



# Reimagining the ESC/ERS 2022 Diagnostic and Treatment Guidelines for Pulmonary Hypertension: **A PANEL CONSENSUS**

The ALA, in partnership with the Pulmonary Hypertension Association, reviewed the 2022 updates to the ESC/ERS Guidelines<sup>1</sup> for the Diagnosis and Treatment of PH at its first-ever in-person PH Roundtable Meeting, attended by an expert panel: **James Klinger**, Brown University; **Vallerie McLaughlin**, University of Michigan; **Anna Hemnes**, Vanderbilt University Medical Center; **Sandeep Sahay**, Houston Methodist; **Tim Williamson**, University of Kansas; **Nicholas Andreas Kolaitis**, University of California San Francisco; **Erika Berman Rosenzweig**, Columbia University; and **Namita Sood**, University of California Davis

The meeting aimed to generate expert opinion and critique on the most recent PH guidelines, and to provide some direction on the recently approved drug sotatercept



## 1 DEFINING PAH

|                                     | 2022 ESC/ERS <sup>1</sup> and 2024 WSPH <sup>2,3</sup> |
|-------------------------------------|--|
| Post-capillary PH                   | mPAP >20 mmHg  |
| Pre-capillary PH                    | mPAP >20 mmHg<br>PAWP ≤15 mmHg<br>PVR >2 Wood units    |
| Isolated post-capillary PH          | mPAP >20 mmHg<br>PAWP >15 mmHg<br>PVR ≤2 Wood units    |
| Combined post- and pre-capillary PH | mPAP >20 mmHg<br>PAWP >15 mmHg<br>PVR >2 Wood units    |



Overall, the panel agreed with the updated hemodynamic thresholds in the 2022 ESC/ERS and the 2024 WSPH recommendations

## CONSIDERATIONS FROM THE PANEL

### 01

Greater standardization of diagnostic tools is needed

### 02

It is important to carry out careful hemodynamic evaluations during RHC

### 03

There are no randomized controlled trials that have successfully demonstrated the efficacy of PAH-specific medications in lpcPH and CpcPH

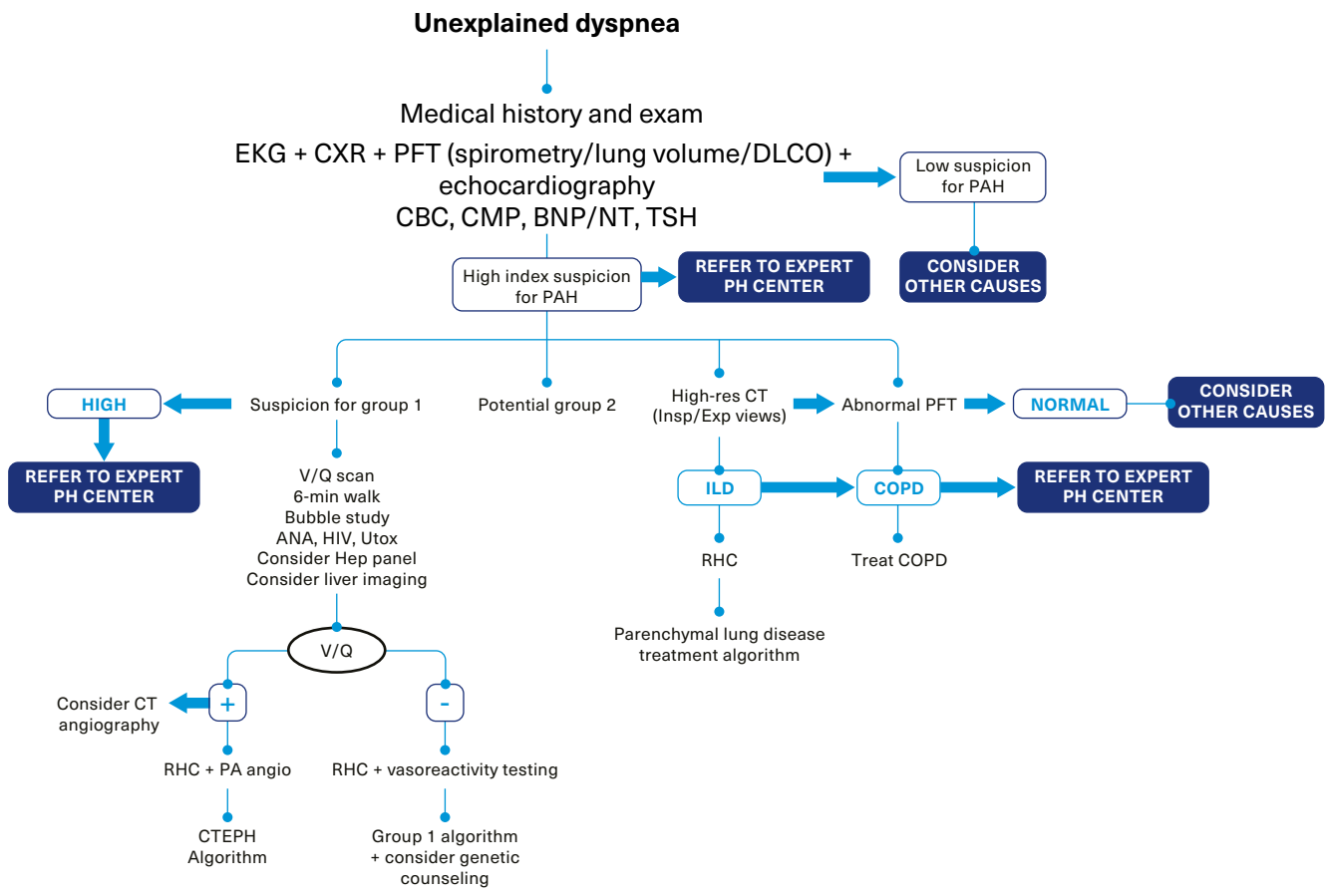


Panel experts agreed with the key indicators of PH and TTE parameters included in the ESC/ERS Guidelines

## 2 DIAGNOSTIC APPROACHES FOR PH

Despite guidelines, there continues to be an unacceptable delay in the diagnosis of PH

For diagnosing unexplained dyspnea, a more streamlined algorithm was suggested by the panel

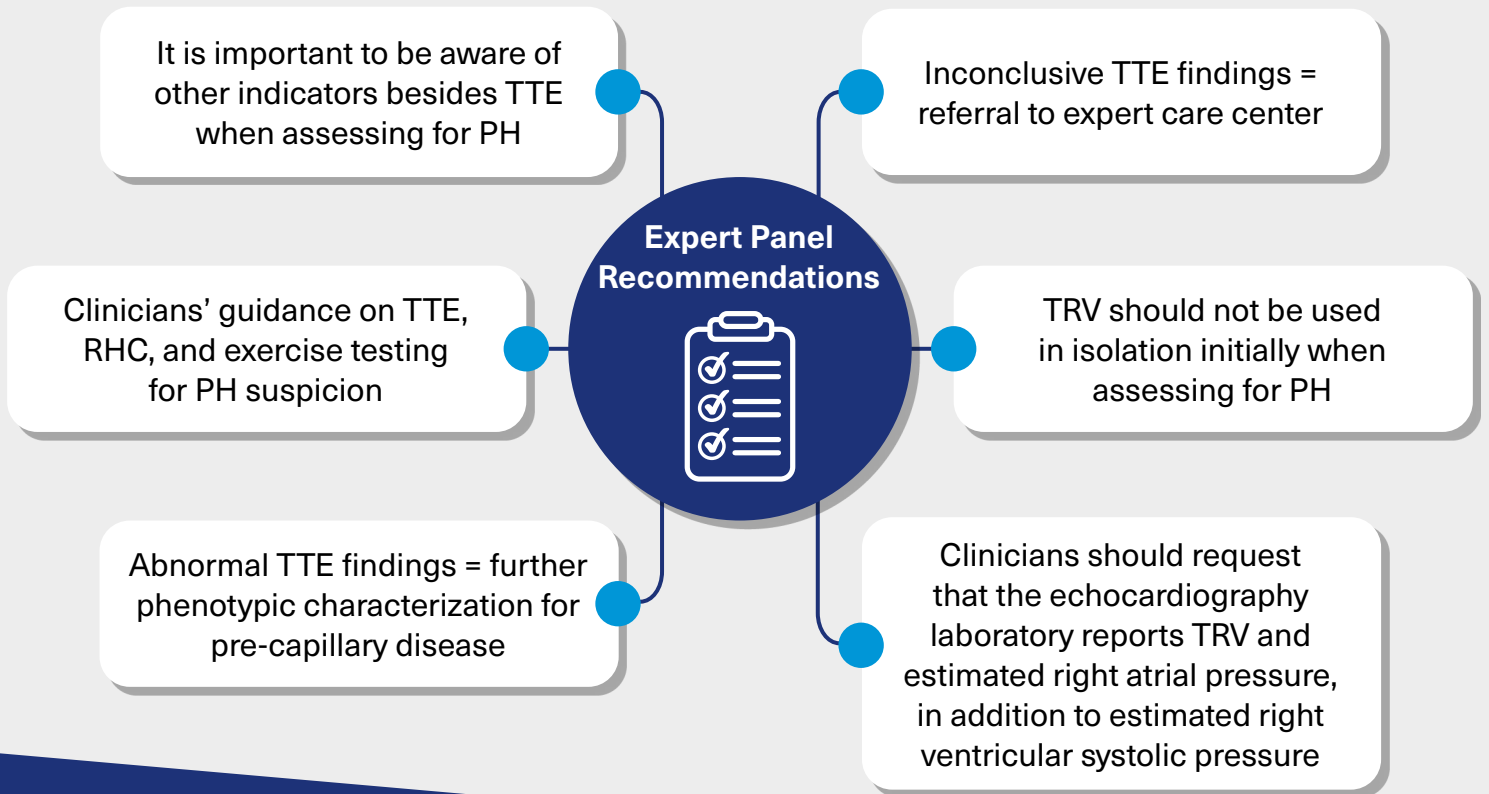


Click here to see the 2022 ESC/ERS algorithm for the diagnosis of unexplained dyspnea (Figure 6)<sup>1</sup>



Click here to see the 2024 WSPH algorithm for the diagnosis of pulmonary hypertension (Figure 1)<sup>2</sup>

## 2 DIAGNOSTIC APPROACHES FOR PH (CONTINUED)



## 3 SCREENING HIGH-RISK POPULATIONS

### Patients who should be screened

#### 2022 ESC/ERS GUIDELINES

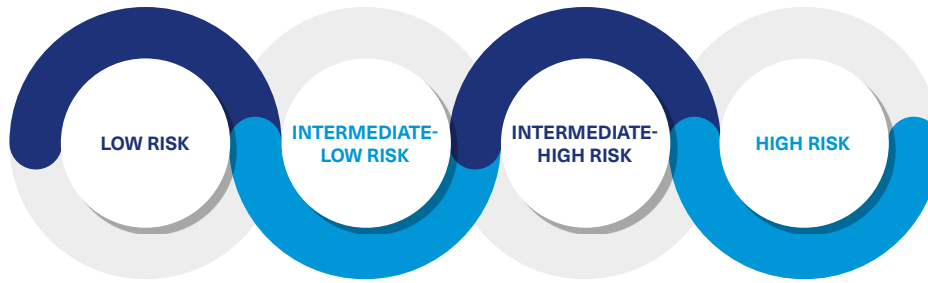
- Asymptomatic patients with SSc, *BMP2* carriers, relatives of patients with HPAH, and patients being evaluated for liver transplant
- Symptomatic patients with portal hypertension, HIV, and non-SSc CTD

#### EXPERT PANEL UPDATES

- Panel agreed with the 2022 ESC/ERS recommendations and suggested extending them to include
  - ✓ Asymptomatic patients with ILD
  - ✓ Symptomatic patients with PoPH, HIV, non-SSc CTD, PE, and methamphetamine use

## 4 RISK STRATIFICATION

The 2022 ESC/ERS Guidelines recommended following a 4-strata model at the follow-up evaluation



Risk stratification should be performed at baseline and during follow-up. The REVEAL risk stratification tool<sup>4</sup> has been validated and is commonly used

More complex risk stratification tools, such as 4-strata models that do not rely solely on functional class, are recommended

When assessing risk for PH, clinicians should consistently use the multivariable stratification tool that they find most suitable

**This model was based on**

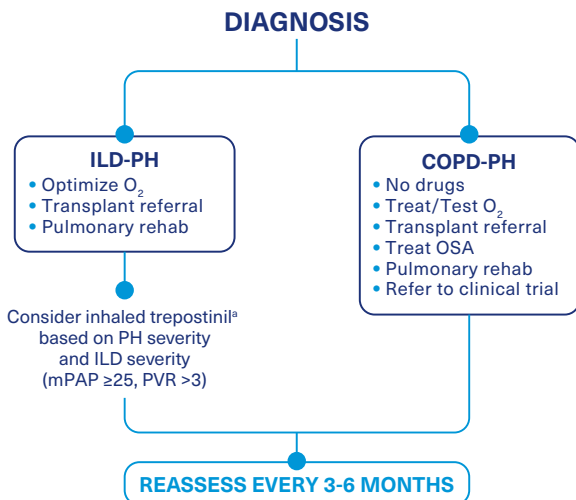
- WHO functional class
- 6-min walking distance
- Brain natriuretic peptide/N-terminal pro-brain natriuretic peptide (BNP/NT)

## 5 TREATMENT ALGORITHMS

The expert panel reviewed the 2024 WSPH and 2022 ESC/ERS treatment algorithms, noting that generally algorithms can oversimplify the treatment decision-making process and that all risk assessment tools have limitations

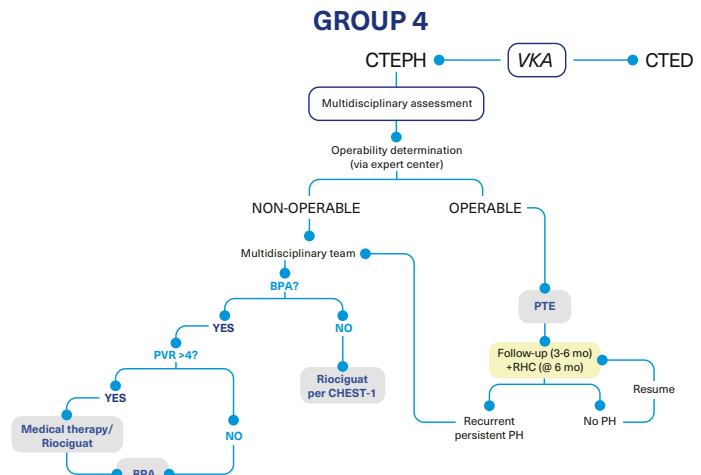
The expert panel suggested new/alternative diagnosis/management algorithms

### a PH in parenchymal lung disease



\*Dry powder or nebulized; dry powder anecdotally associated with more cough.

### b Patients with CTEPH



Click here to see the 2022 ESC/ERS algorithm for the management of CTEPH (Figure 14)<sup>1</sup>



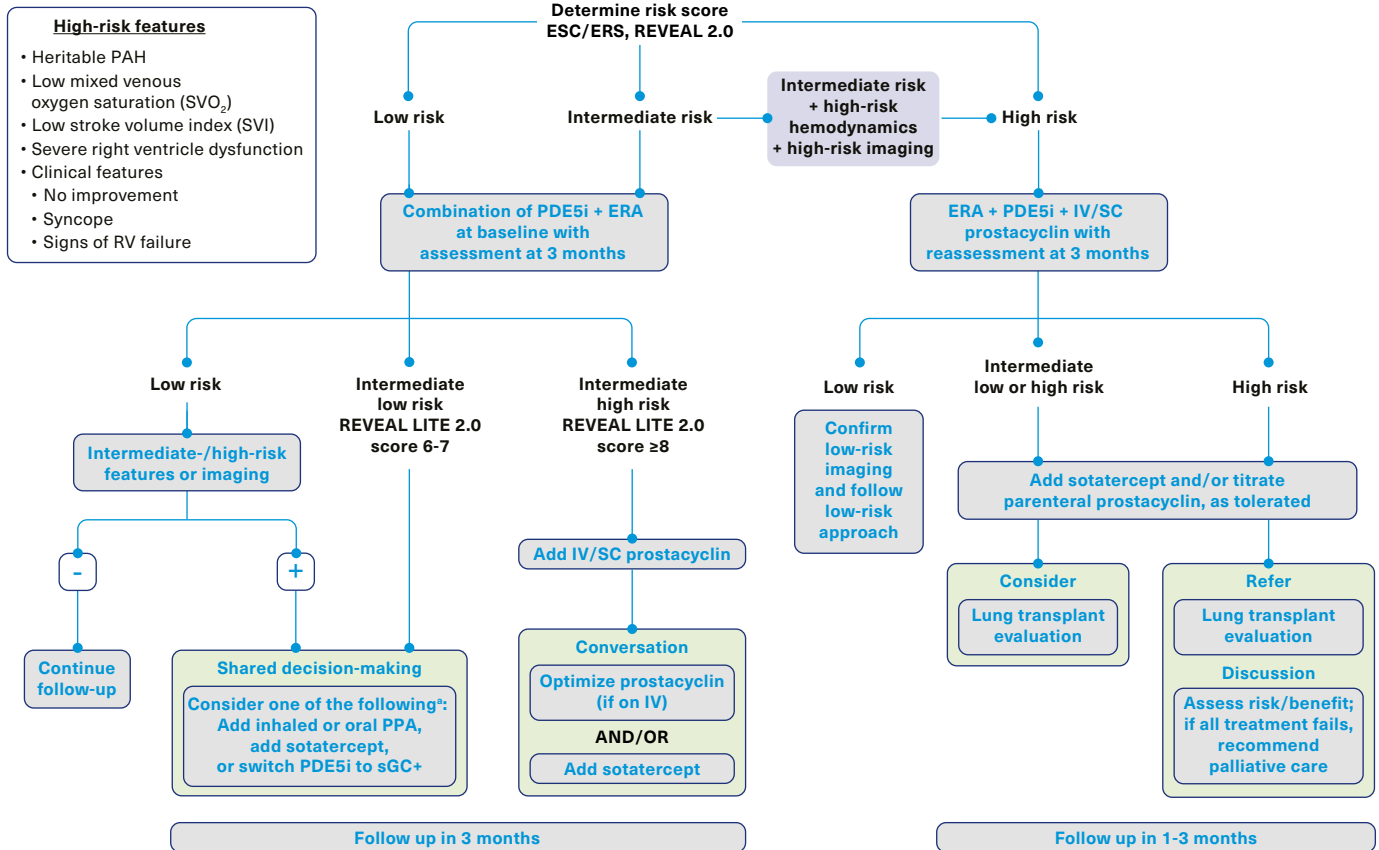
# 5 TREATMENT ALGORITHMS (CONTINUED)

## C Patients with confirmed PAH

### Confirmed PAH

- Comorbidities**
- Hypertension
  - Obesity
  - Atrial fibrillation
  - Diabetes
  - Coronary artery disease
  - Etc

- General measures**
- Diuretics
  - Oxygen
  - Rehabilitation
  - Pregnancy counseling/behavioral change program



\*Blinded clinical studies have demonstrated efficacy when inhaled/oral PPA or sotalercept are added to existing treatments. An open-label study has demonstrated efficacy when patients are switched from PDE5i to sGC+ treatment.

Click here to see the 2022 ESC/ERS algorithm for the treatment of PAH (Figure 9)<sup>1</sup>

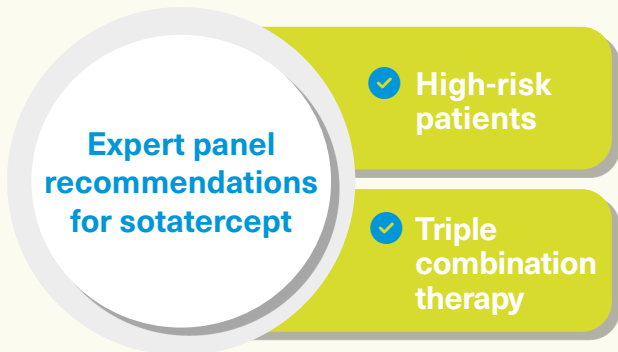
Click here to see the 2024 WSPH algorithm for the treatment of confirmed PAH (Figure 1)<sup>3</sup>

Click here to see a 2024 US perspective on the treatment of PAH<sup>5, b</sup>

<sup>b</sup>Summary only. Purchase required for full article.

## 6 INCORPORATING SOTATERCEPT

Sotatercept was approved by the US FDA in March 2024 for treatment of PAH<sup>6</sup>



- Other PAH treatments, including parenteral prostacyclin, should be optimized before sotatercept is prescribed
- There is no evidence to support discontinuing other treatments if patients respond to sotatercept
- Clinicians and their patients should be aware of the adverse event profile

## SUMMARY OF CONSIDERATIONS FOR FUTURE GUIDELINES

- Greater standardization of diagnostic tools is needed
- Unacceptable delays in PH diagnosis remain
- Additional streamlined versions of the diagnostic algorithm for patients with unexplained dyspnea or suspected PH could be useful
- Asymptomatic patients with SSc, *BMP2* carriers, and relatives of patients with HPAH should be screened
- Symptomatic patients with portal hypertension, HIV, non-SSc CTD, and methamphetamine use should be screened
- Multiple risk assessment tools have been validated; our panel recommends using these risk assessment tools for treatment decisions at baseline and at follow-up evaluation
- Clinicians should use the multivariable stratification tool that they find most suitable for assessing risk of PH
- Algorithms might oversimplify treatment decision-making
- The 4-strata risk assessment used in the ESC/ERS treatment algorithm is useful for stratifying intermediate-risk patients into "intermediate-low" and "intermediate-high" risk groups
- Shared decision-making should be adopted when considering PH treatment options
- Sotatercept should be considered as additional therapy in patients who fail to achieve low-risk status despite dual or triple combination therapy

ALA, American Lung Association; ANA, antinuclear antibody; BNP/NT, brain natriuretic peptide/N-terminal pro b-type natriuretic peptide; BPA, balloon pulmonary angioplasty; CBC, complete blood count; CHEST-1, Chronic Thromboembolic Pulmonary Hypertension Soluble Guanylate Cyclase Stimulator Trial-1; CMP, comprehensive metabolic panel; COPD, chronic obstructive pulmonary disease; CpcPH, combined pre- and post-capillary pulmonary hypertension; CT, computed tomography; CTD, connective tissue disease; CTED, chronic thromboembolic disease; CTEPH, chronic thromboembolic pulmonary hypertension; CXR, chest x-ray; DLCO, diffusing capacity for carbon monoxide; EKG, electrocardiogram; ERA, endothelin receptor antagonist; ERS, European Respiratory Society; ESC, European Society of Cardiology; FDA, US Food and Drug Administration; HIV, human immunodeficiency virus; HPAH, heritable pulmonary arterial hypertension; ILD, interstitial lung disease; Insp/Exp, inspiration/expiration; IpcPH, isolated post-capillary pulmonary hypertension; IV, intravenous; mPAP, mean pulmonary artery pressure; OSA, obstructive sleep apnea; PA angio, pulmonary angiogram; PAH, pulmonary arterial hypertension; PAWP, pulmonary arterial wedge pressure; PDE5i, phosphodiesterase 5 inhibitor; PE, pulmonary embolism; PFT, pulmonary function test; PH, pulmonary hypertension; PoPH, portopulmonary hypertension; PPA, prostacyclin pathway agents; PTE, pulmonary thromboendarterectomy; PVR, pulmonary vascular resistance; REVEAL, Registry to Evaluate Early and Long-term PAH Disease Management; RHC, right heart catheterization; RV, right ventricle; SC, subcutaneous; sGC, soluble guanylate cyclase; SSc, systemic sclerosis; TRV, tricuspid regurgitation velocity; TSH, thyroid-stimulating hormone; TTE, transthoracic echocardiogram; Utox, urine toxicology scan; V/Q, ventilation/perfusion; VKA, vitamin K antagonist; WHO, World Health Organization; WSPH, World Symposium on Pulmonary Hypertension.

### References:

1. Humbert M, et al. *Eur Respir J.* 2023;61:2200879. 2. Kovacs G, et al. *Eur Respir J.* 2024:2401324. doi: 10.1183/13993003.01324-2024. Online ahead of print. 3. Chin KM, et al. *Eur Respir J.* 2024:2401325. doi: 10.1183/13993003.01325-2024. Online ahead of print. 4. Benza RL, et al. *Chest.* 2021;159:337-346. 5. Sahay S, et al. *Am J Respir Crit Care Med.* 2024;210:581-592. 6. Merck [press release]. Accessed April 23, 2024. <https://www.merck.com/news/fda-approves-mercks-winrevair-sotatercept-csrk-a-first-in-class-treatment-for-adults-with-pulmonary-arterial-hypertension-pah-who-group-1/>.

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