



Complete Summary

GUIDELINE TITLE

An empiric integrative approach to the management of cough: ACCP evidence-based clinical practice guidelines.

BIBLIOGRAPHIC SOURCE(S)

Pratter MR, Brightling CE, Boulet LP, Irwin RS. An empiric integrative approach to the management of cough: ACCP evidence-based clinical practice guidelines. Chest 2006 Jan;129(1 Suppl):222S-31S. [43 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On November 18, 2005, the U.S. Food and Drug Administration (FDA) notified manufacturers of Advair Diskus, Foradil Aerolizer, and Serevent Diskus to update their existing product labels with new warnings and a Medication Guide for patients to alert health care professionals and patients that these medicines may increase the chance of severe asthma episodes, and death when those episodes occur. All of these products contain long-acting beta2-adrenergic agonists (LABA). Even though LABAs decrease the frequency of asthma episodes, these medicines may make asthma episodes more severe when they occur. A Medication Guide with information about these risks will be given to patients when a prescription for a LABA is filled or refilled. See the [FDA Web site](#) for more information.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

SCOPE

DISEASE/CONDITION(S)

Acute, subacute, and chronic cough, including:

- Upper airway cough syndrome (UACS)
- Asthma-induced chronic cough
- Nonasthmatic eosinophilic bronchitis (NAEB)
- Gastroesophageal reflux disease (GERD)-induced chronic cough

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Pulmonary Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To review the literature to provide a comprehensive approach, including algorithms for the clinician to follow in evaluating and treating the patient with acute, subacute, and chronic cough

TARGET POPULATION

Patient with acute, subacute, or chronic cough

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Medical history
2. Physical examination
3. Chest radiograph

4. Chest computed tomography scan
5. Spirometry
6. Bronchoscopy
7. Transbronchoscopic biopsy
8. Video-assisted thoracic surgery biopsy
9. High-resolution CT (HRCT) chest scan
10. Allergy testing
11. Evaluation of patient's home or workplace for potential environmental causes
12. Bronchoprovocation challenge
13. Sputum test for assessment of number of eosinophils
14. 24-hour esophageal pH monitoring
15. Upper gastrointestinal (GI) endoscopy
16. Barium swallow study

Treatment

1. First-generation antihistamine-decongestant (A/D)
2. Inhaled corticosteroids (ICSs) and beta-agonists, leukotriene inhibitors, oral corticosteroid therapy
3. Corticosteroid therapy
4. Treatment for gastroesophageal reflux disease (GERD)
5. Assistance with smoking cessation
6. Referral to a cough specialist (for patients with cough whose condition remains undiagnosed)

MAJOR OUTCOMES CONSIDERED

- Utility of diagnostic investigations
- Symptom resolution (including cough)
- Etiology of cough

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

The evidence review procedures included section-specific targeted searches as well as a formal systematic review on selected topics.

Formal Systematic Reviews

Formal systematic reviews on selected topics covered in the guideline were performed by the Center for Clinical Health Policy Research at Duke University Medical Center. For the key questions addressed by the formal systematic reviews see the section titled "Methodology and Grading of the Evidence for the Diagnosis and Management of Cough" (see "Availability of Companion Documents" field).

Literature Search Strategy

The Duke University research team conducted a systematic and comprehensive literature review that began with searches of MEDLINE from 1966 through August 2003 with limits of articles published in the English language and with human subjects. Search terms included the medical subject heading term "cough" combined with a published strategy for identifying randomized controlled trials (RCTs). A separate search combined the medical subject heading terms "bronchiectasis," "cystic fibrosis," and "respiratory therapy" with the RCT strategy. However, searches using terms related to the therapeutic use of specific agents, including "antitussive agents," "expectorants," "bronchodilator agents," "ipratropium," "albuterol," "orciprenaline," and "cromolyn sodium" had poor specificity in the absence of the term "cough," and thus were not used. Additional searches were targeted to double-blind RCTs of nonspecific antitussive therapy and protussive drugs (e.g., expectorant, mucolytic, mucus-modifying agents) for all indications other than those listed in question 2 in the section titled "Methodology and Grading of the Evidence for the Diagnosis and Management of Cough" (see "Availability of Companion Documents" field) that reported on cough clearance or cough symptoms and had been published since the previous American College of Chest Physicians cough guidelines were published. The trials identified in this search were provided to the section authors.

In addition to MEDLINE, the Duke University research team searched the National Guideline Clearinghouse and the Cochrane Library (including the Cochrane Database of Systematic reviews, the Cochrane Controlled trial register, and the Database of Abstracts of Reviews of Effectiveness). Additional studies were identified from the reference lists of review articles and by querying experts in the field.

Inclusion and Exclusion Criteria

The criteria for the inclusion and exclusion of articles were developed for each research question and are shown in Table 1 in the section titled "Methodology and Grading of the Evidence for the Diagnosis and Management of Cough" (see the "Availability of Companion Documents" field). The abstracts of all articles were reviewed by two physicians (one with methodological expertise and one with content area expertise), and those meeting the inclusion criteria were selected for review in full text.

Section-Specific Review

MEDLINE was searched (through May 2004) for studies published in the English language since 1980 on human subjects using the medical subject heading terms "cough," "treatment of cough," and "empiric treatment of cough." Case series were selected and prospective descriptive clinical trials. Any references from these studies that were pertinent to the topic were also obtained.

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 (RCTs) or meta-analyses

Fair = evidence based on other controlled trials or RCTs 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

Note from the National Guideline Clearinghouse (NGC): The evidence review procedures included section-specific targeted searches as well as a formal systematic review on selected topics. Formal systematic reviews on selected topics covered in the guideline were performed by the Center for Clinical Health Policy Research at Duke University Medical Center. For more information see the section titled "Methodology and Grading of the Evidence for the Diagnosis and Management of Cough" (see "Availability of Companion Documents" field).

Formal Systematic Reviews

Synthesis

Details from "included" articles (see the "Description of Methods Used to Collect/Select the Evidence" field) were extracted and recorded into evidence tables. No quantitative synthesis, such as meta-analysis, was performed, but aggregated data were described and analyzed qualitatively.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Expert Consensus (Consensus Development Conference)
Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations were formulated by an international panel of 26 experts representing seven clinical specialties. Many were members of the American College of Chest Physicians (ACCP), but representatives from other medical associations, including the American College of Physicians, Canadian Thoracic Society, and American Thoracic Society, also participated on the panel. These experts convened on several occasions, including a panel conference in Boston, MA, in November 2004, in which they deliberated the final content and recommendations, the rating of the quality of the evidence, the estimation of benefits to the patient population, and the grading of the strength of the recommendations. Authors were selected, or in some cases writing committees were formed, for each topic to review evidence, write an article, and draft guidelines. These assignments were made by the steering committee based on the authors' known expertise in that specific area of the diagnosis and treatment of cough, and their research and writing skills.

The recommendations were graded, by consensus of the panel, using the ACCP Health and Science Policy Grading System, which is based on the following two components: quality of the evidence; and the net benefit of the diagnostic or therapeutic procedure. The quality of evidence is rated according to the study design and strength of the other methodologies used in the included studies. The net benefit of the recommendation is based on the estimated benefit to the specific patient population described in each recommendation and not for an individual patient. The authors of each recommendation proposed their best estimate of the net benefit, and the entire panel considered these choices for each recommendation. At the conference, the panel revised the assessments of net benefit for many recommendations to be consistent across all recommendations.

When there was insufficient evidence, the panel used informal group consensus techniques to refine or develop recommendations based on the expert opinion of the panel. Eighty percent of the panel was in attendance at the final conference to collaborate on the final wording and grading of the recommendations. Even those recommendations that were based on expert opinion were considered to be worthy of inclusion, as they were the recommendations of an international and multidisciplinary team with considerable expertise in the diagnosis and treatment of patients with cough.

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 = There is evidence of benefit that clearly exceeds the minimum clinically significant benefit and evidence of little harm

Intermediate = Clear evidence of benefit but with some evidence of harms, with a net benefit between that defined for "substantial" and "small/weak"

Small/weak = There is evidence of a benefit that may not clearly exceed the minimum clinically significant benefit, or there is evidence of harms that substantially reduce (but do not eliminate) the benefit such that it may not clearly exceed the minimum clinically significant benefit

None = Evidence shows that either there is no benefit or the benefits equal the harms

Conflicting = Evidence is inconsistent with regard to benefits and/or harms such that the net benefit is uncertain

Negative = Expected harms exceed the expected benefits to the population

Table: Relationship of Strength of the Recommendations Scale to Quality of Evidence and Net Benefits

Quality of Evidence	Net Benefit					
	Substantial	Intermediate	Small/Weak	None	Conflicting	Negative
Good	A	A	B	D	I	D
Fair	A	B	C	D	I	D
Low	B	B	C	I	I	D
Expert Opinion	E/A	E/B	E/C	I	I	E/D

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 executive committee of the panel extensively reviewed each section of the guideline manuscript during the writing process. The November 2004 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 section of the guidelines was reviewed and approved by the Clinical Pulmonary Medicine, Respiratory Care, Pediatric Chest Medicine, Environmental and Occupational and Airways Disorders NetWorks of the American College of Chest Physicians (ACCP), as well as the ACCP Health and Science Policy Committee, and subsequently by the ACCP Board of Regents.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

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

1. In patients with cough, the starting point is the medical history and physical examination. Although the timing and characteristics of the cough are of little diagnostic value, the medical history is important to determine whether the patient is receiving an angiotensin-converting enzyme (ACE) inhibitor, is a smoker, or has evidence of a serious life-threatening or systemic disease. **Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A**
2. In patients with an acute cough, first determine whether the acute cough is a reflection of a serious illness such as pneumonia or pulmonary embolism, or, as is usually the case, a manifestation of a nonlife-threatening disease such as a respiratory tract infection (e.g., common cold or lower respiratory tract infection), an exacerbation of a preexisting condition (e.g., chronic obstructive pulmonary disease (COPD), upper airway cough syndrome (UACS), asthma, or bronchiectasis), or an environmental or occupational exposure to some noxious or irritating agent (e.g., allergic or irritant-induced rhinitis). **Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A**
3. In patients with a subacute cough, first determine whether it is a postinfectious cough or not. If it is postinfectious, determine whether it is a result of UACS, transient bronchial hyperresponsiveness, asthma, pertussis, or an acute exacerbation of chronic bronchitis. If it is noninfectious, manage the cough the same way as chronic cough (see clinical algorithm entitled "Subacute cough algorithm for the management of patients ≥ 15 years of age with cough lasting 3 to 8 weeks", in the original guideline document). **Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A**
- 4a. In patients with chronic cough, systematically direct empiric treatment at the most common causes of cough (ie, UACS, asthma, nonasthmatic eosinophilic

bronchitis (NAEB), and gastroesophageal reflux disease [GERD]). **Level of evidence, low; benefit, substantial; grade of recommendation, B**

4b. In patients with chronic cough, therapy should be given in sequential and additive steps because more than one cause of cough may be present. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

5. Patients with a chronic cough who smoke should be counseled and assisted with smoking cessation. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

6. In a patient with cough who is receiving an ACE inhibitor, therapy with the drug should be stopped and the drug should be replaced. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

7. In patients with chronic cough, initial empiric treatment should begin with an oral first-generation antihistamine/decongestant (A/D). **Level of evidence, low; benefit, substantial; grade of recommendation, B**

8a. In patients whose chronic cough persists after treatment for UACS, the possibility that asthma is the cause of cough should be worked up next. The medical history is sometimes suggestive, but is not reliable in either ruling in or ruling out asthma. Therefore, ideally, bronchoprovocation challenge (BPC), if spirometry does not indicate reversible airflow obstruction, should be performed in the evaluation for asthma as a cause of cough. In the absence of the availability of BPC, an empiric trial of antiasthma therapy should be administered. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

8b. In patients with chronic cough, in whom the diagnoses of UACS and asthma have been eliminated or treated without the elimination of cough; NAEB should be considered next with a properly performed induced sputum test for eosinophils. If a properly performed induced sputum test to determine whether eosinophilic bronchitis is present cannot be performed, an empiric trial of corticosteroids should be the next step. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

9. In the majority of patients with suspected cough due to asthma, ideally, before starting an oral corticosteroid regimen, a BPC should be performed and, if the result is positive, some combination therapy of inhaled corticosteroids (ICSs), inhaled beta-agonists, or oral leukotriene inhibitors should be administered. A limited trial of oral corticosteroids, however, should be administered in some patients who are suspected of having asthma-induced cough before eliminating the diagnosis from further consideration. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

10. In patients whose cough responds only partially or not at all to interventions for UACS and asthma or NAEB, treatment for GERD should be instituted next. **Level of evidence, low; benefit, substantial; grade of recommendation, B**

11. In patients with cough whose condition remains undiagnosed after all of the above has been done, referral to a cough specialist is indicated. **Level of**

evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

For more complete diagnosis and treatment recommendations (as indicated in the algorithm of the original guideline document), please refer to the following National Guideline Clearinghouse (NGC) summaries of the American College of Chest Physician's guidelines:

- [Chronic upper airway cough syndrome secondary to rhinosinus diseases \(previously referred to as postnatal drip\): ACCP evidence-based clinical practice guidelines](#)
- [Cough and the common cold: ACCP evidence-based clinical practice guidelines](#)
- [Chronic cough due to asthma: ACCP evidence-based clinical practice guideline](#)
- [Chronic cough due to gastroesophageal reflux disease: ACCP evidence-based clinical practice guidelines](#)
- [Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines](#)
- [Chronic cough due to chronic bronchitis: ACCP evidence-based clinical practice guidelines](#)
- [Chronic cough due to bronchiectasis: ACCP evidence-based clinical practice guidelines](#)
- [Habit cough, tic cough, and psychogenic cough in adult and pediatric populations: ACCP evidence-based clinical practice guidelines](#)
- [Cough: occupational and environmental considerations: ACCP evidence-based clinical practice guidelines](#)

Definitions:

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Low	B	B	C	I	I	D
Expert Opinion	E/A	E/B	E/C	I	I	E/D

CLINICAL ALGORITHM(S)

The following clinical algorithms are provided in the section titled "Diagnosis and Management of Cough Executive Summary" (see "Availability of Companion Documents" field)"

- Acute cough algorithm for the management of patients ≥ 15 years of age with cough lasting < 3 weeks
- Subacute cough algorithm for the management of patients ≥ 15 years of age with cough lasting 3 to 8 weeks
- Chronic cough algorithm for the management of patients ≥ 15 years of age with cough lasting > 8 weeks
- Approach to a child < 15 years of age with chronic cough
- Approach to a child ≤ 14 years of age with chronic specific cough

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

Appropriate management and effective treatment of patients with acute, subacute, and chronic cough

POTENTIAL HARMS

Not 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

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

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

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Pratter MR, Brightling CE, Boulet LP, Irwin RS. An empiric integrative approach to the management of cough: ACCP evidence-based clinical practice guidelines. Chest 2006 Jan;129(1 Suppl):222S-31S. [43 references] [PubMed](#)

ADAPTATION

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

DATE RELEASED

2006 Jan

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on the Diagnosis and Management of Cough

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The American College of Chest Physicians (ACCP) has a very stringent approach to the issue of potential or perceived conflicts of interest. This policy is published on the ACCP Web site at www.chestnet.org. All conflicts of interest within the preceding 5 years were required to be disclosed by all panelists, including those who did not have writing responsibilities, at face-to-face meetings, the final conference, and prior to submission for publication.

The most recent of these are documented in the published guideline supplement. Furthermore, the panel was instructed in this matter, verbally and in writing, prior to the deliberations of the final conference.

ENDORSER(S)

American Thoracic Society - Medical Specialty Society
Canadian Thoracic Society - Medical Specialty Society

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:

- Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.

Background and Methodology Information

- Introduction to the diagnosis and management of cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Methodology and grading of the evidence for the diagnosis and management of cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.

Additional Background Information

- Anatomy and neurophysiology of the cough reflex: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Global physiology and pathophysiology of cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Complications of cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Overview of common causes of chronic cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Assessing cough severity and efficacy of therapy in clinical research: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Potential future therapies for the management of cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.
- Future directions in the clinical management of cough: ACCP evidence-based clinical practice guidelines. Northbrook, IL: ACCP, 2006 Jan.

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.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 4, 2006. The information was verified by the guideline developer on June 5, 2006.

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