PVDOMICS Current Writing Committees
February 1, 2024

Writing Committee	Topic	Leads	Paper Published	Description
1	PVDOMICS study design	Hemnes, Beck, Leopold	Circ Res. 2017; 121:1136-1139. PMID: 29074534 PMCID: PMC5685561	
2	a) Main clinical descriptive; b) clustering; c) mixed groups	Hemnes, Horn, Leopold, Beck	Main clinicial paper 2a) JACC 80(7), 697-718, 2022	2b) The cluster analysis will take an agnostic approach to identifying new clusters of patients with similar phenotypes, regardless of WSPH group. The cluster analyses will be performed using clinical variables, omics variables, and mixed clinical and omics variables. Findings will be related to clinical outcomes. 2c) Definitions, comparison of clinical variables, outcomes & analysis of our mixed group taxonomy vs non mixed PH.
3	RHC Methods	Wilson	Circ Heart Failure. 2020;13, March 2020; e006363. PMID: 32088984 PMCID: PMC7046052	
4	Echo Methods	Jellis	Euro Heart J Cardiovasc Imaging. 2022 Jun 21;23(7):958-969. PMID: 34097027.	
5	CMRI Methods	Kwon		This manuscript will provide an overview of standardized cardiac MRI techniques and protocol that are being employed to comprehensively assess cardiovascular structure, function, tissue characterization, and flow quantification across participating sites in the PVDOMICS program,
6	Six Minute Walk Test	Rischard, Highland		Aim is to uncover clinical and phenotypically important characteristics across the spectrum of pulmonary vascular disease that influence the 6 minute walk test and distance. This WC may include several analysis such as-mixed disease in Group 1 PH, heart rate recovery and prognosis in PH, the characteristics affecting 6-minute walk distance in Group 3 PH, among others.
7	Hemodynamic and clinical char. between WSPH pure and mixed Groups 1vs3 and 2vs3	Borlaug, Jacob		Examine cardiovascular physiology from previous empiric data that determine function and survival in WSPH G1 versus mixed lung disease (1,3) versus G3PH versus lung disease alone (G3 comparators).
8	CT and main PA measurements across WSPH Groups	Lempel, Mathai		Composite indices using CT measurements to predict diagnosis and severity of PH.
9	Relationship between imaging parameters and invasive hemodynamics and NTproBNP	Frantz, Jellis, Kwon		Examination of the relationship between imaging parameters including particularly echo and MRI assessments of the right heart and invasive hemodynamics regarding predicting RV decompensation as assessed by invasive hemodynamics. Imaging predictors of clinical outcome including death/transplantation.
10	Sleep disordered breathing and cardiopulmonary indices in WSPH Grp 1	Lowery, Mehra, Hill	JACC 82(10), 1989-2005, 2023; PMID: 37968017	Plan to examine the prevalence of sleep disordered behavior (SDB) and sub-phenotypes of obstructive sleep apnea (OSA), central sleep apnea (CSA) and degree of nocturnal hypoxia in different Group 1 PAH subtypes. Furthermore, we plan to assess predictors of these SDB sub-phenotypes including patient characteristics such as age, sex, race and body mass index. Finally, we plan to investigate the association of SDB sub-phenotypes including apnea-hypopnea index, central vs obstructive apnea pattern and indices of nocturnal hypoxia with 1-year transplantation and mortality outcomes.
11	Gas Exchange	Frantz, DuBrock		Define the prevalence, mechanisms and clinical risk factors for abnormal gas exchange within and across PH groups and comparators. Define the association between abnormal gas exchange and chest imaging features. Define the association between abnormal gas exchange and symptoms, quality of life exercise capacity and outcome across PH groups and comparator.
12	PH Reclassification: The effect of changing PH definitions on the PVDOMICS cohort	Leopold, Frantz		Reclassification of the PVDOMICS cohort using the new WSPH definition of PH (mPA > 20 mmHg) and/or PVR > 2.2 WU will yield new clusters of clinical and omics variables.
13	RV Diastolic Stiffness and Right Atrial Function Across the Spectrum of Pulmonary Hypertension	Vanderpool		The aim is to investigate the differences in RV diastolic stiffness across the WHO groups of PH.
14	Health-Related Quality of Life Across the Spectrum of Pulmonary Hypertension	Mathai, Balasubramanian		To characterize HRQOL in PH across WSPH groups and identify clinical factors including demographic, physiologic, and hemodynamic markers of disease severity associated with HRQOL.
15	Health related quality of life differences between patients at-risk of and those with established PH	Mathai, Balasubramanian, Hassoun, Frantz		Will assess HRQOL between at-risk and established PH populations to determine associations between markers of disease severity and HRQOL exist. Further, we will determine if differences in HRQOL between at-risk and established PH exist.
16	Diffusing capacity as a clinical predictor of PH in COPD	Mathai, McCormack, Hassoun		We propose examining DLCO between at-risk COPD individuals and those with established COPD-PH to evaluate whether DLCO may be useful as a screening tool for PH in COPD. Further, we will determine whether DLCO is associated with exercise capacity, quality of life, and hemodynamic parameters of disease severity across both at-risk and established COPD-PH populations. We will examine these hypotheses in patients across all WHO groups who have spirometric evidence of COPD and a smoking history and in those patients with Group 3 PH with COPD as a sensitivity analysis.
17	Hemodynamic Phenotypes	Hemnes, Leopold		Clinical and omics profiling of different hemodynamic phenotypes identified in the PVDOMICS cohort will be done. This will be used to determine if hemodynamic profiles cluster and can be identified by omics markers.
18	Acute Vasoreactivity Testing During Right Heart Catheterization in Chronic Thromboembolic Pulmonary Hypertension (CTEPH)	Frantz, Berman	Pulmonary Circulation. PMID: 36618713 PMCID: PMC9817070 On-line 2023 Jan 6 DOI: 10.1002/pul2.12181	Describe frequency and extent of acute vasoreactivity to oxygen and nitric oxide in CTEPH, and association with outcome.
19	Super-responders to acute vasodilator testing and/or long-term treatment with CCB or other PH agent	Berman		We aim to analyze all groups of WSPH patients who have a robust hemodynamic and clinical response to: 1) acute vasodilator testing and/or 2) long-term treatment with calcium channel blockade or 3) any other targeted PH agent (or combination of agents) used for the treatment of pulmonary hypertension.
20	Atrial arrhythmias and PH across WSPH groups	Berman		This study is investigating the incidence of atrial arrhythmias at the time of enrollment of PH patients across WSPH groups and the clinical phenotype of those with arrhythmias vs those without.
21	The effect of the left atrium and pulmonary vascular disease	Horn		Left atrial abnormalities is a cumulative assessment reflecrting LA pressure and is a determining factor of post capillary PH. This study will address the degree to which it is abnormal in non Group 2 PH pateints and adversely effects PH/RV hemodynamics
22	Assessing the burden of CV risk factors and disease across PVDOMICS cohorts	Leopold		Cardiovascular risk factors and established cardiovascular disease is common among patients with pulmonary hypertension. This study will examine the prevalence of these factors among patients with WSPH groups 1, 3, 4 and 5 compare to WSPH group 2 patients. Studies will include assessment of clinical variables and omics
23	Inter-race and ethnicity comparisons in PH	Rischard		Aim is to characterize the similarities and differences of race/ethnicity across the spectrum of pulmonary vascular disease. This WC is comprised of several current analysis such as a general description of race and ethnicity in PVDOMICS, geo-mapping environmental exposures with race/ethnicity in PVD, and examining the social determinants of health with race/ethnicity in PVD.
24	Adjustment of NTproBNP by body measures improves prediction of right HF	Frantz		Describe the impact on NTproBNP levels of: body composition, age, renal function, diabetes mellitus, ethnicity, atrial fibrillation, sinus tachycardia, and paced rhythm.
25	Sex Differences in Right Ventric. Response to PH	Shelburne, Hemnes, Rischard		Describe sex-based differences in PH etiology, rv function, and metabolomics across the spectrum of pulmonary vascular disease.
26	Metabolomics CTEPH	Berman, Frantz		This paper will examine the metabolomic profiles of CTEPH subjects in the PVDOMICS cohort and compare to non-CTEPH subjects to determine whether there are unique metabolic profiles that characterize CTEPH.
27	Metabolomics BWH endothelial fct & PV remodeling	Leopold, Horn		
28	Metabolomics Columbia - clinical phenotypes AVT responders	Berman, Frantz		This study will look specifically at the metabolic phenotypes of AVT responders
29	Metabolomics RV compensation	Frantz, Horn, Rischard		This study will look at differences in metabolomic profiling that reflects RV-PA profiling. Wei wil look across the spectrum independent of WSPH Group.
30	Metabolomics Cornell CV Meds	Horn, Berman		This study will look at metabolomic profiling that reflects PH and CV medications
31	Metabolomics JHU Ssc-PAH	Hassoun, Griffths, Hemnes	Arthritis & Rheumatology. Paper on-line, Jun 19. doi: 10.1002/art.42632. PMID: 37335853	ARH DEFERS TO HASSOUN/GRIFFTHS TO DESCRIBE
32	Metabolomics Mayo HFpEF	Frantz, Horn		To examine the baseline (enrollment) and longitudinal follow up data to determine whether there are 1) significant alterations in metabolomics over time and 2) whether these changes are associated with clinical outcomes. The L-OMICS data acquisition will
33	Metabolomics Vanderbilt Mixed Grp 1/2	Hemnes, Leopold		Metabolomic profiling will be performed for patients with combined pre- and post-capillary PH and comapred to Group 1 and Group 2 PH. Clinical variables will be correlated,

PVDOMICS Current Writing Committees
February 1, 2024

34	Beta-Adrenergic Receptor (bar) levels are related to right ventricular function	Erzurum, Farha, Horn		downregulation of bARs. We will test this hypothesis by quantitation of ?AR levels on the surface of circulating white blood cells in PVDOMICs patient participants in comparison to healthy and disease controls, and determine if the lowest ?AR levels are in the most severe PH. Further to test the hypothesis, we will investigate if the ?AR levels and its messenger cAMP correlate with parameters of RV function as measured by echo and MRI and CPET O2 pulse.
35	Congenital heart disease related pulmonary hypertension	Berman, Chung, Griffths		Patients with PH and CHD including the presence of any atrial level shunt are heterogeneous in CHD type and physiology and with deep OMIC phenotyping analyses we aim to determine whether the deep OMIC features are similar to non CHD associated PH.
36	RV dysfunction in WSPH Group3	Rischard, Borlaug		1)To compare resting lung mechanics/gas exchange between Pure G1 PAH, G1,3 PAH, G3PH, and G3 comparators (excluding sleep disordered breathing); 2) To compare RV afterload between Pure G1 PAH, G1,3 PAH, G3 PH, and G3 comparators; 3) 3) To compare RV function between Pure G1 PAH, G1,3 PAH, G3 PH, and G3 comparators.
37	The Impact of Obstructive Lung Disease Across the Spectrum of Pulmonary Hypertension	Mathai		We hypothesize that chronic obstructive pulmonary disease (COPD) is common in patients with all forms of PH. Further, we hypothesize that COPD will be associated with worse symptoms, functional capacity, and disease severity in patients with both COPD and PH compared to patients with PH without COPD across all WSPH groups.
38	Clinical features of post-acute Sars Co-V2 (PASC) infection in the PVDOMICS cohort	Funke, Hemnes		Questions to be answered: 1) compare PVDOMICs enrollees with and without COVID-19 infection to determine if there are different clinical or Omic features in the two groups, 2) compare outcomes (death/transplant) in enrollees with and without COVID-19 infection, 3) compare clinical features of disease severity pre- and post-COVID to evaluate for evidence of new or worsened pulmonary hypertension and RV dysfunction (RVSP, RV diameter, RV function on echo, six minute walk distance, oxygen desaturation, quality of life metrics).
39	Frequency of Acute Vasodilator Response (AVR) in incident and prevalent PAH patients (Group 1)	Hassoun, Naranjo-Tovar	Pulmonary Circ On-line publ. 2023 Aug 21. doi: 10.1002/pul2.12281 PMID: 37614830	Questions to be answered: 1) Prevalence of AVR in Group 1 (IPAH vs subgroups) in the PVDOMICS cohort; 2) Prevalence of AVR in incident versus prevalent patients in Group 1; 3) Effect of inhaled O2 vs iNO vs combined iO2 and iNO in Group 1 patients; 4) Effect of PAH drugs on AVR in Group 1 (prevalent cohort)
40	Tryptophan, purine, and polyamine metabolites predict development of PAH in systemic sclerosis	Simpson, Hassoun	AJP Lung on-line 03 Oct 2023 https://doi.org/10.1152/ajplung.00177.2023	Questions to be answered: 1) ability of tryptophan, purine, and polyamine metabolites to discriminate PAH from among disease comparators and healthy controls; 2) associations between metabolites of interest and hemodynamic measures of disease severity; 3) associations between metabolites and measures of RV function; 4) associations between metabolites and clinical outcomes, including survival.
41	Impact of functinal iron deficiency on exercise physiology	Martens, Tang	European Heart Journal. 2023 Jun 9;44(22):1979-1991. doi: 10.1093/eurheartj/ehad149. PMID: 36879444	Our hypothesis is that iron deficiency is common in patients with pulmonary hypertension and is associated with diminished maximal exercise capacity (measured by CPET), submaximal exercise capacity (measured by maximal walking distance) and diminished quality of life. Additionally iron deficiency would be associated with more pronounced right ventricular remodeling , pulmonary vascular remodeling and diminished right ventricular contractile reserve (in iCPET subgroup).
42	Defining Degrees of Right Ventricular Size and Function in Pulmonary Hypertension from the PVDOMICS Study	Mukherjee, Kim		We seek to establish quantitative measures of RV chamber size and function in the PVDOMICS study participants with pulmonary hypertension (PH) across age, sex, and race/ethnic groups by quartiles of PH severity which will be incorporated in the planned American Society of Echocardiography guideline document.
43	Inter-reader variability in manually contoured right and left ventricular volumes across the spectrum of pulmonary vascular disease	Rischard, Kwon, Tang		1) To compare inter-site, inter reader variability in manual contouring of the right and left ventricular volumes;) To compare intra-site, inter reader variability in manual contouring of the right and left ventricular volumes; 3) To degin a systematic approach to manual ventricular contouring of the right and left ventricle based on consensus strategy to improve inter-reader reliability (pre and post intervention testing).
44	Platelet mitochondrial function as a predictor of right ventricular function	Farha, Asosingh, Hassoun, Erzurum		Mitochondrial flow analyses will be evaluated to determine the relationship between mitochondrial functions and PH characteristics, particularly cardiac function.
45	LOMICS and PVD: Examining omic signatures of PH longitudinally	Berman		To examine the baseline (enrollment) and longitudinal follow up data to determine whether there are 1) significant alterations in metabolomics over time and 2) whether these changes are associated with clinical outcomes. The L-OMICS data acquisition will be complete and I would aim to begin these analyses as soon as the data is available.
46	Fatty acids in COPD	Chung, Horn, Rischard		1) Is there a different metabolomic (lipidomic) signature between COPD patients with pulmonary hypertension and/or RV dysfunction than those without? 2) Does COPD severity (FEV1), PVR and RV function correlate with increased fatty acid metabolism dysregulation?
47	CHIP	Farha		1) Determine whether CHIP occurs at higher frequencies in PH and is associated with more severe disease. 2) Investigate the interactions between somatic CHIP variants and known PAH germline mutations
48	Metabolic profiles in sleep disordered breathing	Mehra, Ahmad		To elucidate metabolomics signatures of sleep disordered beathing and hypoxemia as contributors to PH with a focus on Group 1 pulmonary arterial hypertension (PAH).
49	Adipose Tissue Depots	Funke, Hemnes		We hypothesize that in PVDOMICS enrollees with Group 1 PAH and Group 2 PH, increased total adipose tissue, thoracic visceral adipose tissue (VAT), thoracic subcutaneous adipose tissue (SAT), and hepatic fat content will be associated with more impaired pulmonary hemodynamics and right ventricular function and worse clinical outcomes.
50	Metabolomic Signatures of PVD with or without Iron Deficiency	Martens, Tang		Our hypothesis is that the recently defined definition of iron deficiency in PH (TSAT<21%) is associated with pronounced metabolic alterations, which might be linked to right ventricular remodeling.
51	Sarcopenia Across the Spectrum of PH	Tang		Impact of sarcopenia across the spectrum of Pulmonary Vascular Diseases
52	Prognostic information from echo and CMR	Rischard, Badagliacca		In contrast to prediction of hemodynamic/RV decompensation, this project will integrate cardiac imaging with risk score to predict mortality and HR QOL in WSPH Group 1 and Group 1 comparators.
53	Air pollution effect on PH	Rischard, Lim		1. We aim to examine the association of air pollution exposure ≤ 5 years from enrollment across all PH groups, comparators, and controls to pulmonary vascular disease, HRQOL, function, mortality and to RV function. 2. We aim to examine the association between air pollution exposure and PH COMPERA risk (total and component) score among WSPH Group 1 subjects.
54	Reproductive history	Hurbon, Rischard, Hemnes		This research will explore relationships between reproductive hormones with right ventricular function and degree of pulmonary vascular disease.
55	CTEPH w/o hypertension	Heresi		The main hypothesis of this proposal is that chronic thromboembolic pulmonary disease (CTEPD) without pulmonary hypertension (PH) represents an intermediate phenotype between health and overt chronic thromboembolic pulmonary hypertension (CTEPH) .
56	CKD	Dao, Leopold		The main hypothesis of this proposal is that decreased kidney function or chronic kidney disease (CKD) is associated with a higher prevalence of pulmonary vascular disease (PVD) and worse clinical outcomes among participants in PVDOMICs. We also hypothesize that CKD serves as a disease modifier for patients with PVD.
57	PCWP	Rischard		Aims are: 1) To define populations where PCWP by end-exhalation and respiratory averaging are discordant, 2) to examine the circumstances where provocative testing aids in the interpretation of PCWP discordance, 3) to determine the influence of the V-wave on PCWP measurement.
58	Spirometry impact on Grp	Mathai		The main hypothesis of this proposal is that the assignment of group according to the 6th WSPH will vary based upon method of interpretation of pulmonary function testing.
59	Systemic immune dysfct.	Farha		The PVDOMICS cohort will allow us to investigate the immune reponse across all PH groups and we will use the deep clinical phenotype and outcome data to help answer whether the immune response has clinical implication in PH.
60	Lipidomics	Simpson, Hassoun		We hypothesize that high-resolution lipidomics will 1) reveal novel associations between specific lipid species and particular WSPH classifications, 2) yield distinct signatures of right ventricular-pulmonary vascular function.
61	HRQOL and RV function	Mathai		We hypothesize that health-related quality of life (HRQOL) will be associated with right ventricular (RV) function as assessed by non-invasive measures across the spectrum of pulmonary hypertension (PH) and that the strength of this association will vary by underlying PH etiology and that these differences between WSPH groups will persist when adjusting for demographic characteristics and hemodynamic severity.