



2017

Use of Management Pathways or Algorithms in Children With Chronic Cough CHEST Guideline and Expert Panel Report

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Use of Management Pathways or Algorithms in Children With Chronic Cough

CHEST Guideline and Expert Panel Report



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BACKGROUND: Using management algorithms or pathways potentially improves clinical outcomes. We undertook systematic reviews to examine various aspects in the generic approach (use of cough algorithms and tests) to the management of chronic cough in children (aged ≤ 14 years) based on key questions (KQs) using the Population, Intervention, Comparison, Outcome format.

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 patients' values and preferences and the clinical context were used to form recommendations. Delphi methodology was used to obtain the final grading.

RESULTS: Combining data from systematic reviews addressing five KQs, we found high-quality evidence that a systematic approach to the management of chronic cough improves clinical outcomes. Although there was evidence from several pathways, the highest evidence was from the use of the CHEST approach. However, there was no or little evidence to address some of the KQs posed.

CONCLUSIONS: Compared with the 2006 Cough Guidelines, there is now high-quality evidence that in children aged ≤ 14 years with chronic cough (> 4 weeks' duration), the use of cough management protocols (or algorithms) improves clinical outcomes, and cough management or testing algorithms should differ depending on the associated characteristics of the cough and clinical history. A chest radiograph and, when age appropriate, spirometry (pre- and post- β_2 agonist) should be undertaken. Other tests should not be routinely performed and undertaken in accordance with the clinical setting and the child's clinical symptoms and signs (eg, tests for tuberculosis when the child has been exposed).

CHEST 2017; 151(4):875-883

KEY WORDS: cough; evidence-based medicine; guidelines; pediatrics

ABBREVIATIONS: ACCP = American College of Chest Physicians; AHR = airway hyperresponsiveness; KQ = key question; LR = likelihood ratio; PC-QOL = Parent Cough-Specific Quality of Life; PedsQL = Pediatric Quality of Life Inventory; PICO = Population, Intervention, Comparison, Outcome; PV = predictive value; QoL = quality of life; RCT = randomized controlled trial

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Summary of Recommendations/Suggestions

1. For children aged ≤ 14 years, we suggest defining chronic cough as the presence of daily cough of at least 4 weeks in duration (Ungraded, Consensus Based Statement).
2. For children aged ≤ 14 years with chronic cough, we suggest that an assessment of the effect of cough on the child and the family be undertaken as part of the clinical consultation (Ungraded, Consensus Based Statement).
3. For children aged ≤ 14 years with chronic cough, we recommend using pediatric-specific cough management protocols or algorithms (Grade 1B).
4. For children aged ≤ 14 years with chronic cough, we recommend taking a systematic approach (such as using a validated guideline) to determine the cause of the cough (Grade 1A).
5. For children aged ≤ 14 years with chronic cough, we recommend basing the management or testing algorithm on cough characteristics and the associated clinical history, such as using specific cough pointers like presence of productive/wet cough (Grade 1A).
6. For children aged ≤ 14 years with chronic cough, we recommend basing the management on the etiology of the cough. An empirical approach aimed at treating upper airway cough syndrome due to a rhinosinus condition, gastroesophageal reflux disease, and/or asthma should not be used unless other features consistent with these conditions are present (Grade 1A).
7. For children aged ≤ 14 years with chronic cough, we suggest that if an empirical trial is used based on features consistent with a hypothesized diagnosis, the trial should be of a defined limited duration in order to confirm or refute the hypothesized diagnosis (Ungraded, Consensus Based Statement).
8. For children aged ≤ 14 years with chronic cough, we recommend that a chest radiograph and, when age

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

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DOI: <http://dx.doi.org/10.1016/j.chest.2016.12.025>

appropriate, spirometry (pre- and post- β_2 agonist) be undertaken (Grade 1B).

9. For children aged ≤ 14 years with chronic cough, we suggest undertaking tests evaluating recent *Bordetella pertussis* infection when pertussis is clinically suspected (Ungraded, Consensus Based Statement).

10. For children aged ≤ 14 years with chronic cough, we recommend not routinely performing additional tests (eg, skin prick test, Mantoux, bronchoscopy, chest CT); these should be individualized and undertaken in accordance with the clinical setting and the child's clinical symptoms and signs (Grade 1B).

11. For children aged > 6 years and ≤ 14 years with chronic cough and asthma clinically suspected, we suggest that a test for airway hyperresponsiveness (AHR) be considered (Grade 2C).

Chronic cough among children is associated with impaired quality of life,¹ multiple physician visits,² and adverse effects from inappropriate use of medications.³ Also, it may signify a serious underlying disease such as bronchiectasis or an inhaled foreign body.¹ Further, early diagnosis is important, as delayed diagnosis (eg, foreign body) may cause chronic respiratory morbidity,⁴ whereas early diagnosis of chronic disease leads to appropriate management and subsequent resolution of cough and improved quality of life (QoL).¹ Use of cough algorithms or pathways can potentially lead to earlier diagnosis and reduce morbidity, unnecessary costs, and medication use associated with chronic cough.

In the management of chronic cough (ie, cough of more than 4 weeks' duration), investigations are undertaken to confirm or rule out specific causes. When undertaking investigations in children, the pediatric-specific issues and risk-benefit ratio needs to be taken into consideration. For example, although respiratory function tests are standard assessments in adults, most young children are unable to generate reliable data from pulmonary function tests (such as spirometry and AHR challenges) until the age of 6 years in most clinical laboratories. Chest CT scans are associated with higher adverse events in young children (future cancer)⁵ and may require a general anesthetic in children aged < 3 years.

The 2006 American College of Chest Physicians (CHEST) guidelines on chronic cough in children⁶ advocated use of a cough pathway based on available but

limited evidence in that era. Research in chronic cough has progressed in the past decade, and hence we undertook systematic reviews addressing key questions (KQs) using the Population, Intervention, Comparison, Outcome (PICO) format relating to various aspects of cough algorithms/pathways⁷ and routine tests (e-Appendix 1). The 5 KQs were the following:

- KQ1: In children aged ≤ 14 years with chronic cough (> 4 weeks' duration), does the use of cough management protocols (or algorithms) improve clinical outcomes?
- KQ2: In children aged ≤ 14 years with chronic cough (> 4 weeks' duration), should the cough or testing algorithm differ depending on the duration and/or severity?
- KQ3: In children aged ≤ 14 years with chronic cough (> 4 weeks' duration), should the cough or testing

algorithm differ depending on the associated characteristics of the cough and clinical history?

- KQ4: In children aged ≤ 14 years, what testing or tests should be routinely done in clinical practice when evaluating chronic cough of at least 4 weeks' duration?
- KQ5: When evaluating children aged ≤ 14 years with chronic cough (of at least 4 weeks' duration), what is the role of pulmonary function studies and bronchial provocation in clinical practice?

In this paper, our overall aim was to present the recommendations and the summary of evidence behind these recommendations relating to the assessment and use of management pathways or algorithms in children with chronic cough. Systematic reviews addressing PICO-formatted KQs relating to various aspects of cough algorithms were undertaken and previously published in part and are best read together with this document.⁷

Methods

For the CHEST cough guidelines, it was a priori determined that the age cutoff for pediatric and adult components was 14 years. We used a standard method⁸ as previously described by Vertigan, et al⁹: "The methodology used by the CHEST Guideline Oversight Committee to select the Expert Cough Panel Chair and the international panel of experts, perform the synthesis of the evidence and develop the recommendations and suggestions has been published.^{8,10} Key questions and parameters of eligibility were developed for this topic. Existing guidelines, systematic reviews, and primary studies were assessed for relevance and quality, and were used to support the evidence-based graded recommendations or suggestions. A highly structured consensus-based Delphi approach was employed to provide expert advice on all guidance statements. The total number of eligible voters for each guideline statement varied based on the number of managed individuals recused from voting on any particular statements because of their potential conflicts of interest. Transparency of process was documented. Further details of the methods have been published elsewhere.^{8,10} Consistent with recent recommendations from the Institute of Medicine, the Panel conducted a comprehensive, systematic review of the literature to provide the evidence base for this guideline."

Guideline Framework

As previously described,⁹ "the ACCP has adopted the GRADE framework (The Grading of Recommendations Assessment, Development and Evaluation). This framework separates the process of rating the quality of evidence from that of determining the

strength of recommendation. The quality of evidence is based on the five domains of risk of bias, inconsistency, indirectness, reporting bias and imprecision. The quality of evidence (ie, the confidence in estimates) is rated as high (A), moderate (B), low or very low (C). The strength of recommendation is determined based on the quality of evidence, balance of benefits and harms, patients' values and preferences, and availability of resources. Recommendations can be strong or weak."

State of the Available Evidence

Searches for the systematic reviews were undertaken externally by librarians (Nancy Harger, MLS and Judy Nordberg, MLS) from the University of Massachusetts Medical School, Worcester, MA. These searches were undertaken between February 28, 2015 and August 14, 2015 using an a priori established protocol for each KQ.⁷ The evidence for three KQs was summarized in a previous publication⁷ (and key tables and figures in e-Appendix 1, e-Tables 1-3, and e-Figs 1-3) and reproduced in e-Appendix 1, e-Tables 4 and 5, and e-Figures 4 and 5 along with the data relevant for KQs 4 and 5.

The systematic reviews⁷ (and e-Appendix 1, e-Tables 4 and 5, e-Figs 4 and 5) identified high-quality evidence to support some recommendations but not all. When there was insufficient evidence for diagnosis and management recommendations, the panel heavily placed great emphasis on patient values, preferences, ease and cost of tests, and availability of potential therapies. The panel also made several suggestions for future research.

Results

The first eight recommendations and/or suggestions were derived from systematic reviews that addressed KQs 1 to 3 summarized in e-Tables 1-3 and e-Figures 1-3.⁷ The subsequent four recommendations/suggestions were derived from systematic reviews that addressed KQs 4 and 5 (all summarized in e-Tables 4 and 5 and e-Figs 4 and 5).

Summary of Evidence and Interpretation

The definition of the duration of chronic cough is controversial, because in a minority of children, cough after viral infections lasts > 4 weeks. In our systematic review,⁷ (e-Tables 1 and 2), we found no studies that addressed the question of whether the cough management or testing algorithm should differ depending on the

duration of chronic cough (KQ 2). Also to date, there are no published studies that have clinically assessed the possible reasons and/or outcomes of the group of children with acute cough that persists for > 4 weeks.

In reviewing published national guidelines, we found that all but one¹¹ guideline defined chronic cough in children as a duration lasting > 4 weeks (e-Table 2). All the guidelines (such as those of ACCP,⁶ and the Thoracic Society of Australia and New Zealand¹²) that use the shorter time frame do not advocate the use of medications or investigations for all children at that time point, recognizing that the cough subsides without any specific treatment in a number of children (ie, assumed “resolved spontaneously”).^{1,13} The shorter time frame is recommended for reasons outlined in previous publications.^{1,12} One such reason is to ensure that all children with chronic cough are carefully assessed and not quickly dismissed as having a postviral cough. This is particularly important in children, as chronic cough may be due to a serious underlying condition, and earlier diagnosis and treatment results in less damage (eg, retained foreign body⁴ and bronchiectasis¹⁴). Indeed, a serious potentially progressive underlying respiratory illness (bronchiectasis, aspiration lung disease, or cystic fibrosis) was documented in 18% of children in a multicenter study that used a cough algorithm.¹ Thus, for safety reasons, we advocated that chronic cough should be defined as that lasting > 4 weeks.

1. For children aged ≤ 14 years, we suggest defining chronic cough as the presence of daily cough of at least 4 weeks in duration (Ungraded, Consensus Based Statement).

Summary of Evidence and Interpretation

Our systematic review⁷ found no eligible studies that examined whether the cough testing algorithm should differ depending on the severity of the cough (e-Table 2). Almost all existing nationally based cough guidelines suggest that cough severity should be assessed, along with burden and expectations. However, these recommendations are generic, with little detail regarding how to assess cough severity.

Although cough is often dismissed by health professionals as a minimal ailment, cough causes substantial burden. In a prospective multicenter cohort study¹ involving 346 children who first presented to pediatric pulmonologists with a chronic cough, the burden of chronic cough (measured by a generic

health-related QoL [Pediatric Quality of Life Inventory {PedsQL}¹⁵] and a cough-specific QoL [Parent Cough-Specific Quality of Life {PC-QOL}^{16,17}]) differed significantly between clinical settings but was not influenced by age or cause of cough. Also, duration of cough and cough score were no different in children with a serious underlying disease compared with those with less serious conditions.¹ This suggests that it is the cough itself, rather than the underlying cause, that drives the disease burden at the point of referral. Further, the cohort’s¹ mean normalized PedsQL score of 74.7 was in the realm of children with other chronic illnesses (cardiac, 79.4; diabetes, 76.6; obesity, 75; and gastrointestinal conditions, 72.4).¹⁸

2. For children aged ≤ 14 years with chronic cough, we suggest that an assessment of the effect of cough on the child and the family be undertaken as part of the clinical consultation (Ungraded, Consensus Based Statement).

Summary of Evidence and Interpretation

Our systematic review⁷ found high-quality evidence that in children aged ≤ 14 years with chronic cough (> 4 weeks’ duration), the use of children-specific cough management protocols (or algorithms) improves clinical outcomes (e-Table 1). When data were available, findings from randomized controlled trials (RCTs) were consistent with those derived from cohort studies.⁷ All studies within the past decade used systematic evaluation of the child.

The highest evidence for the type of chronic cough pathway was that derived from the American College of Chest Physicians,⁶ as the evidence was derived from an RCT¹⁹ and several cohort studies.²⁰⁻²² The evidence for other pathways was restricted to single studies (e-Table 1). The variations in algorithms raise the question of whether algorithms that are specific to the clinical setting should be used, such as in developing countries, where the most common causes of cough are likely different (eg, tuberculosis, parasitic disease). However, irrespective of the relative prevalence of different conditions, the correct diagnosis would be obtained if a cough pathway such as the CHEST guideline is used.

3. For children aged ≤ 14 years with chronic cough, we recommend using pediatric-specific cough management protocols or algorithms (Grade 1B).

4. For children aged ≤ 14 years with chronic cough, we recommend taking a systematic approach (such as

using a validated guideline) to determine the cause of the cough (Grade 1A).

Summary of Evidence and Interpretation

Our systematic reviews⁷ also found high-quality evidence that in children (aged ≤ 14 years) with chronic cough, the cough management or testing algorithm should differ depending on the associated characteristics of the cough and clinical history (e-Tables 3a, 3b). We⁷ found that all included studies demonstrated that cough management should differ depending on clinical history, including cough characteristics. None of the studies used an empirical approach. At a divergent point, all studies used the concept of wet or productive cough, but the point of when this divergence occurred differed between the algorithms.⁷ A study that specifically examined the use of cough pointers²² found that the presence of any specific cough pointer indicating a cause of chronic cough (as opposed to resolution without specific treatment) had sensitivity of 1.0 (95% CI, 0.98-1.0), specificity of 0.95 (95% CI, 0.82-0.99), positive predictive value (PV) of 0.99 (95% CI, 0.97-1.0), negative PV of 1.0 (95% CI, 0.9-1.0), positive likelihood ratio (LR) of 20 (95% CI, 5.2-77.2), and negative LR of 0 (95% CI, 0-0.03). However, recognition of cough pointers (Table 1)²³ is dependent on accurate identification (ie, expertise of physicians and the caregiver's history).

Our systematic review⁷ also found that the majority of children in all the studies received treatment specific for the underlying cause rather than an empirical approach

based on treatment of gastroesophageal reflux disease, upper airway cough syndrome due to a rhinosinus condition, or asthma (e-Table 3). However, in some situations, an empirical trial is required, such as using inhaled corticosteroids when the cough is dry and objective testing cannot be undertaken in a young child. Ascribing causes for the cough has an inherent high risk of bias related to the placebo and “period effects” (the natural resolution of cough over time²⁴) evident in cough-related intervention studies.²⁵ These risks of bias can be reduced by limiting the time frame in which “response to treatment” is considered,²⁵ when an RCT is not undertaken.

5. For children aged ≤ 14 years with chronic cough, we recommend basing the management or testing algorithm on cough characteristics and the associated clinical history, such as using specific cough pointers like presence of productive/wet cough (Grade 1A).

6. For children aged ≤ 14 years with chronic cough, we recommend basing the management on the etiology of the cough. An empirical approach aimed at treating upper airways cough syndrome due to a rhinosinus condition, gastroesophageal reflux disease, and/or asthma should not be used unless other features consistent with these conditions are present (Grade 1A).

7. For children aged ≤ 14 years with chronic cough, we suggest that if an empirical trial is used based on features consistent with a hypothesized diagnosis, the

TABLE 1] Extended List of Cough Pointers (Modified From Previous Papers)^{6,12,23}

Systemic	Pulmonary
<ul style="list-style-type: none"> • Cardiac abnormalities 	<ul style="list-style-type: none"> • Chest pain
<ul style="list-style-type: none"> • Digital clubbing 	<ul style="list-style-type: none"> • Daily moist or productive cough
<ul style="list-style-type: none"> • Failure to thrive 	<ul style="list-style-type: none"> • Hemoptysis
<ul style="list-style-type: none"> • Medications or drugs associated with chronic cough (angiotensin-converting enzyme inhibitors, illicit drug use) 	<ul style="list-style-type: none"> • Abnormal cough characteristics (brassy, plastic bronchitis, paroxysmal with/without posttussive vomiting, staccato, cough from birth)
<ul style="list-style-type: none"> • Neurodevelopmental abnormality 	<ul style="list-style-type: none"> • Recurrent pneumonia
<ul style="list-style-type: none"> • Fever 	<ul style="list-style-type: none"> • Hypoxia/cyanosis
<ul style="list-style-type: none"> • Immune deficiency (primary or secondary) 	<ul style="list-style-type: none"> • History of previous lung disease or predisposing causes (eg, neonatal lung disease, foreign body aspiration)
<ul style="list-style-type: none"> • Feeding difficulties 	<ul style="list-style-type: none"> • Exertional dyspnea
<ul style="list-style-type: none"> • History of contacts (eg, tuberculosis) 	<ul style="list-style-type: none"> • Dyspnea at rest or tachypnea
	<ul style="list-style-type: none"> • Chest wall deformity
	<ul style="list-style-type: none"> • Auscultatory findings (eg, stridor, wheeze, crackles)
	<ul style="list-style-type: none"> • Chest radiograph abnormalities
	<ul style="list-style-type: none"> • Pulmonary function test abnormalities

trial should be of a defined limited duration in order to confirm or refute the hypothesized diagnosis (Ungraded, Consensus Based Statement).

Summary of Evidence and Interpretation

Of the studies included in our systematic reviews,⁷ less than one-half of the studies a priori defined how cough was measured and what constituted cough resolution and/or considered the period effect (e-Tables 1 and 3). Many also lacked standardization of defining cough outcomes. Thus, further high-quality studies using validated tools,²⁶ particularly in primary care settings, are needed. This includes use of methods that take into account the period effect and use of a priori definitions for cause and response using validated pediatric-specific cough outcome measures such as the PC-QOL.^{16,27}

Several but not all guidelines recommend that chest radiographs and spirometry be undertaken in all children presenting with chronic cough (Table 2).²⁸⁻³² In KQ4, our systematic review examined whether any routine investigations should be undertaken in all children with chronic cough, and in KQ5, we evaluated specific cohorts that related to more complex lung function tests.

For KQ4 (e-Fig 4, e-Table 4), we identified one RCT,¹⁹ undertaken in pediatric pulmonology clinics, in which management was based on identification of cough pointers (Table 1) that included abnormalities detected on the chest radiograph and spirometry. The rest of the included studies were lower-quality studies; two were retrospective studies^{33,34} and nine were

prospective studies.^{20-22,35-40} One of the prospective studies⁴¹ included children in the RCT¹⁹ that calculated the LRs of the utility of spirometry and chest radiograph. For both tests, the positive LRs were infinite, but negative LRs were not highly negative, indicating that both tests are good for ruling in disease when abnormalities are present but poor at ruling out disease. For example, abnormal spirometry values at baseline with bronchodilator reversibility provide objective evidence consistent with asthma. However, asthma cannot be ruled out when spirometry values are normal. Results from these studies indicate that the risk-benefit ratio of both spirometry and chest radiograph clearly favors the benefit arm.

Although our search identified several studies evaluating the prevalence of recent *B pertussis* infection in children with cough, these studies^{42,43} did not fulfill our systematic review's inclusion criteria of cough duration.^{36,37} Although the studies reported a mean cough duration of > 4 weeks (range not given), the inclusion criteria for both studies was > 2 weeks. Nevertheless, these studies, conducted in primary care, suggested that appropriate tests to evaluate for recent pertussis infection should be undertaken when clinically appropriate. The most appropriate test (culture, polymerase chain reaction, or serologic analysis) is dependent on the child's age and duration of symptoms.⁴⁴ The 2006 ACCP guideline⁶ advocated that testing for recent *B pertussis* infection be undertaken when clinically suspected (eg, contact, posttussive vomiting, whoop), as described in several studies.^{19-22,40}

TABLE 2] Summary of Pediatric Chronic Cough Guidelines on the Use of Routine Tests

Study/Year	Country	Society	Suggested Routine Tests
Chang et al ¹² /2006	Australia	Thoracic Society of Australia and New Zealand	Yes Spirometry ^a and chest radiography
Chang and Glomb ⁶ /2006	United States	American College of Chest Physicians	Yes Spirometry ^a and chest radiography
Gibson et al ²⁸ /2010	Australia	Australian Lung Foundation	Yes Spirometry ^a and chest radiography
Kohno et al ²⁹ /2006	Japan	Japanese Respiratory Society	No
Leconte et al ³⁰ /2008	Belgium	Primary care	No Tests based on clinical suspicion
Lu ³¹ /2014	China	Multiple societies	Yes (based on translated article) Chest radiography
Shields et al ¹¹ /2008	England	British Thoracic Society	Yes Spirometry ^a and chest radiography
Zacharasiewicz et al ³² /2014	Austria	Austrian Society of Pediatrics, Austrian Society Pneumology	Yes Spirometry ^a and chest radiography

^aSpirometry if age appropriate (usually when aged > 5 years but in some centers, spirometry can be undertaken in children > 3 years).

Other than chest radiograph and spirometry, few studies have systematically undertaken tests in the cohorts of children. Skin prick testing to assess atopy, undertaken in several studies,^{33,35,38} was generally not useful in aiding the diagnosis of chronic cough. This is not surprising, as although atopy increases the probability of having asthma, its presence or absence is a poor sole distinguishing feature for pediatric asthma.⁴⁵ In a study involving 202 children, atopy (defined by skin prick testing) did not influence cough receptor sensitivity to capsaicin.⁴⁶

One study³⁶ undertaken in a setting with a high prevalence (relative to affluent countries) of tuberculosis found that sequential testing (including a Mantoux test) identified tuberculosis in 22% of the 94 children. This study³⁶ and other studies^{19-22,37,39,40} that undertook tests in accordance with the clinical findings suggest that other than chest radiograph and spirometry, other tests should be targeted. Another such example is provided by data from an Iranian study⁴⁷ (excluded because inclusion criteria was > 2 weeks of cough), that described a high frequency of *Toxocara* IgG, peripheral blood eosinophilia, and hypereosinophilia (14%, 55%, and 80%, respectively) in children with chronic cough.

8. For children aged ≤ 14 years with chronic cough, we recommend that a chest radiograph and, when age appropriate, spirometry (pre- and post-β₂ agonist) be undertaken (Grade 1B).

9. For children aged ≤ 14 years with chronic cough, we suggest undertaking tests evaluating recent *Bordetella pertussis* infection when pertussis is clinically suspected (Ungraded, Consensus Based Statement).

10. For children aged ≤ 14 years with chronic cough, we recommend not routinely performing additional tests (eg, skin prick test, Mantoux, bronchoscopy, chest CT); these should be individualized and undertaken in accordance with the clinical setting and the child's clinical symptoms and signs (Grade 1B).

Summary of Evidence and Interpretation

Four relevant studies^{33,35,38,48} were included in the systematic review for KQ5 (e-Fig 5, e-Table 5). There were no RCTs. One was a retrospective study and three were prospective single-center studies that undertook different types of bronchoprovocation investigations. The definition of presence of AHR varied among the studies. One study³⁸ included children with wheeze, two^{33,35} excluded a history of wheeze, and the remaining study⁴⁸ did not specify or

mention wheeze in the inclusion or exclusion criteria. However, one³⁵ of the studies that excluded children with wheeze included children with exertional dyspnea. None of the studies were of high quality, but all studies showed that AHR suggestive of asthma was demonstrated in a subgroup of children with chronic cough. Oral theophylline was used in two studies,^{33,35} and both reported rapid cessation of cough. Some children in the latter study,³³ a retrospective review of charts, were also treated with an oral or inhaled short-acting β₂ agonist. Thus, there are insufficient data to recommend that testing for AHR should be undertaken in all children with chronic cough. When asthma is suspected and/or other symptoms are present (eg, history of wheeze, exertional dyspnea, history of atopy), we suggest that testing for AHR should be considered (if possible) when the spirometry values are normal and other concurrent evidence of asthma is not evident. As it is beyond our scope to discuss the role of AHR and skin prick testing in the evaluation of asthma or rhinitis, readers are referred to asthma and/or rhinitis guidelines. As testing for AHR in clinical laboratories (as opposed to research laboratories) is only validly performed in children aged > 6 years, the recommendation is restricted to this age group.

11. For children aged > 6 years and ≤ 14 years with chronic cough and asthma clinically suspected, we suggest that a test for airway hyperresponsiveness (AHR) be considered (Grade 2C).

Areas for Further Research

To advance and improve the management of chronic cough in children, suggested areas of research include the following:

1. Undertake multicenter cohort studies in various clinical settings (community and hospital) that assess the outcomes of children with acute cough that then progresses to chronic cough.
2. Undertake RCTs on the efficacy of cough in various clinical settings, particularly in primary care. When doing so, we suggest that validated cough outcomes, a priori definitions, and “period effect” considerations be used.
3. Delineate the risk-benefit ratio of using different definitions of cough durations (eg, 4 weeks, 8 weeks, 3 months).
4. Determine if the use of cough algorithms, found to improve clinical outcomes in settings outside of primary care, are beneficial in primary care, with

- appropriate training given to primary care practitioners.
- Evaluate whether cough management or testing algorithms should depend on the duration and/or severity in children with chronic cough.
 - Determine the most appropriate age cutoff used for pediatric vs adult chronic cough guidelines (eg, 12, 14, 18 years).

Conclusions

In the past decade, the availability of single-center and multicenter studies from several countries has improved the evidence base of the 2006 CHEST Cough Guidelines⁶ approach. The new recommendations formulated from systematic reviews addressing five KQs were endorsed by the CHEST Expert Cough Panel. Although there is high-quality evidence for some of the new recommendations, many questions remain, particularly in primary care for which there is scarcity of data.

Acknowledgments

Author contributions: A. C., J. O., and R. I. drafted the key questions. A. C. and J. O. selected the studies, extracted data and undertook the bias assessment. A. C. drafted the recommendations and manuscript, had full access to the data and takes responsibility for the integrity of all of the data and the accuracy of the data analysis. J. O. and R. I. contributed to the data analyses and interpretation and critically reviewed the manuscript. B. R. and M. W. critically reviewed the manuscript. All contributed to modification of the recommendations.

Financial/nonfinancial disclosures: The authors have reported to CHEST the following: A. B. C. is supported by a National Health and Medical Research Council (NHMRC) practitioner fellowship [grant 1058213] and has been awarded multiple grants from the NHMRC related to diseases associated with pediatric cough. She is an author of several of the papers included in this review. J. J. O. is on the Board of Directors of the American Board of Allergy and Immunology; is an Associate Editor of the *Annals of Allergy and Allergy Watch* and a reviewer for Up to Date; has performed clinical research for Boehringer Ingelheim, AstraZeneca, Glaxo, Medimmune, and Novartis; is on the adjudication committee for AstraZeneca and Novartis; is on the data safety monitoring board for Ohio State University; and is a consultant for Glaxo, Myelin, Church and Dwight, and Meda. None declared (M. M. W., B. K. R., K. W., G. C. C., R. S. I.). Moreover, although R. S. I. is the Editor in Chief of CHEST, the review and all editorial decisions regarding this manuscript were made independently by others.

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 systematic reviews. The authors thank CHEST for supporting this work.

Role of sponsors: CHEST was the sole supporter of these guidelines, this article, and the innovations addressed within.

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

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