THE MANAGEMENT OF CHRONIC COUGH

THE PRACTICE OF MANAGING CHRONIC COUGH

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment for the Requirements for the Degree of Master of Science

MASTER OF SCIENCE (2022) (Rehabilitation Science)	McMaster University
TITLE:	The Practice of Managing Chronic Cough
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NUMBER OF PAGES:	X, 127

ABSRACT

This thesis focuses on chronic cough topics, in both the general population and those with chronic respiratory diseases. Study one consists of a systematic review in which the primary aim was to summarize the effect of non-pharmacological therapies on cough-specific quality of life in individuals with and without chronic respiratory diseases. For study two, we conducted a nationwide survey study, which was administered to healthcare providers working in pulmonary rehabilitation (PR) facilities. Given that education was a common component in non-pharmacological interventions, seen in study one, the overall goal of study two was to determine whether chronic cough is assessed and/or managed within PR, as education is also a foundational pillar in PR. The implications of this work seek to inform healthcare providers of alternative chronic cough management therapies, by bringing awareness to the importance of conducting formal cough assessment and management in PR.

ACKNOWLEDGEMENTS

Over the course of my degree, I have had the opportunity to get to know many wonderful people in the Rehabilitation Sciences program. I am truly appreciative of everyone I have met along the way, as you have all played a part in the completion of my MSc degree.

I would like to deeply thank my supervisor, Dr. Dina Brooks, who's continuous guidance, support, and encouragement made this degree possible. I also truly grateful for you agreeing to take me under your wing as a graduate student. You are a kind, selfless, and caring individual who continues to inspire me and whom I admire deeply. I continue to be amazed at all your accomplishments and brilliance.

I thank my wonderful supervisory committee, Dr. Michelle Kho, and Dr. Roger Goldstein, who's insights and thoughtful advice helped push my work forward. Your perspectives and in-depth knowledge of the field not only improved the quality of my work but allowed me to grow my knowledge and skills.

I gratefully would also like to thank my exceptional mentor, Dr. Ana Oliveira. Thank you for your offering hours of your time and for being patient with me throughout my degree. Under your mentorship and guidance, you pushed me to enhance my strengths, as well as continue to encourage me to push my capabilities to new heights.

Lastly, I am deeply grateful for all the support and encouragement I receive from my parents, Iva, and Josip. I thank you for continuing to push me towards achieving my goals and dreams. Without you, I would not be where I am today, nor who I am today.

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LIST OF ABBREVIATIONS

ACE - Angiotensin-converting enzyme
ACT - Airway Clearance Techniques
ATS - American Thoracic Society
BCT - Behavioural cough therapy
CAPE-V - Consensus of Auditory-Perceptual Evaluation of Voice
CC - Chronic Cough
CCT - Cough control therapy
CINAHL - Cumulative Index of Nursing and Allied Health Literature
COPD - Chronic obstructive pulmonary disease
ERS - European Respiratory Society
GERD - Gastroesophageal reflux disease
HADS - Hospital Anxiety and Depression scale
HiREB - Hamilton Integrated Research Ethics Board
HR-QOL - Health-related quality of life
ILD - Interstitial lung disease
LCM – Leicester Cough Monitor
LCQ - Leicester Cough Questionnaire
MD - Mean differences
MESH - Medical subject heading
OSA - Obstructive sleep apnea
OTC - Over-the-counter
PNDS - Postnasal drip syndrome
PR - Pulmonary Rehabilitation
PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PSALTI - Physiotherapy Speech and Language Therapy Intervention
PVFM - Paradoxical vocal fold movement
RCT - Randomized Control Trial
RoB - Risk-of-Bias
SD - Standard deviation
UACS - Upper airway cough syndrome
VAS - Visual Analogue Scale

CHAPTER 1

1.1 INTRODUCTION AND LITERATURE REVIEW

This chapter will characterize and describe chronic respiratory disease and cough. Details surrounding etiology and epidemiology of cough, types of coughs, diagnosis, and management of cough will be discussed, as well as a discussion of pulmonary rehabilitation (PR). This chapter will provide the rationale for evaluating non-pharmacological chronic cough management strategies in individuals with and without chronic respiratory diseases and offer healthcare provider perspectives on assessment and management strategies of chronic cough across Canada. The objectives of the studies will be outlined.

1.2 CHRONIC RESPIRATORY DISEASE

1.2.1 Types and Prevalence

Chronic respiratory diseases describe a group of various respiratory disorders that primarily affect an individual's respiratory system, which is consequently associated with multiple co-morbidities, such as hypertension and cardiovascular disease [1]. With no cure, chronic respiratory disease is a leading cause of death and disability worldwide, with approximately 545 million people affected globally, an increase of 40% since 1990 [2]. With one in five Canadians living with a respiratory disease, its management remains highly relevant [2].

The most common lung diseases in Canada are chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), asthma, lung cancer, cystic fibrosis, obstructive sleep apnea (OSA), and tuberculosis; with COPD, asthma, and lung cancer being the most prevalent [3]. Although chronic inflammation underlies most chronic respiratory diseases, the nature and

source of the inflammation differ, which allows for differentiating and characterizing the various respiratory diseases [4].

COPD is characterized as a progressive lung disease in which chronic inflammation leads to airflow obstruction, due to non-reversible airway abnormalities [4,5]. Pollutants and tobacco use are often associated with the etiology of COPD, which leads to lung inflammation and decline of lung function [6]. The prolonged inflammation causes alveolar abnormalities, resulting in airflow limitation [6]. COPD is associated with co-morbidities such as coronary heart disease, anxiety and depression disorders, malnutrition, and sleep disturbance [7], producing numerous symptoms which impact a person's quality of life [5]. The cost of COPD hospitalizations is estimated to be at $1.5 billion a year in Canada alone [3].

Asthma is also characterized by chronic lung inflammation leading to airflow obstruction, but unlike COPD, the effects of asthma on the airway are reversible through medications and removal of the trigger [4,8]. In Canada, asthma accounts for an estimated total of 80% of all chronic respiratory diseases, resulting in high economic burdens, as annual costs related to asthma care approximate to $141 million in Ontario alone [9].

Lung cancer is a respiratory disease caused by molecular changes due to abnormal cellular signalling, impacting the individual's bronchioles and alveoli [10]. 85% of lung cancer cases are attributed to smoking or exposure to various toxic environmental hazards [11], with the remaining 15% of cases found in non-smokers [10]. There is currently limited knowledge about the etiology of lung cancer in non-smokers, as they seem to differ in multiple aspects in terms of epidemiology, molecular function, and clinical approach [10]. With a 5-year survival rate of less than 15% [10], lung cancer remains to be the leading cause of cancer-related deaths worldwide, and is the most common cancer diagnosed globally [11].

Despite each chronic respiratory disease differing in etiology and pathophysiology, individuals with a chronic respiratory disease present with similar symptoms such as shortness of breath (dyspnea), anxiety, fatigue, and chronic cough [4,12]. Chronic cough will be the overall focus of this thesis.

1.3 COUGH

1.3.1 Etiology and Epidemiology of Cough

Cough is the body's primary defensive mechanism to aid in expelling foreign and toxic particles from the respiratory system [13]. Cough, which is associated with multiple comorbidities, remains to be the most common reason for medical referral and doctor visits annually [14]. Cough is categorized into three distinct categories: acute cough, subacute cough, and chronic cough [15]. Acute cough is a cough lasting for four weeks or less and often results from a common upper respiratory infection, while a chronic cough may result from underlying chronic respiratory disease [15]. An acute cough can lead to subacute cough, lasting between 4 and 8 weeks [15]. Chronic cough is defined as a cough lasting for 8 weeks or more, and is often attributed to various chronic respiratory disease diagnoses [13]. Refractory cough is a chronic cough that persists despite optimal treatment for the underlying conditions [16].

The prevalence rates of chronic cough vary worldwide. Song and colleagues (2015) found global estimates to be around 18% for Australia, 13% in Europe, 11% for America, and 7% in Asia [17]. In Canada, Satia and colleagues (2021) found the prevalence of chronic cough to be between 16-18% in adults aged 45 and older [12]. Common risk factors for chronic cough include diagnosis of chronic respiratory diseases, such as gastroesophageal reflux disease

(GERD), asthma, COPD, and current tobacco use. Increases in airway inflammation from these risk factors result in cough hypersensitivity, thus increasing cough frequency [13,18].

Smoking is a major contributor to chronic cough and it is also responsible for causing 80-90% of all COPD cases [19,20]. Since chronic respiratory diseases are major risk factor for developing a chronic cough, tobacco use greatly influences cough prevalence and cough-related behaviours [18]. The mechanism of action behind active smoking on chronic respiratory diseases, leading to cough, is influenced by multiple processes. Primarily, the inhalation of particles and gases causes a cellular inflammatory response leading to narrowing of airways and increased mucus production [21]. This results in reduced airflow, along with a decreased ability to clear lungs of mucus, consequently increasing a person's risk of developing lung infections and permanent damage to the lungs [21].

Trends in chronic cough prevalence are influenced by age and sex [16,18]. As age increases, the prevalence of chronic cough also increases [18]. When factoring for both sex and age, females in their sixties have the highest prevalence of chronic cough [13,18], with overall chronic cough prevalence rates at the highest levels in males in their eighties [13,18]. Females are also more commonly found to seek medical assistance for cough-related symptoms in comparison to males [13]. Kastelik and colleagues (2002) and Kelsall and colleagues (2009) both found females to have a heightened cough reflex sensitivity, which may provide reasoning to why chronic cough is more prevalent in females [22,23].

1.3.2 Diagnosis of Cough

Diagnosing chronic cough involves a multi-component approach, to gain insight into the most appropriate targeted treatment approaches. Baseline assessments of patients typically

involve a combination of clinical history, as well as, an individual's lifestyle habits and health-related behaviours [15]. For example, a history of smoking combined with the symptom of excessive sputum production, may be an indicator of airflow obstruction, which results in a productive chronic cough [15], while, in comparison, a previous history of angiotensin-converting enzyme (ACE) inhibitor use, may result in a non-productive (dry) cough [15]. In analyzing and being able to narrow down cough origin, the most effective cough management strategies may be more easily identified.

The standard line of approach after lifestyle and symptom analysis may differ between physicians [15]. A chest radiograph is a common approach in the early stages of obtaining a diagnosis [15]. Further cough testing involves spirometry, cough challenges, objective cough assessments, sputum analysis, exhaled breadth concentrate analysis, bronchial hyperresponsiveness, and quality of life assessments [15,24].

Objective assessments of cough aim to describe cough sensitivity and frequency [25]. In particular, cough challenges assess cough reflex sensitivity and involve the inhalation of capsaicin or citric acid, provoking the cough reflex [26]. Although cough challenges are valid and reliable for chronic cough, they lack validation for use in people with chronic respiratory diseases [25]. Furthermore, a downside to using cough challenges is that they are effective at studying mechanisms of disease, however do not capture the efficacy of specific cough therapies [25].

The Leicester Cough Monitor (LCM) and VitaloJak are the most commonly used cough monitors and are considered the gold standard for cough frequency assessment [25]. The LCM is an automated digital monitor and recorder that records sound continuously for the period it is worn by a patient [25]. While similar, the VitaloJak is also another type of digital monitor and

recorder, however sound analysis is manual, requiring more labour and time for sound analysis [25]. The LCM is considered to be the most valid, reliable, and responsive measure of cough frequency, however it also lacks validation for use in people with chronic respiratory disease [12,27].

Subjective measures of cough include self-report questionnaires used to either assess patient-perceived cough severity or health-related quality of life (HR-QOL). The Visual Analogue Scale (VAS) is widely used in research as it is time-efficient and responsive to change for cough severity, however it still lacks validity [25]. The Leicester Cough Questionnaire (LCQ) is another commonly used self-report measure of HR-QOL which encompasses physical, psychological, and social domains [25]. The LCQ is a valid, reliable, and responsive measure, which has been validated for use in a couple of chronic respiratory diseases such as COPD [28], and bronchiectasis [25,29].

1.3.3 Impact of Cough

Chronic cough affects multiple domains of an individual's life including sleep, social life, mood and behaviour, which, consequently, not only impacts a person's HR-QOL, but also places substantial economic challenges on healthcare systems [27]. With chronic cough burdening mental-health and wellbeing, a person may feel the effects of social isolation due to feelings of embarrassment from coughing in public, thus resulting in cough-induced anxiety and depression [27]. Approximately, 42% of patients being treated for chronic cough are prescribed anti-anxiety and/or depression medications [30]. French and colleagues (1988) found that health deterioration from chronic cough was mostly attributed to negative impacts on a person's psychosocial wellbeing [31]. A more recent study from the same research group found that quality of life,

cough severity, and psychological symptoms, such as anxiety and depression, are all interrelated and dependent on each other [32]. These findings demonstrate the need for interventions that directly target cough severity, improvement in cough-related HR-QOL and psychological symptoms [32].

Poor sleep quality is often an under-recognized symptom of chronic cough which not only impacts quality of life but further exacerbates the symptoms of disease [33]. With more than 50% of people with chronic cough experiencing sleep disruption, nocturnal cough is a major determinant of HR-QOL [34]. Poor sleep quality is closely related to impaired daytime function and progression of chronic respiratory disease symptoms, leading to worsened disease prognosis and increased mortality [35]. In general, 50% of people with chronic respiratory diseases associate their sleep disruption to chronic cough [34]. As such, the impact that COPD has on sleep is extreme, as 78% of COPD patients report poor sleep quality [33]. Fisher and colleagues (2018) found that sleep disruption is closely associated with COPD severity and current smoking behaviours [35].

Factoring in the effect that lack of sleep has on activities of daily living, along with the negatively perceived social impacts of coughing in public, people with chronic cough may experience income loss due to decreased productivity or embarrassment from cough [36]. A survey conducted by Kubo and colleagues (2021) found that work productivity was lower and activity impairment was significantly higher in people with chronic cough [36,37]. Kubo and colleagues (2021) also noted that those who had daily interaction with others, were more likely to quit their jobs due to their cough [36,37].

With chronic cough affecting the individual, society, and the healthcare system, evidence-based approaches for the management of chronic cough are needed. In the following

section, the management of chronic cough will be discussed in terms of various pharmacological and nonpharmacological management strategies.

1.4 MANAGING CHRONIC COUGH

Pharmaceutical and nonpharmaceutical therapies are the two main forms of chronic cough management [13,38]. Depending on the type of cough, productive versus non-productive, approaches to cough therapy may differ. Forms of various cough management therapies (combination therapy) may be combined to increase therapy effectiveness and provide optimal results for both non-productive and productive cough. The overall goal of non-productive chronic cough management is to suppress the cough, while the overall goal of productive chronic cough management is to help clear excess mucus from the airways [39]. Non-productive cough therapies include cough desensitization and reduction in cough severity and frequency [13], while therapies for productive cough aim to help mucus expectoration [39].

Guidelines offered by the American College of Chest Physicians and European Respiratory Society provide evidence-based recommendations to help guide healthcare providers in choosing the optimal management plan for their patient [40]. The following section aims to further describe the various categories and approaches to cough management.

1.4.1 Pharmacological Cough Management

Pharmacological cough therapies are the primary line of treatment for healthcare providers when seeking cough management therapies, as approximately 85% of patients who visit physicians due to cough-related concerns receive a prescription [30]. Pharmacological management of cough encompasses a broad spectrum of medications with treatment approaches

differing based on cough origin and type of cough [30,40]. The course of treatment for cough is also influenced by any underlying health conditions to which the presence of cough may be attributed to, such as COPD, asthma, ILD, OSA and GERD [30,38]. Refractory chronic cough, defined as a cough that persists despite medical treatment of underlying health conditions, may require a different management path, such as cough suppression, as there are no underlying conditions that need to be treated prior to addressing the cough as its own entity [38].

Common and traditional types of pharmacological treatments for chronic cough involve over-the-counter (OTC) medications, antitussives, and neuromodulators [40]. OTC cough medicines describe a group of pharmaceutical products in which attainment of a prescription is not required. OTC is used as a form of self-diagnosis and treatment [40], and it is estimated that $1 billion to $3.5 billion is spent annually on OTC treatment modalities in just the United States alone [30]. Although OTC can have an immediate effect on cough suppression, these medications raise the issue of overuse and abuse, as they only provide temporary symptom relief and are not appropriate for use in chronic users due to safety concerns [30,40].

Antitussives work to inhibit cough through either the central nervous system, peripheral nervous system, or both [41]. Classification of antitussives is based on which components of the nervous system they act on, and further classified into opiates, non-opiates, or antihistamine categories [41]. Centrally acting antitussives work by increasing cough threshold, while peripherally acting antitussives provide a temporary soothing effect on the throat or desensitize nerve endings to control cough [41]. Antitussives may possess addictive properties for the user, and side-effects such as drowsiness, nausea, and dizziness, which may limit an individual's activities of daily living [41].

Neuromodulators are another form of pharmacological cough therapy, in which gabapentin and pregabalin are the most commonly types of neuromodulators [40]. Both gabapentin and pregabalin were originally approved for chronic pain, however in more recent years, chronic cough has also been added to the scope of these medications [40]. Ryan and colleagues (2012) examined the effects of gabapentin use in people with refractory chronic cough and found that gabapentin significantly improved the LCQ scores and cough severity [40,42]. Despite the positive effect neuromodulators can have on cough control, individuals taking these medications often discontinue their use due to the severity of the side-effects which include drowsiness, confusion, fatigue, and blurred vision [40]. After discontinuation of neuromodulator use, improvements in cough were not sustained in the long-term [40].

Although ongoing pharmaceutical advances offer effective results in subsidizing cough symptoms alone, factoring in the cost along with adverse effects from medications resulting in treatment discontinuation [40,43], the need for exploring alternative methods for cough management is crucial and is also recognized by international respiratory societies [44].

1.4.2 Nonpharmacological Cough Management

Nonpharmacological therapies for non-productive cough work towards maximizing cough HR-QOL, cough suppression, and cough severity, while minimizing the typical side effects associated with traditional pharmacological treatment [38]. Nonpharmacological cough therapies can include speech-language pathology interventions, behavioural cough therapy (BCT), cough control therapy (CCT), or a combination between physiotherapy and speech-language therapy methodology to deliver a cough control intervention known as PSALTI [38].

Nonpharmacological non-productive cough therapy can be used in a multi-component therapy form aimed at targeting different areas influencing cough [45]. These therapeutical components include cough education, laryngeal hygiene, cough control techniques, and psychoeducational counselling, delivered through either speech-language pathologists and/or physiotherapists [45]. Even though therapy components can be delivered through different healthcare professionals, the mechanism of action behind the multi-component approach to cough remains the same, which will be discussed further on in this section.

For productive chronic cough, non-pharmacological therapies focus on increasing expectoration of secretions by using methods such as airway clearance techniques (ACT). ACT's are delivered by physiotherapists and can involve the use of different techniques such as postural drainage, manual techniques, and respiratory techniques [46]. ACT is typically a cost-effective form of non-pharmacological cough management in those with productive cough, showing positive results in cough efficacy [46]. Mechanisms of ACT aim to increase secretion expectoration by increasing the person's expiratory flow, oscillate airflow, and overall lung volumes [46].

Nonpharmacological cough therapies are often not considered as a primary line of treatment in cough management, particularly in individuals who have underlying medical conditions [38]. However, research suggests that nonpharmacological therapies provide effective results in cough suppression for those with non-productive cough, while also showing improvements in cough-related quality of life [38]. Mohammed and colleagues 2020 found that 86% of participants with underlying respiratory diseases rated improvements in their cough and cough symptoms [45]. This finding suggests a positive advantage to those seeking alternatives to pharmacological management.

Mechanism of Action for Nonpharmacological Use in Non-Productive Cough

The mechanism of action behind improvements in non-productive cough and cough-related symptoms with non-pharmacological cough management is not yet fully understood [38]. As multi-modal therapies target different domains of cough, it is hypothesized that cough sensitivity is reduced, cough is controlled through improvements in laryngeal function, and cough suppression abilities increase [38,47]. Increasing the understanding of the mechanism of action behind the cough reflex, may also potentially increase the insights and possible explanations as to how nonpharmacological cough therapies can be an effective form of cough management [47]. For example, neural cough inhibition is impaired in those suffering from chronic cough, resulting in an increased cough sensitivity, as well as urge to cough [47]. Speech-language pathology interventions are found to reduce cough hypersensitivity by targeting laryngeal muscle tension, while also working to reduce urge to cough by teaching the body how to recognize a cough response and to substitute it with a different learned behaviour [47]. Despite this evidence behind a reduction in cough following speech-language therapy interventions, further research is needed to help strengthen evidence behind the mechanisms of action [47].

It is also beneficial for an individual to understand their own cough in the sense of cough triggers, proper breathing, and exercises to aid in cough control [38,47]. As PR offers an educative and exercise approach to increasing HR-QOL in people with chronic respiratory diseases [48], PR *could* be an appropriate method of chronic cough management. However, it is unknown whether chronic cough is an assessment and/or management goal of PR. In the up-coming section, PR with be discussed in greater depth and detail.

1.5 PULMONARY REHABILITATION

1.5.1 Pulmonary Rehabilitation and Effectiveness

With the aim of improving HR-QOL in people with chronic respiratory diseases by reducing symptoms and improving functional capacity, PR strives to promote and improve a person's overall holistic well-being [48]. Exercise and educational components are the foundational aspects of PR programs; these components offer a patient-centered approach in improving activities of daily living through targeted muscle strength and functional exercises, as well as, incorporating health promotion and behaviour change initiatives [48,49]. PR not only results in improvements in physical capacity, but also results in decreases in hospitalizations and mortality, as well as in anxiety and depression scores [48,49].

PR programs incorporate the use of various healthcare providers including, but not limited to, physicians, physiotherapists, occupational therapists, respiratory therapists, and dietitians [50]. Exercise sessions are typically offered in a group format, which may also be an influencing factor in improving PR attendance and adherence rates [48,50]. Furthermore, psychosocial counselling, nutritional evaluation, and education are further examples of various sub-components included in PR [51].

1.5.2 Barriers and Accessibility to PR

Despite evidence suggesting that PR offers a vast array of benefits to people with chronic respiratory diseases, lack of awareness regarding PR is considered to be a major barrier for both patients and healthcare providers [52–54]. The American Thoracic Society (ATS) and European Respiratory Society (ERS) released guidelines and recommendations on the implementation and

delivery of PR, ways to increase PR knowledge, and patient access [52,53]. In 2015, Canada had only 155 existing PR programs, despite registering over six million Canadians living with a respiratory disease [51]. A geographic location is a major barrier in patient access; those living in remote or rural areas would benefit from local access to PR programs [51,52].

1.5.3 Management of cough and PR

PR has beneficial effects in various chronic respiratory diseases such as COPD, ILD, asthma, bronchiectasis, and cystic fibrosis [48,49,55]. With chronic cough being highly prevalent and a common symptom in chronic respiratory diseases [12], PR would seem to be an appropriate setting for the management of chronic cough. As PR significantly improves HR-QOL by managing physical components of health, including reducing shortness of breath, improving breathing, and increasing exercise and functional capacity, improvements in these domains could possibly aid in the management of chronic cough [49,56,57]. Education in PR could include strategies on cough management. However, little is known about whether chronic cough is assessed or managed during PR.

1.6 GOALS AND OBJECTIVES

In summary, taking into consideration the increasing global prevalence of chronic cough and chronic respiratory diseases, along with the burden of disease on quality of life, the need to investigate the efficacy of existing therapies for chronic cough is relevant and crucial. The overall aim of this thesis seeks to investigate and provide an update in advances of non-pharmacological management of non-productive chronic cough, as well as describe whether chronic cough is assessed and/or managed in PR programs across Canada.

1.7 OUTLINE OF THESIS

1.7.1 Chapter 2: Non-pharmacological management of non-productive chronic cough in adults: A systematic review

The first paper of this thesis aims to describe non-pharmacological management therapies for non-productive chronic cough. Despite three reviews conducted in the past decade on non-pharmacological cough management, this is the first review in more than a decade to look at all forms of non-pharmacological therapies in, both, individuals with refractory chronic cough and people with chronic respiratory diseases [58–60]. More recent reviews conducted on non-pharmacological cough therapies have either looked at specific therapies alone, such as Slinger and colleagues (2019) only describing speech-language pathology interventions for chronic cough [58], or Chamberlain and colleagues (2014) and Wamkpah and colleagues (2022), whom only included people with refractory chronic cough [59,60]. This review seeks to add to the existing literature [58–61] by providing an update on non-pharmacological therapies in all chronic cough populations, to help guide clinicians and healthcare providers seeking alternative cough management techniques.

1.7.2 Chapter 3: Evaluation and Management of Chronic Cough during Pulmonary Rehabilitation- a Canadian Survey Study

The second paper in this thesis aims to describe how chronic cough is assessed and managed in PR programs across Canada. This study is a cross-sectional survey study in which healthcare providers from identified PR programs, from each province, were contacted for survey participation. As PR programs work on improving functionality and decreasing burden of disease

[49], this study seeks to identify if chronic cough is assessed or managed in accordance with the overall goals of the PR program. The objectives and aims of this study are described below:

1. Describe how chronic cough is assessed in PR programs across Canada
2. Describe how chronic cough is managed in PR programs across Canada
3. Describe factors that impact chronic cough assessment and management, such as:
    a. Chronic vs. acute
    b. Productive vs. non-productive
    c. Type of disease
    d. Severity of disease
4. Describe the barriers and facilitators of chronic cough assessment and management in PR across Canada

1.7.3 Chapter 4: Overall Discussion and Conclusion

The final chapter of this thesis will provide a summary of the findings for non-pharmacological therapies for non-productive chronic cough in individuals with refractory chronic cough or chronic respiratory diseases, along with a summary of assessment and management techniques used by healthcare providers in PR programs across Canada. Interpretation of the findings will be discussed, leading to a discussion regarding the studies' limitations, and strives to provide guidance for future research in this field.

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CHAPTER 2:

Non-pharmacological management of non-productive chronic cough in adults: A systematic review

Published in *Frontiers in Rehabilitation Sciences, Pulmonary Rehabilitation Section*

Citation:
Ilicic, A. M., Oliveira, A., Habash, R., Kang, Y., Kho, M., Goldstein, R., & Brooks, D. Non-pharmacological management of non-productive chronic cough in adults: A systematic review. *Frontiers in Rehabilitation Sciences*, 91. Doi: https://doi.org/10.3389/fresc.2022.905257

2. 1 Abstract

Background. Chronic cough is a common reason for medical referral and its prevalence is on the rise. With only one pharmaceutical therapy currently under review for the treatment of refractory chronic cough, exploring non-pharmacological chronic cough management therapies is important. This systematic review summarizes the effectiveness of non-pharmacological chronic cough therapies in adults with non-productive refractory chronic cough or cough due to chronic respiratory diseases.

Methods. We searched Medline, Embase, Cochrane, CINAHL, and Scopus from inception to September 2021. Randomized controlled trials published in English, Portuguese, or French, and examining the effects of non-pharmacological therapies in adults with chronic non-productive cough (>8 weeks; <2 teaspoons sputum) were included. Mean differences, medians, and odds ratios were calculated as appropriate.

Results. 16,546 articles were identified and six articles representing five unique studies were included. Studies evaluated 228 individuals with refractory chronic cough or chronic cough due to a chronic respiratory disease (162 women (71%); 52±11 to 61±8 years old). Obstructive sleep apnea was the only chronic respiratory disease studied. Non-pharmacological therapies included education, cough suppression, breathing techniques, mindfulness, and continuous positive airway pressure. When standing alone, non-pharmacological cough therapies improved cough-specific HR-QoL when not associated with interventions (mean diff MD 1.53 to 4.54), cough frequency (MD 0.59 95%CI 0.36 to 0.95), and voice outcomes (MD 0.3 to 1) when compared to control interventions.

Conclusion. The evidence of non-pharmacological therapies for non-productive chronic cough is limited. Existing studies reflect the heterogeneity in study design, sample size, and outcome

measures. Thus, clinical recommendations for using the most effective interventions remain to be confirmed.

2.2 Introduction

Cough is one of the body's most important reflexes, acting as a primary defense mechanism to clear the upper airways. When cough becomes chronic, defined as lasting for eight weeks or more [1], it can drastically impair activities of daily living and health-related quality of life [1,2], contributing to a downward spiral of fatigue, embarrassment, frustration, anxiety, depression, and social isolation [3,4]. These negative psychosocial impacts are aggravated by the stigma associated with coughing, especially during the recent covid-19 pandemic [5].

The global prevalence of chronic cough in otherwise healthy individuals is increasing, with a prevalence of 16-18% in Canada [2], 18% in the USA [1], and 33% in Europe [1]. In people with chronic respiratory diseases, its prevalence has been reported to be 30-90% [6]. Chronic cough is also one of the most common reasons for medical referrals [2]. Costs associated with chronic cough correspond, on average, to $3266 per patient, which includes multiple medical appointments, prescription medications, and hospitalizations [7]. Despite medical management, patients often report minimal or no improvement in their chronic cough and turn to over-the-counter medications, at an estimated annual cost of $1-3.5 billion for temporary symptom relief [7]. Thus, treating chronic cough has become a priority, both, among otherwise healthy individuals and those with underlying chronic respiratory diseases [6,8].

The two main forms of chronic cough management are pharmacological and non-pharmacological therapy [9–11]. Currently there is only one pharmaceutical therapy under review for the treatment of refractory chronic cough [12], but approval is pending. Other commonly used pharmacological therapies include antacids, pro-motility agents, and neuromodulators [6], however, their effectiveness is limited and may be associated with significant adverse effects such as dizziness, fatigue, cognitive changes, nausea, and risk of

withdrawal [5]. Non-pharmacological therapies include, but are not limited to, education, cough suppression, and breathing techniques. They have been reported to be equally effective, with fewer side effects, compared to pharmacological therapies [6,13], however, there is a paucity of information regarding which non-pharmacological therapies are most effective. Four systematic reviews of non-pharmacological management of chronic cough have been published in the past decade [9,14–16], however they focused mainly on speech language pathology, neglecting other therapies such as behavioural therapies or relaxation [14,16], or focused on people with only refractory chronic cough, excluding those with chronic cough due to chronic respiratory diseases [9,15]. Our systematic review adds to this field of research by including, both, people with refractory chronic cough or chronic respiratory diseases, and seeking to identify all non-pharmacological therapies. This updated systematic review will help guide healthcare providers in the implementation of effective cough management therapies for individuals with either refractory chronic cough or chronic respiratory diseases.

The primary objective of this systematic review is to summarize the effects of non-pharmacological cough management strategies on cough-related quality of life in adults with non-productive refractory chronic cough or with an underlying chronic respiratory disease. The secondary objectives are to summarize the characteristics of individuals participating in non-pharmacological cough management strategies, the structure and components of different cough management strategies reported in the literature, and the effects of cough management strategies on health-specific and cough-related outcomes.

2.3 Methods

This systematic review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [17,18] (Supplementary Material A). The protocol was registered with the International Prospective Register of Systematic Reviews network (no. CRD42020200015) and approved on August 21st, 2020.

2.3.1 Literature Search

Prior to conducting a search, a librarian was consulted to determine effective search strategies. Two authors (A.O. and A.M.I) conducted a search of the following databases: Medline, Embase, Cochrane, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Scopus from inception to September 2020. The search was updated in September 2021. For each database, a search utilizing both keywords and medical subject heading (MESH), designed to identify all non-pharmacological cough interventions for people with chronic cough, was performed within the titles and abstracts of records. An example of the search strategy, conducted in MEDLINE, is reported in Supplementary Material B.

2.3.2 Eligibility Criteria

Articles were deemed eligible if the following criteria was met: 1) randomized controlled trials (RCTs); 2) included adults (≥18 years) with refractory chronic cough (>8 weeks) or those with underlying chronic lung diseases, 3) reported minimum to no sputum production (i.e., < 2 teaspoons/day); 4) examining the effectiveness of non-pharmacological therapies alone (e.g., cough education, laryngeal irritation reduction strategies, cough control, psychoeducational

strategies or behavioural therapies) and were 5) written in English, Portuguese, or French. Articles were excluded if: 1) patients presented with an acute respiratory condition (cough <8 weeks); 2) the duration of cough was not defined; 3) interventions included pharmaceuticals, dietary supplements, or surgery; 4) invasive non-pharmacological interventions (e.g., acupuncture), 5) abstracts in conference proceedings, systematic reviews, dissertations, editorials, case reports, or book chapters. All articles were included independently of the outcome assessed, except for capsaicin and citric acid cough challenge, which were excluded as these tests are used to study mechanisms of disease rather than efficacy of the specified cough therapies [19].

2.3.3 Study Selection

Citations were first managed in EndNote X8.2 (Clarivate, Philadelphia, Pennsylvania, USA) for duplicates screening and removal and were then uploaded to Covidence (Covidence, Boston, Massachusetts, USA) for the study selection process. Four independent reviewers worked in pairs (A.O., A.M.I., R.H., and Y.K.) to screen the titles and abstracts: consensus between at least two reviewers was needed before a final decision to include or exclude the study was made. Remaining article full texts were then independently screened by two reviewers (A.O. and A.M.I.). All disagreements were resolved via consensus and a third reviewer was consulted (D.B.) if a consensus could not be reached.

2.3.4 Data Extraction

Data from the eligible articles was extracted using a data extraction form, designed prior to data collection, which included information regarding study characteristics, program

characteristics, and results. Article characteristics included the first author's last name, year of publication, country of origin, experimental and control interventions, follow-up period duration, drop-out rates at any point in the study, participant's comorbidities, and demographics (i.e., total number of participants, age, and gender) per experimental and control groups. When dropout rates were not reported in the articles, they were calculated as (total randomized – total completed the study protocol)/total randomized) * 100. Program characteristics included the duration and frequency of the intervention, equipment used, inclusion and exclusion criteria, outcomes and outcome measures, and results. Data extraction was pilot tested by two reviewers (A.O. and A.M.I.) in one study to clarify any discrepancies. Data from the remaining articles were extracted by one reviewer (A.M.I.) and verified by a second reviewer (A.O.).

2.3.5 Risk of Bias Assessment

Risk of bias assessments were conducted using the Revised Cochrane risk-of-bias tool for randomized trials (RoB) [17,20], which evaluates 5 domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result [1]. Authors (A.O. and A.M.I.) piloted the risk of bias assessment on one article and then conducted the assessment for the remaining articles individually. Disagreements were solved by consensus.

2.3.6 Data Analysis

A meta-analysis was planned to be conducted if the articles were similar enough to be grouped together (i.e., present with similar interventions, populations, and outcomes). When a meta-analysis was not possible to conduct, the median and interquartile ranges, mean differences (MD) and 95% confidence intervals (95%CI), or odds ratios were extracted directly from the

studies or calculated using Review Manager 5.4.1, according to the Cochrane Handbook for Systematic Reviews of Interventions [18].

2.4 Results

2.4.1 Literature Search and Study Selection

The database search identified 16,546 records. After duplicate removal (n=3,882), 12,664 records underwent title and abstract screening and 153 were identified for full-text screening. At this stage, 147 records were excluded for not meeting the eligibility criteria (Supplementary Material C). This yielded a total of six records (five unique studies – Vertigan et al. 2006 [21] and Vertigan et al. 2008 [22] analysed the same sample of participants and thus were counted as one unique study) included in this review [21–26]. The PRISMA flowchart of the study selection process is provided in Figure 1. A meta-analysis was not possible to conduct due to heterogeneity of study populations, interventions, and outcomes used.

2.4.2 Study Characteristics

Included articles were published between 2006 and 2020, and studies took place in Australia (n=2), the United-Kingdom (n=2), and the United States of America (n=1). One article reported on a multicentre study [24] and the remaining five, on single-centre studies [21–23,25,26], totalling 228 participants (114 in the experimental groups, 114 in the control group), among the five studies (Figure 2). Sample sizes ranged from 9 to 43 with dropouts ranging from 0% to 35% in experimental groups and 0% to 34% in control groups. A detailed description of study characteristics is presented in Table 1.

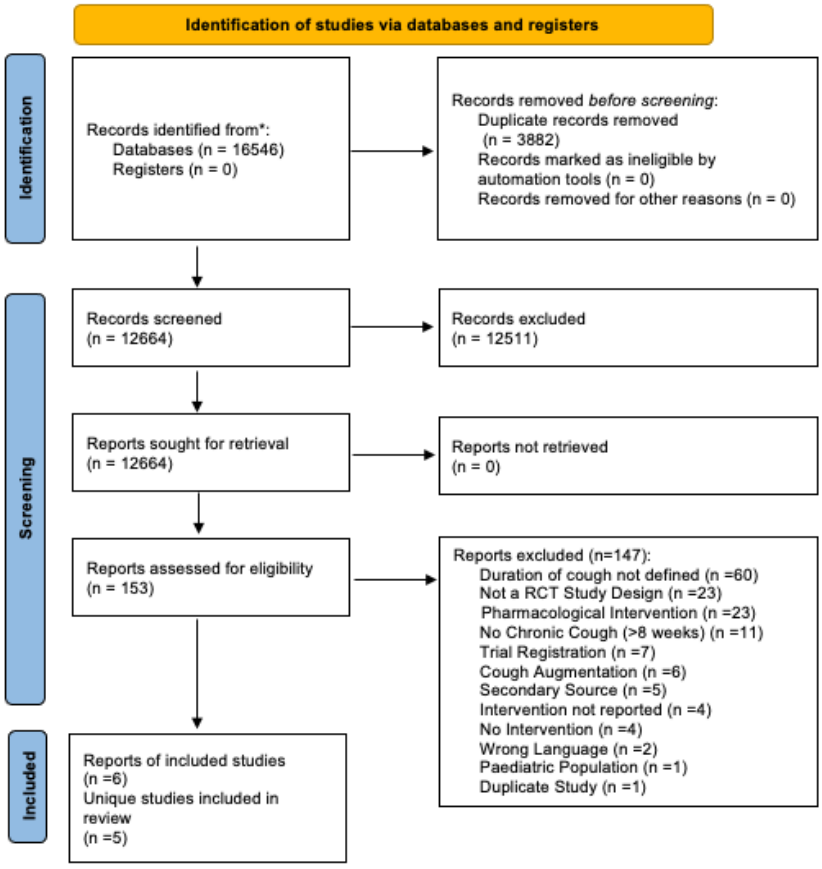

Figure 1 – Flowchart of records and studies included in the systematic review

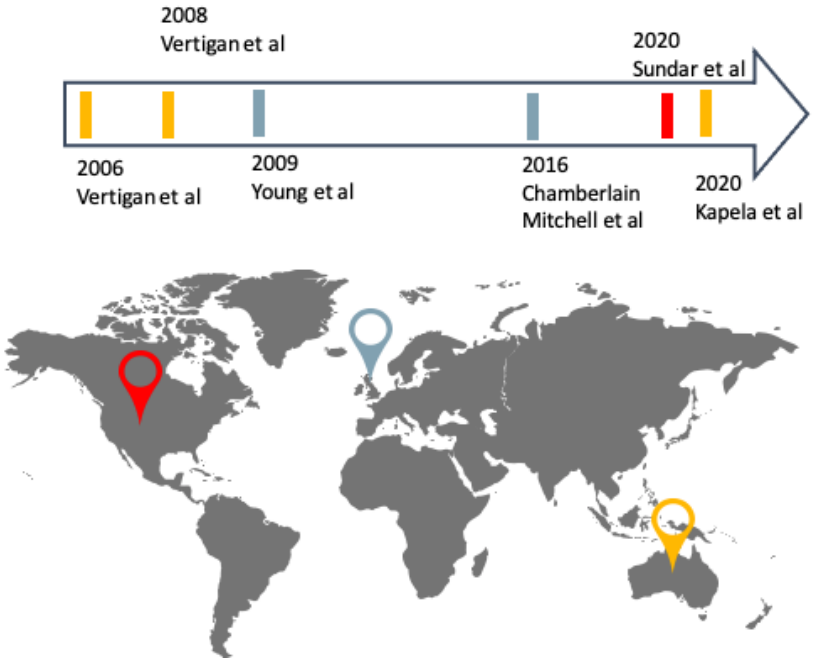

Figure 2: Countries of origin and date of publication of records included in the review.

TABLE 1: Study Characteristics

Author, year	Country	Interventions	Co-morbidities	Experimental Group				Control Group			
				n	Drop-out Rates (%)	Age (years)	Sex (M) (N, %)	n	Drop-out Rates (%)	Age (years)	Sex (M) (N, %)
Vertigan 2006*[21]	Australia	Experimental: SPEICH-C Control: healthy lifestyle education	Asthma PNDS GERD PVFM	43	8.5	57.5±13.8	8, 19	44	12	61.3±13.2	15, 34
Vertigan, 2008*[22]				40	14.8	58.9±13.6	7, 18	43	16	61.5±13.3	15, 35
Young, 2009 [23]	UK	Experimental 1: Mindfulness Experimental 2: Cough Suppression Control: No intervention	Asthma GERD UACS	Cough Suppression: 9 Mindfulness: 10	0	Cough Suppression 61.1±8.4 Mindfulness: 60.2±8.1	Cough Suppression 4, 44 Mindfulness: 3, 30	11	0	54.2±10.8	3, 27
Chamberlain 2017 [24]	UK	Experimental: PSALTI Control: Healthy Lifestyle Advice	N/A	34	35	61 [53-67]	9, 26	41	34	56 [48-67]	15, 37
Sundar, 2020 [25]	USA	Experimental: CPAP Control: Sham CPAP	OSA	9	25	52.4±10.9	2, 22	9	10	62.7 ± 6.3	5, 56
Kapela, 2020 [26]	Australia	Experimental: SPEICH-C + breathing videos Control: SPEICH-C	GERD Rhinosinusitis Asthma ACE inhibitor withdrawal	9	11	59±17	0, 0	9	11	57±9	2, 22

Abbreviations: ACE; Angiotensin Converting Enzyme; CPAP, Continuous Positive Airway Pressure; GERD, Gastroesophageal Reflux Disease; OSA; Obstructive Sleep Apnea; PSALTI, Physiotherapy, Speech and Language Therapy Intervention; PNDS, Postnasal Drip Syndrome; PVFM, Paradoxical Vocal Fold Movement; SLP, Speech-language Pathology; SPEICH-C, Speech Pathology Evaluation, and Intervention for Chronic Cough; UACS, Upper Airway Cough Syndrome; UK, United Kingdom; USA; United States of America. *Vertigan et al. published two separate studies, however using the same population for both. For our review, study table summaries are provided together due to the nature of the article origin. *Participant totals were calculated using the highest participant number in either Vertigan et al. article. As the participant population was derived from the same data, study numbers were only counted once.

Eligibility criteria was comparable across the majority of the included articles and required that participants have a cough lasting for eight weeks or more [21–26], have a refractory chronic cough (failed treatment for other possible causes of cough such as asthma, COPD, GERD, rhinitis) [21,22,24,26] or a chronic cough from an associated chronic respiratory disease (OSA) [25], and had normal chest imaging [21,22,24,25]. Articles excluded participants if there was history of a recent upper respiratory tract infection in the past four-six weeks [21–26].

In both experimental and control groups, participants were mainly women (experimental: n= 88; 77%; control: n= 74; 65%) with ages ranging from 52±11 to 61±8 years old in experimental groups and 54±11 to 63±6 years in control groups. Comorbidities in both groups included GERD [21–23,26], asthma [21–23,26], upper airway cough syndrome (UACS) [23], ACE inhibitor withdrawal [21,22,26], postnasal drip syndrome (PNDS) [21,22], paradoxical vocal fold movement (PVFM) [21,22], OSA [25], and rhinitis [26].

2.4.3 Intervention Characteristics

Duration of interventions ranged from one to eight weeks, with two articles not reporting the length of the intervention [22,26]. The experimental group interventions included mindfulness [23], cough suppression [23], continuous positive airway pressure (CPAP) therapy [25], education strategies to reduce cough, laryngeal hygiene and hydration strategies, cough control, and psychoeducational counselling delivered through speech-language therapy [21,22], speech language pathology with video breathing exercises [26], and through physiotherapy and speech and language therapy (PSALTI) [24]. The control interventions were healthy lifestyle education and advice [19,20,22], sham CPAP therapy [25], strategies to reduce cough, laryngeal hygiene, hydration, cough control, and psychoeducational counselling by a speech language

pathologist (SLP) without breathing exercises [26] or no intervention [23]. A detailed description of interventions characteristics is presented in Table 2.

2.4.4 Effects of Interventions

Out of the six included articles, three reported the effects of interventions on cough-related quality of life (primary outcome) [24–26], one reported on general and disease-specific health-related quality of life [23], two on cough frequency (objective cough counts) [23,24], four articles reported on symptoms (i.e., breathing [21], cough [21], upper airway symptoms [21], urge to cough [23], cough severity [24,26], anxiety and depression [23,24]), and five articles reported on other outcomes such as sinonasal disease, markers of airway inflammation, and voice [21,22,24–26]. In total, seventeen outcome measures were used to evaluate cough interventions, with the LCQ most commonly used in three articles [24–26]. Outcome scores were collected at baseline [21–26], and one week [23], 4-weeks [24], 6-weeks [25], 8-weeks [21,22] and 3-months after baseline [24,25]. One article reported outcomes after a number of sessions (1-6) rather than a fixed time [26]. A detailed description of the effects of interventions can be found in Table 3.

2.4.4.1 Primary outcome measure – Cough-related quality of life

Three articles provided data for cough-related quality of life immediately after the intervention using the LCQ [24–26]. CPAP therapy (MD 4.54 95%CI 3.44 to 5.64), as well as the PSALTI (ES 1.53 95%CI 0.21 to 2.85) resulted in significant improvements on the LCQ total score compared with control groups [24,25]. Kapela et al., 2020 showed that adding video recordings of breathing exercises to a standard intervention which included cough education,

laryngeal irritation reduction and cough suppression strategies, and psycho-educational counselling, is not of added value (MD -2.90 95%CI -5.16 to -0.64) [26]. One study reported on the mid-term effects (3 months) of PSALTI, showing no differences between the control and experimental group (MD 0.01 95%CI−1.62 to 1.64). Effects of these interventions on cough-related quality of life are in figure 3.

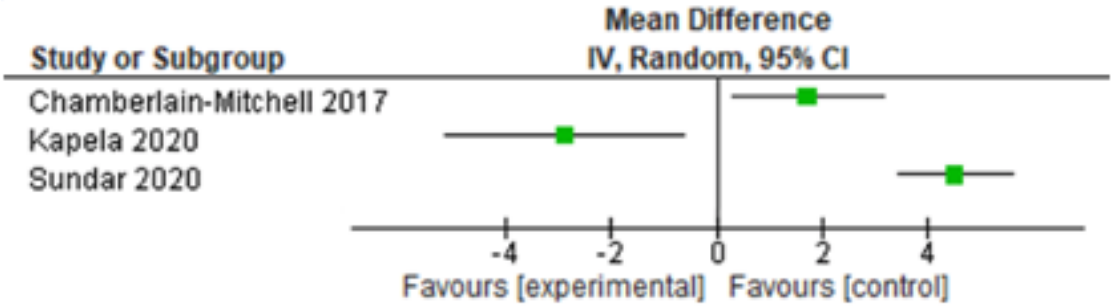

Figure 3: Effects of non-pharmacological interventions on cough-related quality of life.

2.4.4.2 Objective cough measure

One study, objectively, evaluated cough counts using the LCM [24], finding significant differences between the PSALTI and control groups for cough frequency (MD 0.59 95%CI 0.36 to 0.95 cough counts/hour) [24].

2.4.4.3 Symptoms and health-related quality of life

Symptoms evaluated included breathing, voice, upper airway, and limitation symptoms with a Symptom Score (i.e., 5-point Likert scale) [21,26], urge to cough with the Modified Borg Scale [21,23], cough severity using the visual analogue scale [24], and anxiety and depression using the Spielberger State–Trait Anxiety Inventory and the Hospital Anxiety and Depression scale [23]. No difference in the Symptom Total Score was observed by the addition of a video of

breathing exercises to a standard intervention including cough education, laryngeal irritation reduction and cough suppression strategies, and psycho-educational counselling (MD 1.00 95%CI -5.56 to 7.56 points) [26]. Mindfulness (Median 0 IQR 0 to 2 points) and cough suppression (Median 0 IQR -1 to 1 points) were not superior to each other nor to the control group (Median 0 IQR -2 to 1 points) for improving participants' urge to cough [23]. Symptoms of anxiety and depression did not change significantly with mindfulness or voluntary cough suppression (data not reported) [23], or PSALTI (HADS-Anxiety MD -0.42 95%CI -1.96 to 1.13 points; HADS-Depression MD -0.44 95%CI -1.69 to 0.81 points) [24].

Health-related quality of life was evaluated by the Short-Form 36 (SF-36) [24], the asthma life questionnaire (ALQ) [25] and the GERD health-related quality of life questionnaire (GERD-QOL) [25]. The CPAP therapy and the PSALTI did not result in significant differences in health-related quality of life scores (ALQ MD -4.44 95%CI -7.18 to 1.70 points; GERD-QOL MD -3.44 95%CI -4.78 to 2.10 points; SF-36 physical component MD 0.56 95%CI -2.52 to 3.64 points; SF-36 mental component MD 0.81 95%CI -3.10to 4.72 points) [24,25].

2.4.4.4 Voice

Three studies evaluated voice outcomes [21,22,24,26] using the SLP's perceptual voice ratings, acoustic analysis, electroglottography [22], the vocal performance questionnaire [24], and the Consensus of Auditory-Perceptual Evaluation of Voice (CAPE-V) [26]. The cough education, laryngeal irritation reduction and cough suppression strategies, and psycho-educational counselling multi-component therapy, delivered through speech-language therapy, resulted in significant improvements in the perceptual ratings of breathy, rough, strain, glottal fry voice (MD from 0.3 to 1 points) [22]. No difference in the CAPE-V was observed between those

attending the multi-component therapy delivered through speech-language therapy alone, or speech-language therapy paired with video recordings [26]. No significant differences were observed between the PSALTI and control groups for changes in voice impairments (MD 3.9 95%CI -0.33 to 8.12 points) [24].

2.4.4.5 Other outcome measures

Other outcome measures evaluated included the SLP's clinical judgement about the performance of the techniques [21] and effectiveness of the cough education, laryngeal irritation reduction, cough suppression strategies, psycho-educational counselling (rated as successful or partially successful or unsuccessful) [21], the accuracy of the patients' technique [26], the severity of sinonasal disease [25], and airway inflammatory markers from exhaled breath condensate. [25]. The SLPs judged cough education, laryngeal irritation reduction, cough suppression strategies and psycho-educational counselling as significantly successful in improving outcomes compared to the control group (OR 48.13 95%CI 13.53 to 171.25) [21]. Adding a video of breathing exercises to a standard speech language pathology intervention resulted in no improvements to patient's accuracy in performing the speech language pathology techniques. CPAP in the OSA population did not affect the sinonasal questionnaire scores (MD -7.79 95%CI -11.83 to -3.75 points) or airway inflammatory markers compared with sham-CPAP [25].

TABLE 2: Intervention Characteristics

Author, year	Cough Therapy	Components	Duration & Frequency	Equipment	Inclusion Criteria	Exclusion Criteria
Vertigan, 2006 [21] Vertigan, 2008 [22]	SPEICH-C	1) Education 2) Cough control 3) Psycho-educational counselling 4) Vocal Hygiene Education	8 weeks 4 sessions: 30 min each	N/A	1) >18 years; 2) Ability to attend the sessions; 3) Cough >8 weeks despite optimal medical treatment 4) sought medical attention	1) recent URI; 2) Untreated underling condition; 3) abnormal chest X-ray; 4) COPD; 5) neurological voice disorder
Young, 2009 [23]	*Two groups:* 1) Mindfulness 2) Voluntary Suppression	Mindfulness: Controlled breathing and Meditation Cough suppression: Voluntary	1 week Mindfulness: 30 min/day then 15min/day training exercise prior to second cough challenge. Cough suppression: performed during the challenge	Mindfulness: audiocassette for home practice	1) Cough >8 weeks despite optimal medical treatment; 2) Referral to a cough clinic	1) Did not have a measurable C5; 2) URI in past 4 weeks; 3) Current treatment with opiates, ACE inhibitors, OTC cough medicine; 4) Current smokers
Chamberlain, 2017 [24]	PSALTI:	1)education; 2) laryngeal hygiene and hydration; 3) cough suppression techniques; 4) breathing exercises; 5) psychoeducational counselling	4 weeks 4 sessions: 45 min each	N/A	1) Older than 18 years; 2) Chronic cough (>8 weeks) despite optimal medical treatment for underlying conditions; 3) Normal Chest x-ray; 4) < 10mL sputum/day	1) URI within 4 weeks; 2) ACE inhibitors; 3) Current smokers; 4) Respiratory disease; 5) Vocal cord nodules, malignancy, or active aspiration

Sundar et al., 2020 [25]	CPAP Therapy	CPAP equipment provided by Philips-Respironics Inc.	6 weeks	CPAP equipment provided by Philips-Respironics Inc	1) Older than 18 years; 2) Chronic cough (>8 weeks) despite optimal medical treatment for underlying conditions; 3) Smoking < 5 pack years and a history of more than 10 years; 4) Normal chest imagology tests; 6) FEV1/FVC > 0.7, FVC > 70% predicted and DLCO>50% predicted; 7) Diagnosis of OSA	1) Pregnancy; 2) Positive methacholine challenge test; 3) Asthma; 4) Pneumonia < 6 months; 5) Congestive heart failure, renal disease, liver disease, pulmonary embolism, stroke or neurodegenerative disease, malignancy; 6) > 70 years; 7) Use of supplemental oxygen or CPAP; 8) Opiates, benzodiazepines; 9) Alcoholism, drug dependence or illicit drug use; 10) Prior GI or laryngeal surgery; 11) Craniofacial abnormalities that preclude CPAP placement.
Kapela, 2020 [26]	SPEICH-C + pre-recorded SPEICH-C technique videos	SPEICH-C Component: 1) Education 2) Reduce laryngeal irritation 3) Cough suppression strategies 4) Psycho-educational counselling SPEICH-C technique videos: Videos demonstrating therapy exercises	1 to 6 sessions	Computer or DVD player	1) Older than 18 years old; 2) access to a computer of DVD player; 3) Chronic cough (>8 weeks) despite optimal medical treatment for underlying conditions; 4) sought medical attention due to cough	1) Current smoker or ceased smoking less than 6 weeks prior to enrollment; 2) Recent upper respiratory tract infection; 3) Cognitive disorders precluding participation; 4) Untreated associated conditions including asthma, rhinosinusitis, gastro-oesophageal reflux disease, use of angiotensin-converting-enzyme inhibitors, or lung disease.

Abbreviations: ACE; Angiotensin Converting Enzyme; COPD, Chronic Obstructive Pulmonary Disease; CPAP, Continuous Positive Airway Pressure; FEV1, Forced expiratory volume in 1 second; FVC, Forced Vital Capacity; DLCO, Diffusing Capacity of the Lung for Carbon Monoxide; GERD, Gastroesophageal Reflux Disease; OSA; Obstructive Sleep Apnea; OTC, Over the counter; PSALTI, Physiotherapy, Speech and Language Therapy Intervention; PNDS, Postnasal Drip Syndrome; SPEICH-C, Speech Pathology Evaluation and Intervention for Chronic Cough; UACS, Upper Airway Cough Syndrome; X-Ray, Energetic High-Frequency Electromagnetic Radiation.

TABLE 3: Result Characteristics

Author, year	Interventions	Outcomes	Outcome Measures	Results	Summary of Findings
Vertigan, 2006 [21]	Experimental: SPEICH-C Control: Equivalent course of healthy lifestyle education	1) Symptoms: breathing; cough; voice; upper airway, limitations 2) limitation of symptoms on everyday activity clinical judgement	**1) Symptom rating 5-point scale** a) Total score b) Breathing c) Voice d) Upper airway e) Limitations 2) Clinical Judgment (Successful vs. Partially successful vs. Unsuccessful)	1) Symptoms (Pre/post scores): - Total score - EG: 35.4±16 vs. 22.7±18; CG: 29.9±13.5 vs. 28.8±16.5 (p<0.001) - Breathing - EG: 7.9±4.1 vs. 5±4.2; CG: 6.6±4.7 vs. 5.5±3.5 (p<0.001) - Cough - EG: 8.8±2.8 vs. 4.9±3; CG: 7.5±.3.6 vs. 6.3±3.5 (p=0.003) - Voice - EG: 7.2±6 vs. 4.7±5.2; CG: 6.5±.4.6 vs. 6.2±5 (p=0.005) - Upper airway - EG: 9.2±6.6 vs. 6.5±6.3; CG: 7.4±.4.9 vs. 7.4±5.5 (p=0.002) - Limitations - EG: 2.3±1.2 vs. 1.6±1; CG: 2.2±.1.1 vs. 2±1 (p=0.011) 2) Clinical Judgment (Successful vs. Partially successful vs. Unsuccessful) EG: 38 vs. 3 vs. 2; CG: 6 vs. 3 vs. 35 (p<0.001)	SPEICH-C resulted in better outcomes on the 5-point symptom rating scale and on the clinical judgement scores in comparison to the control group.
Vertigan, 2008 [22]	Experimental: SPEICH-C Control: Equivalent course of healthy lifestyle education	1) Perceptual Voice Outcomes 2) Acoustic outcomes & Electroglottography	**1) Ratings of the reading the grandfather passage** 2) Praat acoustics analysis program & laryngograph Speech Studio, Laryngograph	1) Reading the grandfather passage (Pre/post scores) - High Pitch - EG: 1.0±0.2 vs. 1.1±0.5; CG: 1.1±0.2 vs. 1.0±0.2 (p=0.273) - Low Pitch - EG: 1.2±0.5 vs. 1.1±0.4; CG: 1.4±0.6 vs. 1.3±0.7 (p=0.899) - Monotone - EG: 1.3±0.5 vs. 1.2±0.6; CG: 1.2±0.5 vs. 1.2±0.4 (p=0.777) - Soft - EG: 1.3±0.8 vs. 1.1±0.5; CG: 1.3±0.6 vs. 1.1±0.4 (p=0.902) - Loud - EG: 1.0±0.2 vs. 1.0±0.0; CG: 1.0±0.0 vs. 1.0±0.0 (p=0.344) - Breathy - EG: 2.4±1.2 vs. 1.5±0.9; CG: . 2.4±1.2 vs. 2.4±1.0 (p<0.001) - Strain - EG: 2.7±1.3 vs. 1.9±1.1; CG: 2.6±1.0 vs. 2.6±1.0 (p<0.001)	SPEICH-C resulted in better voice outcomes breathing, strain, and rough scores on perceptual in comparison to the control group. No significant differences between groups were observed for changes in acoustic and electroglottography outcomes.

				- Rough - EG: 2.7±1.2 vs. 1.9±1.2; CG: 2.6±1.1 vs. 2.8±1.1 (p<0.001) - Glottal Fry - EG: 2.1±1.2 vs. 1.3±0.7; CG: 2.0±1.2 vs. 2.1±1.1 (p=0.001) - Pitch Breaks - EG: 1.1±0.5 vs. 1.1±0.0; CG: 1.1±0.3 vs. 1.1±0.2 (p=0.478) - Phonation breaks - EG: Pre 1.1±0.6 vs. Post 1.0±0.0; CG: Pre 1.1±0.3 vs. Post 1.0±0.2 (p=0.439) - Voice arrests - EG: Pre 1.1±0.6 vs. Post 1.0±0.0; CG: Pre 1.0±0.0 vs. Post 1.1±0.4 (p=0.042) - Falsetto - EG: Pre 1.0±0.2 vs. Post 1.0±0.0; CG: Pre 1.0±0.0 vs. Post 1.0±0.0 (p=0.344) 2) Praat acoustics analysis program & Laryngograph (Pre/post scores) - MPT - EG: 9.4±6.4 vs. 11.0±5.6; CG: 10.8±6.4 vs. 11.6±6.6 (p=0.422) - SDF - EG: 18.6±12.3 vs. 17.7±14.2; CG: 25.0±16.2 vs. 23.7±17.3 (p=0.970) - Jitter - EG: 2.6±2.5 vs. 1.6±1.3; CG: 2.4±1.6 vs. 2.1±1.5 (p=0.209) - HNR - EG: 17.1±5.9 vs. 19.7±5.0; CG: 19.0±5.1 vs. 18.6±5.5 (p=0.200) - DFx (male) - EG: 97.3±13.1 vs. 96.7±12.3; CG: 105.7±16.6 vs. Post 103.0±16.3 (p=0.746) - DFx (female) - EG: 167.4±27.1 vs. 167.7±21.6; CG: 178.3±29.8 vs. 177.1±32.0 (p=0.801) -Qx - EG: 39.3±17.9 vs. 43.3±19.5; CG: 33.2±16.6 vs. 37.2±19.0 (p=0.449)	
Young, 2009 [23]	Experimental 1: Mindfulness	1) Urge to cough	1) Modified Borg Scale	1) Modified Borg scale (Pre/post mean differences)	No significant differences between groups were observed for changes in urge to cough.

	Experimental 2: Cough Suppression Control: No intervention			- Urge to cough – Voluntary suppression 0.0 (-1.0 to 1.0); mindfulness 0.0 (0.0 to 2.0); CG: 0.0 (-2.0 to 1.0); (p= 0.7)	
Chamberlain, 2017 [24]	Experimental: PSALTI Control: Healthy Lifestyle Advice	**1) Cough- related QoL** 2) Objective Cough frequency 3) Cough severity	**1) LCQ** 2) LCM 3) VAS 4) VPQ 5) SF-36 6) HADS	Pre/post mean differences 1) LCQ Total score - EG: 3.40 (2.26 to 4.55); CG: 1.66 (0.78 to 2.54) (p=0.024) 2) LCM (Cf/hr) - EG: Mean diff 0.55 (0.33 to 0.75); CG: 0.82 (0.60 to 1.22) (p=0.030) 3) VAS - EG: -21.18 (-29.83 to -12.53); CG: -11.84 (-20.11 to -3.57) (p=0.084) 4) VPQ - EG: 4.04 (0.12 to 7.97); CG: 0.73 (-1.94 to 3.39) (p=0.070) 5) SF-36 - SF-36 PCS - EG: 1.62 (–0.96 to 4.21); CG: 0.50 (-1.30 to 2.31) (0.717) - SF-36 MCS - EG: 0.53 (-2.69 to 3.75); CG: -0.26 (-2.92 to 2.40) (p=0.680) 6) HADS - HADS-Anxiety - EG: -1.27 (-2.51 to -0.032); CG: -0.90 (-1.96 to 0.17) (p=0.590) - HADS-Depression - EG: -0.68 (-1.57 to 0.21); CG: -0.21 (-1.11 to 0.69) (p=0.486)	PSALTI significantly improved cough-related quality of life and objective cough frequency in comparison to the control group. No significant differences between groups were observed for changes in cough severity, voice outcomes and symptoms of anxiety and depression.
Sundar, 2020 [25]	Experimental: CPAP therapy Control: Sham CPAP therapy	**1) Cough- related QoL** 2) Sino-nasal Disease 3) Airway Inflammation Markers	**1) LCQ** 2) SNOT- 20 3) GERD-QoL 4) ALQ 5) Exhaled Breath Condensate	Pre/post scores 1) LCQ Total score - EG: 10.63±3.94 vs. 17.24±3.97; CG: 12.62±4.13 vs. 14.69±3.94 (p=0.016) 2) SNOT-20 - EG: 46±14.8 vs. 29.77±20.95; CG: 34.88±14.63 vs. 26.44±13.99 (p=0.27) 3) GERD-QoL - EG: 9.44±8.93 vs. 4.44±4.85; CG: 6.33±6.72 vs. 5.77±7.66 (p=0.27) 4) ALQ - EG: 8.88±2.47 vs. 4.88±2.47; CG: 7.44±3.53 vs. 6.88±3.05 (p=0.09) 5) Exhaled Breath Condensate	CPAP significantly improved cough-related quality of life in comparison to the control group. No significant differences between groups were observed for changes in the severity of sinonasal disease and airway inflammation markers

				- NOX (umol/L) - EG: 3.34±2.07 vs. 2.91±2.32; CG: 3.35±2.81 vs. 5.26±0.18 (p=0.258) - IL- 8 (pg/mL) - EG: 1.52 ± 1.41 vs. 1.00 ± 0.21; CG: 1.02 ± 0.24 vs. 1.04 ± 0.18 (p=0.594) - 8iso (pg/mL) - EG: 4.92 ± 2.23 vs. 7.35 ± 3.47; CG: 3.99 ± 1.89 vs. 5.04 ± 2.13 (p=0.156) - H2O2 nmol/L - EG: 2458.02 ± 324.88 vs. 1654.07 ± 239.71; CG: 1714.42 ± 337.1 vs. 1468.04 ± 143.58 (p=0.643)	
Kapela, 2020 [26]	Experimental: SPEICH-C + pre-recorded SLP technique videos Control: SPEICH-C	1) Cough- related QoL 2) Symptom and limitation outcomes 3) Voice outcomes **4) Accuracy performing the technique**	1) LCQ 2) Symptom severity and frequency rating scale 3) CAPE-V **4) Clinical Judgment (Correct vs. incorrect)**	Pre/Post Mean Differences 1) LCQ Total Score – EG: 15.3±3.00 vs. 16.8±2.70; CG: 11.20±3.30 vs. 15.6±2.40 (p=0.796) 2) Symptom Frequency and Severity Total Score – EG: 25.9±9.20 vs. 19.5±9.20; CG: 22.5±8.30 vs. 17.1±7.50 (p=0.941) 3) CAPE-V – EG: 21.9±16.6 vs. 15.5±12.5; CG: 9.80±5.10 vs. 6.00±3.30 (p=0.575) 4) Rater judgement (Correct vs. Incorrect) – EG 7 vs. 1 vs. CG 7 vs. 0	No significant differences between groups were observed for changes in cough-related quality of life, symptom severity and frequency rating, voice outcomes, and technique performances.

Abbreviations: ACE, Angiotensin Converting Enzyme; *ALQ* asthma life questionnaire; CAPE-V, Consensus of Auditory-Perceptual Evaluation of Voice; CG, Control Group; CPAP, Continuous Positive Airway Pressure; EBC exhaled breath condensate measurements; EG, Experimental Group; GERD, Gastroesophageal Reflux Disease; GERD-QOL GERD health- related quality of life questionnaire; HADS, Hospital Anxiety and Depression Scale; H202, Hydrogen Peroxide; IL-8, Interleukin-8; 8-isopg, 8-isoprostanes; LCM, Leicester Cough Monitor; LCQ, Leicester Cough Questionnaire; NOX, Nitrates/Nitrites; OSA; Obstructive Sleep Apnea; PSALTI, Physiotherapy, Speech and Language Therapy Intervention; PNDS, Postnasal Drip Syndrome; QoL, Quality of Life; SPEICH-C, Speech Pathology Evaluation and Intervention for Chronic Cough; SF-36, Short-form 36 Questionnaire; SNOT-20 sinonasal outcomes-20 questionnaire; Spielberg STAI, Spielberg State-Trait Anxiety Inventory; UACS, Upper Airway Cough Syndrome; VAS, Visual Analogue Scale; VPQ, Vocal Performance Questionnaire.

* Outcome measures presented in bolded format indicate the primary outcome measure of each article. Vertigan et al 2006 and Vertigan et al. 2008 reported no primary outcome measure.

2.4.5 Risk of Bias Assessment

Most articles presented "some concerns" (n=5) in the overall risk of bias [22–26], with one study presenting with a high overall risk of bias [21]. The main source of bias emerged from the absence of studies' registration reporting on outcomes and planned analysis. Such absence prevented the establishment of conclusions about the selection or non/selection of reported outcomes and analyses. Two articles presented high risk of bias on the "deviations from intended interventions" domain [21,23] and one study on the "measurement of the outcome" domain [3]. Four of the included articles were single-blinded [21–24], one study was double-blinded [25], and one study did not blind the participants nor the investigators [26].The detailed risk of bias evaluation can be found in Figure 4.

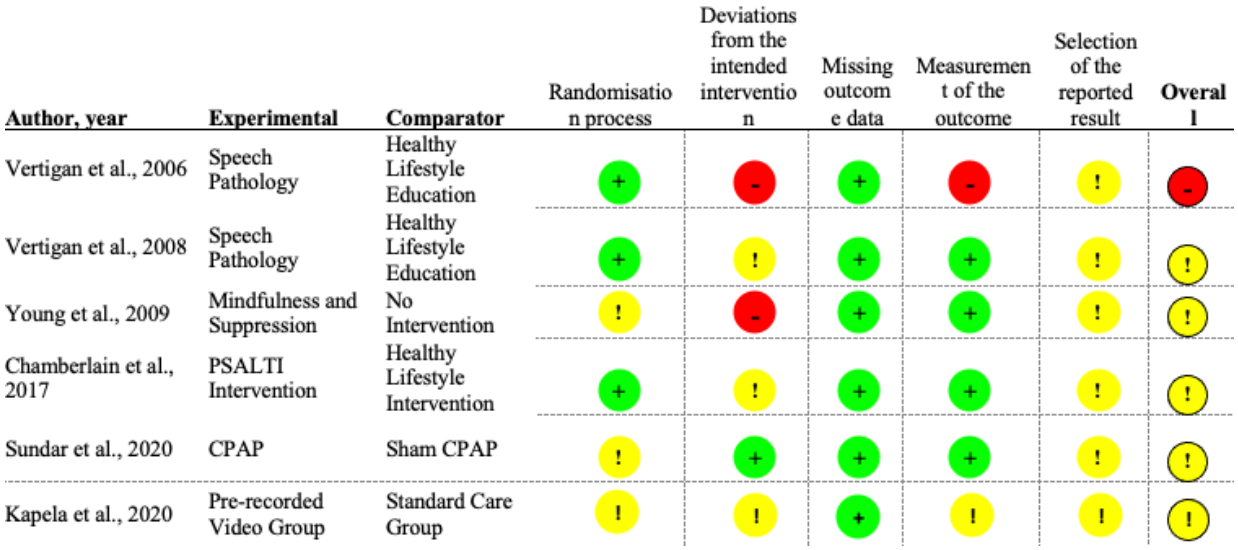

Figure 4**:** Risk of Bias Summary [1]

2.5 Discussion

Non-pharmacological cough therapies improved cough-specific quality of life [24,25], cough frequency [24], and voice outcomes, such as breathy, rough, strain and glottal fry voice [22]. No improvements were observed for urge to cough [24], cough severity [24,26], anxiety

and depression [23,24], severity of sinonasal disease [25], or airway inflammatory markers [25]. Small sample sizes, small effects, and large confidence intervals precluded confidence in establishing the impact of the identified nonpharmacological cough therapies. Variations in outcome measures and sampling times added to the study design heterogeneity, which prevented the pooling of results.

Physiotherapists and SLPs used similar therapies to treat non-productive chronic cough (i.e., education, laryngeal irritation reduction strategies, cough control, and psychoeducational strategies) [21,22,24,26]. The mechanism of actions of these multicomponent therapies is thought to be driven by a synergistic relationship between the various components to reduce sensory input triggering cough [27]. For example, education provided basic knowledge of cough, which then increased the likelihood of cough control strategies being effective [27]. Comparisons between single and multicomponent therapies could not be made, as time points varied, and no study specifically compared single versus multicomponent therapies. CPAP did improve cough in those with OSA, possibly by its impact on lung inflation or on gastro-esophageal reflux [23, 26, 27], however, its use in other chronic respiratory diseases is unexplored. A recent systematic review explored multimodal treatments for refractory chronic cough and concluded that medical therapy, speech language therapy, and procedural therapy all improve outcomes of chronic cough [9]. In this review, all study designs were included and speech-language therapy was described as including a large number of interventions, such as physiotherapy and behavioural therapy and no distinction between them was performed, which could have influenced the conclusions presented [9]. Our review compliments these results, by presenting the data from people with chronic respiratory diseases, including only the highest

evidence available (RCTs) and differentiating between different disciplines and techniques performed for people with refractory chronic cough.

Of the seventeen outcome measures that were used in the studies to evaluate cough interventions, thirteen have adequately described their measurement properties for chronic cough and four have been validated for people with chronic respiratory diseases [29–32]. The LCQ and the LCM appear to be the most valid, reliable, and responsive measures [19], but they lack validation for cough associated with underlying chronic respiratory diseases [2,6]. The absence of disease-specific measures will also limit the extent to which the outcomes used may be applicable to underlying obstructive and interstitial lung disease [28, 32,33,34].

Despite three additional reviews published since 2010 looking at non-pharmacological management of chronic cough, this is the first systematic review in more than a decade to report on the effects of non-pharmacological cough therapies for, both, people with non-productive refractory cough and chronic respiratory diseases, and the results highlight the paucity of articles on this topic despite it being so prevalent. Nevertheless, this review is not without limitations. The quality of our findings was limited by the heterogeneity of the studies published. The duration of the interventions varied between one to eight weeks. We acknowledge that a one-week intervention may be unlikely to influence cough symptoms lasting for several years. Nevertheless, given the paucity of data in the field, and the uncertainty regarding the best design for providing non-pharmacological interventions, we decided to include all studies independently of frequency and duration of sessions to report on all the available evidence to date. Language competency limited our inclusion to studies in English, Portuguese and French. We excluded alternative medicine techniques, such as acupuncture and treatments that required ingestion of herbal medications, vitamins, and teas. We also excluded any therapies in which the use of

pharmacological and non-pharmacologic treatments were paired. Lastly, comorbidities of articles reporting on individuals with refractory chronic cough included asthma, a chronic respiratory condition, except for Sundar et al. [25], in which chronic cough was not refractory, but attributed to the OSA. Results for patients with refractory chronic cough and asthma were not reported separately, and thus, no conclusions can be made regarding the effects of non-pharmacological therapy specifically for individuals with asthma. Furthermore, although therapies delivered through speech-language pathology and physiotherapy offer promising results as a form of nonpharmacological cough management, the long-term effects of this therapy are unknown and need to be further investigated.

2.5.1 Implications for research and practice

Our findings highlight the need for relevant, well-designed studies in order to help guide clinicians to better manage refractory cough, both for individuals with no prior respiratory conditions, and those with documented underlying respiratory tract disorders. Prior to doing so, the optimal administration of non-pharmacological management strategies, as well as their role as part of dual pharmacologic and non-pharmacologic therapy, remains unclear.

2.6 Conclusion

Non-pharmacological cough therapies improve cough-specific quality of life, cough frequency, and voice outcomes in some studies. Although their effectiveness alone or in combination with pharmacological therapies remains highly relevant, current evidence of effectiveness is insufficient for clinical recommendations to assist with the management of refractory cough or non-productive chronic cough associated with chronic respiratory diseases.

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CHAPTER 3:

Cough Assessment and Management in Pulmonary Rehabilitation – a Canadian Survey

Submitted to the *COPD: Chronic Obstructive Pulmonary Disease Journal*

3.1 Abstract

Background: PR is a cornerstone intervention for controlling respiratory symptoms and improving health-related quality of life in people with chronic respiratory diseases. Chronic cough affects up to 90% of people with chronic respiratory diseases, however, it is currently unknown whether chronic cough is assessed and/or managed in PR.

Objective: The primary objective was to determine if chronic cough is assessed and managed in PR. Secondary objectives were to determine factors such as how chronic cough is assessed and managed in PR, what factors impact chronic cough assessment and management, and the barriers and facilitators impacting chronic cough assessment and management.

Methods: This was a cross-sectional study. PR programs in Canada were identified via online websites. A representative from each program was invited via email to complete an online survey including the following topics: PR demographics, assessment and management practices, and barriers and facilitators. Descriptive statistics were used to analyse data.

Results: Of 133 PR programs contacted, 31 returned a completed survey (23% response rate). Surveys were mostly completed by respiratory therapists (42%). Approximately half (52%) of PR programs reported enrolling patients with chronic cough. Of those, 45% reported assessing chronic cough and 62% reported its management. Inadequate knowledge of assessment and management techniques was commonly identified to be a barrier and increased education was suggested as a possible facilitator.

Conclusion: Based on PR programs that responded to our survey, chronic cough is a prevalent symptom, however it is scarcely assessed and managed. Need of structured education and use of standardized strategies were reported as facilitators to the assessment and management of chronic cough in PR.

3.2 Introduction

Chronic respiratory diseases affects over three million Canadians, with COPD, asthma, and ILD, being some of the most prevalent in Canada [1]. Despite each disease differing in their underlying pathophysiology, many have similar clinical presentations, including dyspnea and chronic cough [2]. Dyspnea has been largely studied [3], but there is limited information regarding the assessment and management of chronic cough.

Cough is one of the most important sensory reflexes needed for survival [4]. However, when the cough becomes chronic, i.e., persists for 8 weeks or more, and is triggered by innocuous stimuli, such as talking, laughing, and exercising; it can have a serious impact on patients' daily lives [5]. A cough due to an underlying disease may be relieved when treating the primary cause; however, if it persists despite medical treatment for other health conditions, it is known as a refractory chronic cough [6]. Prevalence rates of chronic cough, either refractory or with an underlying cause, have been on a rise, with a reported prevalence of 16-18% in Canada [7], and can rise up to 90% in those with a chronic respiratory disease [8].

The burden of chronic cough is severe for patients, healthcare services, and societies. A constant feeling of having something 'stuck in the throat', coughing to low levels of stimulation, and inability to stop coughing are reported [9]. Cough can also be related to urinary incontinence, poor sleep, difficulties with relationships and social interactions, and work-related problems (55% productivity loss with costs of $11,610 per employee/year) [10]. This can affect a patient's physical and mental health (e.g., fatigue, anxiety, and depression) [11]. Additionally, its impacts have been aggravated by the stigma associated with coughing during COVID-19 pandemic.

Chronic cough can be managed using pharmacological and non-pharmacological interventions. Non-pharmacological interventions may involve cough suppression for non-productive cough [12–17] and cough augmentation for productive cough [18]. CCT can be delivered by physiotherapists or SLPs and it includes several components such as education, laryngeal hygiene, cough suppression techniques, breathing exercises, and counselling [19]. The underlying mechanisms of CCT are still scarcely studied but are known to improve cough reflex sensitivity, cough frequency, and cough-related quality of life [19]. CCT has been shown promising results for people with refractory chronic cough [19] with no adverse effects.

PR is a multidisciplinary, comprehensive, evidence-based intervention used to improve symptoms, exercise capacity, and quality of life in those who have chronic respiratory diseases [20–22]. Two important core components of PR, education on behaviour change and promotion of hydration and breathing techniques [20,23], are also components of CCT. However, there is limited evidence as to how chronic cough is addressed in PR programs.

Therefore, this study aims to determine if chronic cough is assessed and/or managed in PR. We also seek to identify how chronic cough is assessed and managed in PR, what factors impact chronic cough assessment and management, and barriers and facilitators to chronic cough assessment and management

3.3 Methods

3.3.1 Survey Instrument Development

This was a cross-sectional survey study conducted across Canadian PR programs and developed according to the Consensus-Based Checklist for Reporting of Survey Studies (CROSS), seen in Appendix D. This is a study that was conducted across Canadian PR

programs. The survey questionnaire was developed using a similar format to those of previous PR surveys [2,24], with the addition of cough-specific questions. The survey was divided into the following domains: demographic characteristics of the PR program (type of PR program, such as inpatient vs. outpatient, program capacity, and composition of the healthcare team); cough assessment (method of cough assessment, outcome measures used, and differences assessing cough among different respiratory chronic diseases); cough management (interventions used and differences between the management of productive and non-productive cough, as well as among different respiratory diseases); barriers and facilitators to cough assessment and management [2,24]. The online survey was generated using LimeSurvey (LimeSurvey GmbH, Hamburg, Germany) and was tested by two additional members of the study team and piloted by another healthcare professional experienced in PR. The healthcare professional testing the survey was asked to comment on 1) observations regarding survey informational aspects, 2) comprehensiveness and clarity, 3) easiness of navigation, 4) grammar and spelling, and 5) time for completion. The survey was revised based on this feedback. The time to complete the survey was between 15-20 minutes. To account for human input error, the survey software forced the entry of only numbers for numeric questions, for example, and informed participants if mandatory questions have not been filled. The survey can be found in Appendix E.

3.3.2 Study Design and Participant Recruitment

The population of this study consisted of PR programs in Canada. Programs were identified through lists obtained from the Canadian Thoracic Society (CTS) and provincial and municipal healthcare websites. Programs were contacted by email or phone and asked to identify a member of the PR program who could answer the survey in representation of that program.

This member had to be a healthcare provider, working with patients in PR, to qualify for answering the survey.

3.3.3 Procedure

This study obtained ethics approval from the Hamilton Integrated Research Ethics Board (HiREB) in May 2021 (Project ID: 13097). The representatives of the identified PR programs were sent an introductory email describing the study purpose and rationale, along with the guarantee that confidentiality would be maintained. The email also contained the survey hyperlink. Digital consent was obtained via LimeSurvey by asking participants to click on the "agree" box on the first page of the survey if they were willing to participate. Follow up emails were sent two, four, and six weeks after the initial email [2,24]. The survey recruitment occurred between September 2021 and December 2021.

3.3.4 Data Analysis Plan

Descriptive statistics were used to describe data for survey variables, using means and standard deviation (SD), as well as medians and interquartile ranges (IQR), where applicable. Statistical analyses were computed using Microsoft Excel (Microsoft Corporation, USA). As this study is exploratory and preliminary, no sample size calculation was performed. Missing data was not imputed [25].

3.4 Results

3.4.1 Program Characteristics

A total of 133 PR programs were invited to participate. Of those, 31 completed the survey (23% response rate). Response rate was defined as the number of responses received

divided by the total number of PR programs invited to participate. Eighty-seven programs (85%) provided no reason for declining participation, fourteen (14%) stated that they were unwilling, and one (1%) was not able to respond accurately.

Table 1 indicates a breakdown of PR program characteristics. Survey responses were collected across six provinces: Ontario (n=7; 32%), British Columbia (n=5; 23%), Saskatchewan (n=4; 18%), Alberta (n=3; 14%), Manitoba (n=1; 4%), Prince Edward Island (n=1; 4%), and New Brunswick (n=1; 4%). Nine survey respondents' locations were unidentified. No PR programs were identified in Yukon, Northwest Territories or Nunavut. The PR programs were mainly outpatient (n=27; 93%). Most surveys were completed by respiratory therapists (n=13; 42%), followed by physiotherapists (n=8; 26%) and nurses (n=6; 19%), with an average of 8.6 ± 6.0 years of experience working in PR.

Program characteristics for each type of PR program offered is in Figure 1. Maintenance programs reported enrolling more patients at a given time, with longer session durations. Several respondents (n=7; 58%) reported that their maintenance programs run indefinite and we were not able to be included in some of the data on time duration. Only programs with a fixed time duration were included in the figure.

TABLE 1. PR Program Characteristics

Locations in Canada, n (%)	
Unreported*	9 (29.0)
ON	7 (22.5)
BC	5 (16.1)
SK	4 (12.9)
AB	3 (9.7)
Eastern Provinces (PEI, NB)	2 (6.5)
MB	1 (3.2)
Healthcare professionals, n (%)	
Respiratory Therapist	13 (42.9)
Physiotherapist	8 (25.8)
Nurse	6 (19.4)
Other*	6 (18.1)
Years of experience, mean (SD)	8.6 ± 6.0
Type of program offered, n (%)	
Out-patient	27 (93.1)
Maintenance	12 (42.9)
Home Program	9 (31.0)
In-patient	1 (3.6)
Virtual Out-patient	1 (3.6)
Number of patients with chronic cough median (Q1-Q3)	50 (28.75 – 80.0)

Legend: AB, Alberta; BC, British Columbia; IQR, interquartile range; MB, Manitoba; NB, New Brunswick; ON, Ontario; PEI, Prince Edward Island; SD, standard deviation; SK, Saskatchewan.
*Unreported: Refers to healthcare providers not reporting the geographical location of the PR program.
** "Other" includes kinesiologists (n=2; 6.5%), an exercise physiologist, (n=1; 3.2%), a respirologist (n=1; 3.2%), an exercise therapist (n=1; 3.2%), and a personal trainer (n=1; 3.2%).

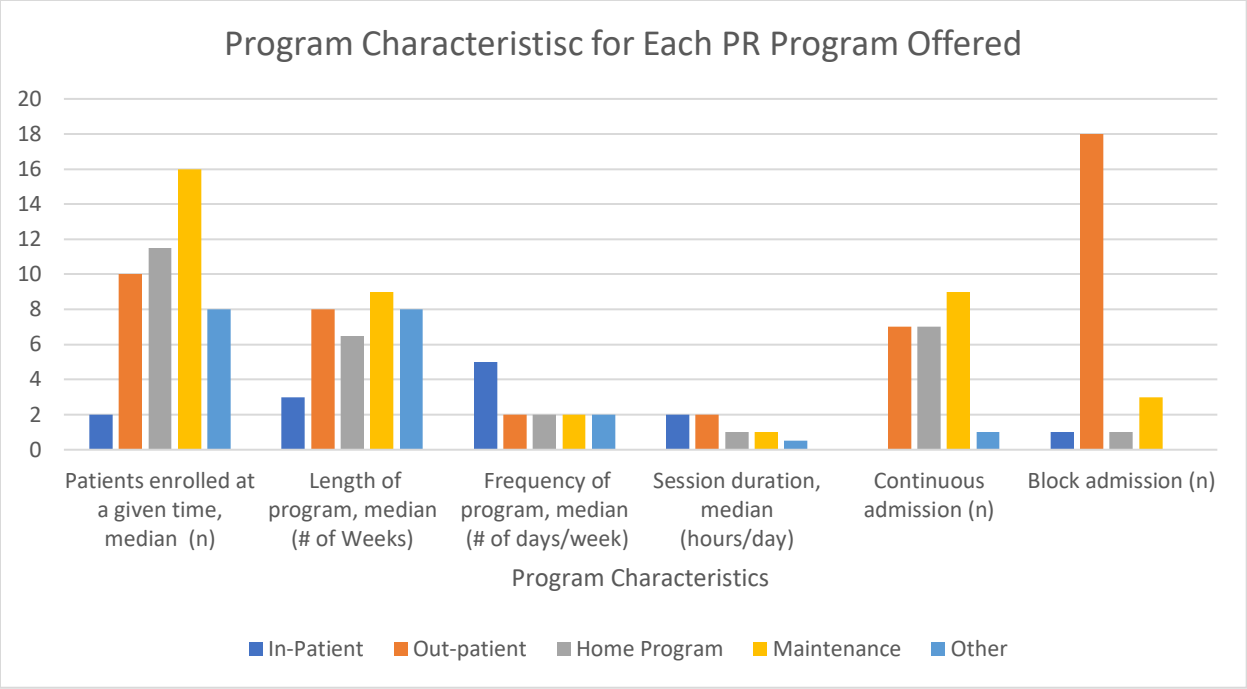

Figure 1: Program characteristics based on type of pulmonary rehabilitation program offered.
**"Other" type of PR offered included virtual PR. To note, many maintenance programs run indefinitely and on rolling admission.*

Of the 31 PR programs completers, the majority reported that COPD was the most represented patient diagnosis in PR (median 80%; Q1 30% – Q3 100%) and half (median 50%; Q1 28.75% – Q3 80%) reported having patients presenting with a chronic cough. The median distribution of respiratory diseases managed in PR programs is presented in Figure 2.

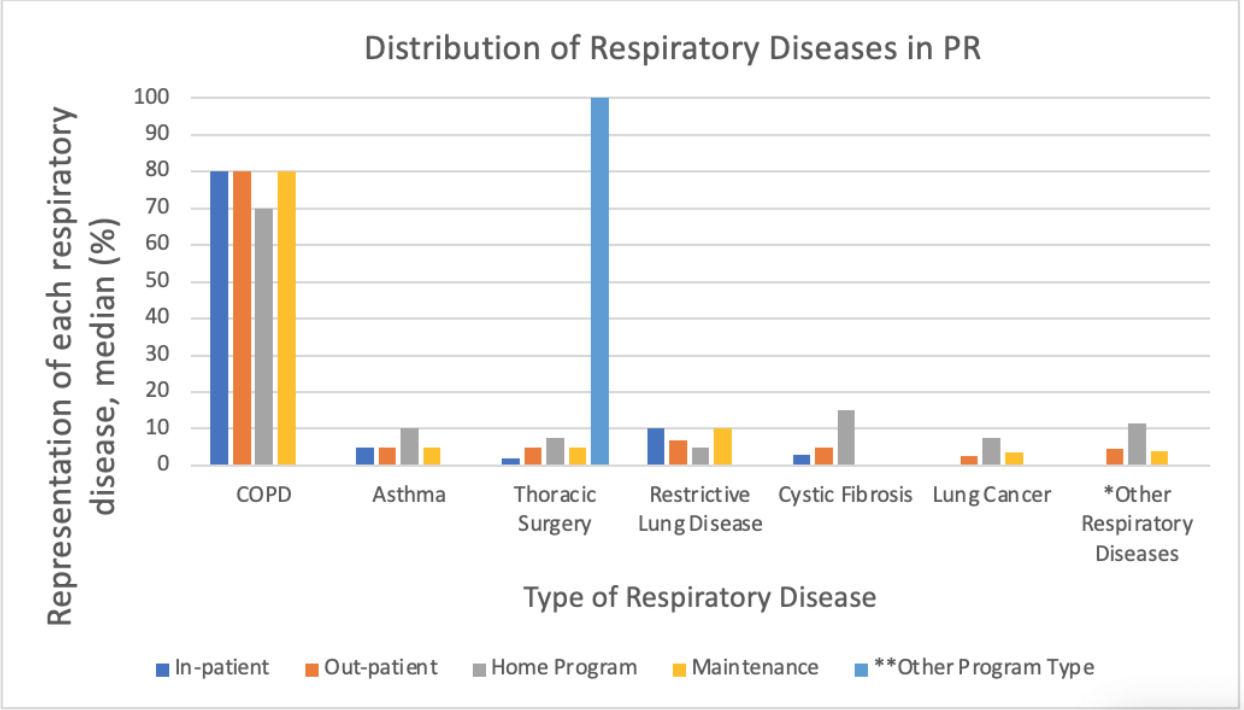

Figure 2: Distribution of respiratory diseases managed in pulmonary rehabilitation programs.
**"Other Respiratory Diseases": respiratory diseases managed in PR include bronchiectasis, pulmonary hypertension, embolism, empyema, bullae, pneumothorax, atelectasis, obesity hypoventilation syndrome, post-covid symptoms. ** "Other Program Type": Out-patient virtual program*

3.4.2 Cough Assessment

Table 2 provides details regarding cough assessment. Fourteen respondents (45%) reported assessing chronic cough. Cough assessment was most frequently conducted at the beginning (n=14; 100%) and end of PR (n=7; 50%) by a physiotherapist (n=7; 50%) or respiratory therapist (n=6; 43%). The assessment included mainly the patient's history (n=13; 93%) and cough questionnaires and scales (n=8; 57%) to evaluate cough frequency (n=13; 93%), type of cough (n=12; 86%), cough triggers (n=12; 86%) and risk factors for cough (n=12; 86%). Items less commonly collected during the assessment are duration of cough (n=9; 64%), factors relieving cough (n=8; 57%) and impacts of cough (n=7; 50%). The distribution of healthcare providers assessing cough is presented in Figure 3 (A).

TABLE 2. Assessment of Chronic Cough in PR Programs

Healthcare professional assessing cough, n (%)	
Physiotherapist	7 (50.0)
Respiratory Therapist	6 (42.9)
Nurse	4 (28.6)
Exercise Physiologist	1 (7.1)
Kinesiologist	1 (7.1)
Assessment point, n (%)	
Beginning of Program	14 (100)
End of Program	7 (50.0)
Monthly	3 (21.4)
Each Session	2 (14.3)
As Needed	2 (14.3)
Weekly	1 (7.1)
Outcome measures, n (%)	
Patient History	13 (92.9)
Questionnaire/Scale	8 (57.1)
Physical Examination	4 (28.6)
Objective Assessment	3 (21.4)
Other: As-needed basis	1 (7.1)
Aspects of cough assessed, n (%)	
Frequency of Cough	13 (92.9)
Type of Cough	12 (85.7)
Cough Triggers	12 (85.7)
Risk Factors for Cough	12 (85.7)
Duration of Cough	9 (64.3)
Relieving Factors	8 (57.1)
Impacts of Cough	7 (50.0)
Other: (Continence and sputum)	1 (7.1)

3.4.3 Cough Management

Table 3 provides details of cough management. A total of 16 respondents (62%) reported managing chronic cough. Non-productive chronic cough was primarily managed through breathing exercises (n=13; 81%), education (n=12; 75%), medication (n=11; 69%), and smoking cessation (n=10; 63%). Less commonly, it was managed through ACTs (n=8; 50%), behaviour change techniques (n=5; 31%) and cough suppression techniques (n=4; 25%). Productive cough was managed using airway clearance techniques (n=15; 94%), medication (n=12; 75%),

breathing exercises (n=11; 69%), and smoking cessation (n=9; 56%). The distribution of healthcare providers managing cough is presented in Figure 3 (B).

TABLE 3. Management of Chronic Cough in PR Programs

Techniques used, n (%)	
Non-productive Chronic Cough	
Breathing Exercises	13 (81.3)
Education	12 (75.0)
Medication	11 (68.8)
Smoking Cessation	10 (62.5)
Airway Clearance Techniques	8 (50.0)
Behaviour Change Techniques	5 (31.3)
Cough Suppression Techniques	4 (25.0)
Productive Chronic Cough	
Airway Clearance Techniques	15 (93.8)
Medication	12 (75.0)
Breathing Exercises	11 (68.8)
Smoking Cessation	9 (56.3)
Behaviour Change Techniques	6 (37.5)
Education	5 (31.3)
Cough Suppression Techniques	1 (6.3)

Most respondents surveyed, indicated that management strategies for chronic cough did not differ based on the respiratory diagnosis (n=9; 56%), or the severity of disease (n=15; 94%). Details of the different chronic cough management strategies provided based on diagnosis are summarized in Appendix F (non-productive cough) and Appendix G (productive cough).

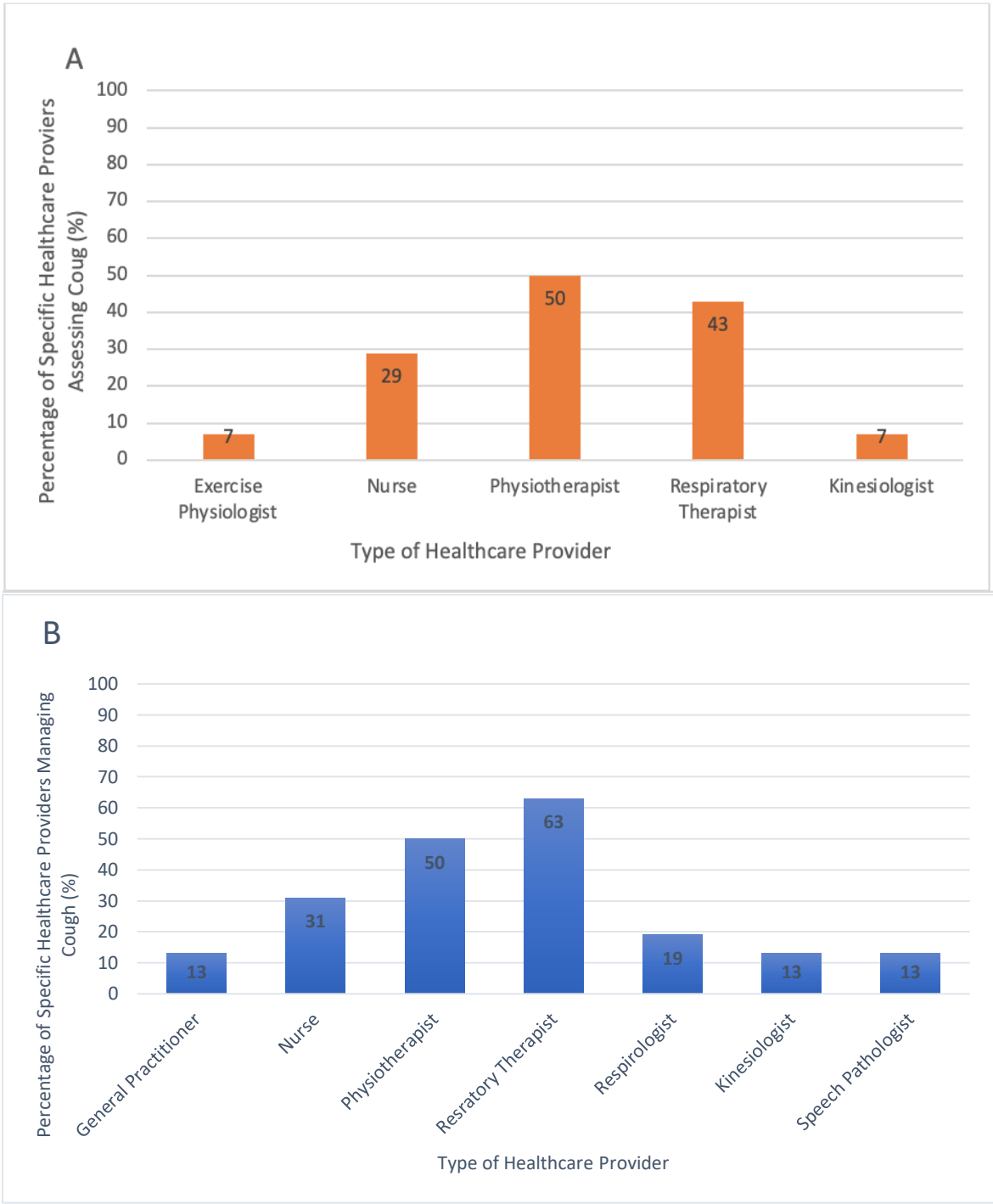

Figure 3: Healthcare Providers (A) Assessing and (B) Managing Cough

3.4.4 Barriers and Facilitators to Cough Assessment and Management

The most commonly identified barrier for cough management was inadequate knowledge on how to assess (n=10; 83%) and treat (n=6; 60%) chronic cough. Other reported reasons for

not assessing/managing chronic cough were lack of patients presenting with a chronic cough in PR (n=2; 67%), and lack of time (n=1; 33%).

The most commonly suggested facilitators for cough assessment and management included providing education and training to healthcare professionals on i) the benefits of PR on chronic cough, ii) valid assessment tools and outcome measures (n=2; 17%) and iii) conducting cough assessment (n=8; 67%) and management (n=4; 44%). The need for increasing the current staff of PR programs was also noted as a facilitator to conduct cough assessment (n=3; 25%) and management in PR (n=4; 44%).

3.5 Discussion

This study shows that most respondents representing PR programs (52%) enroll patients with chronic cough, with 45% reporting assessing and 63% reporting managing chronic cough. Gathering of patient history, use of questionnaires and scales and physical examination were commonly ways for cough assessment. Breathing exercises were the most used strategy for non-productive cough management, while airway clearance techniques were common practice in the management of productive cough. Healthcare professionals also reported an insufficient understanding of cough assessment and management to implement it in their PR practice.

PR programs who responded to the survey do not routinely assess chronic cough, although about half of the respondents reported having patients who present with it. The absence of formal evaluation using valid measurement tools likely prevents a more detailed understanding of the cough characteristics and of the effectiveness of cough management techniques. A detailed history will provide important information regarding characteristics and

triggers, as well as lifestyle and health-related behaviours, that may guide management strategies [26,27], or referral to a cough specialist.

No respondents reported the use of cough-specific measures such as the Leicester Cough Questionnaire (LCQ), a patient reported outcome used in clinical trials and easy to implement in clinical practice [28,29]. The LCQ evaluates cough domains of physical, psychological and social health, takes 5 minutes to complete, and has been reported as valid, reliable, and responsive to therapy in COPD [29] and bronchiectasis [30,31], and namely to PR interventions [32]. Its evaluation, predominantly on the impact of cough symptoms on health related quality of life, means that it provides limited information on other cough characteristics such as cough severity [33]. Encouraging recent research efforts have focussed on the characteristics of cough identified by patients, including urge to cough sensations and cough symptoms, as a prelude to the development of a more comprehensive cough questionnaire [9]. Cough counters are considered the gold standard for cough frequency assessment [30,34] but none of the respondents used them as assessment tools. Similarly, automated solutions using smartphone technology have been reported for those with asthma and chronic refractory cough, but are not yet in widespread use pending studies of feasibility and validation [7,8,35].

Once characterized, optimal management differed in PR programs, between productive and non-productive cough. With ACTs and medication being used for productive chronic cough [36] and breathing exercises plus education to personalize strategies for non-productive cough management. In a recent review of non-pharmacological cough management by our group, we reported that multi-component therapies incorporating both breathing exercises and cough education were the most effective non-pharmacological treatment in improving cough-related quality of life [37]. Similarly, in a recent meta-analysis, Wamkpah and colleagues noted that

non-pharmacological multi-component therapies delivered by SLPs or physiotherapists had positive effects in improving cough and cough-related outcomes [38].

Although the use of antitussive drugs for non-productive chronic cough management has limited efficacy and frequent side-effects [39], 69% of respondents reported using them for non-productive chronic cough, likely because of lack of education of both healthcare providers and patients on alternative approaches even including smoking cessation. Healthcare professionals surveyed identified the need for more education to adequately assess and manage chronic cough in PR. Although national and international professional respiratory organizations have published guidelines on the management of lung disease [40,41], there has been minimal training of rehabilitation providers on the management of chronic cough in PR [42]. The latter presents a unique opportunity as patients have frequent contact with healthcare professionals over several weeks, an ideal environment for reinforcing and supporting learning.

3.5.1 Implications for practice and research

This study identifies that patients enrolled in PR programs across Canada, commonly present with chronic cough but some healthcare professionals lack systematised knowledge and education on how to assess and manage them. Knowledge translation of effective existing therapies would seem a natural step even as tools and treatments continue to be better refined. PR programs provide an important opportunity to improve the wellbeing of those with refractory chronic cough. Our observations should be expanded to improve accuracy and assess generalizability across jurisdictions.

Staffing shortages in healthcare is a current and prevalent barrier in Canada. Therefore, it was to be expected that our survey identified lack of staffing to be a barrier to cough

management. A solution to this barrier may not be as simple as increasing staffing numbers in pulmonary rehabilitation centres, due to ongoing staffing shortages of healthcare workers from the COVID-19 pandemic. One possible solution to minimizing this barrier is to rather increase the upskilling of existing staff than to increase staffing altogether. In doing so, existing staff will obtain the abilities and skillset to manage cough symptoms and increase their reach with patients, still within their scope of work. By managing cough effectively, perhaps the burden of cough on healthcare systems would lessen, therefore lessening the burden on existing staff.

3.5.2 Strengths and Limitations

This is the first study looking at chronic cough assessment and management in PR programs. It includes healthcare professional perspectives across many Canadian PR facilities, regarding barriers and facilitators to improved cough management. Although we have a representative sample of Canadian PR programs, as we were able to gather data from most of the provinces, the results are limited by the modest response rate, in part because the study took place during the ongoing COVID-19 pandemic which limited access to PR as part of the initial national health protection regulations. The low response rate may also be attributed to the lack of staffing in PR, leading to lack of time to complete the survey.

3.6 Conclusion

Although more than half of respondents reported enrolling patients with chronic cough, only 45% reported assessing and 63% reported managing it. Lack of formal education on how to assess and treat chronic cough was the main barrier identified. Cough is a burdensome symptom and sign. The application of formal assessment using valid tools will facilitate our understanding

of its characteristics as well as the impact of treatment strategies that can be implemented as part of a PR program.

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CHAPTER 4: DISCUSSION & CONCLUSION

4.1 Overall Findings of Thesis

Global prevalence rates of chronic cough are on the rise and, consequently, chronic cough is reported to be one of the most common reasons for medical referral [1]. Despite chronic cough being of such a high prevalence (16-18% in Canada [1] and up to 90% in people with chronic respiratory diseases [2]), literature surrounding chronic cough assessment and management strategies is scarce. The purpose of this thesis was to explore the effectiveness and application of non-pharmacological interventions in the management of chronic cough. To achieve the overall goals, a systematic review of non-pharmacological chronic cough management strategies was conducted (chapter two), as well as a cross-sectional survey exploring the use of non-pharmacological cough management strategies in Canadian PR programs (chapter three).

The findings of our systematic review, in chapter two, revealed that some non-pharmacological management strategies can have positive effects on improving cough-specific quality of life (QoL), cough frequency, and various voice outcomes. These therapies consist of combination therapies involving education, laryngeal hygiene, cough control, and psychoeducational counselling, and CPAP. A common feature among effective interventions was having a cough education section [3–7]. Despite non-pharmacological therapies revealing promising results in certain domains, there was heterogeneity in study design, sample size, and outcome measures, thus preventing any formal clinical recommendations to be made regarding the use of non-pharmacological therapies.

The LCQ was the primary outcome measure in study two, the systematic review. LCQ mean scores range from 1-7 for each domain, with total scores ranging from 3-21[8]. Increases in

scores correlate with increases in cough-related quality of life [8]. Nguyen and colleagues (2022), suggest that mean improvement scores with a 1.3-point increase or greater, following an intervention, can be considered clinically meaningful [8]. Therefore, the use of the LCQ demonstrates that CPAP therapy and the PSALTI do contribute to increased cough-related quality of life following interventions. These findings demonstrate the positive influence of cough management on quality of life, thus proving the need for further investigation of non-pharmacological therapies.

Taking into consideration one of the findings from our systematic review, in which an educational component was an integral piece to effective non-pharmacological therapies, we hypothesized that PR would be an appropriate area to include chronic cough management [9]. Our survey study (chapter three) showed that over 50% of PR programs in Canada have patients who present with chronic cough. This number may be an underestimation, as only 45% of PR programs formally assess patients for chronic cough. According to healthcare professionals in PR programs, the most common barrier to cough assessment and management in PR is the lack of education regarding assessment and management techniques. This result was strengthened with one of the main identified facilitators being a need for increased education for healthcare providers. These findings highlight potential areas of interest for future studies in the field of chronic cough and PR.

4.2 Contributions to Knowledge & Literature

Although there are four existing systematic reviews on non-pharmacological cough management strategies, chapter two aimed to provide an update in the literature regarding existing non-pharmacological therapies [10–13]. Existing reviews such as Molassiotis and

colleagues (2010) and Slinger and colleagues (2019) only included speech language therapy interventions, therefore excluding other forms of non-pharmacological management [10,11]. Chamberlain and colleagues (2014), as well as Wamkpah and colleagues (2020), only included people with refractory chronic cough in their reviews, which consequently excluded a large population of people suffering from chronic cough due to an underlying chronic respiratory disease [5,13]. However, our review sought to include both, people with both refractory chronic cough and chronic cough due to a chronic respiratory disease, while encompassing all non-pharmacological interventions in existing literature.

Various therapies delivered through physiotherapy, speech language therapy, mindfulness, and CPAP were identified and included in this review, thus offering greater generalizability than pre-existing reviews in this field. Furthermore, OSA was the only identified chronic respiratory disease, which highlights the paucity of information surrounding alternative management strategies for people with chronic respiratory disease, for which chronic cough can affect up to 90% of that population.

Our study was the first to investigate if PR programs assess and manage chronic cough. In chapter three, we demonstrated that healthcare providers, themselves, recognize the need for formal education in PR to increase the rates of assessment and management of chronic cough in PR.

4.3 Clinical Implications

There are currently no approved pharmacological methods for the treatment of chronic cough, therefore non-pharmacological cough management strategies could be considered and incorporated as forms of cough management [14,15]. The survey revealed that the main barrier

to cough assessment and management was lack of knowledge of how to do it during PR, with the main facilitator being increased education regarding cough assessment and management. PR programs would benefit from the inclusion of structured education for healthcare providers, aiming to inform practices surrounding the use of proper cough assessment and management techniques. This could help with chronic cough recognition within PR goals and aims.

4.4 Thesis Strengths and Limitations

4.4.1 Strengths

We have conducted the first systematic review in more than a decade to report on the effects of non-pharmacological cough therapies for, both, people with non-productive refractory cough and chronic respiratory diseases. Our review is also the only review to include all forms of non-pharmacological therapies; not limited to one form (e.g., only speech language pathology). By doing so, we aimed to include a wide variety of study participants and interventions to try and encompass as many studies as possible in this field.

The survey study was unique, as it was the first study to address the assessment and management of chronic cough within PR programs. With feedback received from participants, insight into various influential factors affecting chronic cough assessment and management in PR was gathered from those who interact most with patients in PR.

4.4.2 Limitations

The results of the two reported studies should also be considered alongside their limitations. In our systematic review, several alternative techniques (such as acupuncture and uptake of vitamins and teas) were excluded, as we were seeking to identify non-invasive procedures. We also excluded numerous studies in which non-pharmacological interventions

were paired with the simultaneous use of medications. This limited the inclusion of papers and the findings. Secondly, OSA was the only formally included chronic respiratory disease in the systematic review. Results for patients with refractory chronic cough and asthma were not reported separately in studies, and thus, no conclusions can be made regarding the effects of non-pharmacological therapy specifically for individuals with asthma. Thirdly, speech language pathology and physiotherapy offer promising results as a form of nonpharmacological cough management; however, the long-term effects of these therapies are unknown and need to be further investigated. Lastly, the most important limitation to consider from chapter two is that the quality of our findings was limited by the heterogeneity of the studies published, thus limiting our ability to make any formal clinical recommendations.

Chapter three is a notable study due to its clinical originality and relevance. However, a low response rate could have reduced the validity of our findings. The impact of COVID-19 negatively impacted the response rate for the survey, as some PR programs reported not having time to complete the survey due to lack of staffing.

4.5 Research Implications

The findings from our systematic review and survey study demonstrate the need for further research around optimal care for chronic cough. As traditional pharmacological methods for chronic cough management have low success rates in the long-term due to strong side-effects [16,17], future research could benefit from focusing in the direction of alternative non-pharmacological management strategies.

Chapter two confirmed that there are beneficial non-pharmacological therapies which work towards improving cough-related quality of life in people with chronic cough, however due

to the scarcity of literature on non-pharmacological chronic cough management, further research is needed. There is also a need to further investigate if non-pharmacological therapies would benefit from being combined with pharmaceutical therapies, as one study conducted by Vertigan and colleagues (2016) demonstrated the efficacy of combined speech-pathology treatment with pregabalin in improving symptoms and quality of life [6]. The study of optimal administration and integration of non-pharmacological therapies is also needed.

Chapter three showed how chronic cough is not systematically managed in PR despite affecting more than half of participants in PR programs. Specific themes emerged regarding chronic cough assessment and management barriers and facilitators. However, due to the study low response rate (23%), this study needs to be replicated on a larger scale, as well as in other global populations to allow for identification of other identified barriers and facilitators. If similar emerging themes are noticed, perhaps standardized global guidelines regarding chronic cough assessment and management in PR could be produced. In the meantime, future research should focus on replicating this study on a larger scale and population.

4.6 Conclusion

In conclusion, this thesis provided an update to the literature on existing non-pharmacological chronic cough management strategies, as well as an insight into whether chronic cough is assessed and managed within Canadian PR programs. Non-pharmacological therapies showed promising results in improving cough-specific quality of life, cough frequency, and voice outcomes, however due to the heterogeneity of the results, no direct clinical recommendations could be made. As seen in chapter three, chronic cough affects more than half of patients enrolled in PR programs in Canada, but its assessment and management are not

structured among programs. Only 45% of survey respondents report assessing for chronic cough, while 63% report managing chronic cough. Healthcare provider-perceived barriers and facilitators to conducting chronic cough assessment and management, demonstrate the need for professional education in PR. These findings provide opportunities and possible avenues for further research to help facilitate the integration of optimal non-pharmacological management of chronic cough in clinical practice through various initiatives.

4.7 References

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APPENDICES

Appendix A: PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	26
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	27
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	29
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	30
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	31
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	31
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix B
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	32
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	32
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	33
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding	33

Section and Topic	Item #	Checklist item	Location where item is reported
		sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	33
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	33
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Table 2
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Lines 177-183
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	33
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	33
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	33
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	33
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	33
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	33
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Appendix C

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Figure 4
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	34
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	38
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	37
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	38
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	49
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	38
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	50
	23b	Discuss any limitations of the evidence included in the review.	51
	23c	Discuss any limitations of the review processes used.	51
	23d	Discuss implications of the results for practice, policy, and future research.	52
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	31
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	31
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	/

Section and Topic	Item #	Checklist item	Location where item is reported
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	n/a
Competing interests	26	Declare any competing interests of review authors.	n/a
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	/

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Appendix B: Example of Search Strategy

MEDLINE Search Terms – to be performed in title, abstract and keywords

CONCEPT: Chronic Respiratory Disease

MeSh headings: exp respiratory tract diseases/ or exp bronchial diseases/ or exp asthma/ or bronchiectasis/ or bronchitis/ or exp bronchiolitis/ or exp bronchiolitis obliterans/ or exp tracheobronchomalacia/ or exp granuloma, respiratory tract/ or granuloma, laryngeal/ or laryngeal neoplasms/ or laryngomalacia/ or exp lung diseases/ or exp pulmonary aspergillosis/ or exp lung diseases, interstitial/ or exp alveolitis, extrinsic allergic/ or exp histiocytosis, langerhans-cell/ or exp lung diseases, obstructive/ or exp bronchitis/ or exp pulmonary disease, chronic obstructive/ or exp pneumoconiosis/ or exp silicosis/ or exp lung neoplasms/ or exp carcinoma, bronchogenic/ or pneumonia/ or exp bronchopneumonia/ or exp pulmonary fibrosis/ or exp idiopathic pulmonary fibrosis/ or exp idiopathic interstitial pneumonias/ or exp pleural diseases/ or exp pleural neoplasms/ or exp respiratory hypersensitivity/ or exp respiratory system abnormalities/ or exp respiratory tract neoplasms/ or exp bronchial neoplasms/ or exp thoracic diseases/ or exp tracheal diseases/

OR

Key words: (COPD or (chronic adj3 bronchitis) or emphysema or ILD or respiratory diseas* or bronchial diseas* or asthm* or bronchiectas* or lung cancer or bronchitis or bronchiolitis or bronchiolitis obliterans or tracheobronchomalacia or granuloma, respiratory tract or laryngeal granuloma or laryngeal neoplasm* or laryngomalacia or lung disease* or pulmonary aspergillosis or alveolitis or Langerhans cell or (obstructive adj3 disease*) or chronic obstructive pulmonary disease or pneumoconiosis or silicosis or lung neoplasm* or carcinoma or pneumon* or bronchopneumon* or (idiopathic adj3 fibros*) or (idiopathic adj3 pneumon*) or pleural diseas* or pleural neoplasm* or respiratory hypersensitivity or (respiratory adj3 abnormalit*) or respiratory tract neoplasm* or bronchial neoplasm* or thoracic disease* or tracheal disease* or asbestosis or silicosis or beryliosis or pleuroparenchymal fibroelastosis or (interstitial adj3 disease) or granulomatous* or sclerosis or polymyositis or dermatomyositis or lupus or Hamman-Rich syndrome or bagassosis or histiocytosis).tw,kf.

AND

CONCEPT: Cough

MeSh headings: Cough/

OR

Key words: chronic cough*.tw,kf.

AND

CONCEPT: Non-pharmacological Interventions

MeSh headings: exp Therapeutics/ or Airway Management/ or physical therapy modalities/ or exp exercise movement techniques/ or exp musculoskeletal manipulations/ or rehabilitation/ or exp exercise therapy/ or exp Speech Therapy/ or exp Complementary Therapies/

OR

Key words: (therapeutic* or management or physiotherapy or speech thera* or language thera* or complementary thera* or alternative medicine or alternative thera* or intervention* or treatment* or rehabilitation* or nonpharmacologic*).tw,kf.

Appendix C: List of Excluded Articles

Reference	Reason for exclusion
M. Zidan, H. Shaarawy, Assessment of the prevalence of obstructive sleep apnea in patients with undiagnosed chronic cough, Eur. Respir. J. 40 (2012). http://erj.ersjournals.com/content/40/Suppl_56/P1877.abstract?sid=22a4d8a0-8e17-4be5-b95d-3be3bf155dd9http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed13&NEWS=N&AN=71924234 NS -.	Abstract in conference proceedings
A.B. Zakrisson, M. Arne, M. Hasselgren, K. Lisspers, B. Stallberg, K. Theander, A complex intervention of self-management for patients with COPD or CHF in primary care improved performance and satisfaction with regard to own selected activities; A longitudinal follow-up, J. Adv. Nurs. 75 (2019) 175-186. https://doi.org/10.1111/jan.13899.	Abstract in conference proceedings
L. Yardley, J. Joseph, S. Michie, M. Weal, G. Wills, P. Little, Evaluation of a Web-based intervention providing tailored advice for self-management of minor respiratory symptoms: exploratory randomized controlled trial, J. Med. Internet Res. 12 (2010) e66. https://doi.org/10.2196/jmir.1599.	Abstract in conference proceedings
D. Xue, S. Han, S. Jiang, H. Sun, Y. Chen, Y. Li, W. Wang, Y. Feng, K. Wang, P. Li, Comprehensive geriatric assessment and traditional Chinese medicine intervention benefit symptom control in elderly patients with advanced non-small cell lung cancer, Med. Oncol. 32 (2015) 1–7. https://doi.org/10.1007/s12032-015-0563-5.	Abstract in conference proceedings
R.H. Wilson, S.M. Farber, W. Mandel, A new agent of therapeutic value in pulmonary insufficiency and irritative cough, Antibiot. Med. Clin. Ther. (New York, NY). 5 (1958) 567–572. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=13571961 NS -.	Abstract in conference proceedings
S.H. Yu, A.M. Guo, X.J. Zhang, Effects of self-management education on quality of life of patients with chronic obstructive pulmonary disease, Int. J. Nurs. Sci. 1 (2014) 53-57. https://doi.org/10.1016/j.ijnss.2014.02.014.	Case-series
J. Yorke, M. Lloyd-Williams, J. Smith, F. Blackhall, A. Harle, J. Warden, J. Ellis, M. Pilling, J. Haines, K. Luker, et al., Management of the respiratory distress symptom cluster in lung cancer: a randomised controlled feasibility trial, Support. Care Cancer. 23 (2015) 3373-3384. https://doi.org/10.1007/s00520-015-2810-x.	Case-series
N. Yokohori, M. Hasegawa, A. Sato, H. Katsura, Severe sleep apnea syndrome associated with chronic cough without daytime sleepiness, Eur. Respir. J. 46 (2015). https://doi.org/http://dx.doi.org/10.1183/13993003.congress2015.PA3598.	Case-report

N. Yokohori, M. Hasegawa, A. Sato, H. Katsura, Utility of continuous positive airway pressure therapy for treating chronic coughs in patients with obstructive sleep apnea, Intern. Med. 53 (2014) 1079–1082. https://doi.org/http://dx.doi.org/10.2169/internalmedicine.53.1855.	Abstract in conference proceedings
P. Weiner, R. Magadle, M. Beckerman, M. Weiner, N. Berar-Yanay, Specific expiratory muscle training in COPD, Chest. 124 (2003) 468-473. https://doi.org/10.1378/chest.124.2.468.	Observational Study
W. Wei, L. Yu, Y. Wang, X. Li, Z. Qiu, L. Wang, B. Liu, S. Liang, H. Lu, Z. Qiu, Efficacy and safety of modified sequential three-step empirical therapy for chronic cough, Respirology. 15 (2010) 830–836. https://doi.org/https://dx.doi.org/10.1111/j.1440-1843.2010.01785.x.	Pre-Post Design
D. Vilozni, M. Lavie, M. Ofek, I. Sarouk, O. Efrati, Cough Characteristics and FVC Maneuver in Cystic Fibrosis, Respir. Care. 59 (2014) 1912–1917. https://doi.org/10.4187/respcare.03290.	Case-report
S. Verver, M. Poelman, A. Bögels, S.L. Chisholm, F.W. Dekker, Effects of instruction by practice assistants on inhaler technique and respiratory symptoms of patients. A controlled randomized videotaped intervention study, Fam. Pract. 13 (1996) 35-40. https://doi.org/10.1093/fampra/13.1.35.	Observational Study
A.E. Vertigan, D.G. Theodoros, P.G. Gibson, A.L. Winkworth, Voice and Upper Airway Symptoms in People With Chronic Cough and Paradoxical Vocal Fold Movement, J. Voice. 21 (2007) 361–383. https://doi.org/http://dx.doi.org/10.1016/j.jvoice.2005.12.008.	Case-report
A.E. Vertigan, S.M. Kapela, I. Franke, P.G. Gibson, The Effect of a Vocal Loading Test on Cough and Phonation in Patients With Chronic Cough, J. Voice. 31 (2017) 763–772. https://doi.org/https://dx.doi.org/10.1016/j.jvoice.2017.03.020.	Case-report
A.E. Vertigan, P.G. Gibson, Urge to cough and its application to the behavioural treatment of cough, Bratisl. Lek. Listy. 112 (2011) 102–108. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=21452759 NS -.	Case-report
C.P. van der Schans, T.W. van der Mark, G. de Vries, D.A. Piers, H. Beekhuis, J.E. Dankert-Roelse, D.S. Postma, G.H. Koeter, Effect of positive expiratory pressure breathing in patients with cystic fibrosis, Thorax. 46 (1991) 252–256. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=2038733 NS -.	Case-report
L. Wang, X. Kang, Z. Liu, L. Liu, S. Liu, Y. Bian, G. Li, Efficacy of acupuncture combined with Chinese herb in refractory chronic cough, Am. J. Respir. Crit. Care Med. 189 (2014). https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01131442/full NS -.	Case-report
R.D. Turner, G.H. Bothamley, Chronic cough and a normal chest X-ray-a simple systematic approach to exclude common causes before referral to secondary care: A retrospective cohort study, Npj Prim. Care Respir. Med. 26 (2016). https://doi.org/10.1038/npjpcrm.2015.81.	Retrospective Cohort

G. Taipin, C. Zukun, T. Xiantao, L. Zili, Z. Miansheng, T. Guo, Z. Chen, X. Tai, Z. Liu, M. Zhu, Space-time acupuncture for intractable cough after lupus nephropathy: A case report and literature review, Medicine (Baltimore). 96 (2017) 1–3. https://doi.org/10.1097/MD.0000000000009309.	Case-report
K.M. Sundar, S.E. Daly, A.M. Willis, A longitudinal study of CPAP therapy for patients with chronic cough and obstructive sleep apnoea, Cough. 9 (2013) 19. https://doi.org/http://dx.doi.org/10.1186/1745-9974-9-19.	Retrospective Cohort
K.M. Sundar, S.E. Daly, M.J. Pearce, W.T. Alward, Chronic cough and obstructive sleep apnea in a community-based pulmonary practice, Cough. 6 (2010). https://doi.org/10.1186/1745-9974-6-2.	Observational Study
K.M. Sundar, S.E. Daly, Clinical profile of chronic cough patients improving with therapy for sleep apnoea, Pulm. Pharmacol. Ther. 24 (2011) e4–e5. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed12&NEWS=N&AN=70733466 NS -.	Pharmacological intervention
K. Sundar, S. Daly, A. Willis, Prospective study of the prevalence of obstructive sleep apnea (OSA) in patients with chronic cough and impact of nocturnal continuous positive airway pressure therapy (CPAP) on the course of chronic cough, Chest. 142 (2012). https://doi.org/http://dx.doi.org/10.1378/chest.1387645.	Case-report
M. Sumitani, S. Nanjo, N. Miyamoto, S. Yoshida, M. Tsuda, M. Nishijima, S. Shoji, K. Tomii, N. Katakami, K. Miyamoto, Persistent dry cough effectively may be treated by soft extensible chest band, Chest. 142 (2012). https://doi.org/http://dx.doi.org/10.1378/chest.1388250.	Duration of cough not defined
N.C. Sullivan, Assessment and management of persistent cough in adults, Clin. Excell. Nurse Pract. 1 (1997) 417–422. http://libaccess.mcmaster.ca/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=107251100&site=ehost-live NS -.	Duration of cough not defined
C.L. Su, L.L. Chiang, T.Y. Chiang, C.T. Yu, H.P. Kuo, H.C. Lin, Domiciliary positive expiratory pressure improves pulmonary function and exercise capacity in patients with chronic obstructive pulmonary disease, J. Formos. Med. Assoc. / Taiwan Yi Zhi. 106 (2007) 204-211. https://doi.org/10.1016/S0929-6646(09)60241-2.	Duration of cough not defined
P. Sonnerfors, G. Faager, A.K. Nordlin, U. Einarsson, Pulmonary rehabilitation including interactive 3D visualization technique, in COPD, Eur. Respir. J. 54 (2019). https://doi.org/10.1183/13993003.congress-2019.PA569.	Pharmacological intervention
R.S. Soni, B. Ebersole, N. Jamal, Treatment of Chronic Cough, Otolaryngol. Head. Neck Surg. 156 (2017) 103–108. https://doi.org/https://dx.doi.org/10.1177/0194599816675299.	Duration of cough not defined
G. Simpson, Investigation and management of persistent dry cough, Thorax. 54 (1999) 469–470.	Duration of cough not defined

http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=10409073 NS -.	
S.W. Simon, Symptomatic treatment of asthmatic bronchitis, J. Am. Geriatr. Soc. 8 (1960) 107–111. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=14446944 NS -.	Pharmacological intervention
M. Tomruk, E. Keles, S. Ozalevli, A.O. Alpaydin, Effects of thoracic kinesio taping on pulmonary functions, respiratory muscle strength and functional capacity in COPD patients: a pilot randomized controlled study, Eur. Respir. J. 50 (2017). https://doi.org/10.1183/1393003.congress-2017.PA1534.	Secondary source
T. Toljamo, M. Kaukonen, P. Nieminen, V.L. Kinnula, Early detection of COPD combined with individualized counselling for smoking cessation: a two-year prospective study, Scand. J. Prim. Health Care. 28 (2010) 41–46. https://doi.org/10.3109/02813431003630105.	Duration of cough not defined
S.J. Stenekes, A. Hughes, M.-C. Gregoire, G. Frager, W.M. Robinson, P.J. McGrath, Frequency and self-management of pain, dyspnea, and cough in cystic fibrosis, J. Pain Symptom Manage. 38 (2009) 837–848. https://doi.org/https://dx.doi.org/10.1016/j.jpainsymman.2009.04.029.	No chronic cough (defined as >=8weeks)
A.C. Shembel, C.A. Rosen, T.G. Zullo, J.L. Gartner-Schmidt, Development and validation of the cough severity index: A severity index for chronic cough related to the upper airway, Laryngoscope. 123 (2013) 1931–1936. https://doi.org/http://dx.doi.org/10.1002/lary.23916.	Duration of cough not defined
J.C. Schraa, J.F. Dirks, Hypnotic treatment of the alexithymic patient: a case report, Am. J. Clin. Hypn. 23 (1981) 207–210. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med2&NEWS=N&AN=7246472 NS -.	Duration of cough not defined
L. Slovarp, B.K. Loomis, A. Glaspey, Assessing referral and practice patterns of patients with chronic cough referred for behavioral cough suppression therapy, Chronic Respir. Dis. 15 (2018) 296–305. https://doi.org/10.1177/1479972318755722.	Duration of cough not defined
P. Sivasothy, L. Brown, I.E. Smith, J.M. Shneerson, Effect of manually assisted cough and mechanical insufflation on cough flow of normal subjects, patients with chronic obstructive pulmonary disease (COPD), and patients with respiratory muscle weakness, Thorax. 56 (2001) 438–444. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=11359958 NS -.	Duration of cough not defined
B. Sitkauskiene, K. Stravinskaite, R. Sakalauskas, P. V Dicpinigaitis, Changes in cough reflex sensitivity after cessation and resumption of cigarette smoking, Pulm. Pharmacol. Ther. 20 (2007) 240–243. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=17045500 NS -.	Duration of cough not defined
V. Singh, D.C. Khandelwal, R. Khandelwal, S. Abusaria, Pulmonary rehabilitation in patients with chronic obstructive pulmonary disease, Indian J. Chest Dis. Allied Sci. 45 (2003) 13-17.	Paediatric population

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00430952/full NS -.	
J. Selby, E. Bailey, F. Gillies, J.H. Hull, Time to re-group: a novel approach to the delivery of speech and language therapy for chronic refractory cough, Thorax. 72 (2017) A141-. https://doi.org/10.1136/thoraxjnl-2017-210983.249.	No chronic cough (defined as >=8weeks)
G. Rutten, J. Van Eijk, M. Beek, H. Van der Velden, Patient education about cough: effect on the consulting behaviour of general practice patients, Br. J. Gen. Pract. 41 (1991) 289-292. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00080116/full NS -.	Intervention not reported
L. Rose, D. McKim, D. Leasa, M. Nonoyama, A. Tandon, M. Kaminska, C. O'Connell, A. Loewen, B. Connolly, P. Murphy, N. Hart, J. Road, Monitoring Cough Effectiveness and Use of Airway Clearance Strategies: A Canadian and UK Survey, Respir. Care. 63 (2018) 1506–1513. https://doi.org/https://dx.doi.org/10.4187/respcare.06321.	Duration of cough not defined
B. Riegel, J.E. Warmoth, S.J. Middaugh, W.G. Kee, L.C. Nicholson, D.M. Melton, D.K. Parikh, J.C. Rosenberg, Psychogenic cough treated with biofeedback and psychotherapy. A review and case report, Am. J. Phys. Med. Rehabil. 74 (1995) 155–158. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=7710731 NS -.	Duration of cough not defined
M. Ribeiro, C.A. De Castro Pereira, L.E. Nery, O.S. Beppu, C.O. Silva, A prospective longitudinal study of clinical characteristics, laboratory findings, diagnostic spectrum and outcomes of specific therapy in adult patients with chronic cough in a general respiratory clinic, Int. J. Clin. Pract. 60 (2006) 799–805. https://doi.org/http://dx.doi.org/10.1111/j.1368-5031.2006.00876.x.	Duration of cough not defined
A.A. Raj, D.I. Pavord, S.S. Birring, Clinical cough IV:what is the minimal important difference for the Leicester Cough Questionnaire?, Handb. Exp. Pharmacol. (2009) 311–320. https://doi.org/https://dx.doi.org/10.1007/978-3-540-79842-2_16.	Duration of cough not defined
R.H. Poe, R. V Harder, R.H. Israel, M.C. Kallay, Chronic persistent cough. Experience in diagnosis and outcome using an anatomic diagnostic protocol, Chest. 95 (1989) 723–728. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=2924600 NS -.	Pharmacological intervention
C. Pisinger, N.S. Godtfredsen, T. Jørgensen, Smoking reduction and cessation reduce chronic cough in a general population: the Inter99 study, Clin Respir J. 2 (2008) 41–46. https://doi.org/10.1111/j.1752-699x.2007.00029.x.	No chronic cough (defined as >=8weeks)
A.S. Patel, G. Watkin, B. Willig, K. Mutalithas, H. Bellas, R. Garrod, I.D. Pavord, S.S. Birring, Improvement in health status following cough-suppression physiotherapy for patients with chronic cough, Chron. Respir. Dis. 8 (2011) 253–258. https://doi.org/https://dx.doi.org/10.1177/1479972311422547.	Cough augmentation

A.D. Palmer, R.K. Bolognone, S. Thomsen, D. Britton, J. Schindler, D.J. Graville, The Safety and Efficacy of Expiratory Muscle Strength Training for Rehabilitation After Supracricoid Partial Laryngectomy: A Pilot Investigation, Ann. Otol. Rhinol. Laryngol. 128 (2019) 169–176. https://doi.org/https://dx.doi.org/10.1177/0003489418812901.	Duration of cough not defined
H.J. Pai, R.S. Azevedo, A.L.F. Braga, L.C. Martins, B.M. Saraiva-Romanholo, M. de A. Martins, C.A. Lin, A randomized, controlled, crossover study in patients with mild and moderate asthma undergoing treatment with traditional Chinese acupuncture, Clinics (Sao Paulo). 70 (2015) 663–669. https://doi.org/https://dx.doi.org/10.6061/clinics/2015(10)01.	No chronic cough (defined as >=8weeks)
Nct, Sham CPAP vs. Straight CPAP for Chronic Cough, Https://Clinicaltrials.Gov/Show/NCT03172130. (2017). https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01594649/full NS -.	Duration of cough not defined
Nct, Cystic Fibrosis- Children and Adults Tai Chi Study, Https://Clinicaltrials.Gov/Show/NCT02054377. (2014). https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01543468/full NS -.	Pharmacological intervention
Nct, Does CBT Improve the Perception/Impact of Cough and Breathlessness in IPF Patients, Https://Clinicaltrials.Gov/Show/NCT01738711. (2012). https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01539028/full NS -.	Duration of cough not defined
P.R. Munford, D. Reardon, R.P. Liberman, L. Allen, Behavioral treatment of hysterical coughing and mutism: a case study, J. Consult. Clin. Psychol. 44 (1976) 1008–1014. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=11229 NS -.	No intervention
Nct, Cough Desensitization Therapy for Cough Hypersensitivity Syndrome, Https://Clinicaltrials.Gov/Show/NCT04256733. (2020). https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02080113/full NS -.	No chronic cough (defined as >=8weeks)
Nct, Feasibility & Effect of a Tele-rehabilitation Program in Pulmonary Sarcoidosis Pulmonary Sarcoidosis, Https://Clinicaltrials.Gov/Show/NCT03914027. (2019). https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01931282/full NS -.	Duration of cough not defined
A.H. Morice, S. Faruqi, C.E. Wright, R. Thompson, J.M. Bland, Cough hypersensitivity syndrome: a distinct clinical entity, Lung. 189 (2011) 73–79. https://doi.org/https://dx.doi.org/10.1007/s00408-010-9272-1.	Pharmacological intervention
F.J. Molina-Saldarriaga, N.J. Fonseca-Ruiz, D.P. Cuesta-Castro, A. Esteban, F. Frutos-Vivar, Spontaneous breathing trial in chronic obstructive pulmonary disease: continuous positive airway pressure (CPAP) versus T-piece, Med. Intensiva. 34 (2010) 453-458. https://doi.org/10.1016/j.medin.2010.03.007.	Pharmacological intervention

S.J. Mohammed, J. Steer, J. Ellis, L. Kellett, N. Kurji-Smith, S.M. Parker, Non-pharmacological cough suppression therapy for cough associated with underlying lung disease, Thorax. 73 (2018) A98–A99. https://doi.org/http://dx.doi.org/10.1136/thorax-2018-212555.164.	Trial registration
S. Mohammed, J. Steer, J. Ellis, S.M. Parker, Nonpharmacological cough control therapy for chronic refractory cough and cough associated with underlying lung disease, ERJ Open Res. 6 (2020) 243–2019. https://doi.org/http://dx.doi.org/10.1183/23120541.00243-2019.	Duration of cough not defined
A. Miles, M. Jardine, F. Johnston, M. de Lisle, P. Friary, J. Allen, Effect of Lee Silverman Voice Treatment (LSVT LOUD R) on swallowing and cough in Parkinson's disease: A pilot study, J. Neurol. Sci. 383 (2017) 180–187. https://doi.org/https://dx.doi.org/10.1016/j.jns.2017.11.015.	Cough augmentation
H.C. Long, M.H. Zhang, L. Yu, X.H. Li, X.F. Zhou, B.R. Xiao, Y.J. Liu, Z.L. Wang, C.T. Liu, A pilot study of a simple management strategy for patients with chronic cough in Chengdu, Respirology. 17 (2012) 12. https://doi.org/http://dx.doi.org/10.1111/j.1440-1843.2012.02288.x.	Intervention not reported
S.F. Lillie, J. Haines, A. Vyas, S.J. Fowler, Speech and language therapy by SkypeTM for vocal cord dysfunction and chronic cough, Thorax. 69 (2014) A126–A127. https://doi.org/http://dx.doi.org/10.1136/thoraxjnl-2014-206260.253.	Duration of cough not defined
D. Masmoudi, A. Krid, S. Chakroun, H. Trabelsi, L. Triki, H. Zouari, I. Kammoun, K. Masmoudi, M. Chaabouni, Does continuous positive airway pressure improve the sub-maximal exercise capacity in obese patients with severe obstructive sleep-apnea-hypopnea-syndrome ?, Eur. Respir. J. 54 (2019). https://doi.org/http://dx.doi.org/10.1183/13993003.congress-2019.PA4173.	Trial registration
D.J. Maselli, J.I. Peters, In refractory chronic cough, physiotherapy plus speech and language therapy improved quality of life at 4 weeks, Ann. Intern. Med. 166 (2017) JC3. https://doi.org/http://dx.doi.org/10.7326/ACPJC-2017-166-2-003.	Duration of cough not defined
D. Marimuthu, F. Nasir, B. Singh, Laryngeal Amyloidosis: A Case Report, Int. Med. J. 26 (2019) 51–52. http://libaccess.mcmaster.ca/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=134551668&site=ehost-live NS -.	Duration of cough not defined
B.M. Levine, Systematic evaluation and treatment of chronic cough in a community setting, Allergy Asthma Proc. 29 (2008) 336–342. https://doi.org/http://dx.doi.org/10.2500/aap.2008.29.3122.	Cough augmentation
S.T. Kulnik, S.S. Birring, J. Moxham, G.F. Rafferty, L. Kalra, Does respiratory muscle training improve cough flow in acute stroke? Pilot randomized controlled trial, Stroke (00392499). 46 (2015) 447–453. https://doi.org/10.1161/STROKEAHA.114.007110.	No chronic cough (defined as >=8weeks)
K. Krakowiak, M. Dabrowska, F. Bula, A. Lobacz, D. Rojek, E.M. Grabczak, A. Krzeski, R. Krenke, Speech therapy - a non-	Duration of cough not defined

pharmacological method to manage difficult-to-treat chronic cough, Adv. Respir. Med. 85 (2017) 116–120. https://doi.org/http://dx.doi.org/10.5603/ARM.2017.0018.	
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T. Murry, T. Virtue, J. Datema, C. Liem, B. Crawley, P. Krishna, Expiratory muscle strength training as treatment for chronic cough, Lung. 198 (2020) 39. https://doi.org/http://dx.doi.org/10.1007/s00408-020-00328-3.	Repeat
A.E. Vertigan, S.L. Kapela, N.M. Ryan, S.S. Birring, P. McElduff, P.G. Gibson, Pregabalin and Speech Pathology Combination Therapy for Refractory Chronic Cough: a Randomized Controlled Trial, Chest. 149 (2016) 639-648. https://doi.org/10.1378/chest.15-1271.	Pharmacological intervention

Appendix D: Checklist for Reporting of Survey Studies (CROSS)

Section/topic	Item	Item description	Reported on page #
Title and abstract			
Title and abstract	1a	State the word "survey" along with a commonly used term in title or abstract to introduce the study's design.	58
	1b	Provide an informative summary in the abstract, covering background, objectives, methods, findings/results, interpretation/discussion, and conclusions.	59
Introduction			
Background	2	Provide a background about the rationale of study, what has been previously done, and why this survey is needed.	60
Purpose/aim	3	Identify specific purposes, aims, goals, or objectives of the study.	61
Methods			
Study design	4	Specify the study design in the methods section with a commonly used term (e.g., cross-sectional or longitudinal).	61
Data collection methods	5a	Describe the questionnaire (e.g., number of sections, number of questions, number and names of instruments used).	62
	5b	Describe all questionnaire instruments that were used in the survey to measure particular concepts. Report target population, reported validity and reliability information, scoring/classification procedure, and reference links (if any).	62
	5c	Provide information on pretesting of the questionnaire, if performed (in the article or in an online supplement). Report the method of pretesting, number of times questionnaire was pre-tested, number and demographics of participants used for pretesting, and the level of similarity of demographics between pre-testing participants and sample population.	62
	5d	Questionnaire if possible, should be fully provided (in the article, or as appendices or as an online supplement).	Appendix E
Sample characteristics	6a	Describe the study population (i.e., background, locations, eligibility criteria for participant inclusion in survey, exclusion criteria).	62
	6b	Describe the sampling techniques used (e.g., single stage or multistage sampling, simple random sampling, stratified sampling, cluster sampling, convenience sampling). Specify the locations of sample participants whenever clustered sampling was applied.	62
	6c	Provide information on sample size, along with details of sample size calculation.	63
	6d	74	92
Survey administration	7a	Provide information on modes of questionnaire administration, including the type and number of contacts, the location where the survey was conducted (e.g., outpatient room or by use of online tools, such as SurveyMonkey).	62
	7b	Provide information of survey's time frame, such as periods of recruitment, exposure, and follow-up days.	63
	7c	Provide information on the entry process: –>For non-web-based surveys, provide approaches to minimize human error in data entry. –>For web-based surveys, provide approaches to prevent "multiple participation" of participants.	62

Study preparation	8	Describe any preparation process before conducting the survey (e.g., interviewers' training process, advertising the survey).	62
Ethical considerations	9a	Provide information on ethical approval for the survey if obtained, including informed consent, institutional review board [IRB] approval, Helsinki declaration, and good clinical practice [GCP] declaration (as appropriate).	63
	9b	Provide information about survey anonymity and confidentiality and describe what mechanisms were used to protect unauthorized access.	63
Statistical analysis	10a	Describe statistical methods and analytical approach. Report the statistical software that was used for data analysis.	63
	10b	Report any modification of variables used in the analysis, along with reference (if available).	n/a
	10c	Report details about how missing data was handled. Include rate of missing items, missing data mechanism (i.e., missing completely at random [MCAR], missing at random [MAR] or missing not at random [MNAR]) and methods used to deal with missing data (e.g., multiple imputation).	63
	10d	State how non-response error was addressed.	n/a
	10e	For longitudinal surveys, state how loss to follow-up was addressed.	n/a
	10f	Indicate whether any methods such as weighting of items or propensity scores have been used to adjust for non-representativeness of the sample.	n/a
	10g	Describe any sensitivity analysis conducted.	n/a
Results			
Respondent characteristics	11a	Report numbers of individuals at each stage of the study. Consider using a flow diagram, if possible.	63
	11b	Provide reasons for non-participation at each stage, if possible.	64
	11c	Report response rate, present the definition of response rate or the formula used to calculate response rate.	63
	11d	Provide information to define how unique visitors are determined. Report number of unique visitors along with relevant proportions (e.g., view proportion, participation proportion, completion proportion).	n/a
Descriptive results	12	Provide characteristics of study participants, as well as information on potential confounders and assessed outcomes.	64
Main findings	13a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates along with 95% confidence intervals and p-values.	n/a
	13b	For multivariable analysis, provide information on the model building process, model fit statistics, and model assumptions (as appropriate).	n/a
	13c	Provide details about any sensitivity analysis performed. If there are considerable amount of missing data, report sensitivity analyses comparing the results of complete cases with that of the imputed dataset (if possible).	n/a
Discussion			
Limitations	14	Discuss the limitations of the study, considering sources of potential biases and imprecisions, such as non-representativeness of sample, study design, important uncontrolled confounders.	74
Interpretations	15	Give a cautious overall interpretation of results, based on potential biases and imprecisions and suggest areas for future research.	73

Generalizability	16	Discuss the external validity of the results.	74
Other sections			
Role of funding source	17	State whether any funding organization has had any roles in the survey's design, implementation, and analysis.	n/a
Conflict of interest	18	Declare any potential conflict of interest.	n/a
Acknowledgements	19	Provide names of organizations/persons that are acknowledged along with their contribution to the research.	n/a

From: Sharma A, Minh Duc NT, Luu Lam Thang T, Nam NH, Ng SJ, Abbas KS, Huy NT, Marušić A, Paul CL, Kwok J, Karbwang J. A consensus-based checklist for reporting of survey studies (CROSS). Journal of general internal medicine. 2021 Oct;36(10):3179-87.

Appendix E: Survey Instrument

SURVEY INSTRUMENT

☐ Our facility **DOES NOT** have a pulmonary rehabilitation program.
Thank you. You do not need to complete the survey.

☐ Si vous préférez répondre au questionnaire en français, veuillez contacter Ana Maria Ilicic au ilicica@mcmaster.ca

The information is meant to reflect the way a pulmonary rehabilitation (PR) program addresses cough. We are looking for a member of the PR team who would be familiar with the details of the PR program.

Do you feel like you can represent this program?

YES NO

If "Yes" is selected please continue to Part A of the survey.

If "No" is selected please answer the following:

Is there an email to contact someone from your PR program who is better equipped to answer this survey?

Email: _____

Thank you. You do not need to complete the survey.

Part A: Participant Information

1. What type of healthcare professional are you certified as? *(Please check all that apply)*

Dietitian
Exercise Physiologist
General Practitioner
Nurse
Occupational Therapist
Pharmacist
Physiatrist
Physical Therapist
Psychologist
Respiratory Therapist
Respirologist
Kinesiologist
Speech Pathologist
Other *Specify:*

2. How many years of experience do you have in a PR setting?
(Please specify in years)

_____ years(s)

Part B: Program Information

3. What type of PR program does your facility offer? *(Please check all that apply)*

□ Inpatient □ Outpatient
□ Home Program □ Maintenance
□ Other: _____

4. For each PR program please answer the following questions:

	Type of Program				
	In-patient	**Out-patient**	**Home Program**	**Maintenance**	**Other**
How many patients can be enrolled at a given time?					

What is the length of the program? (# of weeks)					
What is the frequency of the program? (# of days/week)					
What is the duration of the sessions? (hours/day)					
Do you admit on a continuous basis or in block? (C= continuous, B= block, NA= not applicable)					

5. What percentages of patients in your PR program have been diagnosed with the following conditions?

		Type of Program				
		In-patient	**Out-patient**	**Home Program**	**Maint-enance**	**Other**
COPD						
Asthma						
Thoracic Surgery	Pre					
	Post					
Restrictive Lung Disease	Parenchymal					
	Thoracic					
	Neuromuscular					
Cystic Fibrosis						
Lung Cancer						
Other *(please specify)*: _____ _____ _____						

* *Please ensure the total adds up to 100%.*

Part C: Chronic Cough in Pulmonary Rehabilitation

We are interested in **chronic cough**; therefore, the following questions all pertain to chronic cough, which is **defined as a cough lasting 8 weeks or greater**.

6. What percentage of the patient's in your PR program present chronic cough? *(Please use numbers from 0 to 100)*

   _____ %

7. Does your PR program assess patients for chronic cough? *(Please check one)*

   YES NO

If "yes" is selected please fill out questions 10-13, if "no" is selected, please go to question 14

IF YES:

8. How often do you assess patients for chronic cough? (*Please check all that apply)*

   ☐ Beginning of Program
   ☐ Each Session
   ☐ Weekly
   ☐ Monthly
   ☐ End of Program
   ☐ Other: _____

9. Which healthcare professional performs the chronic cough assessment?
   (*Please check all that apply)*

   Dietitian
   Exercise Physiologist
   General Practitioner
   Nurse
   Occupational Therapist
   Pharmacist
   Physiatrist
   Physical Therapist
   Psychologist
   Respiratory Therapist
   Respirologist
   Kinesiologist
   Speech Pathologist
   Other *Specify:*

10. How is chronic cough assessed in your program? (*Please check all that apply)*

- ☐ Physical Examination
  - *Specify:* _____
- ☐ Patient Report/ Patient History
  - *Specify:* _____
- ☐ Questionnaire/Scale
  - *Specify:* _____
- ☐ Objective Assessment (e.g. cough counter)
  - *Specify:* _____
- ☐ Other:
  - *Specify:* _____

11. What aspects of chronic cough does your PR program assess? (*Please check all that apply)*

- ☐ Type of cough
- ☐ Duration of cough
- ☐ Frequency of cough
- ☐ Cough triggers
- ☐ Cough relief
- ☐ Risk factors for cough (e.g., smoking, coffee/alcohol ingestion, medication)
- ☐ Impacts of cough (e.g., cough related quality of life, social interactions)
- ☐ Other: _____

IF NO was selected for question 7:

12. A) What are the barriers/reasons for **not** assessing chronic cough in your PR program? (*Please check all that apply)*

- ☐ Lack of time
- ☐ Lack of outcome measures
- ☐ Lack of staff
- ☐ Lack of chronic cough within patient cohort
- ☐ Lack of evidence in chronic cough assessment
- ☐ Inadequate knowledge about chronic cough assessment
- ☐ Other: _____

B) If more than one reason was selected, please rank answers from most to least common

_____

_____

_____

13. What could facilitate chronic cough assessment in your PR program?

_____
_____
_____
_____
_____
_____

Part D: Cough Management

14. Does your PR program treat/manage chronic cough? *(Please check one)*

YES NO

If "yes" is selected please fill out questions 17-22, if "no" is selected, please go to question 21

IF YES:

15. Which healthcare professional performs chronic cough management? (*Please check all that apply)*

Dietitian
Exercise Physiologist
General Practitioner
Nurse
Occupational Therapist
Pharmacist
Physiatrist
Physical Therapist
Psychologist
Respiratory Therapist
Respirologist
Kinesiologist
Speech Pathologist
Other *Specify:*

16. A) How is non-productive (dry) chronic cough managed in your program? *(Please check all that apply and provide a brief description)*

- ☐ Medication
- ☐ Breathing Exercises
  - *Specify:* _____
- ☐ Behaviour Change Techniques
  - *Specify:* _____
- ☐ Smoking Cessation
- ☐ CPAP
- ☐ Cough Suppression Techniques
  - *Specify:* _____
- ☐ Airway clearance techniques
  - *Specify:* _____
- ☐ Education
  - *Specify*_____
- ☐ Other: _____

B) How is productive (wet) chronic cough managed in your program? *(Please check all that apply and provide a brief description)*

- ☐ Medication
- ☐ Breathing Exercises
  - *Specify:* _____
- ☐ Behaviour Change Techniques
  - *Specify:* _____
- ☐ Smoking Cessation
- ☐ CPAP
- ☐ Cough Suppression Techniques
  - *Specify:* _____
- ☐ Airway clearance techniques
  - *Specify:* _____
- ☐ Education
  - *Specify:* _____
- ☐ Other: _____
  _____

17. A) Does your PR program use different management strategies for different types of respiratory diseases? *(Please check one)*

YES NO

B) If yes, please specify:

_____
_____
_____
_____

18. How is non-productive (dry) chronic cough managed in your program for specific diseases? *(Please check all that apply)*

		Management strategies								
		Medication	**Breathing exercises**	**BCT**	**Smoking Cessation**	**CPAP**	**CST**	**ACT**	**Education**	**Other**
COPD										
Asthma										
Thoracic Surgery	Pre									
	Post									
Restrictive Lung Disease	Parenchymal									
	Thoracic									
	Neuromuscular									
Cystic Fibrosis										
Lung Cancer										
Other *(please specify)*: _____ _____ _____										

Legend: BCT, behaviour change techniques; CPAP, continuous positive airway pressure; CST, cough suppression techniques; ACT, airway clearance techniques

19. How is productive (wet) chronic cough managed in your program for specific diseases? *(Please check all that apply)*

		Management strategies								
		Medication	**Breathing exercises**	**BCT**	**Smoking Cessation**	**CPAP**	**CST**	**ACT**	**Education**	**Other**
COPD										
Asthma										
Thoracic Surgery	Pre									
	Post									
Restrictive Lung Disease	Parenchymal									
	Thoracic									
	Neuromuscular									
Cystic Fibrosis										
Lung Cancer										

Other *(please specify)*: _____ _____ _____									

Legend: BCT, behaviour change techniques; CPAP, continuous positive airway pressure; CST, cough suppression techniques; ACT, airway clearance techniques

20. A) Does the severity of the disease impact the management of chronic cough in your PR program? *(Please check one)*

YES NO

B) If yes is selected, how does it impact cough management?

_____
_____
_____

21. A) What are the barriers/reasons for **not** managing cough in your PR program? (*Please check all that apply)*

- ☐ Lack of time
- ☐ Lack of equipment for intervention
- ☐ Lack of staff
- ☐ Lack of chronic cough within patient cohort
- ☐ Lack of evidence in chronic cough management
- ☐ Inadequate knowledge about chronic cough management
- ☐ Other: _____

B) If more than one reason was selected, please rank answers from most to least common:

_____
_____
_____

22. What could facilitate chronic cough management in your PR program?

_____
_____
_____

Part E: Conclusion

23. Are there any additional comments in regard to chronic cough assessment or management that you would like to share with us?

    _____
    _____
    _____
    _____
    _____

24. When the research is completed, would you like us to send you a copy of the findings? *(Please check one)*

    YES NO

If "Yes" is selected please provide your contact information in Part F of the survey.

Part F: Optional

This is optional. Please fill this in if you are interested in being informed of the final results of the study.

Facility: _____

Email: _____

Thank you for completing this survey!

Appendix F:

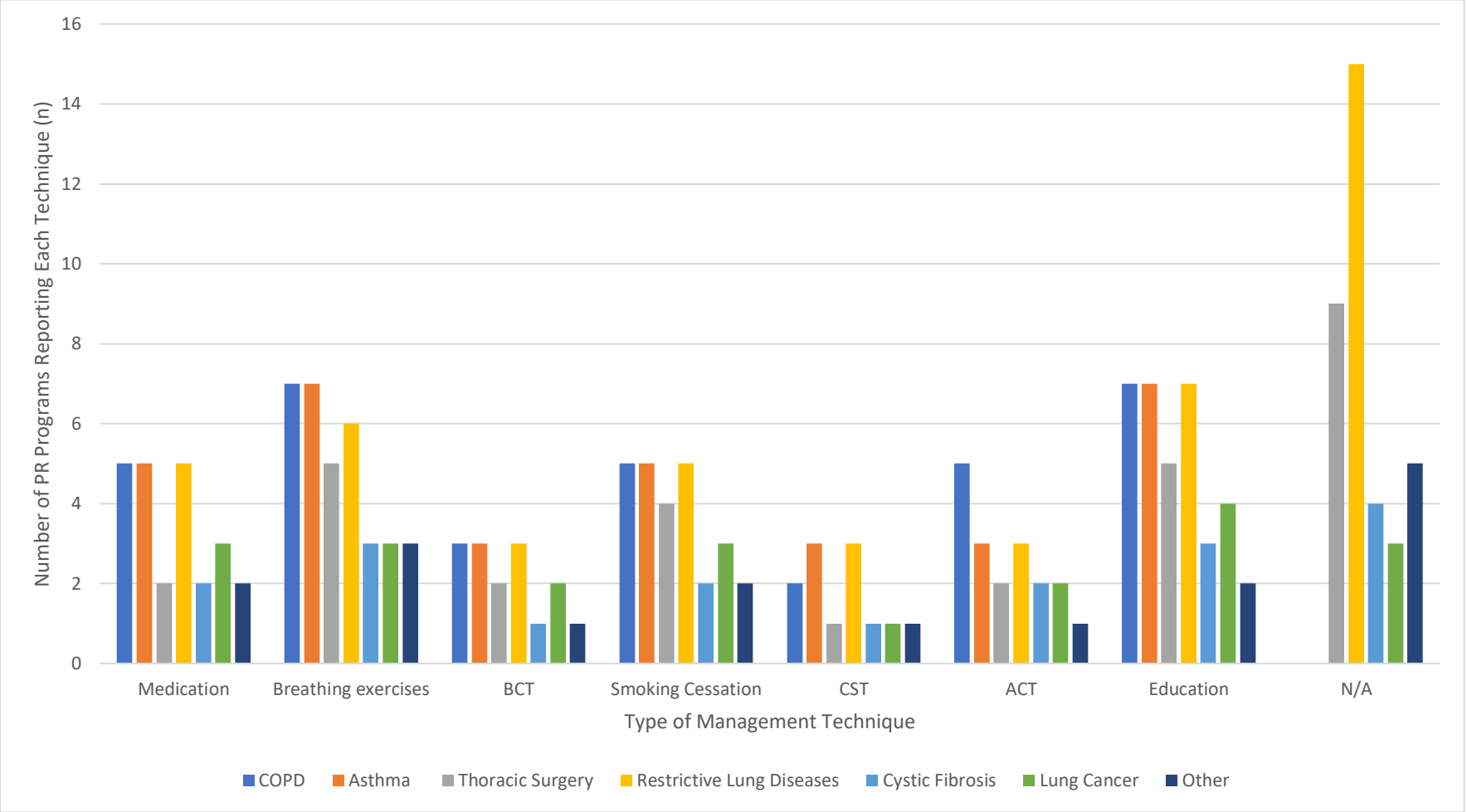

Figure 1 Distribution of various management techniques used for non-productive chronic cough, differing based on type of respiratory disease.
**" Other" respiratory diseases include post-covid support, bronchiectasis, and treatment depending on symptoms alone.*

Appendix G:

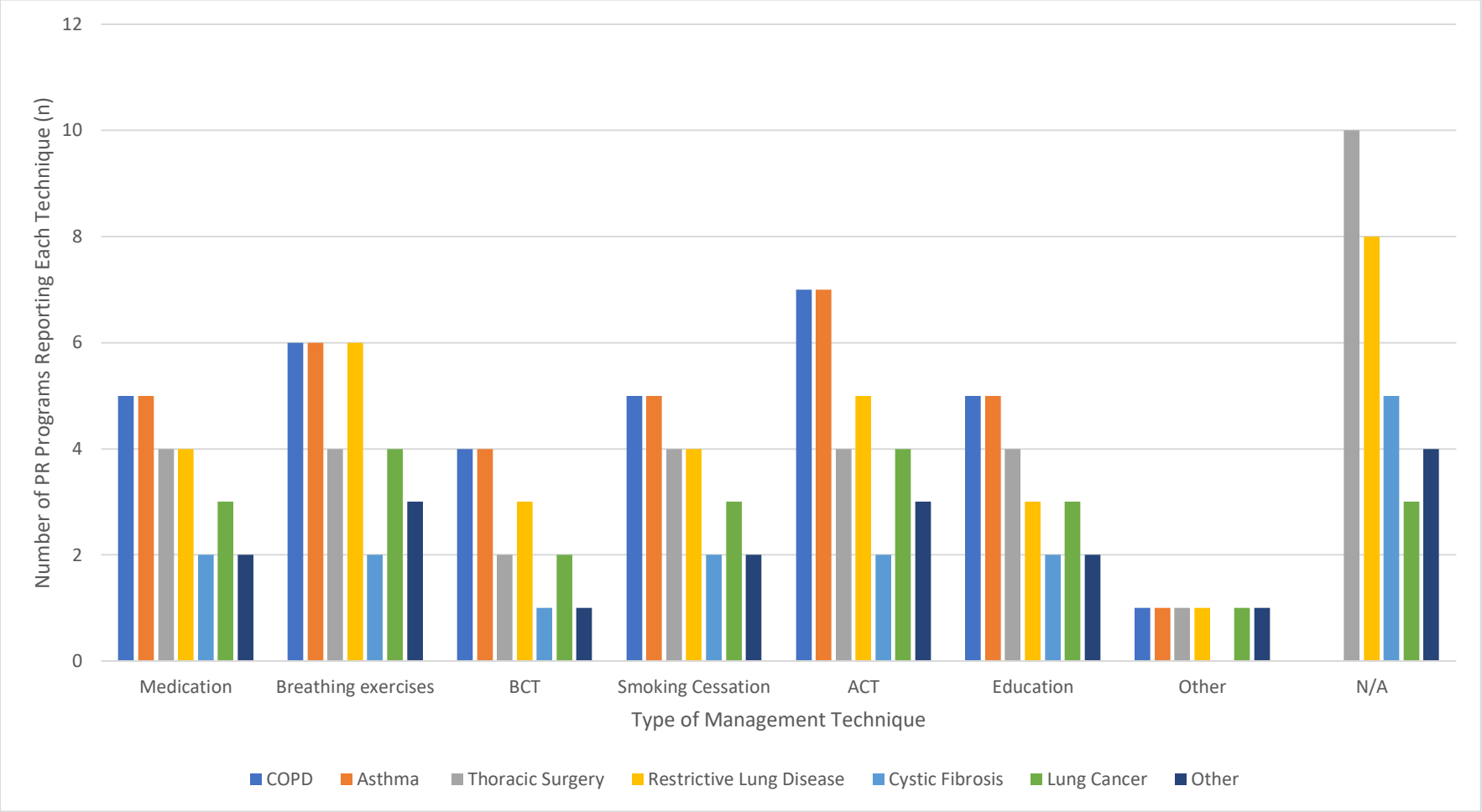

Figure 2: Distribution of various management techniques used for productive chronic cough, differing based on type of respiratory disease.
** "Other" management techniques include ruling out heart failure; "Other" types of respiratory diseases managed in PR include post-covid symptoms, bronchiectasis, and Kartagener's Syndrome*