American Lung Association.

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[1] 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[1] and 2024 WSPH[2,3]
Post-capillary PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 Wood units
Isolated post-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 Wood units
Combined post- and pre-capillary PH	mPAP >20 mmHg PAWP >15 mmHg 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

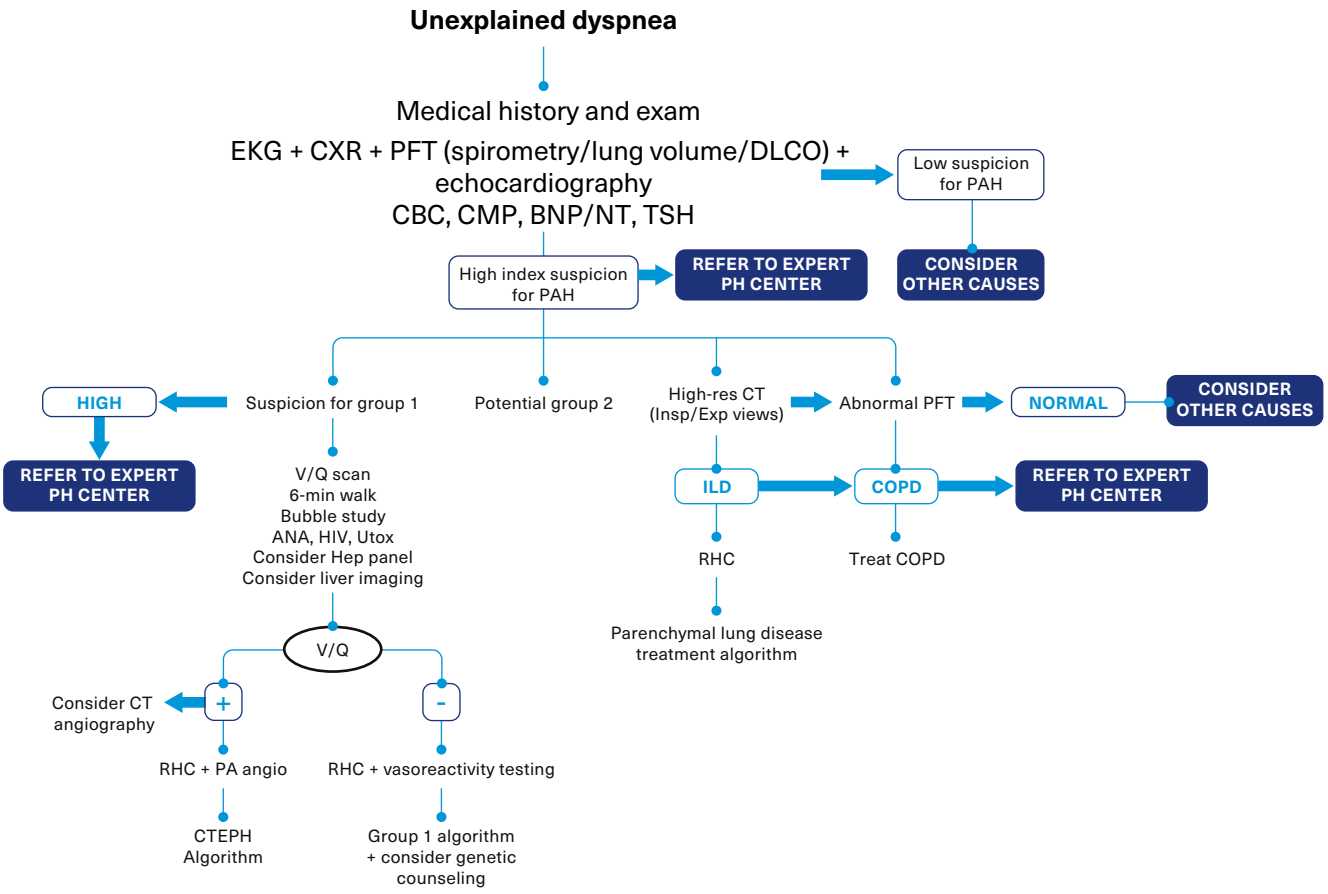
There are no randomized controlled trials that have successfully demonstrated the efficacy of PAH-specific medications in IpcPH and CpcPH

2 DIAGNOSTIC APPROACHES FOR PH

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

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

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)[1]

Click here to see the 2024 WSPH algorithm for the diagnosis of pulmonary hypertension (Figure 1)[2]

2 DIAGNOSTIC APPROACHES FOR PH (CONTINUED)

Expert Panel Recommendations

- It is important to be aware of other indicators besides TTE when assessing for PH
- Inconclusive TTE findings = referral to expert care center
- Clinicians' guidance on TTE, RHC, and exercise testing for PH suspicion
- TRV should not be used in isolation initially when assessing for PH
- Abnormal TTE findings = further phenotypic characterization for pre-capillary disease
- Clinicians should request that the echocardiography laboratory reports TRV and estimated right atrial pressure, in addition to estimated right ventricular systolic pressure

3 SCREENING HIGH-RISK POPULATIONS

Patients who should be screened

2022 ESC/ERS GUIDELINES

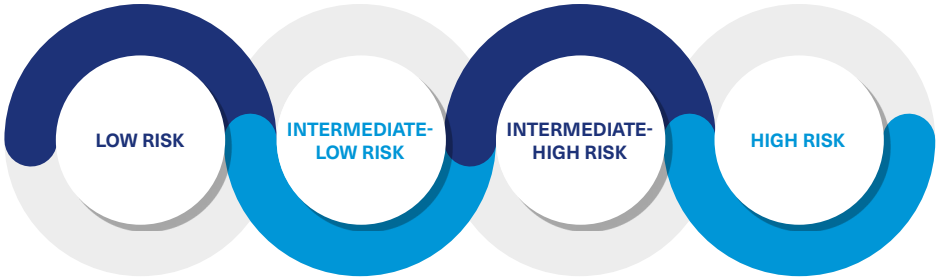
- Asymptomatic patients with SSc, *BMPR2* carriers, relatives of patients with HPAH, and patients being evaluated for liver transplant
- Symptomatic patients with portal hypertension, HIV, and non-SSc CTD

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[4] 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

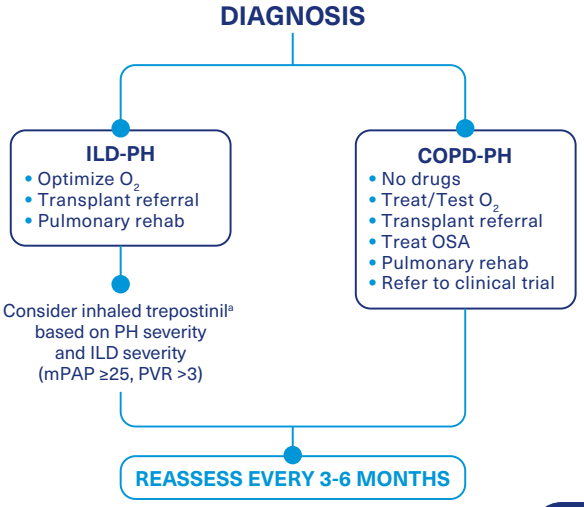
- WHO functional class
- 6-min walking distance
- Brain natriuretic peptide/N-terminal pro-brain natriuretic peptide (BNP/NT)

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

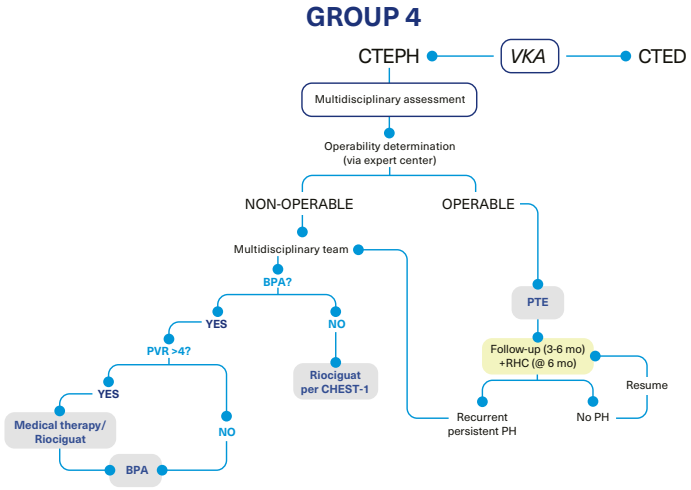
The expert panel suggested new/alternative diagnosis/management algorithms

a PH in parenchymal lung disease



[a]Dry powder or nebulized; dry powder anecdotally associated with more cough.

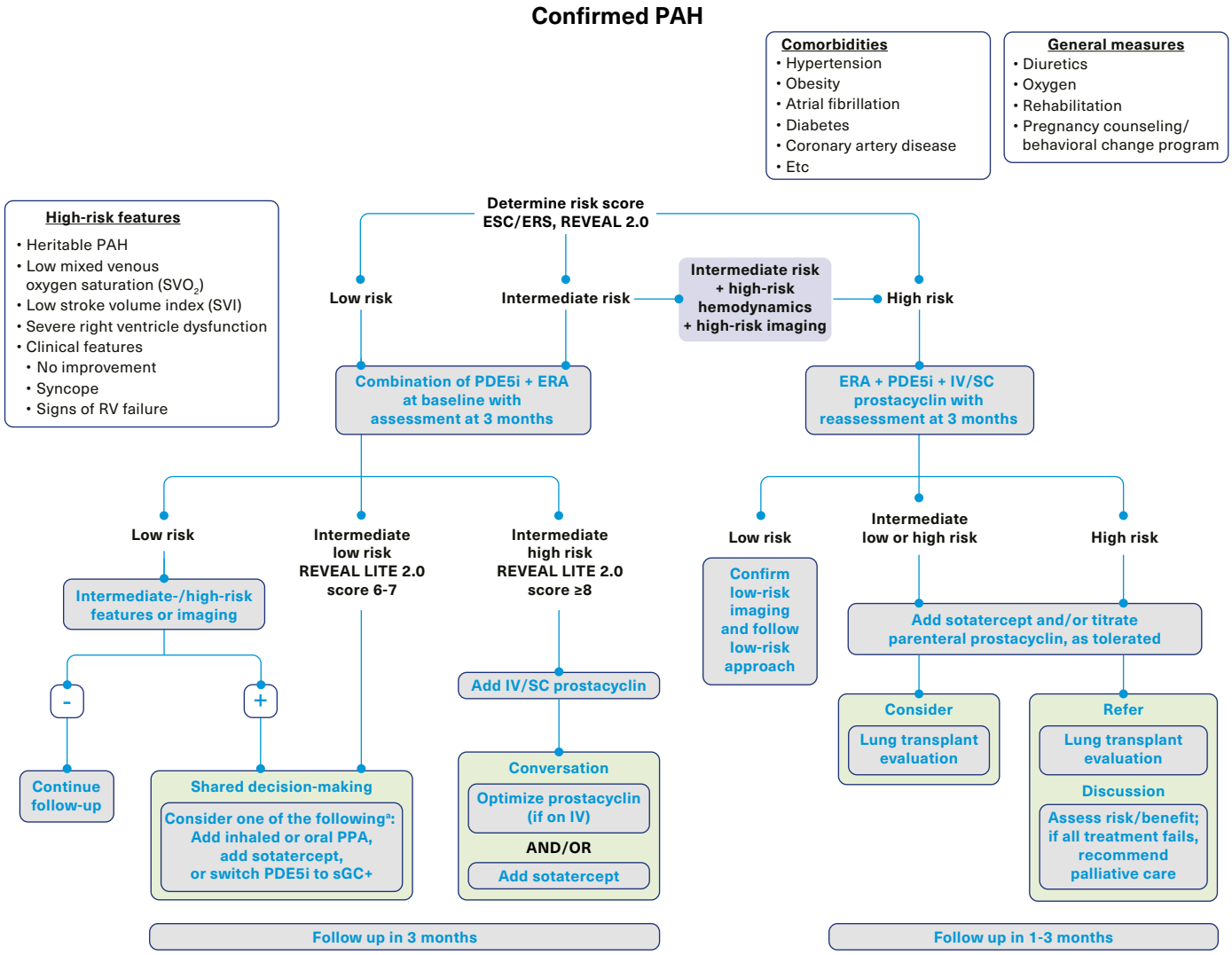
b Patients with CTEPH



Click here to see the 2022 ESC/ERS algorithm for the management of CTEPH (Figure 14)[1]

5 TREATMENT ALGORITHMS (CONTINUED)

C Patients with confirmed PAH



[a]Blinded clinical studies have demonstrated efficacy when inhaled/oral PPA or sotatercept are added to existing treatments. An open-label study has demonstrated efficacy when patients are switchedfrom PDE5i to sGC+ treatment.

Click here to see the 2022 ESC/ERS algorithm for the treatment of PAH (Figure 9)[1]

Click here to see the 2024 WSPH algorithm for the treatment of confirmed PAH (Figure 1)[3]

Click here to see a 2024 US perspective on the treatment of PAH[5, b]

[b]Summary only. Purchase required for full article.

6 INCORPORATING SOTATERCEPT

Sotatercept was approved by the US FDA in March 2024 for treatment of PAH[6]

Expert panel recommendations for sotatercept

- High-risk patients
- Triple combination therapy

- 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, *BMPR2* 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/.

Disclaimer: Support for this program was provided by Merck

American Lung Association.