±12	48±13¶,+	41±11#,§			
CI L·min^{-1}·m^{-2}	2.7±0.9	2.7±0.9¶	2.9±0.7#,§			
P_{pcw} mmHg	13±7	9±3¶,+,§	24±5#,+,§,/			
PVR dyn·s·cm^{-5}	654±430	780±449¶,+	289±225#,+,§			
Sv,O_2 %	63±9	63±9§	64±8§			
FEV_1 % pred	73±22	77±20¶,+,§	67±20#,+,§			
FVC % pred	85±24	88±22¶,+	76±22#,§			
$T_{L,CO}$ % pred	54±22	55±23¶,+,§	62±17+,/			
Maximal therapy						
None	28	11	87			
CCB	1	2	1			
Oral monoRx	46	49	12			
Oral comb	8	13	0			
Prostanoid monoRx	8	10	0			
Prostanoid comb	9	15	0			



Data are presented as mean±SD or %, unless otherwise stated. PAH: pulmonary arterial hypertension; PH-LHD: pulmonary hypertension associated with left heart disease; PH-lung: pulmonary hypertension associated with lung disease; CTEPH: chronic thromboembolic pulmonary hypertension; PH-misc: miscellaneous pulmonary hypertension; WHO: World Health Organization functional class; ISWD: incremental shuttle walking distance; $\bar{P}_{ra}$: mean right atrial pressure; $\bar{P}_{pa}$: mean pulmonary artery pressure; CI: cardiac index; P_{pcw}: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance; Sv,O_2: mixed venous oxygen saturation; FEV_1: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; $T_{L,CO}$: transfer factor of the lung for carbon monoxide; CCB: calcium-channel blocker; oral monoRx: oral monotherapy; oral comb: combination phosphodiesterase-5 inhibitor and endothelin receptor antagonist; prostanoid monoRx: prostanoid monotherapy; prostanoid comb: prostanoid in combination with any other targeted therapy. #: $p<0.05$ in comparison to group 1; ¶: $p<0.05$ in comparison to group 2; +: $p<0.05$ in comparison to group 3; §: $p<0.05$ in comparison to group 4; /: $p<0.05$ in comparison to group 5.

Pulmonary Hypertension Registries(III)

Pulmonary Arterial Hypertension in France
Results from a National Registry

Marc Humbert, Olivier Sitbon, Ari Chaouat, Michèle Bertocchi, Gilbert Habib, Virginie Gressin, Azzedine Yaici, Emmanuel Weitzenblum, Jean-François Cordier, François Chabot, Claire Dromer, Christophe Pison, Martine Reynaud-Gaubert, Alain Haloun, Marcel Laurent, Eric Hachulla, and Gérald Simonneau

Service de Pneumologie, Centre des Maladies Vasculaires Pulmonaires, Hôpital Antoin
Université Paris-Sud, Clamart, France; Service de Pneumologie, Hôpital Hautepierre, S
Lyon; Service de Cardiologie, Hôpital de la Timone; Service de Pneumologie, Hôpital
France, Paris; Service de Pneumologie, Hôpital de Brabois, Vandoeuvre-les-Nancy; Ser
Bordeaux; Département Médecine Aiguë Spécialisée, Hôpital Michallon, Grenoble; Se
Service de Cardiologie, Hôpital Pontchaillou, Rennes; and Service de Médecine Intern

RAP, mmHg	7 (4)	8 (7)
mPAP, mmHg	41.5 (19.7)	44.3 (14.5)
CO, L/min	4.8 (2.3)	4.0 (1.6)
CI, L/min/m2	2.8 (1.1)	2.2 (1.1)
PVR, WU	6.2 (5.1)	7.4 (6.1)
SVO2, %	70.9 (9)	66.0 (10)

Greek PAHTool Registry

TABLE 2. SIX-MINUTE WALK DISTANCE AND HEMODYNAMIC PARA
NEW YORK HEART ASSOCIATION FUNCTIONAL CLASS AT DIAGNOS
ARTERIAL HYPERTENSION

	NYHA I–II	NYHA III	NYHA IV	p Value
6-min walk test				
n	134	359	55	
Distance, m	415 ± 86	319 ± 92	192 ± 96	< 0.0001
Percentage of reference values				
Male patients	68.1 ± 14.1	58.8 ± 14.7	36.5 ± 17.9	< 0.0001
Female patients	67.9 ± 22.2	53.9 ± 16.4	34.1 ± 15.8	< 0.0001
Hemodynamic parameters, n	162	405	77	
RAP, mm Hg	6 ± 4	9 ± 5	11 ± 7	< 0.0001
mPAP, mm Hg	50 ± 17	56 ± 15	56 ± 13	0.0002
PAWP, mm Hg	8 ± 3	8 ± 3	8 ± 4	0.75
Cardiac index, L/min/m²	2.9 ± 0.9	2.4 ± 0.7	2.1 ± 0.8	< 0.0001
Sv_{O_2}, %	67 ± 8	62 ± 8	54 ± 9	< 0.0001
PVRI, mm Hg/L/min/m²	15.8 ± 9.7	21.5 ± 9.8	25.1 ± 10.1	< 0.0001

For definition of abbreviations, *see* Table 1.
Data expressed as mean ± SD.

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Greek Pulmonary Hypertension Registry
Key messages

Greek PAHTool Registry

- 371 patients with PH were recorded, with PAH as the most frequent cause.
- Nearly half patients were newly diagnosed.
- Female sex was the dominant sex among all groups except from group 3.
- The majority of patients (60%) had no or mild symptoms.
- The most common comorbidities were hypertension and obesity.

Greek Pulmonary Hypertension Registry
Key messages

Greek PAHTool Registry

- There were significant differences in hemodynamics between PH groups.
- PAH patients with no or mild symptoms (I/II), were of younger age, covered a greater distance in 6MWT and had a higher CO, CI, SVO2% and a lower PVR in RHC than more symptomatic ones (WHO III/IV).
- Based on symptoms, FC and hemodynamics, we can hypothesize that PH patients in Greece are recruited in the registry at an earlier stage, compared to other registries
    - Strong hospital affiliations to expert centers
    - Wide spread use of echocardiogram
    - Reimbursement issues
- We provide for the first time reliable multicenter data of PH patients in Greece