National Heart, Lung, and Blood Institute

Challenges and Solutions for Early and Accurate Diagnosis in Pulmonary Vascular Disease (PVD)

November 2-3, 2026

Program Book

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Agenda

Day 1 (November 2, 2026)

Introduction and Workshop Overview

10:00 a.m.–10:15 a.m. **Introduction of Speakers**

Lei Xiao, M.D., Ph.D., National Heart, Lung, and Blood Institute (NHLBI)

10:15 a.m.–10:20 a.m. **Opening Remarks from NHLBI**

Marishka Brown, Ph.D., Division of Lung Diseases (DLD), NHLBI

10:20 a.m.–10:35 a.m. **Opening Remarks from Workshop Co-Chairs**

Bradley Maron, M.D., University of Maryland

Roham Zamanian, M.D., FCCP, Stanford University

10:35 a.m.–10:45 a.m. **Historical Context to Early Pulmonary Hypertension (PH)**

Bradley Maron, M.D., University of Maryland

10:45 a.m.–10:55 a.m. **Workshop Objectives**

Roham Zamanian, M.D., FCCP, Stanford University

Session 1: Fundamental Considerations of Early PH: Current State and Challenges

10:55 a.m.–11:10 a.m. **Definitions and Concepts of Early PH**

Kara Goss, M.D., UT University of Texas Southwestern Medical Center

11:10 a.m.–11:25 a.m. **Public Health Campaigns for Early PH Detection**

Peter Leary, M.D., Ph.D., University of Washington

11:25 a.m.–11:40 a.m. **Early PH Detection in the World Health Organization (WHO) Classification**

Serpil Erzurum, M.D., Cleveland Clinic

11:40 a.m.–11:55 a.m. **Early PH Pathobiology: The Journey Toward a Multistage Model of Pathogenesis**

Bradley Wertheim, M.D., Brigham and Women's Hospital

11:55 a.m.–12:15 p.m. **Session 1 Breakouts**

Breakout Room 1: Definition of early PH from different viewpoints (physicians, patients, industry, regulatory officials, molecular scientists)

Moderator:
Kelly Chin, M.D., UT Southwestern Medical Center

Breakout Room 2: Is the goal to detect early PH or to detect PH earlier?

Moderator:
Raymond Benza, M.D., Old Dominion University, Eastern Virginia Medical School

Breakout Room 3: How does early PH fit into the WHO classification system, and how may the "early PH" definition differ among WHO classification groups?

Moderator:
Adam Andruska, M.D., Stanford University

12:15 p.m.–12:30 p.m. **Session 1 Group Discussion**

12:30 p.m.–1:05 p.m. **Lunch Break**

Session 2: AI- and Non-AI-Assisted Technology to Detect Early PH, Part 1

1:05 p.m.–1:20 p.m. **Understanding AI: From Patterns to Trustworthy Clinical Decisions**

Syed Ahmad Chan Bukhari, Ph.D., St. John's University

1:20 p.m.–1:35 p.m. **Digital Stethoscope for Early PH Detection**

Gaurav Choudhary, M.D., Brown University

1:35 p.m.–1:50 p.m. **Electrocardiograms (ECGs) for Early PH Detection**

Hilary DuBrock, M.D., Mayo Clinic

1:50 p.m.–2:05 p.m. **Echocardiography for Early PH Detection**

David Ouyang, M.D., Cedars-Sinai Medical Center

2:05 p.m.–2:20 p.m. **Session 2 Group Discussion**

Session 3: AI- and Non-AI-Assisted Technology to Detect Early PH, Part 2

2:20 p.m.–2:35 p.m. **AI Caveats—and Opportunities—in Early PVD Detection**

Katherine Goodman, J.D., Ph.D., University of Maryland School of Medicine

2:35 p.m.–2:50 p.m. **Computerized Tomography (CT) of the Chest for Early PH Detection**

Farbod (Nick) Rahaghi, M.D., Ph.D., University of California, Los Angeles

2:50 p.m.–3:05 p.m. **Molecular Technologies for Early PH Detection**

Maria Giovanna Trivieri, M.D., Ph.D., Icahn School of Medicine at Mount Sinai

3:05 p.m.–3:20 p.m. **Hyperpolarized Xenon MRI to Phenotype PH**

Sudarshan Rajagopal, M.D., Ph.D., Duke University

3:20 p.m.–3:40 p.m. **Session 2 and 3 Breakouts**

Breakout Room 1: What role does imaging play in early PH recognition for non-high-risk subgroups? What are the advantages, limitations, and potential caveats, including radiation exposure, costs, and incidental findings?

Moderator:
Monica Mukherjee, M.D., Johns Hopkins University

Breakout Room 2: What populations or cohorts should undergo specific imaging, screening, or diagnostic modalities, and why?

Moderator:
Shelsey Johnson, M.D., Brigham and Women's Hospital

Breakout Room 3: What performance characteristics are acceptable for screening technologies, considering sensitivity, specificity, and rates of false positives and false negatives?

Moderator:
Steven Kawut, M.D., M.S., University of Pennsylvania

3:40 p.m.–3:55 p.m. **Session 3 Group Discussion**

3:55 p.m.–4:10 p.m. **Break**

Session 4: Biomarkers

4:10 p.m.–4:25 p.m. **New Blood-Derived Biomarkers for Early PH Detection or Risk Stratification**

Patricia Thistlethwaite, M.D., Ph.D., University of California, San Diego

4:25 p.m.–4:40 p.m. **Multiomics and Composite Biomarkers for Early PH Detection or Risk Stratification**

Anna Hemnes, M.D., Vanderbilt University Medical Center

4:40 p.m.–4:55 p.m. **Genetic and Genomic Susceptibility for Early PH Detection**

Micheala Aldred, Ph.D., Indiana University

4:55 p.m.–5:15 p.m. **Session 4 Breakouts**

Breakout Room 1: How do multi-omic peripheral biomarkers relate to what is locally occurring in the lung vasculature or lungs?

Moderator:
Catherine Simpson, M.D., Johns Hopkins University

Breakout Room 2: Can we infer early disease biomarkers/profiles from studies conducted in end-stage patients receiving PAH therapies?

Moderator:
Arun Jose, M.D., University of Cincinnati

Breakout Room 3: What characteristics should define an optimal biomarker for early PH detection?

Moderator:
Andrew Sweatt, M.D., Stanford University

5:15 p.m.–5:30 p.m. **Session 4 Group Discussion**

5:30 p.m. **Adjourn**

Day 2 (November 3, 2026)

Session 5: Exercise Physiology to Uncover Early PH

10:00 a.m.–10:15 a.m. **Early RV Changes in Early PH Detection**

Ryan Tedford, M.D., Medical University of South Carolina

10:15 a.m.–10:30 a.m. **Provocative RHC to Uncover Early PH**

Barry Borlaug, M.D., Mayo Clinic

10:30 a.m.–10:45 a.m. **The Use of Passively Sensed Real-world Data from Smartphones and Wearable to Support Early Detection and Monitoring of PAH**

Allan Lawrie, Ph.D., Imperial College London

10:45 a.m.–11:05 a.m. **Session 5 Breakouts**

Breakout Room 1: How available are conductance and exercise RHC procedures, and how clinically useful are they, considering the risks, benefits, and costs?

Moderator:
Steven Hsu, M.D., Johns Hopkins University

Breakout Room 2: Is exercise PH diagnosis clinically useful?

Moderator:
Katarina Zeder, M.D., Ph.D., University of Maryland

Breakout Room 3: How reliable and accurate are actigraphy and wearable devices for early PH detection?

Moderator:
Jasleen Minhas, M.D., University of Pennsylvania

11:05 a.m.–11:25 a.m. **Session 5 Group Discussion**

Session 6: Population Screening and Health System Implementation Challenges

11:25 a.m.–11:40 a.m. **Screening Considerations for Early PH Detection in the General Population**

Evan Brittain, M.D., Vanderbilt University

11:40 a.m.–11:55 a.m. **Challenges and Opportunities for Early PH Detection in Health Deserts and Low- and Middle-Income Countries**

Ana Mocumbi, M.D., Ph.D., Universidade Eduardo Mondlane (Mozambique)

11:55 a.m.–12:10 p.m. **Real-World Implementation of Early PH Detection**

Thomas Maddox, M.D., Washington University in St. Louis

12:10 p.m.–12:30 p.m. **Session 6 Breakouts**

Breakout Room 1: How should health systems manage large numbers of patients identified through broad screening approaches?

Moderator:
Anjali Vaidya, M.D., Temple University

Breakout Room 2: How can early PH recognition be implemented in the general population, and what are the implications for healthcare systems?

Moderator:
Francois Haddad, M.D., Stanford University

Breakout Room 3: What criteria or thresholds should be used to discontinue screening?

Moderator:
Evelyn Horn, M.D., Weill Cornell Medical College

12:30 p.m.–12:45 p.m. **Session 6 Group Discussion**

12:45 p.m.–1:30 p.m. **Lunch Break**

Session 7: Trial Considerations for Early PH

1:30 p.m.–1:45 p.m. **Trial Design Considerations for Early PH Detection**

Robert Frantz, M.D., Mayo Clinic

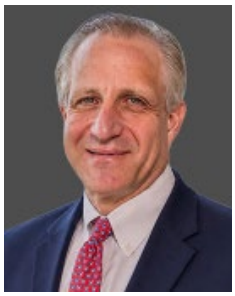
1:45 p.m.–2:00 p.m. **Therapeutic Targets for Early PH**

Corey Ventetuolo, M.D., Brown University

2:00 p.m.–2:15 p.m.	**Current Evidence for the Treatment of Early PH** Paul Hassoun, M.D., Johns Hopkins University
2:15 p.m.–2:35 p.m.	**Session 7 Breakouts** **Breakout Room 1: What is the optimal management strategy for early PH?** Moderator: Nicholas Hill, M.D., Tufts University **Breakout Room 2: What does the ideal clinical trial for early PH look like?** Moderator: Franz Rischard, D.O., University of Arizona College of Medicine-Tucson **Breakout Room 3: How large should trials related to early PH be, and how should patients be enrolled?** Moderator: Stephen Mathai, M.D., Johns Hopkins University
2:35 p.m.–2:50 p.m.	**Session 7 Group Discussion**
2:50 p.m.–3:05 p.m.	**Break**
Session 8	
3:05 p.m.–5:05 p.m.	**Open Discussion Led by Workshop Co-Chairs** Bradley Maron, M.D., University of Maryland Roham Zamanian, M.D., FCCP, Stanford University
5:05 p.m.	**Adjourn**

Workshop Organizing Committee

Workshop Co-Chairs



Bradley Maron, M.D., University of Maryland

Dr. Bradley Maron is the Editor-in-Chief of *Circulation*, Senior Associate Dean for Precision Medicine and the Melvin Sharoky Professor of Medicine at the University of Maryland School of Medicine, and Co-Executive Director of the University of Maryland-Institute for Health Computing (UM-IHC) in North Bethesda, Maryland. His research interfaces with redox biochemistry, network medicine, and next-generation bioinformatics to discover novel mechanisms underpinning cardiovascular disease. He is a world authority on the clinical management of pulmonary hypertension and right heart failure and has led collaborative international projects contributing to drug development programs, personalized medicine approaches that optimize phenotyping, prognostication, and treatment selection for patients with complex diseases, and epidemiological reports establishing cardiovascular risk. His work led to the contemporary hemodynamic criteria used to diagnose pulmonary hypertension in clinical practice worldwide. Dr. Maron holds co-inventorship of several innovations and is funded by the National Institutes of Health, among other foundations. He is the President of the Pulmonary Vascular Research Institute, a member of the American Society of Clinical Investigation, and a recipient of numerous distinguished awards for clinical expertise and medical education.

Roham Zamanian, M.D., FCCP, Stanford University

Dr. Roham Zamanian is a professor of medicine in the Department of Medicine and the director of the Stanford Adult Pulmonary Hypertension Program. His career has focused on translational and clinical research on pulmonary vascular diseases with a specific focus on pulmonary arterial hypertension (PAH). As a faculty member of the Vera Moulton Wall Center for Pulmonary Vascular Disease, he is dedicated to establishing and growing the translational capacity of the program. To that end, he has developed the Stanford Pulmonary Hypertension Biobank and helped improve and implement the Wall Center Pulmonary Hypertension Database. He has a long track record of mentoring junior fellows and faculty in clinical research, helping them develop independent research careers and secure funding. His academic mission is to design and implement leading-edge clinical trials as part of translational research at Stanford University and mentor early-career academic researchers. He has taken part in, designed, and served as principal investigator or co-investigator on a large number of government-, industry-, and National Institutes of Health–funded investigator-initiated research studies. He has a proven record of excellent study integrity and successful project completion, resulting in clinical evaluation and development of three novel PAH therapeutics.

NHLBI Members

John Sheridan, Ph.D., Restrictive and Vascular Lung Diseases, Division of Lung Diseases, National Heart, Lung, and Blood Institute

Dr. John Sheridan is the acting deputy director of the Division of Lung Diseases (DLD) and chief of the Restrictive and Vascular Lung Diseases Branch. As branch chief, he oversees research on interstitial lung diseases, pulmonary fibrosis, pulmonary hypertension, right heart failure, sarcoidosis, lymphangioleiomyomatosis, and other rare lung diseases. Prior to joining DLD, he was the director of research at the Cystic Fibrosis Foundation, where he led research programs on cell and gene therapies to advance the discovery of gene editing, mRNA technologies, delivery mechanisms, and stem cell therapies to treat cystic fibrosis.

Roy Sutliff, Ph.D., Restrictive and Vascular Lung Diseases, Division of Lung Diseases, National Heart, Lung, and Blood Institute

Dr. Roy Sutliff is a program officer in the Restrictive and Vascular Lung Diseases branch of the Division of Lung Diseases (DLD) at the National Heart, Lung, and Blood Institute (NHLBI). He works with Dr. Lei Xiao to oversee the pulmonary hypertension portfolio and manages a portfolio of over 100 grants comprising approximately 30 percent career development awards, 60 percent investigator-initiated awards, and 10 percent small business grants. Dr. Sutliff completed his B.S. in biochemistry at Temple University, his Ph.D. at Drexel University, and his postdoctoral fellowship at the University of Cincinnati. He first joined the Department of Pathology at Emory University in 1999 and later moved to the Pulmonary Division at Emory University, where he attained the rank of professor. He also served as the director of graduate studies for the Molecular and Systems Pharmacology Program, was active in the Laney Graduate School, and oversaw international exchange and recruitment programs. He has published over 90 research articles on preclinical models of pulmonary hypertension.

Lei Xiao, M.D., Ph.D., Division of Lung Diseases, National Heart, Lung, and Blood Institute

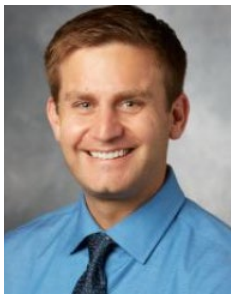
Dr. Lei Xiao has been a program director in the Division of Lung Diseases (DLD) within the National Heart, Lung, and Blood Institute (NHLBI) since 2014, overseeing research grants in pulmonary vascular disease. Dr. Xiao earned his M.D. from Peking University Health Science Center in 1993 and his Ph.D. in pharmacology from Creighton University in 1998. He completed his postdoctoral training in cardiology at Boston University (BU) in 2001 and served as an assistant professor of medicine at BU and then at the University of Illinois Chicago (UIC). Prior to joining NHLBI in 2014, Dr. Xiao served as the director of research education in the section of pulmonary, critical care, sleep, and allergy in the Department of Medicine at UIC. Dr. Xiao was also the principal investigator of several NHLBI R01 grants, an American Heart Association National

Scientist Development Grant, and other research grants. He has received numerous national and international research and academic awards, including the first-place award for two consecutive years at the New England Cardiovascular Research Competition, the Jay N. Cohn New Investigator Award from the Heart Failure Society of America, the Fok Ying-Tung Prize for Outstanding Chinese Doctor Worldwide from the World Association of Chinese Doctors, and multiple NHLBI Director's Awards. He has also served as an editor or reviewer for many academic journals and as a reviewer for grant-review study sections.

Junior Faculty Members

Adam Andruska, M.D., Stanford University

Dr. Adam Andruska is an assistant professor of pulmonary, allergy, and critical care medicine at Stanford University. He conducts basic and translational research investigating how inflammation drives the development of vascular pathology in pulmonary arterial hypertension and associated lung diseases. Dr. Andruska's lab focuses on two areas: (1) identifying helper T cell subtypes and secreted ligands that drive vascular neointimal lesion growth in pulmonary hypertension, and (2) understanding how tertiary lymphoid structures develop in the lung to harbor pathologic helper T cells. The lab uses single-cell, spatial, and deep-tissue imaging technologies to map and interrogate cell–cell interactions between immune lineages and the pulmonary vasculature. He also cares for patients in the adult pulmonary hypertension service and in the medical intensive care unit.



Andrew Sweatt, M.D., Stanford University

Dr. Andrew Sweatt is board certified in internal medicine, pulmonary disease, and critical care medicine. He subspecializes in the evaluation and treatment of pulmonary hypertension. He completed his subspecialty fellowship training in 2016 and joined the multidisciplinary pulmonary hypertension team at Stanford University as a clinician and translational researcher. He sees patients at the main Stanford University campus and East Bay site in Emeryville.

Katarina Zeder, M.D., Ph.D., University of Maryland

Dr. Katarina Zeder is a physician-scientist specializing in pulmonary hypertension (PH), combining clinical expertise with translational research to improve early diagnosis, understanding of the disease, and patient management. Her research focuses on five major areas: (1) pulmonary vascular physiology and early detection of PH through exercise testing; (2) clinical and histopathological characterization of PH in chronic obstructive pulmonary disease; (3) PH in kidney disease; (4) artificial intelligence–driven approaches to PH diagnosis within the electronic health record; and (5) global PH epidemiology.

Dr. Zeder earned her medical degree and Ph.D. from the Medical University of Graz in Austria. In 2023, she completed a research fellowship at Harvard Medical School before joining the University of Maryland School of Medicine and the Institute for Health Computing as a research associate in 2024.

Speaker and Moderator Information

Introduction and Workshop Overview

Marishka Brown, Ph.D., Division of Lung Diseases, National Heart, Lung, and Blood Institute

Dr. Marishka Brown is a distinguished biomedical scientist and federal public health leader at the National Institutes of Health (NIH). She is the acting director of the Division of Lung Diseases (DLD) and the director of the National Center on Sleep Disorders Research (NCSDR) within the National Heart, Lung, and Blood Institute. She provides executive leadership for a research portfolio that spans pulmonology, critical care, sleep, and circadian biology. Dr. Brown joined DLD as a program director within NCSDR and oversaw the Sleep Disorders Medicine program. Her NIH career began as an American Association for the Advancement of Science, Science & Technology Policy fellow in the Office of Strategic Coordination, within the Office of the Director. Dr. Brown received her education from the University of Maryland, Baltimore, and her fellowship training at the University of Pennsylvania.

Bradley Maron, M.D., University of Maryland

Historical Context to Early Pulmonary Hypertension (PH)

Pulmonary hypertension is a progressive and debilitating disease that is most often diagnosed late due to nonspecific symptoms and a low clinical index of suspicion among clinicians. In studies focusing on incident patients with pulmonary arterial hypertension, for example, the mean pulmonary artery pressure was 49 mmHg, well above the lower limit of clinical risk (~20 mmHg). Identifying patients early in their disease course is well-positioned to improve clinical care. Nonetheless, efforts to improve early diagnosis of pulmonary arterial hypertension (PAH) and other treatable forms of pulmonary hypertension have been hindered by challenges inherent to identifying at-risk patients in clinical practice. Integration of contemporary technology (including AI), public health campaigns, utilization of established risk factors associated with PAH, and emphasis on biomolecular pathways that define early (as opposed to late) presentation of pulmonary vascular disease may be useful for launching programs that diagnose patients earlier, at scale. This workshop program aims to galvanize contemporary concepts across the basic, translational, clinical, and epidemiological research spectrum to establish the framework of a plan that improves the diagnostic yield of early pulmonary hypertension. The goal is to synthesize

the basis of an approach that accomplishes these objectives by focusing on methods that are feasible, safe, testable, and effective.

Session 1: Fundamental Considerations of Early PH: Current State and Challenges

Kara Goss, M.D., UT Southwestern Medical Center

Dr. Kara Goss is an R01-funded physician-scientist in the Division of Pulmonary and Critical Care Medicine at UT Southwestern Medical Center. Trained in internal medicine, pediatrics, and adult pulmonary and critical care, including pulmonary hypertension and right ventricular failure, she has developed unique lifespan expertise in the long-term cardiopulmonary effects of extreme preterm birth. Her work uses state-of-the-art imaging and physiologic assessments to study this emerging high-risk population. Clinically, she specializes in the care of adults born preterm and she manages a full range of pulmonary vascular diseases through the UT Southwestern Pulmonary Hypertension Clinical Program.

Definitions and Concepts of Early PH

Pulmonary hypertension (PH) is hemodynamically defined as a mean pulmonary artery pressure (mPAP) >20 mmHg, with early PH most commonly used to describe mPAP 21-24 mmHg with pulmonary vascular resistance (PVR) 2-3 Wood units. Conceptually, early PH can also encompass a group that temporally is likely to progress to overt PH (e.g., elevated PVR preceding overt PH, or exercise-induced PH), or those 'at risk' due to the presence of underlying pulmonary vascular disease (PVD). In the most classic sense, PVD is identified by histopathological remodeling, including medial smooth muscle hypertrophy and distal neomuscularization, that precedes largely irreversible plexiform lesions and intimal fibrosis, though clinically it is sometimes used to describe any structural remodeling of the pulmonary vascular tree.

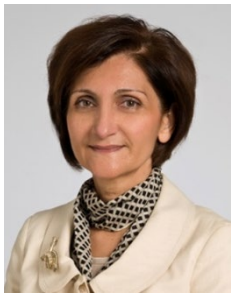
Peter Leary, M.D., Ph.D., University of Washington

Dr. Peter Leary is professor of medicine and adjunct professor of epidemiology at the University of Washington, where he serves as director of the Pulmonary Vascular Disease Program. He is a physician-scientist whose research integrates clinical epidemiology, translational science, and multi-omics to improve the understanding and treatment of pulmonary vascular disease. His work has focused on pulmonary arterial hypertension (PAH), right ventricular adaptation, and pulmonary vascular disease phenotyping, with a particular interest in identifying repurposed therapeutic targets and improving precision medicine approaches. Dr. Leary has led or contributed to numerous National Heart, Lung, and Blood Institute–funded studies and currently serves as principal investigator of multiple National Institutes of Health–supported clinical and translational research programs. He played a leadership role in developing the Pulmonary Hypertension Association Registry and chaired the Global Burden of Disease Pulmonary Hypertension Writing Group. His work has helped define the epidemiology, geographic

variation, and healthcare delivery of PAH in the United States and globally. Dr. Leary serves on the Scientific Leadership Council of the Pulmonary Hypertension Association. He has published over a hundred peer-reviewed manuscripts spanning epidemiology, clinical trials, implementation science, and translational pulmonary vascular research.

Public Health Campaigns for Early PH Detection

Public health campaigns for early detection of pulmonary hypertension (PH) require an appropriate population, an actionable therapeutic window, and an accurate test. Pulmonary arterial hypertension (PAH) may offer a compelling biological rationale for earlier intervention, but evidence that treating it earlier changes its natural history remains insufficient to strongly support robust screening. In addition, current diagnostic approaches cannot reliably identify disease before it develops, and their performance is inadequate for general population screening. Because PAH is rare, even highly specific tests generate substantial numbers of false positives, prompting costly investigations, potential misclassification, and unnecessary treatment. Earlier case finding is more defensible in selected populations with increased disease prevalence, including systemic sclerosis, certain congenital heart diseases, liver transplant candidates, and carriers of pathogenic PAH variants. Broader campaigns targeting unexplained dyspnea or methamphetamine exposure require better characterization of disease prevalence, ideally improved tests, and integration with expert evaluation. Priorities include developing highly specific biomarkers of early disease and susceptibility, validating tests within defined risk groups, and conducting trials that distinguish treatment timing from treatment intensity. Prevention studies in genetically or clinically enriched populations are also needed. Completing these research tasks is essential before expanding public health campaigns intended to improve outcomes through earlier detection.



Serpil Erzurum, M.D., Cleveland Clinic

Dr. Serpil Erzurum is chief research and academic officer (CRAO) of the Cleveland Clinic health system. As CRAO, Dr. Erzurum leads the strategic growth of enterprise-wide medical and scientific education programs; clinical, basic, and translational research; and technology development for the delivery of innovative care. A practicing pulmonologist and active scientist, Dr. Erzurum holds the Alfred Lerner Memorial Chair in Innovative Biomedical Research and is professor of medicine at the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University. Her scientific contributions and leadership in pulmonary research have led to diagnostic and therapeutic advances in lung diseases and helped to identify human physiologic adaptive responses to high-altitude hypoxia. She has published more than 300 peer-reviewed articles and has been the principal investigator on more than 20 federal grants, including multi-investigator program project grants and network trials. She is an elected member of the National Academy of Medicine, the American Society for Clinical Investigation, and the Association of American Physicians, serving as its president from 2017–2018. She has served as chair of the Pulmonary Disease Board of the American Board of Internal Medicine. Dr. Erzurum earned her

medical degree from Northeast Ohio Medical University and completed residency training in internal medicine at the Baylor College of Medicine. She completed fellowship training at the University of Colorado Health Sciences Center and postdoctoral training at the National Heart, Lung, and Blood Institute in Bethesda, MD.

Early PH Detection in the World Health Organization (WHO) Classification

The Pulmonary Vascular Disease Phenomics cohort (PVDOMICS; NCT02980887) was designed to redefine heterogeneous pulmonary vascular diseases through deep clinical and biological phenotyping [Hemnes et al. *Circulation Research* 2017]. The network is a rich resource to test the hypothesis that molecular biomarkers can accurately define pulmonary vascular disease along a continuum. A biomarker-defined process can tell us what type of disease biology is present, how strongly the pathway is activated and how the biology evolves over time. Unique characteristics of PVDOMICS allow us to test this concept. The network spans all WSPH Groups 1–5 and includes those with heart, lung, blood and sleep disorders [HLBS] at-risk for PH but not having PH by WSPH hemodynamic criteria [N = 1,193 across six sites [Brigham & Women's, Columbia & Cornell, Mayo, Vanderbilt, U Arizona, Johns Hopkins], of which N = 750 had incident or prevalent PH, N = 347 HLBS At-Risk comparators, and N = 96 healthy controls]. Deep clinical phenotyping was performed with right heart catheterization, cardiopulmonary exercise test, echocardiogram, magnetic resonance imaging, chest computed tomography, lung functions, sleep studies with centralized quality control and quantification of data. Blood samples were obtained at rest and during exercise from numerous vascular beds for multi-omics profiling.

Findings confirm that clinical disease classification is inadequate [Hemnes et al *J Am Coll Cardiol* 2022]. There is substantial overlap across WSPH categories; ~34% of patients cannot be assigned to a single WSPH group. Mixed phenotypes are common in WSPH Group 1. Many patients labeled as Group 1 also exhibit Group 2 and Group 3 features. Pulmonary imaging abnormalities span all WSPH groups—not just Group 3. These findings support the concept that the WSPH clinical definition is unable to accurately classify distinct types of pulmonary vascular disease. Ongoing work is now evaluating biomarker-defined endotypes, including abnormalities in the arginine/nitric oxide pathway. Findings show that arginine/nitric oxide abnormalities are shared across all five PH groups, but vary in magnitude, indicating a continuum of endothelial dysfunction rather than distinct, group-specific patterns [Farha et al. *Antioxidants & Redox Signaling* 2025]. Importantly, biomarker-defined PH clusters are able to predict transplant-free survival better than conventional WSPH classifications [Farha et al. *Journal of the American Heart Association* 2026]. The cluster with the poorest survival had the lowest arginine bioavailability and nitrate levels, consistent with endothelial dysfunction and loss of pulmonary microvasculature. Altogether, these findings support the potential of biomarkers to identify biologically distinct PH subtypes, improve prognostic stratification, and provide insights into disease progression across the PH continuum.

References: *Hemnes et al. Circulation Research* 2017; Hemnes et al *J Am Coll Cardiol* 2022; Rischard et al *Circ Heart Fail*. 2023; Lowery et al *J Am Coll Cardiol*. 2023; Simpson et al. *Am J*

Physiol Lung Cell Mol Physiol. 2023; Balasubramanian et al. *Chest*. 2024; Naranjo et al. *Pulm Circ*. 2023; Borlaug et al. *Eur J Heart Fail*. 2024; Rischard et al. *Circ Heart Fail*. 2023; Reddy et al. *Eur J Heart Fail*. 2024; Farha et al. *Antioxidants & Redox Signaling*. 2025; Farha et al. *Journal of the American Heart Association* 2026.

Bradley Wertheim, M.D., Brigham and Women's Hospital

Dr. Bradley Wertheim is a member of the Pulmonary Vascular Disease Program at Brigham and Women's Hospital and the co-director of the pulmonary vascular section of the Veterans Affairs Boston Healthcare System. He is an assistant professor of medicine at Harvard Medical School. He holds a B.S. in biochemistry from Lafayette College and an M.D. from Harvard Medical School. He completed his internal medicine residency at Massachusetts General Hospital, followed by fellowships in pulmonary and critical care medicine, pulmonary vascular disease, and pulmonary vascular and systems biology at Brigham and Women's Hospital. His laboratory is funded by the National Heart, Lung, and Blood Institute to study the pathogenesis of vascular collagen deposition in early-stage pulmonary arterial hypertension.

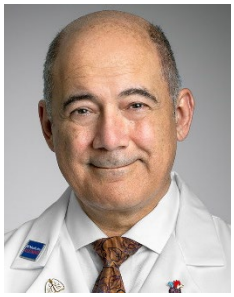
Early Pulmonary Hypertension Pathobiology: The Journey Toward a Multistage Model of Pathogenesis

Although understanding of advanced-stage pulmonary arterial hypertension (PAH) has grown over the last 30 years, only superficial insight exists into the biological mechanisms regulating disease onset and acceleration prior to the onset of clinical symptoms. Elsewhere in biomedical research, efforts to understand the preclinical phase of disease have led to transformative approaches in oncology (such as the paradigm of multi-stage carcinogenesis), cardiovascular medicine, and infectious disease management. However, owing to challenges including patient identification, experimental reductionism, and barriers to obtaining human samples from target tissues (lung, heart) from at-risk/early-stage patients, a similar multi-stage model of PH pathogenesis has not been achieved. This presentation will analyze how investigators have studied biological disease mechanisms in early pulmonary vascular disease to date, through the lens of PAH and other forms of pulmonary hypertension (PH). The discussion will conclude with aspirational strategies to define the temporal biology of PH and elaborate a unified model of multi-stage PH pathogenesis.

Session 1 Breakouts Moderators

Kelly Chin, M.D., UT Southwestern Medical Center

Dr. Kelly Chin is a professor of medicine in the Department of Internal Medicine at UT Southwestern Medical Center and a member of the Division of Pulmonary and Critical Care Medicine. She completed training in internal medicine and earned an M.S. in clinical sciences at UT Southwestern. Dr. Chin also completed a fellowship in pulmonary and critical care medicine at the University of California, San Diego. She currently serves as director of pulmonary hypertension clinical research at UT Southwestern, and she previously served as the director of UT Southwestern's pulmonary hypertension program from 2010–2023. She is active in clinical research, serving as a principal investigator and steering committee member for multiple clinical trials in pulmonary hypertension. She also served as an associate editor for *Circulation* from 2015–2026.



Raymond Benza, M.D., Old Dominion University, Eastern Virginia Medical School

Dr. Raymond Benza is a professor of medicine and section head of cardiology at Eastern Virginia Medical School, which is part of the Macon and Joan Brock Virginia Health Sciences at Old Dominion University. He also serves as the George and Linda Kaufman Academic Chair of Cardiology at Sentara Health. He formerly served as the chief of cardiology at The Ohio State University, the system director of pulmonary vascular disease at Mount Sinai in New York, and the system director of advanced heart failure, transplant, and mechanical circulatory devices at the Allegheny Health Network in Pittsburgh. He is a fellow of the American College of Physicians, the American Heart Association, the American College of Chest Physicians, and the American College of Cardiology. He is a diplomate of the American Board of Internal Medicine with certification in the subspecialties of cardiovascular diseases and advanced heart failure and transplantation. Dr. Benza currently holds administrative positions in the Pulmonary Vascular Research Institute and the International Society for Heart and Lung Transplantation, and he is the former treasurer of that society. He served on President Barack Obama's Advisory Committee on Organ Transplantation in the Health Resources and Services Administration for 4 years. Dr. Benza was knighted in 2015 by his Royal Highness Vittorio Emanuele of Italy for his philanthropic work on behalf of patients with pulmonary arterial hypertension, and he was admitted to the Association of University Cardiologists. He serves on the editorial boards of multiple journals and is the steering committee chair for multiple industry trials in heart failure and pulmonary hypertension. His primary clinical interests are the evaluation and treatment of advanced congestive heart failure, cardiac transplantation, and pulmonary arterial hypertension. He participates in major clinical studies of new therapies for the treatment of heart failure, mechanical support, and pulmonary hypertension. Dr. Benza is a funded investigator for the National Institutes of Health

for his work in pulmonary arterial hypertension focusing on risk stratification, pharmacogenomics, and new device therapies for the disease.

Session 2: AI- and Non-AI-Assisted Technology to Detect Early PH, Part 1

Syed Ahmad Chan Bukhari, Ph.D., St. John's University

Dr. Syed Ahmad Chan Bukhari is an associate professor of computer science and director of research in the Collins College of Professional Studies at St. John's University in New York. He leads the Bukhari Lab, where his research focuses on trustworthy artificial intelligence (AI), biomedical knowledge graphs, neuro-symbolic reasoning, clinical natural language processing, and health data interoperability. His work bridges AI methodology with biomedical data science, clinical prediction, and decision support. His research has been supported by the National Institutes of Health and the National Science Foundation. Previously, he conducted research at the Yale School of Medicine and Stanford University's CEDAR Metadata Center. His scientific interests include robust and interpretable AI, knowledge-guided reasoning, uncertainty-aware learning, and human-centered clinical AI. Through interdisciplinary collaborations, he aims to develop AI methods that are transparent, reproducible, and rigorously evaluated for challenging healthcare problems.

Understanding AI: From Patterns to Trustworthy Clinical Decisions

Artificial intelligence (AI) is increasingly capable of recognizing patterns in electrocardiograms, medical images, clinical notes, and longitudinal patient records. For pulmonary hypertension (PH), however, a promising risk signal is not yet an earlier, more accurate, or clinically useful decision. This presentation offers a clinician-oriented introduction to contemporary AI, including predictive machine learning, multimodal learning, generative AI, and agentic systems. Using selected published studies in PH, it will illustrate both emerging capabilities and important evidence gaps related to clinical context, generalizability, reference standards, and prospective validation.

The presentation will then explore research directions in knowledge-guided and causal reasoning, uncertainty-aware models, and carefully supervised AI agents. Emphasis will be placed on trustworthy human-AI collaboration, transparent evidence, fairness, and outcomes that matter to patients and health systems. The goal is to identify promising opportunities for interdisciplinary research that can help clinicians connect fragmented clinical signals, recognize disease more responsibly, and evaluate whether AI-assisted pathways genuinely improve the timing and quality of care.

Gaurav Choudhary, M.D., Brown University

Dr. Gaurav Choudhary is the Ruth and Paul Levinger professor of cardiology at the Warren Alpert Medical School of Brown University and director of cardiovascular research at Brown University and the Brown University Health Cardiovascular Institute. He also serves as chief of research at the VA Providence Healthcare System. Dr. Choudhary is a practicing cardiologist and co-director of the VA Providence Pulmonary Hypertension Clinic. His research, funded by the National Institutes of Health and the Department of Veterans Affairs, focuses on pulmonary hypertension and right ventricular (RV) dysfunction, spanning clinical epidemiology, pulmonary vascular biology, mechanisms of RV remodeling, and translational science. His work aims to improve the early detection, risk stratification, and treatment of pulmonary hypertension. He was co-principal investigator of a National Heart, Lung, and Blood Institute–funded project developing deep learning methods to detect pulmonary hypertension using digital stethoscope recordings and single-lead electrocardiography. His current interests include integrating artificial intelligence with noninvasive cardiovascular technologies to develop accessible, scalable screening tools for earlier recognition of pulmonary hypertension and RV dysfunction.

Digital Stethoscope for Early PH Detection

Pulmonary hypertension (PH) is a progressive condition associated with significant morbidity and mortality, yet diagnosis is frequently delayed. Limited access to echocardiography and specialized diagnostic testing contributes to underrecognition, particularly in primary care and resource-limited settings. Artificial intelligence (AI)-enabled digital stethoscopes offer a potentially scalable approach to earlier detection.

This presentation will describe the development and evaluation of a deep learning-based algorithm using digital stethoscope recordings to identify elevated right ventricular systolic pressure (RVSP), a marker of possible PH. A vision transformer-based model was pretrained on over 600,000 unlabeled recordings and fine-tuned using 15,595 recordings from 1,665 patients, with echocardiographic RVSP ≥40 mmHg defining the screening target. In an independent test cohort of 373 patients, the algorithm achieved an area under the receiver operating characteristic curve (AUROC) of 0.882 at the patient level, with 78.3% sensitivity and 80.1% specificity.

The presentation will also explore opportunities to improve screening performance by integrating complementary AI-derived findings, including cardiac murmurs, ventricular dysfunction, and electrocardiographic abnormalities. Future directions include validation against invasive hemodynamics, differentiation of PH subtypes, longitudinal monitoring, and prospective evaluation of clinical implementation.

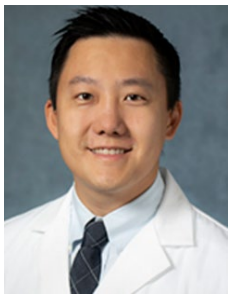
AI-enabled digital auscultation has the potential to transform PH screening by providing an accessible, noninvasive point-of-care tool to facilitate earlier recognition, appropriate referral, and timely diagnosis.

Hilary DuBrock, M.D., Mayo Clinic

Dr. Hilary DuBrock is a professor of medicine at the Mayo Clinic in Rochester, MN, co-director of the Pulmonary Hypertension (PH) Clinic and program director of the Mayo Clinic PH fellowship. Dr. DuBrock's clinical and research interests include PH, pulmonary vascular complications of liver disease, and the use of artificial intelligence to aid in the early diagnosis of PH.

Electrocardiograms (ECGs) for Early PH Detection

Pulmonary hypertension (PH) is a progressive condition characterized by an elevated mean pulmonary arterial pressure, which can lead to right ventricular failure and death. Due to non-specific symptoms, PH is commonly associated with significant diagnostic delays of 2-3 years. Electrocardiograms are simple, non-invasive, and inexpensive tests commonly performed in the PH diagnostic journey, but traditional ECG interpretation has limited sensitivity for PH diagnosis. Artificial intelligence (AI)-enhanced ECG analysis may identify subtle electrical signatures of PH earlier in the disease course. In this presentation, the evidence regarding conventional and AI-enhanced ECG for early PH detection will be discussed. Important challenges, including false-positive results, interpretability, implementation, and the need for prospective studies to determine whether AI-ECG can meaningfully accelerate PH diagnosis and improve clinical outcomes, will also be discussed.



David Ouyang, M.D., Cedars-Sinai Medical Center

Dr. David Ouyang is a physician-scientist and cardiologist with subspecialty expertise in noninvasive imaging and a technical background in programming, statistics, and deep learning. As a statistician, he has always been fascinated by how to understand, visualize, and interpret data. With the exponential rise in the amount of data being collected in clinical care, there are substantial opportunities to use these data to personalize care and improve diagnosis and treatment of cardiovascular disease. Dr. Ouyang's goal as an investigator is to apply his expertise in echocardiography and deep learning to medical imaging while leveraging clinically generated data to inform scientific discovery. His previous work has demonstrated the ability of convolutional neural networks to identify systemic human phenotypes that modify cardiovascular risk but were previously thought not to be apparent on echocardiographic images, as well as to characterize cardiac function more precisely than human interpreters. As an advanced cardiac imager and cardiologist, Dr. Ouyang hopes to enhance the use of cardiovascular imaging in clinical care.

Echocardiography for Early PH Detection

Pulmonary hypertension (PH), defined by an elevated mean pulmonary artery pressure >20 mmHg, is often recognized late. With rapid image acquisition, no ionizing radiation, and low cost,

transthoracic echocardiography serves as the frontline test for PH and guides referral for right heart catheterization (RHC). Screening rests on right ventricular systolic pressure (RVSP), derived as 4 × (peak tricuspid regurgitation velocity [TRV])^2 plus a right atrial pressure inferred from the inferior vena cava. Suboptimal Doppler signals, torrential tricuspid regurgitation, and categorical right atrial pressure estimates yield 95% limits of agreement with RHC as wide as ±40 mmHg; about half of estimates differ from RHC by >10 mmHg, 22–56% of studies have no measurable TRV, and mild PH falls below current TRV thresholds. Much of this error reflects heterogeneity in acquisition and expert interpretation, and artificial intelligence (AI) improves upon standard measures; in EchoNet-RCT, the first prospective, blinded randomized clinical trial for AI in echocardiography, cardiologists revised AI ejection fraction assessments less often than sonographer assessments (16.8% vs 27.2%). Automated TRV measurement achieves diagnostic accuracy comparable to expert readers against RHC, and our open-source EchoNet-Measurements automates right heart, pulmonary artery, and inferior vena cava measurements. Multi-view foundation models such as EchoPrime, trained on over 12 million videos, estimate pulmonary artery pressure and right ventricular function, and could extend assessment to patients without a measurable TRV and to opportunistic archive screening. This talk reviews these results alongside AI-ECG and multimodal approaches and proposes research priorities, including paired echocardiography–RHC datasets, models trained on invasive hemodynamics rather than echocardiography-derived labels, and prospective randomized evaluation of AI-guided PH detection and referral.

Session 3: AI- and Non-AI-Assisted Technology to Detect Early PH, Part 2

Katherine Goodman, J.D., Ph.D., University of Maryland School of Medicine

Dr. Katherine Goodman is an associate professor of epidemiology and founding director of the Center for Health AI Evaluation at the University of Maryland School of Medicine and director of the Generative AI Lab at the University of Maryland Institute for Health Computing. Her research sits at the intersection of artificial intelligence (AI), clinical data science, and health law, with a particular focus on leveraging large volumes of unstructured electronic health record data and patient-reported outcomes to improve diagnostic timeliness and algorithmic safety across clinical domains. A former U.S. Food and Drug Administration law attorney, Dr. Goodman brings legal and regulatory expertise to emerging questions surrounding clinical decision support tools, healthcare applications of generative AI, and medical device regulation. Her scholarship examining clinical AI governance, safety, and ethics has appeared in leading journals, including The Journal of the American Medical Association and *The New England Journal of Medicine*.

AI Caveats—and Opportunities—in Early PVD Detection

Artificial intelligence (AI) offers opportunities to improve the timeliness of pulmonary vascular disease (PVD) detection, but translating promising models into clinical benefit requires attention to where and how AI enters the diagnostic process. This presentation examines two practical

caveats that can inform study design. First, the regulatory status of clinical AI depends on its intended function, with important distinctions between analysis of images or physiologic signals versus clinical text. These distinctions shape feasible research and implementation pathways. Second, the low prevalence and heterogeneous presentation of pulmonary vascular diseases complicate screening; even highly accurate prediction models may produce many more false positives than true positives. Strategies include enriching for higher-risk patients, focusing on persistent symptoms unexplained by other conditions, and achieving sufficient sample size to study subtle or atypical presentations.

These challenges also create opportunities for academic research. AI-scribe transcripts may preserve granular symptom descriptions and temporal clues lost in conventional clinical notes if healthcare systems retain transcripts for appropriate research use. Additionally, patient-facing conversational AI may enable repeated, longitudinal characterization of persistent or evolving symptoms, collected from patients at home. Finally, locally deployed large language models (LLMs) and federated research approaches may support multicenter analyses without centrally pooling raw clinical text that could violate HIPAA requirements. Together, these strategies offer a path for navigating regulatory and methodological caveats to develop testable approaches for earlier and more clinically useful PVD detection.

Farbod Rahaghi, M.D., Ph.D., University of California, Los Angeles

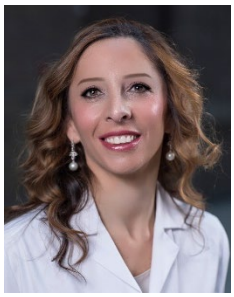
Dr. Farbod Rahaghi is an associate professor of medicine at the David Geffen School of Medicine at UCLA and a physician-scientist specializing in pulmonary and critical care medicine, with a focus on pulmonary vascular disease. Dr. Rahaghi earned his medical degree and Ph.D. in bioengineering from the University of California, San Diego. He completed his internal medicine residency at Duke University and his pulmonary and critical care fellowship at Harvard Medical School's Brigham and Women's Hospital and Massachusetts General Hospital, where he subsequently served on the faculty before joining UCLA.

His research integrates advanced medical imaging, quantitative analysis, and artificial intelligence to improve the diagnosis, characterization, and management of cardiopulmonary diseases such as pulmonary hypertension, pulmonary embolism, and parenchymal lung disease. His work in imaging has focused on the application of computed tomography to quantify vascular structure and identify clinically meaningful disease phenotypes. He is also interested in leveraging large clinical datasets and machine learning to advance personalized approaches to pulmonary vascular disease.

Computerized Tomography (CT) of the Chest for Early PH Detection

This talk will discuss the current strengths and limitations of clinical CT imaging for screening for PH. The talk will discuss what paradigms are being advanced to enhance this capability. The interplay between these advances and the subtle but importantly related concept of detection of early disease (that is, measuring vasculopathy) and a vision for its potential role, particularly in at-

risk populations, will then be discussed. Lastly, the emergence of new technology and how this will enhance CT's ability to be used in PH will be discussed.



Maria Giovanna Trivieri, M.D., Ph.D., Icahn School of Medicine at Mount Sinai

Dr. Maria Giovanna Trivieri is associate professor of medicine and radiology and medical director of the Pulmonary Hypertension Program at the Icahn School of Medicine at Mount Sinai, with an additional appointment in the Black Family Stem Cell Institute. A physician-scientist with international training in Italy, Canada, and the United States, she integrates basic cardiovascular science with clinical investigation to study pulmonary vascular disease and cardiomyopathies.

Her research combines molecular imaging with human stem cell disease models to investigate disease mechanisms and to identify potential diagnostic and therapeutic targets. She has led studies using hybrid PET/MRI to characterize pulmonary vascular abnormalities in pulmonary hypertension and examine their relationship to hemodynamics and clinical risk. Her broader imaging portfolio includes cardiac sarcoidosis, amyloidosis, arrhythmic mitral valve prolapse, and transplant rejection.

Her research has received support from the National Institutes of Health, the American Heart Association, the U.S. Department of War, and industry sources. She is particularly interested in translating molecular imaging signals into validated tools for earlier recognition and characterization of pulmonary vascular disease and right ventricular remodeling.

Molecular Technologies for Early PH Detection

Molecular imaging offers an opportunity to identify pulmonary vascular and right ventricular changes before conventional measures reveal functional deterioration. This presentation reviews emerging PET technologies for early detection and disease characterization in pulmonary hypertension, focusing on FDG as a marker of glucose utilization, VEGFR-targeted tracers as indicators of vascular biology, and FAPI as a marker of fibroblast activation.

Evidence from experimental models and clinical studies illustrates the distinct questions these tracers can address. Pulmonary artery FDG uptake has been associated with pulmonary hypertension in sarcoidosis and observed in patients with precapillary disease despite otherwise favorable clinical risk assessments. VEGFR-targeted PET has shown increased lung tracer uptake before pulmonary pressure elevation in a rat model. Clinical FAPI studies have linked right ventricular uptake to impaired function, remodeling, and subsequent clinical worsening in established pulmonary arterial hypertension.

The presentation distinguishes evidence for disease activity and prognosis from evidence required to demonstrate earlier diagnosis or benefit from PET-guided treatment. It also examines challenges related to tracer specificity, acquisition protocols, signal localization, and

reproducibility. Finally, it proposes priorities for prospective studies in at-risk populations, including standardized imaging, blinded interpretation, appropriate reference standards, and longitudinal assessment of disease progression and clinical impact. Whether acting on an earlier molecular signal improves patient outcomes remains a central question.

Sudarshan Rajagopal, M.D., Ph.D., Duke University

Dr. Sudarshan Rajagopal is an associate professor of medicine in the Division of Cardiology at the Duke University School of Medicine, and he is the co-director of the Duke Pulmonary Vascular Disease Center. As a physician, he sees patients across the spectrum of pulmonary hypertension (PH). The major goal of his basic research is to discover and characterize basic signaling and physiological mechanisms whose dysfunction contributes to PH. As a postdoctoral fellow in the laboratory of Dr. Robert Lefkowitz, he focused on "biased agonism," a novel paradigm for G protein-coupled receptor (GPCR) signaling in which receptors can signal through distinct pathways depending on the ligand that binds to them. His research group has made fundamental discoveries on mechanisms underlying biased agonism and the effects of GPCR-biased signaling. He has established an active translational research program focused on implementing novel imaging approaches to evaluate disease activity in pulmonary arterial hypertension (PAH) and CTEPH and on applying artificial intelligence approaches to imaging and real-world data in PH. In collaboration with Dr. Bastiaan Driehuys, he has used hyperpolarized xenon magnetic resonance imaging to probe pulmonary capillary hemodynamics to diagnose PH and monitor response to therapy.

Hyperpolarized Xenon MRI to Phenotype Pulmonary Hypertension

Pulmonary hypertension (PH) is a heterogeneous group of disorders that result in an increase in mean pulmonary artery pressure. Diagnosis and screening of PH are based largely on methods that do not directly probe the pulmonary vasculature, but rather on changes in right heart function (echocardiography) or in pulmonary vascular resistance (right heart catheterization) that only become abnormal once there is already significant disease. Noninvasive tools for probing the pulmonary vasculature remain limited, but hyperpolarized xenon-129 (^{129}Xe) magnetic resonance imaging (MRI) offers a unique window into 3D lung function. Because xenon dissolves into lung tissue and binds hemoglobin, a single breath-hold can image gas exchange from airspaces into the lung parenchyma (membrane) and transfer into red blood cells (RBCs). It also captures cardiogenic oscillations in the RBC signal.

This presentation will review the principles of ^{129}Xe MRI and the distinct functional signatures that differentiate obstructive, interstitial, and pulmonary vascular diseases. Most notably, ^{129}Xe MRI has specific signatures associated with PH that differentiate it from other chronic lung diseases, including reduced RBC transfer with relatively preserved ventilation and barrier uptake, and altered RBC signal oscillations that report on pulmonary vascular resistance and distinguish pre-capillary from post-capillary disease. These signatures have also shown promise as biomarkers for therapeutic response. Lastly, unpublished data will show how ^{129}Xe MRI can phenotype

patients with PH, a step toward more precise, physiology-based classification and individualized treatment.

Session 2 and 3 Breakouts Moderators

Monica Mukherjee, M.D., Johns Hopkins University

Dr. Monica Mukherjee is a professor of medicine in the Division of Cardiology at Johns Hopkins University and a physician-scientist specializing in quantitative echocardiography, multimodality cardiovascular imaging, right ventricular physiology, and pulmonary vascular disease. Her research program investigates mechanisms of right ventricular adaptation to pulmonary vascular load and develops noninvasive imaging approaches to identify maladaptation before overt right heart failure. Dr. Mukherjee's work has characterized distinct patterns of right ventricular dysfunction in systemic sclerosis, demonstrated the utility of exercise provocation for detecting early cardiopulmonary abnormalities, and advanced physiologically informed measures of right ventricular–pulmonary arterial coupling. Through the integration of multimodality imaging, invasive hemodynamics, pressure-volume analysis, and multicenter studies, her research seeks to improve disease phenotyping and risk stratification. Her research has received support from the National Institutes of Health, U.S. Department of War, National Scleroderma Foundation, and CHEST Foundation. She served as chair of the writing committee for the 2025 ASE Right Heart Guidelines and the 2026 AHA scientific statement on myocardial inflammation. She serves on the ASE board of directors, chairs the AHA Cardiac Imaging and Intervention Committee, and holds editorial positions with *Circulation, Circulation: Cardiovascular Imaging, Journal of the American Heart Association,* and the *Journal of the American Society of Echocardiography*.

Shelsey Johnson, M.D., Brigham and Women's Hospital

Dr. Shelsey Johnson is a junior faculty member in the Division of Pulmonary and Critical Care Medicine at Brigham and Women's Hospital in Boston, MA. She is a physician-scientist whose clinical research focuses on early diagnosis and phenotyping of pulmonary hypertension associated with chronic obstructive pulmonary disease through the use of quantitative chest computed tomography data. Her work is supported by a K23 award from the National Heart, Lung, and Blood Institute.

Steven Kawut, M.D., M.S., University of Pennsylvania

Dr. Steven Kawut is the director of the Pulmonary Hypertension/Pulmonary Vascular Disease Program, a senior scholar in the Center for Clinical Epidemiology and Biostatistics, and a tenured professor of medicine and epidemiology at the Perelman School of Medicine at the University of Pennsylvania. His clinical and research interests focus on pulmonary vascular disease and lung transplantation. He has published more than 350 peer-

reviewed articles on topics such as pulmonary arterial hypertension and right ventricular dysfunction. He has received funding from the National Institutes of Health (NIH) for 25 years. He serves on the editorial board of the *American Journal of Respiratory and Critical Care Medicine*. He has served on several study sections and on the Data and Safety Monitoring Boards of NIH-funded and industry-funded single-center and multicenter randomized clinical trials. He has mentored more than 60 individuals in clinical research.

Session 4: Biomarkers

Patricia Thistlethwaite, M.D., Ph.D., University of California, San Diego

Dr. Patricia Thistlethwaite is a distinguished professor of surgery and director of the Division of Cardiothoracic Surgery at the University of California, San Diego. She served as the first woman president of the Western Thoracic Surgical Society. Dr. Thistlethwaite's clinical interests include lung cancer, minimally invasive pulmonary and mediastinal surgery, and heart and lung transplantation. In addition to her clinical work, Dr. Thistlethwaite has run a molecular biology laboratory focused on pulmonary vascular disease with funding from the National Institutes of Health for the past 27 years. She earned the Honorary Knowledge and Discovery Award (recognizing the top 5 percent of researchers in the United States) from the American Health Council, the Jenesis Trailblazer Award from United Therapeutics, the Certificate of Excellence Award from the Pulmonary Vascular Research Institute, and has been named a Castle Connolly Top Doctor and an Exceptional Woman in Medicine for the past 23 years. She has authored more than 180 peer-reviewed papers.

New Blood-Derived Biomarkers for Early PH Detection or Risk Stratification

A major barrier to the diagnosis and treatment of pulmonary arterial hypertension is the lack of a widely used, non-invasive blood test that is highly sensitive and specific for diagnosing and following the course of individuals with this disease, including patients with early-stage pulmonary arterial hypertension.

In recent years, there has been a plethora of newly identified biomarkers for the diagnosis and prognosis of pulmonary arterial hypertension. Although published studies have addressed the use of biomarkers in newly diagnosed and established disease, few biomarkers have been specifically validated for diagnosis and risk stratification in early pulmonary arterial hypertension. This talk will highlight areas of interest, including single-peptide biomarkers, miRNA, long non-coding RNA, cell-free DNA, circulating progenitor cells, and methylation signatures in circulating CD4+ T-cells.

Anna Hemnes, M.D., Vanderbilt University Medical Center

Dr. Anna Hemnes is professor of medicine at Vanderbilt University Medical Center, where she holds the Hugh Jackson Morgan chair in medicine and serves as chair of the Department of Medicine. She is a translational physician-scientist whose research focuses on altered metabolism in pulmonary vascular disease. Her laboratory investigates the effects of BMPR2 mutations on insulin-mediated intracellular signaling in the pulmonary vasculature and right ventricle. Her clinical research examines the role of insulin resistance and metabolic syndrome in pulmonary vascular disease, including genetic susceptibility and deep molecular phenotyping. This work led to a landmark publication identifying an omic signature of vasodilator-responsive pulmonary arterial hypertension; the study was among the earliest demonstrations of precision medicine in an ultrarare pulmonary vascular disease. Building on these findings, her group is developing blood-based omics approaches to predict responses to U.S. Food and Drug Administration–approved therapies for pulmonary arterial hypertension. In addition to her research, Dr. Hemnes maintains an active clinical practice in the Vanderbilt Center for Pulmonary Vascular Disease. She cares for patients with pulmonary vascular disorders and has successfully recruited patients into numerous clinical studies investigating pulmonary hypertension, diagnostic approaches, and novel disease classifications. Her work bridges basic science, translational discovery, and clinical investigation to advance understanding and treatment of pulmonary vascular disease and improve patient outcomes.

Multi-Omics and Composite Biomarkers for Early PH Detection or Risk Stratification

Pulmonary hypertension is a disease that usually develops insidiously over months or years and by the time of presentation is thought to affect a substantial portion of the lung's vasculature. As a result, delayed presentation is the norm for most patients and better tools for screening at-risk populations and early identification predictors for members of the general population who do not have known risk. Moreover, in patients with established pulmonary hypertension, we choose therapies based on clinical risk characteristics rather than molecular characterization of disease process that dictates choice of effective therapies. This talk will discuss the unmet need in pulmonary hypertension for molecular markers of disease presence, optimal therapeutic choice, and risk for poor outcomes. Ideal features of biomarkers and early attempts to address this fundamental question will be reviewed.

Micheala Aldred, Ph.D., Indiana University

Dr. Micheala Aldred graduated from University College London with a first-class degree in genetics. Her Ph.D. studies were conducted at the MRC Human Genetics Unit, in Edinburgh, Scotland, where she worked on the genetics of X-linked retinitis pigmentosa. Her postdoctoral training at the University of Cambridge and Ohio State University included experience in cancer genetics and chromosome deletion syndromes. Dr. Aldred ran the clinical molecular genetics diagnostic laboratory at the University of Leicester for 5 years, where she worked with

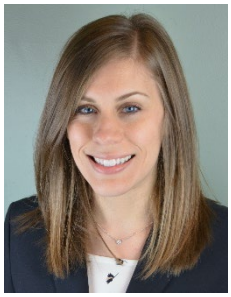
professor Richard Trembath on the genetics of pulmonary arterial hypertension (PAH), and was part of the international consortium that identified bone morphogenetic protein receptor type 2 (*BMPR2*) gene mutations in familial PAH. Prior to moving to Indianapolis, Dr. Aldred held faculty appointments at the University of Leicester and in the Genomic Medicine Institute at Cleveland Clinic.

Dr. Aldred's research applies her wide-ranging experience in inherited diseases and cancer genetics to the study of PAH and hereditary hemorrhagic telangiectasia (HHT). PAH is a potentially fatal disorder characterized by proliferative changes in the vessels of the lungs, leading to a sustained elevation in pulmonary artery pressure. This increased pressure in turn affects the heart and may lead to right heart failure. Dr. Aldred has recently identified somatic chromosomal alterations in endothelial cells from the lungs of patients with PAH. Her work now focuses on characterizing the molecular basis for these changes and their functional roles in the disease process. Her group has also shown that mutations in the *BMPR2* gene or in *SMAD9*, a downstream mediator of bone morphogenetic protein (BMP) signaling, can disrupt BMP-regulated microRNA processing, thus highlighting a new pathway that may be important in the pathogenesis of PAH. This work has culminated in testing drugs that could bypass the genetic defect, raising the possibility of personalized therapy for patients with the familial form of PAH. This project has now broadened to include HHT, a related vascular disorder that is also caused by mutations in the BMP signaling pathway. Dr. Aldred's research is funded by an Outstanding Investigator Award from the National Institutes of Health, and she is an active participant in several national and international pulmonary hypertension consortia.

Genetic and Genomic Susceptibility for Early PH Detection

To date, twelve genes have been definitively associated with PAH, and nine more have a lower evidence base. However, pathogenic variants in these genes are rare. Only about 6% of PAH patients have a family history, while 10% to 20% of patients with idiopathic PAH are found to harbor a mutation upon sequencing. First-degree relatives of individuals with a pathogenic variant can opt to undergo predictive genetic testing and, if found to carry the same variant, regular surveillance may aid early diagnosis. In the general population, however, Group 1 PH is rare, and thus it is not feasible to undertake genetic screening to identify individuals who are at increased risk. The role of common variants is still an emerging field, but the identification of functional enhancer variants that influence expression of the transcription factor SOX17 is exemplary. For non-Group 1 PH, very little is known about potential genetic contributors, but here the at-risk populations are much larger, and genetic testing may have greater utility if robust polygenic risk scores can be identified. Large-scale sequencing studies will be required to achieve this goal. Perhaps the greatest yield may come not from early diagnosis but from pharmacogenomic studies that help better target treatments to those most likely to respond.

Session 4 Breakouts Moderators



Catherine Simpson, M.D., Johns Hopkins University

Dr. Catherine Simpson is an associate professor of medicine in the Division of Pulmonary and Critical Care Medicine at the Johns Hopkins University School of Medicine. She is also a physician-scientist in the Johns Hopkins Pulmonary Hypertension Program and the associate program director for research in the Pulmonary and Critical Care Medicine Fellowship Program.

Dr. Simpson leads a translational research program focused on understanding biological heterogeneity in pulmonary vascular disease and the mechanisms underlying right ventricular adaptation and failure. Her research integrates high-dimensional molecular data, including metabolomics, proteomics, and single-cell transcriptomics, with detailed clinical phenotyping and cardiovascular physiology to identify molecular endophenotypes, clinically informative biomarkers, and potential therapeutic targets. These research efforts are funded by National Heart, Lung, and Blood Institute R01 and R03 awards and an Innovative Project Award from the American Heart Association. A central goal of her work is to translate molecular discoveries into improved disease classification, risk stratification, and personalized treatment strategies for patients with pulmonary hypertension.

Arun Jose, M.D., University of Cincinnati

Dr. Arun Jose earned his undergraduate degree in biomedical engineering from Johns Hopkins University, where he remained for his medical degree and internal medicine residency training in the Osler Program at The Johns Hopkins Hospital. He completed fellowship training in pulmonary and critical care medicine at George Washington University, followed by a master's degree in clinical and translational research at the University of Cincinnati, where he remained as a faculty member. He is currently an associate professor of medicine, a pulmonary hypertension specialist, and director of pulmonary hypertension at the Cincinnati VA Medical Center. He is also a fellow of the American College of Chest Physicians and the American Thoracic Society. Dr. Jose's current research interests include clarifying the biochemical mechanisms that drive pulmonary vascular disease due to liver disease, exploring the role of the gut microbiome and circulating metabolome in pulmonary arterial hypertension, and developing clinical biomarkers with prognostic value in different forms of pulmonary hypertension.

Session 5: Exercise Physiology to Uncover Early PH

Ryan Tedford, M.D., Medical University of South Carolina

Dr. Ryan Tedford is a professor of medicine in the Division of Cardiology and holds the Dr. Peter C. Gazes Endowed Chair in Heart Failure at the Medical University of South Carolina (MUSC) in Charleston, SC. He currently serves as the section head of heart failure and the medical director of cardiac transplantation. He also established and directs the Advanced Heart Failure and Transplant Fellowship Program at MUSC. Dr. Tedford is an internationally recognized clinical researcher and has published more than 350 works, including peer-reviewed original research articles, invited expert reviews, editorials, and book chapters. His research focuses on hemodynamic assessment of right ventricular function and its interaction with the pulmonary circulation and left heart. This research spans the fields of pulmonary hypertension (PH), left heart disease, exercise physiology, hemodynamics, systemic sclerosis, and mechanical circulatory support. He serves on numerous scientific advisory boards and clinical trial steering committees. He co-chaired the task force on PH due to left heart disease for the 7th World Symposium on Pulmonary Hypertension. He is currently a deputy editor for *Circulation*. He previously served as deputy editor for the *Journal of Heart and Lung Transplantation* and on the editorial boards of *Circulation: Heart Failure*, *CHEST*, and *JACC: Heart Failure*.

Early RV Changes in Early PH Detection

Early detection of pulmonary hypertension (PH) requires recognition of right ventricular (RV) maladaptation before overt RV failure develops. Traditional measures of RV function, including TAPSE, RV fractional area change, and RV ejection fraction, may remain relatively preserved during early disease. Measures of RV-pulmonary artery (PA) coupling may identify abnormalities in RV adaptation at an earlier stage. Emerging less-invasive approaches and surrogate measures of RV-PA coupling may improve sensitivity and facilitate longitudinal assessment, particularly when invasive measures are impractical.

Assessment of RV reserve provides an additional opportunity to uncover early disease by evaluating the ability of the RV to augment function in response to stress. Exercise right-heart catheterization, stress echocardiography, and advanced imaging can characterize RV and pulmonary vascular reserve. However, the physiologic response, and potentially the ability to discriminate early disease, vary according to the stressor employed, including exercise, volume loading, and pharmacologic challenge. Integrating resting measures of RV-PA coupling with dynamic assessment of RV reserve may ultimately provide a more sensitive framework for identifying early pulmonary vascular disease and detecting clinically meaningful PH before conventional resting measures become abnormal.

Barry Borlaug, M.D., Mayo Clinic

Dr. Barry Borlaug is a consultant in the Division of Circulatory Failure, Department of Cardiovascular Medicine, with a joint appointment in the Division of Interventional Cardiology. Dr. Borlaug also serves as chair of cardiovascular research at the Mayo Clinic Rochester. He joined the staff of the Mayo Clinic in 2006 and holds the academic rank of professor of medicine at the Mayo Clinic College of Medicine and Science. He is the Endowed William J. and Sharon A. Schoen professor of cardiology.

Dr. Borlaug is an invasive cardiologist who specializes in treating patients with congestive heart failure. He conducts cardiac catheterization procedures, with a special interest in comprehensive invasive hemodynamic assessment. His research focuses on the mechanisms, diagnosis, and treatment of heart failure—particularly heart failure with preserved ejection fraction. His team is pursuing several clinical studies examining the abnormalities that contribute to functional limitations and symptoms of heart failure. Dr. Borlaug's lab also conducts clinical trials seeking to identify novel therapies to improve functional status and long-term outcomes in patients with heart failure. His research is funded by the National Heart, Lung, and Blood Institute; the U.S. Department of War; and industry grants. He serves in steering committee leadership roles for multicenter industry-sponsored trials in addition to his federally funded and foundation-funded studies. Dr. Borlaug has published over 600 peer-reviewed articles as well as multiple book chapters and abstracts. Dr. Borlaug has a long track record of mentorship, with over 50 current and former trainees, and currently serves as program director for the Mayo Clinic Cardiovascular National Institutes of Health–funded T32 training grant.

Provocative RHC to Uncover Early Pulmonary Hypertension

Pulmonary hypertension (PH) remains under-recognized in patients with exertional dyspnea. Exercise right heart catheterization (RHC) provides a physiologic stress test that can uncover abnormalities not apparent at rest and identify early PH related to HF with preserved ejection fraction (HFpEF), as well as precapillary exercise-induced PH.

Invasive hemodynamic exercise testing can reveal marked increases in pulmonary artery pressure (PAP) and pulmonary artery wedge pressure (PAWP) despite normal resting values. In HFpEF, approximately one-third of affected patients have normal resting PAWP; these patients have an increased risk of heart failure hospitalization or death compared to patients with normal exertional PAWP. An abnormal PAP-cardiac output relationship during exercise with normal PAWP can identify an early precapillary pulmonary vascular phenotype. Exercise PH is prognostically important, and longitudinal observations in HFpEF and systemic sclerosis suggest that exercise-induced hemodynamic abnormalities may precede the development of resting PH.

Exercise RHC offers diagnostic information beyond resting hemodynamics by interrogating cardiovascular reserve under the conditions in which patients experience symptoms. Current diagnostic criteria include an exercise PAWP ≥25 mmHg or PAWP/cardiac output slope ≥2

mmHg/L/min for HFpEF and an mPAP/cardiac output slope ≥3 mmHg/L/min with normal PAWP for precapillary exercise PH. Importantly, emerging evidence suggests that exercise-induced PH represents a potentially treatable stage of disease, with stronger therapeutic evidence currently available for HFpEF than for precapillary PH; this remains an important gap where more evidence is needed.

When exercise testing is not feasible, saline loading or passive leg raise can improve diagnostic sensitivity compared with resting measurements alone, although these provocations produce less robust hemodynamic stress than exercise.

Combining invasive hemodynamics with cardiopulmonary exercise testing, blood sampling, and ventilatory measurements can further define the mechanisms limiting oxygen delivery and utilization. A proactive, physiologically provocative approach to RHC may therefore enable earlier and more accurate phenotyping of patients with unexplained exertional symptoms, identify pulmonary vascular and left-heart disease before resting abnormalities become overt, and create opportunities for earlier disease-specific intervention.

Allan Lawrie, Ph.D., Imperial College London

Dr. Allan Lawrie is chair of pulmonary vascular diseases at Imperial College London and leads multidisciplinary research focused on improving the detection, monitoring, and treatment of pulmonary vascular disease. His research spans molecular mechanisms, drug-target development, digital health, and artificial intelligence in pulmonary arterial hypertension (PAH), with a strong translational focus. He leads research programs that leverage passively sensed real-world data from smartphones and wearable devices linked to health records to identify early signals of disease, monitor changes in health status, and develop scalable digital biomarkers. Working across large population cohorts, his team combines activity, physiological, behavioral, and environmental data with machine learning approaches to improve early diagnosis and longitudinal monitoring of PAH and other cardiovascular diseases. Dr. Lawrie has established collaborations across academic, clinical, technology, and industry sectors to accelerate the translation of digital health innovations into clinical practice.

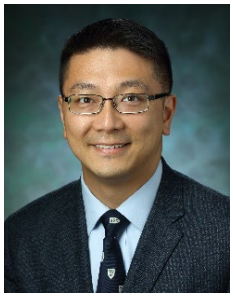
The use of passively sensed real-world data from smartphones and wearable to support early detection and monitoring of PAH

Pulmonary arterial hypertension (PAH) is a progressive disease that is frequently diagnosed late, often following a prolonged period of non-specific symptoms. Earlier identification of individuals at risk and improved approaches to longitudinal monitoring remain major unmet needs in pulmonary vascular disease.

The rapid adoption of smartphones and wearable devices has created new opportunities to capture continuous, passively sensed measures of health in real-world settings. Data on physical activity, mobility, sleep, heart rate, and behavior can provide insights into functional status that

may complement or even precede traditional clinical assessments. This presentation will discuss emerging evidence supporting the use of digital phenotyping and consumer technologies. It will highlight recent work demonstrating that smartphone-derived physical activity measures can identify patients with PAH and that these measured variables are associated with disease severity, supporting the feasibility of real-world digital biomarkers for patient monitoring. To conclude, the presentation will outline ongoing and planned work through the My Heart Counts program to combine passively collected smartphone and wearable data with electronic health records and advanced machine learning approaches to develop scalable strategies for population-level screening, risk stratification, and remote monitoring of pulmonary vascular disease.

Session 5 Breakouts Moderators



Steven Hsu, M.D., Johns Hopkins University

Dr. Steven Hsu is associate professor of medicine in the Division of Cardiology at the Johns Hopkins University School of Medicine, where he directs a translational research program studying the right ventricle (RV) in pulmonary hypertension, heart failure, and left ventricular assist device support. His work examines how the RV adapts and ultimately fails in response to increasing pulmonary vascular load, with a focus on RV contractility-afterload uncoupling. His laboratory combines invasive pressure-volume loop phenotyping in patients with biomechanical studies of isolated RV myocytes, linking whole-heart hemodynamics to sarcomere-level mechanisms. The goal is to detect RV-pulmonary arterial uncoupling before overt clinical decline and identify new ways to diagnose this condition. Dr. Hsu's research is supported by R01 awards from the National Heart, Lung, and Blood Institute and by a prior K23 award. Clinically, he cares for patients with advanced heart failure as medical director of mechanical circulatory support and is a member of the Miller-Coulson Academy of Clinical Excellence at Johns Hopkins.

Jasleen Minhas, M.D., University of Pennsylvania

Dr. Jasleen Minhas is a physician-scientist at the University of Pennsylvania. She is board certified in internal medicine, pulmonary disease, and critical care medicine, and she holds a master of science in clinical epidemiology. Her research focuses on wearable and sensor-based measurements for remote sensing in pulmonary arterial hypertension (PAH), using advanced statistical methods to analyze data from accelerometers, heart-rate monitors, and other sensors to characterize patients and support earlier detection and monitoring. She also conducts qualitative research eliciting patient perspectives on wearable devices and physical activity in PAH to ensure that monitoring approaches are acceptable and meaningful to the people who use them. She helps lead the organization, data pipelines, and analysis for Physical ACTivity in Pulmonary Hypertension, an ancillary study of the Pulmonary Hypertension Association Registry spanning 25 centers across the United States. Dr. Minhas is supported by a K23 award from the

National Heart, Lung, and Blood Institute and has received the ATS Early Career Investigator Award in Pulmonary Vascular Disease and the Jenesis Early Career Award for pulmonary hypertension.

Session 6: Population Screening and Health System Implementation Challenges

Evan Brittain, M.D., Vanderbilt University

Dr. Evan Brittain is Professor of Medicine in the Division of Cardiovascular Medicine at Vanderbilt University Medical Center, Vice Chair for Research in the Department of Medicine, and Co-Director of the Vanderbilt Pulmonary Circulation Center. His research focuses on the epidemiologic, molecular, and genetic determinants of pulmonary vascular disease and right ventricular failure. His research program integrates large electronic health record cohorts, human genetics, cardiovascular imaging, digital health, translational studies, and clinical trials to understand pulmonary hypertension and right heart disease. Dr. Brittain also directs Vanderbilt's Physician-Scientist Training Program and serves as Assistant Dean for Physician-Researcher Training and Director of the Office of Medical Student Research at Vanderbilt University School of Medicine.

Screening Considerations for Early PH Detection in the General Population

Earlier recognition of pulmonary hypertension (PH) could enable evaluation and treatment before advanced pulmonary vascular and right ventricular disease develops. The classic Wilson-Jungner principles provide a useful framework for considering screening in PH. The target condition should be important, detectable at an earlier stage, amenable to acceptable testing and effective intervention, and identified through a strategy in which benefits justify downstream costs and harms. These considerations make indiscriminate population screening for PH challenging, particularly given the low prevalence of pulmonary arterial hypertension (PAH). Risk-enriched screening is an attractive alternative.

The electronic health record (EHR) may provide a particularly powerful environment for this approach. Patients with unrecognized PH are already interacting with healthcare systems and accumulating potentially informative signals across time, including symptoms, associated conditions, laboratory values, physiologic measurements, imaging findings, and patterns of healthcare utilization. Rather than relying on a single screening test, these longitudinal data could be integrated to identify individuals whose phenotype increasingly resembles PH or PAH and who warrant focused evaluation. Phenotype risk scores provide one model for aggregating otherwise nonspecific clinical findings, while existing physiologic abnormalities, including echocardiographic evidence of PH, represent another opportunity to identify potentially unrecognized disease. EHR-linked genomic biobanks may provide an additional strategy for identifying genetically enriched populations, allowing integration of genotype information with evidence of disease expression.

Together, the EHR permits a layered approach to PH detection that concentrates screening within populations seeking care, where diagnostic yield is substantially greater. Future research should determine whether such EHR-enabled strategies can improve timely recognition of clinically important PH and PAH while limiting unnecessary downstream testing.

Ana Olga Mocumbi, M.D., Ph.D., Universidade Eduardo Mondlane (Mozambique)

Dr. Ana Olga Mocumbi is an associate professor of cardiology at Universidade Eduardo Mondlane, an affiliated professor in the Department of Global Health at the University of Washington, and a lead researcher at the Non-Communicable Diseases Division at Instituto Nacional de Saúde.

Her career focuses on poverty-related chronic diseases, particularly neglected cardiovascular diseases, with an emphasis on task shifting and incorporating new technologies to improve care delivery and research in low-income settings. Her main research interests are social determinants of health, cardiomyopathies, rheumatic heart disease, heart failure in children, pulmonary hypertension, and women's cardiovascular health.

Dr. Mocumbi is an active contributor to the Pulmonary Vascular Research Institute, the Pan-African Society of Cardiology (where she co-chairs the Task Force for Access to Reproductive Health Services for Women with Cardiovascular Disease), is co-chair of the World Heart Federation Science Committee, and is co-chair of the Non-Communicable Diseases and Injuries Poverty Network.

She is currently deputy editor for global cardiovascular health at *Circulation*.

Challenges and Opportunities for Early PH Detection in Health Deserts and Low- and Middle-Income Countries

Early and accurate diagnosis of pulmonary vascular disease (PVD) is usually challenging due to significant clinical obstacles. The disease remains clinically silent until structural damage is advanced, and its initial signs mimic several common diseases.

Some diagnostic challenges must be highlighted. First, delayed presentation and non-specific symptoms: early symptoms—such as exertional dyspnea (shortness of breath) and fatigue—are vague and easily misattributed to asthma, obesity, COPD, or left heart failure. Secondly, diagnostic delay averages 12 to 33 months from symptom onset, leading 70% to 80% of patients to present in advanced WHO functional class III or IV. Thirdly, due to late hemodynamic definition, standard screening protocols rely on a resting mean pulmonary artery pressure ≥ 25 mmHg, when extensive vascular remodeling has already occurred. Moreover, comorbidities and differential diagnoses such as valvular heart disease, left heart failure, pulmonary infections or chronic lung disease create restrictive or pseudo-obstructive patterns on pulmonary function tests and technical artifacts on imaging that complicate the diagnosis. Finally, resource and infrastructure

gaps are particularly important in under-resourced settings, where advanced diagnostics - such as transthoracic echocardiography, ventilation/perfusion scans, high-resolution CT, and the diagnostic gold standard (right heart catheterization) - are frequently limited to specialized tertiary urban centers.

In low- and middle-income countries, endemic diseases (such as schistosomiasis, tuberculosis, HIV, rheumatic heart disease and cardiomyopathies) further complicate workflows. The solutions for diagnosis include using simplified algorithms based on non-invasive diagnostics, building referral networks to a few centers of excellence and specialized cardiovascular clinics, with invasive right heart catheterization being used to confirm diagnoses and differentiate pre-capillary from post-capillary pulmonary hypertension. Prevention includes improving the diagnosis and timely management of both infectious and congenital heart diseases.

Thomas Maddox, M.D., Washington University in St. Louis

Dr. Thomas Maddox is a professor of medicine in the Cardiovascular Division and director of clinical innovation in the Department of Medicine at Washington University School of Medicine in St. Louis. His work focuses on redesigning care delivery using digital health, artificial intelligence, clinical informatics, and implementation science, with an emphasis on translating predictive and decision-support tools into measurable clinical and operational impact. He previously served as executive director of the BJC HealthCare/Washington University in St. Louis Healthcare Innovation Lab and vice president for digital products and innovation at BJC HealthCare.

Nationally, Dr. Maddox is a deputy editor for artificial intelligence at *Circulation*, president of the Healthcare Innovators Professional Society, and a member of the U.S. Food and Drug Administration's Digital Health Advisory Committee. He is board certified in cardiovascular disease and clinical informatics, and he has held leadership roles with the American College of Cardiology, the American Heart Association, and the National Academy of Medicine.

Real-World Implementation of Early Pulmonary Hypertension Detection

Advances in pulmonary hypertension (PH) detection are expanding the population in whom pulmonary vascular disease may be recognized earlier. Lower hemodynamic thresholds, electronic health record phenotyping, artificial intelligence-enabled electrocardiography and imaging, and other multimodal approaches increasingly allow health systems to identify patients who might previously have been missed or diagnosed later in their disease course. However, improved detection also creates an important implementation challenge: every additional signal generates demand for clinical review, diagnostic testing, specialty expertise, and, when appropriate, right-heart catheterization.

This presentation will examine early PH detection as a care-delivery pathway rather than an isolated diagnostic test. A proposed implementation framework will move from identification of

at-risk populations through risk enrichment, clinical triage, standardized evaluation, specialist referral, confirmatory testing, and closed-loop follow-up. Particular emphasis will be placed on two potential rate-limiting steps: clear ownership of positive signals and adequate health system capacity to act on them.

A tiered approach may help align the intensity of evaluation with underlying risk, reserving systematic screening for established high-risk populations while using triggered or opportunistic approaches in clinically enriched and broader populations. Centralized intake, standardized diagnostic pathways, asynchronous specialist review, and explicit escalation criteria may further expand effective PH diagnostic capacity without requiring every positive screen to generate an immediate specialty visit.

Ultimately, the next phase of early PH detection research should move beyond retrospective model performance toward prospective implementation studies that determine whether these strategies shorten time to diagnosis, improve appropriate treatment, and produce better outcomes without an unacceptable false-positive burden, excess resource use, or inequity. The intervention to be tested is therefore not simply the detection algorithm but the health system pathway surrounding it.

Session 6 Breakouts Moderators

Anjali Vaidya, M.D., Temple University

Dr. Anjali Vaidya is an internationally recognized expert in pulmonary hypertension (PH), right heart failure, echocardiography, and chronic thromboembolic pulmonary hypertension (CTEPH). She is director of Temple University Hospital's Advanced Pulmonary Hypertension, Right Heart Failure, and CTEPH Program, an assistant dean, and a professor of medicine at Temple University's Lewis Katz School of Medicine in Philadelphia, PA. She is the recipient of the Pulmonary Hypertension Association's Outstanding Physician Award.

Dr. Vaidya earned her medical degree from the Boston University School of Medicine and completed residency, cardiology fellowship, and additional fellowship training in advanced echocardiography, PH, and advanced heart failure and cardiac transplantation at the University of Pennsylvania (Penn), where she served as chief resident and a fellow, and as co-director of PH prior to being recruited to Temple.

Dr. Vaidya is the founder of Temple's Pulmonary Hypertension Fellowship, one of few such fellowships in the United States, and serves as the associate program director of Temple's Cardiology Fellowship. Dr. Vaidya is passionate about educating and has received multiple Penn and Temple University Teaching and Mentorship awards. She published the virtual echocardiography screening tool and developed a novel automated EMR algorithm designed to identify patients with pulmonary arterial hypertension earlier than is possible in routine clinical practice.

Francois Haddad, M.D., Stanford University

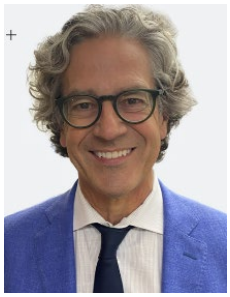
Dr. Francois Haddad is a clinical professor of medicine who specializes in the field of cardiovascular imaging, pulmonary hypertension, advanced heart failure, and transplantation. Dr. Haddad has more than 20 years of experience in cardiology. He directs the Stanford Cardiovascular Institute's Biomarker and Phenotypic Core Laboratory, which is dedicated to translational studies in cardiovascular medicine. The laboratory focuses on (1) identifying early biomarkers of heart failure and aging, (2) developing bioengineering approaches to cardiovascular disease modeling, and (3) developing novel informatics approaches for the detection and risk stratification of disease. He is involved in several precision medicine initiatives including Project Baseline, the Integrated Personalized Omics Profiling Initiative, and the Right Heart Network Collaborative Projects.

Evelyn Horn, M.D., Weill Cornell Medical College

Dr. Evelyn Horn is a professor of clinical medicine and the founding director of the Advanced Heart Failure, Mechanical Assist, and Pulmonary Hypertension Programs at Weill Cornell Medical College. She holds an adjunct appointment at Columbia University. Dr. Horn earned a degree in mathematical economics from Brown University and a medical degree from the Mount Sinai School of Medicine, where she also completed her internship and residency. She completed cardiology training at Cedars-Sinai and UCLA and a research fellowship at the Columbia College of Physicians & Surgeons. She remained at Columbia University in various capacities for more than 20 years, including as director of the Circulatory Physiology Fellowship Program, director of Clinical Services for Heart Failure, associate director of the combined Pediatric and Adult Pulmonary Hypertension Center, director of the High-Risk Cardiac Obstetrics Program, and director of the Pulmonary Vascular Program of the Center for Advanced Cardiac Care before being recruited by Weill Cornell to establish the advanced heart failure program.

She started her research career as a CHEST physician-scientist studying the role of the G protein–beta receptor complex in heart failure, transplantation, and arrhythmias. She has been involved with most of the groundbreaking pulmonary hypertension (PH) studies and many of the classic systolic heart failure studies, the initial biventricular pacing heart failure and LVAD protocols and has remained as a principal investigator in multiple industry-sponsored and National Institutes of Health–sponsored studies for HFrEF, HFpEF, LVADs, and PH. She was part of the National Heart, Lung, and Blood Institute's PVDOMICS study to reexamine clinical phenotyping, endophenotyping, and omics data in pulmonary vascular disease across the PH spectrum. Dr. Horn also led the adjudication committee and was instrumental in the mixed PH taxonomy. She remains actively engaged in the crossroads of pulmonary vascular disease and heart failure worlds and ventricular-vascular remodeling.

Session 7: Trial Considerations for Early PH



Robert Frantz, M.D., Mayo Clinic

Dr. Robert Frantz is professor of medicine in the Department of Cardiovascular Medicine at the Mayo Clinic in Rochester, MN. He is also the director of the Mayo Pulmonary Hypertension Clinic. Dr. Frantz works in the Cardiac Catheterization Laboratory, performing complex resting and exercise hemodynamic studies, vasodilator challenges, and pulmonary angiography in patients with suspected chronic thromboembolic pulmonary hypertension (CTEPH). He coordinates the Mayo Clinic CTEPH program, performs pulmonary angiography, and coordinates the Balloon Pulmonary Angioplasty program. He has been involved in many of the clinical trials of investigational therapies for pulmonary arterial hypertension (PAH). He is the site principal investigator for the National Heart, Lung, and Blood Institute–funded Pulmonary Vascular Disease Omics program. He previously served as vice chair of the Mayo Clinic institutional review board. His research interests include early identification of pulmonary hypertension utilizing artificial intelligence electrocardiogram algorithms, the long-term tolerability and safety of sotatercept, the optimal treatment of PAH with features of pulmonary veno-occlusive disease, and the role of investigational antiproliferative therapies in the treatment of PAH. He also works with the advanced heart failure and heart transplant programs at the Mayo Clinic.

Trial Design Considerations for Early PH Detection

Clinical trial designs for early detection of pulmonary hypertension require innovative thinking regarding screening methodology, inclusion criteria, extent of phenotyping, and whether to seek/include multiple forms of suspected pulmonary hypertension. Pulmonary hypertension poses increased risk for adverse outcomes regardless of associated disease state, so from a public health perspective, earlier detection of all forms of PH is laudable. “Earlier detection” and “early-stage” PH are different things. Earlier detection approaches may include patients with risk of PH, such as scleroderma or a known genetic mutation, and finding them while PVR is still 2-3 Wood units. Alternatively, it could involve screening the general population or screening patients with dyspnea. Screening tools may include an AI ECG assessment, HFpEF risk score calculation, NT-proBNP, and other investigational “liquid biopsy” techniques, and/or a noncontrast chest CT looking for pulmonary artery enlargement and/or early pulmonary parenchymal disease (emphysema, fibrosis).

The choice of treatment strategy(ies), endpoints, and study duration are additional critical elements. Many screening strategies may identify PH in the broad sense and then require additional phenotyping for further classification. The balance between sufficient phenotyping to choose appropriate therapy while maintaining fiscal feasibility is an important consideration. Use of research funds to identify possible PH, followed by a combination of clinically indicated testing and research-funded testing, may be a suitable approach. Inclusion of patients at participating

sites that are already being clinically phenotyped and found to have early PH (e.g., PVR 2-3 WU) is reasonable but not likely to be a sufficient population.

A screening strategy that detects multiple forms of PH, and then, with an embedded trial design with multiple intervention arms tailored to the suspected form of PH, is advised. For suspected early PH associated with HFpEF risk factors, including obesity, randomization to intervention with diet, exercise, meticulous management of systemic hypertension, detection and treatment of sleep-disordered breathing, and GLP-1 agonists or placebo/conventional care is a consideration. For early detected pulmonary fibrosis/Group III PH, inhaled treprostinil vs. placebo, given the known effects of inhaled treprostinil on both the PH element and risk of progressive fibrosis, is an option. For early Group 1 PAH, PDE5i + ERA, or an antiproliferative such as sotatercept vs. observation/placebo, can be considered.

Endpoints may include combined all-cause cardiovascular events, hospitalization, death, and clinical progression, including a rise in NT-proBNP and worsening functional class/exercise capacity.

Corey Ventetuolo, M.D., Brown University

Dr. Corey Ventetuolo is a professor of medicine and health services, policy, and practice at Brown University, where she directs the Division of Pulmonary, Critical Care and Sleep Medicine. She is also the inaugural director of the Center for Advanced Lung Care and medical director of the Adult Extracorporeal Membrane Oxygenation Program at Brown University Health. Her research focuses on sexual dimorphism in pulmonary vascular disease and on novel methods of endotyping patients, including precision treatment approaches guided by pulmonary artery endothelial cell biopsies obtained at the point of care. She also studies new mechanisms underlying interorgan crosstalk in pulmonary hypertension and during extracorporeal life support. Dr. Ventetuolo is an associate editor of the *American Journal of Respiratory and Critical Care Medicine* and chair of the Pulmonary Circulation Assembly of the American Thoracic Society. Her work is supported by the National Institutes of Health and the American Heart Association.

Therapeutic Targets for Early PH

Pulmonary arterial hypertension (PAH) is usually diagnosed years after onset, when vascular remodeling is advanced. The established treatment pathways and all approved therapies were tested in patients with established disease. Yet the processes that initiate the disease likely begin long before clinical disease manifests, including endothelial dysfunction, imbalanced BMPR2 and activin signaling, smooth muscle proliferation, inflammation, and metabolic reprogramming. These are the logical targets for early intervention.

Epidemiology stands between these targets and the patients who could benefit. Low prevalence and nonspecific symptoms make early cases hard to find outside enriched groups such as systemic sclerosis and heritable mutation carriers. Mildly elevated pressures under the lowered

hemodynamic definition are far more often due to left heart or lung disease than to early PAH. And a rare subset of a rare disease offers few patients for trials. This talk reviews the candidate targets in early pulmonary vascular disease and poses three questions: which pathways drive early disease, how to identify patients in whom those pathways are active, and how to test target-directed therapy in a small population.

Paul Hassoun, M.D., Johns Hopkins University

Dr. Paul Hassoun is professor of medicine at the Johns Hopkins University School of Medicine and the director of the Pulmonary Hypertension Program at Johns Hopkins Hospital. He received his medical degree from the Faculté de Médecine Lariboisière-Saint Louis at the University of Paris in France, completed an internship and residency at Brigham and Women's Hospital, and completed a fellowship in pulmonary and critical care medicine at Massachusetts General Hospital. Both hospitals are affiliated with Harvard Medical School. Dr. Hassoun served as chair of the American Thoracic Society (ATS) Pulmonary Circulation Program Committee (2009) and the Pulmonary Circulation Assembly (2011–2012) and as a member of the ATS Publications Policy Committee. He served as president of the Pulmonary Vascular Research Institute (2018–2019). Dr. Hassoun serves on the editorial board of the *American Journal of Respiratory and Critical Care Medicine* (2010–present), *CHEST* (2006–2015), and the *European Respiratory Review* (2008–2015). He currently serves as associate editor of the *European Respiratory Journal* (2013–present) and served as associate editor of the *Journal of Clinical Investigation* (2017–2022). Dr. Hassoun has led a successful research program in pulmonary vascular and endothelial cell biology and has maintained continuous National Institutes of Health funding since 1989.

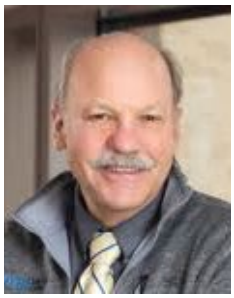
Current Evidence for Treatment of Early PH

Early detection of pulmonary arterial hypertension (PAH) has improved substantially but remains an important unmet need. PAH often presents with nonspecific exertional dyspnea and fatigue, so diagnosis often occurs after substantial pulmonary vascular and right ventricular disease has developed. While idiopathic PAH might be difficult to diagnose early with population-wide screening, early diagnosis of other forms of PAH is possible and highly encouraged in populations at risk, such as those with connective tissue diseases. The strongest evidence for this argument is in systemic sclerosis (SSc), where annual assessment is recommended using combinations of symptoms, pulmonary function tests, particularly reduced DLCO, biomarkers such as BNP/NT-proBNP, and screening transthoracic echocardiography. The DETECT algorithm, developed specifically for SSc patients at higher risk, can identify patients who warrant echocardiography and ultimately right-heart catheterization (RHC); however, it remains imperfect. Screening is also recommended for carriers of pathogenic PAH-associated variants in families with heritable PAH, and in other cohorts at risk of PAH, such as those with portal hypertension, HIV, severe lung disease, left heart disease, or congenital heart disease.

The field should be moving toward detecting preclinical or very early pulmonary vascular disease, rather than simply diagnosing established PAH earlier (early preclinical diagnosis versus diagnosis of early PAH or PH). Echocardiography remains central but has imperfect sensitivity, particularly when resting pulmonary pressures are still normal. CPET, exercise echocardiography, cardiac MRI, circulating biomarkers, and multimodal algorithms are being investigated to detect abnormalities before resting hemodynamics become diagnostic. The 2022 ESC/ERS definition lowered the hemodynamic threshold for PH to mean pulmonary artery pressure >20 mmHg, with PAH additionally requiring PVR >2 Wood units and PAWP ≤15 mmHg. However, the guidelines explicitly note that the clinical significance and treatment of patients in the mild/preclinical hemodynamic range remain areas for further research. These new thresholds have clear implications in SSc-associated PH. However, even in SSc-associated PH, early pulmonary vascular disease may not necessarily develop into PAH since WSPH Groups 2 or 3 are also quite common complications and may not warrant PAH therapy.

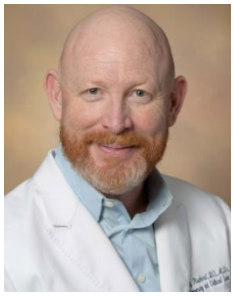
Thus, there are reasonably mature risk-based screening approaches for selected high-risk populations, but no validated, broadly applicable strategy for detecting PAH in the general population or reliably identifying the disease at its earliest biological stage.

Session 7 Breakouts Moderators



Nicholas Hill, M.D., Tufts University

Dr. Nicholas Hill is chief emeritus and research director of the Division of Pulmonary, Critical Care and Sleep Medicine at Tufts Medical Center in Boston, MA, and professor of medicine at Tufts University School of Medicine. He earned his M.D. from Dartmouth Medical School in 1975. He completed his internship and residency in medicine at Tufts-New England Medical Center and Boston VA Medical Center. He completed fellowships in cardiovascular medicine at the University of Massachusetts Medical Center and in pulmonary medicine at the Boston University School of Medicine. He is board certified in internal medicine, pulmonary disease, and critical care medicine. He has conducted extensive research and written extensively in the fields of noninvasive ventilation and pulmonary hypertension for more than 40 years. He has edited several books on these topics. He is past president of the American Thoracic Society and has received a Distinguished Scholar Award in Critical Care from the Chest Foundation of the American College of Chest Physicians. Additionally, Dr. Hill received an Award for Excellence in Pulmonary Hypertension Care from the Pulmonary Hypertension Association and a Career Achievement Award from Geisel School of Medicine at Dartmouth.



Franz Rischard, D.O., University of Arizona College of Medicine-Tucson

Dr. Franz Rischard is a professor of medicine, the medical director of the Pulmonary Hypertension Program, and an associate dean of clinical research at the University of Arizona College of Medicine–Tucson. Over more than 25 years at the University of Arizona, he has helped build the Pulmonary Hypertension Program into a national center for clinical care, training, and research. Dr. Rischard chairs the Pulmonary Vascular Research Institute Exercise Task Force and has published more than 100 peer-reviewed manuscripts. He has served as principal or co-principal investigator on 15 research grants, including awards from the National Institutes of Health and the American Heart Association, and as a site principal investigator or steering committee member for more than 70 clinical trials. His research focuses on right ventricular adaptation and disease reverse remodeling in pulmonary vascular disease, as well as health equity and the effects of social adversity in pulmonary hypertension. He is committed to mentoring residents, fellows, and junior faculty members in pulmonary hypertension and clinical research.

Stephen Mathai, M.D., Johns Hopkins University

Dr. Stephen Mathai is a professor of medicine and a member of the Johns Hopkins Pulmonary Hypertension Program at the Johns Hopkins University School of Medicine. His clinical and research interests focus on early diagnosis, treatment, and outcomes assessment in patients with pulmonary vascular disease, particularly those with underlying conditions that predispose them to pulmonary hypertension, such as connective tissue disease. He is the director of inpatient services at The Johns Hopkins Hospital and is co-director of the Ann Dana Kusch Multidisciplinary Program for Interstitial Lung Disease and Pulmonary Hypertension. He has held leadership positions in national and international organizations, including the American College of Chest Physicians, the Rare Disease Advisory Panel of the Patient-Centered Outcomes Research Institute, and the World Symposium on Pulmonary Hypertension Association Clinical Trials Task Force and Treatment Task Force.