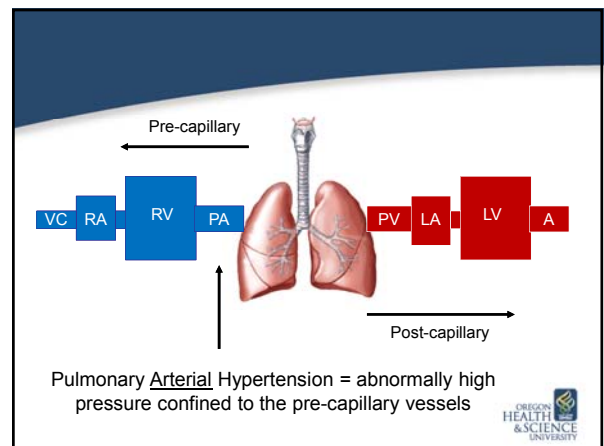
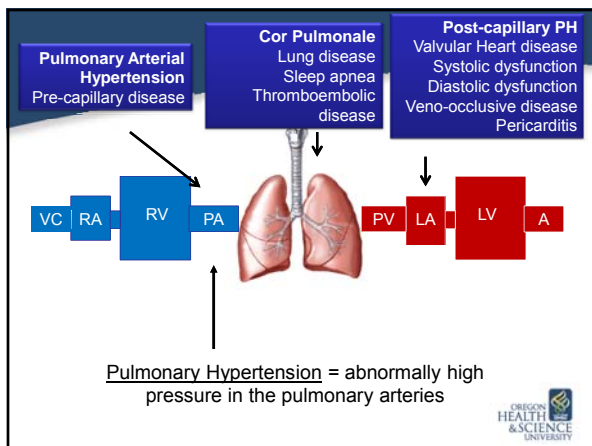
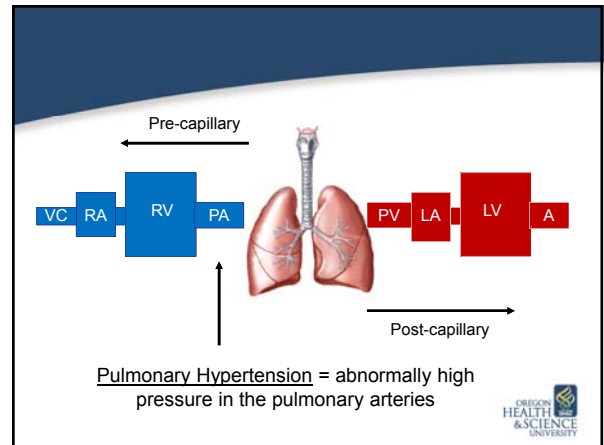
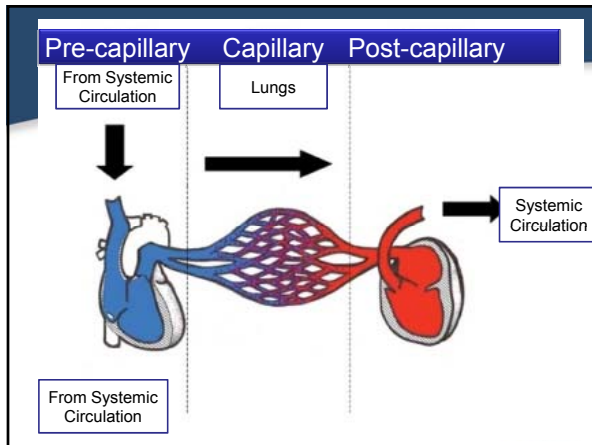



# Pulmonary Artery HTN Diagnosis


Akram Khan, MD  
Assistant Professor  
Pulmonary And Critical Care Medicine

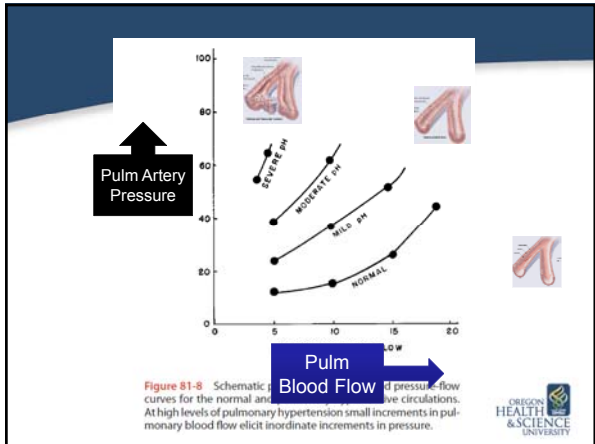
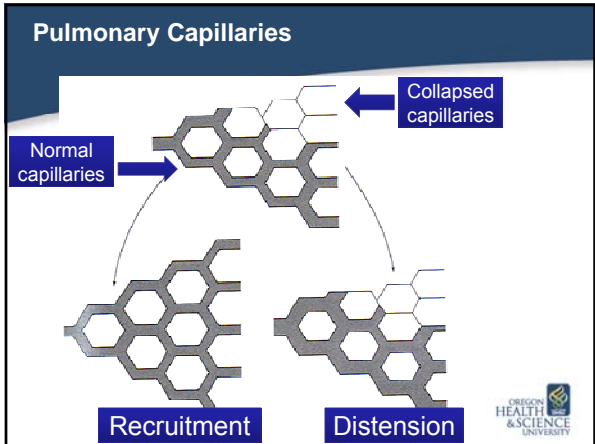
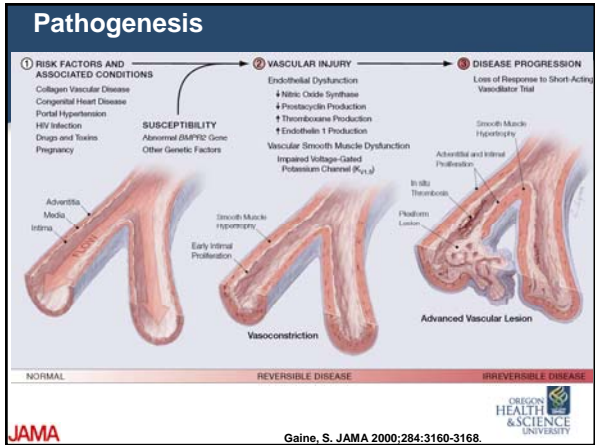
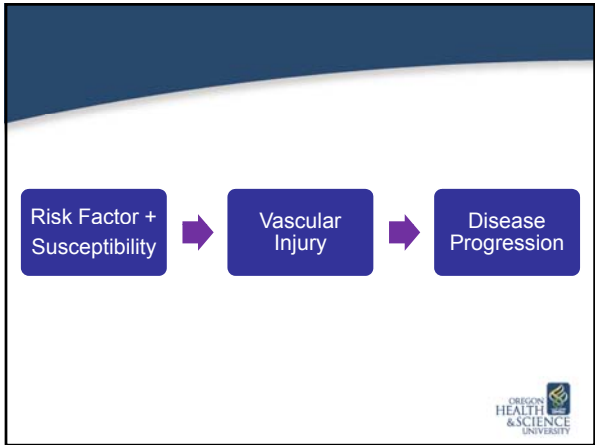
# PULMONARY PHYSIOLOGY

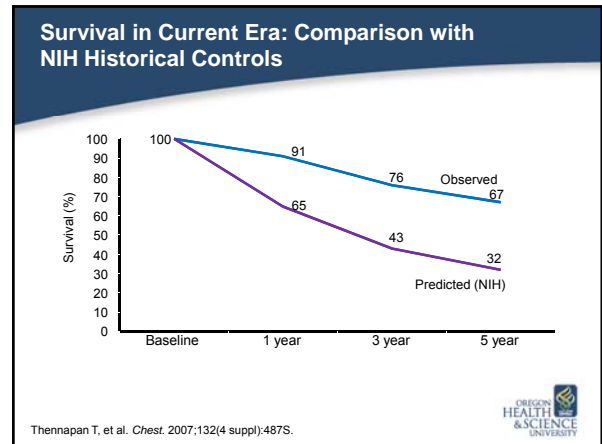
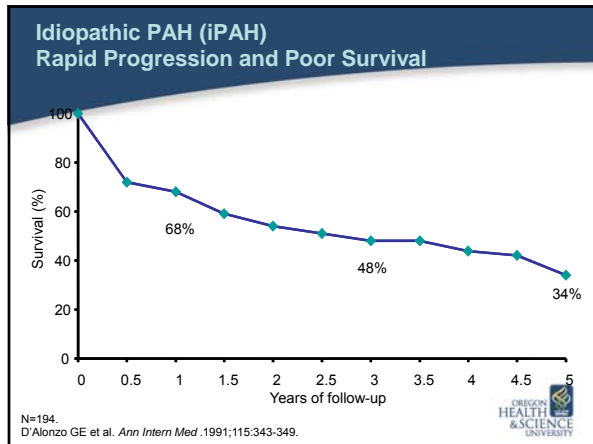


# EPIDEMIOLOGY & PATHOPHYSIOLOGY



- ## Clinical Classification of Pulmonary Hypertension 2008 Dana Point
- Pulmonary Artery Hypertension
  - PH with L heart disease
  - PH associated with lung diseases and/or hypoxia
  - Chronic Thromboembolic PH (CTEPH)
  - Multifactorial / Misc.
- Publication pending
- 





### Prevalence of PAH: French National Registry

- Consecutive adult patients
  - ≥18 years of age
  - 17 French specialty centers
- B/W Oct 2002 - Oct 2003
- Prevalence of PAH: 15.0 cases/million
  - Prevalence of iPAH: 5.9 cases/million

Humbert M et al. *Am J Respir Crit Care Med*. 2006;173:1023-1030.

### Prevalence of PAH: French National Registry

- Time interval b/w symptom onset and diagnosis: 27 months
- Mean age ~ 50yrs
- Twice as many women as men

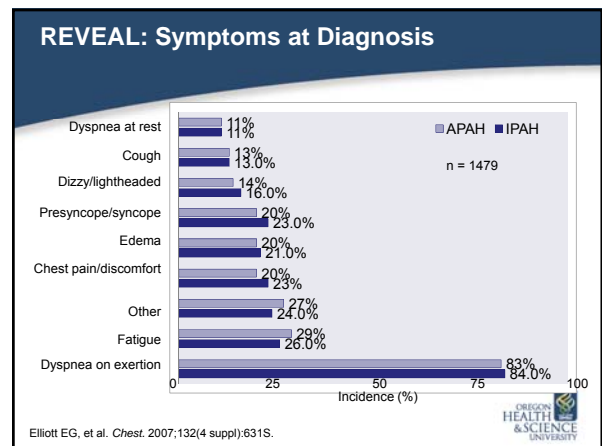
Humbert M et al. *Am J Respir Crit Care Med*. 2006;173:1023-1030.

### REVEAL: Database Characteristics

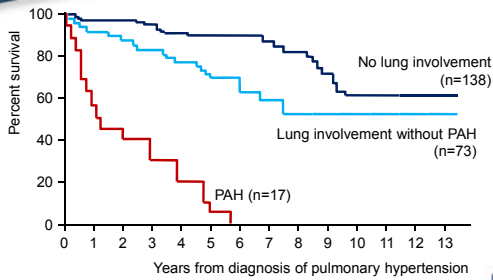
- 50-center US database
- Median time from initial symptoms to RHC
  - 14 months
- Median time from to first visit to pulmonary hypertension clinic
  - 15 months
- Average body mass index
  - 28.9 + 18.4 kg/m<sup>2</sup>

	iPAH (n = 685)	APAH (n = 760)
Female-to-male ratio	3.42:1	4.43:1
Mean age at diagnosis (years)	45-54	45-54

Badesh DB, et al. *Chest*. 2007;132(4 suppl):473S.



### PAH Associated With Scleroderma



Koh ET et al. *Br J Rheumatol*. 1996;35:989-993



### PAH Associated With Connective Tissue Diseases (CTD)

- Prevalence: 10-15%
  - 33% Systemic sclerosis
  - 50% CREST
  - Overestimate: lack of RHC confirmation
- Systemic sclerosis: 75% of PAH associated with CTD
- Rapidly progressive PAH disease course
  - 1-year survival: 45% to 69%

Coghlan JG et al. *Lupus*. 2006;15:138-142. Mukerjee D et al. *Ann Rheum Dis*. 2003;62:1088-1093. Kawut SM et al. *Chest*. 2003;123:344-350. Braunwald E, Zipes BP, Lippa P, eds. *Heart Disease*. 2 vols. 6th ed. Philadelphia, PA: WB Saunders CO:2001:170, 173, 372, 499, 1908, 1912, 1918-1921.



### PAH Associated with Congenital Heart Disease (CHD)

- ~1.8 M Americans have congenital heart defect
  - 6 cases/1000 in general population
- 1.6–12.5 cases/million of PAH associated with CHD in adults
- Eisenmenger syndrome more common with large defects
  - Almost all cases of truncus arteriosus
  - 50% with large VSD
  - 10% with large ASD

Marelli AJ et al. *Circulation*. 2007;115:163-172. Gallè N et al. *Drugs*. 2008;68:1049-1066. The Task Force on Diagnosis and Treatment of Pulmonary Arterial Hypertension of the European Society of Cardiology. *Eur Heart J*. 2004;25:2243-2278.



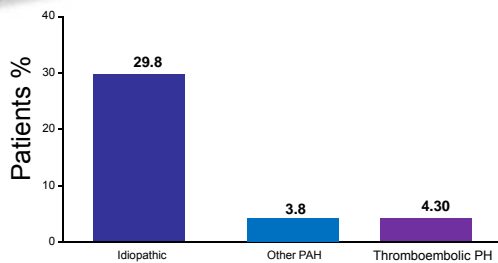
### PAH Associated with HIV

- PAH occurs in 1 in 200 patients with HIV infection
  - PAH a significant mortality factor when present
  - With improved outcomes due to highly active antiretroviral therapy (HAART)
  - Near complete normalization of pressures with vasodilator therapy

Opravil M et al. *Am J Respir Crit Care Med*. 1997;155:990-995. Speich R et al. *Chest*. 1991;100:1268-1271. Nunes H et al. *Am J Respir Crit Care Med*. 2003;167:1433-1439.



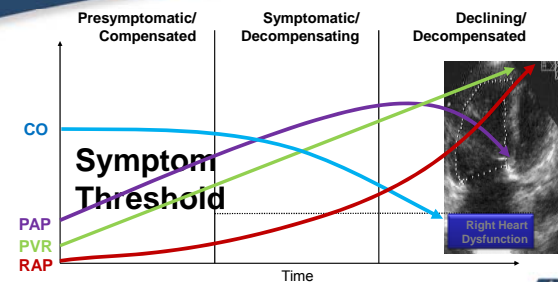
### Methamphetamine Use as a Risk Factor for PAH\*



\*Retrospective analysis at single PH center of adults with PH. Chin KM et al. *Chest*. 2006;130:1657-1663

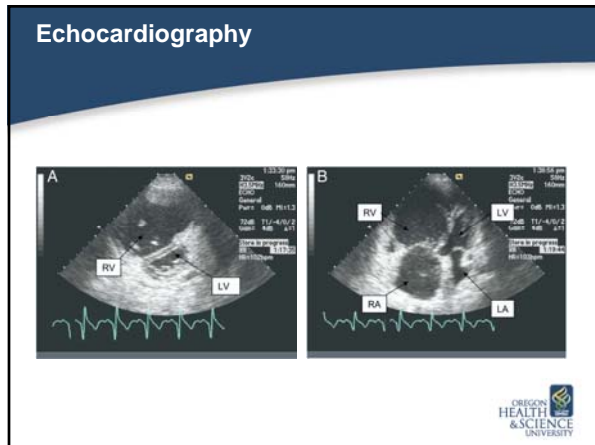
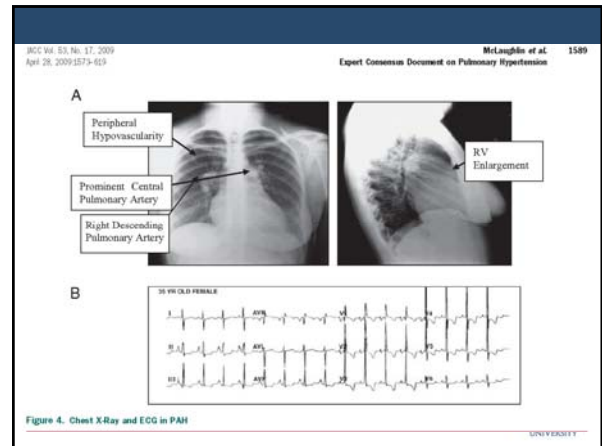
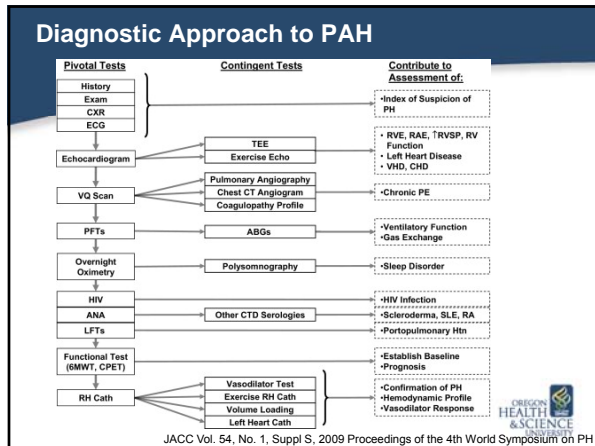


### PAH Progression



CO=cardiac output; PAP=pulmonary arterial pressure; PVR=pulmonary vascular resistance; RAP=right atrial pressure.

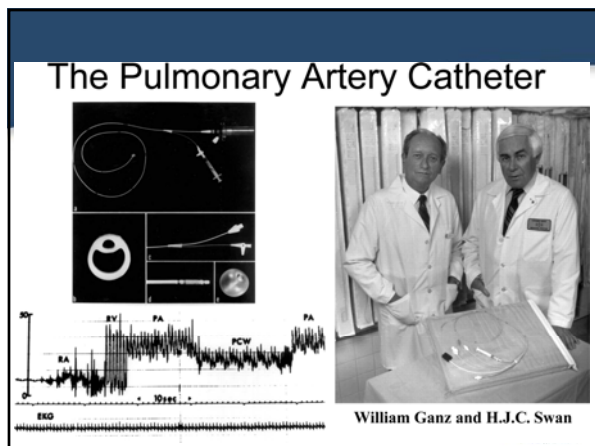




## Severity of Pulmonary Hypertension

Degree of Disease	Mean Pulmonary Artery Pressure (mm Hg) Cath	Systolic Pulmonary Artery Pressure (mm Hg) Echo
Mild	25-50	40-60
Moderate	41-55	60-80
Severe	>55	>80

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## Right Heart Catheterization

- Required to
  - Confirm diagnosis
  - Calculate PVR
  - Guide therapy for PAH
- Exclude other etiologies for PH
  - Intracardiac or extracardiac shunts
  - Left-heart disease


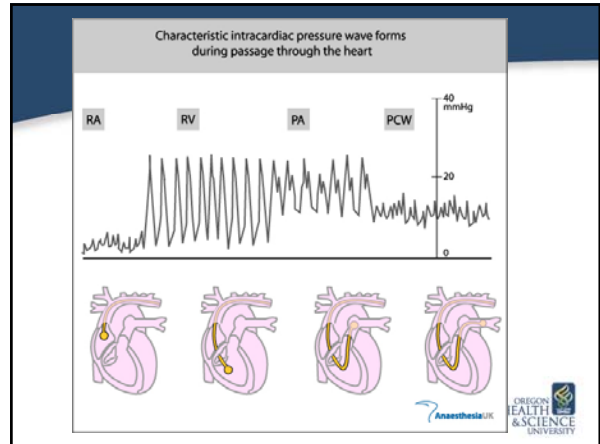
McGoan M. Chest. 2004;126:14S-34S.

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## Right Heart Catheterization

- Measure degree of right-heart dysfunction
  - Right atrial pressure
  - Cardiac output
- Vasodilator testing

McGoan M. *Chest*. 2004;126:14S-34S.

## Normal Pulmonary Hemodynamic Values


Normal Pulmonary Hemodynamic Values	
Cardiac Output (liters/min)	4-6
Right atrial pressure (mmHg)	2-8
Pulmonary artery pressure (mm Hg)	
Systolic	16-24
Diastolic	5-12
Mean	9-16
Pulmonary wedge pressure (mm Hg)	5-12
Pulmonary vascular resistance (dynes/sec/cm <sup>-5</sup> )	80-160

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## Definition of PAH by Right Heart Catheterization

Increased mean pulmonary arterial pressure (mPAP)	≥25 mm Hg at rest, or ≥30 mm Hg during exercise
Normal pulmonary capillary wedge pressure (PCWP)	≤15 mm Hg
Increased pulmonary vascular resistance (PVR)	>3 woods units

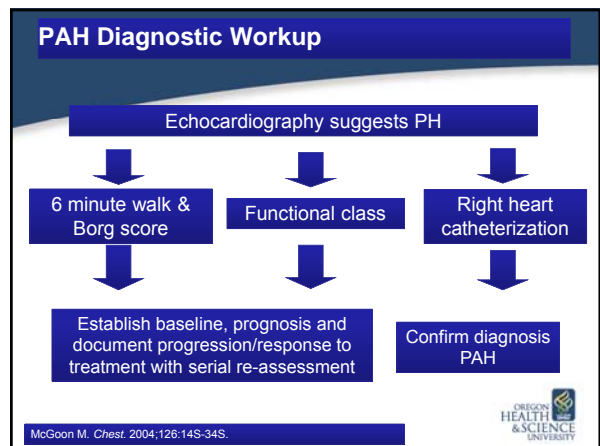
Rubin L.J. *Chest*. 1993;104:236-250.



## Severity of Pulmonary Hypertension

Degree of Disease	Mean Pulmonary Artery Pressure (mm Hg) Cath	Systolic Pulmonary Artery Pressure (mm Hg) Echo
Mild	25-50	40-60
Moderate	41-55	60-80
Severe	>55	>80

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### Case Presentation: History

- 52 year old male
  - 7 month h/o **progressively worsening dyspnea**
- Walking slowly causes immediate severe dyspnea & dizziness (**WHO III**)
- Symptoms subside at rest



### Case Presentation: History

- **2 syncopal episodes**, both while walking at a brisk pace
- No cough, chest pain, or wheezing
- No other significant medical history
- Takes no medications



### Clinical Problem 1

- Physical exam
  - Temp 37C
  - BP 105/60,
  - Pulse 102 at rest and 120 after walking,
  - RR 20/min
  - BMI 32 kg/m<sup>2</sup>.
  - Jugular venous distention +
  - Lungs: Clear to auscultation with no wheezes or crackles



### Clinical Problem 1

- Physical exam
  - **Fixed splitting of the S2**
  - **Increased pulmonic component**
  - Grade 1-2/6 **holosystolic murmur at left sternal border near the fourth rib that increases with inspiration**
  - Lower extremity edema, No cyanosis or clubbing



### Clinical Problem 1

- Diagnostic Data
  - CBC (**polycythemia vera can lead to PAH**) and resting ABG are normal
  - **ECG rightward QRS axis and large R waves in V1**
  - Spirometry & plethysmography are normal
  - Chest radiograph shows no infiltrates or masses



### Clinical Problem 1

- Which of the following is the best next step in the evaluation of this patient?
  - A. Bronchoscopy and trans-bronchial lung biopsy
    - Interstitial Lung Disease
  - B. Methacholine challenge test
    - Asthma
  - C. Right-heart catheterization & pulmonary angiography
    - Pulmonary Hypertension
  - D. Trans-thoracic echocardiography
    - Pulmonary Hypertension



## Clinical Problem 1

- ANSWER: D
  - Transthoracic echocardiography
- In patients with suspected pulmonary HTN
  - TTE can suggest the presence of pulm HTN
  - Evaluate for cardiac causes of elevated pulm artery pressure



## Goals of Management of PAH

- Improve survival
- Prevent worsening
- Improve hemodynamics
- Maintain or improve functional class
- Improve exercise capacity
- Improve daily functioning and quality of life



## Considerations for Selecting Initial Therapy for PAH

- Severity of symptoms
- Physical examination (right-heart failure?)
- Rate of progression
- Echocardiogram (RV size and function)
- Right heart catheterization
  - Mean PA pressure and cardiac index



## Considerations for Selecting Initial Therapy for PAH

- **6-minute walk distance**
- BNP/NT-pro-BNP
- Capability of patient to handle parenteral therapy



## Considerations for Selecting Initial Therapy for PAH

- Parenteral therapy is first choice in very advanced patients
- Other issues
  - Drug-drug interactions
  - Adverse events
  - Comorbid conditions (eg, diabetes)
  - Route of administration
  - Dosing intervals
  - Cost

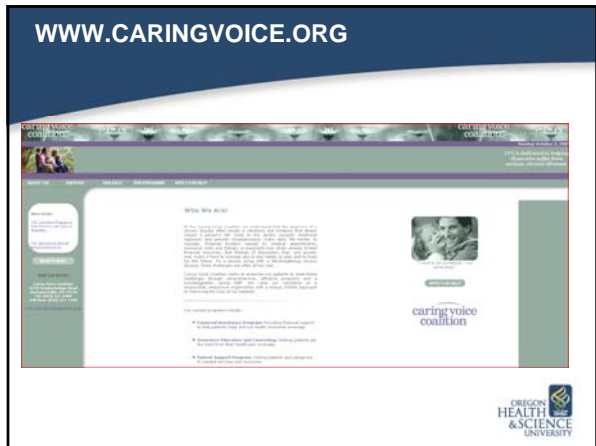


## Cost Analysis

- Approximate annual cost
  - Sildenafil \$12 761
  - Bosentan \$55 890
  - Ambrisentan \$56 736
  - Iloprost \$92 146
- Based on a 70-kg patient at the lower end of the dosing spectrum
  - Epoprostenol \$33 153
  - Treprostinil \$97 615







### PAH Determinants of Risk

Lower Risk	Determinants of Risk	Higher Risk
No	Clinical evidence of RV failure	Yes
Gradual	Progression	Rapid
II, III	WHO class	IV
Longer (>400 m)	6MW distance	Shorter (<300 m)
Minimally elevated	BNP	Very elevated
Minimal RV dysfunction	Echocardiographic findings	Pericardial effusion, significant RV dysfunction
Normal/near normal RAP and CI	Hemodynamics	High RAP, low CI

McLaughlin VV, McGoon MD. *Circulation*. 2006;114:1417-1431.

