



## Complete Summary

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### GUIDELINE TITLE

Prognosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines.

### BIBLIOGRAPHIC SOURCE(S)

McLaughlin VV, Presberg KW, Doyle RL, Abman SH, McCrory DC, Fortin T, Ahearn G. Prognosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest 2004 Jul;126(1 Suppl):78S-92S. [45 references]  
[PubMed](#)

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY  
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## SCOPE

### DISEASE/CONDITION(S)

Idiopathic pulmonary arterial hypertension

### GUIDELINE CATEGORY

Evaluation  
Risk Assessment

### CLINICAL SPECIALTY

Cardiology  
Internal Medicine

Pulmonary Medicine  
Thoracic Surgery

## **INTENDED USERS**

Physicians

## **GUIDELINE OBJECTIVE(S)**

To provide appropriate evidence based recommendations to assess the prognosis of patients with pulmonary arterial hypertension (PAH). Specifically, the guideline seeks to answer two questions: what is the expected survival of patients with PAH, and what are the clinical factors associated with survival in patients with PAH?

## **TARGET POPULATION**

Patients with idiopathic pulmonary arterial hypertension

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Risk Assessment/Prognosis**

Evaluation of:

1. New York Heart Association functional class
2. Presence of pericardial effusion
3. Hemodynamics, including mean right atrial pressure cardiac index, mean pulmonary arterial pressure)
4. Doppler echocardiography right ventricular (RV) (Tei) index
5. Maximum oxygen consumption
6. Brain natriuretic peptide levels
7. Diffusing capacity of the lung for carbon monoxide
8. Response to medical therapy
9. Underlying etiologies (e.g., scleroderma, congenital heart disease, human immunodeficiency virus infection, portopulmonary hypertension, idiopathic pulmonary arterial hypertension)
10. Patient demographics (age, gender, time of onset of symptoms to diagnosis)

Applicable testing procedures:

1. 6-minute walk test
2. Cardiopulmonary exercise test
3. Electrocardiogram
4. Doppler echocardiogram

## **MAJOR OUTCOMES CONSIDERED**

- Expected survival in pulmonary arterial hypertension (PAH)
- Survival in PAH associated with underlying etiology
- Impact of medical therapy on survival in PAH

- Survival in children with PAH
- Clinical factors associated with survival
  - Demographics
  - Hemodynamics
  - Vasodilator responsiveness
  - Echocardiographic findings
  - Exercise tolerance
  - Electrocardiographic findings
  - New York Heart Association functional class
  - Serum biomarkers, such as atrial natriuretic peptide, brain natriuretic peptide, catecholamines, and uric acid
  - Pulmonary function

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

*Note from National Guideline Clearinghouse (NGC):* The Center for Clinical Health Policy Research at Duke University identified and evaluated evidence on this topic, working with the guideline development panel to formulate key questions suitable for systematic literature synthesis.

#### Search Strategy

Computerized searches of the MEDLINE bibliographic database from 1992 to October 2002 were conducted. The developers searched using the term *hypertension, pulmonary*. The search was limited to articles concerning human subjects that were published in the English language and accompanied by an abstract. In addition, the developer searched the reference lists of included studies, practice guidelines, systematic reviews, and meta-analyses, and consulted with clinical experts to identify relevant studies missed by the search strategy or published before 1992.

#### Study Selection

The developers selected studies that described survival over time and considered studies among patients with known or suspected idiopathic pulmonary arterial hypertension (IPAH) or PAH associated with connective tissue diseases, chronic liver disease with portal hypertension, congenital heart disease (CHD) and Eisenmenger syndrome, human immunodeficiency virus (HIV) infection, and chronic thromboembolic disease. The developers excluded studies of pulmonary hypertension associated with chronic obstructive pulmonary disease (COPD), other parenchymal lung disease, high altitude, or cardiac disease (e.g., left-heart failure or valvular heart disease) except CHD. They also excluded studies of neonates and case series with < 10 subjects.

Two physicians (one with methodologic expertise and one with content area expertise) reviewed the abstracts of candidate articles and selected a subset to review in full text. Full-text articles were again reviewed by two physicians to determine whether they were study reports or review articles, and were pertinent to the key questions.

## **NUMBER OF SOURCE DOCUMENTS**

Not stated

## **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Expert Consensus  
Weighting According to a Rating Scheme (Scheme Given)

## **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

### **Quality of the Evidence**

**Good** = evidence based on good randomized controlled trials or meta-analyses

**Fair** = evidence based on other controlled trials or randomized controlled trials with minor flaws

**Low** = evidence based on nonrandomized, case-control, or other observational studies

**Expert opinion** = evidence based on the consensus of the carefully selected panel of experts in the topic field. There are no studies that meet the criteria for inclusion in the literature review.

## **METHODS USED TO ANALYZE THE EVIDENCE**

Systematic Review with Evidence Tables

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

The studies retrieved from the literature search were reviewed and classified according to primary diagnosis (idiopathic pulmonary arterial hypertension [IPAH] vs. PAH associated with another disease), treatment strategy, survival rates, risk factors, and type of analysis done.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Informal Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

An international panel of 19 experts representing five medical experts was assembled. Representatives from other medical and patient advocacy associations were also invited to join the panel (including the American College of Cardiology, American College of Rheumatology, and the Pulmonary Hypertension Association). These experts convened on several occasions, including the culminating panel conference in September 2003, in which they deliberated over the composition of the final recommendations and grading of the current state of the evidence, benefits to the patient, and the strength of the recommendations.

Guideline development was led by an executive committee including the chair, the leader of the methodology support group, and the American College of Chest Physicians project manager, which supervised the guideline development process, methodologic issues, panel composition, structure of the final document, and activities of the writing committees. Each writing committee, led by a group leader who served as primary author and editor of that chapter, conferred with the methodology team on inclusion/exclusion criteria, relevant research questions, and important literature that was not readily identified. These individuals continue with their responsibilities to assist in the development of the implementation tools.

When the evidence was insufficient for evidence-based recommendations, the panel used informal group consensus techniques to develop recommendations based on the expert opinion of the panel. With every member of the panel attending the final conference, the expert-based opinions are truly representative of geographically diverse and multispecialty inclusive practice patterns of the complete panel.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Strength of Recommendations**

A = strong recommendation  
B = moderate recommendation  
C = weak recommendation  
D = negative recommendation  
I = no recommendation possible (inconclusive)  
E/A = strong recommendation based on expert opinion only  
E/B = moderate recommendation based on expert opinion only  
E/C = weak recommendation based on expert opinion only  
E/D = negative recommendation based on expert opinion only

### **Net Benefit**

Substantial  
Intermediate  
Small/weak  
None  
Conflicting  
Negative

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

External Peer Review  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The writing groups and the executive committee of the panel extensively reviewed each chapter during the writing process. The final conference provided an opportunity for the entire panel to review the latest drafts. Following final revisions and one final review by the executive committee, each chapter of the guidelines was reviewed and approved by the American College of Chest Physicians (ACCP) Health and Science Policy Committee, the ACCP Pulmonary Vascular NetWork, and then by the ACCP Board of Regents. The guidelines have not been field tested.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Rating schemes for level of evidence, strength of recommendation, and net benefit follow the "Major Recommendations."

As the majority of the evidence reviewed in the original guideline document is applicable to patients with idiopathic pulmonary arterial hypertension (IPAH), the following recommendations pertain to patients with IPAH. In most instances, data are insufficient to make recommendations for patients with pulmonary arterial hypertension (PAH) due to diagnosis other than IPAH. In patients with IPAH, the following parameters, as assessed at baseline, may be used to predict a worse prognosis:

1. Advanced New York Heart Association functional class (NYHA-FC). **Quality of evidence: good; net benefit: substantial; strength of recommendation: A.**
2. Low 6 -minute walk test (6MWT) distance. **Quality of evidence: good; net benefit: substantial; strength of recommendation: A.**
3. Presence of a pericardial effusion. **Quality of evidence: good; net benefit: substantial; strength of recommendation: A.**
4. Elevated mean right atrial pressure (mRAP). **Quality of evidence: fair; net benefit: substantial; strength of recommendation: A.**
5. Reduced cardiac index (CI). **Quality of evidence: fair; net benefit: substantial; strength of recommendation: A.**
6. Elevated mean pulmonary arterial pressure (mPAP). **Quality of evidence: fair; net benefit: intermediate; strength of recommendation: B.**
7. Elevated Doppler Echocardiography right ventricular (RV) (Tei) index. **Quality of evidence: low; net benefit: intermediate; strength of recommendation: C.**

8. Low VO<sub>2</sub>max (maximum oxygen consumption) and low peak exercise systolic blood pressure (SBP) and diastolic blood pressure (DBP) as determined by cardiopulmonary exercise test (CPET). **Quality of evidence: low; net benefit: intermediate; strength of recommendation: C.**
9. Electrocardiogram (ECG) findings of increased P-wave amplitude in lead II, qR pattern in lead V<sub>1</sub>, and World Health Organization criteria for RV hypertrophy. **Quality of evidence: low; net benefit: intermediate; strength of recommendation: C.**
10. Elevated brain natriuretic peptide (BNP) (>180 pg/mL). **Quality of evidence: low; net benefit: intermediate; strength of recommendation: C.**
11. In patients with IPAH treated with epoprostenol, persistence of NYHA-FC III or IV status after at least 3 months of therapy may be used to predict a worse prognosis. **Quality of evidence: fair; net benefit: substantial; strength of recommendation: A.**
12. In patients with scleroderma-associated PAH, reduced diffusing capacity of the lung for carbon monoxide (DLCO) (<45% of predicted) may be used to predict a worse prognosis. **Quality of evidence: low; net benefit: small/weak; strength of recommendation: C.**
13. In pediatric patients with IPAH, younger age at diagnosis may be used to predict a worse prognosis. **Quality of evidence: low; net benefit: small/weak; strength of recommendation: C.**

## **Definitions**

### **Quality of the Evidence**

**Good** = evidence based on good randomized controlled trials or meta-analyses

**Fair** = evidence based on other controlled trials or randomized controlled trials with minor flaws

**Low** = evidence based on nonrandomized, case-control, or other observational studies

**Expert opinion** = evidence based on the consensus of the carefully selected panel of experts in the topic field. There are no studies that meet the criteria for inclusion in the literature review.

### **Strength of Recommendations**

A = strong recommendation

B = moderate recommendation

C = weak recommendation

D = negative recommendation

I = no recommendation possible (inconclusive)

E/A = strong recommendation based on expert opinion only

E/B = moderate recommendation based on expert opinion only

E/C = weak recommendation based on expert opinion only

E/D = negative recommendation based on expert opinion only

### **Net Benefit**

Substantial  
Intermediate  
Small/weak  
None  
Conflicting  
Negative

## **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Assessment of prognosis of patients with pulmonary arterial hypertension (PAH) is important, as it influences both medical therapy and referral for transplantation. The guideline provides evidence-based recommendations to assess the prognosis of these patients.

### **POTENTIAL HARMS**

None stated

## **QUALIFYING STATEMENTS**

### **QUALIFYING STATEMENTS**

- The information provided in the guideline should be used in conjunction with clinical judgment. Although the guideline provides recommendations that are based on evidence from studies involving various populations, the recommendations may not apply to every individual patient. It is important for the physician to take into consideration the role of patient preferences and the availability of local resources.
- The American College of Chest Physicians (ACCP) is sensitive to concerns that nationally and/or internationally developed guidelines are not always applicable in local settings. Further, guideline recommendations are just that, recommendations not dictates. In treating patients, individual circumstances, preferences, and resources do play a role in the course of treatment at every decision level. Although the science behind evidence-based medicine is rigorous, there are always exceptions. The recommendations are intended to guide healthcare decisions. These recommendations can be adapted to be applicable at various levels.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation tools have been developed, including a quick reference guide in print and personal digital assistant format, and educational slide presentations for physicians and other health-care practitioners.

### IMPLEMENTATION TOOLS

Patient Resources  
Personal Digital Assistant (PDA) Downloads  
Quick Reference Guides/Physician Guides  
Resources  
Slide Presentation  
Tool Kits

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

McLaughlin VV, Presberg KW, Doyle RL, Abman SH, McCrory DC, Fortin T, Ahearn G. Prognosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest 2004 Jul;126(1 Suppl):78S-92S. [45 references]  
[PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Jul

### GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

## **SOURCE(S) OF FUNDING**

Funding for both the evidence reviews and guideline development was provided through an unrestricted educational grant from GlaxoSmithKline, Texas Biotechnology Corporation, and Actelion Pharmaceuticals US. Representatives from these companies were not granted right of review, nor were they allowed participation in any portion of the guideline development.

## **GUIDELINE COMMITTEE**

American College of Chest Physicians (ACCP) Expert Panel on Pulmonary Artery Hypertension

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

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## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

The following participants have disclosed information regarding potential or real conflicts of interest and commitment:

Steven H. Abman, MD: scientific advisory board for INO Therapeutics; consultant for Pfizer.

Charles W. Atwood, Jr., MD, FCCP: research support from Respironics, Inc.

David B. Badesch, MD, FCCP: consultant or Speaker's Bureau for Glaxo Wellcome/GlaxoSmithKline, Actelion, InterMune, Encysive, Myogen, Astra-Merck, Astra-Zeneca, Exhale Therapeutics/CoTherix, Forrest Labs, INO Therapeutics, Berlex; research support from Glaxo Wellcome/GlaxoSmithKline, United Therapeutics, Boehringer Ingelheim, Actelion, Encysive, ICOS/Texas Biotechnologies/Encysive, Myogen, INO Therapeutics, Scleroderma Foundation, National Institutes of Health, National Heart, Lung, and Blood Institute, United Therapeutics, Pfizer, American Lung Association.

Robyn J. Barst, MD: consultant and research support from Actelion, Encysive, Exhale Therapeutics, INO, Myogen, United Therapeutics, Pfizer GlaxoSmithKline; unrestricted education grants from GlaxoSmithKline, Encysive, Actelion.

Richard N. Channick, MD, FCCP: research support from Actelion, Pfizer, Myogen, United Therapeutics; consultant and Speaker's Bureau for Actelion.

Ramona L. Doyle, MD, FCCP: Speaker's Bureau for Actelion; clinical research for Actelion, Myogen, United Therapeutics.

David D. Gutterman, MD, FCCP: stock options with Johnson & Johnson; relative who is a Vice-President at GlaxoSmithKline.

James E. Loyd, MD, FCCP: relationships with GlaxoSmithKline, United Therapeutics, Actelion, ICOS/Texas Biotechnology, Westat, PRA International, Pfizer, Exhale Therapeutics.

Michael D. McGoan, MD: past research support from Glaxo Wellcome, United Therapeutics, Actelion; research support from Texas Biotech/Encysive, Myogen, Pfizer, Medtronic.

Vallerie V. McLaughlin, MD, FCCP: consultant for Actelion, United Therapeutics, Exhale Therapeutics; Speaker's Bureau for Actelion; research funding from Actelion, United Therapeutics, Pfizer, Encysive/Texas Biotechnologies, Glaxo Wellcome, Exhale Therapeutics, Myogen.

Stuart Rich, MD: research funding from Actelion, Pfizer, United Therapeutics, Encysive, Myogen; consultant for Actelion, Pfizer, United Therapeutics, GlaxoSmithKline.

Lewis J. Rubin, MD, FCCP: consultant for Actelion, Myogen, Schering, Exhale Therapeutics, United Therapeutics, Pfizer, Celgene; investigator for Actelion, Myogen, Exhale, Pfizer, Celgene; no stock holdings or other ownerships or positions.

Gerald Simonneau, MD: consultant and investigator for Glaxo Wellcome, Pfizer, Actelion, Schering, Myogen, United Therapeutics.

Virginia D. Steen, MD: relationships with Arthritis Foundation, Scleroderma Foundation, Actelion.

Fredrick M. Wigley, MD: research funding from Biogen, Pfizer, Actelion; consultant to Genzyme.

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

#### Background Articles

- Rubin, LJ. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Introduction. Chest 2004 Jul;126(1 Suppl):7S-10S.
- Rubin LJ. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Executive summary. Chest 2004 Jul;126(1 Suppl):4S-6S.
- McCrory DC, Lewis SZ. Methodology and grading for pulmonary hypertension evidence review and guideline development. Chest 2004 Jul;126(1 Suppl):11S-13S.

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

Additional implementation tools are available:

- Clinical Resource: Pulmonary Arterial Hypertension. Northbrook, IL. ACCP, 2004.

Ordering information is available from the [American College of Chest Physicians \(ACCP\) Web site](#).

#### **PATIENT RESOURCES**

The following is available:

- A patient's guide to pulmonary hypertension. In: Clinical resource: pulmonary arterial hypertension. Northbrook (IL): American College of Chest Physicians (ACCP). 2004.

Ordering information is available from the [American College of Chest Physicians \(ACCP\) Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

#### **NGC STATUS**

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