

Classification of Cough as a Symptom in Adults and Management Algorithms

CHEST Guideline and Expert Panel Report



Richard S. Irwin, MD, Master FCCP; Cynthia L. French, PhD, RN, ANP-BC, FCCP; Anne B. Chang, MBBS, PhD, MPH; Kenneth W. Altman, MD, PhD; on behalf of the CHEST Expert Cough Panel*

BACKGROUND: We performed systematic reviews using the population, intervention, comparison, outcome (PICO) format to answer the following key clinical question: Are the CHEST 2006 classifications of acute, subacute and chronic cough and associated management algorithms in adults that were based on durations of cough useful?

METHODS: We used the CHEST Expert Cough Panel's protocol for the systematic reviews and the American College of Chest Physicians (CHEST) methodological guidelines and Grading of Recommendations Assessment, Development, and Evaluation framework. Data from the systematic reviews in conjunction with patient values and preferences and the clinical context were used to form recommendations or suggestions. Delphi methodology was used to obtain the final grading.

RESULTS: With respect to acute cough (< 3 weeks), only three studies met our criteria for quality assessment, and all had a high risk of bias. As predicted by the 2006 CHEST Cough Guidelines, the most common causes were respiratory infections, most likely of viral cause, followed by exacerbations of underlying diseases such as asthma and COPD and pneumonia. The subjects resided on three continents: North America, Europe, and Asia. With respect to subacute cough (duration, 3-8 weeks), only two studies met our criteria for quality assessment, and both had a high risk of bias. As predicted by the 2006 guidelines, the most common causes were postinfectious cough and exacerbation of underlying diseases such as asthma, COPD, and upper airway cough syndrome (UACS). The subjects resided in countries in Asia. With respect to chronic cough (> 8 weeks), 11 studies met our criteria for quality assessment, and all had a high risk of bias. As predicted by the 2006 guidelines, the most common causes were UACS from rhinosinus conditions, asthma, gastroesophageal reflux disease, nonasthmatic eosinophilic bronchitis, combinations of these four conditions, and, less commonly, a variety of miscellaneous conditions and atopic cough in Asian countries. The subjects resided on four continents: North America, South America, Europe, and Asia.

CONCLUSIONS: Although the quality of evidence was low, the published literature since 2006 suggests that CHEST's 2006 Cough Guidelines and management algorithms for acute, subacute, and chronic cough in adults appeared useful in diagnosing and treating patients with cough around the globe. These same algorithms have been updated to reflect the advances in cough management as of 2017. CHEST 2018; 153(1):196-209

KEY WORDS: cough; evidence-based medicine; guidelines; management algorithms for acute, subacute, and chronic cough in adults

ABBREVIATIONS: AECOPD = acute exacerbation of COPD; CHEST = American College of Chest Physicians; PICO = population, intervention, comparator, outcome; QoL = quality of life; NAM = National Academy of Medicine; UACS = upper airway cough syndrome

AFFILIATIONS: From the UMassMemorial Medical Center (Drs Irwin and French), Worcester, MA; the Menzies School of Health Research and Respiratory Department (Dr Chang), Lady Cilento Children's Hospital, Qld Uni of Technology Queensland, Australia;

Summary of Suggestions

1. For adult patients complaining of cough, we suggest that acute cough be defined as being < 3 weeks in duration (Grade 2C).

2. For adult patients complaining of cough, we suggest that subacute cough be defined as being between 3 and 8 weeks in duration (Grade 2C).

3. For adult patients complaining of cough, we suggest that chronic cough be defined as being > 8 weeks in duration (Grade 2C).

4. For adult patients seeking medical care complaining of cough, we suggest that estimating the duration of cough is the first step in narrowing the list of potential diagnoses (Grade 2C).

5. For adult patients around the globe complaining of cough, we suggest that the cough be managed using evidence-based guidelines that are based upon duration of cough (Grade 2C).

Remark: The updated CHEST cough guidelines and algorithms have been based upon systematic reviews that meet National Academy of Medicine (NAM) standards and cough guidelines that meet the NAM criteria of trustworthy clinical practice guidelines.

Because a carefully taken history with detailed questioning of the character, timing, and complications of

chronic cough in adults had not been shown to be useful in diagnosing the cause of the cough,¹ the world's first cough guideline developed by the first American College of Chest Physicians (CHEST) Expert Cough Panel suggested in 1998 that cough be classified according to its duration.² Although all coughs are acute at the outset, the panel believed that it was the duration of the cough at the time of patient presentation to health-care providers that helped narrow the list of possible diagnoses in adults. Although the first expert cough panel classified cough duration into acute (ie, lasting < 3 weeks) and chronic (ie, lasting 3-8 weeks) categories, the second ACCP Expert Cough Panel suggested in 2006³ that cough continue to be classified according to its duration but that there should be three not two categories. Based on literature that had accumulated between 1998 and 2006, the panel believed that cough should be reclassified into acute (ie, < 3 weeks), subacute (ie, 3-8 weeks), and chronic (ie, > 8 weeks) categories and suggested management algorithms for these categories that suggested the likeliest and most common diagnostic possibilities in each category.⁴

We performed a systematic review to answer the following key clinical question: Are the CHEST 2006 classifications of acute, subacute, and chronic cough and associated management algorithms in adults that were based on durations of cough³ useful?

Methods

We used the published methodology of the CHEST Guideline Oversight Committee⁵ to select the Expert Cough Panel Chair and the International Panel of Experts to perform a systematic review, synthesize evidence, and develop recommendations and practice management suggestions. After generating the key clinical question for this systematic review, Population, Intervention, Comparison,

Outcome (PICO) elements were derived to inform the literature review. The question was formulated after polling the existing writing group for key clinical questions related to how best to classify cough. The writing committee unanimously chose to focus on the durations of acute, subacute, and chronic cough and how they had been defined in the 2006 Cough Guidelines.³ The resultant PICO elements that formed the basis of the subsequent systematic review are presented in [Table 1](#).

Literature Search

The methods used for this systematic review conformed to those outlined in the article "Methodologies for the Development of CHEST Guidelines and Expert Panel Reports."⁵ Librarians from the University of Massachusetts Medical School undertook searches to answer the question for acute, subacute, and chronic cough. For chronic cough, articles were identified from searches of electronic databases (PubMed and SCOPUS) commencing from their initiation through February 23, 2016. PubMed was relied on to pick up any Cochrane systematic reviews for chronic cough. For acute and subacute cough, articles were identified from searches of PubMed, SCOPUS, and the Cochrane Database of Systematic Reviews from their initiation through February 23, 2016. The reference lists of retrieved articles were examined for additional citations. The search terms used are presented in [e-Tables 1 and 2](#). The titles and abstracts of the search results were independently evaluated by two reviewers (R. S. I. and C. L. F.) to identify potentially relevant articles. The full texts of all potentially relevant articles were retrieved, and two reviewers (R. S. I. and C. L. F.) independently

and the Institute for Voice and Swallowing (Dr Altman), Baylor College of Medicine, Houston, TX.

FUNDING/SUPPORT: The authors have reported to *CHEST* that no funding was received for this study.

DISCLAIMER: American College of Chest Physician guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at <http://www.chestnet.org/Guidelines-and-Resources/Guidelines-and-Consensus-Statements/CHEST-Guidelines>.

CORRESPONDENCE TO: Richard S. Irwin, MD, Master FCCP, UMassMemorial Medical Center, 55 Lake Ave N, Worcester MA 01655; e-mail: richard.irwin@umassmemorial.org

Copyright © 2017 American College of Chest Physicians. Published by Elsevier Inc. All rights reserved.

DOI: <https://doi.org/10.1016/j.chest.2017.10.016>

TABLE 1] Key Clinical Question and PICO Elements That Guided the Systematic Reviews
Key question: Are the CHEST 2006 classifications of acute, subacute, and chronic cough and associated management algorithms in adults that were based on durations of cough useful in diagnosing and treating the cough?

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Patient population (P)	<ol style="list-style-type: none"> Adults complaining of acute cough (< 3 wk duration) Adults complaining of subacute cough (3-8 wk duration) Adults complaining of chronic cough (> 8 wk duration) English-language publications Peer-reviewed articles Relevant systematic reviews and meta-analyses 	Children Non-English language publications Not a before and after clinical study with at least 25 subjects enrolled
Intervention (I)	Cough management protocols or pathways	None
Comparator (C)	Nonuse of cough management protocols or pathways	None
Outcome (O)	Final diagnosis based on favorable response of cough to treatment	Diagnosis not based on response of cough to treatment

reviewed all retrieved studies. Although a third reviewer was available to adjudicate any disagreements, there were no disagreements. Because a review of articles published before 2006 used a variety of definitions of acute and chronic cough, and subacute cough had not yet been defined, and because the CHEST management algorithms for cough were not published until 2006, we decided to include only articles published in 2006 and afterward in our analysis.

Quality Assessment

Included articles underwent methodological assessment. Quality assessment was carried out if the articles met the following criteria: (1) they were published during 2006 or later; (2) they defined acute, subacute, or chronic cough (or a combination of the three) based on the duration, as described in the methods sections of the articles, and reported the actual durations in the results sections of the articles; and (3) they reported the spectrum and frequency of causes of cough in the study subjects based on response to treatment as described in the results sections of the articles. For randomized controlled trials, quality assessment was carried out with the Cochrane Risk of Bias Tool.⁶ For observational studies, quality assessment was performed with the Cochrane risk of bias tool for cohort studies.⁷ For systematic reviews, quality assessment was done with the Documentation and Appraisal Review Tool.⁸

Results

The selections of studies that addresses the key clinical question are shown in [Figures 1 and 2](#).

Key Clinical Question: Are the CHEST 2006 classifications of acute, subacute, and chronic cough and associated management algorithms that were based on durations of cough useful in diagnosing and treating the cough?

With respect to acute cough, only three studies met our criteria for quality assessment, and all had a high

Practice Recommendations/Suggestions

The findings of this systematic review were used to support the evidence-graded recommendations or suggestions. A structured consensus-based modified Delphi approach was used to provide expert advice on guidance statements. In this regard, for a recommendation or suggestion to be approved by the Expert Cough Panel, 75% of the eligible panel members had to vote, and 80% of those voting had to strongly agree or agree with the statement.⁵ In the context of practice recommendations, a strong recommendation applies to almost all patients, whereas a weak recommendation is conditional and applies to only some patients. The strength of recommendation here is based on consideration of three factors: balance of benefits to harms, patient values and preferences, and resource considerations. Harms incorporate risks and burdens to the patients that can include convenience or lack of convenience, difficulty of administration, and invasiveness. These, in turn, impact patient preferences. A patient representative who had been a member of the Cough Panel provided patient-centered input for this guideline and approved of the suggestions contained herein. The resource considerations go beyond economics and should also factor in time and other indirect costs. The authors of these recommendations or suggestions have considered these parameters in determining the strength of the recommendations or suggestions and associated grades.⁵

risk of bias ([Table 2](#)).⁹⁻¹¹ Although all studies were prospective and none mentioned any harms, none had a control group or used a validated outcome tool for cough assessment. Two of the three studies defined acute cough in the methods section of the articles as < 3 weeks; the third study defined it as no more than 28 days. In the results sections of these studies, all the subjects (N = 308) sought medical attention for complaints of cough < 3 weeks' duration. The most common causes of acute cough were respiratory infections, most likely of viral cause, followed by

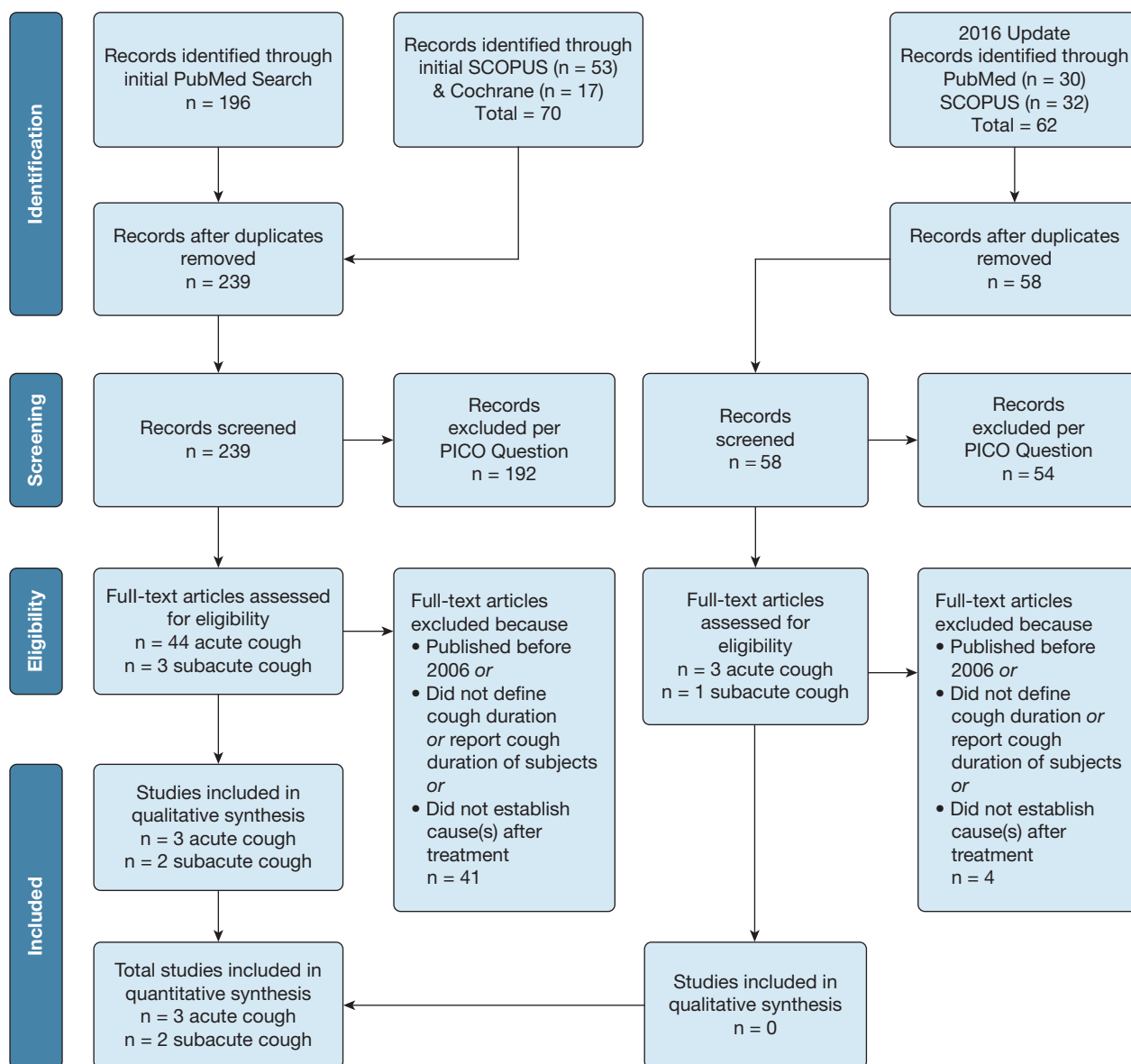


Figure 1 – Selection of studies that addressed the key clinical question for acute and subacute cough: Are the CHEST 2006 classifications of acute and subacute cough and associated management algorithms in adults that were based on durations of cough useful? From Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Plos Med. 6(7):e1000097.

exacerbations of underlying diseases such as asthma and COPD, and pneumonia. The subjects in these three articles resided on three continents: North America, Europe, and Asia. These results are consistent with what CHEST’s 2006 Cough Guidelines predicted and revealed the appropriateness, on a global basis, of the 2006 management algorithm for acute cough. For the acute cough management algorithm to accurately reflect the guidelines on cough

due to tuberculosis that is in preparation and cough in the immunocompromised host,¹² the 2006 adult acute cough diagnostic algorithm has been updated (Fig 3) to include the suggestions that (1) tuberculosis, as a specific infection, be considered in all patients complaining of cough in endemic areas, regardless of cough duration, and in high-risk populations, regardless of cough duration, even if chest radiographs are normal; (2) a history should be

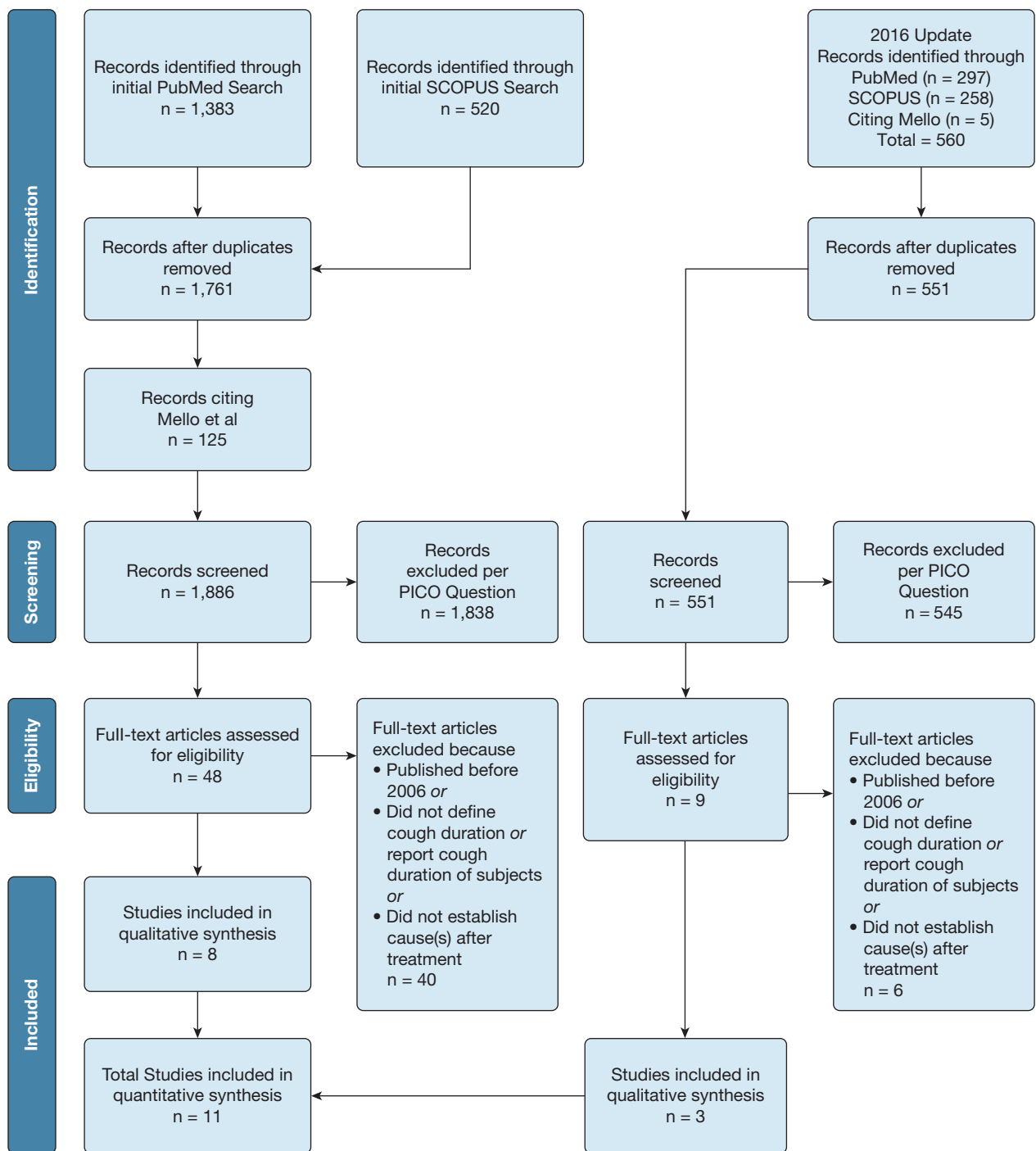


Figure 2 – Selection of studies that addressed the key clinical question for chronic cough: Are the CHEST 2006 classifications of chronic cough and associated management algorithms in adults that were based on durations of cough useful? From Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Plos Med.* 6(7):e1000097.

sought for hemoptysis or other potential life-threatening symptoms and, if present, immediately addressed and evaluated (ie, red flags); (3) a validated cough severity tool be routinely used to assess the

outcome of therapy (Fig 4)¹³; and (4) patients be routinely followed in a clinic or by telephone within 4-6 weeks after the initial evaluation.¹⁴ If cough persists, a follow-up appointment should be arranged.

TABLE 2] Summary of Extracted Data for Acute Cough in Adults

Study/Year	Design	Sample Size	Duration	Common Causes	Study Quality
Godycki-Cwirko et al ⁹ /2011 Europe	Prospective; ≤ 28 d; no validated cough tool	221	4 d median	Respiratory infection (90.5%) URT (42.5%) LRT (48%) AECOPD (3.6%) Asthma (1.4%) Unspecified (4.5%)	High risk of bias; no harms reported
Worrall ¹⁰ /2008 Canada	Prospective; ≤ 14 d; no validated cough tool	62	< 6 d mean	URI (71%) Asthma (19%) Influenza (6%) Pneumonia (3%)	High risk of bias; no harms reported
Yamasaki et al ¹¹ /2010 Japan	Prospective; < 21 d; no validated cough tool	25	< 3 wk all subjects	RTI (72%) Asthma (28%)	High risk of bias; no harms reported

AECOPD = acute exacerbation of COPD; LRT = lower respiratory tract; RI = respiratory infection; URT = upper respiratory tract.

Suggestion 1. For adult patients complaining of cough, we suggest that acute cough be defined as being < 3 weeks in duration (Grade 2C).

With respect to subacute cough, only two studies met our criteria for quality assessment, and all had a high risk of bias (Table 3).^{11,15} Although both were

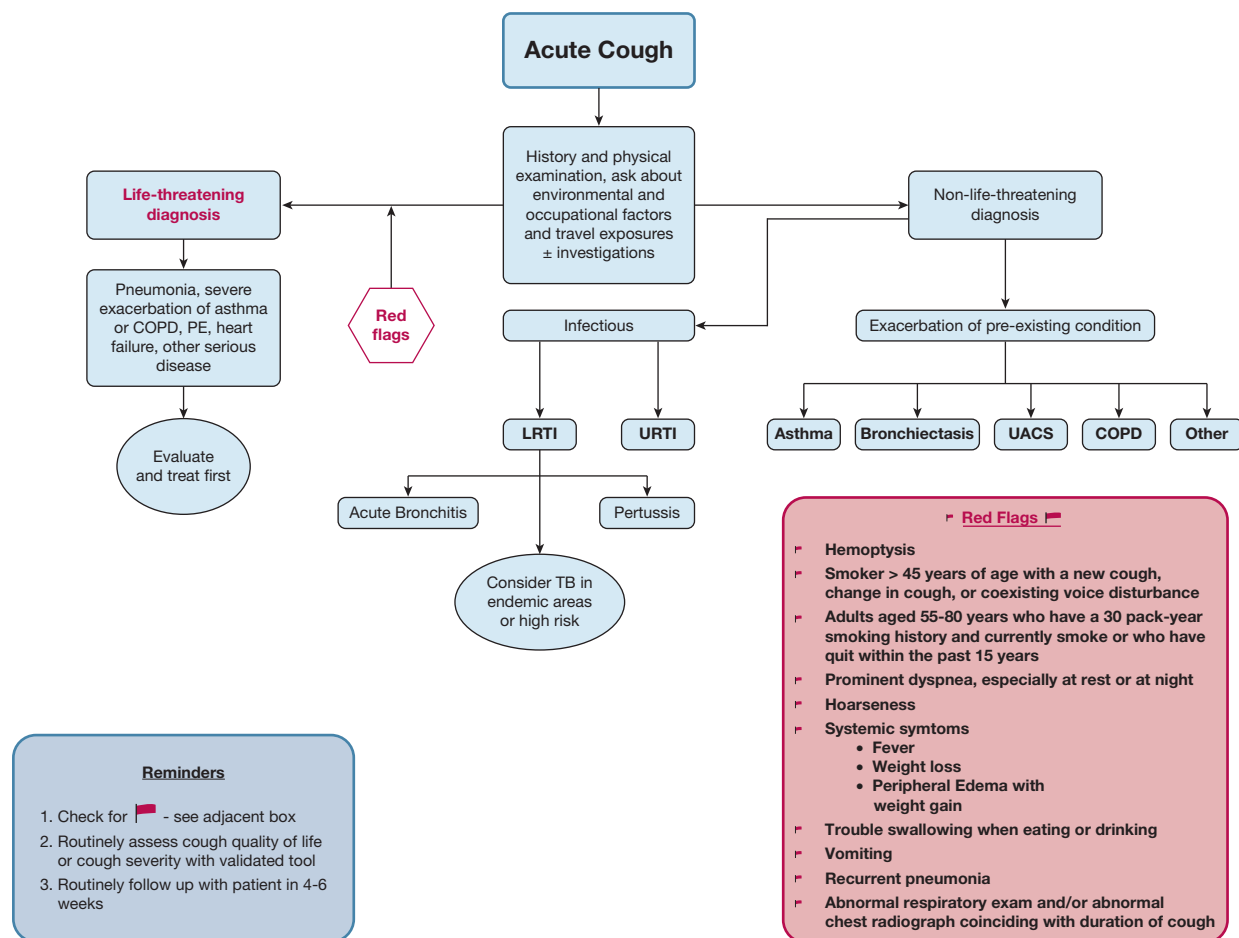
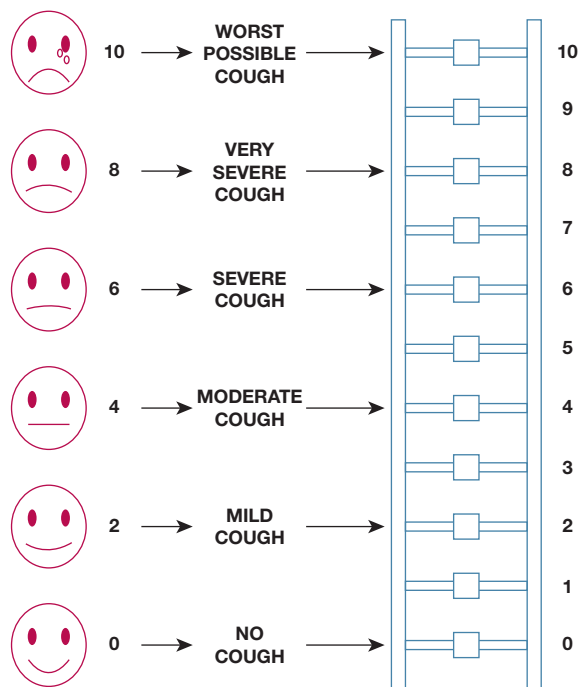


Figure 3 – Acute cough algorithm for the management of patients ≥ 15 years of age with cough lasting < 3 weeks. Always screen for the presence of red flags as a clue to a potentially life-threatening condition. Always consider the presence of TB in endemic areas or high-risk populations even if chest radiographs are normal. Remember to routinely assess cough severity or quality of life before and after treatment and routinely follow patients 4-6 weeks after initial visit. LRTI = lower respiratory tract infection; PE = pulmonary embolism; UACS = upper airway cough syndrome; URI = upper respiratory tract infection.

A
Please check the rung on the ladder that best describes the **severity of your cough taking timing, intensity, distress, and quality into account** over the past week.



B
Please check the box on the rung of the ladder that best describes your overall quality of life (satisfaction or happiness with life) related to your cough over the past week.

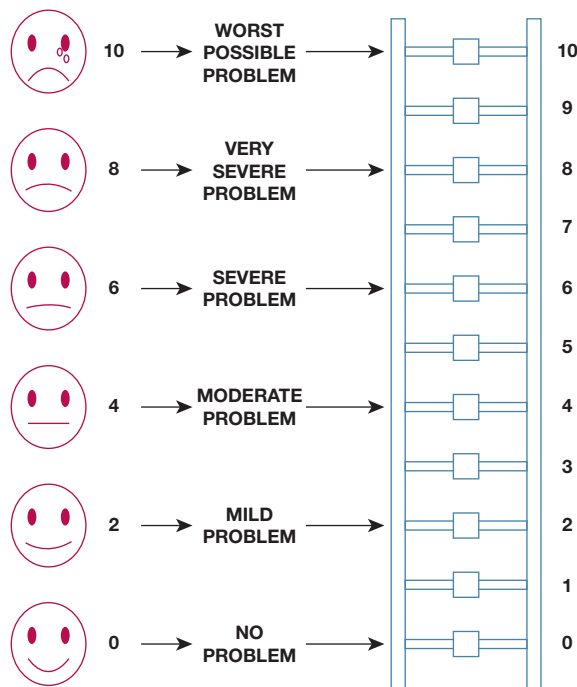


Figure 4 – Representative Punum ladders to assess (A) cough severity or (B) overall quality of life.

prospective studies and none mentioned any harms, none had a control group or used a validated outcome tool for cough assessment. Both studies defined

subacute cough in the methods section of the articles as being between 3 and 8 weeks' duration. In the results section of the articles, all the subjects

TABLE 3] Summary of Extracted Data for Subacute Cough in Adults

Study/Year	Design	Sample Size	Duration	Common Causes	Study Quality
Kwon et al ¹⁵ /2006 Korea	Prospective; 3-8 wk; (did not check for pertussis); excluded abnormal chest film, smokers, or ACEI use; no validated cough tool	184	3-8 wk all subjects	PI (48.4%) PNDS (33.2%) Asthma (15.8%) NAEB (5.4%)	High risk of bias; no harms reported
Yamasaki ¹¹ /2010 Japan	Prospective; 3 to 8 wk; no validated cough tool; no exclusions noted	41	3-8 wk all subjects	Asthma (58.5%) PI (12.2%) Unknown (12.2%) RTI (7.3%) AECOPD (4.8%) Sinobronchial syndrome (2.4%) Bronchiolitis due to rheumatoid arthritis (2.4%)	High risk of bias; no harms reported

ACEI = angiotensin-converting enzyme inhibitor; NAEB = nonasthmatic eosinophilic bronchitis; PI = postinfectious; PNDS = postnasal drip syndrome; RTI = respiratory tract infection. See Table 2 legend for expansion of other abbreviations.

(N = 225) sought medical attention complaining of cough between 3 and 8 weeks. The most common causes of subacute cough were postinfectious cough and exacerbations of underlying diseases such as asthma, COPD, and upper airway cough syndrome (UACS). The subjects in these two studies resided in countries in Asia. These results are consistent with what CHEST's 2006 Cough Guidelines predicted and revealed the continued appropriateness of the 2006 management algorithm for subacute cough in adults. Nevertheless, they have been updated (Fig 5) to include the suggestions that (1) history should be sought for hemoptysis or other potential life-threatening symptoms and, if present, should be immediately addressed and evaluated (ie, red flags); (2) a validated cough severity or quality of life tool be routinely used to assess the outcome of therapy; (3) environmental and occupational exposures be considered and addressed if present,^{16,17} as they are in the acute cough algorithm; and (3) patients be routinely followed up in the clinic or by telephone within 4 to 6 weeks after the initial evaluation. If cough persists, a follow-up appointment should be arranged.

Suggestion 2. For adult patients complaining of cough, we suggest that subacute cough be defined as being between 3 and 8 weeks in duration (Grade 2C).

With respect to chronic cough, although all studies were prospective and none mentioned any harms, 11 studies met our criteria for quality assessment and all had a high risk of bias (Table 4).¹⁸⁻²⁸ Although 10 were prospective studies, none mentioned any harms. Although six used a validated cough outcome tool, none had a control group. Ten of the 11 studies defined chronic cough in the methods sections of the articles as ≥ 8 weeks, and the 11th one used a definition of ≥ 4 weeks. However, in the results sections of these articles, all the subjects (N = 2,220) sought medical attention complaining of cough ≥ 8 weeks' duration. The most common causes of chronic cough were UACS from a variety of rhinosinus conditions, asthma, gastroesophageal reflux disease, nonasthmatic eosinophilic bronchitis, combinations of these four conditions, and less commonly, a variety of miscellaneous conditions and atopic cough in Asian countries. The subjects in these 11 articles resided on four continents: North America, South America, Europe, and Asia. These results are consistent with what CHEST's 2006 Cough Guidelines predicted and reveal

the continued appropriateness of the 2006 management algorithm for chronic cough in adults. Nevertheless, they have been updated (Fig 6) to include the suggestions that (1) history should be sought for hemoptysis or other potential life-threatening symptom and, if present, should be immediately addressed and evaluated (ie, red flags); (2) a validated cough severity tool be routinely used to assess outcome of therapy; (3) environmental and occupational exposures be considered and addressed if present, as they are in the acute cough algorithm; (4) recognition that acid suppression alone is no longer recommended for treating cough due to gastroesophageal reflux disease²⁹; (5) sitagliptin,³⁰ as well as angiotensin-converting enzyme inhibitors, be discontinued to see if the drug is responsible for the cough; (6) patients be routinely followed in the clinic within 4 to 6 weeks after the initial evaluation; and (7) referral to a well-recognized cough clinic should be considered for the refractory unexplained chronic cough.

Suggestion 3. For adult patients complaining of cough, we suggest that chronic cough be defined as being > 8 weeks in duration (Grade 2C).

The results of our systematic review suggest that the CHEST 2006 adult classifications of acute, subacute, and chronic cough and associated management algorithms that were based on durations of cough have been useful to clinical investigators around the globe. Not only were the classifications followed but also the most common causes of each category were predicted by the 2006 Cough Guideline. Nevertheless, for the 2006 management algorithms to reflect the updated cough guidelines and contemporary literature, they have been updated (Figs 3, 5, 6).

Suggestion 4. For adult patients seeking medical care complaining of cough, we suggest that estimating the duration of cough is the first step in narrowing the list of potential diagnoses (Grade 2C).

Suggestion 5. For adult patients around the globe complaining of cough, we suggest that the cough be managed using evidence-based guidelines that are based upon duration of cough (Grade 2C).

Remark: The updated cough guidelines and algorithms have been based upon systematic reviews that meet the National Academy of Medicine (NAM) standards³¹ and cough guidelines that meet the NAM criteria of trustworthy clinical practice guidelines.³²⁻³⁴

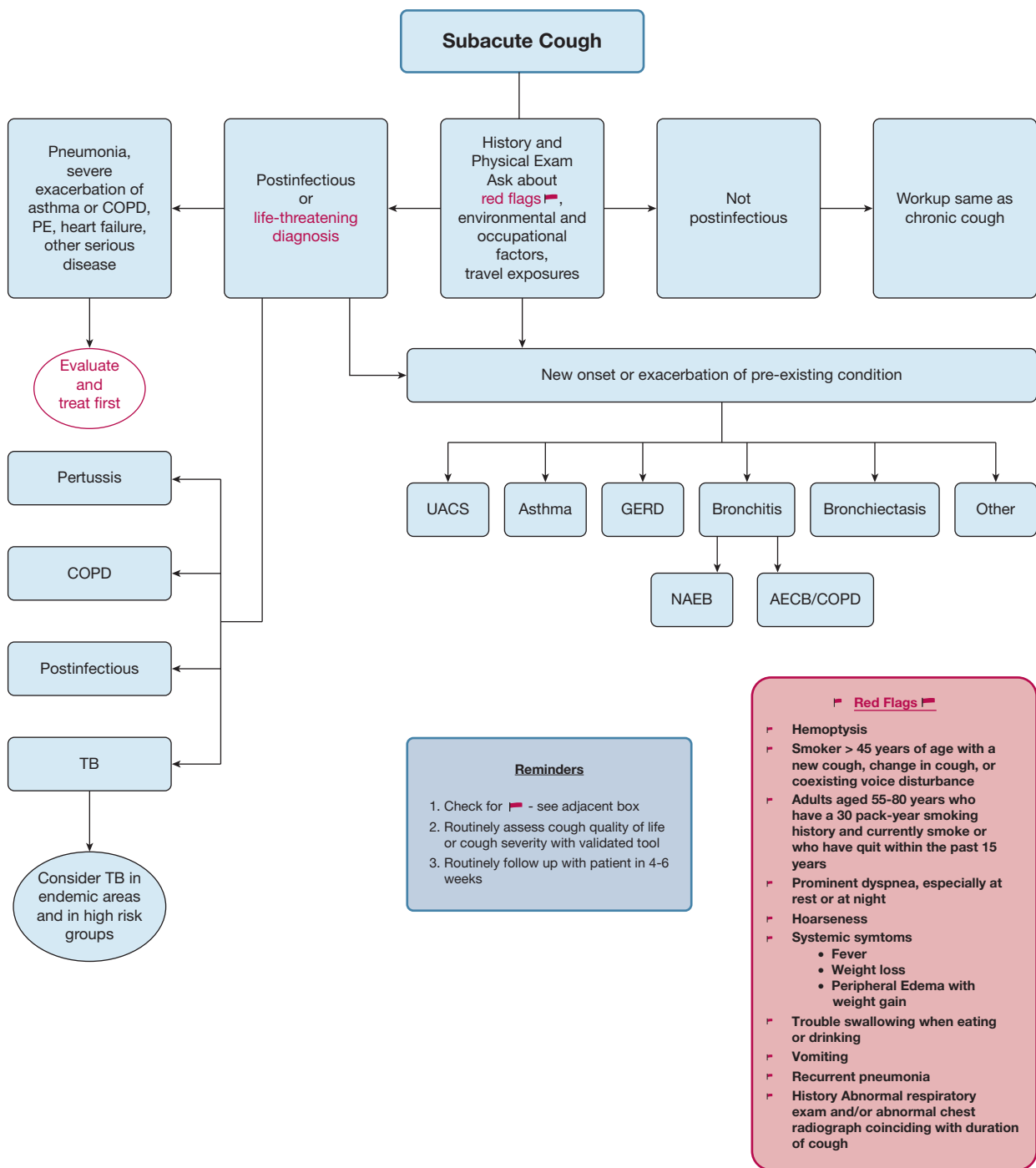


Figure 5 – Subacute cough algorithm for the management of patients ≥ 15 years of age with cough lasting 3 to 8 weeks. Always screen for the presence of red flags as a clue to a potentially life-threatening condition as well as historical clues for environmental and occupational factors that might be contributing to the cough. Always consider the presence of TB in endemic areas or high-risk populations even if chest radiographs are normal. Remember to routinely assess cough severity or quality of life before and after treatment and routinely follow patients 4 to 6 weeks after initial visit. AECB = acute exacerbation of chronic bronchitis; GERD = gastroesophageal reflux disease; NAEB = nonasthmatic eosinophilic bronchitis. See Figure 1 and 3 legends for expansion of other abbreviations.

Areas for Future Research

To advance the field, there are a number of potential research endeavors that should be undertaken. They are enumerated here.

1. Because there has been a paucity of studies describing the spectrum and frequency of causes of acute and subacute cough, prospective before and after intervention studies need to be performed

TABLE 4] Summary of Extracted Data for Chronic Cough in Adults

Study/Year	Design	Sample Size	Duration	Common Causes	Study Quality
Fletcher et al ¹⁸ /2010 USA	Prospective; no exclusions; ≥ 8 wk; validated cough tool used	103	Mean, 71.9 \pm 86 m; range, 2-456 m	GERD (85.4%) UACS (81.8%) Asthma (14.6%) Bronchiolitis (7.8%) Unexplained (3.9%) Pharyngeal dysfunction (1.9%) Multiple causes (67%)	High risk of bias; no harms reported
Irwin et al ¹⁹ /2006 USA	Prospective; no exclusions; > 8 wk; no validated tool	24	Mean, 8.6 \pm 7.4 y	Unexplained (46%) Extrapulmonary (33%) PNDS PNDS + GERD GERD GERD + ACEI Intrapulmonary (21%) Asthma Asthma + GERD GERD + PNDS Bronchiolitis Industrial bronchitis	High risk of bias; no harms reported
Lai et al ²⁰ /2013 China	Prospective; Current smokers excluded; ≥ 8 wk; No validated tool	704	Median, 12 m Range, 2-696 m	CVA (32.6%) UACS (18.6%) Multiple causes (8%) NAEB (17.2%) AC (13.2%) GERD (4.6%) Unexplained (8.4%) Others (5.4%)	High risk of bias; no harms reported
Yu et al ²¹ /2011 China	Prospective; current smokers excluded; ≥ 8 wk; no validated tool	109	Median, 6 m Range, 2-480 m	CVA (41.3%) UACS (24.8%) NAEB (6.4%) GERD (6.4%) Combined causes: UACS + CVA UACS + GERD GERD + CVA GERD + NAEB UACS + CVA + GERD Other (5.5%) Unexplained (2.7%)	High risk of bias; no harms reported
Lee et al ²² /2007 South Korea	Prospective; no exclusions; ≥ 4 wk; validated cough tool used	378	Median, 2 m Range, 1-36 m	PNDS (67.5%) Asthma (38.1%) GERD (7.7%) Unexplained (3.1%) Mycobacterial infection (1.8%) Bronchiectasis (1.5%)	High risk of bias; no harms reported
Levine ²³ /2008 USA	Prospective; no exclusions; ≥ 8 wk; validated cough tool used	390	Median, 6.5 y Range, 2 m-60 y	Rhinitis 67.4% GERD 50.1% Chronic sinusitis 23.6% Asthma 15% ACEI 11.5% Unexplained 27%	High risk of bias; no harms reported
Ogawa et al ²⁴ /2009 Japan	Retrospective; no exclusions; ≥ 8 wk; no validated tool	70	Median, 4.5 m Range, 2-181 m	Unexplained (27%) Asthma (37%) Atopic cough (24%) Sinobronchial syndrome (12.8%) GERD (1.4%) Psychogenic (1.4%)	High risk of bias; no harms reported

(Continued)

TABLE 4] (Continued)

Study/Year	Design	Sample Size	Duration	Common Causes	Study Quality
Ribeiro et al ²⁵ / 2006 Brazil	Prospective; no exclusions; ≥ 8 wk; validated cough tool used	147	Median, 24 wk Range, 8-54 wk	Multiple causes (9%) Asthma (29%) COPD (11%) NAEB (10%) UACS (9%) GERD (9%) Unexplained (8%) Drug induced (5%) ILD (2.5%) Lung cancer (2%) Bronchiectasis (1%) TB (1%)	High risk of bias; no harms reported
Dabrowska et al ²⁷ /2014 Poland	Prospective; smokers excluded; > 8 wk; validated cough tool used	68	Median, 24 m Range, 10 wk-30 y	Multiple causes (72%) GERD (37%) UACS (28%) Asthma (14%) NAEB (7%) Unexplained (3%) Other (11%)	High risk of bias; no harms rereported
Deng et al ²⁸ / 2016 China	Prospective; excluded CHF, ACEI, smokers, diabetes, cancer, pregnancy, prior RI; ≥ 8 wk; validated cough tool used	96	Median, 4 m Range, 2-100 m	CRC (46.7%) NAEB CVA Atopic cough PNDS (27.5%) GERD (10.8%) Unexplained (15%)	High risk of bias; no harms reported
Dabrowska et al ²⁶ /2015 Poland	Prospective; excluded smokers, abnormal PFTs or chest film; > 8 wk; no validated cough tool	131	Median, 24 m Range, 2.5-360 m	Multiple causes (56%) GERD (62%) UACS (46%) Asthma (25%) NAEB (15%) Unexplained (3%) Other (21%)	High risk of bias; no harms reported

CRC = corticosteroid-responsive cough; CVA = cough variant asthma; GERD = gastroesophageal reflux disease; ILD = interstitial lung disease; PFTs = pulmonary function tests; UACS = upper airway cough syndrome. See Table 2 and 3 legends for expansion of other abbreviations.

- using validated cough outcome tools to document improvement in the acute and subacute cough with treatment.
- Because of the relative paucity of studies that used validated cough outcome tools in describing the spectrum and frequency of causes of chronic cough, prospective before and after intervention studies need to be performed using such tools to document improvement in chronic cough with treatment.
- To determine the reliability and validity and efficacy of the 2017 CHEST cough management algorithms for acute, subacute, and chronic cough, prospective randomized clinical trials, with usual care control groups, will need to be undertaken with validated cough outcome tools.
- For ease of use and to potentially increase adherence to the cough management guidelines by clinicians and patients, an electronic version of the acute, subacute, and chronic guidelines will need to be developed. An electronic version will also have the potential to facilitate not only the use of management algorithms but also the dissemination and implementation of the practice guidelines. Based on a systematic review that assessed intervention fidelity on the part of the investigators who carried out and published results of outcome studies on the effects of treatment in subjects with chronic cough, it is clear that efforts need to be devoted to improving fidelity to guidelines,¹⁴ and an electronic version may offer an opportunity for improvement.³⁵

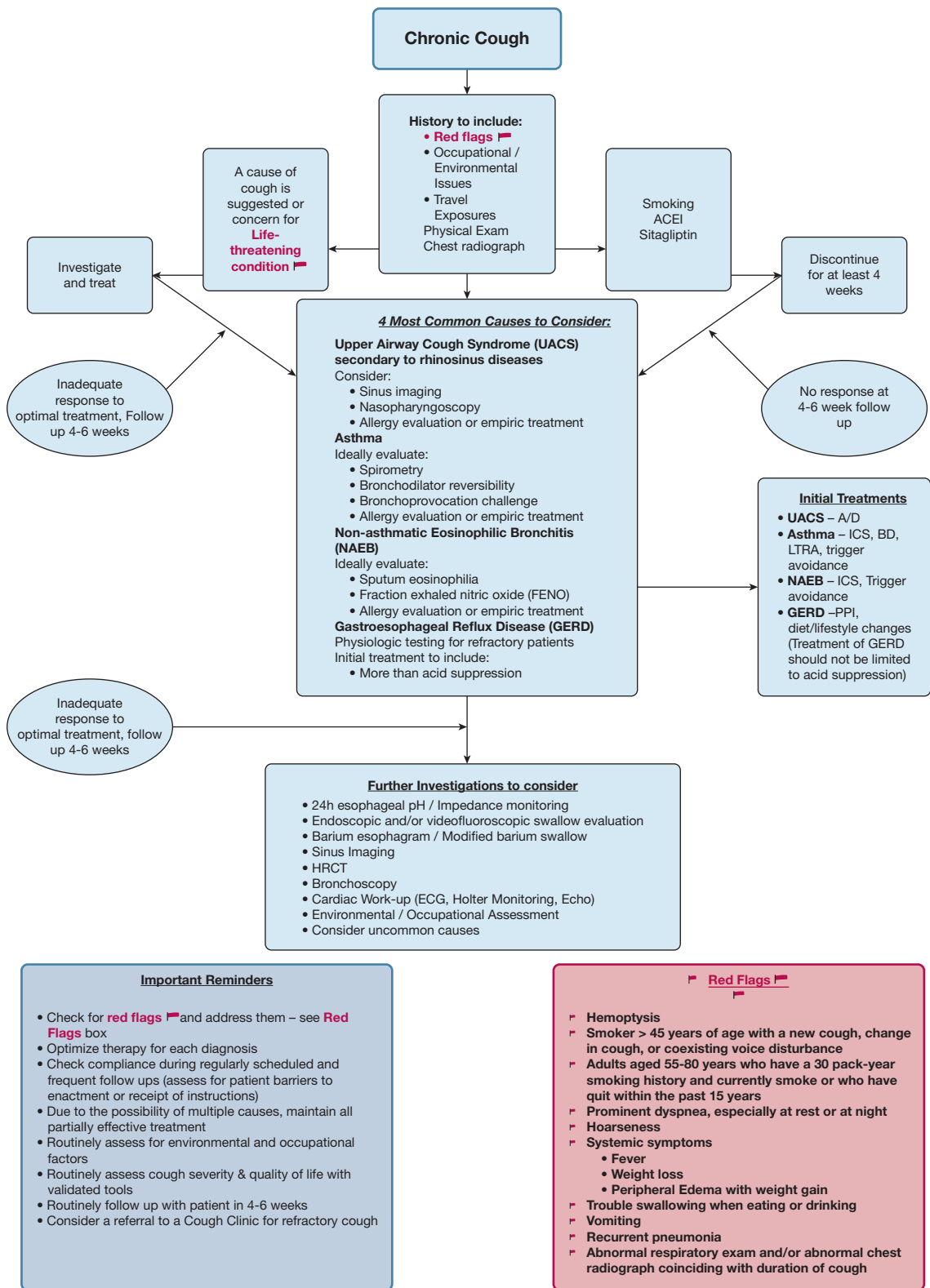


Figure 6 – Chronic cough algorithm for the management of patients ≥ 15 years of age with cough lasting > 8 weeks. Always screen for red flags as a clue to a potentially life-threatening condition, as well as historical clues for environmental and occupational factors that might be contributing to the cough. Always evaluate whether sitagliptin as well as angiotensin-converting enzyme inhibitors are contributing to the patient's cough. Always consider the presence of TB in endemic areas or high-risk populations even if chest radiographs are normal. Be aware that treatment of cough due to GERD should not be limited to acid suppression. Remember to routinely assess cough severity or quality of life before and after treatment and routinely follow patients 4 to 6 weeks after the initial visit. Consider referral to a recognized cough clinic for patients with refractory unexplained chronic cough. ACEI = angiotensin-converting enzyme inhibitor; A/D = antihistamine/decongestant; BD = bronchodilator; HRCT = high-resolution CT; ICS = inhaled corticosteroid; LTRA = leukotriene antagonist; PPI = proton pump inhibitor. See Figure 3 and 4 legends for expansion of other abbreviations.

Conclusions

Since publication of the 2006 CHEST Cough Guidelines, the field of how cough is classified and managed has advanced. Although the classification and management of acute, subacute, and chronic cough based on its duration were proposed in the 2006 guidelines, it was not known until this systematic review that the definitions were being used around the globe and that the management algorithms would accurately predict the most common causes of acute, subacute, and chronic cough. Although the suggestions generally reflect those made in the 2006 guidelines (albeit worded in a different way), the strength of the evidence for them has increased because they are based on a systematic review. This article has also identified gaps in our knowledge and areas for future research.

Acknowledgments

Author contributions: R. S. I. and C. L. F. developed the key clinical question and performed the systematic review. R. S. I. created the first draft of the manuscript. All authors read and critically reviewed all drafts of the manuscript and approved the final version.

Financial/nonfinancial disclosures: The authors have reported to CHEST the following: R. S. I. and C. L. F. are codevelopers of the Cough Quality of Life Questionnaire and have received less than \$400 each in the past 6 years to support its further development. Although R. S. I. is the Editor in Chief of CHEST, the review and all editorial decisions regarding this manuscript were independently made by others. K. W. A. discloses consultations with KayPentax, receiving \$300, Bayer, receiving \$800, and 5AM Ventures, receiving \$550, which was all donated to the American Laryngological Association. None declared (A. B. C.).

***Collaborators:** Members of the CHEST Expert Cough Panel: Todd M. Adams, MD (Webhannet Internal Medicine Associates of York Hospital), Kenneth W. Altman, MD, PhD (Baylor College of Medicine, Houston, TX), Elie Azoulay, MD, PhD (University of Paris, Paris, France), Alan F. Barker, MD (Oregon Health & Science University, Portland, OR), Surinder S. Birring, MBChB, MD (Division of Asthma, Allergy and Lung Biology, King's College London, Denmark Hill, London, United Kingdom), Fiona Blackhall, MD, PhD (University of Manchester, Department of Medical Oncology, Manchester, England), Donald C. Bolser, PhD (College of Veterinary Medicine, University of Florida, Gainesville, FL), Louis-Philippe Boulet, MD, FCCP (Institut universitaire de cardiologie et de pneumologie de Québec, Christopher Brightling, MBBS, PhD, FCCP (University of Leicester, Glenfield Hospital, Leicester, United Kingdom), Priscilla Callahan-Lyon, MD (Adamstown, MD), Anne B. Chang, MBBS, PhD, MPH (Royal Children's Hospital, Queensland, Australia), Terrie Cowley (The TMJ Association, Milwaukee, WI), Satoru Ebihara, MD, PhD (Department of Rehabilitation Medicine, Toho University School of Medicine, Tokyo, Japan), Ali A. El Solh, MD, MPH (University at Buffalo, State University of New York, Buffalo, NY), Patricio Escalante, MD, MSc, FCCP (Mayo Clinic, Rochester, MN), Stephen K. Field, MD (University of Calgary, Calgary, AB, Canada), Dina Fisher, MD, MSc (University of Calgary, Respiratory Medicine, Calgary, AB, Canada), Cynthia T. French, PhD, FCCP (UMass Memorial Medical Center, Worcester, MA), Peter Gibson, MBBS (Hunter Medical Research Institute, New South Wales, Australia), Philip Gold, MD, MACP, FCCP (Loma Linda University, Loma Linda, CA), Susan M. Harding, MD, FCCP (Division of Pulmonary, Allergy, and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, AL), Anthony Harnden, MBChB, MSc (University of Oxford, Oxford, England), Adam T. Hill, MBChB, MD (Royal Infirmary and University of Edinburgh, Edinburgh, Scotland), Richard S. Irwin, MD, Master

FCCP (UMass Memorial Medical Center, Worcester, MA), Joanne Kavanagh, MBChB, (Division of Asthma, Allergy, and Lung Biology, King's College London, Denmark Hill, London, United Kingdom), Karina A. Keogh, MD (Mayo Clinic, Rochester, MN), Kefang Lai, MD, PhD (First Affiliated Hospital of Guangzhou Medical College, Guangzhou, China), Andrew P. Lane, MD (Johns Hopkins University School of Medicine, Baltimore, MD), Kaiser Lim, MD (Mayo Clinic, Rochester, MN), J. Mark Madison, MD, FCCP (UMass Memorial Medical Center, Worcester, MA), Mark A. Malesker, PharmD, FCCP (Creighton University School of Pharmacy and Health Professions, Omaha, NE), Stuart Mazzone, PhD, FCCP (University of Queensland, Queensland, Australia), Alex Molassoitis, PhD, MSc, RN (Hong Kong Polytechnic University, Hong Kong, China), M. Hassan Murad, MD, MPH (Mayo Clinic, Rochester, MN), Mangala Narasimhan, DO, FCCP (Hofstra-Northwell Health, Manhasset, NY), Huong Q. Nguyen, PhD, RN (Kaiser Permanente, Pasadena, CA), Peter Newcombe, PhD (School of Psychology University of Queensland, Queensland, Australia), John Oppenheimer, MD (UMDNJ-Rutgers University), Marcos I. Restrepo, MD, MSc, FCCP (South Texas Veterans Health Care System, San Antonio, TX), Mark Rosen, MD, Master FCCP (Icahn School of Medicine at Mount Sinai, New York, NY), Bruce Rubin, MEngr, MD, MBA (Virginia Commonwealth University, Richmond, VA), Jay H. Ryu, MD, FCCP (Mayo Clinic, Rochester, MN), Susan M. Tarlo, MBBS, FCCP (Toronto Western Hospital, Toronto, ON, Canada), Julie Turmel, PhD (Quebec Heart and Lung Institute, Laval University, Quebec), Anne E. Vertigan, PhD, MBA, BAppSc (SpPath) (John Hunter Hospital, New South Wales, Australia), Gang Wang, MD, PhD (Sichuan University, West China Hospital, Chengdu, China), Miles Weinberger, MD, FCCP (University of Iowa Hospitals and Clinics, Iowa City, IA).

Endorsements: This guideline has been endorsed by the American College of Allergy, Asthma, and Immunology (ACAAI), American Thoracic Society (ATS), Asian Pacific Society for Respiriology (APSR), Canadian Thoracic Society (CTS), and Irish Thoracic Society (ITS).

Other contributions: We are grateful to Nancy Harger, MLS, and Judy Nordberg, MLS, Education and Clinical Services Librarians working in the University of Massachusetts Medical School Library in Worcester, MA, who undertook all the searches for these previously published systematic reviews.

Additional information: The e-Tables can be found in the Supplemental Materials section of the online article.

References

1. Mello CJ, Irwin RS, Curley FJ. Predictive values of the character, timing, and complications of chronic cough in diagnosing its cause. *Arch Intern Med.* 1996;156(9):997-1003.
2. Irwin RS, Boulet LP, Cloutier MM, et al. Managing cough as a defense mechanism and as a symptom. A consensus panel report of the American College of Chest Physicians. *Chest.* 1998;114(2 suppl Managing):133S-181S.
3. Irwin RS, Baumann MH, Bolser DC, et al. Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest.* 2006;129(1 suppl):1S-23S.
4. Pratter MR, Brightling CE, Boulet LP, et al. An empiric integrative approach to the management of cough: ACCP evidence-based clinical practice guidelines. *Chest.* 2006;129(1 suppl):222S-231S.
5. Lewis SZ, Diekemper R, Ornelas J, et al. Methodologies for the development of CHEST guidelines and expert panel reports. *Chest.* 2014;146(1):182-192.
6. Higgins J, Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. <http://www.cochrane-handbook.org>. Accessed August 10, 2017.
7. Cochrane Bias Methods Group. Tool to assess risk of bias in cohort studies. <https://sites.google.com/site/riskofbiastool/>. Accessed August 10, 2017.
8. Diekemper R, Ireland B, Merz L. Development of the Documentation and Appraisal Review Tool for systematic reviews. *World J Meta-Anal.* 2015;3(3):142-150.

9. Godycki-Cwirko M, Hood K, Nocun M, et al. Presentation, antibiotic management and associated outcome in Polish adults presenting with acute cough/LRTI. *Fam Pract.* 2011;28(6):608-614.
10. Worrall GJ. One hundred coughs: family practice case series. *Can Fam Physician.* 2008;54(2):236-237.
11. Yamasaki A, Hanaki K, Tomita K, et al. Cough and asthma diagnosis: physicians' diagnosis and treatment of patients complaining of acute, subacute and chronic cough in rural areas of Japan. *Int J Gen Med.* 2010:3101-3107.
12. Rosen MJ, Ireland B, Narasimhan M, et al. Cough in ambulatory immunocompromised adults: CHEST Expert Panel Report. *Chest.* 2017;152(5):1038-1042.
13. Boulet LP, Coeytaux RR, McCrory DC, et al. Tools for assessing outcomes in studies of chronic cough: CHEST guideline and expert panel report. *Chest.* 2015;147(3):804-814.
14. French CT, Diekemper RL, Irwin RS, et al. Assessment of intervention fidelity and recommendations for researchers conducting studies on the diagnosis and treatment of chronic cough in the adult: CHEST guideline and expert panel report. *Chest.* 2015;148(1):32-54.
15. Kwon NH, Oh MJ, Min TH, et al. Causes and clinical features of subacute cough. *Chest.* 2006;129(5):1142-1147.
16. Tarlo SM, Altman KW, French CT, et al. Evaluation of occupational and environmental factors in the assessment of chronic cough in adults: a systematic review. *Chest.* 2016;149(1):143-160.
17. Tarlo SM, Altman KW, Oppenheimer J, et al. Occupational and environmental contributions to chronic cough in adults: CHEST expert panel report. *Chest.* 2016;150(4):894-907.
18. Fletcher KE, French CT, Irwin RS, et al. A prospective global measure, the Punum Ladder, provides more valid assessments of quality of life than a retrospective transition measure. *J Clin Epidemiol.* 2010;63(10):1123-1131.
19. Irwin RS, Ownbey R, Cagle PT, et al. Interpreting the histopathology of chronic cough: a prospective, controlled, comparative study. *Chest.* 2006;130(2):362-370.
20. Lai K, Chen R, Lin J, et al. A prospective, multicenter survey on causes of chronic cough in China. *Chest.* 2013;143(3):613-620.
21. Yu L, Qiu ZH, Wei WL, et al. Discrepancy between presumptive and definite causes of chronic cough. *Chin Med J (Engl).* 2011;124(24):4138-4143.
22. Lee J, Kim M, Kim JH, et al. A cheaper, faster way to resolve chronic cough. *J Fam Pract.* 2007;56(8):641-646.
23. Levine BM. Systematic evaluation and treatment of chronic cough in a community setting. *Allergy Asthma Proc.* 2008;29(3):336-342.
24. Ogawa H, Fujimura M, Takeuchi Y, et al. The importance of basidiomycetous fungi cultured from the sputum of chronic idiopathic cough: a study to determine the existence of recognizable clinical patterns to distinguish CIC from non-CIC. *Respir Med.* 2009;103(10):1492-1497.
25. Ribeiro M, Pereira CAD, Nery LE, et al. A prospective longitudinal study of clinical characteristics, laboratory findings, diagnostic spectrum and outcomes of specific therapy in adult patients with chronic cough in a general respiratory clinic. *Int J Clin Pract.* 2006;60(7):799-805.
26. Dabrowska M, Grabczak EM, Arcimowicz M, et al. Causes of chronic cough in non-smoking patients. *Adv Exp Med Biol.* 2015;873:25-33.
27. Dabrowska M, Grabczak EM, Arcimowicz M, et al. Chronic cough—assessment of treatment efficacy based on two questionnaires. *Arch Med Sci.* 2014;10(5):962-969.
28. Deng HY, Luo W, Zhang M, et al. Initial empirical treatment based on clinical feature of chronic cough. *Clin Respir J.* 2016;10(5):622-630.
29. Kahrilas PJ, Altman KW, Chang AB, et al. Chronic cough due to gastroesophageal reflux in adults: CHEST guideline and expert panel report. *Chest.* 2016;150(6):1341-1360.
30. Baraniuk JN, Jamieson MJ. Rhinorrhea, cough and fatigue in patients taking sitagliptin. *Allergy Asthma Clin Immunol.* 2010;6(1):8.
31. Institute of Medicine of the National Academies. Finding what works in healthcare: standards for systematic reviews. March 2011. <http://www.nationalacademies.org/hmd/~media/Files/Report%20Files/2011/Finding-What-Works-in-Health-Care-Standards-for-Systematic-Reviews/Standards%20for%20Systematic%20Review%202010%20Insert.pdf>. Accessed April 14, 2017.
32. Lewis SZ, Diekemper RL, French CT, et al. Methodologies for the development of the management of cough: CHEST guideline and expert panel report. *Chest.* 2014;146(5):1395-1402.
33. Institute of Medicine of the National Academies. Clinical practice guidelines we can trust. March, 2011. <http://www.nationalacademies.org/hmd/~media/Files/Report%20Files/2011/Clinical-Practice-Guidelines-We-Can-Trust/Clinical%20Practice%20Guidelines%202011%20Insert.pdf>. Accessed April 14, 2017.
34. Jiang M, Guan WJ, Fang ZF, et al. A critical review of the quality of cough clinical practice guidelines. *Chest.* 2016;150(4):777-788.
35. Lobach DF, Hammond WE. Development and evaluation of a computer-assisted management protocol (CAMP): improved compliance with care guidelines for diabetes mellitus. *Proc Annu Symp Comput Appl Med Care.* 1994:787-791.