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Understanding the Role of Early Diagnosis and Treatment in PAH in the Context of Racial and Ethnic Disparities: Nurse Practitioners on the Frontlines of Care

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Disclosures

Advisor: United Therapeutics
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Advisor/Consultant: Acceleron/Merck Bayer, Gossamer Bio, Johnson & Johnson/Janssen, Liquidia

Learning Objectives

- Outline the latest pulmonary arterial hypertension (PAH) guidelines on early diagnosis and initiation of therapy, considering how racial and ethnic disparities may play into treatment delays and patient outcomes
- Describe a guideline-directed, evidence-based management plan for PAH that includes consideration of current guidelines, combination therapies, escalation strategies, and current clinical trial data and patient-characteristics
- Discuss how to incorporate patient-focused management tactics to address racial and ethnic disparities and the practical considerations of patients with PAH

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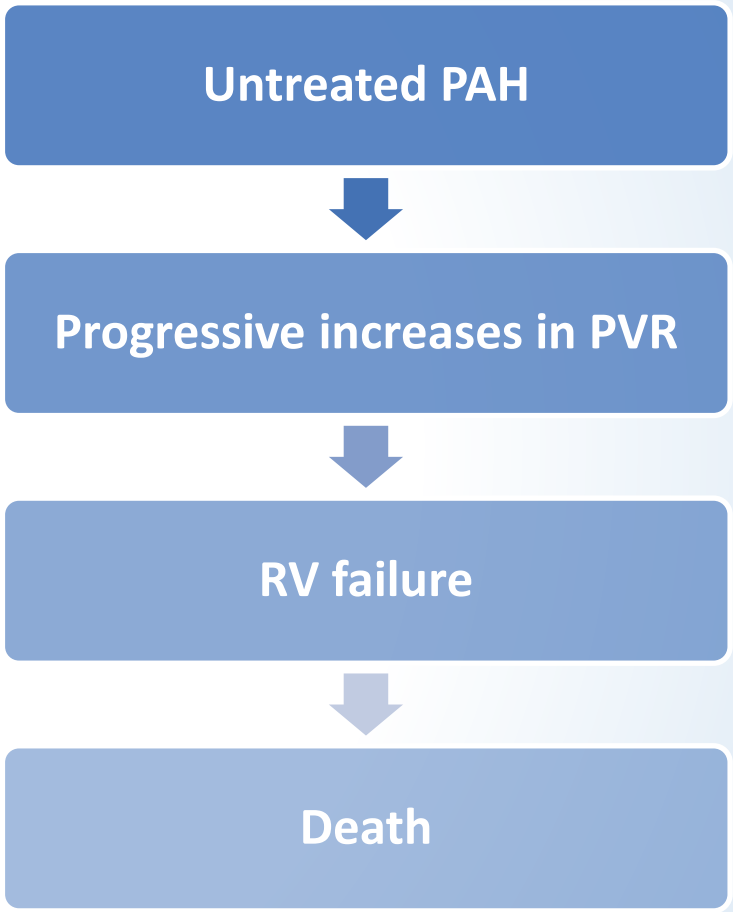
PAH and the Role of NPs in Early Detection and Treatment

Pulmonary Arterial Hypertension

- Rare progressive disease
- ~500–1000 new cases each year in US
- More common in women
- All ages
- Most severe pulmonary hypertensive disease
- 5-Y mortality rate
  - ~40% if untreated



PVR, pulmonary vascular resistance; RV, right ventricle; Y, year.

Farber HW, et al. *Chest*. 2015;148(4):1043-1054; Galiè N, et al. *Adv Ther.* 2022;39:796-810; Humbert M, et al. *N Engl J Med*. 2004;351(14):1425-1436; National Organization for Rare Disorders. Pulmonary arterial hypertension. Available at: https://rarediseases.org/rare-diseases/pulmonary-arterial-hypertension/; Vazquez ZGS, et al. *Lung*. 2020;198(4):581-596.

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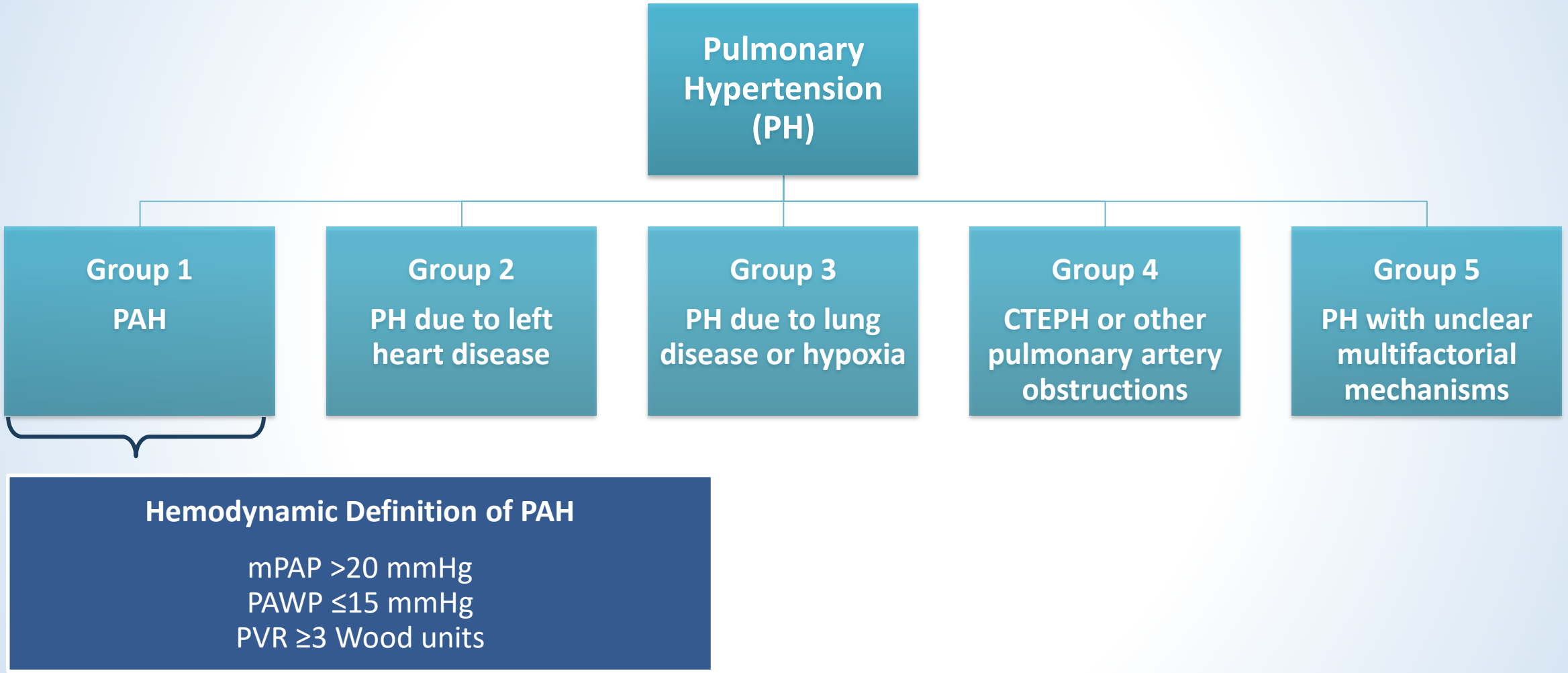
WHO Classification of Pulmonary Hypertension



CTEPH, chronic thromboembolic pulmonary hypertension; mPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure.

Hoeper MM, et al. *Lancet Respir Med*. 2016;4:306-22.

PAH Subtypes

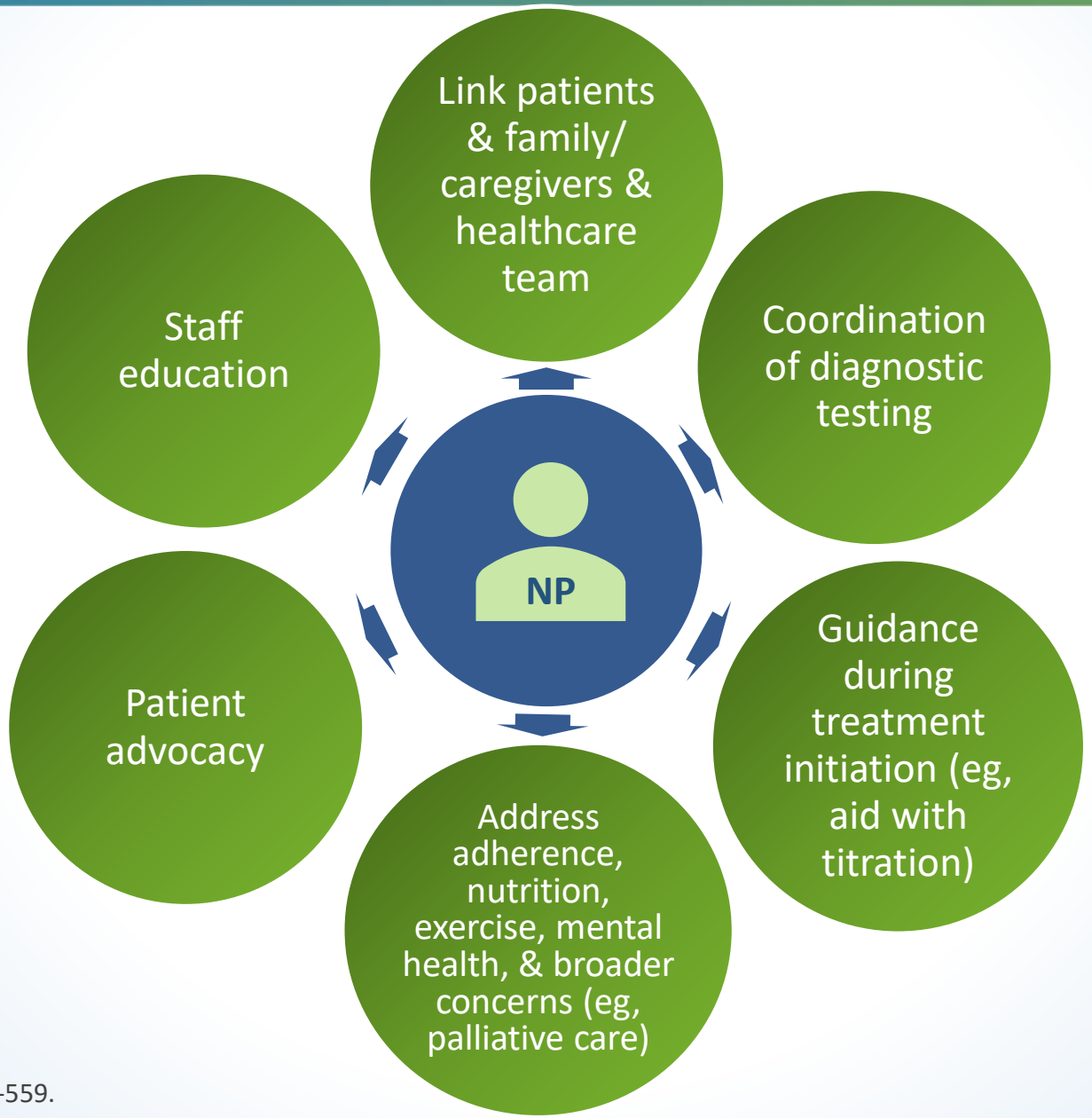
- Idiopathic
- Heritable
- Drug & toxin-induced
- Condition-associated:
  - CTD
  - HIV infection
  - Portal hypertension
  - CHD
  - Schistosomiasis

- PVOD & pulmonary capillary hemangiomatosis
- Persistent PH of the newborn

CHD, coronary heart disease; CTD, connective tissue disease; HIV, human immunodeficiency virus; PVOD, pulmonary veno-occlusive disease.

Hoeper MM, et al. *Lancet Respir Med*. 2016;4:306-22.

The Central Role of Nurse Practitioners in PAH Care



Wapner J, Matura LA. *J Nurse Pract.* 2015;11:551-559.

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Impact of Race/Ethnicity on PAH Care and Outcomes

Associations Between Socioeconomic Status, Race/Ethnicity, and Disparities in PAH Outcomes

Patients

- REVEAL registry
  - 5Y study
  - 55 US centers
  - N=3,515
- Stratified into four income categories:
  - ZIP code–based median income from 2000 US Census data

Observational Data

- Higher frequency of Black and Hispanic individuals in the lower two income categories vs the higher two income categories
- Patients in lower income groups:
  - Longer time to PAH recognition
  - More functional class 3–4 patients at the time of PAH diagnosis

REVEAL, Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management.
Talwar A, et al. *Am J Resp Criti Care Med*. 2017;196:e32-e47.

Racial Disparities in Time to Diagnostic RHC: Results of a Small-Scale, Retrospective, Cross-Sectional Analysis

Study Patients

- Patients with PAH at the University of Illinois
- N=73
  - AA: 35
  - EA: 24
  - HA: 14

Findings

- Delay in time to dRHC after first abnormal TTE for AA patients was 650d greater vs others (*P*=.005)
  - AA: 928 +/- 420d
  - EA: 232 +/- 186d
  - HA: 365 +/- 497d
- Time between most recent TTE & dRHC was not statistically different (*P*=.092)
  - AA: 88 +/- 45d
  - EA: 51 +/- 30d
  - HA: 43 +/- 16d

AA, African American; d, day; dRHC, diagnostic right heart catheterization; EA, European American; HA, Hispanic American; RHC, right heart catheterization; TTE, transthoracic echocardiography.

Krow et al. *Am J Respir Crit Care Med.* 2020;201:A3793

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Racial Differences in Patterns of PAH Treatment

Study Patients

- Patients with PAH enrolled in the PAH Biobank
- N=1837
  - NHW: 79%
  - AA: 11%
  - Hispanic: 10%*

Study Findings

Medication Prescription

- Hispanics **treated less often** vs NHWs (OR†=0.55; 95% CI=0.40–0.77)

Prescription of PAH-Specific Medication

- No group differences in class of PAH-specific medications prescribed
- % of patients with PAH who were prescribed PAH-specific medications varied by race (*P*<.001)
  - **78% of AA**
  - **70% of NHW**
  - **57% of Hispanics**

*(99% White) †OR adjusted for age, sex, RAP, CI, disease sub-type and center volume.

CI, confidence interval; NHW, non-Hispanic White; RAP, right atrial pressure.

Al-Naamani N, et al. *Pulm Circ*. 2017;7:793-796.

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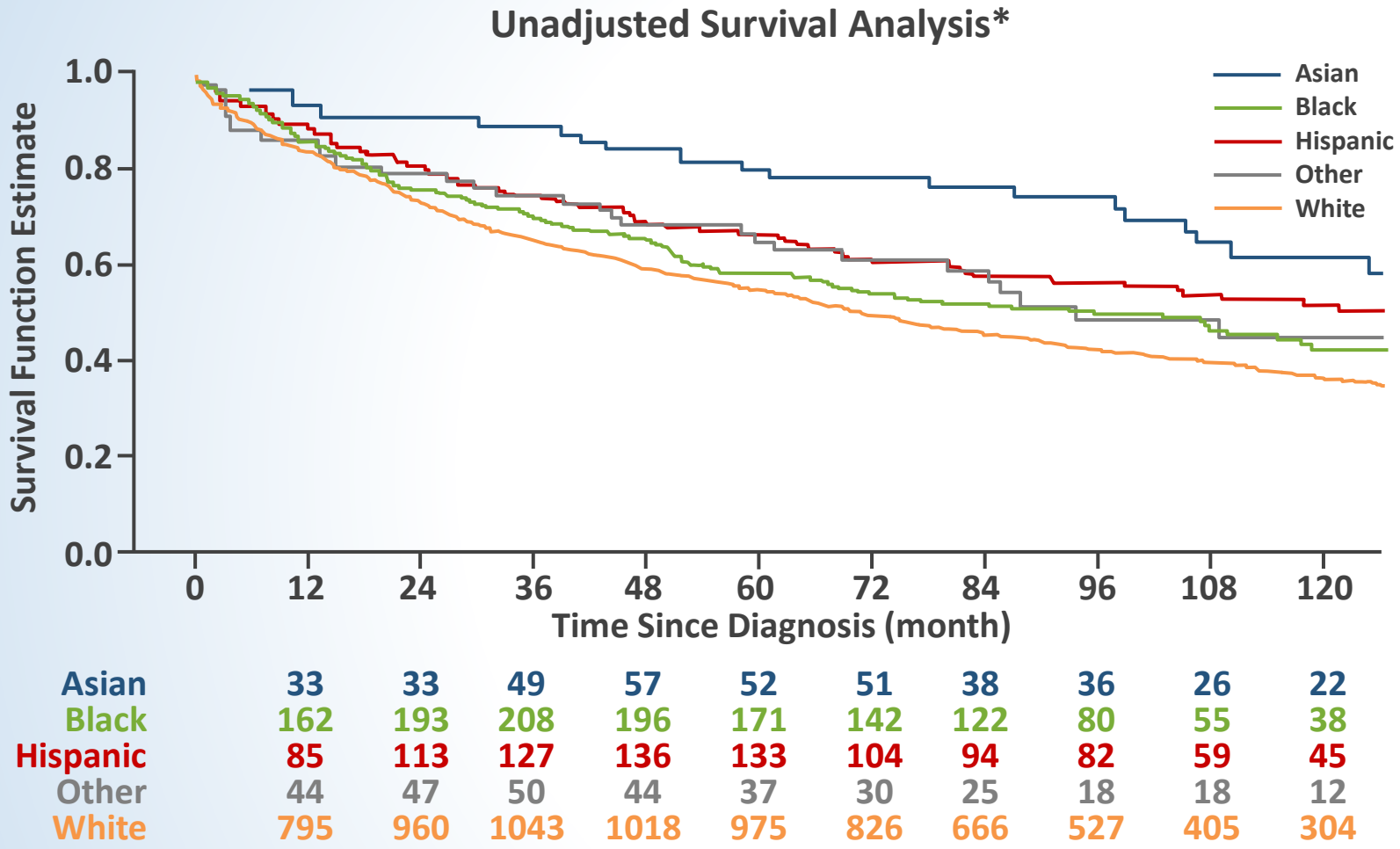
REVEAL Registry: Impact of Race on Survival in Patients With PAH



Race	N	HR (95% CI) vs White Patients	*P* Value
Asian	100	0.541 (0.358–0.819)	0.0037
Black	393	0.813 (0.672–0.982)	0.0319
Hispanic	263	0.709 (0.560–0.897)	0.0041
Other	88	0.788 (0.541–1.149)	0.2157
White	2202	—	—

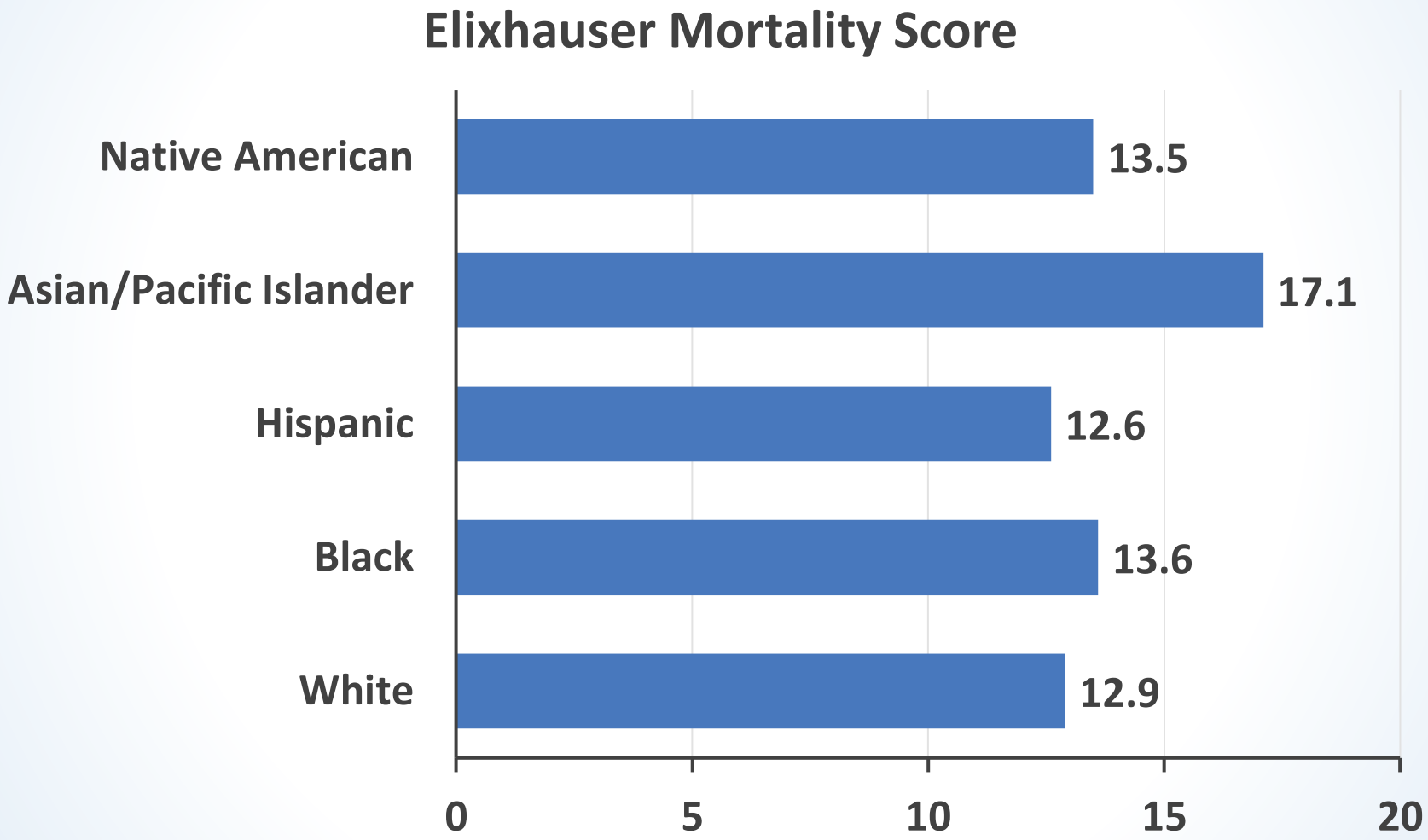
Analysis of the REVEAL registry did not find race/ethnicity to be a significant predictor of mortality.

*Unadjusted survival analysis. Unadjusted Cox model; only left truncation for time since diagnosis was included; †Survival analysis limited to patients aged ≤60 years, using left truncation analysis. Unadjusted Cox model; only left truncation for time since diagnosis was included.

HR, hazard ratio.

Medrek S, et al. *J Heart Lung Transplant*. 2020;39:321-330.

Differences in Outcomes in Hospitalized Patients With PAH by Race/Ethnicity



Gaznabi S, et al. *J Heart Lung Transplant*. 2020;39:S511.

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Diagnosis of PAH

Clinical Manifestations of PH

Initial (nonspecific, induced by exertion)	Advanced (progressing RV failure, occur at rest)	Specific to underlying/ associated diseases or comorbidities
• Common: – Dyspnea – Fatigue – Weakness – Angina	• Abdominal distension • Ankle edema • Syncope	• Hemoptysis • Hoarseness • Wheeze • Angina • Telangiectasia, digital ulceration, & sclerodactyly (SSc) • Inspiratory crackles (ILD) • Spider naevi, testicular atrophy, & palmar erythema (liver disease) • Digital clubbing (PVOD, cyanotic CHD, ILD, or liver disease)

SSc, systemic scleroderma; ILD, intersitial lung disease.

Galie N, et al. *Eur Heart J*. 2016;37(1):67-119.

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Physical Signs of PAH

May be present initially	• Parasternal lift • Loud P2 • RV third heart sound • Pansystolic murmur of tricuspid regurgitation • Diastolic murmur of pulmonary regurgitation
More common in advanced disease	• Elevated JVP • Hepatomegaly • Ascites • Peripheral edema • Cool extremities
Not usually present	• Wheezes • Crackles

JVP, jugular venous pressure.

Galie N, et al. *Eur Heart J*. 2016;37(1):67-119.

Differential Diagnosis

- CHF/cardiomyopathy
- CAD
- Left heart diseases
- Valvular disease
- PE
- Lung diseases (eg, COPD)

CHF, congestive heart failure; CAD, coronary artery disease; PE, pulmonary embolism; COPD, chronic obstructive pulmonary disease.

Galie N, et al. *Eur Heart J*. 2016;37(1):67–119; National Organization for Rare Disorders. Pulmonary arterial hypertension. Available at: https://rarediseases.org/rare-diseases/pulmonary-arterial-hypertension/ ; Stringham R, et al. *Am Fam Physician*. 2010;82(4):370-377.

Diagnostic Evaluation for PAH

- Early referral and recognition
- Echocardiography
- V/Q scan
- PFTs
- Chest CT (usually HRCT)
- Biomarkers (BNP or NT-proBNP)
- 6MWT
- RHC/hemodynamic diagnosis

6MWT, 6-minute walk test; BNP, brain natriuretic peptide; CT, computed tomography; HRCT, high resolution CT; NT-proBNP, N-terminal pro-BNP; PFTs, pulmonary function tests; V/Q scan, ventilation-perfusion scintigram.

Frost A, et al. *Eur Respir J*. 2019;53(1):1801904; Galie N, et al. *Eur Heart J*. 2016;37(1):67–119; Klinger JR, et al. *Chest*. 2019;155(3):565-586.

Guidelines for Echocardiographic Evaluation of Patients With Suspected PH

Echocardiographic Probability of PH in Symptomatic Patients With a Suspicion of PH

Peak TRV (m/s)	Presence of Other Echo 'PH Signs'*	Echocardiographic Probability of PH
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

Echocardiographic Signs Suggesting PH Used to Assess the Probability of PH in Addition to TRV Measurement

A: The Ventricles*	B: Pulmonary Artery*	C: Inferior Vena Cava and Right Atrium*
Right ventricle/left ventricle basal diameter ratio >1.0	RV outflow Doppler acceleration time <105 msec and/or midsystolic notching	Inferior cava diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LV eccentricity index >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/sec	Right atrial area (end-systole) >18 cm^2
	PA diameter >25 mm	

Echocardiography is recommended to assess the "level of probability of PH," and results should be interpreted to support the decision to initiate cardiac catheterization.

*See table at right; **Echocardiographic signs from ≥2 different categories (A/B/C) from the list should be present to alter the level of echocardiographic probability of PH.
LV, left ventricular; PA, pulmonary artery; TRV, tricuspid regurgitation velocity.
Galie N, et al. *Eur Heart J*. 2016;37(1):67-119.

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Which Patients Should Be Screened?

- ✓ CTD (eg, scleroderma, RA, GPA, SLE)
- ✓ HIV (if symptomatic)
- ✓ Sickle cell disease
- ✓ Liver disease
- ✓ Congenital heart disease (if symptomatic)

RA, rheumatoid arthritis; GPA, granulomatosis with polyangiitis; SLE, systemic lupus erythematosus.

Kiely DG, et al. *Eur Heart J Suppl*. 2019;21:K9-k20; Klings ES, et al. *Am J Respir Crit Care Med*. 2014;189:727-40.

Echocardiographic Measurement for Estimating PAP

- RVSP = 4 (velocity of TR)^2 + RA pressure

  = 4(4)^2 + 20

  = ~84 mmHg

RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation; RA, right atrial; PASP, pulmonary artery systolic pressure.
Images courtesy of John Ryan, MD, University of Utah.

Checklist for Echocardiographic Assessments When PH Is Suspected

- Estimate pulmonary artery systolic pressure
- Evaluate severity of TR
- Evaluate right heart size and function
- Exclude left heart valvular disease and systolic dysfunction
- Exclude congenital heart disease
- Differentiate PAH from PH due to LHD
- Estimate RA pressure
- Evaluate for pericardial effusion

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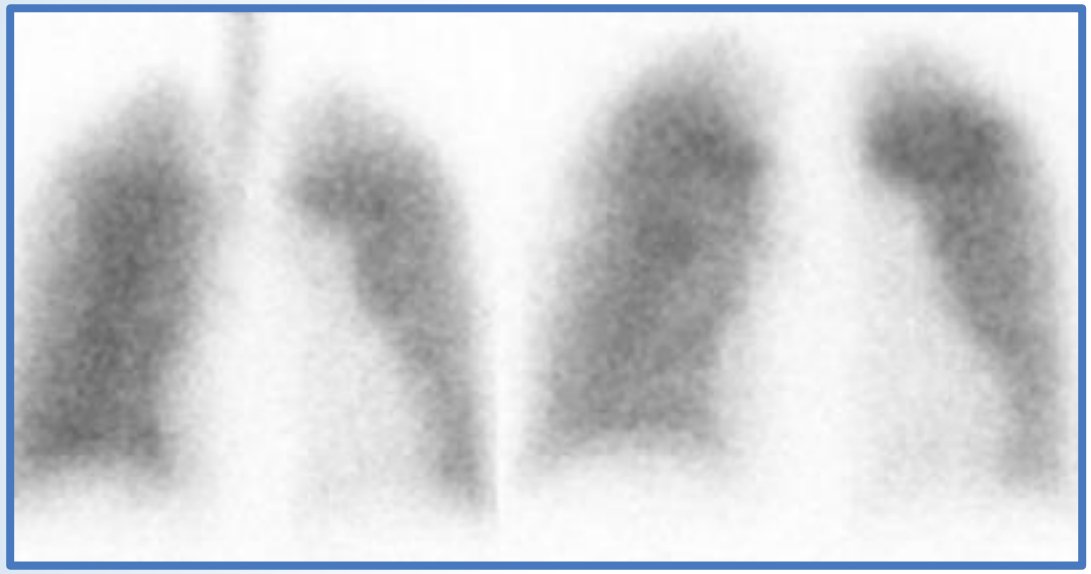
LHD, left heart disease.

V/Q Scan

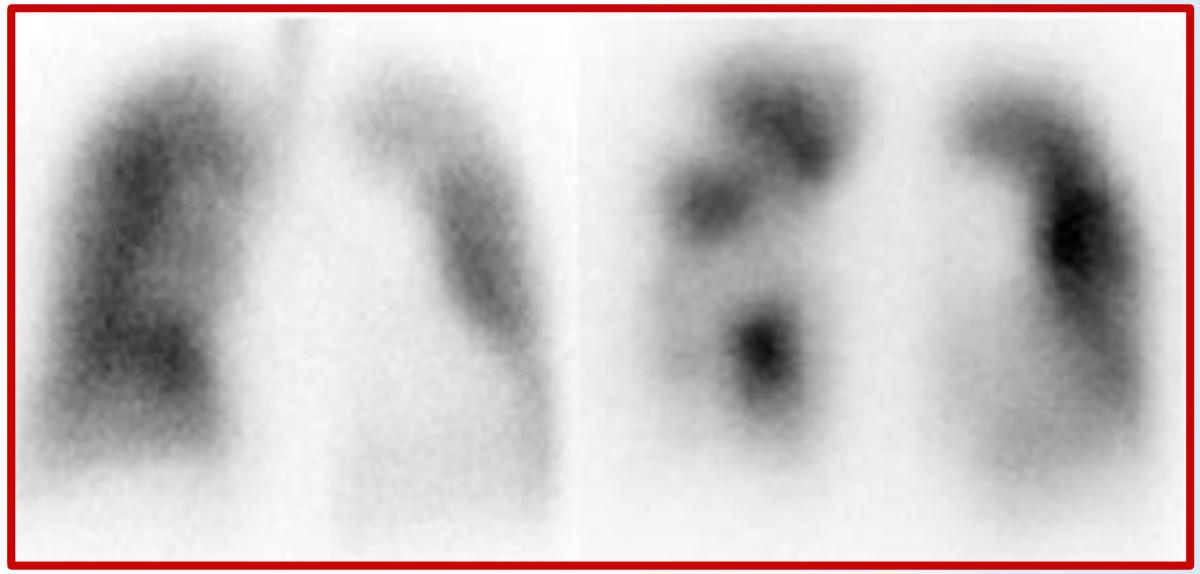
Ventilation Perfusion



Normal or Mottled Pattern

PAH

Ventilation Perfusion



At least one segmental perfusion defect inconsistent with ventilation scan findings

CTEPH

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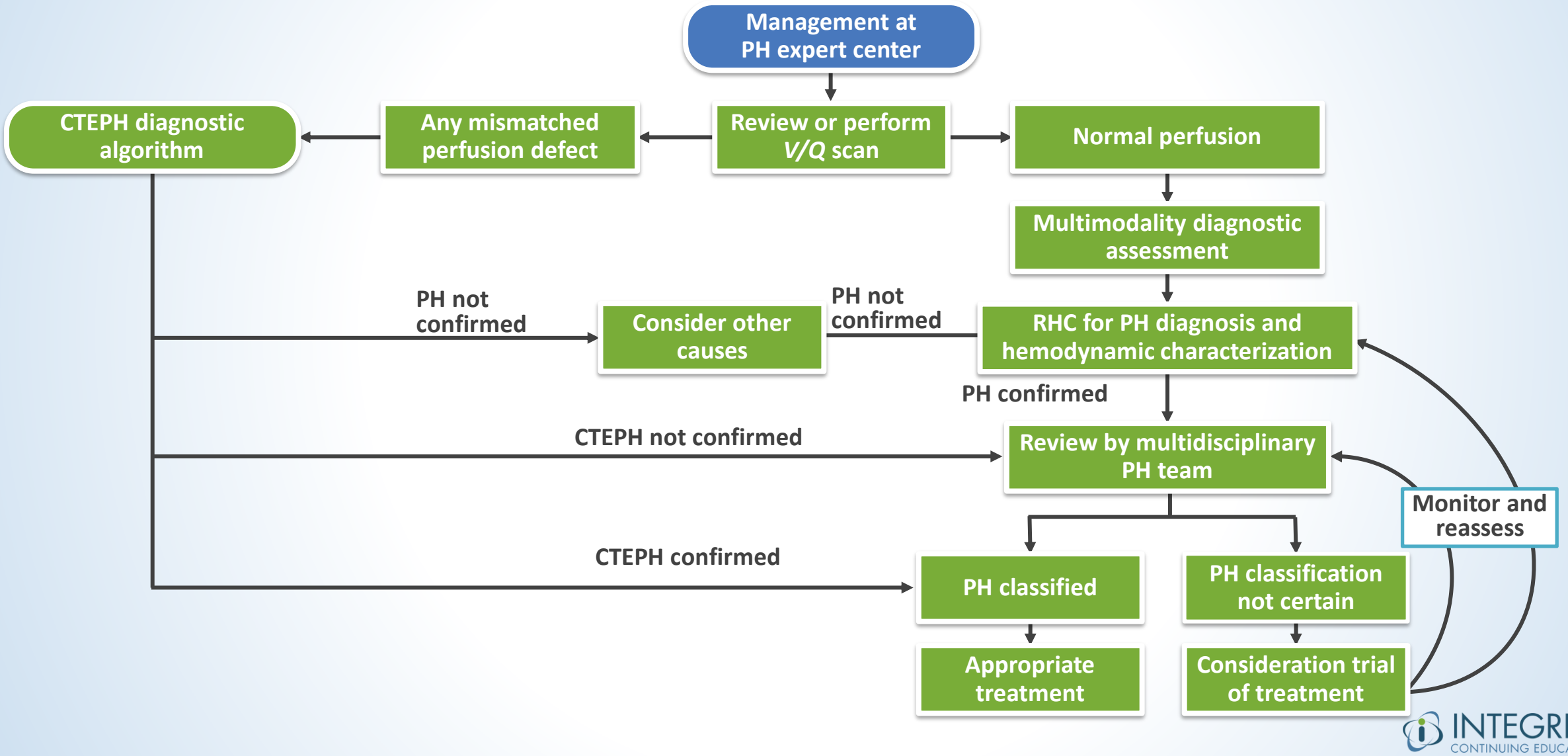
Tanabe N, et al. *Respir Investig*. 2013;51(3):134-146.

PH Diagnostic Algorithm: 2018 6th World Symposium



Adapted from Galie N, et al. *Eur Respir J.* 2019; 53 1801889.

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Risk Assessment of Patients With PAH

WHO Functional Classification of PH*

Class I

- No limitation of physical activity
- Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope

Class II

- Slight limitation of physical activity
- Comfortable at rest
- Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope

Class III

- Marked limitation of physical activity
- Comfortable at rest
- Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope

Class IV

- Unable to carry out any physical activity without symptoms
- Manifest signs of right HF
- Dyspnea and/or fatigue may even be present at rest
- Discomfort increased by any physical activity
- Syncope

*Functional classification of pulmonary hypertension modified after the New York Heart Association functional classification according to the WHO 1998.

HF, heart failure; WHO, World Health Organization.

Galiè N, et al. *Eur Heart J*. 2009;30(20):2493-537.

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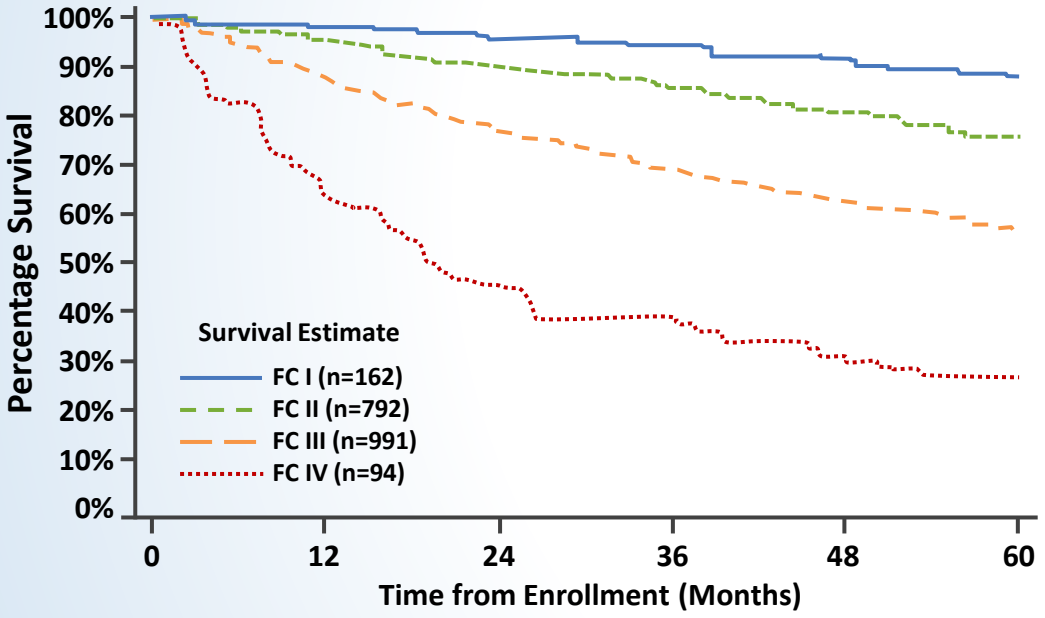
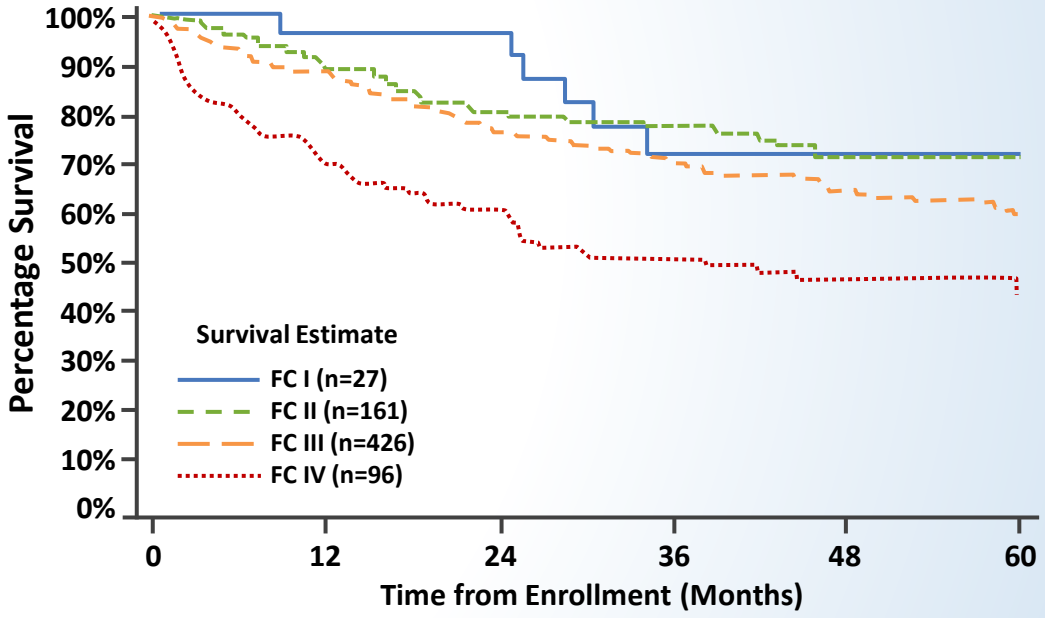
5-Year Survival Among Patients With PAH by WHO FC

REVEAL Registry

Previously Diagnosed at Enrollment



Newly Diagnosed at Enrollment



NYHA FC is one of the most important predictors of survival among patients with PAH.

FC, functional class; NYHA, New York Heart Association.

Farber HW, et al. *Chest*. 2015;148:1043-1054.

ERS/ESC Risk Assessment of Prognosis in PAH

Determinants of Prognosis*	Estimated 1-Year Mortality		
	Low Risk (<5%)	Intermediate Risk (5%–10%)	High Risk (>10%)
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope	Repeated syncope
WHO functional class	I, II	III	IV
6-minute walking distance	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% predicted) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% predicted) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% predicted) VE/VCO_2 slope ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/l	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, cardiac magnetic resonance imaging)	Right atrium area <18 cm^2 No pericardial effusion	Right atrium area 18–26 cm^2 No or minimal, pericardial effusion	Right atrium area >26 cm^2 Pericardial effusion
Hemodynamics	RAP <8 mmHg Cardiac index ≥2.5 l/min/m^2 SvO_2 >65%	RAP 8–14 mmHg Cardiac index 2.0–2.4 l/min/m^2 SvO_2 60–65%	RAP >14 mmHg Cardiac index <2.0 l/min/m^2 SvO_2 <60%

*Mostly based on expert opinion and validated for idiopathic PAH.

SvO_2, mixed venous oxygen saturation; VE/VCO_2, minute ventilation-carbon dioxide output; VO_2, oxygen uptake.

Galie N, et al. *Eur Heart J*. 2016;37(1):67–119.

REVEAL Lite 2

Parameter	Variables Included in Scoring	REVEAL Lite 2
Renal insufficiency	eGFR <60 mL/min/1.73 m^2 or defined by clinical judgment if eGFR is unavailable:	+1
NYHA or WHO FC	FCI: FC III: FC IV:	–1 +1 +2
Vital signs	SBP <110 mm Hg: HR >96 bpm:	+1 +1
6MWD	≥440 min: 320- <440 min: <165 min:	–2 –1 +1
BNP/NT-proBNP	BNP <50 pg/mL or NT-proBNP <300 pg/mL: BNP 200- <800 pg/mL: BNP ≥800 pg/mL OR NT-proBNP ≥1100 pg/mL:	–2 +1 +2
Total score		Sum of above scores +6

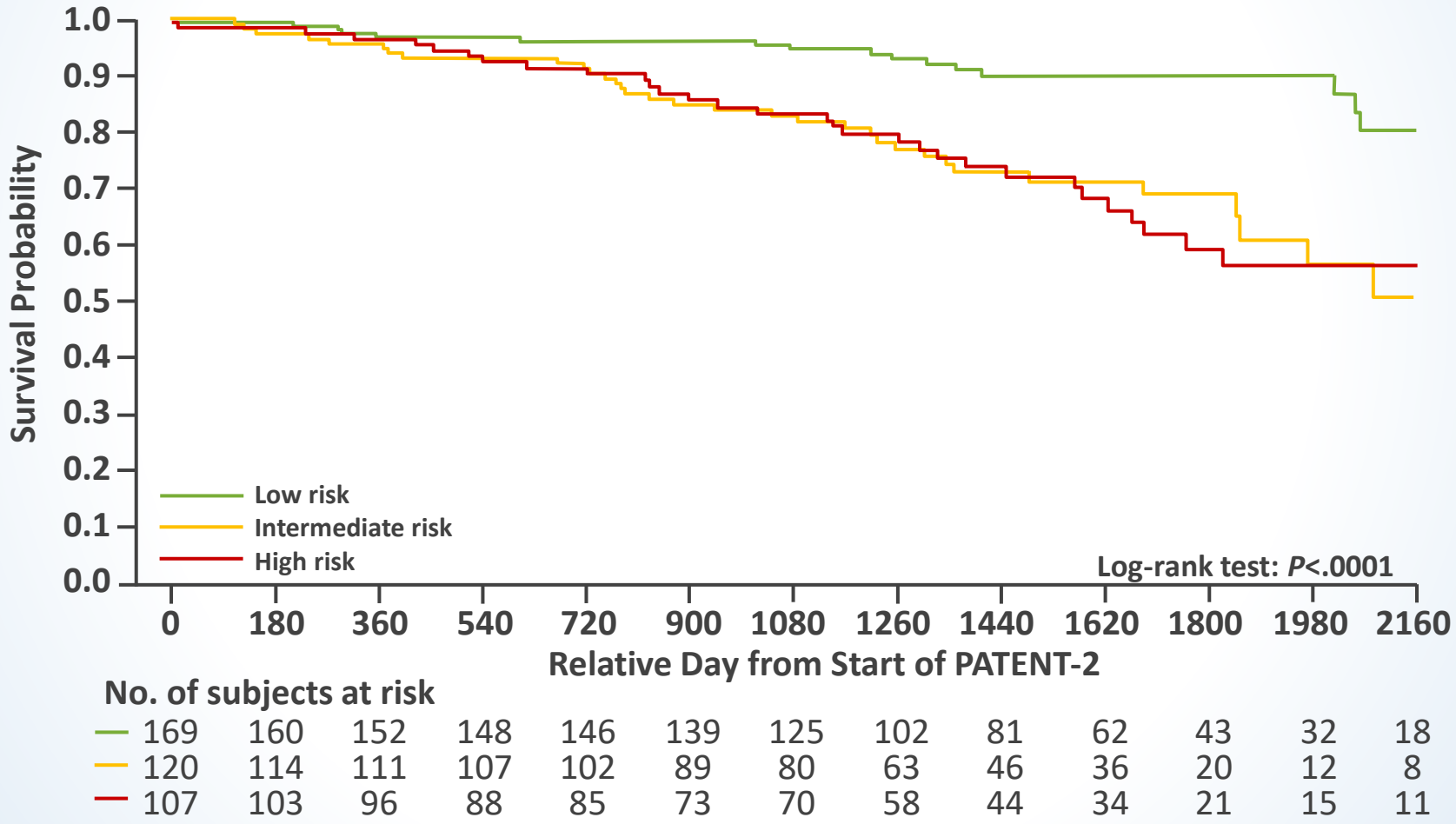
Scoring

1 to 5: Low risk
6 or 7: Intermediate risk
≥8: High risk

DLCO, diffusing capacity of the lungs for carbon monoxide; eGFR, estimated glomerular filtration rate; HR, heart rate; SBP, systolic blood pressure.
Adapted from: Benza RL, et al. *Chest*. 2021;159:337-346.

Changes in REVEAL Lite 2 Score Predict Outcomes in Patients With PAH

Kaplan-Meier analysis for survival by stratified REVEAL Lite 2 risk strata at A, baseline and B, PATENT-1 Week 12. Day 0 of survival time considered in this analysis was the start of PATENT-2.



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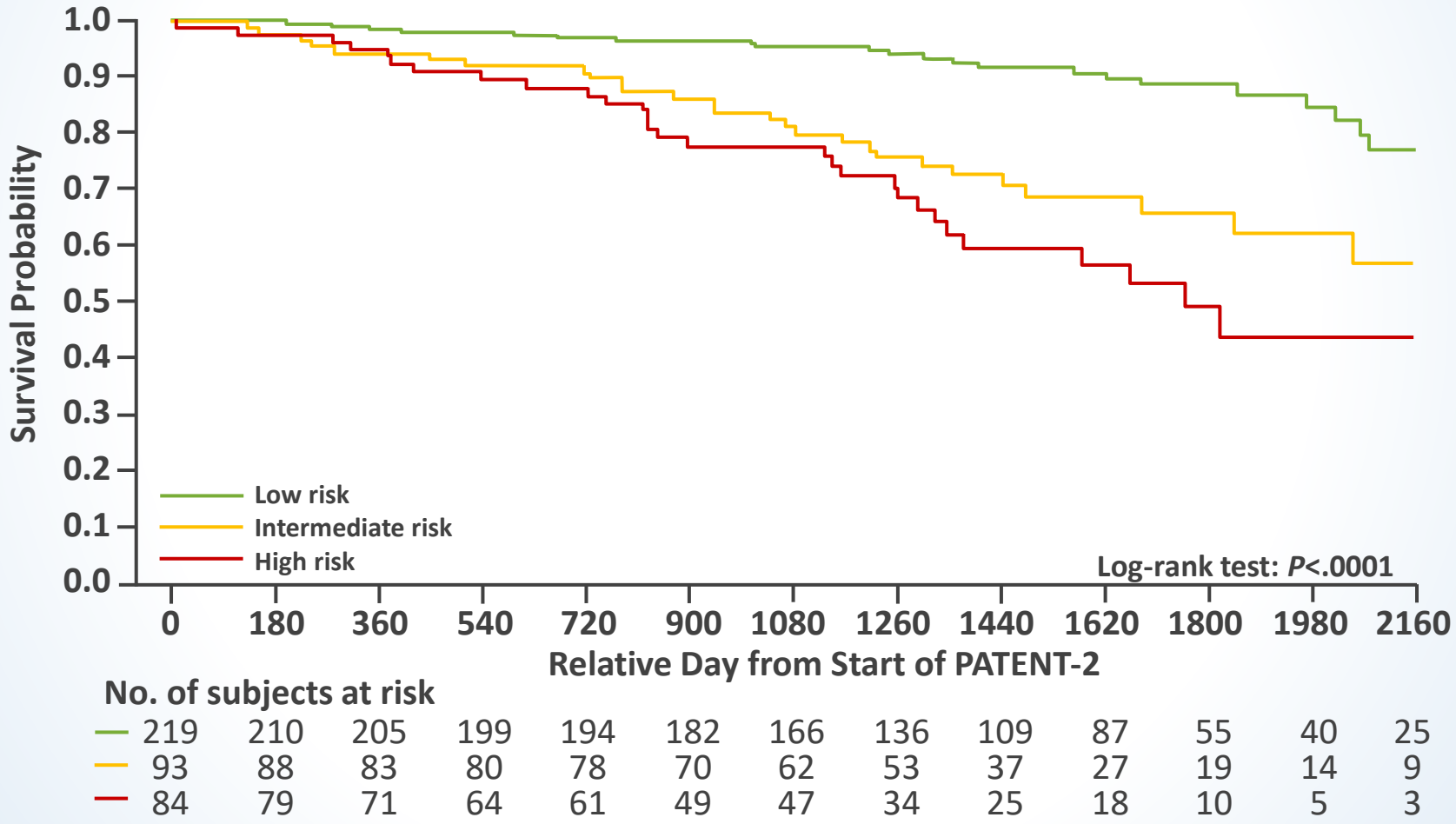
Benza RL, et al. *J Heart Lung Transplant*. 2022;41:411-420.

Changes in REVEAL Lite 2 Score Predict Outcomes in Patients With PAH

Kaplan-Meier analysis for survival by stratified REVEAL Lite 2 risk strata at A, baseline and B, PATENT-1 Week 12. Day 0 of survival time considered in this analysis was the start of PATENT-2.



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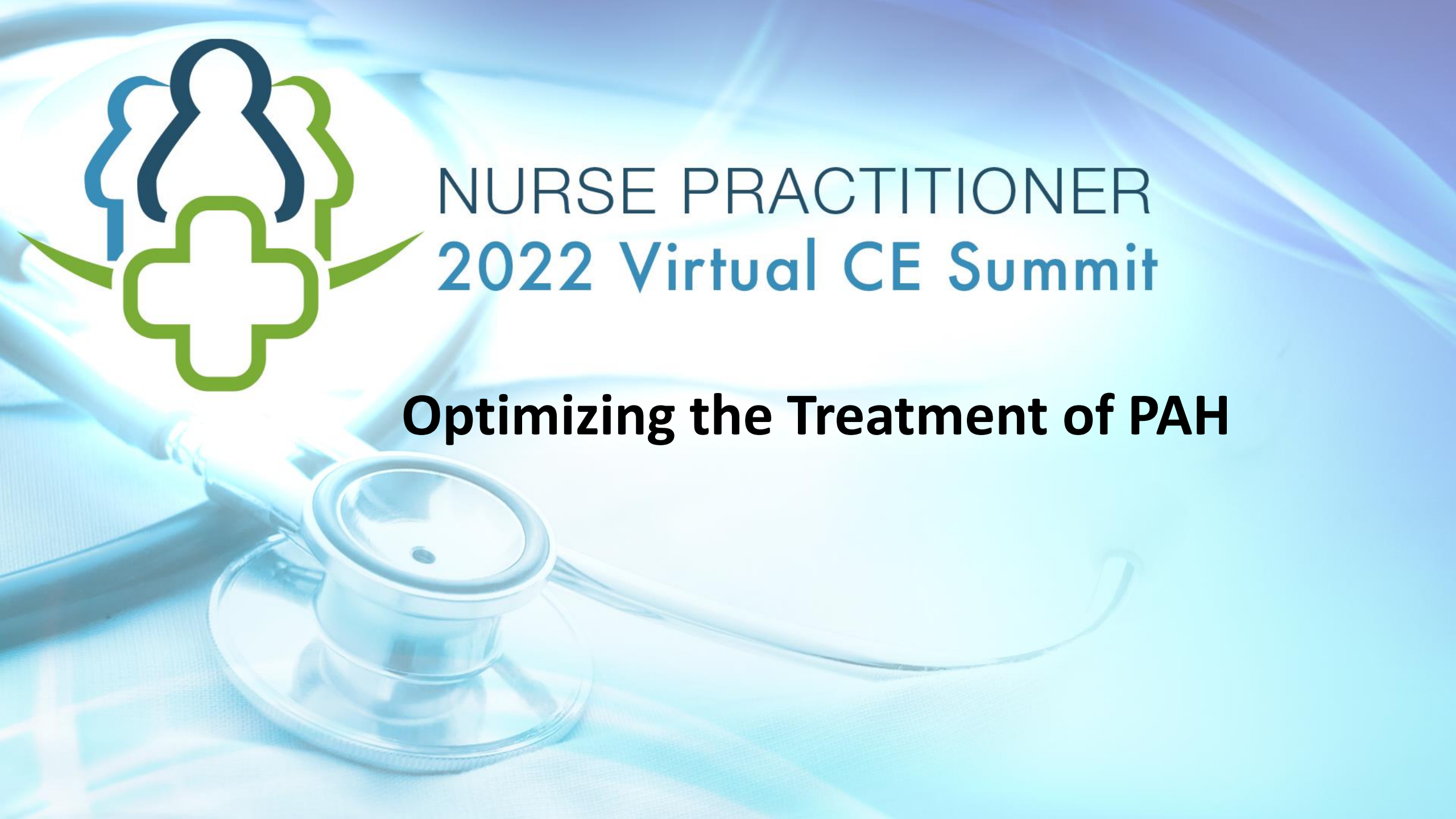
Benza RL, et al. *J Heart Lung Transplant*. 2022;41:411-420.



Optimizing the Treatment of PAH

PAH Treatment Goals

LT, liver transplant; QOL, quality of life.

General Management of Confirmed PAH

- Evaluate severity in a systematic & consistent manner
- Coordinate care between local physicians & PH centers
- Aggressively treat contributing causes
- Participate in supervised exercise activity
- Maintain current immunizations (influenza, pneumococcal pneumonia, COVID)
- Consider when to incorporate palliative care services

Avoid the following:

- Pregnancy (if pregnancy does occur, PH center care is suggested)
- High altitude (if necessary, use supplemental O_2 as needed to maintain saturations >91%)
- Nonessential surgery (if necessary, PH center care is suggested)
- Avoid intubation (if necessary, PH center care is suggested)

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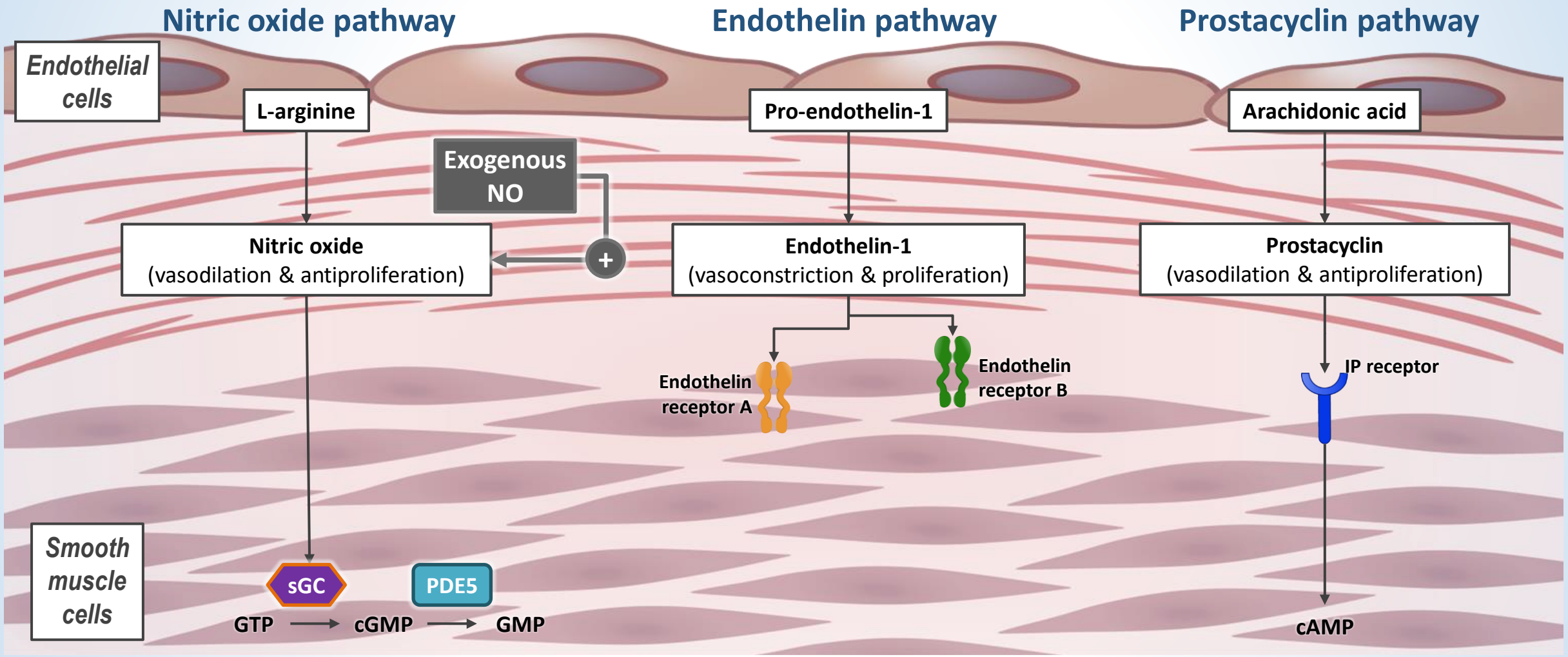
Klinger JR, et al. *Chest*. 2019;155:565-586.

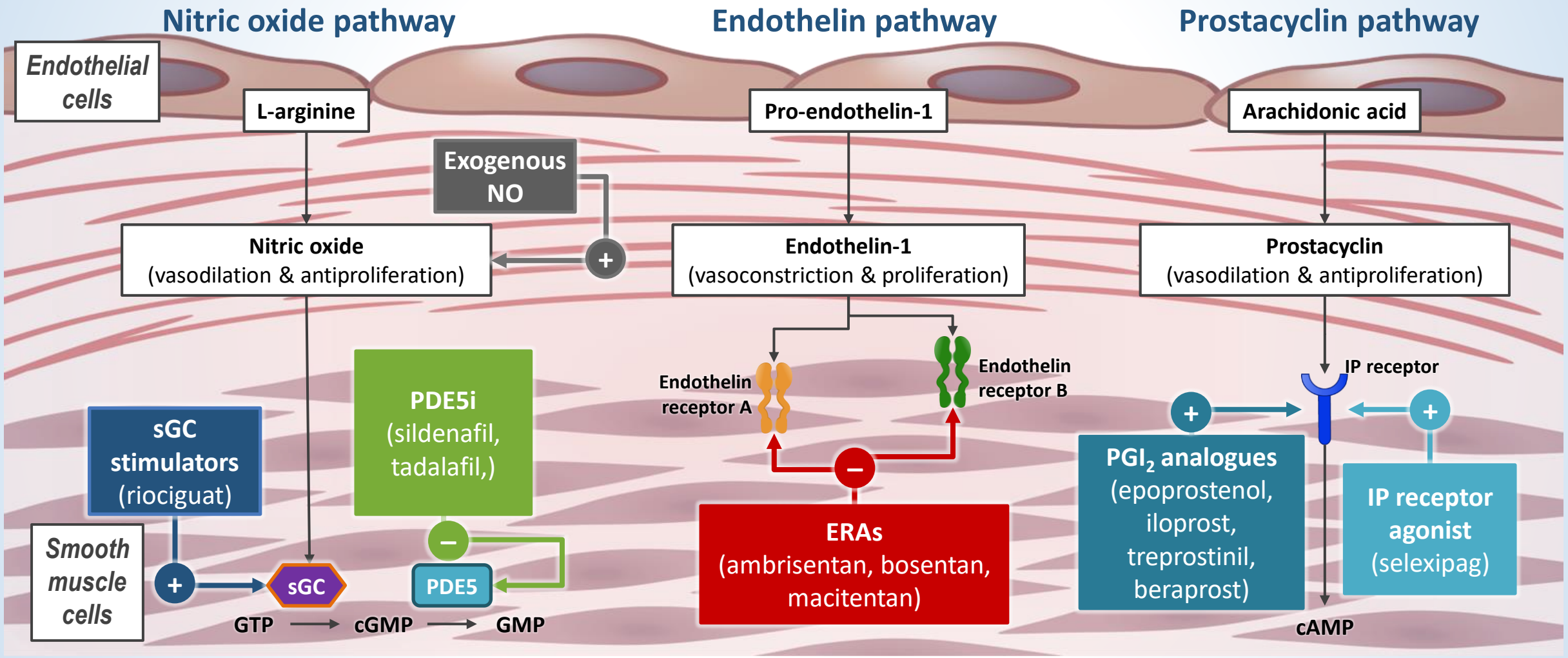
Therapeutic Targets of Approved PAH Treatments



cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; IP, prostacyclin receptor; GTP, guanosine triphosphate; NO, nitric oxide; PDE5, phosphodiesterase type 5 inhibitor; sGC, soluble guanylate cyclase.

Humbert M. *Eur Res Rev*. 2010;19:59-63.; Yerly P, et al. *Swiss Med Wkly*. 2016;146:w14305-w14305.

Therapeutic Targets of Approved PAH Treatments



ERA, endothelin receptor antagonist; PDE5i, PDE5 inhibitors; PGI_2, prostacyclin.

Humbert M. *Eur Res Rev.* 2010;19:59-63.; Yerly P, et al. *Swiss Med Wkly*. 2016;146:w14305-w14305.

Select Trials in PAH

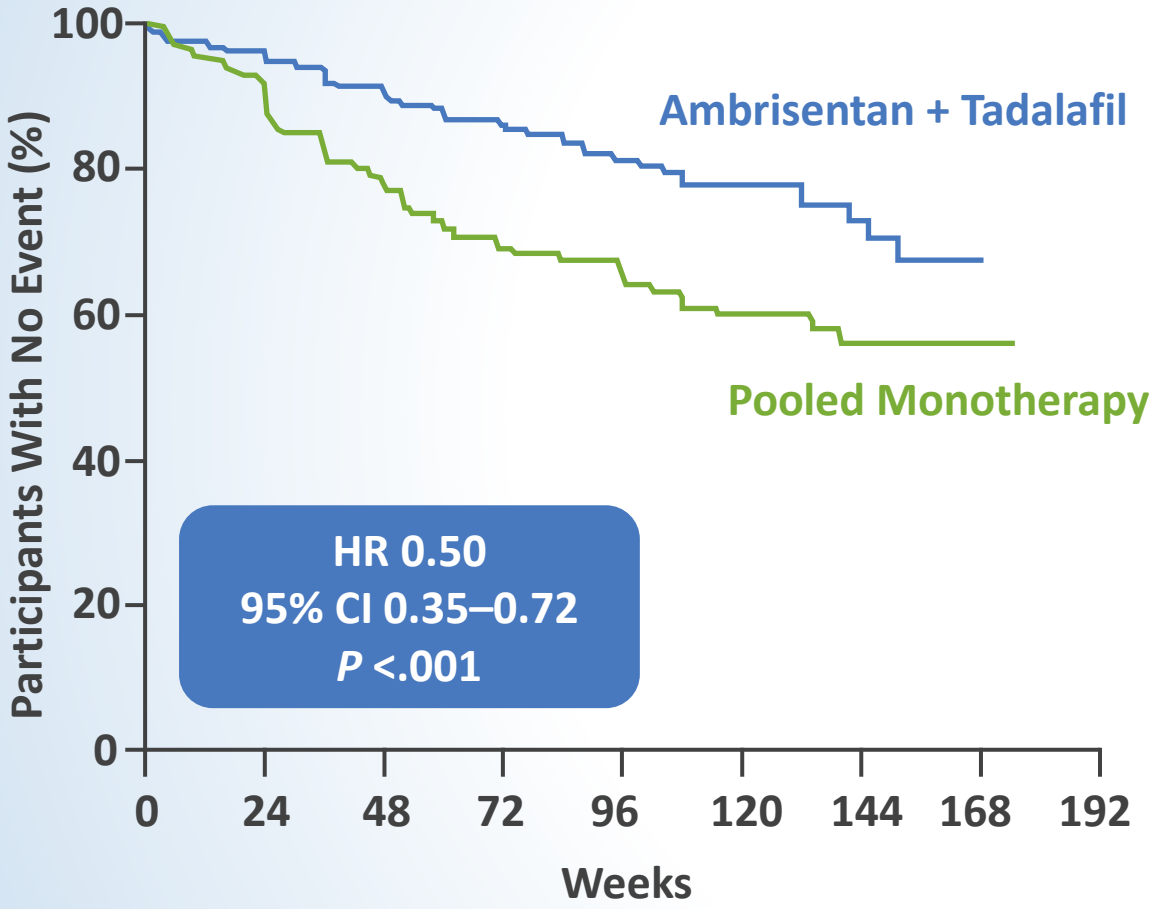
Clinical Trial	Treatments	Efficacy Findings	Safety and Tolerability
SERAPHIN	• Macitentan 3 mg (n=250) or 10 mg (n=242) • PBO (n=250)	• Risk for worsening ↓ with 3-mg & 10-mg MAC vs PBO	• AEs more common with MAC: headache, nasopharyngitis, anemia
GRIPHON	• Selexipag (N=574) • PBO (N=582)	• Proportion of patients without an event* ↑ with selexipag vs PBO	• AEs more common with selexipag: headache, diarrhea, nausea, jaw pain
FREEDOM-EV	• Treprostinil (n=345) • PBO (n=345)	• Clinical worsening ↓ with TRE vs PBO	• AEs most common with TRE: headache, diarrhea, flushing, nausea, vomiting
PATENT 1 & 2	• Riociguat up to 2.5 mg TID (n=254) or 1.5 mg TID (n=63) • PBO (n=126)	• Improved 6MWD, PVR, NT-proBNP, WHO FC, time to clinical worsening, & dyspnea • 6MWD & WHO FC improvements persisted at 2Y	• Most common SAE with PBO & 2.5 mg–maximum group: syncope (4% & 1%, respectively)

*Death from any cause or PAH-related complication ≤7d after last dose.

AE, adverse event; MAC, macitentan; PBO, placebo; SAE, serious adverse event; TID, three times a day; TRE, treprostinil.

Pulido T, et al. *N Engl J Med*. 2013;369(9):809-818; Sitbon O, et al. *N Engl J Med*. 2015;373:2522-33; White RJ, et al. *Am J Respir Crit Care Med*. 2020;201(6):707-717.

AMBITION: Combined Ambrisentan and Tadalafil in Patients With PAH



- Study objective:
  - Evaluate effect of initial combination therapy with ambrisentan & tadalafil on long-term PAH outcomes
- Treatment:
  - AMB + TAD (COMB; n=253) vs AMB or TAD alone (MONO; n=247)
- Primary endpoint:
- Time to clinical failure
- Findings:
  - Clinical failure risk ↓ with COMB vs MONO (risk reduction: HR=0.50; 95%CI, 0.35 to 0.72; *P* <.001)
  - COMB vs MONO showed greater ↓ from baseline in NT-proBNP, clinical response rate, & 6MWT improvement
  - AEs more common with COMB vs MONO: peripheral edema, headache, nasal congestion, anemia

AMB, ambrisentan; COMB, combination therapy; MONO, monotherapy; TAD, tadalafil.

Galiè N, et al. *N Engl J Med*. 2015;373(9):834-844.

TRITON: Triple vs Dual Combination Therapy for Patients With Newly Diagnosed PAH

TRITON: Multicenter, double-blind, randomized, placebo-controlled, phase 3b study

Newly diagnosed, treatment-naïve patients with PAH

n=123	Macitentan 10 mg OD	Tadalafil 40 mg OD	Selexipag 200-1600 µg BID
n=124	Macitentan 10 mg OD	Tadalafil 40 mg OD	Placebo 200-1600 µg BID

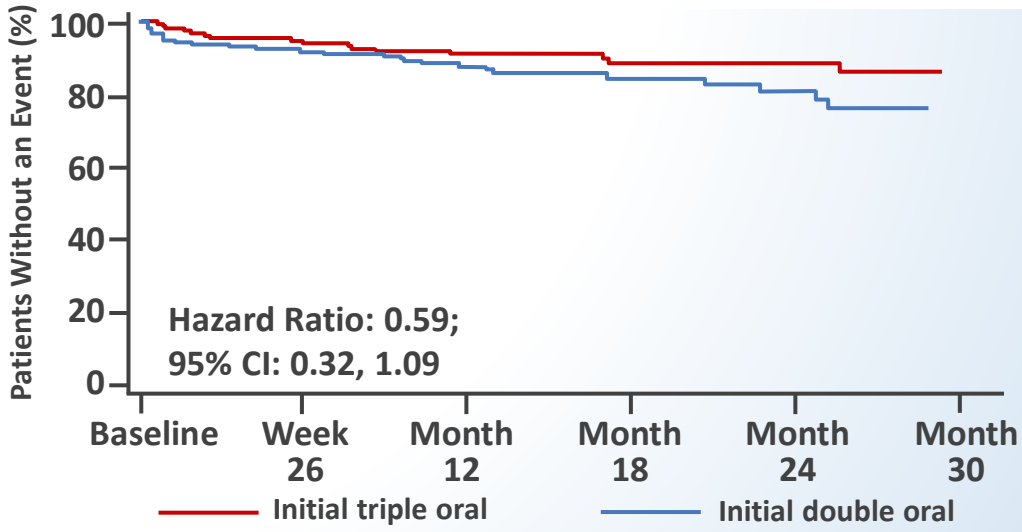
Change from Baseline to Week 26

	Initial triple	Initial double	Treatment effect
Primary Endpoint			
Pulmonary vascular resistance 	-54%	-52%	No difference
Secondary Endpoints (Exploratory Analyses)			
6-minute walk distance 	+55 m	+56 m	No difference
NT-proBNP 	-74%	-75%	

Time to First Disease Progression Event

Secondary Endpoints (Exploratory Analyses)

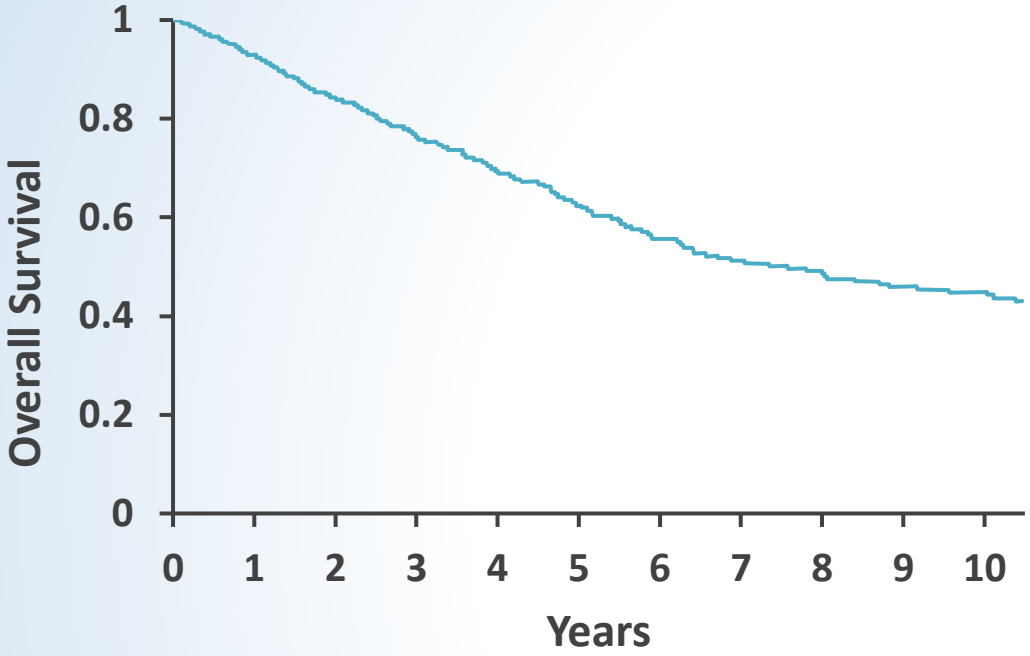
41% reduction in risk of disease progression with initial triple oral vs initial double oral combination therapy



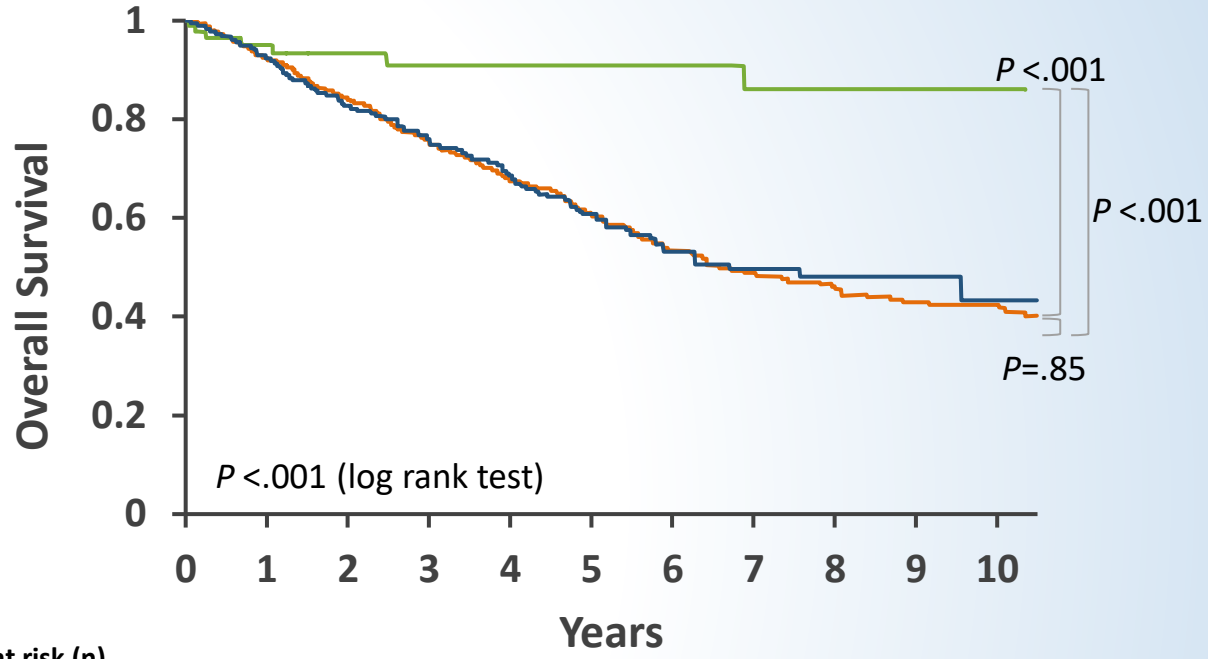
BID, twice a day; OD, once daily.

Chin KM, et al. *J Am Coll Cardiol*. 2021;78:1393-1403.

Effect of Upfront Triple vs Dual Combination Therapy on Overall Survival in Patients With PAH: Retrospective Analysis



Patients at risk (n)	1611	1265	982	748	569	425	311	224	157	103	69
Overall survival		93%		77%		62%					44%
98% CI		0.91-0.94		0.74-0.79		0.59-0.65					0.41-0.49



Patients, at risk (n)											
Triple combo	76	59	52	40	30	26	22	17	10	6	1
Dual combo	551	418	299	225	169	115	79	46	24	12	7
Monotherapy	984	786	630	484	369	284	210	161	123	85	61

Overall survival (95% CI)					
Triple combo	94% (0.89-1.00)	91% (0.83-0.98)	91% (0.83-0.98)		86% (0.74-0.97)
Dual combo	93% (0.90-0.95)	76% (0.72-0.80)	61% (0.55-0.66)		43% (0.33-0.54)
Monotherapy	92% (0.91-0.94)	76% (0.73-0.79)	61% (0.57-0.65)		43% (0.38-0.47)

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Boucly A, et al. *Am J Respir Crit Care Med*. 2021;204(7):842-854.

Initial Treatment Strategy for PAH

Baseline
Multiparametric risk stratification

Select initial therapies using shared decision-making

Low	Intermediate – Aggressive Titration	Intermediate – Maximal Medical Therapy	High
Dual oral therapy	Dual oral therapy	Triple therapy with IV/SQ PCA	Triple with IV/SQ PCA

3 months
Reassess risk

Escalate therapy—consider parenteral prostanoid for most non-low risk

Low	Intermediate – Aggressive Titration	Intermediate – Maximal Medical Therapy	High
Structured follow-up	Escalate to triple therapy	Triple with IV/SQ PCA	Triple with IV/SQ PCA

6 months
Reassess risk

Low risk or not low risk—not low risk should receive parenteral prostanoid

Low	Intermediate-High – Maximal Medical Therapy
Structured follow-up	Triple with IV/SQ PCA

Upfront Maximal Medical Therapy for Intermediate Risk

Why not for all
- Inconvenient
- Side effects
- Risk of complications
- Cost

Why to consider
- Potentially life prolonging
- Risk prediction ≠ clinical response
- Intermediate risk ≠ stable
- Delayed start, never catch up
- Treatments more effective early
- High 5-year mortality

IV, intravenous; PCA, prostacyclin analog; SQ, subcutaneous.

Cascino TM, et al. *Am J Respir Crit Care Med*. 2021;204(7):756-759.

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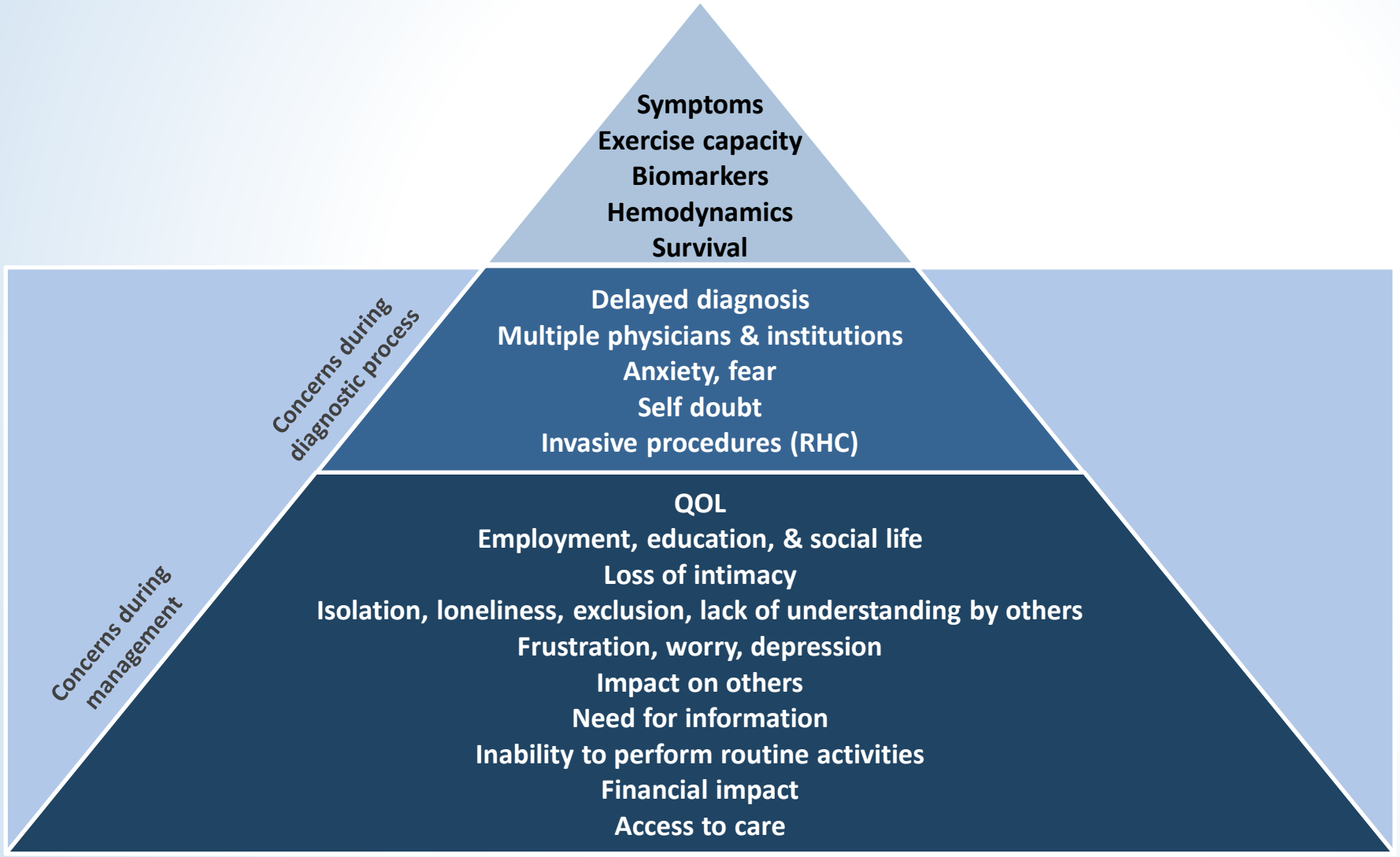
Patient-Focused Management of PAH

Concerns Regarding PAH Management: The Patient Perspective



Surveys of patients and caregivers suggest that traditional parameters of PH severity may be the "tip of the iceberg" when the broader range of patient concerns is considered.

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McGoon MD, et al. *Eur Respir J*. 2019;53(1):1801919.

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Patient Case Study

Case Patient

A 60-year-old Hispanic woman with history of limited cutaneous SSc presents with 3 mos of progressive dyspnea, light-headedness, and fatigue. She has no chest pain, syncope, or palpitations. Her physical exam revealed sclerodactyly and telangiectasia of her hands and legs, pronounced P2, and trivial systolic murmur but was otherwise within normal limits.

Audience Discussion Question

Which of the following would you include as part of the initial evaluation for this patient?

A. EKG
B. Echo
C. PFTs
D. V/Q scan
E. HIV
F. Autoimmune testing
G. 6MWD
H. BNP
I. Cardiac MRI
J. RHC

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Echo, echocardiogram; EKG, electrocardiogram; MRI, magnetic resonance imaging.

Initial Evaluation

Initial Evaluation Findings	
EKG: Right axis deviation	**Autoimmune testing:** + ANA + SCL-70
Echo: Moderate right ventricular enlargement with mild RV dysfunction. Normal LA, LVEF 60%	**6MWD:** 350 m
PFTs: Mild restriction and reduced DLCO of 40%	**BNP:** 125 ng/L
V/Q scan: Normal	**HIV:** Negative

ANA, antinuclear antibody; LA, left atrium.

Audience Discussion Question

Based on the results of initial evaluation, the patient undergoes diagnostic RHC and is diagnosed with SSc-PAH. How would you characterize her level of risk?

A. Low
B. Intermediate
C. High

Audience Discussion Question

In addition to disease risk, what kinds of factors would most strongly influence your PAH management plan for the patient?

A. Home environment
B. Economic factors
C. Patient preferences

Discussion Question

Which of the following treatment regimens would you prescribe for this patient?

A. Monotherapy with an ERA, PDE5i, or prostacyclin analogue
B. Dual therapy with an ERA + PDE5i
C. Triple therapy with an ERA + PDE5i + prostacyclin analogue

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Program Summary

Summary of Key Points

- PAH is a chronic vascular disease characterized by abnormal thickening of the arterial wall leading to increased PVR, RV failure, and eventually heart failure, if untreated.
- Early recognition, accurate diagnosis, and treatment tailored based on disease risk are crucial for reducing morbidity and mortality.
- Evolving evidence suggests that race/ethnicity has an important impact on the prevalence and outcomes of PAH, and should be taken into account when establishing a treatment plan.
- A range of therapies targeting the NO, endothelial, and prostacyclin pathways are approved for PAH and have shown good efficacy, particularly when used in combination.
- In addition to appropriate pharmacotherapy, patients with PAH also require management that addresses a range of concerns, including QoL issues, psychological well-being, and financial burden.

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Thank You!