

# Etiologies of Chronic Cough in Pediatric Cohorts

## CHEST Guideline and Expert Panel Report

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## **e-Appendix 1.**

### **Further details on Methods**

For the CHEST cough guidelines, it was *a-priori* determined that the age cut-off for pediatric and adult components was 14-years. We used a standard method<sup>1</sup> as previously described by Vertigan et al:<sup>2</sup> “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.<sup>1,3</sup> 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.<sup>1,3</sup> 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”. During the Delphi approach, those with a ‘conflict of interest’ are requested not to vote.

### **Guideline Framework**

As previously described,<sup>2</sup> “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 (i.e., 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”. The framework used included consumer or patient input as part of the Delphi approach.

### Key Clinical Questions and PIRT / Study Selection Criteria

**Key question (KQ) 1:** In children with chronic (>4 weeks) cough, are the common etiology different from adults?

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Patient Population	<ul style="list-style-type: none"> <li>Humans</li> <li>Children with chronic cough (&gt; 4 weeks)</li> </ul>	Adults (aged >14 years)
Index Test	Etiologies of chronic cough	None
Comparator	<ul style="list-style-type: none"> <li>Etiology of cough in adults (in published reviews)</li> </ul>	None
Target Condition	<ul style="list-style-type: none"> <li>Chronic Cough</li> </ul>	Known bronchiectasis or cystic fibrosis
Timing	<ul style="list-style-type: none"> <li>Timing not limited</li> </ul>	None
Setting	<ul style="list-style-type: none"> <li>Inpatient and outpatient</li> </ul>	None
Study design	<ul style="list-style-type: none"> <li>Evaluation studies</li> <li>Case series</li> </ul>	<ul style="list-style-type: none"> <li>Not a clinical study (e.g., editorial, non-systematic review, letter to the editor)</li> </ul>
Publications	<ul style="list-style-type: none"> <li>English-language only</li> <li>Peer-reviewed articles</li> <li>Relevant systematic review, meta-analysis, or methods article (used only for background and as potential sources of additional relevant material)</li> </ul>	<ul style="list-style-type: none"> <li>Non-English-language publications</li> <li>Case studies</li> <li>Review papers published before 2000</li> <li>Series reporting or focusing on single etiology only</li> </ul>

**KQ2:** In children with chronic (>4 weeks) cough, are the common etiology age and/or setting dependent

<b>Study Characteristic</b>	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Patient Population	<ul style="list-style-type: none"> <li>Humans</li> <li>Children with chronic cough</li> </ul>	Adults (aged >14 years)
Index Test	<ul style="list-style-type: none"> <li>Age</li> <li>Setting (e.g. primary, secondary, country)</li> </ul>	None
Comparator	<ul style="list-style-type: none"> <li>Different ages and settings using same methods</li> </ul>	None
Target Condition	<ul style="list-style-type: none"> <li>Chronic cough</li> </ul>	Known bronchiectasis or cystic fibrosis
Timing	<ul style="list-style-type: none"> <li>Timing not limited</li> </ul>	None
Setting	<ul style="list-style-type: none"> <li>Inpatient and outpatient</li> </ul>	None
Study design	<ul style="list-style-type: none"> <li>Evaluation studies</li> <li>case series</li> </ul>	<ul style="list-style-type: none"> <li>Not a clinical study (e.g., editorial, non-systematic review, letter to the editor)</li> </ul>
Publications	<ul style="list-style-type: none"> <li>English-language only</li> <li>Peer-reviewed articles</li> <li>Relevant systematic review, meta-analysis, or methods article (used only for background and as potential sources of additional relevant material)</li> </ul>	<ul style="list-style-type: none"> <li>Non-English-language publications</li> <li>Case studies</li> <li>Review papers published before 2000</li> <li>Series reporting or focusing on single etiology only</li> </ul>

**KQ1 and KQ2** were combined in the search as, advised by the librarians (Nancy Harger, MLS and Judy Nordberg, MLS), the broad concepts of child, chronic cough, and etiology from KQ1 will be contained in KQ2 as well. Search undertaken on 9th Jan 2016

#### **PubMed:**

##### BASE SEARCH

((("Cough/diagnosis"[Mesh] OR "Cough/etiology"[Mesh]) AND chronic) OR chronic cough[tiab] OR idiopathic cough OR "refractory cough" OR (unresponsive[tiab] AND cough[tiab]) OR "intractable cough" OR "psychogenic cough" OR (unresolved[tiab] AND cough[tiab]) OR "unexplained cough" OR "persistent cough" OR (chronic disease[mh] AND cough) OR "pediatric cough" OR "pediatric chronic cough") AND (etiology OR etiologies OR cause OR causality OR risk factors[mh] OR risk factor\*[tiab]))

Results: 4188

Base search with Limits: article type, English, All Child, Humans

((("Cough/diagnosis"[Mesh] OR "Cough/etiology"[Mesh]) AND chronic) OR chronic cough[tiab] OR idiopathic cough OR "refractory cough" OR (unresponsive[tiab] AND cough[tiab]) OR "intractable cough" OR "psychogenic cough" OR (unresolved[tiab] AND cough[tiab]) OR "unexplained cough" OR "persistent cough" OR (chronic disease[mh] AND cough) OR "pediatric cough" OR "pediatric chronic cough") AND (etiology OR etiologies OR cause OR causality OR risk factors[mh] OR risk factor\*[tiab]) NOT (editorial[pt] OR comment[pt] OR letter[pt])) Filters: Case Reports; Clinical Conference; Clinical Study; Clinical Trial; Clinical Trial, Phase I; Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Comparative Study; Consensus Development Conference; Consensus Development Conference, NIH; Controlled Clinical Trial; Evaluation Studies; Guideline; Multicenter Study; Observational Study; Practice Guideline; Randomized Controlled Trial; Research Support, American Recovery and Reinvestment Act; Research Support, N.I.H., Extramural; Research Support, N.I.H., Intramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Research Support, U.S. Government; Validation Studies; Humans; English; Child: birth-18 years

**Results: 557 plus 36 recent articles**

**SCOPUS:** search adapted for Scopus

TITLE-ABS-KEY(("chronic cough" OR "idiopathic cough" OR "refractory cough" OR (unresponsive AND cough) OR "intractable cough" OR "psychogenic cough" OR (unresolved AND cough) OR "unexplained cough" OR "persistent cough" OR ("chronic disease" AND cough) OR "pediatric cough" OR "pediatric chronic cough") AND (etiology OR etiologies OR cause OR causality OR "risk factors") AND (child OR

children OR infant OR newborn OR preschool OR adolescent OR toddler OR neonate OR pediatric)) AND ( LIMIT-TO(LANGUAGE,"English" ) ) AND ( LIMIT-TO(DOCTYPE,"ar" ) OR LIMIT-TO(DOCTYPE,"re" ) OR LIMIT-TO(DOCTYPE,"cp" ) OR LIMIT-TO(DOCTYPE,"ip" ) )

**Results: 583 deduped in ENDNOTE library with PubMed: 364**

#### **Web of Science:**

**TOPIC:** (("chronic cough" OR "idiopathic cough" OR "refractory cough" OR (unresponsive AND cough) OR "intractable cough" OR "psychogenic cough" OR (unresolved AND cough) OR "unexplained cough" OR "persistent cough" OR ("chronic disease" AND cough) OR "pediatric cough" OR "pediatric chronic cough") AND (etiology OR etiologies OR cause OR causality OR "risk factors") AND (child OR children OR infant OR newborn OR preschool OR adolescent OR toddler OR neonate OR pediatric))

**Refined by: DOCUMENT TYPES:** ( ARTICLE OR PROCEEDINGS PAPER OR REVIEW OR MEETING ABSTRACT ) AND **LANGUAGES:** ( ENGLISH )

**Timespan:** All years. **Indexes:** SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC.

**Results: 316 then deduped in ENDNOTE library: 151**

#### **Cochrane Central Register**

Used Scopus search string

**Results: 12**

(Total for KQ1/2: 557+ 36 + 364 + 151 + 12 = 1120)

See table in main text for included studies.

**Key question 3:** Is OSA an etiology of chronic cough in children? If so, when should OSA be considered a cause of chronic cough in children

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Patient Population	<ul style="list-style-type: none"> <li>Humans</li> <li>Children with chronic cough</li> </ul>	Adults (aged >14 years)
Index Test	<ul style="list-style-type: none"> <li>Obstructive sleep apnea (OSA)</li> </ul>	None
Comparator	<ul style="list-style-type: none"> <li>Conditions other than OSA</li> </ul>	None
Target Condition	<ul style="list-style-type: none"> <li>Chronic cough</li> </ul>	None
Timing	<ul style="list-style-type: none"> <li>Timing not limited</li> </ul>	None
Setting	<ul style="list-style-type: none"> <li>Inpatient and outpatient</li> </ul>	None
Study design	<ul style="list-style-type: none"> <li>Evaluation studies</li> <li>Case series</li> </ul>	<ul style="list-style-type: none"> <li>Not a clinical study (e.g., editorial, non-systematic review, letter to the editor)</li> </ul>
Publications	<ul style="list-style-type: none"> <li>English-language only</li> <li>Peer-reviewed articles</li> <li>Relevant systematic review, meta-analysis, or methods article (used only for background and as potential sources of additional relevant material)</li> </ul>	<ul style="list-style-type: none"> <li>Non-English-language publications</li> </ul>

Search date: original search on July 2015 (repeat search on Pubmed only in Oct 2016 found no additional articles)

### PubMed

(sleep apnea, obstructive[mh] OR obstructive sleep apnea[tiab] OR sleep apnea[tiab] OR OSA[tiab] OR (hypopnoea AND sleep) OR (apnoea AND sleep)) AND ("chronic cough" OR "idiopathic cough" OR "refractory cough" OR "unresponsive cough" OR "intractable cough" OR "psychogenic cough" OR "unresolved cough" OR "unexplained cough" OR "productive cough" OR (cough AND chronic disease[mh])) *Filter English*

**Results: 38**

### **Web of Science**

((("obstructive sleep apnea" OR "sleep apnea" OR OSA OR "sleep hypopnoea" OR "sleep apnoea") AND ("chronic cough" OR "idiopathic cough" OR "refractory cough" OR "unresponsive cough" OR "intractable cough" OR "psychogenic cough" OR "unresolved cough" OR "unexplained cough" OR "productive cough" OR (cough AND chronic disease))) AND (pediatric OR paediatric OR child OR children OR infant OR neonate OR toddler OR preschool OR adolescent)

**Results: 9**

**After deduplication against "All References" in EndNote, Results = 4**

### **SCOPUS**

TITLE-ABS-KEY(("obstructive sleep apnea" OR "sleep apnea" OR OSA OR "sleep hypopnoea" OR "sleep apnoea") AND ("chronic cough" OR "idiopathic cough" OR "refractory cough" OR "unresponsive cough" OR "intractable cough" OR "psychogenic cough" OR "unresolved cough" OR "unexplained cough" OR "productive cough" OR (cough AND chronic disease))) AND (pediatric OR paediatric OR child OR children OR infant OR neonate OR toddler OR preschool OR adolescent) AND (human OR humans) AND ( LIMIT-TO(LANGUAGE,"English" ) )

**Results: 46**

**After deduplication against "All References" in EndNote, Results = 30**

### **CENTRAL (Cochrane)**

**Results: 0**

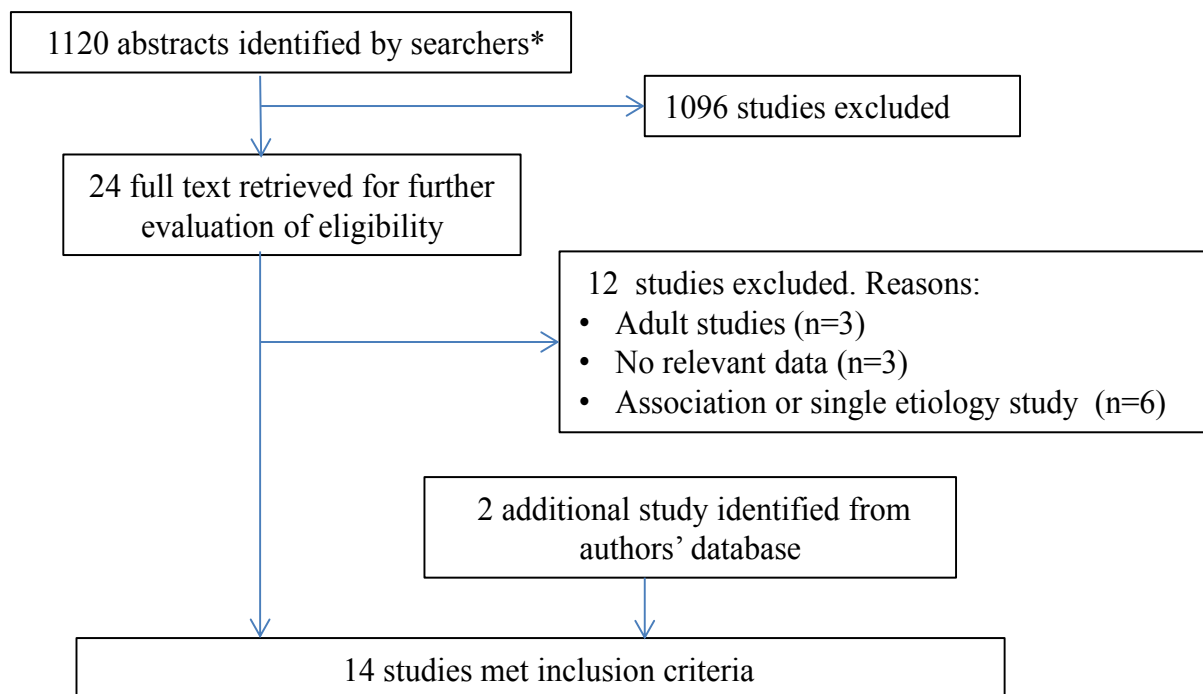
(Total KQ3: 38 + 4 + 30 = 72)



**e-Figure 1**

Selection of studies for key questions

1. In children with chronic (>4 weeks) cough, are the common etiology different from adults?
2. In children with chronic (>4 weeks) cough, are the common etiology age and/or setting dependent?

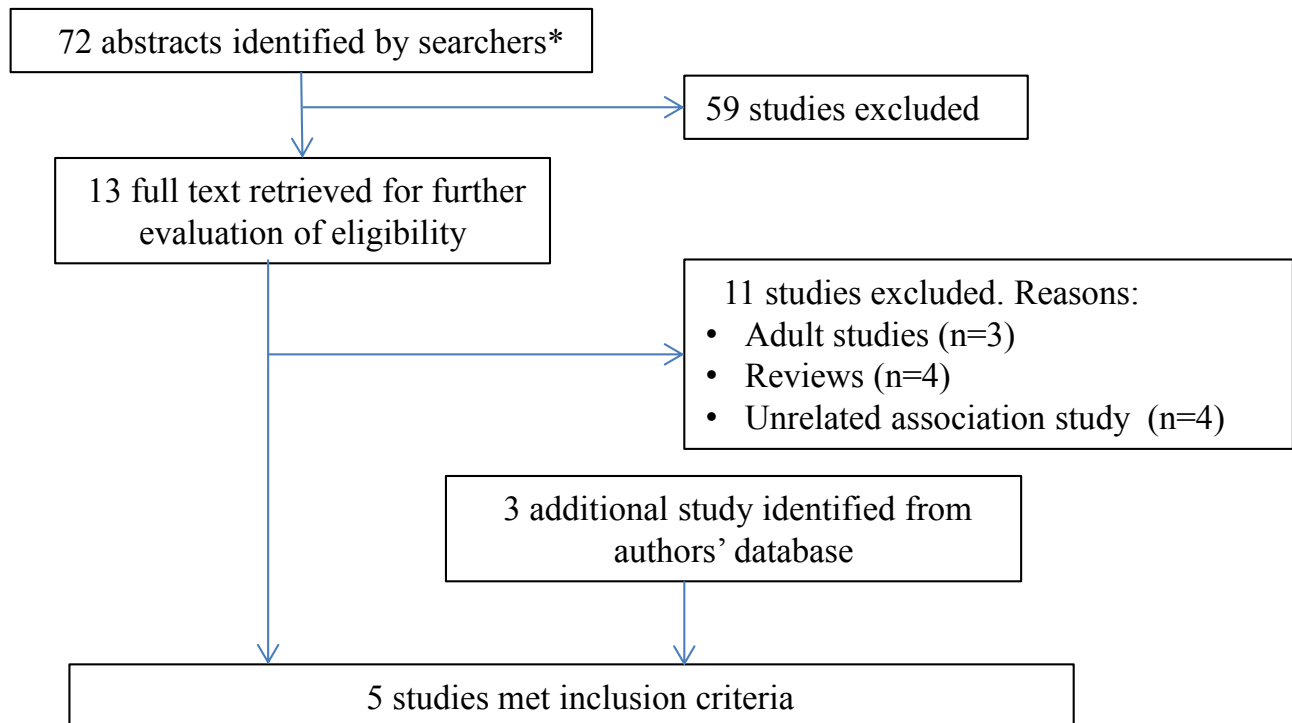


\*Searchers were undertaken by Nancy Harger, MLS and Judy Nordberg, MLS, Education and Clinical Services Librarians working in the University of Massachusetts Medical School Library in Worcester, MA

Duplication removed by librarians

**e-Figure 2**

Selection of studies for key question 3 - Is OSA an etiology of chronic cough in children? If so, when should OSA be considered a cause of chronic cough in children



\*Searchers were undertaken by Nancy Harger, MLS and Judy Nordberg, MLS, Education and Clinical Services Librarians working in the University of Massachusetts Medical School Library in Worcester, MA

Duplication removed by librarians

### References

- 1 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.
- 2 Vertigan AE, Murad MH, Pringsheim T et al. Somatic Cough Syndrome (previously referred to as psychogenic cough) and Tic Cough (previously referred to as habit cough) in Adults and Children: Chest Guideline and Expert Panel Report. *Chest* 2015; 148(1):24-31.
- 3 Irwin RS, French CT, Lewis SZ et al. Overview of the management of cough: CHEST Guideline and Expert Panel Report. *Chest* 2014; 146(4):885-889.