Pulmonary Hypertension/Right Heart Failure: Update and Developing a Rural PH Practice

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MN Statewide CV Summit

5/21/2021

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Disclosures

Consultant with Edwards Lifesciences

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Objectives

1. Review updated pulmonary hypertension (PH) definition.
2. Differentiate Group 1 (PAH) versus Groups 2-5 PH.
3. Compare PH prevalence in rural MN to national registries

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What is Pulmonary Hypertension?

- ↑Pressure in pulmonary vasculature
- Progressive RV failure & subsequent death
- Why it matters → PAH 85%-91% 1 yr survival -- 58% 5-yr survival
- Median 2.7 years from symptoms to diagnosis

Benza RL et al. Circ, 2010; 122:164-172.

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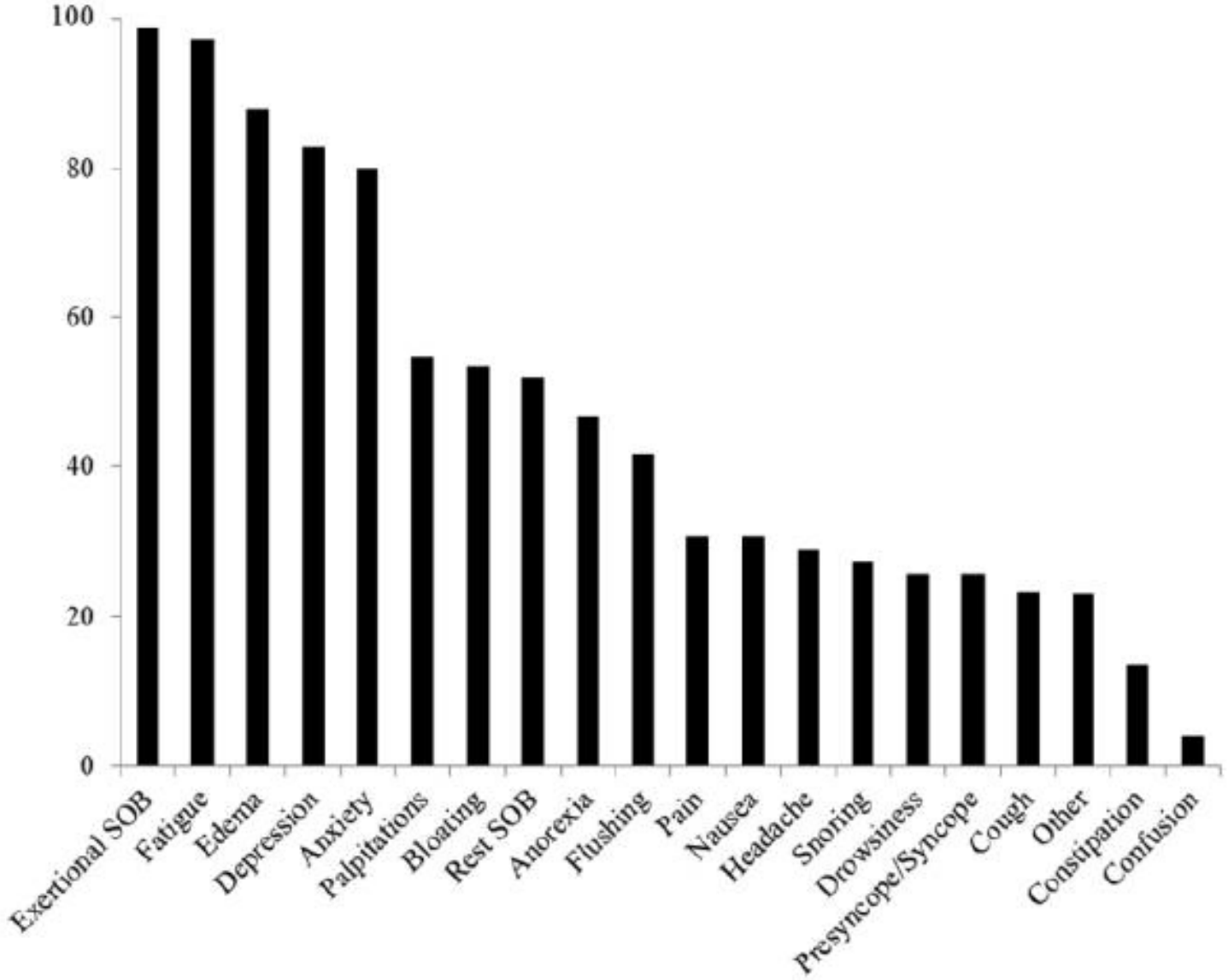

Figure 1. Symptoms encountered most often in patients with pulmonary arterial hypertension. Y-axis shows percent of respondents. SOB: shortness of breath.

Fenstad et al. 2014, Pulm Circ, 4(3):504-10.

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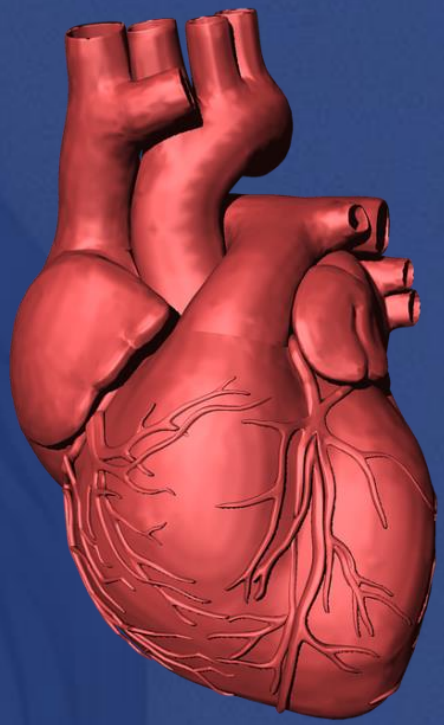
PAH Evaluation and Workup



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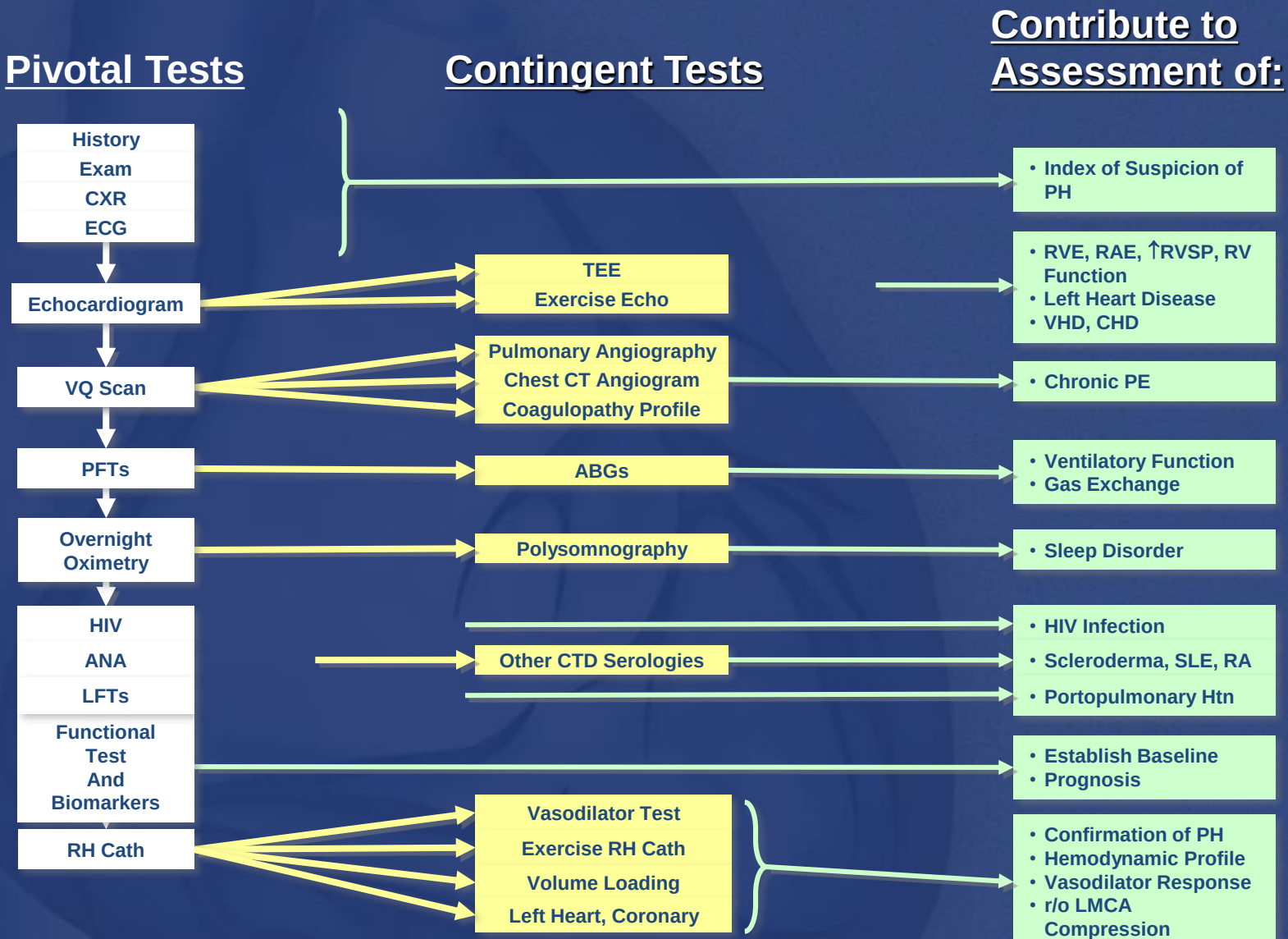
Approach to PH Evaluation

Diagnosis



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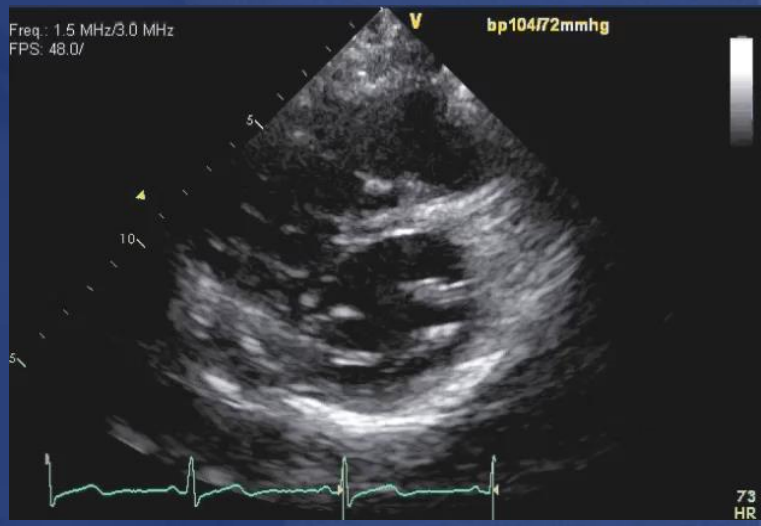
Echo is a Screening Test

- Normal RV pressure < 30 mmHg
- Estimate RVSP with modified Bernoulli equation
  - Can over or underestimate
- RV size and function: TAPSE, S', FAC



Lang RM et al. JASE. 2015; 28(1):1-39.

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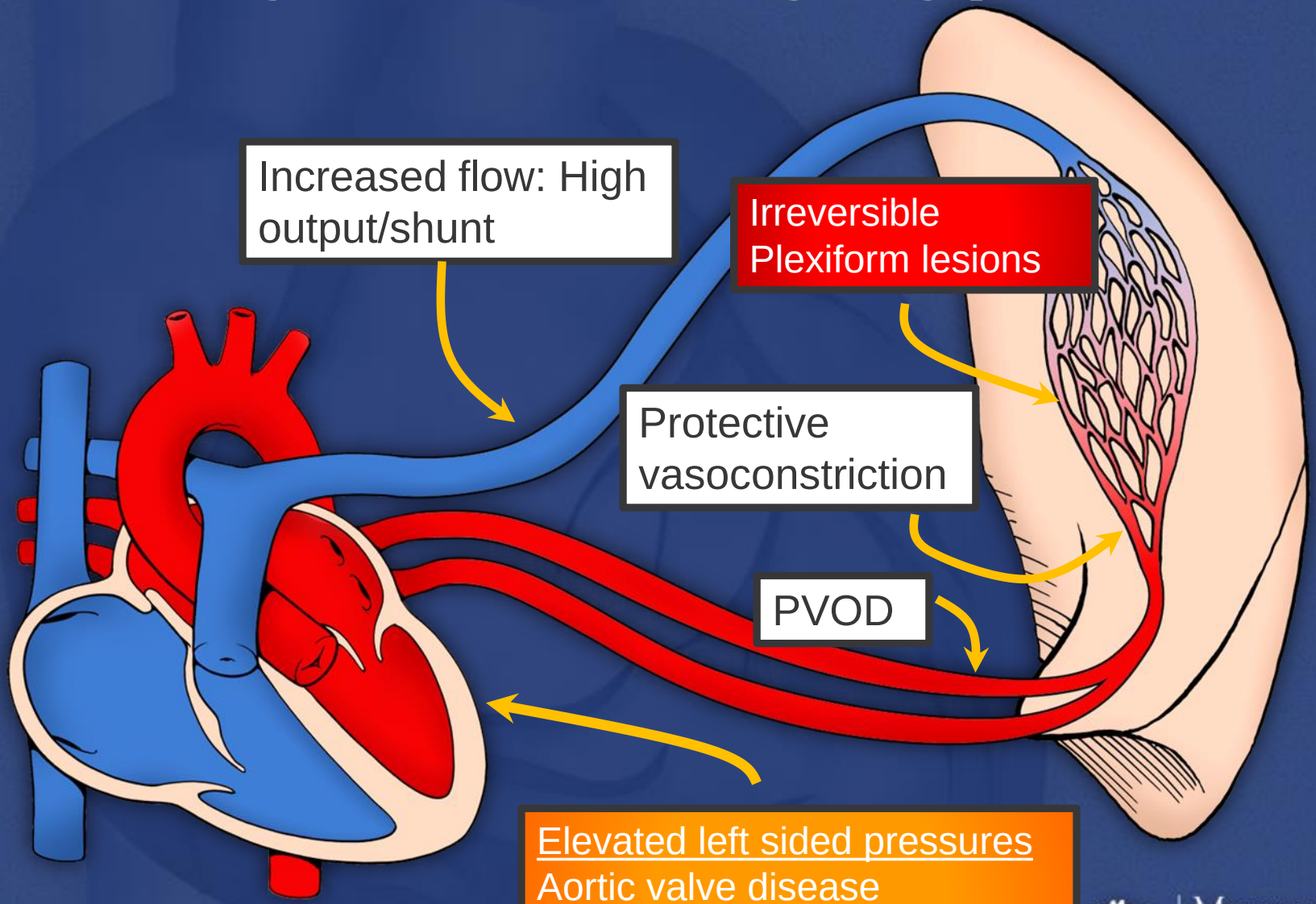
Anatomy - Pulmonary Hypertension



Modified slide from Rick Nishimura MD

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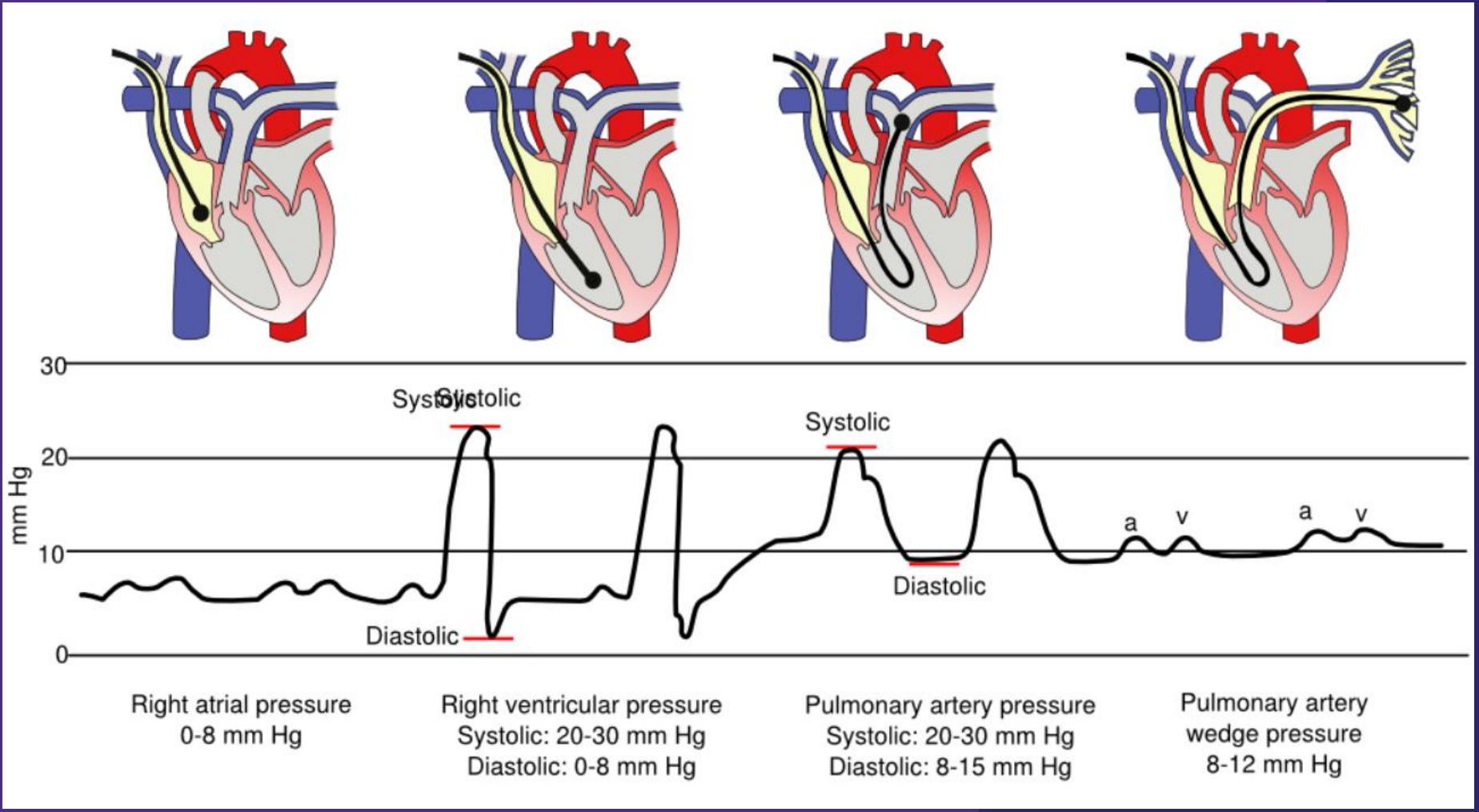
Right Heart Catheterization



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Right Heart Catheterization

- Gold standard for diagnosis
- PAH = Mean PA pressure > 20 mm Hg
  - In PAH → PAWP ≤ 15 mm Hg
  - PVR ≥ 3.0 Wood Units
- Vasodilator response

Positive Vasodilator Test:
1. mPAP ↓by ≥ 10 mmHg
2. mPAP < 40 mmHg
3. Normal or ↑ in CO

***4.5-10% of patients

Table 7. Agents for Acute Vasodilator Testing

	Epoprostenol	Adenosine	Nitric Oxide
Route of Administration	Intravenous infusion	Intravenous infusion	Inhaled
Dose Titration	2 ng/kg/min every 10 to 15 min	50 mcg/kg/min every 2 min	None
Dose Range	2 to 10 ng/kg/min	50 to 250 mcg/kg/min	10 to 80 ppm
Side Effects	Headache, nausea, lightheadedness	Dyspnea, chest pain, AV block	Increased left heart filling pressure in susceptible patients

Definitions	Characteristics	Clinical Groups
Pre-capillary PH	• mPAP >20 mmHg • PAWP ≤15 mmHg • PVR ≥3 WU	1, 3, 4, & 5
Isolated post-capillary PH	• mPAP >20 mmHg • PAWP >15 mmHg • PVR <3 WU	2 & 5
Combined pre & post-capillary PH	• mPAP >20 mmHg • PAWP >15 mmHg • PVR ≥3 WU	2 & 5

Frost A et al. ERJ, 2019;53(1).

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PH Classification

The 5 Groups

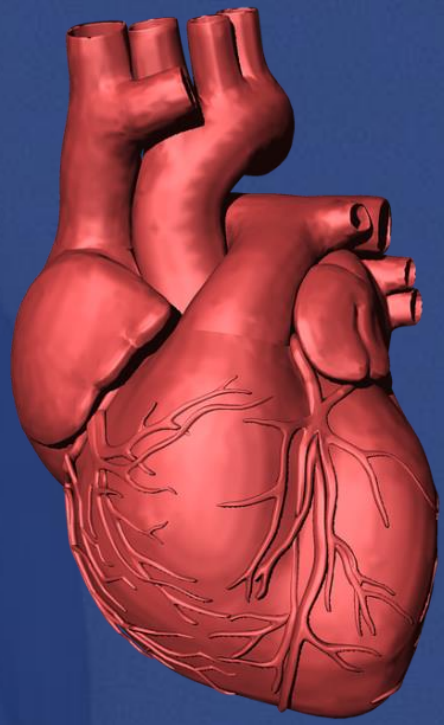

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Table 1 Updated Classification of Pulmonary Hypertension*

1. Pulmonary arterial hypertension
   - 1.1 Idiopathic PAH
   - 1.2 Heritable PAH
   - 1.2.1 BMPR2
   - 1.2.2 ALK-1, ENG, **SMAD9**, **CAV1**, **KCNK3**
   - 1.2.3 Unknown
   - 1.3 Drug and toxin induced
   - 1.4 Associated with:
   - 1.4.1 Connective tissue disease
   - 1.4.2 HIV infection
   - 1.4.3 Portal hypertension
   - 1.4.4 Congenital heart diseases
   - 1.4.5 Schistosomiasis

   PAH

1′ Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis

1″. Persistent pulmonary hypertension of the newborn (PPHN)

2. Pulmonary hypertension due to left heart disease
   - 2.1 Left ventricular systolic dysfunction
   - 2.2 Left ventricular diastolic dysfunction
   - 2.3 Valvular disease
   - **2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies**

   Left Heart

3. Pulmonary hypertension due to lung diseases and/or hypoxia
   - 3.1 Chronic obstructive pulmonary disease
   - 3.2 Interstitial lung disease
   - 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
   - 3.4 Sleep-disordered breathing
   - 3.5 Alveolar hypoventilation disorders
   - 3.6 Chronic exposure to high altitude
   - 3.7 Developmental lung diseases

   Lungs

1998 – 2nd World Symposium

2008 – 4th World Symposium (Dana Point)

2013 – 5th World Symposium (Nice, France)

2018 – 6th World Symposium – updated PH definition

Simonneau G. JACC 2013, 62(25S).

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4. Chronic thromboembolic pulmonary hypertension (CTEPH)

VTE

5. Pulmonary hypertension with unclear multifactorial mechanisms

5.1 Hematologic disorders: **chronic hemolytic anemia**, myeloproliferative disorders, splenectomy

5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis

Misc

5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders

5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure, **segmental PH**

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*5th WSPH Nice 2013. Main modifications to the previous Dana Point classification are in bold.

BMPR = bone morphogenic protein receptor type II; CAV1 = caveolin-1; ENG = endoglin; HIV = human immunodeficiency virus; PAH = pulmonary arterial hypertension.

Simonneau G. JACC 2013, 62(25S).

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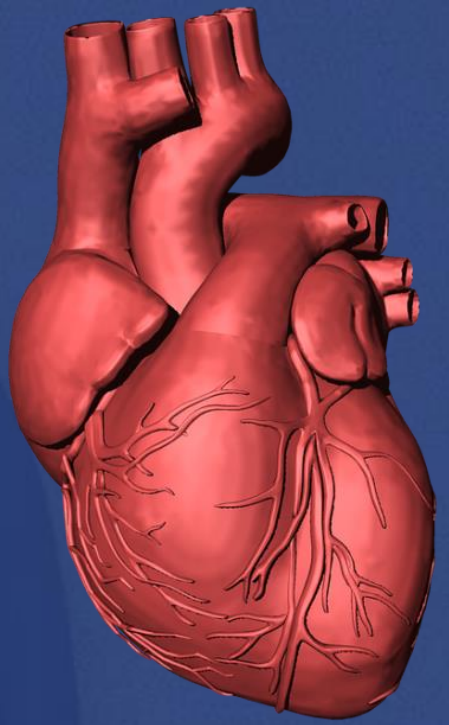
PH Epidemiology



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PAH Epidemiology

- Idiopatic & heritable PAH incidence: estimated at 5-15 per million
- 10-15% of patients with Scleroderma
- 3-10% of patients with congenital heart disease (shunts)
- 2-16% of patients with portal hypertension

McGoon MD et al. JACC 2013, 62(25S):D51.

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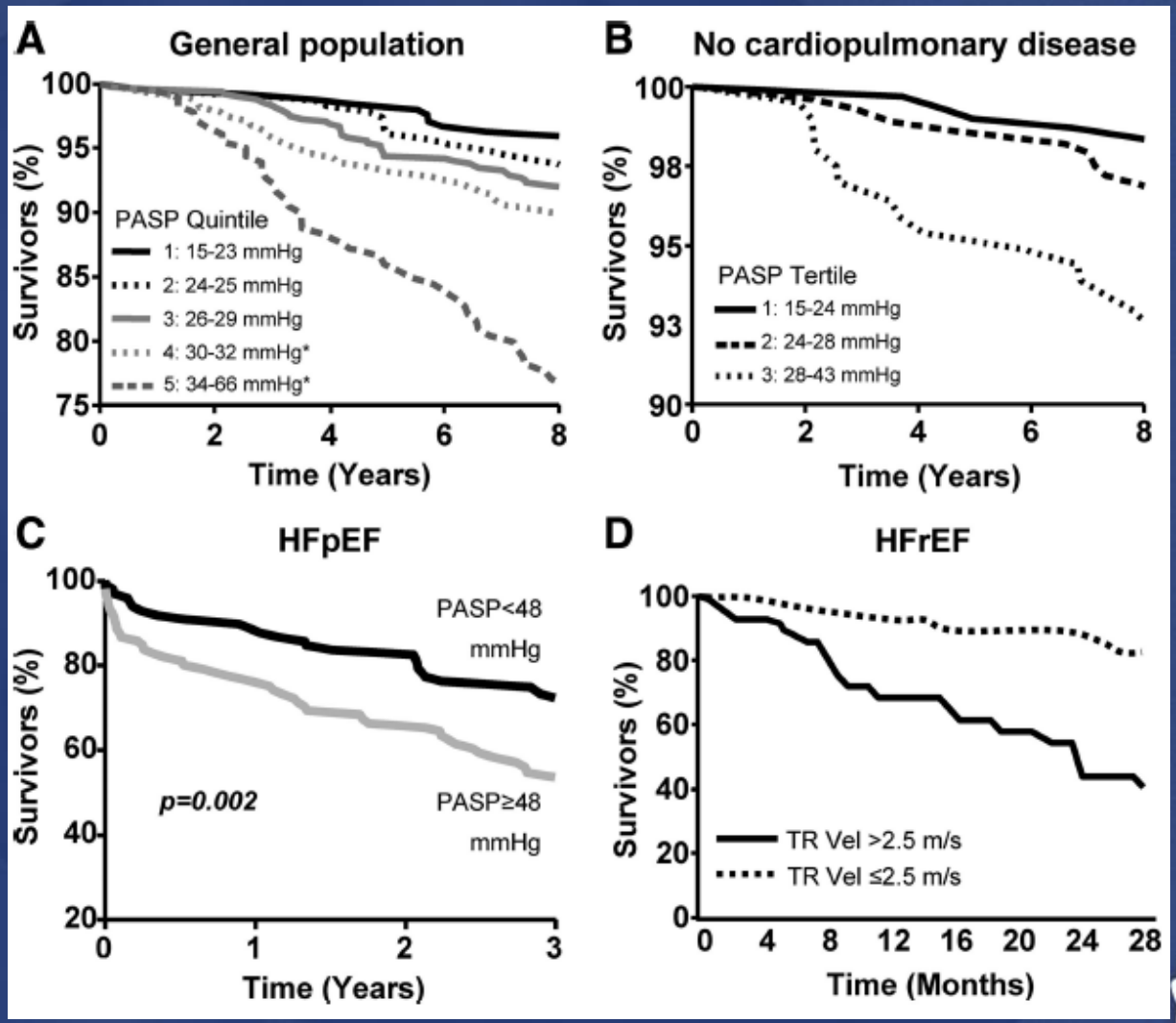
PH as a Comorbidity = ↑ Mortality in HFpEF & HFrEF



Guazzi M. Circ, 2012; 126:975-90.

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Chronic Thromboembolic PH
CTEPH = Group 4 PH

- 1-5% incidence after PE
- 25% pts w/ no PE history
- 96% sensitivity of VQ scan vs. 51% w/ CT

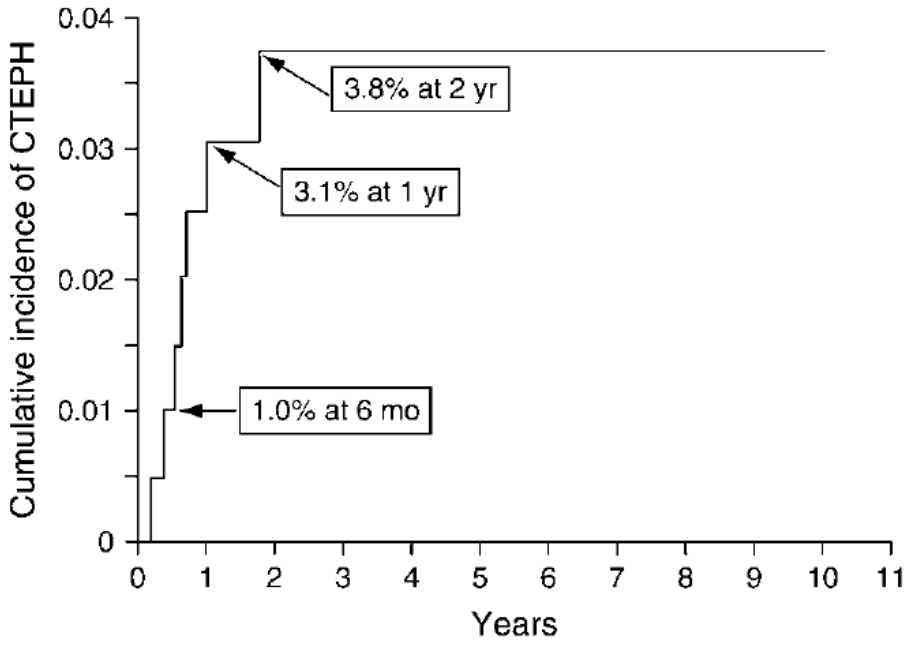

Figure 1. Cumulative incidence of chronic thromboembolic pulmonary hypertension (CTEPH) after a first episode of pulmonary embolism without prior deep vein thrombosis. Reproduced by permission from Reference 30.

Tapson V, Humbert M. Proc Am Thor Soc, 2006;564-67.

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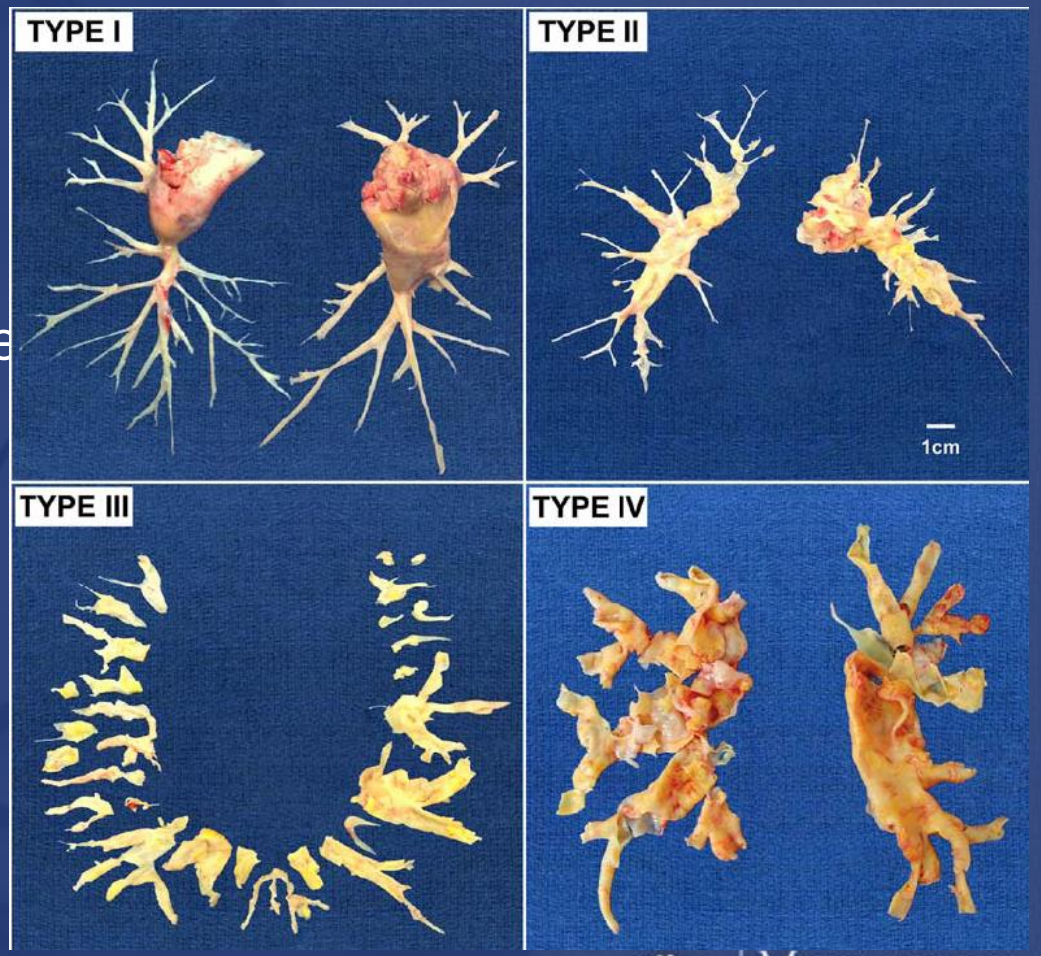
CTEPH Treatment

- Proximal disease = surgery (PTEA)
  - 11-35% of pts will have residual PH
- Distal disease = Medication
  - Anticoagulation
  - PH-directed meds
  - Balloon pulmonary angioplasty



Lang IM, Madini M. Circ, 2014, 130:508-518.

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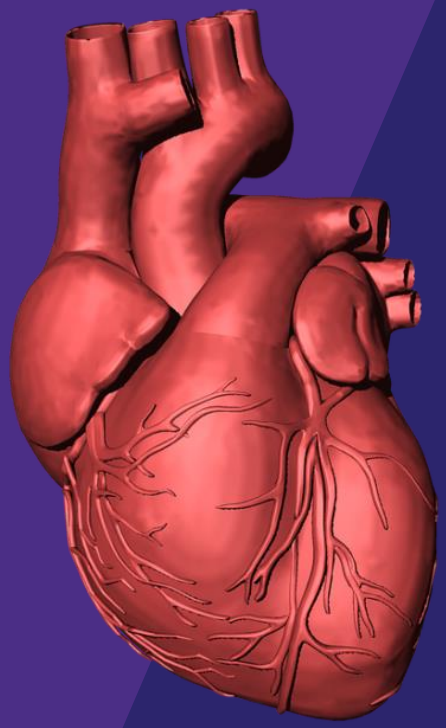
PAH Pathophysiology



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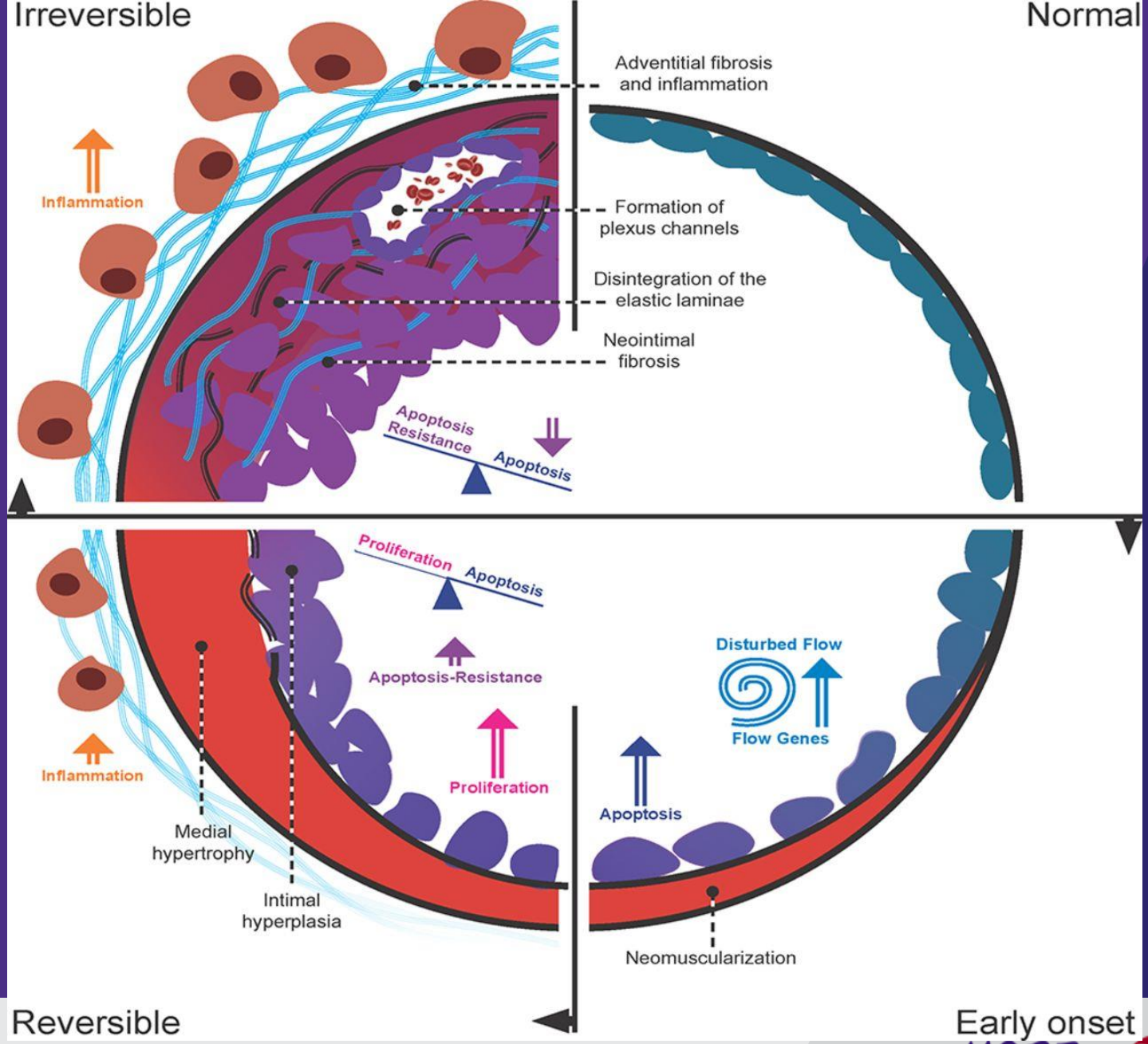

Van der Feen DE et al. Heart. 2019;105:276-282.

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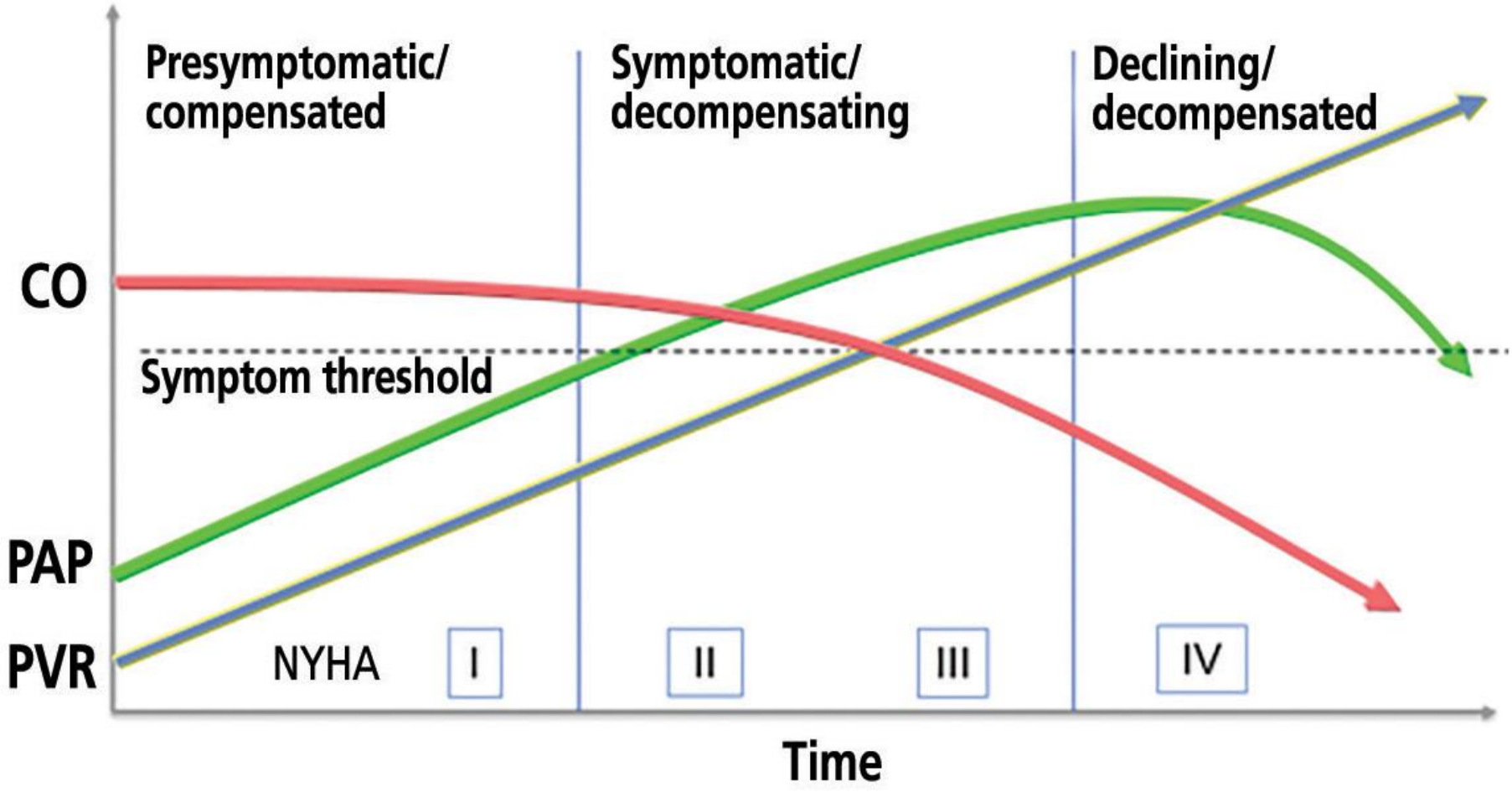

CO = cardiac output; NYHA = New York Heart Association functional class; PAP = pulmonary arterial pressure; PVR = pulmonary vascular resistance

Bhatnagar A et al. Clev Clin J Med, 2018, 85(6):468-480.

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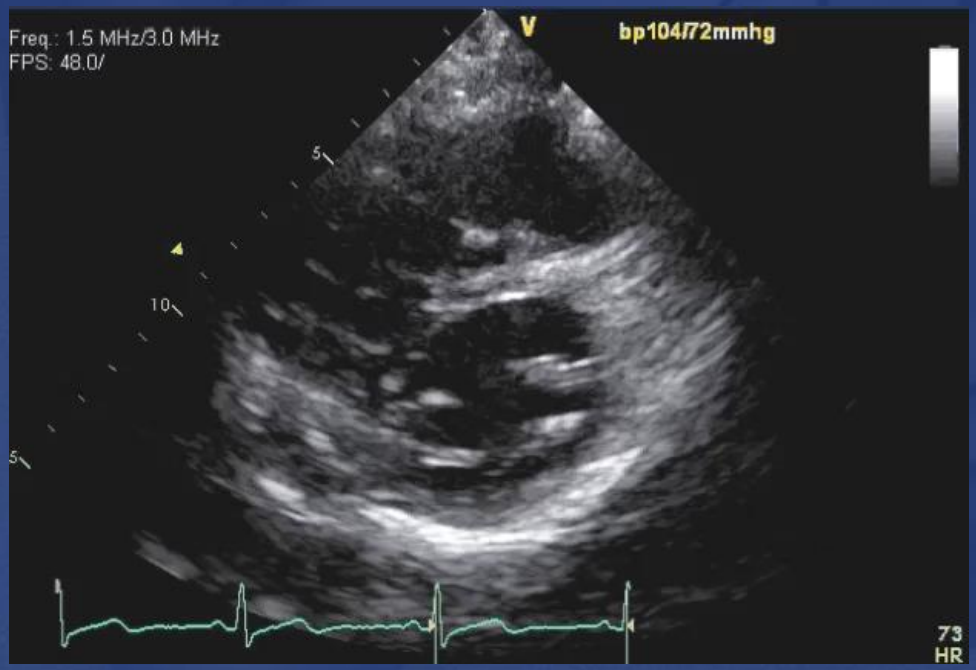
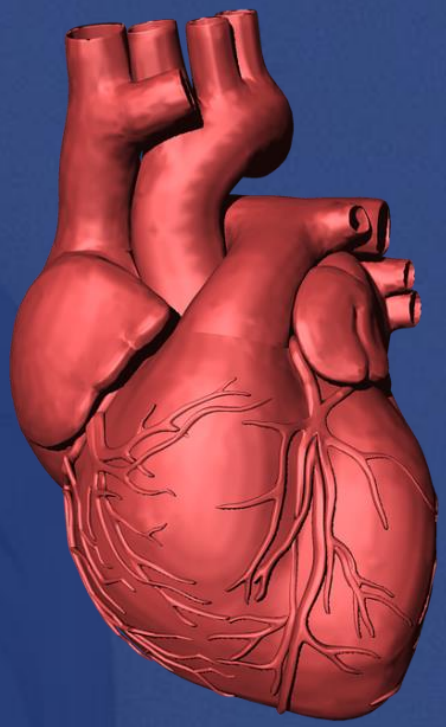
PH Research

Rural vs. Urban Population





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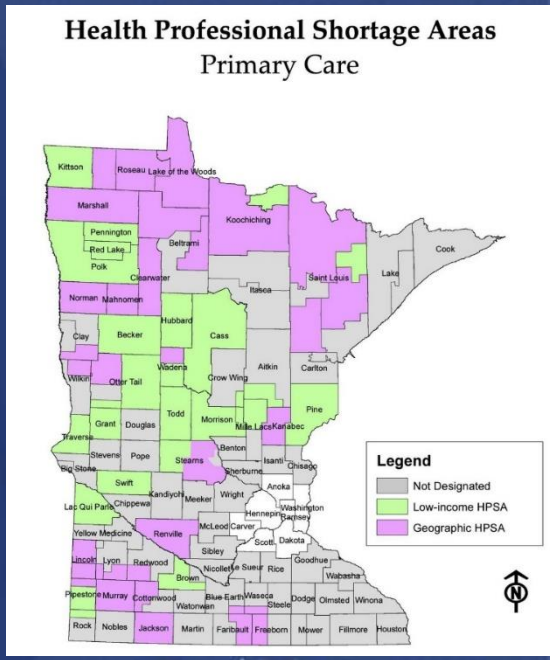
Rural vs. Urban PH

- Different demographics & socioeconomic pressures than urban communities
- >25% of MN in rural communities (1.38+ million people)
- Lack of access to specialist physicians:
  - 30 specialists/100,000 pts vs. 263 per 100,000 pts



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Rural vs. Urban PH

- PH registries heavily weighted to urban population
- PH classification & prevalence is underreported in rural areas

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Rural vs. Urban PH

- Retrospective consecutive pts w/ RVSP ≥ 50 mmHg or PH symptoms
- PAH = mPA ≥ 25mmHg & PAWP ≤ 15 with PVR > 3.0 WU
- Consecutive patients -- 1/1/2010-3/31/2020

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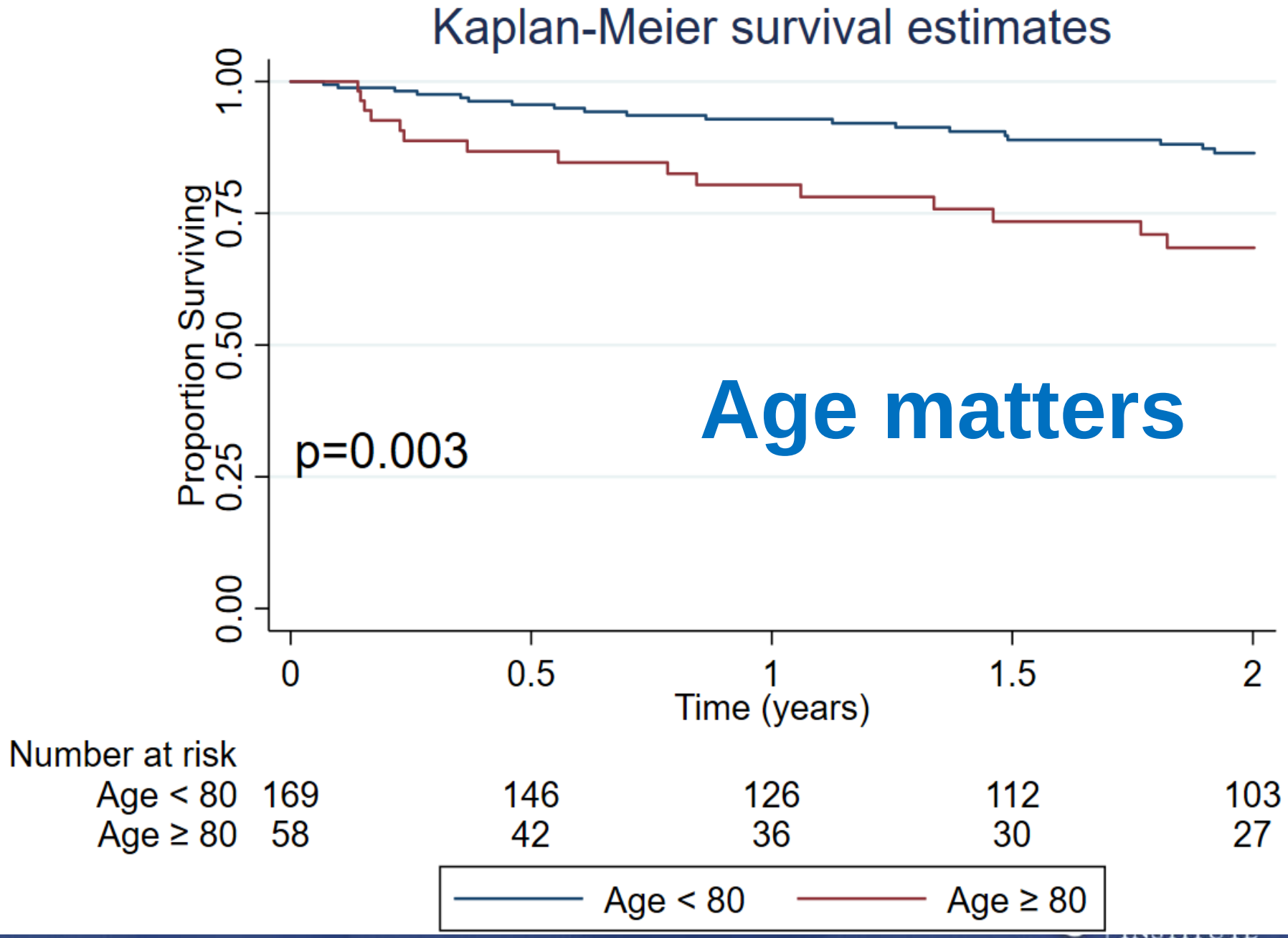
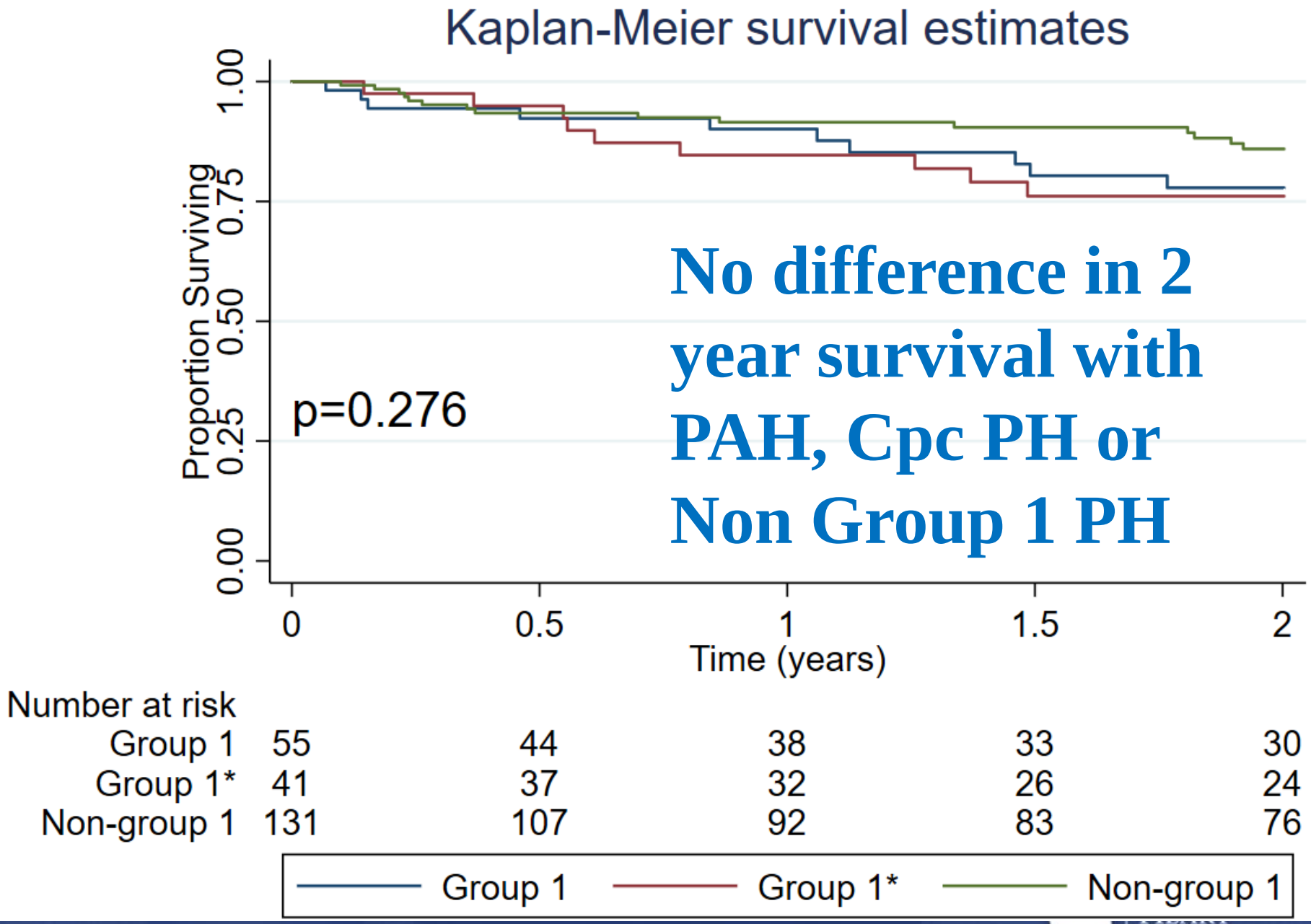
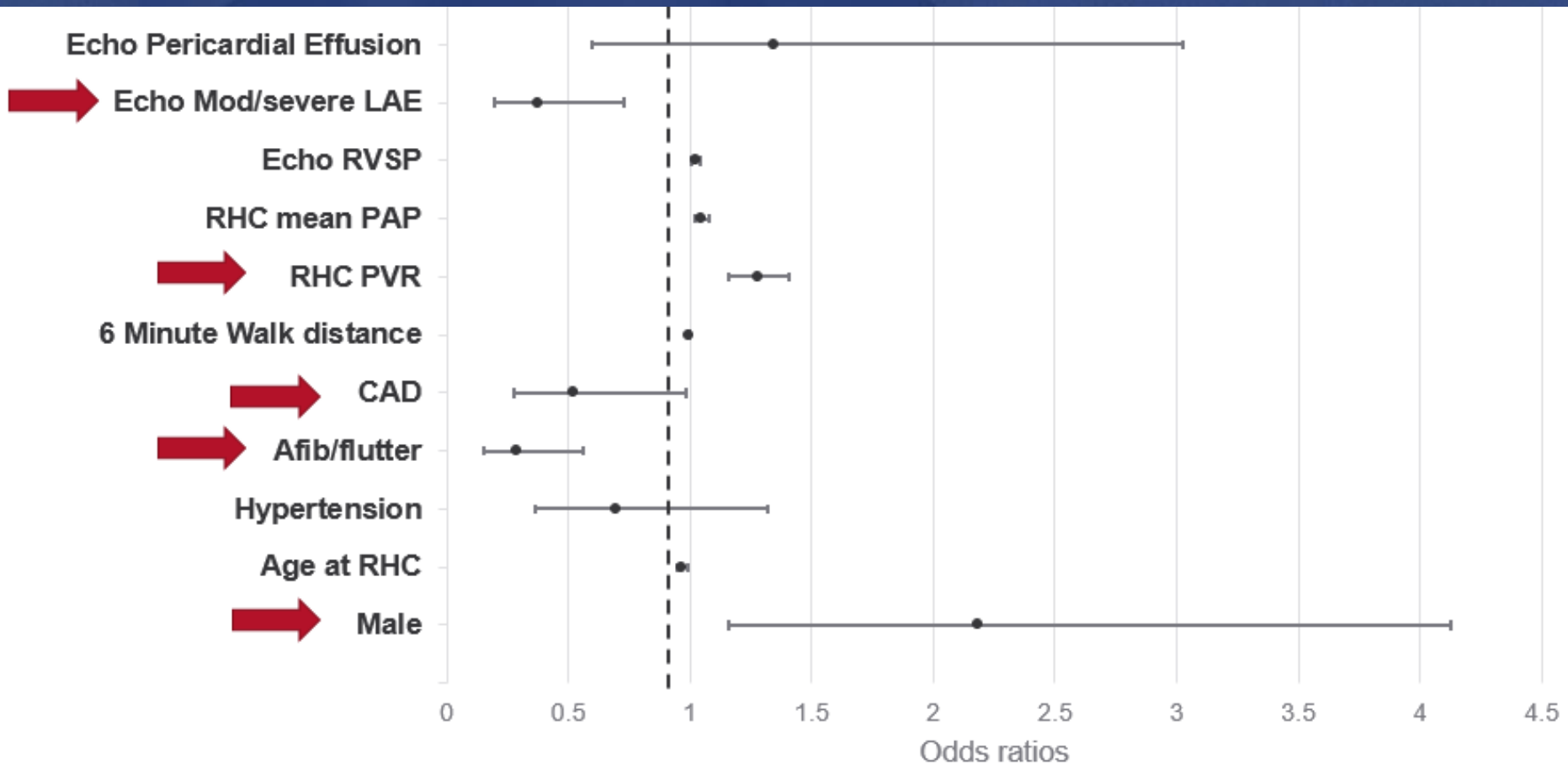
Patient Characteristics

	All pts (n=229)	Group 1 (n=56)	Group 1* (n=41)	Non-group 1 (n=132)	p-values
Male (%)	123 (54)	38 (68)	22 (54)	63 (48)	**0.041**
BMI @ first consult Mean ± SD	32±8.9	29.1±7.6	30.8±7.4	33.6±8.8	**0.002**
Age at RHC Mean ± SD	72.2±11.9	68.5±14.1	74.6±10.5	73±10.9	**0.023**
Coronary artery disease (%)	101 (44)	18 (32)	16 (39)	67 (51)	0.056
Atrial fibrillation (%)	111 (48)	15 (26.8)	28 (68)	68 (52)	**<0.001**
Connective tissue disease (%)	6 (3)	2 (4)	2 (5)	2 (2)	0.377
BNP median (IQR)	280.5 (137.5, 505.8)	316 (148, 801)	186.5 (112, 725.8)	287 (139.5, 443.5)	0.548


Kaplan-Meier survival estimates
Proportion Surviving
0.00
0.25
0.50
0.75
1.00
p=0.003
Age matters
0
0.5
1
1.5
2
Time (years)
Number at risk
Age < 80 169 146 126 112 103
Age ≥ 80 58 42 36 30 27
Age < 80
Age ≥ 80


Kaplan-Meier survival estimates
Proportion Surviving
1.00
0.75
0.50
0.25
0.00
p=0.276
No difference in 2 year survival with PAH, Cpc PH or Non Group 1 PH
0
0.5
1
1.5
2
Time (years)
Number at risk
Group 1 55 44 38 33 30
Group 1* 41 37 32 26 24
Non-group 1 131 107 92 83 76
Group 1
Group 1*
Non-group 1

PAH Predictors



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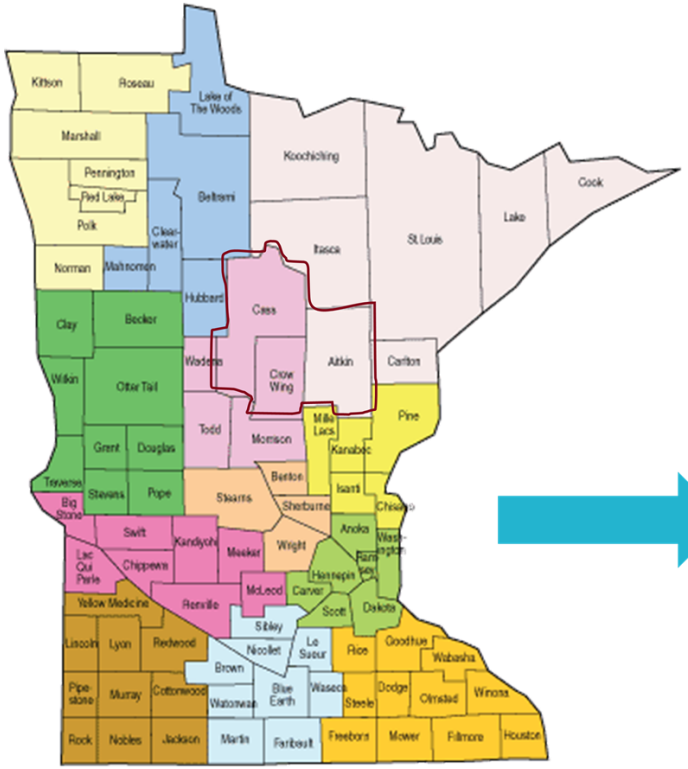
Prevalence of PH in Rural Minnesota



Population: 28,567

Cass County, MN
PAH: 560/million
Group 1*+2: 420/million

Population: 62,500

Aitkin County, MN
PAH: 370/million
Group 1*+2: 1543/million

Population: 16,202

Crow Wing County, MN
PAH: 368/million
Group 1*+2: 1360/million

Conclusions

- PAH prevalence in rural Minnesota appears significantly higher than the estimated 15-50 cases/million compared to national data.
- Why? Lower socioeconomic area, access to care, environmental exposures? Or Nationwide trend of underrecognition?

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Take Home Messages

- 5 groups for PH (Group 1 = PAH)
  - RHC is gold standard
- PH = mean PA pressure >20 mmHg
  - PAH = PAWP ≤ 15 & PVR ≥ 3.0 Wood Units
- PH is underreported in rural population

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Questions

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