

United States Pulmonary Hypertension Scientific Registry

Baseline Characteristics

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e-Appendix 1. List of USPHSR participating Pulmonary Hypertension centers, their location, institutional review board (IRB) committee name, and project approval number.

Site Name	Location	IRB Name	Number	Type of Number
University of Colorado	Aurora, CO	University Research, University of Colorado Denver, Colorado Multiple Institutional Review Board	PAM004-1	Submission ID
Allegheny General Hospital	Pittsburgh, PA	Allegheny Health Network Research Institute	RC-6270	Not Applicable
Mayo Clinic, Jacksonville	Jacksonville, FL	Mayo Clinic Institutional Review Board	16007417	Application Number
Washington University	St. Louis, MO	Washington University in St. Louis Human Research Protection Office	201612118	IRB ID Number
University of Arizona	Tucson, AZ	The University of Arizona Human Subjects Protection Program	1710951702	Protocol Number
Intermountain Medical Center	Salt Lake City, UT	Intermountain Healthcare Research Institutional Review Board	1050403	IRB Number
University of Cincinnati	Cincinnati, OH	University of Cincinnati Institutional Review Board	2017-4874	Study ID
Boston University	Boston, MA	Boston Medical, Boston University, Office of the Institutional Review Board	H-35388	IRB Number
Duke University	Durham, NC	Duke Medicine Institutional Review Board for Clinical Investigations	Pro00074764	Protocol ID
Mayo Clinic, Rochester	Rochester, MN	Mayo Clinic Institutional Review Board	16-006159	Application Number
Tufts University	Boston, MA	Tufts Health Sciences, Health Sciences Campus Institutional Review Board	12772	IRB Number
Vanderbilt University	Nashville, TN	Vanderbilt University Institutional Review Board	170116	IRB Number
Houston Methodist Hospital	Houston, TX	Houston Methodist Institutional Review Board	Pro00015112	Protocol ID
University of Pittsburgh	Pittsburgh, PA	University of Pittsburgh Institutional Review Board	PRO16110373	IRB Number
University of Rochester	Rochester, NY	University of Rochester Office for Human Subject Protection Research Subjects Review Board	RSRB00063320	RSRB

e-Table 1. Comorbidities by WHO Group 1 and APAH sub-group at enrollment in PAH Biobank.

Comorbid Condition	All Patients	IPAH	FPAH	PVOD/PCH	APAH (all)	CTD	CHD	PoPH	Drugs/toxins
N	499	218	22	3	256	171	30	22	24
Obesity	104 (20.8)	52 (23.9)	5 (22.7)	1 (33.3)	46 (18)	29 (17)	3 (10)	5 (22.7)	5 (20.8)
Cancer (Non-Skin)	21 (4.2)	11 (5)	0	0	10 (3.9)	8 (4.7)	0	0	2 (8.3)
Ischemic Cardiovascular Event	43 (8.6)	10 (4.6)	2 (9.1)	0	31 (12.1)	20 (11.7)	3 (10)	4 (18.2)	3 (12.5)
Diabetes	75 (15)	29 (13.3)	4 (18.2)	0	42 (16.4)	27 (15.8)	1 (3.3)	7 (31.8)	6 (25)
Hypertension	185 (37.1)	82 (37.6)	2 (9.1)	1 (33.3)	100 (39.1)	73 (42.7)	7 (23.3)	7 (31.8)	11 (45.8)
Cardiomyopathy	9 (1.8)	5 (2.3)	0	0	4 (1.6)	2 (1.2)	0	0	2 (8.3)
Valvular Heart Disease	25 (5)	9 (4.1)	0	0	16 (6.2)	9 (5.3)	4 (13.3)	1 (4.5)	2 (8.3)
Scleroderma	115 (23)	2 (0.9)	0	0	113 (44.1)	113 (66.1)	0	0	0
Rheumatoid Arthritis	24 (4.8)	1 (0.5)	0	0	23 (9.0)	20 (11.7)	1 (3.3)	1 (4.5)	1 (4.2)
Lupus	22 (4.4)	1 (0.5)	0	0	21 (8.2)	21 (12.3)	0	0	0
Other Collagen Vascular Disease	15 (3)	0	0	0	15 (5.9)	14 (8.2)	1 (3.3)	0	0
Deep Vein Thrombosis	16 (3.2)	7 (3.2)	0	0	9 (3.5)	7 (4.1)	0	0	1 (4.2)
Pulmonary Embolism	18 (3.6)	10 (4.6)	0	1 (33.3)	7 (2.7)	5 (2.9)	2 (6.7)	0	0
Hypothyroidism	90 (18)	32 (14.7)	5 (22.7)	1 (33.3)	52 (20.3)	45 (26.3)	1 (3.3)	2 (9.1)	3 (12.5)
Hyperthyroidism	12 (2.4)	4 (1.8)	1 (4.5)	0	7 (2.7)	7 (4.1)	0	0	0
Renal Insufficiency	29 (5.8)	15 (6.9)	0	0	14 (5.5)	7 (4.1)	1 (3.3)	3 (13.6)	3 (12.5)
COPD	43 (8.6)	18 (8.3)	0	1 (33.3)	24 (9.4)	11 (6.4)	5 (16.7)	3 (13.6)	4 (16.7)
ILD/IPF	47 (9.4)	4 (1.8)	0	2 (66.7)	41 (16)	41 (24)	0	0	0
Cirrhosis	29 (5.8)	2 (0.9)	0	0	27 (10.5)	3 (1.8)	1 (3.3)	20 (90.9)	1 (4.2)
Clinical Depression	57 (11.4)	26 (11.9)	1 (4.5)	0	30 (11.7)	14 (8.2)	5 (16.7)	4 (18.2)	4 (16.7)
Hyperlipidemia	48 (9.6)	20 (9.2)	0	0	28 (10.9)	22 (12.9)	2 (6.7)	1 (4.5)	3 (12.5)
Asthma	33 (6.6)	15 (6.9)	2 (9.1)	0	16 (6.2)	9 (5.3)	4 (13.3)	1 (4.5)	1 (4.2)

Values presented as No. (%) unless otherwise noted
 See Tables 1a and 1b for expansion of abbreviations
 COPD – Chronic obstructive pulmonary disease
 ILD/IPF – Interstitial lung disease/Idiopathic pulmonary fibrosis

e-Table 2. Concomitant medications by WHO Group 1 and APAH subgroup at enrollment in PAH Biobank.

Concomitant medications	All Patients	IPAH	FPAH	PVOD/ PCH	APAH (all)	APAH sub-groups			
						CTD	CHD	PoPH	Drugs/ toxins
N	499	218	22	3	256	171	30	22	24
Warfarin	97 (19.4)	63 (28.9)	8 (36.4)	0	26 (10.2)	21 (12.3)	2 (6.7)	0	3 (12.5)
CCB	67 (13.4)	23 (10.6)	0	1 (33.3)	43 (16.8)	36 (21.1)	2 (6.7)	2 (9.1)	3 (12.5)
Long-acting nitrate	2 (0.4)	0	0	0	2 (0.8)	2 (1.2)	0	0	0
ACE Inhibitor	51 (10.2)	21 (9.6)	0	0	30 (11.7)	21 (12.3)	2 (6.7)	1 (4.5)	5 (20.8)
Beta Blocker	97 (19.4)	44 (20.2)	2 (9.1)	0	51 (19.9)	31 (18.1)	9 (30)	7 (31.8)	3 (12.5)
Heparin	2 (0.4)	1 (0.5)	0	0	1 (0.4)	1 (0.6)	0	0	0
Low molecular weight heparin	3 (0.6)	1 (0.5)	0	0	2 (0.8)	1 (0.6)	0	1 (4.5)	0
Direct oral anticoagulant	19 (3.8)	6 (2.8)	0	2 (66.7)	11 (4.3)	8 (4.7)	3 (10)	0	0
Corticosteroid	91 (18.2)	22 (10.1)	3 (13.6)	0	66 (25.8)	58 (33.9)	2 (6.7)	4 (18.2)	1 (4.2)
Aspirin	141 (28.3)	53 (24.3)	3 (13.6)	0	85 (33.2)	69 (40.4)	5 (16.7)	5 (22.7)	5 (20.8)
Other Anti Inflammatory	41 (8.2)	16 (7.3)	2 (9.1)	0	23 (9)	11 (6.4)	4 (13.3)	1 (4.5)	5 (20.8)
NSAID	51 (10.2)	20 (9.2)	1 (4.5)	0	30 (11.7)	18 (10.5)	3 (10)	1 (4.5)	5 (20.8)
Monoclonal Antibodies	1 (0.2)	0	0	0	1 (0.4)	0	1 (3.3)	0	0
Clopidogrel	11 (2.2)	5 (2.3)	0	0	6 (2.3)	5 (2.9)	1 (3.3)	0	0
Diuretic	352 (70.5)	153 (70.2)	15 (68.2)	2 (66.7)	182 (71.1)	123 (71.9)	16 (53.5)	19 (86.4)	21 (87.5)
Oxygen	169 (33.9)	71 (32.6)	3 (13.6)	2 (66.7)	93 (36.3)	62 (36.3)	13 (43.3)	5 (22.7)	8 (33.3)
Digoxin	59 (11.8)	25 (11.5)	5 (22.7)	0	29 (11.3)	23 (13.5)	2 (6.7)	1 (4.5)	3 (4.3)
Statin	122 (24.4)	59 (27.1)	1 (4.5)	0	62 (24.2)	51 (29.8)	3 (10)	3 (13.6)	4 (16.7)
SSRI	111 (22.2)	44 (20.2)	4 (18.2)	0	63 (24.6)	44 (25.7)	5 (16.7)	5 (22.7)	7 (29.2)
Synthetic Thyroid	102 (21)	36 (16.5)	4 (18.2)	1 (33.3)	64 (25)	55 (32.2)	2 (6.7)	2 (9.1)	3 (12.5)
Psychotropic drugs	55 (11)	24 (11.0)	4 (18.2)	2 (66.7)	25 (9.8)	14 (8.2)	8 (26.7)	1 (4.5)	2 (8.3)
Other Antidepressants	45 (9)	19 (8.7)	0	0	26 (10.2)	18 (10.5)	5 (16.7)	1 (4.5)	1 (4.2)
Immunosuppressive medications	73 (14.6)	6 (2.8)	0	1 (33.3)	66 (25.8)	59 (34.5)	2 (6.7)	5 (22.7)	0
Angiotensin receptor blockers	28 (5.6)	12 (5.5)	1 (4.5)	0	15 (5.9)	13 (7.6)	2 (6.7)	0	0
Potassium	114 (22.8)	52 (23.9)	7 (31.8)	1 (33.3)	54 (21.1)	40 (23.4)	4 (13.3)	3 (13.6)	6 (25)
Diabetes Medications	60 (12)	27 (12.4)	2 (9.1)	0	31 (12.1)	19 (11.1)	1 (3.3)	5 (22.7)	5 (20.8)
Other non-PH drug	339 (67.9)	149 (68.3)	13 (59.1)	3 (100)	174 (68)	121 (70.8)	18 (60)	17 (77.3)	13 (54.2)
None	12 (2.4)	8 (3.7)	1 (4.5)	0	3 (1.2)	0	1 (3.3)	1 (4.5)	0

Values presented as No. (%) unless otherwise noted

SSRI – selective serotonin reuptake inhibitor

NSAID – non-steroidal anti-inflammatory drug

CCB – calcium channel blocker

ACE – angiotensin converting enzyme See Tables 1a and 1b for expansion of abbreviations

e-Table 3. Environmental exposures in all USPHSR subjects (male and female) by WHO Group 1, includes anorexigens, soy, well water, and cigarette smoking.

Exposure	All Patients	IPAH	FPAH	PVOD/PCH	APAH (all-subgroups)
Patients, N	494	213	22	3	256
Ever taken Fen-Phen or Phentermine, N (%)	55 (11.4)	21 (10.1)	2 (9.1)	1 (33.3)	31 (12.5)
Ever taken other weight loss drugs, N (%)	84 (17.3)	39 (18.6)	4 (19)	0	41 (16.3)
Prescription, N (%)	24 (28.6)	9 (23.1)	1 (25)	0	14 (34.1)
Soy product consumption, N (%)	98 (19.8)	39 (18.6)	4 (19)	1 (33.3)	53 (20.7)
Soy product consumption duration, N (%)					
1 time per month	38 (38.8)	15 (37.5)	1 (25)	0	22 (41.5)
2 to 3 times per month	29 (29.6)	12 (30)	1 (25)	1 (100)	15 (28.3)
1 time per week	5 (5.1)	1 (2.5)	0	0	4 (7.5)
2 times per week	9 (9.2)	5 (12.5)	0	0	4 (7.5)
3 to 4 times per week	6 (6.1)	2 (5)	1 (25)	0	3 (5.7)
5 to 6 times per week	1 (1)	0	0	0	1 (1.9)
1 time per day	6 (6.1)	2 (5)	1 (25)	0	3 (5.7)
2 or more times per day	4 (4.1)	3 (7.5)	0	0	1 (1.9)
Use of well/spring water, N (%)	207 (41.9)	81 (39.1)	8 (36.4)	1 (33.3)	117 (47.2)
Duration of well/spring water use, N (%)					
Less than 1 year	9 (4.3)	2 (2.5)	0	0	7 (6)
1 to 5 years	27 (13)	8 (9.9)	2 (25)	0	17 (14.5)
5 to 10 years	39 (18.8)	14 (17.3)	1 (12.5)	1 (100)	23 (19.7)
Greater than 10 years	132 (63.8)	57 (70.4)	5 (62.5)	0	70 (59.8)
Current smoker, N (%)	20 (4.1)	7 (3.3)	1 (4.5)	0	12 (4.7)
Pack/years, mean ± SD	11.3 ± 11.7	9.1 ± 7.0	15 ± NA	-	12.1 ± 14.2
Smoking duration, N (%)					
Less than 1 year	3 (15)	0	0	-	3 (25)
2 to 5 years	1 (5)	0	0	-	1 (8.3)
5 to 10 years	1 (5)	1 (14.3)	0	-	0
10 to 30 years	5 (25)	0	1 (100)	-	4 (33.3)
Greater than 30 years	10 (50)	6 (85.7)	0	-	4 (33.3)
Former smoker, N (%)	189 (40)	80 (39)	3 (14.3)	1 (33.3)	105 (43)
Pack/years, mean ± SD	12.9 ± 14.4	10.1 ± 11.0	7.3 ± 6.9	22.5 ± NA	15.1 ± 16.5
Past smoking duration, N (%)					
Less than 1 year	12 (6.3)	6 (7.5)	0	0	6 (5.7)
1 to 2 years	11 (5.8)	7 (8.8)	0	0	4 (3.8)
2 to 5 years	23 (12.2)	13 (16.2)	0	0	10 (9.5)
5 to 10 years	40 (21.2)	18 (22.5)	1 (33.3)	0	21 (20)
10 to 30 years	72 (38.1)	26 (32.5)	2 (66.7)	0	44 (41.9)
Greater than 30 years	31 (16.4)	10 (12.5)	0	1 (100)	20 (19)

e-Table 4. Environmental exposures in all USPHSR subjects (male and female) by WHO Group 1, includes alcohol, marijuana, and recreational drug use

Exposure	All Patients	IPAH	FPAH	PVOD/PCH	APAH (all-subgroups)
Patients, N	494	213	22	3	256
Alcohol consumption, past 1 year, N (%)					
Daily	23 (4.7)	10 (4.7)	0	0	13 (5.1)
5 to 6 times per week	12 (2.4)	6 (2.8)	0	0	6 (2.4)
3 to 4 times per week	15 (3)	10 (4.7)	1 (4.5)	0	4 (1.6)
2 times per week	19 (3.9)	8 (3.8)	0	0	11 (4.3)
1 time per week	27 (5.5)	13 (6.1)	2 (9.1)	0	12 (4.7)
2 to 3 times per month	42 (8.5)	16 (7.5)	2 (9.1)	0	24 (9.4)
Once a month	30 (6.1)	12 (5.7)	1 (4.5)	0	17 (6.7)
3 to 11 times per year	61 (12.4)	23 (10.8)	7 (31.8)	2 (66.7)	29 (11.4)
1 to 2 times per year	93 (18.9)	43 (20.3)	4 (18.2)	1 (33.3)	45 (17.6)
Not in past 1 year	124 (25.2)	49 (23.1)	3 (13.6)	0	72 (28.2)
Never	46 (9.3)	22 (10.4)	2 (9.1)	0	22 (8.6)
Average daily drink consumption in past 1 year, mean ± SD	1.8 ± 1.5	1.8 ± 1.2	1.8 ± 1.2	1.8 ± 1.4	1.9 ± 1.7
Binge drinking^a in last 1 year, N (%)	85 (17.2)	40 (18.8)	5 (22.7)	0	40 (15.6)
Current drug use, N (%)	24 (4.9)	7 (3.3)	1 (4.5)	0	16 (6.2)
Type of drug used, N (%)					
Amphetamine	2 (0.4)	0	0	-	2 (0.8)
Dextroamphetamine	0	0	0	-	0
Cocaine	0	0	0	-	0
PCP	0	0	0	-	0
Marijuana	20 (4)	7 (3.3)	1 (4.8)	-	12 (4.7)
Other^b	3 (0.6)	1 (0.5)	0	-	2 (0.8)
Past drug use, N (%)	130 (26.7)	53 (25.2)	8 (36.4)	1 (33.3)	68 (27)
Type of drug used, N (%)					
Amphetamine	19 (3.8)	5 (2.3)	1 (4.5)	0	13 (5.1)
Methamphetamine	22 (4.5)	6 (2.8)	1 (4.5)	0	15 (5.9)
Dextroamphetamine	2 (0.4)	0	0	0	2 (0.8)
Cocaine	37 (7.5)	16 (7.5)	1 (4.5)	0	20 (7.8)
PCP	4 (0.8)	1 (0.5)	0	0	3 (1.2)
Marijuana	117 (23.7)	51 (23.9)	7 (31.8)	1 (33.3)	58 (22.7)
Other^b	14 (2.8)	4 (1.9)	0	0	10 (3.9)

^aBinge drinking is defined as > 5 drinks for males or > 4 drinks for females in 2 hours

^bOther drugs include ADHD medication, LSD, acid, mushrooms, crack, ecstasy, heroin, mescaline, opium, peyote, and Quaaludes

e-Table 5. Right heart catheterization data at diagnosis for HPAH patients, grouped by the most commonly identified genetic mutations.^b

Right Heart Catheterization Data	All patients (499)	HPAH ^a (76)	ABCC8 (5)	ACVRL1 (5)	BMPR2 (39)	GDF2 (5)	GGCX (3)	TBX4 (3)
MAP, mmHg	93.2 ± 17.4	89.6 ± 14.7	93 ± NA	93.3 ± 18.8	88.3 ± 16.5	-	-	89 ± NA
N	241	35	1	3	21	0	0	1
Mean PAP, mmHg	49.4 ± 13.2	53.4 ± 12.0	50.6 ± 16.0	53.4 ± 5.7	58.0 ± 10.7	49.0 ± 3.7	67.0 ± 10.5	55.0 ± 9.8
N	498	76	5	5	39	5	3	3
PCWP, mmHg	10.2 ± 3.8	9.0 ± 4.1	10.6 ± 5.2	10.0 ± 6.0	9.2 ± 3.4	7.6 ± 2.3	11.0 ± 4.0	11.0 ± 6.2
N	487	75	5	5	38	5	3	3
Mean RAP, mmHg	9.3 ± 5.6	9.5 ± 4.7	9.0 ± 4.1	11.0 ± 5.4	8.7 ± 3.9	9.5 ± 4.4	19 ± NA	9.7 ± 7.6
N	489	71	5	5	36	5	1	3
PVR, Wood units	10.4 ± 5.8	12.1 ± 5.8	11.8 ± 6.8	14.4 ± 10.3	14.3 ± 5.4	10.1 ± 4.6	17.4 ± 9.2	9.6 ± 2.4
N	479	74	5	5	38	5	3	3
Thermodilution CO, L/min	4.5 ± 1.6	4.5 ± 1.1	4.4 ± 0.6	3.8 ± 0.8	4.5 ± 1.2	3.6 ± 1.3	4.55 ± 2.2	4.4 ± 0.1
N	291	35	2	2	17	4	2	2
Thermodilution CI, L/min/m ²	2.4 ± 0.7	2.4 ± 0.6	2.6 ± 0.4	2.1 ± 0.6	2.5 ± 0.7	1.8 ± 0.5	2.9 ± NA	2.6 ± 0.5
N	222	29	2	2	17	3	1	2
Fick CO, L/min	4.3 ± 1.6	4.2 ± 1.4	3.9 ± 1.3	4.4 ± 3.0	3.8 ± 1.2	5.0 ± 1.8	2.6 ± NA	4.7 ± 0.6
N	398	64	5	4	33	3	1	3
Fick CI, L/min/m ²	2.3 ± 0.7	2.2 ± 0.6	2.0 ± 0.4	2.0 ± 1.3	2.1 ± 0.6	1.9 ± 0.2	-	2.6 ± 0.7
N	316	56	5	4	32	2	0	3
SvO ₂ , %	64.0 ± 9.8	63.5 ± 8.9	55.0 ± 17.0	65.0 ± 7.6	63.4 ± 8.6	66.5 ± 7.8	41 ± NA	71.0 ± 4.2
N	289	47	2	4	27	2	1	2

All values mean +/- SD unless otherwise indicated

Please see previous tables for abbreviations

HPAH – Heritable

^aHPAH includes all those with pathogenic/suspected pathogenic mutations and individuals previously classified as FPAH without identified mutations

^bLess common mutations (only found in 1-2 patients) including *ATP13A3*, *BMPR1B*, *EIF2AK4*, *ENG*, *KCNA5*, *KLK1*, *SMAD1*, and *SOX17* are not included