




GUIDELINES

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# Chronic cough in children: an evidence-based clinical practice guideline adapted for the use in Egypt using 'Adapted ADAPTE'

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## Abstract

**Background** We recently adopted a guideline for chronic cough in children in the Egyptian health system. Adapting clinical practice guidelines (CPGs) to the local healthcare setting is a valid alternative to de-novo development that can improve their uptake and implementation without demanding a substantial drain on resources. The objective of this study was to adapt evidence-based recommendations from global high-quality CPGs for children with a chronic cough to suit the Egyptian healthcare context.

**Methods** We followed the Adapted ADAPTE methodological framework for guideline adaptation. This process includes three phases: set-up, adaptation, and finalization. A guideline adaptation group (GAG) and an external review group including clinical content experts and methodologists conducted the process.

**Results** The GAG adapted 10 sections of recommendations from three original CPG(s) including (i) the American College of Chest Physicians (ACCP) 2006–2020, (ii) the European Respiratory Society (ERS) 2019, (iii) the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) 2018. A set of CPG implementation tools was added to enhance implementability including an algorithm, a slide presentation for clinical diagnosis, investigations and treatment of chronic cough, patient education, and online resources.

**Conclusion** The adapted CPG provides pediatricians and related healthcare workers with applicable evidence-based recommendations for chronic cough in children in Egypt. The project also highlighted the utility of Adapted ADAPTE and the invaluable collaboration between the clinical and methodological experts for the adaptation of pediatric national guidelines.

**Keywords** Practice guideline, Adaptation, Evidence-based medicine, Chronic cough, Pediatrics, Pediatric pulmonology, Egypt, Eastern mediterranean region

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## Background

When a child under the age of 14 has a daily cough for longer than 4 weeks, it is considered a chronic cough [1]. It can be divided into a specific and non-specific cough. A non-specific cough is defined as a protracted cough without any symptoms, signs, history, or test results that would suggest a specific diagnosis (specific cough pointers). Specific cough is typically linked to an underlying condition [2].

About 10% of the global population suffers from a chronic cough [3], which has a significant negative socio-economic impact and significantly lowers the quality of life (QOL) [4] for both parents and children [5]. For several months to years, children with a chronic cough may face physical discomfort, sleep disturbances, decreased academic output, and social isolation [6].

There are some clear differences between prepubertal children and adults, such as maturational differences in airway, respiratory muscles and chest wall structure, sleep-related characteristics, respiratory reflexes, and respiratory control [7]. Common pediatric etiologies differ from those in adults [8].

By careful observation, taking a thorough history, and using the information from the history to guide suitable testing and treatment trials, the etiology of chronic cough in children can be properly determined [9]. Either recording simple measures, such as a cough score out of 10, or more detailed, validated measures of cough quality of life (QOL) should be used to evaluate the effects of coughing [10, 11].

For common illnesses that cause coughing, such as rhinitis, rhinosinusitis, asthma, eosinophilic bronchitis, and GERD, investigations and therapeutic trials should involve chest X-rays, spirometry [12], computed tomography [9], flexible bronchoscopy, and alveolar lavage [13]. Additional examinations include immunological testing, nuclear medicine scans, echocardiography, complex sleep polysomnography, barium swallow, and videofluoroscopic evaluation of swallowing [5].

Every child who has a chronic cough should have a thorough evaluation because chronic coughs can indicate a significant underlying medical issue (such as an inhaled foreign body). Children with chronic cough should be given common treatment measures like reducing their exposure to tobacco smoke and other environmental contaminants in addition to etiology-based management [14].

The present clinical practice guideline aims to address major clinical questions regarding, practical diagnostic tools for specific and nonspecific chronic coughs. Also, available therapeutic options for chronic cough in children are included.

Clinical Practice Guidelines (CPGs) are “statements involving recommendations aimed at improving patient care, informed by a systematic review of evidence and an evaluation of the benefits and harms of different healthcare options” [1]. CPGs have been acknowledged as one of the most significant tools for enhancing evidence-based healthcare quality and safety [15, 16].

In healthcare settings with limited resources, CPG adaptation is a viable and effective alternative to CPG development. The CPG produced for various healthcare contexts that reflected the local health system was encouraged to be trans-contextually customized to reduce duplicating of work and use the resources available effectively while avoiding time-wasting activities [17, 18].

The Egyptian Pediatric CPGs Committee (EPG) is the first national initiative to produce pediatric evidence-based CPGs that started in 2018 using one of the CPG formal adaptation methodologies: The Adapted ADAPTE [19].

Because there are currently no published CPGs for chronic cough in Egypt, the supplied evidence-based CPG is proposed as a National CPG using an evidence-based and formal CPG adaptation method.

The objective of this study was to adapt the recommendations from global high-quality CPGs for children with chronic cough to suit the health system and related services in Egypt.

## Methods

We used the ‘Adapted ADAPTE’ adaptation methodology consisting of three phases with modifications in the steps and tools to suit the local context in Egypt [15].

### Phase 1 (set up)

The EPG Pulmonology Group recognized persistent cough in children as the prioritized health topic for this CPG during phase 1. To find qualifying CPGs, an initial exploratory search for chronic cough CPGs was done.

The EPG Pulmonology Group Members who represent multiple Egyptian universities were chosen to form the Chronic Cough Guideline Adaptation Group (CCGAG). The selection of the CCGAG members was transparent and based on voluntary participation as all the EPG CPG projects are not associated with any financial funding or rewards. The clinical members of the CCGAG included both members with prior experience with CPG adaptation and new members. The CCGAG composition was multidisciplinary including physicians, academic faculty staff, consultant pediatricians, pulmonologists, and three CPG methodologists. The preliminary search results encouraged us to move forward with this adaptation project. Six sessions of capacity building on solutions of

evidence-based healthcare, including the CPG adaptation process methodology, were conducted by the CPG methodologists for new members of the CCGAG [18, 19].

The patient population for the adapted CPG is children with chronic cough. The identified target intended users included physicians, pediatricians, primary health care physicians (PHC), practitioners, nurses, and clinical pharmacists.

### Phase 2 (adaptation)

The CCGAG included 16 professors of pulmonology and pediatrics and a general pediatrician, two professors of child health, one clinical pharmacist, and one professor of tropical medicine and infectious disease with prior experience in the evidence-based CPG adaptation methodology.

The PIPOH model, inclusion, and exclusion criteria, and a thorough search strategy containing a list of keywords were used to identify specific health questions for clinical diagnosis, investigations, and therapy. The patient population (P), intervention(s) (I), professionals and clinical specialties (P), outcomes (O), and healthcare settings or context (H) are all part of the PIPOH. In addition to online libraries, we searched bibliographic (e.g., PubMed and Google Scholar) and CPG databases (e.g., Guidelines International Network Library and Registry, DynaMed, and WHO Guidelines).

The Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II) [20] was used to evaluate the eligible Source CPGs. AGREE II is the gold standard for assessing the quality of CPGs that consists of 23 items arranged into 6 domains. The CCGAG members reviewed and appraised three source original CPGs: the American College of Chest Physicians (ACCP) 2006–2020, the European Respiratory Society (ERS) 2019, the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) 2018. This phase concludes with the first draft of the adapted CPG.

In light of the findings of the AGREE II appraisal and comprehensive content evaluation of the source CPGs, members of the CCGAG agreed that the recommendations were clear and based on the most relevant scientific evidence, and they presented care options that could be applied to the local context and be acceptable to children with chronic cough, parents, and carers.

We opted not to perform additional evaluations of the certainty of the body of evidence and the strength of recommendation and instead relied on the high ratings of domain 3 (rigor of development) of the AGREE II appraisal and the evidence base behind the appraised source CPGs because this is one of the accepted choices for the decision of CPG adaptation to accept the evidence and recommendations from the source CPG(s) [16].

Additionally, the CCGAG selected, reviewed, and discussed each recommendation statement against the local healthcare system and context in Egypt through a series of 20 focus group discussions. The final stage of this phase was creating the initial draft of the adapted CPG.

### Phase 3 (finalization)

Phase 3 marked the completion of the first draft of the adapted CPG full document, which included an evaluation of the included recommendations for acceptability and applicability in the Egyptian healthcare system. A national panel of external reviewers comprising professional healthcare practitioners and subject matter clinical experts received and reviewed this adapted CPG draft. The CCGAG considered the reviewers' suggestions, which were incorporated into the finalized adapted CPG. A set of CPG implementation (CPGI) tools was included in the final CPG complete document.

Furthermore, our CCGAG chose to report the adapted Chronic cough CPG utilizing the items of the extension of the Reporting Items for Practice Guidelines in Healthcare (RIGHT) Statement for the reporting of adapted CPGs (i.e., the RIGHT-Ad@pt Tool) [21].

## Results

The total length of this CPG project was from December 2021 to August 2023. There were 20 online meetings for organizing, evaluating, and focus group discussions.

This work marks the fourth CPG adaptation project for the EPG Pulmonology Group using the 'Adapted ADAPTE' as a part of the EPG fourth wave of National CPGs [19].

### Phase 1 (set up)

The CCGAG was developed by a national group with clinical and methodological experience in December 2021. The required resources and abilities were identified and assigned. The CCGAG members all signed declarations of conflicts of interest.

The feasibility of the CPG adaptation procedure was established through a preliminary search for published CPGs. The CPG adaptation working plan template from the Adapted ADAPTE was used to draft and discuss the working plan from the outset [15, 22].

### Phase 2 (adaptation)

The PIPOH model was used in the identification of health questions. The 28 developed questions include 9 questions for clinical diagnosis, 10 questions for investigations, and 9 questions for treatment. Three source CPGs for evaluation, diagnosis, and treatment of chronic cough in children were studied.

According to the ratings of the AGREE II appraisal and in-depth content review, there was a consensus among the CCGAG members to adopt the American College of Chest Physicians (ACCP) 2006–2020 [2], European Respiratory Society (ERS) 2019 [23], Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) 2018 [24] to answer the 28 health questions posted. Other most relevant available evidence was searched for questions not answered within the chosen sources, providing its reference.

The details of AGREE II ratings of ACCP CPG, ERS CPG, and KAAACI CPG were included in the appendix of the supplement (Supplementary 2).

Health questions used to develop this adapted CPG and the summary recommendations are highlighted in Table 1.

For the first and second phases, a review and quality appraisal of the recently published clinical Diagnosis, investigations, and Treatment of Chronic cough in Children Source CPGs was conducted, which included the health questions, inclusion and exclusion criteria, CPG searching and screening results, in addition to the ratings and commentary of the AGREE II appraisal (Supplementary file 2).

The three source CPGs were reviewed and critically appraised including those developed by the American College of Chest Physicians (ACCP) 2006–2020, the European Respiratory Society (ERS) 2019, the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) 2018.

Afterward, we assessed the currency of the included CPGs to ensure the updated status of their recommendations and linked evidence base where no substantial evidence is expected to be released soon that might alter these recommendations.

The CCGAG reviewed and discussed the AGREE II assessment and decided to adopt all the recommendations of the three source CPGs.

Following multiple focus group discussions about CPGI facilitators and barriers, particularly with variable healthcare sectors, available medications, or healthcare provider positions, relevant customization of the recommendations was done.

The CCGAG decided to adopt the pathway of severity assessment and modify the two medication tables from relevant resources. New CPGI tools were provided by the CCGAG based on the adapted CPG: clinical algorithm for diagnosis, an educational slide set, investigations and treatment, patient education, and online resources (Fig. 1).

### Phase 3 (finalization)

Two external reviewers accepted our invitation to participate based on their expertise in managing children

with chronic coughs in addition to their representation of different healthcare sectors in Egypt. The external review comments were collated, revised, considered, and incorporated into the completed adapted CPG full document.

The EPG Pulmonology Group contacted all the Source CPG developers to request permission to adapt their CPGs to the Egyptian healthcare system.

A summary of recommendations is provided in the full CPG document (Table 1).

### Review and update of the adapted CPG

The CCGAG recommended the next review to be after 3 years of its publication after checking for updates in the Source CPG or possibly if a preponderance of published evidence will signal an earlier update of the recommendations.

### Guideline implementation strategies and tools

A set of CPGI tools was integrated into the adapted CPG full document (Fig. 1, and Supplement 1). Furthermore, CPGI strategies were suggested including (i) leadership participation and commitment, (ii) dissemination, (iii) clinical and quality champions, (iv) training and education, (v) audit and feedback, (vi) networking with current organizational programs, and (vi) patients as change advocates [29, 30].

### Facilitators and barriers to implementation

The EPG has identified several potential facilitators and barriers to the implementation of National Pediatric CPGs. These were reported in a separate article [19]. The CCGAG recommends widespread implementation of the GAHAR national standards and the WHO international guidelines for antibiotics stewardship programs.

### Discussion

Cough is a physiological reflex that protects the airways from noxious substances and clears excess secretions. The cough reflex consists of peripheral receptors in the pharynx, carina, bronchi, and bronchioles that send impulses through afferent nerves (vagus and glossopharyngeal nerves) to the cough receptors in the medulla oblongata that send orders to effector muscles (glottis and inspiratory and expiratory muscles) through efferent nerves (vagus, phrenic, and spinal motor nerves) [31]. Although cough is a spontaneous reflex, it is also under voluntary control from cortical and subcortical brain areas [32]. Continuous irritation of the airways leads to afferent signals that constantly activate the medullary cough center. Chronic cough causes could be intrathoracic (lungs parenchyma,

**Table 1** Health questions and key recommendations of the adapted CPG

N	Health questions In evaluating children aged ≤ 14 years with chronic cough:	Guideline	Recommendation statements	Level of evidence	Grade of recommendation
Q1	What is the value of estimating the duration of a cough?	ACCP 2020	For patients seeking medical care complaining of cough, clinicians suggest that estimating the duration of the cough is the first step in narrowing the list of potential diagnoses	C	(Grade 2)
Q2	Should history include specific cough pointers?	ACCP 2020	History should include cough characteristics and the associated clinical history such as using specific cough pointers like the presence of productive/wet cough	A	(Grade 1)
Q3	Should history include red flags?	GPP	History should include symptoms of red flags or other potentially life-threatening symptoms and if present, they should be immediately addressed and evaluated		Glashan and Mahmoud, 2019 [25]
Q4	What is the value of a detailed history to determine environmental exposure to respiratory irritants?	ERS 2019	Exposure to airborne irritants (e.g., tobacco exposure, combustions, traffic-related exposure), allergens, or infection may be a reason for dry chronic cough	EO	
Q5	Is history suggestive of OSA (mouth breathing, snoring, restless sleep, morning somnolence, daytime sleepiness, and poor academic achievement) important for the diagnosis?	Korean 2016	In unexplained or unresponsive chronic cough, obstructive sleep apnea should be included in the differential diagnosis	EO	
Q6	Is a history of drug intake important to evaluate cough?	ERS 2019	Detailed history of drug intake is needed including ACEI and other drugs such as bisphosphonates or calcium channel antagonists and prostanoid eye drops	EO	
Q7	What is the importance of clinical evaluation of upper airway cough syndrome due to a rhinosinus condition, gastroesophageal reflux disease, and/or asthma before starting any empiric therapy for these conditions?	ACCP 2020	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	A	(Grade 1)
Q8	8a- How to suspect asthma from history?	ACCP 2020	Diagnosis of asthma is suggested by the presence of risk factors and/or response to a short (2–4 weeks) therapeutic trial of 400 µg/day of beclomethasone equivalent may be warranted, and these children should be evaluated in 2–4 weeks		Ungraded Consensus-Based Statement
	8 b- How to suspect cough variant asthma by history?	ERS 2019 Korean 2016	Cough variant asthma (CVA) was originally described as asthma with cough as the sole symptom and where treatment with bronchodilators improved coughing	EO EO	
Q9	How to suspect TB by history?	ACCP 2020	Patients with cough with or without fever, night sweats, hemoptysis, weight loss, and/or contact with TB case and -who are at risk of pulmonary TB in a community high in TB prevalence	Consensus	

**Table 1** (continued)

N	Health questions In evaluating children aged ≤ 14 years with chronic cough:	Guideline	Recommendation statements	Level of evidence	Grade of recommendation
Investigations					
Q10	10a-Should the clinician recommend chest radiography? 10b- Should chest CT scan be routinely performed for children with normal physical examination and plain chest X-ray?	ACCP 2006–2020 ERS 2019	The clinician should recommend chest radiography The clinician should not routinely perform a chest CT scan in patients who have normal physical examinations and chest X-rays	B Very low	(Grade 1) Conditional recommendation
Q11	11a- When age is appropriate, should the clinician recommend spirometry (pre- and post-β2 agonist)? 11b- For children aged > 6 years and asthma is clinically suspected, should the clinician suggest a test for airway hyper-responsiveness? 11c- Should FeNO (if available)/blood eosinophil count be used in aiding the diagnosis or predicting the treatment response when asthma is clinically suspected?	ACCP 2006–2020 ACCP 2006–2020 ERS 2019	The clinician should recommend spirometry (pre- and post-β2 agonist) when age is appropriate The clinician should suggest a test for airway hyper-responsiveness (mannitol or methacholine inhalation) This recommendation places a relatively higher value on the predictability of the treatment response and the impact on the treatment decision	B C Very low	(Grade 1) (Grade 2)
Q12	Should the clinician perform additional tests (e.g., skin prick test, Mantoux, bronchoscopy, chest CT)?	ACCP 2006–2020	Clinicians should not routinely perform additional tests	B	(Grade 1)
Q13	Should the clinician suggest undertaking tests for evaluating recent Bordetella pertussis infection when pertussis is clinically suspected?	ACCP 2020	These should be individualized and undertaken according to the child's clinical symptoms and signs The clinician should suggest undertaking tests for evaluating recent Bordetella pertussis infection when pertussis is clinically suspected (if there is post-tussive vomiting, paroxysmal cough, or inspiratory whoop)	B	Ungraded Consensus-Based Statement
Q14	14a- Should the clinician suggest further investigations when a wet cough (unrelated to the underlying disease and with no specific cough pointers) persists after 4 weeks of appropriate antibiotics? 14b- Should the clinician recommend evaluation of immunologic competence for children with wet cough unrelated to underlying disease and with specific cough pointers?	ACCP 2006–2020 ACCP 2006	The clinician should suggest further investigations (e.g., flexible bronchoscopy with quantitative culture and sensitivity with or without chest CT assessment for aspiration) to be undertaken The clinician should recommend an evaluation of the immunologic competence in the presence of criteria suspicious of immunodeficiency (appendix) to assess for an underlying disease	B B	(Grade 1) (Grade 1)
Q15	For children with chronic productive purulent cough, do you recommend investigations to document the presence or absence of bronchiectasis?	ACCP 2012	In patients with suspected bronchiectasis without a characteristic chest radiograph finding, a high-resolution CT (HRCT) scan of the chest should be ordered because it is the diagnostic procedure of choice to confirm the diagnosis	Low	(Grade B)

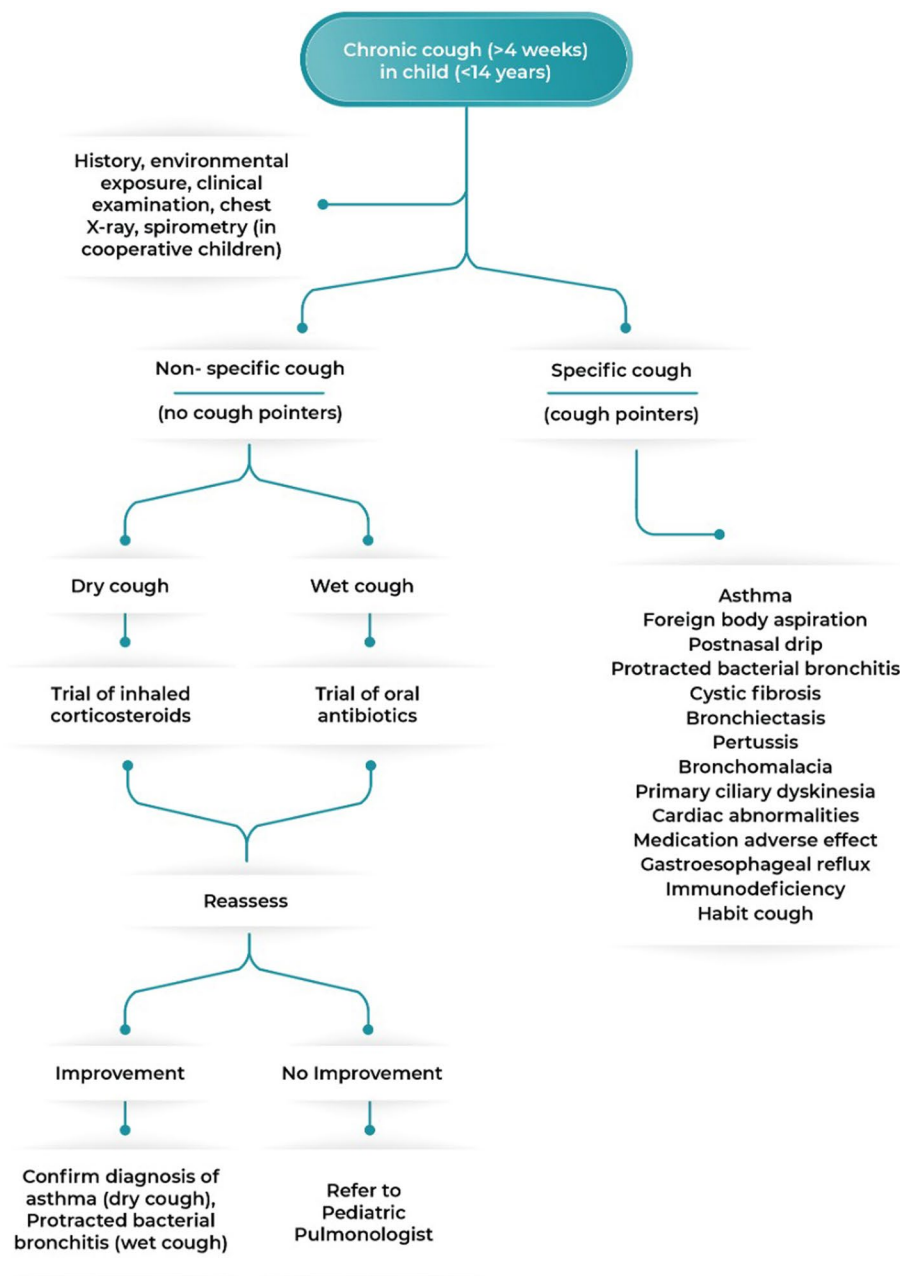
**Table 1** (continued)

N	Health questions In evaluating children aged ≤ 14 years with chronic cough:	Guideline	Recommendation statements	Level of evidence	Grade of recommendation
Q16	16a- In patients evaluated for GERD, what are the most sensitive and specific tests for the diagnosis?	ACCP 2006–2020	A 24-h esophageal pH monitoring test is the most sensitive and specific test	Low	(Grade B)
16b-	Is barium esophagography beneficial for diagnosing GERD as the cause of cough?	ACCP 2012	Barium esophagography may be beneficial. It can be considered if it is the only available test to reveal that GERD is of potential pathologic significance	Low	(Grade B)
16c-	In patients with suspected GERD, are the esophagography findings helpful to rule out GERD as the cause of cough?	ACCP 2012	A normal esophagography finding does not rule out GERD as the cause of the cough	Low	(Grade B)
Q17	17a- Should the clinician suggest screening for TB to patients in high TB prevalence countries or settings?	ACCP 2020	The clinician should suggest screening for TB regardless of cough duration	C	(Grade 2)
17b-	Should the clinician suggest an Xpert MTB/RIF test, when available, to replace sputum microscopy as an initial diagnostic test for patients with a high risk of pulmonary TB but a low risk of drug resistance?	ACCP 2020	The clinician should suggest an Xpert MTB/RIF test, when available, to replace sputum microscopy as an initial diagnostic test		Ungraded Consensus-Based Statement
Q18	For children with upper airway symptoms, should the clinician advise routine laryngoscopy, rhinoscopy, or CT sinuses?	GPP	In patients who report upper airway symptoms laryngoscopy, rhinoscopy or CT sinuses may be performed but not routinely		O'Hara and Jones 2006 [26]
Q19	For children with non-specific cough, if the cough does not resolve within 2 to 4 weeks, should the child be re-evaluated for the emergence of specific etiological pointers?	ACCP 2020	For children with non-specific cough, we suggest that if the cough does not resolve within 2 to 4 weeks, the child should be re-evaluated for the emergence of specific etiological pointers		Ungraded Consensus-Based Statement
Treatment					
Q20	21a- What is the recommended treatment for children aged > 6 years and < 14 years with clinically suspected asthma	ACCP 2020	When risk factors for asthma are present, a short (2–4 weeks) trial of 400 µg/day of beclomethasone equivalent, and re-evaluated	Fair	(Grade B)
21b-	Should asthma medications be used after acute viral bronchiolitis if the cough persists for more than 4 weeks?	ACCP 2020	Asthma medications should not be used for cough unless other evidence of asthma is present		Ungraded consensus-based statement
Q21	Should an empirical approach aiming at treating upper airway cough syndrome due to a rhinosinus condition, gastroesophageal reflux disease, or asthma be used?	ACCP 2020	1 - An empirical approach should not be used unless other features consistent with these conditions are present 2 - If an empirical trial is used, the trial should be of a defined limited duration to confirm or refute the hypothesized diagnosis	A	(Grade 1) Ungraded consensus-based statement 1

**Table 1** (continued)

N	Health questions In evaluating children aged ≤ 14 years with chronic cough:	Guideline	Recommendation statements	Level of evidence	Grade of recommendation
Q22	What are the recommendations for wet or productive cough unrelated to underlying disease and without any other specific cough pointers?	ACCP 2020	<p>1-Two weeks of antibiotics targeting the common respiratory bacteria (Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis) and depending on the local antibiotic sensitivities</p> <p>2- The diagnosis of PBB be made</p> <p>3- When the wet cough persists after 2 weeks of appropriate antibiotics, consider treatment with an additional 2 weeks of the appropriate antibiotic(s)</p> <p>4- When the wet cough persists after 4 weeks of appropriate antibiotics, further investigations as flexible bronchoscopy with quantitative cultures and sensitivities with or without chest CT) can be undertaken</p>	A C B B	(Grade 1) 4 (Grade 1) (Grade 2) (Grade 1)
Q23	What is the treatment in children without an underlying lung disease who have symptoms and signs or tests consistent with gastroesophageal pathological reflux?	ACCP 2020	<p>a) They can be treated for GERD according to evidence-based GERD-specific guidelines</p> <p>(b) Acid suppressive therapy should not be used solely for chronic cough</p>	B C	(Grade 1) (Grade 1)
Q24	What is the suggested treatment for a child diagnosed with somatic cough disorder?	ACCP 2020	<p>Non-pharmacological trials of hypnosis or Suggestion therapy or Reassurance and counseling or Referral to a psychologist or psychiatrist</p> <p>They are managed according to sleep guidelines</p>	C	(Grade 2)
Q25	For children suspected of having OSA, what is the management?	ACCP 2020			Ungraded consensus-based statement
Q26	Should histamine H1-receptor antagonists (H1RAs) be used to treat non-specific chronic coughs?	Korean 2019 GPP	<p>The use of H1RAs in children with non-specific cough must be balanced against well-known adverse events, especially in very young children</p> <p>ACCP is recommended against the empirical use of H1RAs in children with chronic cough unless other features consistent with upper airway cough syndrome due to rhinosinusitis are present</p>	Low	Conditional recommendation Chang et al. 2017 [27]
Q27	Should LTRAs be used to treat non-specific chronic coughs?	Korean 2019	<p>Careful considerations of cost, risk, and benefits are needed until there is sufficient data to determine the efficacy of LTRAs in these children</p>	Very low	Conditional recommendation
Q28	Should neuromodulators (opioids, gabapentin or pregabalin,) be used?	GPP	<p>Cough neuromodulators are not used in children due to reported adverse events, possible toxicity, and lack of clinical trials</p>		Gardiner et al. 2016 [28]





Management of chronic cough

**Fig. 1** Management of chronic cough

airways, pleura, mediastinum, cardiovascular system) or extrathoracic (head and neck especially nose and larynx, upper gastrointestinal tract, or central nervous system as somatic cough syndrome) [33]. Upper respiratory tract infections, bacterial infections, gastroesophageal reflux, and hyperactive airways are the most common causes of chronic cough [34, 35].

A chronic cough could be classified as a specific cough (with cough pointers) or a non-specific cough (without cough pointers) [36]. Non-specific cough could be further classified into dry or wet cough. Cough pointers help direct the diagnosis of specific cough, e.g., clearing the throat with or without other signs of nasal allergy suggesting upper airway disease (post-nasal drip, allergic

rhinitis, or sinusitis), wet cough with stunted growth and or clubbing suggesting cystic fibrosis, bronchiectasis or interstitial lung diseases; choking with feeding suggesting aspiration, and swallowing syndrome; brassy or barking cough suggesting tracheobronchomalacia, or airway compression; fever and weight loss suggesting tuberculosis; bizarre cough that disappears on sleeping suggesting somatic cough syndrome (tick cough); paroxysmal spasmodic cough along with vomiting or an inspiratory whoop suggesting pertussis or pertussis-like illness, staccato cough suggesting chlamydia infection, especially in infants [37].

Chung et al. 2022 used the term “cough hypersensitivity” to describe increased sensitivity of cough receptors, afferent nerves (vagal hypersensitivity), or cough centers to subthreshold stimulus leading to chronic non-specific cough. Also, Laryngeal dysfunction is hypersensitivity of the larynx to triggering stimuli that lead to vocal cord adduction during inspiration and inspiratory stridor, this is usually accompanied by the sensation of tickling and dry throat that triggers cough [32].

The Italian Society of Pediatric Allergy and Immunology and several guidelines [38] recommend the watchful waiting protocol for most cases of chronic dry cough as most of them are post-viral cough that resolves spontaneously, while others [36, 38] recommend doing chest X-rays and spirometry (if the child is cooperative) to avoid missing diagnoses as foreign body aspiration and airway hyperactivity, which is also our recommendation.

The best treatment of non-specific chronic cough in children is based on identifying the etiology of cough and its risk factors, especially environmental factors [32]. The American Academy of Pediatrics does not advocate cough and cold over-the-counter drugs in children younger than 6 years old since evidence-based recommendations have revealed that there are no effective medications to either cure or reduce the symptoms of cough in children [39]. Antibiotics do not affect viral infections, honey, herbal medicine, and fluids were tried in some studies [40].

For a chronic non-specific dry cough, we recommend a 2–4 weeks trial of daily 400 µg of beclomethasone equivalent and re-evaluate the response. The good response suggests airway hyperresponsiveness and asthma treatment should be started if a cough recurred. While in wet non-specific cough, we recommend 2 weeks of antibiotic treatment whereas *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are the most common respiratory pathogens, depending on local antibiotic sensitivity. If oral antibiotics are taken and the patient has a good response, PBB is diagnosed; however, if the wet cough persists after 2 weeks of the recommended antibiotics,

therapy with an additional 2 weeks of the recommended antibiotic(s) may be considered. After taking the recommended antibiotics for 4 weeks and the wet cough still exists, additional testing such as a flexible bronchoscopy with quantitative cultures and sensitivities, with or without a chest CT, can be done.

Speech therapy has also been successfully used in the treatment of somatic cough syndrome or non-specific cough. It includes patient education, vocal cord hygiene, cough suppression education, breathing patterns education, and behavioral modification that helps to distract the patient from the need to cough. Some guidelines suggest that patients with somatic cough syndrome may rarely require neuromodulating drugs [32], but we do not recommend them due to the possible side effects, and lack of clinical trials.

The goal of this study was to adapt global CPGs and their recommendations to the Egyptian healthcare setting for managing patients with chronic coughs across all local healthcare sectors.

The chronic cough CPG adaptation process demonstrates the essential capacity building, knowledge, skills, and hard effort that were critical to this endeavor both clinically and methodologically. The extended timetable observed in this CPG adaptation effort was not unique; we found it in other local CPG adaptation initiatives [41].

Furthermore, considering the scarcity of relevant high-quality randomized controlled trials, systematic reviews, and meta-analyses from the Egyptian setting, adapting CPGs for children with chronic cough is a good and valid alternative to constructing a CPG from scratch.

The use of the ‘Adapted ADAPTE’ method is a strength of this project because it is clearly structured and easy to follow along with a set of supportive tools and resources.

Determining the expected workload, resources, knowledge, and the need for dedicated leadership, project management, clinical, and methodological support according to the CCGAG’s experience, is consistent with published evidence. We addressed these requirements during phase 1 (set-up).

## Conclusions

The ‘Adapted ADAPTE’ is a rigorous and practical approach that was shown to be particularly practicable for national CPG projects when bundled with the AGREE II appraisal.

Our experience with this adaptation process presents invaluable knowledge of its national application in Egypt while also demonstrating its potential suitability for the region. Additional context-specific adaptation steps and tool modifications are recommended and encouraged in variable contexts [19].

## Implications for practice

The availability of a national chronic cough CPG is necessary but inadequate on its own to ensure ultimate healthcare standardization. The effectiveness of dissemination and implementation strategies, as well as other associated quality improvement and safety initiatives to support the delivery of relevant healthcare services, will determine its positive impact on children with chronic cough.

## Future research recommendations

We recommend further research and real-world evidence in the Egyptian context to inform the further review and update of this CPG's recommendations.

### Abbreviations

ACCP	American college of chest physicians
ACEI	Angiotensin-converting enzyme inhibitors
AFCM	Armed Forces College of Medicine
AGREE	Appraisal of Guidelines for Research and Evaluation
CCGAG	Chronic Cough Guideline Adaptation Group
CPGs	Clinical Practice Guidelines
CT	Computed tomography
CVA	Cough variant asthma
EBCPG	Evidence-Based Clinical Practice Guideline
EBM	Evidence-based medicine
EPG	Egyptian Pediatric Clinical Practice Guidelines Committee
ERS	European Respiratory Society
FeNO	Fractional exhaled nitric oxide
GER	Gastro-esophageal reflux
GERD	Gastro-esophageal reflux disease
GOR	Grade of Recommendation
H1Ras	Histamine 1-receptor antagonists
HRCT	High-resolution computed tomography
KAAACI	Korean Academy of Asthma, Allergy, and Clinical Immunology
LOE	Level of Evidence
LTRAs	Leukotriene receptor antagonists
MTB/RIF	Mycobacterium tuberculosis complex resistance to rifampicin
OSA	Obstructive sleep apnea
PHC	Primary health care
PBB	Protracted bacterial bronchitis
pH	Potential of hydrogen
PIPOH	Patients, Interventions, Professionals, Outcomes, Healthcare settings
QOL	Quality of life
RCT	Randomized controlled trial
TB	Tuberculosis

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43054-023-00244-0>.

**Additional file 1.** The EPG Chronic cough CPG Book.

**Additional file 2.** The slide set for educational material for professionals.

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### Authors' contributions

EMF, MHM, TH, HHS, DHH, ASM, SRI, ASM, and YSA have conceptualized and written the first draft of the manuscript and had the responsibility for the decision to submit it for publishing. YSA, AA, and TIO conceptualized the design. Members of the Chronic cough GAG included clinical experts (ASM, AIH, DHH, DTS, EMF, FGB, HGE, HHS, HMM, MHM, MAS, MMR, MME, NAK, SNB, SMH, TH, AA, TO, YSA), TH was the clinical chair. SRI designed the algorithm, and DHH prepared the PowerPoint presentation. All the clinical members of the Chronic Cough GAG selected the topic of the guideline, shared in searching and screening of data, AGREE II appraisal, putting health questions and formulation of adapted recommendation and CPGI tools, and finalization of the adapted full guideline document. AA, TO, and YSA were the CPG methodologists. Prof. Shreef Reda and Prof. Laila Abd El Ghafar were members of the external review group for the clinical content of the adapted CPG. All authors participated in the interpretation of the data, critically reviewed the manuscript, and participated in the editing and reviewing of the manuscript. All authors read and approved the final manuscript.

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### Availability of data and materials

Any relevant material in addition to future revisions and updates will be made available from the official website of the Egyptian Pediatric Clinical Practice Guidelines Committee (EPG) (<http://epg.edu.eg>) and by contacting guideline-committee@gmail.com.

### Declarations

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests. Conflict of interest declaration documents can be made available from the EPG upon request.

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