

# Management of acute cough: recommendations and evaluation of clinical guidelines according to AGREE II

Manejo da tosse aguda: recomendações e avaliação de diretrizes clínicas segundo o AGREE II Manejo de la tos aguda: recomendaciones y evaluación de las guías clínicas según AGREE II

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#### **Abstract**

Introduction: Cough is one of the main causes of demand for care in primary care, as it affects the patient's quality of life. An acute cough is considered a self-limiting problem because it is of low severity and has a short latency period. Objective: The aim of this study was to evaluate the quality of clinical guidelines (CGs) for the treatment of acute cough. Methods: Searches were carried out on the websites of national and international institutions and organizations using the descriptors "cough," "tos," "practice guideline," "guideline," and "guide of clinical practice." The selected guidelines were evaluated by four reviewers using the Appraisal of Guidelines for Research & Evaluation (AGREE II) instrument, and then, they were classified as strongly recommended, recommended with modifications, and non-recommended. Results: A total of 11 international guidelines were selected, published between 2006 and 2019, most from the United States of America. A total of seven guidelines were specific to the treatment of acute cough, only one guideline was focused on pharmaceutical care, and six were focused on the treatment of adults and children. Scope and purpose were the domains that presented the best score; editorial independence (D6) had the highest score variation (0-98%); and applicability (D5) of guidelines had the lowest mean score, 46% (range 2-88%). Regarding interventions, most of the guidelines referred to pharmacological interventions as unnecessary and the most cited non-pharmacological intervention was menthol (ointment). Conclusions: Therefore, it is necessary to carry out more clinical studies of good quality so that the CGs can be revised, to make the recommendations more reliable.

Keywords: Quality of health care; Evidence-based practice; Clinical practice guidelines; Cough.

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Funding:

not applicable.

Ethical approval:

not applicable.

Informed Consent Form:

not applicable.

Provenace:

not commissioned.

Associate Editor:

Leonardo Ferreira Fontenelle

Peer review:

external.

Received: 10/17/2023. Approved: 03/05/2025.

**How to cite:** Winck LM, Boechat MM, Alves BMCS, Barros DSL, Lima RF, Reis TM, et al. Management of acute cough: recommendations and evaluation of clinical guidelines according to agree II. Rev Bras Med Fam Comunidade. 2025;20(47):3991. https://doi.org/10.5712/rbmfc20(47)3991



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#### Resumo

Introdução: A tosse é uma das principais causas de procura de atendimento na atenção primária, pois afeta a qualidade de vida do paciente. A tosse aguda é considerada um problema autolimitado, por ser de baixa gravidade e ter curto período de latência. Objetivo: Avaliar a qualidade das diretrizes clínicas (DCs) para o tratamento da tosse aguda. Métodos: Foram realizadas buscas em sites de instituições e organizações nacionais e internacionais utilizando os descritores "cough", "tos", "practice guideline", "guideline" e "guide of clinical practice". As diretrizes selecionadas foram avaliadas por quatro revisores por meio do instrumento Appraisal of Guidelines for Research & Evaluation (AGREEII) e, em seguida, classificadas como fortemente recomendadas, recomendadas com modificações ou não recomendadas. Resultados: Foram selecionadas onze diretrizes internacionais, publicadas entre 2006 e 2019, sendo a maioria originária dos Estados Unidos. Sete diretrizes eram específicas para o tratamento da tosse aguda, apenas uma diretriz era voltada para a atenção farmacêutica e seis eram voltadas para o tratamento de adultos e crianças. Os domínios "escopo e propósito" apresentaram as melhores pontuações; o domínio "independência editorial" (D6) teve a maior variação de pontuação (0–98%); e a "aplicabilidade" (D5) obteve a menor média de pontuação, com 46% (variação de 2–88%). Em relação às intervenções, a maioria das diretrizes considerou desnecessárias as intervenções farmacológicas, sendo o mentol (pomada) a intervenção não farmacológica mais citada. Conclusões: Torna-se necessário realizar mais estudos clínicos de boa qualidade para que as diretrizes clínicas possam ser revisadas, tornando as recomendações mais confiáveis.

Palavras-chave: Qualidade dos cuidados de saúde; Prática baseada em evidências; Diretrizes de prática clínica; Tosse.

#### Resumen

Introducción: La tos es una de las principales causas de demanda de atención en la atención primaria, ya que afecta la calidad de vida del paciente. La tos aguda se considera un problema autolimitado por su baja gravedad y corto período de latencia. Objetivo: Evaluar la calidad de las guías clínicas (GC) para el tratamiento de la tos aguda. Métodos: Se realizaron búsquedas en sitios web de instituciones y organizaciones nacionales e internacionales utilizando los descriptores "cough", "tos", "practice guideline", "guideline" y "guide of clinical practice". Las guías seleccionadas fueron evaluadas por cuatro revisores utilizando el instrumento Appraisal of Guidelines for Research & Evaluation (AGREEII), y luego se clasificadas como fuertemente recomendadas, recomendadas con modificaciones o no recomendadas. Resultados: Se seleccionaron once guías internacionales publicadas entre 2006 y 2019, la mayoría provenientes de los Estados Unidos. Siete directrices eran específicas para el tratamiento de la tos aguda, solo una se centraba en la atención farmacéutica y seis se centraban en el tratamiento en adultos y niños. Los dominios de alcance y propósito presentaron los mejores puntajes; independencia editorial (D6) tuvo la mayor variación de puntuación (0–98%); y la aplicabilidad (D5) fue el dominio con el puntaje promedio más bajo, 46% (rango del 2–88%). En cuanto a las intervenciones, la mayoría de las directrices se refirieron a las intervenciones farmacológicas como innecesarias y la intervención no farmacológica más citada fue el mentol (ungüento). Conclusiones: Por lo tanto, es necesario realizar más estudios clínicos de buena calidad para que las guías clínicas puedan ser revisadas, con el fin de hacer que sus recomendaciones sean más confiables.

Palabras claves: Calidad de la atención sanitaria; Práctica basada en evidencia; Guías de práctica clínica; Tos.

# INTRODUCTION

Cough is a common symptom in several health problems and can be classified as acute, subacute, and chronic, depending on the duration. Acute cough improves in less than 3 weeks, subacute cough lasts between 3 and 8 weeks, and chronic cough persists for more than 8 weeks. Some guidelines classify cough only as acute and chronic, lasting up to 8 weeks and more than 8 weeks, respectively. It was agreed in this study that acute cough would be that lasting up to 3 weeks, according to the classification in the scientific literature based on evidence. For

In Jiang's study, it was found that cough is one of the main causes of seeking advice in primary care, as it changes the patient's routine and, consequently, his quality of life.<sup>8,9</sup> Cough is associated with sleep disturbances, irritability, throat irritation, tiredness, and pain in the abdomen and chest, due to the strong contraction performed by the muscles to expel the foreign body from the airways, in addition to anxiety from a serious underlying illness.<sup>10</sup> It is also noted that coughing can have a socioeconomic impact due to higher expenses with health technologies and services, as well as being responsible for a decrease in professional performance and an increase in absenteeism at work and at school.<sup>2,10-13</sup>

To ensure quality healthcare, it is necessary for healthcare professionals to have up-to-date knowledge about acute cough and be able to identify cases associated with self-limiting disorders, differentiating them from more complex problems and offering the best treatment options based on evidence. In this context, clinical guidelines (CGs) that assist in decision-making and aim to standardize the correct approach to managing diffuse complaints, such as respiratory disorders, play a crucial role I6

However, it is important to note that the treatment of acute cough can sometimes be controversial. The therapeutic approach may vary depending on the adopted CGs, as well as the individual characteristics of the patient. Some studies may provide conflicting or limited evidence regarding the different medications and interventions available for the treatment of acute cough.<sup>17</sup> This can lead to debates and discussions among healthcare professionals about the best approach to be taken in specific cases.<sup>9-17</sup> The aim of this study was to analyze the main pharmacological and non-pharmacological interventions most recommended by CGs for the treatment of acute cough while also assessing their methodological quality.

## **METHODS**

# Searches for guidelines

Searches were carried out on the websites of national and international institutions and organizations, such as the American College for Chest Physicians (CHEST), the National Institute for Health Care Excellence (NICE), and the National Commission for the Incorporation of Health Technologies in the SUS (CONITEC), between August 2019 and January 2020. The DeCS/MeSH descriptors were used: "cough," "tos," "practice guideline," "guideline," and "guide of clinical practice." Other terms that were also used in the search process included non-DeCS/MeSH descriptors commonly used in the literature: "self-limiting cough," "acute cough," "clinical guideline," "guidance," "clinical guidelines," "self-limiting health problems," and "self-limiting illness."

# Selection of guidelines

Guidelines that presented treatment recommendations for acute cough were included. The symptoms of cough with a short latency period stand out. Guidelines aimed at the management of chronic cough, cough associated with acute asthma exacerbation or chronic obstructive pulmonary disease (COPD), tuberculosis (TB), and other presentations in respiratory symptomatic patients were excluded.

Guidelines published in languages other than Portuguese, English, and Spanish, and guidelines with a specific population, such as athletes, were excluded. The publication date of the documents was not an exclusion criterion, due to the small number of guidelines available for the treatment of acute cough. The selection was carried out independently by two reviewers.

## **Evaluation of the guidelines by the AGREE II instrument**

The selected guidelines were independently assessed by four reviewers, using the Appraisal of Guidelines for Research & Evaluation (AGREE II) instrument, which aims to assess the quality of

CGs, provide a methodological strategy for their development, and inform how the information must be reported, in addition to being able to be used to assess guidelines for any disease and at any stage of healthcare.<sup>17,18</sup>

AGREE II is organized into 23 items categorized into six domains and two items of global assessment, which indicates the general quality of the guideline and whether it can be recommended or not for use. Each domain in the AGREE II instrument evaluates a single dimension of the quality of the guideline, which are: Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, and Editorial Independence. The selected guidelines were classified according to the AGREE II domains based on the calculation of the average scores, with a weight of 2 for the domains of Applicability and Rigor in Development. Three categories were used for classification: for scores >60%, the guidelines were classified as strongly recommended, guidelines with scores between 30 and 60% were classified as recommended with modifications, and results lower than 30% referred to a classification of non-recommendation of the guideline. 17,18

# Statistical analysis of agreement by Kappa method

Statistical analysis of the degree of agreement makes the classification more reliable.<sup>19</sup> In this study, the Fleiss' Kappa (K) concordance test was used to measure the degree of agreement among the four evaluators in assessing the quality of each CG for the treatment of acute cough. Fleiss' Kappa is an extension of Cohen's Kappa that allows for the calculation of agreement among multiple raters.<sup>17,18</sup>

The maximum value of Kappa is 1, which means that the closer to 1, the greater the agreement between judges. On the other hand, the closer to 0, the greater the disagreement between the judges or agreement by chance. Negative values mean that the agreement was lower than expected by chance. The present study obtained a moderate degree of agreement (K=0.44).

#### RESULTS

#### General characteristics of the guidelines

A total of 11 international guidelines were selected, published between 2006 and 2019, of which one was from China, <sup>19</sup> one from Spain, <sup>20</sup> two from Germany, <sup>2,21</sup> three from the United Kingdom, <sup>4,7,25</sup> and four from the United States. <sup>23,24,26,27</sup> A total of seven guidelines were specific to the treatment of acute cough, only one guideline was focused on pharmaceutical care, and six were focused on the treatment of adults and children. Of the 11 guidelines, 2 were consensus-based, and the other 9 guidelines were evidence-based. For the selection of the guidelines, there was no choice of a specific population; adults and children affected by acute cough entered the selection criteria. Chart 1<sup>2,4,7,19,20,21,23-27</sup>, presents the main characteristics of each guideline.

#### General assessment of the quality of the guidelines

Comparing the scores by domain, among the CGs, Scope and Purpose (D1) was the domain that presented the best score and the only one that reached 100%, and Editorial Independence (D6)

Chart 1. General characteristics of each clinical guideline (CG) for acute cough.

CG	Clinical guideline	Year	Issuing company	Country	Target population	Cough type	Development method	Classification system	
CG1	Clinical Practice Guidelines for Diagnosis and Management of Cough-Chinese Thoracic Society (CTS) asthma consortium <sup>19</sup>	2018	стѕ	China	Adult Child	Acute Subacute Chronic	Evidence	GRADE	
CG2	Cough (acute): antimicrobial prescribing <sup>7</sup>	2019	NICE	UK	Adult Child	Acute	Evidence	GRADE	
CG3	Cough and the common cold <sup>26</sup>	2006	CHEST	USA	Adult	Acute	Evidence	CHEST	
CG4	Cough suppressant and pharmacologic protussive therapy: ACCP evidence-based clinical practice guidelines <sup>23</sup>	2006	CHEST	USA	Adult	Acute* Chronic	Evidence	CHEST	
CG5	Diagnosis and management of cough executive summary: ACCP evidence- based clinical practice guidelines <sup>27</sup>	2006	CHEST	USA	Adult Child	Acute Subacute Chronic	Evidence	CHEST	
CG6	Guidelines of the German Respiratory Society for diagnosis and treatment of adults suffering from acute, subacute and chronic cough <sup>2</sup>	2019	GRS	Germany	Adult	Acute Chronic	Evidence	GRADE	
CG7	Pharmacologic and nonpharmacologic treatment for acute cough associated with the common cold: CHEST Expert Panel Report <sup>24</sup>	2017	CHEST	USA	Adult Child	Acute	Evidence	CHEST	
CG8	Protocolos de indicación farmacéutica y criterios de derivación al médico en síntomas menores <sup>19</sup>	2008	semFYC	Spain	Adult	Acute	Consensus	-	
CG9	Recommendations for the management of cough in adults <sup>4</sup>	2006	BTS	UK	Adult	Acute	Consensus	-	
CG10	Respiratory tract infections (selflimiting): prescribing antibiotics <sup>25</sup>	2017	NICE	UK	Adult Child	Acute	Evidence	GRADE	
CG11	Diagnoseund therapie des akuten hustens bei erwachsenen <sup>21</sup>	2014	DEGAM	Germany	Adult	Acute	Evidence	GRADE	

Legend: CTS: Chinese Thoracic Society; NICE: National Institute for Health and Care Excellence; CHEST: American College of Chest Physicians; GRS: German Respiratory Society; semFYC: Sociedad Española de Medicina de Familia y Comunitaria; BTS: British Thoracic Society; DEGAM: German College of General Practitioners and Family Physicians; GRADE: Grading of Recommendations Assessment, Development and Evaluation.

<sup>\*</sup>The guideline is aimed at the treatment of chronic cough, but aspects of the treatment of acute cough were discussed, so it was included in the study.

presented the worst score (0%), in the two guidelines. Editorial Independence (D6) had the highest score variation (0–98%), and Clarity of Presentation (D4) had the lowest variation (75–93%). Applicability (D5) of Guidelines had the lowest mean score, 46% (range 2–88%). The score for each domain of the CGs for cough is shown in Table 1.

**Table 1.** General characteristics of each clinical guideline (CG) for acute cough.

Clinical guideline	Scope and Purpose (%)	Stakeholder Engagement (%)	Development Rigor (%)	Clarity of Presentation (%)	Applicability (%)	Editorial Independence (%)	Classification		
CG1 94.0 85.0		85.0	95.0	93.0	85.0	90.0	Strongly recommended		
CG2	100.0	85.0	80.0	82.0	85.0	63.0	Strongly recommended		
CG3	67.0	8.0	40.0	75.0	2.0	2.0	Recommended with modifications		
CG4	67.0	18.0	51.0	83.0	3.0	0.0	Recommended with modifications		
CG5	81.0	56.0	78.0	89.0	17.0	8.0	Recommended with modifications		
CG6	90.0	79.0	43.0	92.0	24.0	92.0	Strongly recommended		
CG7	93.0	67.0	92.0	92.0	39.0	96.0	Strongly recommended		
CG8	92.0	65.0	24.0	75.0	23.0	0.0	Recommended with modifications		
CG9	93.0	81.0	85.0	89.0	71.0	98.0	Strongly recommended		
CG10	94.0	93.0	98.0	90.0	88.0	58.0	Strongly recommended		
CG11	97.0	81.0	79.0	88.0	55.0	96.0	Strongly recommended		
Average	88.0	65.3	69.5	86.2	44.7	54.8	-		

#### Evaluation by domain

In the domain of Scope and Purpose, the clarity with which the general and specific objectives of the guidelines are presented was evaluated, as well as the target population and which health problem the guideline is directed toward<sup>1,16,29</sup>. This domain had the highest scores, ranging from 67 to 100%, with the CG Cough (acute): antimicrobial prescribing being the best evaluated (100%)<sup>7</sup>. The two guidelines that received the lowest scores were Cough Suppressant and Pharmacologic Protussive Therapy<sup>23,26</sup> and Cough and the Common Cold, as both did not specifically define the target population.

The domain of Stakeholder Involvement analyzes those responsible for developing the guidelines, including the opinion of the target population, and assesses whether the target users are well defined 1,17,18. The results of this domain were discrepant between the documents, as the scores ranged from 8 to 93%, corresponding, respectively, to the Cough and the Common Cold and Respiratory Tract Infections —

Antibiotic Prescribing: Prescribing of Antibiotics for Self-Limiting Respiratory Tract Infections in Adults and Children in Primary Care. 7,22,24

In general, it was observed that the deficits in the domain of Stakeholder Involvement were mainly related to the lack of information about the opinions and experiences of the target population.<sup>1,17,18</sup> Another important point is that the Cough and the Common Cold (8%) and Cough Suppressant and Pharmacologic Protussive Therapy (18%) guidelines were prepared by only one professional, a pulmonologist and a physiologist, respectively.<sup>23,26</sup>

The clarity with which the recommendations are presented, without ambiguous recommendations, and whether the key recommendations are easily identified by the reader, in addition to assessing whether there are other treatment options for the presented health problem, are evaluated in the domain of Clarity of Presentation. It was the second domain with the highest scores, ranging from 75 to 93%. In general, the recommendations were written in simple and easy-to-understand language, and most guidelines addressed other aspects of the clinical issue.<sup>1,17,18</sup>

The domain Applicability assesses which factors facilitate or hinder the implementation of the guideline in practice if there is advice on how to overcome these barriers and which costs are related to the application of the recommendations. This section also observes the guideline implementation criteria and the impact of the recommendations. This was the domain with the lowest average score (44.7%), demonstrating that there was no discussion of methods to overcome the barriers to implementing the recommendations, especially the discussion of resources needed.

In the domain of Editorial Independence, whether the conflicts of interest of the professionals who prepared the guideline are declared, as well as a statement that the funding agency did not influence the recommendations, is evaluated.<sup>14</sup> This domain obtained the most discrepant scores, with a variation between 0 and 98%. Some guidelines did not mention their funding bodies or their conflicts of interest and in others, they were not declared directly, demonstrating a lack of transparency. Conflicts of interest are a key issue to indicate the impartiality and reliability of recommendations.<sup>17,18</sup>

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) recommendation classification system was used by four guidelines. The guidelines developed by CHEST and NICE used their recommendation rating system; however, the NICE guidelines do not clearly show the degree of recommendation and level of evidence.<sup>7,17,18,23,26</sup>

The Spanish guideline Protocols de Indicación Farmacéutica y Criterios de Derivación al Médico in Minor Symptoms<sup>20</sup> was based on consensus and a recommendation classification system was not presented.

Chart 2 shows the pharmacological and non-pharmacological interventions addressed in each guideline. For the construction of the charts, only the recommendations made for the treatment of acute cough were considered, which can be handled by the pharmacist, and the recommendations made for subacute and chronic cough were not considered.

#### DISCUSSION

The Cough Suppressant and Pharmacologic Protussive Therapy guideline<sup>27</sup> did not clearly define the health issue that would be discussed, as it was initially mentioned as a guideline directed toward the treatment of chronic cough; however, several treatment recommendations were made for acute cough.

Chart 2. Summary of pharmacological and non-pharmacological interventions addressed in each guideline.

Clinical guideline	Pharmacological interventions															Non-pharmacological interventions						
	Unnecessary	Dextromethorphan	Clobutinol	Cloperastine	Levodropropizine	Dropropizine	Bromhexine	Ambroxol	Acetylcysteine	Carbocysteine	Guaifenesin	Antibiotics	lvy, Primrose, and Thyme	Andrographis paniculata	Pelargonium	Echinacea	Fluid intake	Steam inhalation	Menthol (ointment)	Vitamin C	Zinc	Honey
CG1	Yes	Yes	-	-	-	_	Yes	Yes	Yes	Yes	Yes	No	-	-	-	-	-	-	Yes	-	-	-
CG2	Yes	Yes	-	-	-	-	-	-	No	No	Yes	No	In	In	In	In	-	-	-	-	-	Yes
CG3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	In	-
CG4	Yes	In	-	-	Yes	-	-	-	-	-	In	-	-	-	-	-	-	-	-	-	No	-
CG5	Yes	-	-	-	-	-	-	-	-	-	-	No	-	-	-	-	-	-	-	-	No	-
CG6	-	In	-	-	-	-	-	In	In	-	In	No	Yes	-	-	-	-	-	-	-	-	In
CG7	Yes	In	-	-	-	-	In	-	In	In	In	-	-	-	-	-	-	-	Yes	-	In	Yes
CG8	Yes	Yes	-	-	-	-	-	-	-	-	-	No	-	-	-	-	Yes	-	-	-	-	-
CG9	Yes	In	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	-	-	Yes
CG10	-	-	-	-	-	-	-	-	-	-	-	No	-	-	-	-	-	-	-	-	-	-
CG11	Yes	-	-	-	-	-	-	-	-	-	-	No					Yes	In	In	No	No	-

Yes: recommended use; No: use not recommended; - Not mentioned; In: Inconclusive.

Most of the guidelines were unable to formulate clear recommendations for each intervention, due to lack of evidence and/or low-quality evidence, with four<sup>2,4,23,24</sup> guidelines considering some of their results as inconclusive for pharmacological recommendations and five<sup>7,21,24,26</sup> guidelines considering some non-pharmacological recommendations inconclusive. A total of eight CGs<sup>4,7,19,20,23,24,27</sup> concluded that no intervention is necessary, as there is a natural remission. In many cases, analyses and pharmacological recommendations were made for the class of drugs and not for the specific drug, which is not advantageous for clinical practice, as the efficacy and safety of each drug must be discussed separately.

The Scope of Purpose domain had the highest average recommendation by the AGREE II instrument for clearly defining the general and specific objectives of the guidelines and the target population, even if not specific, and for identifying which health problem the guideline is directed toward. The CG Cough (acute): antimicrobial prescribing had the highest score, proving that the use of antimicrobials is erroneous.<sup>7</sup>

The Stakeholder Engagement domain, despite a high average of 67%, showed a high discrepancy between CGs 3 (Cough and the Common Cold) and 10 (Respiratory Tract Infections — Antibiotic Prescribing: Prescribing of Antibiotics for Self-Limiting Respiratory Tract Infections in Adults and Children in Primary Care). This confirms that pharmacological measures are not necessary for the management of acute cough, nor is antimicrobial therapy.<sup>7,24</sup>

The Rigor and Development domain already had a higher average, with 71% of approval being strongly recommended by the CGs; however, there was little discussion about the revision of the guidelines and updating extremely important methods since most of the guidelines have already been published for more than 10 years and although there are still deficits in the evidence regarding pharmacological and non-pharmacological treatments for acute cough, some recommendations need to be revised.<sup>1,18,29</sup>

The Clarity of Presentation domain obtained the second highest mean of high recommendation by the CGs, with the alignment of the recommendations of the most reliable forms of acute cough management according to the guidelines, with little discrepancy between them. The Applicability domain had a lower average recommendation by the CGs, and the Stakeholder Engagement domain had discrepancies between the CGs 3, with only 2%, and 4 without recommendations and the CG1<sup>24</sup> with 85% recommendation. It has been stated that non-pharmacological measures are first-line treatment. 18,29

The Editorial Independence domain had the greatest discrepancy between CF 8<sup>20</sup> and clinical guideline 9,<sup>4</sup> demonstrating conflicts of interest between the measures recommended by the CGs. This makes their practices unreliable and also the sample of the target population, which, in addition to not being specific, does not seek health professionals for correct guidance on symptom relief.<sup>1,17,18,29</sup>

According to the British Thoracic Society, no classification system was used in the elaboration of its guideline because it considers the recommendations to be arbitrary, due to the generally low level of evidence. Therefore, the recommendations were made based on the available evidence, and, when necessary, on the clinical experience of the members of the guideline drafting group.<sup>7,24</sup>

However, non-pharmacological measures were recommended as first-line treatment. Honey (for children over 3 years of age), avoiding exposure to secondhand smoke, and avoiding exposure to cough triggers are the safest recommendations for children with acute cough. For adults, smoking cessation and not exposing yourself to factors that trigger coughing are the main recommendations of CGs.<sup>4,7,19,20,23,25,28,29</sup>

These are measures that during the symptoms of acute cough bring comfort to the patient, especially in respiratory complications. They improve the quality of life and help stop the symptoms of acute cough more quickly.

Malesker's criteria consider that even without evident advances in treatment, having been pointed out in the data of his clinical trials in his 2006 update, dozens of pharmacological and non-pharmacological treatment options are found today. They may be available as monotherapy or combined therapy, as shown in Charts 2 and 3.25

According to the guidelines, it is recommended that after a post-viral infection, cough may not require antibacterial treatments.<sup>7,24</sup> For patients with severe cough, antitussives, antihistamines, and decongestants are recommended for short-term use. Over-the-counter cough medicines containing the expectorant guaifenesin (in people aged 12 years and over) are recommended to comfort symptoms only when it affects the quality of life.<sup>7,19</sup> Pelargonium (an herbal medicine; in people aged 12 years and over) is recommended as safe management to comfort cough symptoms.<sup>30</sup>

Non-pharmacological measures like honey and fluid intake were strongly recommended by the CGs as first-line treatment because of the low severity and short latency period. The Food and Drug Administration (FDA), the health regulatory agency of the United States, has approved pharmacological measures for the treatment of cough. However, these are mostly new combinations of previously approved products. In addition, concerns about drug safety have led to recommendations regarding the use of some products in specific populations.<sup>25,28,29</sup>

## CONCLUSION

In general, the guidelines showed quality failures, mainly in the areas of "Stakeholder Involvement," "Development Rigor," "Applicability," and "Editorial Independence," in which there were scores below 50%. There was consensus that the use of pharmacological therapy is not necessary for the treatment

of acute cough. But, it is important to emphasize that the evidence is not clear enough to recommend a specific drug since the clinical studies presented by the guidelines showed that most of the results did not obtain significant differences between the placebo and the drugs, in addition to flaws in the methodological development of studies.

Antibiotics are not recommended for treating acute cough, as they have not demonstrated effectiveness in alleviating symptoms of self-limiting conditions. Moreover, their indiscriminate use can lead to adverse reactions and contribute to the development of antibiotic resistance.

Non-pharmacological measures have been recommended as first-line treatment for acute cough and should be the first choice. The best recommended non-pharmacological measure according to the guidelines would be passive smoking cessation for children and active and passive smoking cessation for adults.

This study has some limitations that should be considered. First, the selection of CGs was based on availability in specific institutional and organizational databases, which may have excluded relevant guidelines published in other sources. Additionally, although the AGREE II instrument is widely used to assess the methodological quality of guidelines, it does not directly measure the effectiveness of recommendations in clinical practice. Finally, the analyzed guidelines varied significantly in scope and methodology, making direct comparisons between them challenging. These limitations should be taken into account when interpreting the results of this study.

Since cough is a symptom of multiple health conditions, there may be challenges in diagnosis and confusion regarding treatment recommendations, which can impact patients' quality of life. Therefore, further high-quality clinical studies are needed to strengthen the evidence base, allowing for guideline updates that provide clearer and more reliable recommendations. Additionally, incorporating patient perspectives is essential to expand the knowledge base on the safety and effectiveness of both pharmacological and non-pharmacological therapies.

## **CONFLICT OF INTERESTS**

Nothing to declare.

## **AUTHORS' CONTRIBUTIONS**

LMW: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft. MMB: Data curation, Formal analysis, Investigation, Writing – original draft. BMCSA: Data curation, Formal analysis, Investigation, Writing – review & editing. DSLB: Data curation, Formal analysis, Methodology, Writing – review & editing. RFL: Data curation, Formal Analysis, Methodology, Writing – review & editing. RSS: Conceptualization, Investigation, Methodology, Supervision, Validation.

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