Cochrane Library

Cochrane Database of Systematic Reviews

Speech and language therapy for management of chronic cough (Review)

Slinger C, Mehdi SB, Milan SJ, Dodd S, Matthews J, Vyas A, Marsden PA

Slinger C, Mehdi SB, Milan SJ, Dodd S, Matthews J, Vyas A, Marsden PA.
Speech and language therapy for management of chronic cough.
Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD013067.
DOI: 10.1002/14651858.CD013067.pub2.

www.cochranelibrary.com

TABLE OF CONTENTS

[Intervention Review]

Speech and language therapy for management of chronic cough

Claire Slinger[1], Syed B Mehdi[1], Stephen J Milan[2], Steven Dodd[3], Jessica Matthews[1], Aashish Vyas[1], Paul A Marsden[1,4,5]

[1]Department of Respiratory Medicine, Lancashire Teaching Hospitals Trust, Preston, UK. [2]Medical School, Lancaster University, Lancaster, UK. [3]Faculty of Health and Medicine, Lancaster University, Lancaster, UK. [4]North West Lung Centre, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK. [5]Division of Infection, Immunity and Respiratory Medicine, School of Biological Sciences, University of Manchester, Manchester, UK

Contact address: Claire Slinger, Department of Respiratory Medicine, Lancashire Teaching Hospitals Trust, Preston, UK. Claire.slinger@lthtr.nhs.uk.

Editorial group: Cochrane Airways Group.
Publication status and date: New, published in Issue 7, 2019.

Citation: Slinger C, Mehdi SB, Milan SJ, Dodd S, Matthews J, Vyas A, Marsden PA. Speech and language therapy for management of chronic cough. *Cochrane Database of Systematic Reviews* 2019, Issue 7. Art. No.: CD013067. DOI: 10.1002/14651858.CD013067.pub2.

ABSTRACT

Background

Cough both protects and clears the airway. Cough has three phases: breathing in (inspiration), closure of the glottis, and a forced expiratory effort. Chronic cough has a negative, far-reaching impact on quality of life. Few effective medical treatments for individuals with unexplained (idiopathic/refractory) chronic cough (UCC) are known. For this group, current guidelines advocate the use of gabapentin. Speech and language therapy (SLT) has been considered as a non-pharmacological option for managing UCC without the risks and side effects associated with pharmacological agents, and this review considers the evidence from randomised controlled trials (RCTs) evaluating the effectiveness of SLT in this context.

Objectives

To evaluate the effectiveness of speech and language therapy for treatment of people with unexplained (idiopathic/refractory) chronic cough.

Search methods

We searched the Cochrane Airways Trials Register, CENTRAL, MEDLINE, Embase, CINAHL, trials registries, and reference lists of included studies. Our most recent search was 8 February 2019.

Selection criteria

We included RCTs in which participants had a diagnosis of UCC having undergone a full diagnostic workup to exclude an underlying cause, as per published guidelines or local protocols, and where the intervention included speech and language therapy techniques for UCC.

Data collection and analysis

Two review authors independently screened the titles and abstracts of 94 records. Two clinical trials, represented in 10 study reports, met our predefined inclusion criteria. Two review authors independently assessed risk of bias for each study and extracted outcome data. We analysed dichotomous data as odds ratios (ORs), and continuous data as mean differences (MDs) or geometric mean differences. We used standard methods recommended by Cochrane. Our primary outcomes were health-related quality of life (HRQoL) and serious adverse events (SAEs).

Main results

We found two studies involving 162 adults that met our inclusion criteria. Neither of the two studies included children. The duration of treatment and length of sessions varied between studies from four sessions delivered weekly, to four sessions over two months. Similarly, length of sessions varied slightly from one 60-minute session and three 45-minute sessions to four 30-minute sessions. The control interventions were healthy lifestyle advice in both studies.

One study contributed HRQoL data, using the Leicester Cough Questionnaire (LCQ), and we judged the quality of the evidence to be low using the GRADE approach. Data were reported as between-group difference from baseline to four weeks (MD 1.53, 95% confidence interval (CI) 0.21 to 2.85; participants = 71), revealing a statistically significant benefit for people receiving a physiotherapy and speech and language therapy intervention (PSALTI) versus control. However, the difference between PSALTI and control was not observed between week four and three months. The same study provided information on SAEs, and there were no SAEs in either the PSALTI or control arms. Using the GRADE approach we judged the quality of evidence for this outcome to be low.

Data were also available for our prespecified secondary outcomes. In each case data were provided by only one study, therefore there were no opportunities for aggregation; we judged the quality of this evidence to be low for each outcome. A significant difference favouring therapy was demonstrated for: objective cough counts (ratio for mean coughs per hour on treatment was 59% (95% CI 37% to 95%) relative to control; participants = 71); symptom score (MD 9.80, 95% CI 4.50 to 15.10; participants = 87); and clinical improvement as defined by trialists (OR 48.13, 95% CI 13.53 to 171.25; participants = 87). There was no significant difference between therapy and control regarding subjective measures of cough (MD on visual analogue scale of cough severity: −9.72, 95% CI −20.80 to 1.36; participants = 71) and cough reflex sensitivity (capsaicin concentration to induce five coughs: 1.11 (95% CI 0.80 to 1.54; participants = 49) times higher on treatment than on control). One study reported data on adverse events, and there were no adverse events reported in either the therapy or control arms of the study.

Authors' conclusions

The paucity of data in this review highlights the need for more controlled trial data examining the efficacy of SLT interventions in the management of UCC. Although a large number of studies were found in the initial search as per protocol, we could include only two studies in the review. In addition, this review highlights that endpoints vary between published studies.

The improvements in HRQoL (LCQ) and reduction in 24-hour cough frequency seen with the PSALTI intervention were statistically significant but short-lived, with the between-group difference lasting up to four weeks only. Further studies are required to replicate these findings and to investigate the effects of SLT interventions over time. It is clear that SLT interventions vary between studies. Further research is needed to understand which aspects of SLT interventions are most effective in reducing cough (both objective cough frequency and subjective measures of cough) and improving HRQoL. We consider these endpoints to be clinically important. It is also important for future studies to report information on adverse events.

Because of the paucity of data, we can draw no robust conclusions regarding the efficacy of SLT interventions for improving outcomes in unexplained chronic cough. Our review identifies the need for further high-quality research, with comparable endpoints to inform robust conclusions.

PLAIN LANGUAGE SUMMARY

Speech and language therapy for chronic cough

Background to the question

People normally cough to protect and clear the airways. For example, when we have a chest infection, we cough to eject bacteria. Or when we breathe in dust, we cough to eject the dust. Some people have chronic, or long-term cough, due to a disease such as asthma, chronic obstructive pulmonary disease (COPD), or gastro-oesophageal reflux disease. However, some people have chronic cough for no obvious reason. This is known as unexplained (idiopathic/refractory) chronic cough (UCC). Coughing over months and years is unpleasant, causing a reduction in quality of life.

Current guidelines recommend the use of gabapentin (a drug usually used to control seizures and reduce nerve pain) to try to stop people with UCC from coughing. However, this drug has side effects including drowsiness.

Speech and language therapy (SLT) has been suggested as a non-drug-based option for managing UCC. Speech and language therapy would avoid the risks and side effects of medication.

Speech and language therapy aims to teach people to control their cough. The person is taught methods to help them suppress the urge to cough. Education is given with the intention to help people understand how the technique works and hopefully get them to stick with it. People also receive vocal hygiene information. Vocal hygiene involves techniques to reduce the trigger to cough. For example, vocal hygiene may involve helping someone breathe through their nose rather than their mouth and avoiding drinking alcohol and caffeine, which can worsen cough. They may also be given psychoeducational counselling to help them learn they have the means to control their cough.

This review assessed the latest evidence regarding the effectiveness of SLT in the management of UCC.

Study characteristics

We found two relevant studies to include in the review. Both studies were randomised controlled trials (a type of study in which participants are assigned to one of two or more treatment groups using a random method) in which participants had a diagnosis of UCC. Participants received either an intervention including SLT techniques or 'healthy lifestyle advice' as a control group. We chose to use health-related quality of life and serious adverse events to judge whether SLT is a useful intervention.

Main results

Only one of the studies comparing SLT to usual care reported data about quality of life (using a questionnaire). After four weeks, participants in the study who were receiving the SLT treatment, physiotherapy and speech and language therapy intervention (PSALTI), had on average an improvement in their quality of life compared to people in the control group. However, this benefit compared to control was short-lived and disappeared after four weeks. This means that although the treatment appeared to work in the shorter term, it may not improve quality of life in the longer term compared to usual care.

We also looked for information about side effects or harms of the treatment. The same study reported that no one experienced serious side effects or harms during the study.

Other ways of measuring the impact of SLT were also considered, and in each case relevant data were only provided by one study. An improvement in objective cough counts (using a cough monitor), symptoms (using symptom scores), and clinical improvement was shown with SLT compared to controls. The included trials reported no difference for other secondary outcomes such as subjective measures of cough or cough reflex sensitivity (measured in the laboratory using airway irritants).

Quality of the evidence

The small number of high-quality, relevant studies found in this review means that we cannot be sure of the overall benefits of SLT in the management of UCC. Improvements in health-related quality of life were associated with the PSALTI intervention over a short period in one study, but further research is required to replicate this finding. Overall, more controlled trials are required to fully examine the potential of SLT for the management of UCC.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [*Explanation*]

Speech and language therapy compared with control for chronic cough

Patient or population: participants with chronic cough
Settings: hospital
Intervention: speech and language therapy
Comparison: Healthy lifestyle advice

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (RCTs)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo programme	Speech and language therapy				
Health-related quality of life Follow-up: 4 weeks	Source data not available in trial report		**MD 1.53** (0.21 to 2.85)	71 (1)	⊕⊕◯◯ Low[1,2]	The statistically significant difference for PSALTI versus control was not maintained between 4 weeks and 3-month follow-up
Serious adverse events Follow-up: 4 weeks	0/41	0/34	Not estimable	75 (1)	⊕⊕◯◯ Low[1,2]	
Objective cough counts (over 24-hour period) Follow-up: 4 weeks	Source data not available in trial report		Ratio for mean coughs per hour on treatment was**0.59** (0.37 to 0.95)	71 (1)	⊕⊕◯◯ Low[1,2]	This statistically significant difference was not maintained for PSALTI versus control between 4 weeks and 3-month follow-up (Chamberlain Mitchell 2017).

Symptoms Follow-up: 2 months	The mean improvement in symptoms in the control group was 2.9	**MD 9.80 better** (4.50 to 15.10)	-	87 (1)	⊕⊕◯◯ Low[1,2]	The data were skewed and were analysed with non-parametric methods by Vertigan 2006, which also gave a significant result favouring speech and language therapy
Clinical improvement (as defined by trialists) Follow-up: 2 months	6/44 demonstrated successful improvement	38/43 demonstrated successful improvement	**OR 48.13** (13.53 to 171.25)	87 (1)	⊕◯◯◯ Very low[1,2,3]	
Subjective measures of cough (e.g. VAS/numerical cough scale score) Follow-up: 4 weeks	Source data not available in trial report		**MD −9.72** (−20.80 to 1.36)	71 (1)	⊕⊕◯◯ Low[1,2]	Similarly, there was no difference for PSALTI versus control between 4 weeks and 3-month follow-up
Cough reflex sensitivity (as measured by cough challenge: capsaicin concentration required to provoke 5 coughs) Follow-up: 4 weeks	Source data not available in trial report		**Capsaicin concentration 1.11** (0.80 to 1.54) times higher in intervention group	49 (1)	⊕⊕◯◯ Low[1,2]	There was no significant difference for PSALTI versus control in the capsaicin cough challenge either in terms of the 2 or 5 cough thresholds (Chamberlain Mitchell 2017).
Adverse events Follow-up: 4 weeks	0/41	0/34	Not estimable	75 (1)	⊕⊕◯◯ Low[1,2]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **IV:** inverse variance; **MD:** mean difference; **OR:** odds ratio; **PSALTI:** physiotherapy and speech and language therapy intervention; **RCT:** randomised controlled trial; **VAS**: visual analogue scale

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]A point was deducted to reflect the study question precluding the opportunity to double-blind.
[2]A point was deducted to reflect imprecision (data from a single study with modest sample size).
[3]A point was deducted to reflect judgement being made of outcome as defined by trialists.

BACKGROUND

Description of the condition

Cough is a reflex action to clear the airways of mucus and irritants such as smoke. Cough is a sequence comprising an inspiratory, glottic (vocal fold) closure, then a forced expiratory effort initially against the closed glottis (Fontana 2008). The duration of cough can be acute (less than three weeks), subacute (between three and eight weeks), or chronic (longer than eight weeks) (Irwin 2006). Details regarding the theory and treatment of cough can be found in several different clinical fields, including otolaryngology, respiratory medicine, speech and language therapy, respiratory physiology, and physiotherapy (Vertigan 2016a).

Unexplained (idiopathic/refractory) chronic cough (UCC) is a cough that persists after common causes have been evaluated and ruled out and medical management options have not offered any convincing relief from symptoms. This condition is a diagnosis of exclusion following a careful diagnostic workup to exclude other causes of cough such as underlying lung/airways disease, gastro-oesophageal reflux, drugs (such as angiotensin-converting enzyme inhibitors (ACEis)), and rhinosinusitis (Gibson 2016a; Morice 2006; Morice 2007; Morice 2007a; Vertigan 2016a).

Evidence suggests that UCC may be caused by neural hyper-responsiveness. The observation that lower concentrations of tussive agents are required to induce cough in participants with UCC compared with healthy controls illustrates an increase in sensitivity of the cough reflex (Prudon 2005). Symptomatically, patients with this condition describe an 'irritation' or 'tickle' within the throat and a heightened urge or need to cough (Hilton 2015). Functional magnetic resonance imaging (fMRI) studies have demonstrated a clear role of the central nervous system in the sensation or urge to cough (Farrell 2014; Leech 2013; Mazzone 2007; Mazzone 2011), as well as a failure of descending inhibition of cough (Ando 2016). It is known that vagal afferent bronchopulmonary C-fibres as well as A-delta fibres are important in cough (Belvisi 2003; Canning 2014). Novel drugs targeting C-fibre receptors have been recently trialed in humans. An oral transient receptor potential vanilloid subtype 1 (TRPV1) antagonist had no effect on cough frequency but did reduce cough reflex sensitivity in participants with UCC (Khalid 2014). Another, more potent, TRPV1 antagonist showed similar results in a more recent randomised controlled trial (RCT) (Belvisi 2017). In contrast, targeting the P2X3 receptor demonstrated a 75% reduction in daytime cough frequency in participants with UCC using a novel P2X3 antagonist (Abdulqawi 2015), supporting the hypothesis of a neural mechanism in UCC.

Furthermore, an overlap has been postulated between chronic cough and other laryngeal dysfunction presentations, such as inducible laryngeal obstruction (ILO), extra-thoracic responsiveness, globus pharyngeus, hyperfunctional muscle tension, muscle tension dysphonia, voice disorders, and dysphagia symptoms (Altman 2002; Irwin 2010; Morrison 1999; Ryan 2009; Song 2014; Vertigan 2006; Vertigan 2012; Vertigan 2013; Vertigan 2016a; Vertigan 2019). Inducible laryngeal obstruction, previously known as vocal cord dysfunction (VCD) or paradoxical vocal form movement (PVFM), is an "inappropriate, transient, reversible narrowing of the larynx in response to external triggers" (Halvorsen 2017), leading to symptoms of shortness of breath, dysphonia, and cough (Vertigan 2016a). Symptoms of ILO are localised to the larynx (Benninger 2011). It has been suggested that these symptoms may represent different manifestations of an underlying hypersensitive and hyper-responsive upper airway (Morrison 1999; Vertigan 2007a; Vertigan 2010; Vertigan 2016a).

Description of the intervention

Speech and language therapy (SLT) offers a non-pharmacological intervention for people with UCC who may have exhausted medical treatment for their condition, or who wish to pursue a non-pharmacological treatment option (Haines 2015; Ryan 2010; Ryan 2014; Vertigan 2006; Vertigan 2016a). Speech and language therapy has been incorporated into the Treatment of unexplained chronic cough: CHEST guideline and expert panel report (Gibson 2016a), which details treatment of UCC, and the Australian cough guidelines summary statement (Gibson 2010). The goal of SLT is to reduce laryngeal irritation that can trigger an individual's urge to cough, and to increase voluntary control of cough by interrupting or preventing coughing episodes, as well as to address symptoms associated with dysphonia and ILO (Vertigan 2016a; Vertigan 2019).

Speech and language therapists are appropriately trained to manage chronic cough via a combination of detailed knowledge of anatomy and physiology of the upper airway, experience in education and training on respiratory physiology and clinical voice disorders, and knowledge of interventions to modify laryngeal behaviour (Altman 2000; Stemple 2009). As there is a hypothesised and clinically recognised overlap between cough and other upper airway and laryngeal disorders, such as ILO, globus pharyngeus, muscle tension dysphonia, and dysphagic symptoms, SLT professionals have the skills required to identify, assess, and manage these overlapping conditions effectively by applying techniques traditionally used to treat muscle tension voice disorders (Blager 1998; Blager 2000; Carney 1997; Chhetri 2014; Dunn 2015; Estill 2009; Estill 2009a; Ryan 2010; TitzeI 2006; Vertigan 2007a). Speech and language therapy assessment can also investigate patient-reported symptoms of dysphagia to identify clinical signs of aspiration that may warrant further investigation (Vertigan 2013; Vertigan 2016a; Irwin 2010).

Given the overlap between chronic cough and other upper airway and laryngeal disorders, videolaryngoscopy may assist differential diagnosis and consequent targeted therapy (Forrest 2012; Vertigan 2016a). Furthermore, the trained SLT professional can provide biovisual feedback with videolaryngoscopy. This has been found to be useful for assisting patients in applying techniques and in

helping to monitor response to SLT in other related conditions such as clinical voice disorders and ILO (Balkissoon 2012; Belafsky 2001; Christopher 2010; Hull 2016; Olin 2017).

The urge to cough and indicators suggestive of ILO can be evaluated through the use of scales (e.g. Davenport 2002) (Ryan 2014; Traister 2014). Hyperfunction in the larynx during voicing can signify laryngeal dysfunction and can serve as a contributory factor to cough reflex sensitivity. Voicing is often cited as a trigger for coughing episodes. A clinical voice assessment can use recognised descriptive rating scales of perceptual voice characteristics, such as rough, breathy, and strained vocal qualities (Hirano 1981; Omori 2011; Ryan 2014; Vertigan 2007a).

The SLT professional can also assess voice production instrumentally (Ryan 2010; Zelcer 2002), for example by using an acoustic voice analysis programme or visualising the larynx via videolaryngoscopy during voice use according to a recognised protocol (RCSLT 2008). Manual assessment of tension in the extrinsic laryngeal musculature is a useful tool for assessing hyperfunction, which can be detected in muscle tension voice disorders (Rubin 2000; Vertigan 2016a).

Vertigan 2012 and Vertigan 2016a outlined a multidimensional SLT intervention for chronic cough management consisting of the following elements.

Education

Education focusses on encouraging adherence, with the aim of acceptance that patients can control their cough and take steps at the first sign of the urge to cough to implement cough suppression strategies such as cough suppression swallow, controlled breathing, relaxed throat breathing, and ILO release breathing (Vertigan 2016). Patients are provided with information on the importance of sustained application of cough suppression techniques (Vertigan 2012), as well as reassurance that their cough is not necessary or beneficial to them.

Education is provided on the perpetuating nature of the cough, and how this can potentially lead to an increased laryngeal sensitivity, laryngeal trauma, and laryngeal tension. Specific goals for therapy are planned with the patient. The ultimate goal of SLT is for the patient to control the cough, even in the presence of the sensation or urge to cough.

Symptom control techniques

The aim of symptom control strategies is to enable the patient to prevent, stop, or interrupt the cough despite having the triggering sensation or urge. The patient is taught to substitute the cough with a competing response (e.g. distraction, cough suppression swallow, relaxed throat breathing, a sip of fluids, laryngeal deconstriction) (Estill 2009; Vertigan 2007a). Laryngeal control techniques for any coexisting inducible laryngeal obstruction can also be included in the therapy intervention (Blager 2000; Boone 1993; Chhetri 2014; Kotby 1993).

A hierarchy for applying control techniques can be devised with the patient; this can include graded exposure to desensitise the patient to particular triggers, and facilitate automaticity of techniques when symptomatic (Vertigan 2016).

Reducing laryngeal irritation via vocal hygiene

Vocal hygiene advice is routinely used in the SLT approach to clinical voice disorders (Blager 1988), and it may be beneficial in the treatment of UCC (Vertigan 2012). Vocal hygiene consists of advice on reducing irritation and trauma to the upper airway, for example the potential harmful effects of smoking, mouth breathing, caffeine, and alcohol on laryngeal mucosa. Easy voicing and adequate hydration are emphasised and demonstrated to reduce the risk of phonotrauma (Boone 1993; Kotby 1993; Murry 2004; Solomon 2014; Vertigan 2007a). Information on diet and behavioural management of gastro-oesophageal and laryngopharyngeal reflux is provided (Koufman 2011; Vertigan 2019).

Psychoeducational counselling

The therapist can assess readiness to engage in SLT, as this may impact the efficacy of therapy (Prochaska 1982). Acceptance that the patient can control the cough (internal locus of control), self-efficacy (Bandura 1986), and the effort required of the patient are made explicit, with emphasis on treatment being 'hard work'. Realistic, targeted goal setting helps the therapist to direct interventions and monitor progress (Murry 2004; Ryan 2010; Vertigan 2012).

Overall goals of speech and language therapy interventions can be summarised as follows (Gibson 2015a).

1. Reduce the sensitivity of the cough reflex.
2. Encourage improvement in voluntary control of cough.
3. Reduce irritation of the larynx.

How the intervention might work

Speech and language therapy interventions aim to improve a person's control over cough and symptoms associated with any overlapping dysphonia and ILO (Vertigan 2016a), but the mechanism(s) by which multimodal SLT interventions may reduce cough severity and frequency, leading to improvement in health-related quality of life, is poorly understood. However, it is postulated that SLT management of UCC can help break the cycle of reciprocal irritation of cough receptors by increasing voluntary cognitive control of the urge to cough, reducing cough reflex sensitivity, reducing laryngeal irritation and laryngeal muscle tension, and also treating any coexisting paradoxical vocal fold movement (Ryan 2010; Vertigan 2016; Vertigan 2019).

Speech and language therapy interventions have been shown to reduce cough sensitivity in participants with UCC (Ryan 2009; Smith 2005; Vertigan 2006; Vertigan 2016). However,

a multicentre RCT demonstrated no differences between intervention and control groups with capsaicin cough challenge (Chamberlain Mitchell 2017). The psychoeducational and control strategies component may support subjective improvement in chronic cough management techniques and may reduce upper airway muscle tension (Canning 2006; Gibson 2009). Improved laryngeal hygiene attained via hydration and education on reduction of laryngeal injury may support lower phonation threshold pressure, thereby reducing stimulation of cough receptors (Casper 2003; Solomon 2014).

Vertigan 2019 details that the overall mechanism for improvement in cough symptoms following multimodal SLT intervention is unknown. However, it could represent both a central action in improved function of the neural cough suppression networks and laryngeal control, and a peripheral action demonstrated by a reduction in laryngeal hypersensitivity.

Why it is important to do this review

Cough is one of the most common reasons why patients seek medical advice (Morice 2006). The reported prevalence of chronic cough in the population varies in the most recent studies from 4%, Colak 2017, to 9.6% (Song 2015). Cough presents a considerable financial burden, with acute cough costing approximately GBP 979 million in the UK, including GBP 875 million in loss of productivity and GBP 104 million in healthcare costs (Morice 2006). The cost of chronic cough to the economy remains unclear. The impact of chronic cough on quality of life is far reaching and can include negative physical, psychological, and social consequences (Decalmer 2007; French 1998; McGarvey 2013). Patient-reported impact has been reported to be comparable to the impact of stroke or Parkinson's disease (Song 2013). Reported psychological and physical morbidities include vomiting, social embarrassment, headaches, low mood, and sleep disturbance (Chamberlain 2013). Urinary incontinence associated with chronic cough is a particularly distressing symptom (Hrisanfow 2013).

Few effective medical treatments for individuals with UCC are known. Current guidelines advocate the use of gabapentin (Gibson 2016a), following improvements in quality of life reported in an RCT of gabapentin in UCC (Ryan 2012). One study demonstrated a reduction in subjective cough scores in response to slow-release morphine sulphate (Morice 2007a). Another study examined amitriptyline in participants with postviral vagal neuropathy and cough, but guidelines do not currently recommend this treatment (Jeyakumar 2006).

Speech and language therapy has been advocated as an attractive non-pharmacological option for managing UCC without the risks and side effects associated with pharmacological agents and is advocated in guidelines (Gibson 2016a). Speech and language therapy was the focus of this review.

OBJECTIVES

To evaluate the effectiveness of speech and language therapy for treatment of people with unexplained (idiopathic/refractory) chronic cough.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs). We included studies reported in full text, those published as an abstract only, and unpublished data. We planned to include cluster trials and first-period data from cross-over trials if these were available, however all of the included studies were of conventional parallel-group design.

Types of participants

We included participants with a diagnosis of unexplained chronic (idiopathic/refractory) cough (UCC) who had undergone a full diagnostic workup to exclude an underlying cause, as per published guidelines or local protocols. Had we identified eligible studies in children (17 years of age and younger), we would have analysed them separately from adult studies, however all of the included studies focused on adult participants.

Types of interventions

We included studies that used recognised speech and language therapy (SLT) techniques for UCC, such as the multidimensional SLT intervention described in the Background section (education, symptom control or vocal hygiene, psychoeducational counselling) and/or other recognised SLT laryngeal control techniques as defined by trialists.

We planned to include other co-interventions, provided they were not part of the randomised treatment.

We included studies comparing SLT and usual care versus usual care, such as reassurance, lifestyle advice, and background medications. We also planned to include studies comparing SLT versus an 'active' control such as non-prescribed/over-the-counter cough products (e.g. lozenges). We included trials that delivered a number of sessions and planned to investigate in subgroup analyses the number of sessions provided wherever possible (Ryan 2010).

Types of outcome measures

Primary outcomes

1. Health-related quality of life (assessed via a validated measure)
2. Serious adverse events

Secondary outcomes

1. Objective cough counts (e.g. using the Leicester Cough Monitor (LCM))
2. Symptoms (preferentially assessed on validated symptom scales)
3. Clinical improvement (as defined by trialists)
4. Subjective measures of cough (e.g. visual analogue scale (VAS)/numerical cough scale score)
5. Cough reflex sensitivity (as measured by cough challenge)
6. Adverse events/side effects

Reporting in the study of one or more of the outcomes listed was not an inclusion criterion for this review.

Search methods for identification of studies

Electronic searches

The Cochrane Airways Group Information Specialist conducted systematic searches in the following sources:

1. Cochrane Airways Trials Register via the Cochrane Register of Studies (CRS-Web), searched on 8 February 2019;
2. Cochrane Central Register of Controlled Trials (CENTRAL), via the Cochrane Register of Studies (CRS-Web), searched on 8 February 2019;
3. MEDLINE Ovid SP from 1946 to 8 February 2019;
4. Embase Ovid SP from 1974 to 8 February 2019;
5. CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature) from 1937 to 8 February 2019;
6. US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov/). searched on 8 February 2019;
7. World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/) searched on 8 February 2019

Search strategies are provided in Appendix 1.

We searched all sources from inception to the present, with no restriction on language of publication.

Searching other resources

We checked the reference lists of all primary studies and review articles for additional references. We searched for errata or retractions from included studies published in full text on PubMed (www.ncbi.nlm.nih.gov/pubmed) and reported within the review the date this was done (February 2019).

Data collection and analysis

Selection of studies

Two review authors (CS and PM) independently screened the titles and abstracts of studies identified by the search and coded them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We retrieved the full-text study reports of all potentially eligible studies, and two review authors (CS and PM) independently screened them for inclusion, while recording reasons for exclusion of ineligible studies. We planned to resolve any disagreements through discussion, consulting a third person/review author (AV) if necessary, however this was not required. We identified and excluded duplicates and collated multiple reports of the same study so that each study, rather than each report, was the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' tables (Moher 2009).

Data extraction and management

We used a data collection form that had been piloted on at least one study in the review to record study characteristics and outcome data. Two review authors (SJM and JM) extracted the following study characteristics from the included studies.

1. Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and locations, study setting, withdrawals, and dates of study.
2. Participants: N, mean age, age range, gender, severity of condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria, and exclusion criteria.
3. Interventions: intervention, comparison, concomitant medications, and excluded medications.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Notes: funding for studies and notable conflicts of interest of trial authors.

Two review authors (SJM and JM) independently extracted outcome data from the included studies. We noted in the 'Characteristics of included studies' table if outcome data were not reported in a manner precluding them from being entered into the Review Manager 5 file (RevMan 2014). We planned to resolve any disagreements by consensus, consulting a third person/review author (PM) if necessary, however this was not required. One review author (SJM) transferred data into the Review Manager 5 file (RevMan 2014). A second review author (CS) double-checked that study characteristics and data had been entered correctly by comparing the data presented in the systematic review against that in the study reports.

Assessment of risk of bias in included studies

Two review authors independently (SJM and JM) assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We planned to resolve any disagreements by discussion, consulting another review author (PM) if necessary, however this was not required. We assessed risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

We judged each potential source of bias as high, low, or unclear and provided a quote from the study report together with a justification for our judgement in the 'Risk of bias' table. We summarised 'Risk of bias' judgements across different studies for each of the domains listed. We considered blinding separately for different key outcomes when necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different than for use of a patient-reported pain scale). When information on risk of bias related to unpublished data or correspondence with a trialist, we noted this in the 'Risk of bias' table.

When considering treatment effects, we took into account risk of bias for studies that contribute to that outcome.

Assessment of bias in conducting the systematic review

We conducted the review according to our published protocol and planned to justify any deviations from it in the Differences between protocol and review section. There was no need to deviate from the protocol (Slinger 2018).

Measures of treatment effect

We analysed dichotomous data as odds ratios (ORs) and continuous data as mean differences (MDs) or geometric MDs. We planned that if data from rating scales were combined in a meta-analysis, we would ensure that they were entered with a consistent direction of effect (e.g. lower scores always indicate improvement). The paucity of data meeting our inclusion criteria precluded further consideration of this issue.

We planned to conduct meta-analyses only when meaningful, that is when treatments, participants, and the underlying clinical question were similar enough for pooling to make sense. Unfortunately, there was no opportunity for aggregation.

We planned to describe skewed data narratively (e.g. as medians and interquartile ranges for each group).

Had multiple trial arms been reported in a single study, we would have included only the relevant arms. All of the trials meeting our inclusion criteria were two-arm studies. In the protocol for this review we stated that "If two comparisons (e.g. intervention A vs usual care and intervention B vs usual care) are combined in the same meta-analysis, we will either combine the active arms or halve the control group to avoid double-counting"; however, this was not an issue with the available data.

Where adjusted analyses were available (analysis of variance (ANOVA) or analysis of covariance (ANCOVA)), we used these as a preference in our meta-analyses. Where both change from baseline and endpoint scores were available for continuous data, we used change from baseline. We planned to avoid doing so in the event of low correlation between measurements in individuals, and there was no apparent indication of this issue. We planned that where a study reported outcomes at multiple time points, we would use change in baseline and endpoint scores.

When both per-protocol/completer and intention-to-treat (ITT) analyses were provided in a single report, we used the latter.

Unit of analysis issues

For dichotomous outcomes, we used participants, rather than events, as the unit of analysis (e.g. number of people experiencing an adverse event, rather than number of adverse events per person). However, we planned that if rate ratios had been reported in a study, we would analyse them accordingly; this was not an issue with the included studies. We planned to meta-analyse data from cluster-RCTs only if available data had been adjusted (or could be adjusted) to account for the clustering. Again, this was not an issue with our included studies.

Dealing with missing data

We contacted the investigators of the included studies to verify key study characteristics and for additional clarifications.

Assessment of heterogeneity

We planned to use the I^2 statistic to measure heterogeneity among the studies in each analysis. Had we identified substantial heterogeneity, we would have reported this and explored possible causes by performing prespecified subgroup analysis. However, there was no opportunity for aggregation.

Assessment of reporting biases

We planned that if we had been able to pool more than 10 studies, we would create and examine a funnel plot to explore possible small-study and publication biases. However, there were insufficient studies meeting our inclusion criteria to pursue this aim.

Data synthesis

We used a random-effects model and planned to perform a sensitivity analysis with a fixed-effect model if necessary.

'Summary of findings' table

We created a 'Summary of findings' table using the following outcomes.

Primary outcomes

1. Health-related quality of life (assessed with a validated measure)
2. Serious adverse events

Secondary outcomes

1. Symptoms
2. Clinical improvement (as defined by trialists)
3. Subjective measures of cough (e.g. VAS/numerical cough score)
4. Cough reflex sensitivity (as measured by cough challenge)
5. Objective cough counts
6. Adverse events/side effects

Reporting in the study of one or more of the outcomes listed here was not an inclusion criterion for the review.

We used the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it relates to studies that contribute data for the prespecified outcomes. We used the methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), employing GRADEpro software (GRADEpro GDT). We justified all decisions to downgrade the quality of studies using footnotes, and included comments to aid the reader's understanding of the review when necessary.

Subgroup analysis and investigation of heterogeneity

We planned to carry out the following subgroup analyses on our two primary outcomes (health-related quality of life and serious adverse events). However, this was not possible due to the paucity of data.

1. Number of sessions of SLT (one to three sessions versus four to six sessions versus seven or more sessions).
2. Speech and language therapist-delivered intervention versus intervention delivered by other healthcare professionals.

We planned to use the formal test for subgroup interactions in Review Manager 5 (RevMan 2014).

Sensitivity analysis

We planned to conduct sensitivity analyses by removing studies when the method of randomisation was judged as unclear or high in the 'Risk of bias' assessment. We also planned to conduct sensitivity analyses by removing studies with an active control arm. Furthermore, we planned to compare the results from a fixed-effect model with those from the random-effects model. However, this was not possible due to the paucity of data.

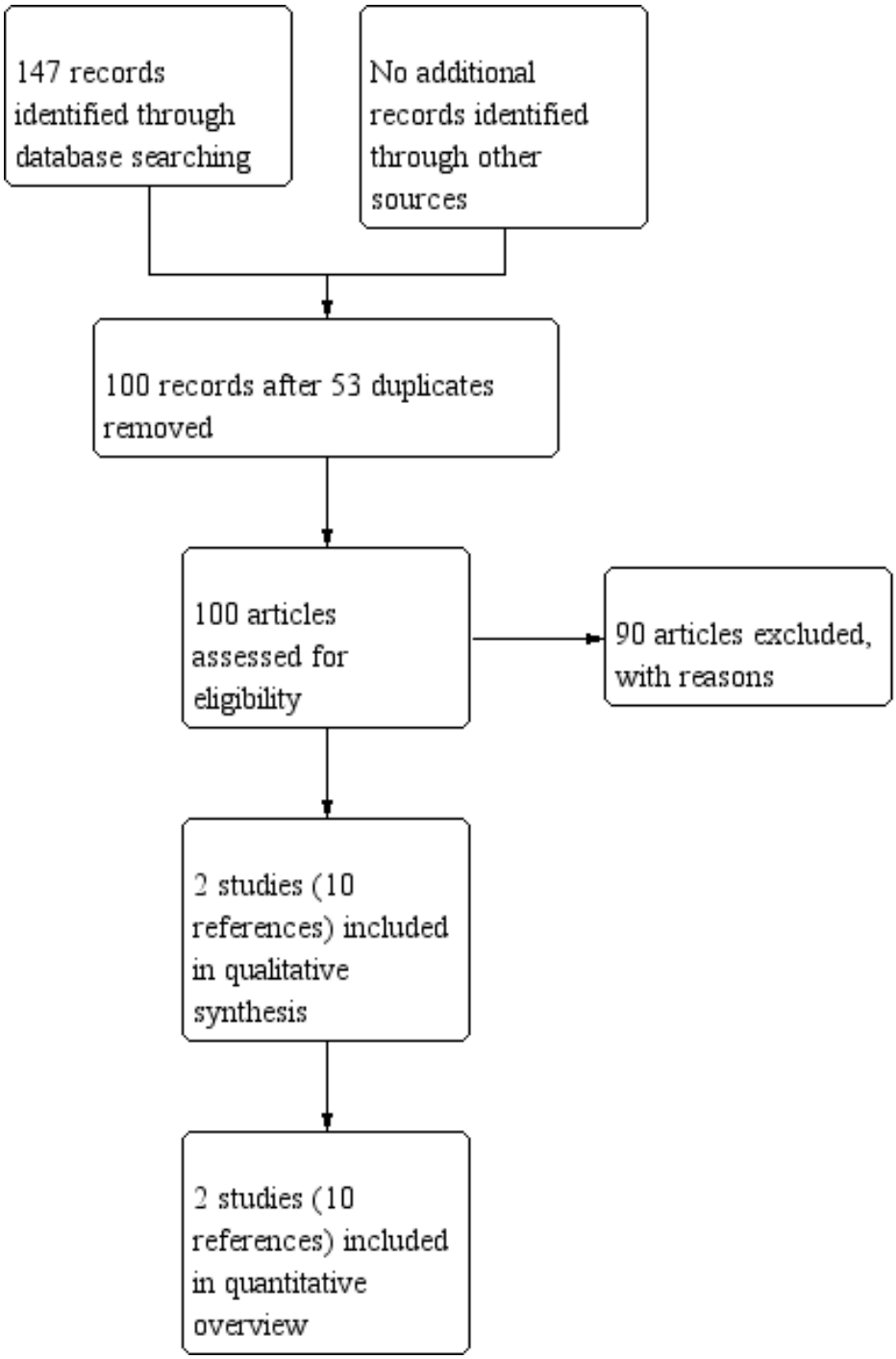
RESULTS

Description of studies

Results of the search

We retrieved 141 references from the literature searches conducted on 9 July 2018. We assessed 94 references after removal of duplicate records (see study flow diagram in Figure 1).

Figure 1. Study flow diagram.



On 8 February 2019 we identified a further six references, with no duplicates. In total we therefore assessed 100 references (see Figure 1).

Included studies

We included two trials with a total of 162 randomised participants. One study was conducted across multiple sites in the UK (Chamberlain Mitchell 2017), and another in Newcastle, Australia (Vertigan 2006). Further clarification on the included studies was requested and received from authors.

Populations

In Vertigan 2006, participants were eligible if cough was persistent for more than two months following medical treatment including treatment for asthma, postnasal drip syndrome, gastro-oesophageal reflux, and withdrawal of angiotensin-converting enzyme inhibitors. The participants underwent thorough respiratory history, hypertonic saline challenge, and induced sputum analysis before inclusion in the study. The study included a total 87 participants, randomised to placebo group (n = 44) and treatment group (n = 43).

The eligibility criteria in Chamberlain Mitchell 2017 included chronic cough (duration of more than two months) with normal chest x-ray, minimal sputum production, and negative and/or failed treatments for asthma, gastro-oesophageal reflux disease, and rhinitis. Patients were excluded if they had vocal cord nodules, evidence of aspiration or malignancy. There were 75 eligible participants who were randomised to control group (n = 41) and physiotherapy and speech and language therapy intervention (PSALTI) group (n = 34).

Interventions

The intervention therapies used in the two included studies had differing titles: Speech Pathology Evaluation and Intervention for CHronic Cough (SPEICH-C) in Vertigan 2006 and PSALTI in Chamberlain Mitchell 2017. However, the content was very similar, comprising four one-to-one sessions of laryngeal hygiene and hydration, cough suppression techniques, and psychoeducational counselling around volitional control and the concept of the idiopathic nature of cough. Both studies used healthy lifestyle advice as a control therapy with a focus on exercise, physical activity, diet and nutritional advice, and stress management.

In one study, both the intervention and control therapies were delivered purely by a speech and language therapist (Vertigan 2006). The other study delivered intervention therapy by either a physiotherapist or speech and language therapist, and the control therapy by a physiotherapist, speech and language therapist, or nurse (Chamberlain Mitchell 2017).

The duration of treatment and length of sessions varied between studies, from four sessions delivered weekly in Chamberlain Mitchell 2017 to four sessions over two months in Vertigan 2006. Similarly, length of sessions varied slightly, from one 1-hour session and three 45-minute sessions in Chamberlain Mitchell 2017 to four 30-minute sessions in Vertigan 2006.

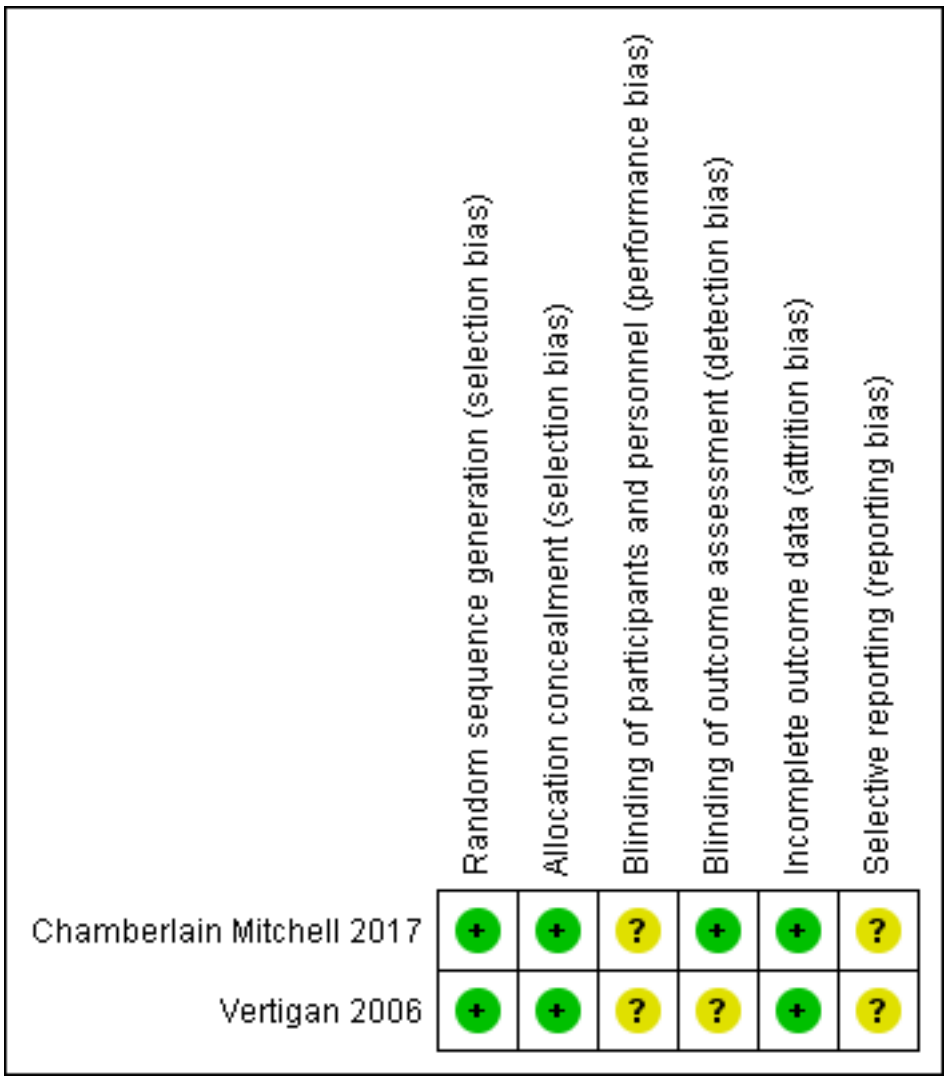
Excluded studies

We excluded 90 records, with reasons given in the Characteristics of excluded studies tables. A study flow diagram is shown in Figure 1. The primary reason for exclusion was: 59 (65%) were not relevant to people with a diagnosis of UCC; 13 (14%) were reviews; eight (9%) were not randomised studies; one (1%) did not include an SLT intervention; one (1%) was an editorial; and one (1%) was a comparison between pregabalin in addition to speech pathology versus speech pathology alone. An additional trial considered the benefit of adding video recordings of speech therapy techniques, demonstrated by a speech pathologist, to support participants' development of the technique for chronic refractory cough (1%).

Risk of bias in included studies

A full 'Risk of bias' assessment for each study can be found in the Characteristics of included studies tables, and a summary of our judgements in Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

We assessed Chamberlain Mitchell 2017 and Vertigan 2006 as at low risk of bias for random sequence generation and allocation concealment.

Blinding

We judged Chamberlain Mitchell 2017 and Vertigan 2006 as at unclear risk of performance bias. We assessed Chamberlain Mitchell 2017 as at low risk and Vertigan 2006 as at unclear risk of detection bias. Our judgments of unclear risk of bias reflect our uncertainty in relation to reporting.

Incomplete outcome data

We assessed Chamberlain Mitchell 2017 and Vertigan 2006 as at low risk of attrition bias.

Selective reporting

We judged Chamberlain Mitchell 2017 and Vertigan 2006 as at unclear risk of reporting bias. As in the assessments of blinding, our judgments of unclear risk of bias reflect our uncertainty in relation to reporting, as we did not have access to trial protocols.

Effects of interventions

See: **Summary of findings for the main comparison** Speech and language therapy compared with healthy lifestyle advice for chronic cough

Primary outcomes

Health-related quality of life (HRQoL)

Only one study contributed data to this outcome, and using the GRADE approach we judged the quality of evidence to be low (Summary of findings for the main comparison). Health-related quality of life was assessed by Chamberlain Mitchell 2017 with the Leicester Cough Questionnaire (LCQ). Data were analysed using ANCOVA and reported as between-group difference from baseline to four weeks (mean difference (MD) 1.53, 95% confidence interval (CI) 0.21 to 2.85; participants = 71; studies = 1; Analysis 1.1), revealing a statistically significant benefit for PSALTI versus control. This difference is also clinically significant as it exceeds the minimum clinically important difference (MCID) of 1.3 in chronic cough (Raj 2009). Our analysis focused on the 71 ITT population participants (of the total 75 entering the study). This statistically significant difference for PSALTI versus control was not maintained between four weeks and three-month follow-up.
There were no differences between the two groups from baseline to four weeks on general health and mood assessments, that is the 36-item Short Form Health Survey (SF-36) and Hospital Anxiety and Depression Scale (HADS) scores.
We did not attempt subgroup analyses due to the paucity of the data.

Serious adverse events

Vertigan 2006 did not report serious adverse events. Chamberlain Mitchell 2017 reported that there were no serious adverse events in either the PSALTI or control arms of the study (Analysis 1.2). We judged the quality of the evidence to be low using the GRADE approach (Summary of findings for the main comparison).

Secondary outcomes

Objective cough counts

Cough frequency per hour over a 24-hour period was measured by Chamberlain Mitchell 2017. This was analysed as geometric means, which compare the ratio of mean cough counts per hour on treatment to control. The Leicester Cough Monitor (LCM) is a validated, objective, semi-automated, and ambulatory cough-monitoring device that was used in this study to assess objective cough frequency (Birring 2008). The device was worn by participants for 24 hours at baseline, at 4 weeks (after the fourth treatment session), and at 3-month follow-up; in each of these sessions the device recorded the number of coughs per hour. The effect estimate favoured PSALTI (versus control), which was associated with a ratio of cough counts per hour of 59% (95% CI 37% to 95%; participants = 71; studies = 1; Analysis 1.3) of cough counts per hour on control. We judged the quality of this evidence to be low using the GRADE approach (Summary of findings for the main comparison). This statistically significant difference for PSALTI versus control was not maintained between four weeks and three-month follow-up.

Symptoms

Vertigan 2006 reported a significant benefit for the SLT intervention (SPEICH-C) versus control for change in total symptoms scores over the four treatment sessions (MD 9.80, 95% CI 4.50 to 15.10; participants = 87; studies = 1; Analysis 1.4). We are aware that these data are skewed, and were analysed with non-parametric methods by Vertigan 2006. In the non-parametric analysis there was a significant difference between groups, favouring SPEICH-C versus control. We judged the quality of the evidence to be low using the GRADE approach (Summary of findings for the main comparison).

Clinical improvement (as defined by trialists)

Vertigan 2006 demonstrated a significant improvement following SPEICH-C versus control for change in symptoms scores of breathing, cough, voice, upper airway, and limitation over the four treatment sessions (odds ratio (OR) 48.13, 95% CI 13.53 to 171.25; participants = 87; studies = 1; Analysis 1.5). Each participant's outcome was categorised by a speech and language therapist as successful, unsuccessful, or partially successful. The assessment was based on the participant's informal reports of the effectiveness of the intervention together with the speech and language therapist's clinical judgement of the participant's understanding and implementation of the intervention. Thirty-eight out 43 participants in the SPEICH-C group were regarded as having a successful outcome in relation to these criteria, whereas only six out of 44 participants in the control group were judged to have a successful outcome. Using the GRADE criteria, we judged the quality of this evidence as very low (Summary of findings for the main comparison).
Chamberlain Mitchell 2017 found no differences between groups with respect to a vocal performance questionnaire from baseline to four weeks.

Subjective measures of cough (e.g. visual analogue scale (VAS)/numerical cough scale score)

Only one study contributed data to this outcome, and we judged the quality of the evidence as low using the GRADE approach (Summary of findings for the main comparison). Cough severity, measured on a VAS (ranging from 0 to 100 mm, with higher scores denoting higher severity) (Boulet 2015), was reported by Chamberlain Mitchell 2017 (MD −9.72, 95% CI −20.80 to 1.36; participants = 71; studies = 1; Analysis 1.6). The mean difference favoured the intervention, but the result is uncertain as the confidence interval includes the possibility of no difference between groups. Similarly, there was no difference for PSALTI versus control between four weeks and three-month follow-up.

Cough reflex sensitivity (as measured by cough challenge)

There was no significant difference between PSALTI and control in the capsaicin cough challenge for either the two or five cough thresholds (capsaicin concentration to induce five coughs: 1.11 (95% CI 0.80 to 1.54) times higher on treatment than on control; participants = 49; studies = 1; Analysis 1.7) (Chamberlain Mitchell 2017). We judged the quality of the evidence to be low using the GRADE approach (Summary of findings for the main comparison).

Adverse events/side effects

Adverse events were not reported by Vertigan 2006. Chamberlain Mitchell 2017 reported no adverse events in either the PSALTI or control conditions (Analysis 1.8). We judged the quality of this evidence as low using the GRADE approach (Summary of findings for the main comparison).

DISCUSSION

Summary of main results

Overall there was a paucity of controlled trial data. We found only two randomised trials that met our inclusion criteria (Chamberlain Mitchell 2017; Vertigan 2006). Both were undertaken in adults with UCC and examined the effect of an intervention versus healthy lifestyle advice. Chamberlain Mitchell 2017 (conducted in the UK) examined the effect of a physiotherapy and speech and language therapy intervention (PSALTI) on HRQoL and measures of cough. Vertigan 2006 (conducted in Australia) studied the effect of a speech therapy intervention (SPEICH-C) on symptom scores.

There was a significant improvement in HRQoL (LCQ) scores at four weeks, but not between four weeks and three months; however, these data were from one study only (Chamberlain Mitchell 2017), as this outcome was not included in Vertigan 2006. No serious adverse events were reported, however information on this outcome was not specifically stated in one of the trials (Vertigan 2006).

We found statistically significant improvements in 24-hour cough frequency at four weeks when comparing PSALTI to control, but this difference was not maintained between four weeks and three months. The effect of PSALTI on subjective measures of cough was uncertain with no statistically significant difference in cough severity measured on a VAS, although the mean difference favoured the intervention. These data were from only one study (Chamberlain Mitchell 2017).

We found statistically significant improvements in symptom scores following the SLT intervention in Vertigan 2006..

Overall completeness and applicability of evidence

Due to the absence of common outcomes in the two studies, opportunities for statistical aggregation did not arise, and consequently, whilst the results are encouraging, the paucity of evidence precludes us from drawing robust conclusions to guide clinical practice.

Only two studies with modest sample sizes met our inclusion criteria. They were both conducted in high-income settings, therefore the global applicability of the evidence is limited. Moreover, the two studies used different outcomes, precluding direct statistical aggregation. The interventions were based either on SLT, Vertigan 2006, or SLT and physiotherapy combined (Chamberlain Mitchell 2017). Both studies appeared to employ similar treatment approaches, as first described by Vertigan 2006. In Chamberlain Mitchell 2017, the Active Cycle of Breathing Technique (ACBT) was introduced if the participant's sputum production was close to the limit of sputum exclusion criteria, and nasal douche for nasal mucus hypersecretion. The benefit of physiotherapy techniques in addition to SLT techniques was not investigated in Chamberlain Mitchell 2017, hence it is not possible to draw conclusions on the relative positive contribution of discipline-specific interventions (Smith 2017).

Quality of the evidence

The overall quality of the evidence presented in this review is low for seven of the eight outcomes included in the GRADE assessment; the quality of the evidence from the remaining outcome 'clinical improvement (as defined by trialists)' was judged as very low when assessed by the GRADE criteria. However, only two studies met our inclusion criteria. Both studies described methods of randomisation, and these were similar. The control and intervention arms for the two studies were comparable and clearly defined, although one study had a two-month intervention arm with no long-term outcome data (Vertigan 2006), and the other study had a four-week intervention arm with four-week

and three-month postintervention outcome data (Chamberlain Mitchell 2017). One study used the treating speech therapist's judgement on clinical outcome and symptom scores (Vertigan 2006), whilst the other study used a validated questionnaire, interval cough monitoring, and VAS to assess the effect of the intervention (Chamberlain Mitchell 2017). The latter study also undertook general health and mood assessments using the SF-36 and HADS. The two studies also used different primary and secondary endpoints. The variance in data collection and analysis meant it was not possible to statistically combine the two studies for any outcome. The quality of the evidence was limited critically by the lack of studies meeting our inclusion criteria, and of those that did meet our inclusion criteria, by the lack of consistency in data collection methodology, duration of follow-up, and primary and secondary endpoints analysed.

The two included studies by Vertigan 2006 and Chamberlain Mitchell 2017 were single-blinded, and symptom ratings were blinded. It was not possible to blind the treating therapist, and there is inevitably the possibility of unconscious bias having been conveyed to the participants; this is not a criticism of these well-conducted studies, but a feature of the interventions, introducing concomitant uncertainty in this regard.

In our GRADE assessment we deducted one point to reflect the study question, which precluded the opportunity to double-blind, and an additional point to reflect imprecision (data from a single study with modest sample size); this was applied to all outcomes considered in the Summary of findings for the main comparison. We deducted a further point for the outcome 'clinical improvement (as defined by trialists)' to reflect that the judgement of efficacy on this outcome was made against criteria defined by the trialists.

Potential biases in the review process

We recognise that there is the possibility of publication bias, which could influence our understanding of the effects of the interventions reported in this review. Studies demonstrating an absent or negative effect of the proposed intervention are less likely to have been presented or accepted for publication. Subsequently, data that are made available for review could, as a result, be biased. Due to the small number of trials included in the review, it was not possible to assess the significance of publication bias formally. However, potentially eligible studies were identified using a robust, systematic search process conducted by experienced specialists using multiple sources including journals, conference publications, electronic databases, reference and citation lists of included studies, and trial registries. It is possible that some studies may have been inaccurately classified as not eligible for inclusion in the review. Due to the small number of studies included, we did not perform a sensitivity analysis to explore the impact of excluding studies that did not meet agreed criteria. Any studies excluded from analysis were done so on the basis of agreed and consistent criteria. There is the potential for errors to occur in data entry for some full-text reports; however, we took measures to double-check all data in an attempt to avoid this during data extraction. All papers included in the review process were independently assessed by two review authors, with data corroborated by a third review author. Owing to the variability in outcomes reported across the included studies, we were unable to statistically combine the overall findings. However, we contacted the chief authors of the included studies, and both were willing and able to provide further clarity on their methodology and interpretation of data. We therefore feel that we have taken thorough measures to minimise risk of bias in this review, and are confident in the merit of outcomes individually reported in the included studies.

Agreements and disagreements with other studies or reviews

We are aware of reviews of chronic cough in the literature that assess diagnosis and management, but they differ in primary objectives and methodologies used. Vertigan 2007 reviews behaviour modification therapies in chronic cough using systematic reviews and case studies to explain the main constructs required to deliver effective non-pharmacological therapies to treat chronic cough. The components of cough suppression therapy are further reviewed by Chamberlain 2013. Each of the four therapy components are reviewed individually and the evidence base considered to provide a structure for the speech and language therapist/respiratory physiotherapist to use to support patient outcome. Ryan 2014 reviewed the treatment of refractory chronic cough with speech and language therapy and gabapentin via RCTs, systematic reviews, and case reports in English publications eight years prior to their paper, concluding that behavioural treatment and pharmacological neuromodulation have a role. Chronic cough can arise due to known respiratory as well as non-respiratory pathology. Molassiotis 2010 undertook a systematic review in adults including RCTs and controlled trials to evaluate the effectiveness of pharmacological and non-pharmacological interventions in the relief of chronic cough excluding malignant disease. Guidelines for the diagnosis and treatment of chronic cough were published in *Chest* (Gibson 2016), using the best available evidence from RCTs and systematic reviews. Eleven RCTs were included, but only one looked at non-pharmacological intervention as the major component of the study. The Chamberlain Mitchell 2017 RCT postdated all these review articles, and its impact on UCC is not assessed. A further review included all studies examining non-pharmacological treatments in UCC focusing on potential mechanisms and the effects of treatment (Chamberlain Mitchell 2019).

There is a paucity of evidence in this area with regard to outcomes of speech and language therapy in the management of chronic cough. The RCTs that do exist use similar methodologies of treatment, but interstudy data analysis is not possible due to the absence of common outcome measures.

It is important to note that Vertigan 2016, although not meeting the inclusion criteria for this review, found that SLT, when combined with the neuromodulator pregabalin, led to a significantly greater improvement in participants' perceived cough severity and cough-related quality of life, when compared to SLT alone. This combination of SLT and pregabalin was also found to improve cough sensitivity. This benefit was sustained after treatment withdrawal. However, due to observed adverse effects of pregabalin, the authors state that this multimodal treatment should be reserved for those with more severe end spectrum cough symptoms. Further studies to help understand who may benefit from combined pharmacological and non-pharmacological approaches, and the timing of each component, may help inform clinical practice further. This study is of clinical interest to professionals working with people with UCC, although data from this single trial would need to be confirmed in subsequent research to provide us with robust evidence to guide clinical practice.

AUTHORS' CONCLUSIONS

Implications for practice

We found only two trials meeting our inclusion criteria, which included a combined total of 162 randomised adult participants. Neither of the studies included children.

We identified positive effects in one study of speech and language therapy (SLT)-based approaches, in combination with physiotherapy, for our predefined primary outcome of health-related quality of life (HRQoL). No adverse events were reported (Chamberlain Mitchell 2017).

However, the between-group benefits of the intervention with regard to HRQoL in Chamberlain Mitchell 2017 were found to be short-lived, and this finding needs to be interpreted with caution when applying it to clinical practice. Vertigan 2006 did not report data on HRQoL.

Further high-quality studies with comparable endpoints are needed to inform robust conclusions and guide clinical practice.

Implications for research

The paucity of data in this review highlights the need for more randomised controlled trial data examining the efficacy of SLT in the management of UCC. This review highlights that endpoints vary between the included studies.

The improvements in HRQoL (Leicester Cough Questionnaire) and reduction in 24-hour cough frequency seen with the physiotherapy and speech and language therapy intervention (PSALTI) were statistically significant but short-lived, with the effect lasting up to 4 weeks only between PSALTI and control groups. Further studies examining SLT intervention in UCC are required to replicate these findings and to investigate the effects of the interventions over time. It is clear that SLT interventions vary between studies. Further research is needed to understand which aspects of the SLT intervention are most effective in reducing cough (both objective cough frequency and subjective measures of cough) and improving HRQoL. We consider these endpoints to be important clinically. It is also important for studies to report any adverse events that occur. Further studies could be designed to understand the essential components of the intervention (Smith 2017).

Further research is needed to investigate whether the results of this review are applicable across cultures and along the age spectrum.

ACKNOWLEDGEMENTS

Rebecca Fortescue was the Editor for this review and commented critically on the review.

We are especially grateful to Emma Dennett, Liz Stovold, and Emma Jackson of Cochrane Airways, and to Rebecca Normansell and Chris Cates (Cochrane Airways Co-ordinating Editors) for the additional guidance provided. We are also particularly grateful to Anne Vertigan and Sarah Chamberlain-Mitchell for their invaluable assistance in providing additional clarification on their studies and confirming that they know of no additional studies that would meet our inclusion criteria.

We are grateful also to Richard Slinger for draft and proof reading of this review.

The Background and Methods sections of this protocol are based on a standard template used by Cochrane Airways.

This project was supported by the National Institute for Health Research (NIHR) via Cochrane Infrastructure funding to Cochrane Airways. The views and opinions expressed therein are those of the review authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS, or the Department of Health.

REFERENCES

References to studies included in this review

Chamberlain Mitchell 2017 *{published data only}*

* Chamberlain Mitchell SAF, Garrod R, Clark L, Douiri A, Parker SM, Ellis J, et al. Physiotherapy, and speech and language therapy intervention for patients with refractory chronic cough: a multicentre randomised control trial. *Thorax* 2017;**72**(2):129–36.

Chamberlain Mitchell SAF, Garrod R, Clarke L, Douiri A, Hull J, Chung KF, et al. Breathing pattern changes in refractory chronic cough with physiotherapy speech and language therapy intervention. *European Respiratory Journal* 2016;**48**(Suppl 60):PA1375.

Chamberlain SAF, Birring SS, Clarke L, Douiri A, Pandyan A, Garrod R. Efficacy of a physiotherapy, speech and language therapy intervention (PSALTI) for patients with refractory chronic cough: a multi-centred RCT. *Physiotherapy* 2015;**101**(Suppl 1):eS206–7.

Chamberlain SAF, Birring SS, Clarke L, Douiri A, Parker SM, Fowler SJ, et al. Efficacy of a physiotherapy, speech and language therapy intervention (PSALTI) on health related quality of life (HRQOL) for patients with refractory chronic cough: a randomised control trial. *Thorax* 2014;**69** (Suppl 2):A78.

ISRCTN73039760. Efficacy of a physiotherapy, speech and language therapy intervention (PSALTI) for patients with chronic cough: a randomised controlled trial. www.isrctn.com/ISRCTN73039760 (first received 29 July 2011).

Maselli DJ, Peters JI. In refractory chronic cough, physiotherapy plus speech and language therapy improved quality of life at 4 weeks. *Annals of Internal Medicine* 2017; **166**(2):JC3.

Vertigan 2006 *{published data only}*

Gibson PG, Vertigan AE. Speech pathology for chronic cough: a new approach. *Pulmonary Pharmacology and Therapeutics* 2009;**22**(2):159–62.

Vertigan A, Theodoros D, Gibson P, Winkworth A. Efficacy of speech pathology treatment for refractory chronic cough. *Respirology* 2006;**11**(Suppl 2):74.

* Vertigan AE, Theodoros DG, Gibson PG, Winkworth AL. Efficacy of speech pathology management for chronic cough: a randomised placebo controlled trial of treatment efficacy. *Thorax* 2006;**61**(12):1065–9.

Vertigan AE, Theodoros DG, Winkworth AL, Gibson PG. A comparison of two approaches to the treatment of chronic cough: perceptual, acoustic, and electroglottographic outcomes. *Journal of Voice* 2008;**22**(5):581–9.

References to studies excluded from this review

Ackerstaff 1995 *{published data only}*

Ackerstaff AH, Hilgers FJM, Aaronson NK, De Boer MF, Meeuwis CA, Knegt PPM, et al. Heat and moisture exchangers as a treatment option in the post-operative rehabilitation of laryngectomized patients. *Clinical Otolaryngology and Allied Sciences* 1995;**20**(6):504–9.

Al-Riyami 2001 *{published data only}*

Al-Riyami BMS, Al-Rawas OAS, Al-Riyami AA, Jasim LG, Mohammed AJ. Prevalence of asthma symptoms in Omani schoolchildren. *Sultan Qaboos University Medical Journal* 2001;**3**(1):21–7.

Bemanin 2015 *{published data only}*

Bemanin MH, Fallahpour M, Arshi S, Nabavi M, Yousofi T, Shariatifar A. First report of asthma prevalence in Afghanistan using international standardized methods. *Eastern Mediterranean Health Journal* 2015;**21**(3):194–8.

Benninger 2011 *{published data only}*

Benninger C, Parsons JP, Mastronarde JG. Vocal cord dysfunction and asthma. *Current Opinion in Pulmonary Medicine* 2011;**17**(1):45–9.

Birring 2017 *{published data only}*

Birring SS, Floyd S, Reilly CC, Cho PSP. Physiotherapy and speech and language therapy intervention for chronic cough. *Pulmonary Pharmacology and Therapeutics* 2017;**47**: 84–7.

Biswas 2015 *{published data only}*

Biswas M, Ades AE, Hamilton W. Symptom lead times in lung and colorectal cancers: what are the benefits of symptom-based approaches to early diagnosis?. *British Journal of Cancer* 2015;**112**(2):271–7.

Brady 2018 *{published data only}*

Brady GC, Roe JWG, O' Brien M, Boaz A, Shaw C. An investigation of the prevalence of swallowing difficulties and impact on quality of life in patients with advanced lung cancer. *Supportive Care in Cancer* 2018;**26**(2):515–9.

Cacciari 2017 *{published data only}*

Cacciari L, Morin M, Dumoulin C. Association between digital assessment (flexibility and strength) and ultrasound morphometric parameters of the pelvic floor. www.ics.org/2017/abstract/741 (accessed prior to 2 October 2018).

Carmel 2016 *{published data only}*

Carmel ME, Deng DY, Greenwell TJ, Zimmern PE. Definition of success after surgery for female stress incontinence or voiding dysfunction: an attempt at standardization. *European Urology Focus* 2016;**2**(3):231–7.

Chamberlain 2013 *{published data only}*

Chamberlain S, Garrod R, Birring SS. Cough suppression therapy: does it work?. *Pulmonary Pharmacology and Therapeutics* 2013;**26**(5):524–7.

Cholera 2016 *{published data only}*

Cholera M, Chainani-Wu N. Management of pemphigus vulgaris. *Advances in Therapy* 2016;**33**:910–58.

Dart 2003 *{published data only}*

Dart RA, Gollub S, Lazar J, Nair C, Schroeder D, Woolf SH. Treatment of systemic hypertension in patients with pulmonary disease: COPD and asthma. *Chest* 2003;**123** (1):222–43.

Faria 2014 *{published data only}*
Faria J, Behar P. Medical and surgical management of congenital laryngomalacia: a case-control study. *Otolaryngology* 2014;**151**(5):845–51.

Fernandez 2015 *{published data only}*
Fernandez G, Dunn S, Nieves C, Melhado K, Lehr G, Pomerantz S, et al. Predictors of postextubation dysphagia in nonstroke patients. *Chest* 2015;**148**(4):P243A.

Finck 2006 *{published data only}*
Finck C. Laryngeal dysfunction after thyroid surgery: diagnosis, evaluation and treatment. *Acta Chirurgica Belgica* 2006;**106**(4):378–87.

Gibson 2014 *{published data only}*
Gibson P. Laryngeal botoxification for severe asthma. *Respirology* 2014;**19**(4):467–8.

Gibson 2015 *{published data only}*
Gibson PG, Vertigan AE. Gabapentin in chronic cough. *Pulmonary Pharmacology and Therapeutics* 2015;**35**:145–8.

Gibson 2016 *{published data only}*
Gibson PG, Wang G, McGarvey L, Vertigan AE, Altman KW, Birring SS, et al. Treatment of unexplained chronic cough: CHEST guideline and Expert Panel Report. *Chest* 2016;**149**(1):27–44.

Goldstein 2007 *{published data only}*
Goldstein R, Bright J, Jones SM, Niven RM. Severe vocal cord dysfunction resistant to all current therapeutic interventions. *Respiratory Medicine* 2007;**101**(4):857–8.

Good 2018 *{published data only}*
Good JT, Rollins DR, Kolakowski CA, Stevens AD, Denson JL, Martin RJ. New insights in the diagnosis of chronic refractory cough. *Respiratory Medicine* 2018;**141**:103–10.

Harvey 2018 *{published data only}*
Harvey PR, Theron BT, Trudgill NJ. Managing a patient with globus pharyngeus. *Frontline Gastroenterology* 2018;**9**: 208–12.

Hertegard 2002 *{published data only}*
Hertegard S, Hallen L, Laurent C, Lindstrom E, Olofsson K, Testad P, et al. Cross-linked hyaluronan used as augmentation substance for treatment of glottal insufficiency: safety aspects and vocal fold function. *Laryngoscope* 2002;**112**(12):2211–9.

Hilgers 1996 *{published data only}*
Hilgers FJM, Ackerstaff AH, Balm AJM, Gregor RT. A new heat and moisture exchanger with speech valve (Provox stomafilter). *Clinical Otolaryngology and Allied Sciences* 1996;**21**(5):414–8.

Hilgers 2003 *{published data only}*
Hilgers FJ, Ackerstaff AH, Van As CJ, Balm AJ, Van den Brekel MW, Tan IB. Development and clinical assessment of a heat and moisture exchanger with a multi-magnet automatic tracheostoma valve (Provox FreeHands HME) for vocal and pulmonary rehabilitation after total laryngectomy. *Acta Oto-Laryngologica* 2003;**123**(1):91–9.

Hull 2005 *{published data only}*
Hull EM, Dumas HM, Crowley RA, Kharasch VS. Tracheostomy speaking valves for children: tolerance and clinical benefits. *Pediatric Rehabilitation* 2005;**8**(3):214–9.

Hunter 2011 *{published data only}*
Hunter KU, Lyden T, Haxer M, Feng FY, Chepeha D, Eisbruch A. What is the clinical relevance of objective swallow studies in head and neck cancer (HNC) patients receiving chemoirradiation (CRT)? Analysis of aspiration in swallow studies vs. risk of aspiration pneumonia. *International Journal of Radiation* 2011;**81**(2 Suppl 1):S174.

Ihalainen 2015 *{published data only}*
Ihalainen T, Rinta-Kiikka I, Ronkainen A, Korpijaakko-Huuhka AM. The incidence of aspiration or penetration in patients with traumatic cervical spinal cord injury (CSCI): a prospective study with twenty subjects. *Dysphagia* 2015;**30** (2):255.

Irons 2010 *{published data only}*
Irons JY, Kenny DT, Chang AB. Singing for children and adults with bronchiectasis. *Cochrane Database of Systematic Reviews* 2010, Issue 2. DOI: 10.1002/ 14651858.CD007729.pub2

Irwin 2010 *{published data only}*
Irwin RS. Unexplained cough in the adult. *Otolaryngologic Clinics of North America* 2010;**43**(1):167-80, xi-xii.

Jensen 2013 *{published data only}*
Jensen JB, Rasmussen N. Phonosurgery of vocal fold polyps, cysts and nodules is beneficial. *Danish Medical Journal* 2013;**60**(2):A4577.

Kapela 2019 *{published data only}*
Kapela SL, Vertigan AE, Gibson PG. Speech pathology intervention for chronic refractory cough: a pilot study examining the benefit of using prerecorded videos as an adjunct to therapy. *Journal of Voice* 2019;**33**:S0892–1997.

Kew 2017 *{published data only}*
Kew KM, Malik P, Aniruddhan K, Normansell R. Shared decision-making for people with asthma. *Cochrane Database of Systematic Reviews* 2017, Issue 10. DOI: 10.1002/ 14651858.CD012330.pub2

Killoran 2012 *{published data only}*
Killoran A, Biglan KM. Therapeutics in Huntington's disease. *Current Treatment Options in Neurology* 2012;**14** (2):137–49.

Kyriakou 2018 *{published data only}*
Kyriakou K, Petinou K, Phinikettos I. Risk factors for voice disorders in university professors in Cyprus. *Journal of Voice* 2018;**32**(5):643.e1–9.

Lukrafka 2010 *{published data only}*
Lukrafka JL, Fuchs SC, Moreira LB, Picon RV, Fischer GB, Fuchs FD. Performance of the ISAAC questionnaire to establish the prevalence of asthma in adolescents: a population-based study. *Journal of Asthma* 2010;**47**(2): 166–9.

Marques 2015 *{published data only}*
Marques SA, Silveira SB, Haddad JM, Passaro AC, Edmund BC, Ferreira EA. Effect of pelvic floor and hip muscle strengthening in the treatment of stress urinary incontinence: randomized blind clinical trial. *International Urogynecology Journal and Pelvic Floor Dysfunction* 2015;**26** (1 Suppl 1):S141–2.

McGarvey 2013 *{published data only}*
McGarvey L. The difficult-to-treat, therapy-resistant cough: why are current cough treatments not working and what can we do?. *Pulmonary Pharmacology and Therapeutics* 2013;**26** (5):528–31.

Mellor 1998 *{published data only}*
Mellor DJ, Mellor AH, McAteer EM. Local anaesthetic infiltration for surgical exodontia of third molar teeth: a double-blind study comparing bupivacaine infiltration with i.v. ketorolac. *British Journal of Anaesthesia* 1998;**81**(4): 511–4.

Mesia 2010 *{published data only}*
Mesia R, Rivera F, Kawecki A, Rottey S, Hitt R, Kienzer H, et al. Quality of life of patients receiving platinum-based chemotherapy plus cetuximab first line for recurrent and/or metastatic squamous cell carcinoma of the head and neck. *Annals of Oncology* 2010;**21**(10):1967–73.

Michaudet 2017 *{published data only}*
Michaudet C, Malaty J. Chronic cough: evaluation and management. *American Family Physician* 2017;**96**(9): 575–80.

Molassiotis 2010 *{published data only}*
Molassiotis A, Bryan G, Caress A, Bailey C, Smith J. Pharmacological and non-pharmacological interventions for cough in adults with respiratory and non-respiratory diseases: a systematic review of the literature. *Respiratory Medicine* 2010;**3**(4):934–44.

Morice 2017 *{published data only}*
Morice AH, Shanks G. Pharmacology of cough in palliative care. *Current Opinion in Supportive and Palliative Care* 2017;**11**(3):147–51.

NCT03457610 *{published data only}*
NCT03457610. Speech therapy in the management of chronic cough. clinicaltrials.gov/show/NCT03457610 (first received 7 March 2018).

Oner 2013 *{published data only}*
Oner O, Celik GE. Psychogenic cough. *Turk Toraks Dergisi* 2013;**14**(Suppl 3):24–6.

Oskam 2013 *{published data only}*
Oskam IM, Verdonck-De Leeuw IM, Aaronson NK, Witte BI, De Bree R, Doornaert P, et al. Prospective evaluation of health-related quality of life in long-term oral and oropharyngeal cancer survivors and the perceived need for supportive care. *Oral Oncology* 2013;**49**(5):443–8.

Park 2017 *{published data only}*
Park JS, Oh DH, Chang MY. Effect of expiratory muscle strength training on swallowing-related muscle strength in community-dwelling elderly individuals: a randomized controlled trial. *Gerodontology* 2017;**34**(1):121–8.

Patterson 2007 *{published data only}*
Patterson MC, Vecchio D, Prady H, Abel L, Wraith JE. Miglustat for treatment of Niemann-Pick C disease: a randomised controlled study. Lancet 2007; Vol. 6, issue 9: 765–72.

Perez 2011 *{published data only}*
Perez J, Guarderas JC, Pongdee T. Botox injections in larynx as a treatment for vocal cord dysfunction. *Annals of Allergy, Asthma and Immunology* 2011;**107**(5 Suppl 1):A59.

Perez 2012 *{published data only}*
Perez JE, Pongdee T, Guarderas J. Botox injections in larynx as a treatment for vocal cord dysfunction. *World Allergy Organization Journal* 2012;**5**(Suppl 2):S119.

Plowman 2016 *{published data only}*
Plowman E, Robison R, Tabor L, Wymer J. Impact of combined inspiratory-expiratory exercise on respiratory and Bulbar function in an individual with ALS. 27th International Symposium on ALS/MND; 2016 Dec 7-9; Dublin. 2016:279.

Pohl 2012 *{published data only}*
Pohl D, Tenembaum S. Treatment of acute disseminated encephalomyelitis. *Current Treatment Options in Neurology* 2012;**14**(3):264–75.

Raggi 2016 *{published data only}*
Raggi RR, Antenucci RA, Benvenuti MB, Ferrari GF, Cuda DC. Recovery of swallowing in two patients in post-acute phase with severe dysphagia from Wallemberg syndrome by combined use of conventional therapy, electro stimulator and IOPI device. 6th European Society for Swallowing Disorders Congress; Oct 14-15; Milan. 2016.

Reverberi 2019 *{published data only}*
Reverberi C, Lombardi F, Lusuardi M, Pratesi A, Di Bari M. Development of the decannulation prediction tool in patients with dysphagia after acquired brain injury. *Journal of the American Medical Directors Association* 2019;**20**(4): 470–75.e1.

Ryan 2009 *{published data only}*
Ryan NM, Gibson PG. Characterization of laryngeal dysfunction in chronic persistent cough. *Laryngoscope* 2009; **119**(4):640–5.

Ryan 2010 *{published data only}*
Ryan NM, Vertigan AE, Bone S, Gibson PG. Cough reflex sensitivity improves with speech language pathology management of refractory chronic cough. *Cough* 2010;**6**:5.

Ryan 2014 *{published data only}*
Ryan NM, Gibson PG. Recent additions in the treatment of cough. *Journal of Thoracic Disease* 2014;**6**(Suppl 7): S739–47.

Ryan 2016 *{published data only}*
Ryan MA, Cohen SM. Long-term follow-up of amitriptyline treatment for idiopathic cough. *Laryngoscope* 2016;**126** (12):2758–63.

Sauni 2013 *{published data only}*
Sauni R, Uitti J, Jauhiainen M, Kreiss K, Sigsgaard T, Verbeek JH. Remediating buildings damaged by dampness

and mould for preventing or reducing respiratory tract symptoms, infections and asthma (Review). *Evidence-Based Child Health* 2013;**8**(3):944–1000.

Selby 2017 ***{published data only}***
Selby J, Bailey E, Gillies F, Hull JH. Time to re-group: a novel approach to the delivery of speech and language therapy for chronic refractory cough. *Thorax* 2017;**72** (Suppl 3):A141.

Shem 2012 ***{published data only}***
Shem K, Castillo K, Wong S, Chang J, Kolakowsky-Hayner S. Dysphagia and respiratory care in individuals with tetraplegia: incidence, associated factors, and preventable complications. *Topics in Spinal Cord Injury Rehabilitation* 2012;**18**(1):15–22.

Sitoh 2000 ***{published data only}***
Sitoh YY, Lee A, Phua SY, Lieu PK, Chan SP. Bedside assessment of swallowing: a useful screening tool for dysphagia in an acute geriatric ward. *Singapore Medical Journal* 2000;**41**(8):376–81.

Smithard 1998 ***{published data only}***
Smithard DG, O'Neill PA, Park C, England R, Renwick DS, Wyatt R, et al. Can bedside assessment reliably exclude aspiration following acute stroke?. *Age and Ageing* 1998;**27** (2):99–106.

Soria 2013 ***{published data only}***
Soria F, Furkim AM, Nunes MC, Pinto G, Lange M, Zetola V. Identification risk of aspiration pneumonia in two groups of patients with stroke. *Dysphagia* 2013;**28**(2):325–6.

Soria 2013a ***{published data only}***
Soria F, Furkim AM, Nunes MC, Albini R, Macri M, Pinto G, et al. Clinical evaluation of swallowing in patients with stroke in the emergency room. *Dysphagia* 2013;**28**(2):308.

Suiter 2014 ***{published data only}***
Suiter DM, Sloggy J, Leder SB. Validation of the Yale swallow protocol: a prospective double-blinded videofluoroscopic study. *Dysphagia* 2014;**29**(2):199–203.

Tong 2016 ***{published data only}***
Tong TE, Ng ML, Yan N. Impact of expiratory muscle strength training (EMST) on phonatory performance in Parkinson's patients. 20th International Congress of Parkinson's Disease and Movement Disorders; 2016 Jun 19-23; Berlin. 2016.

Vertigan 2007 ***{published data only}***
Vertigan AE, Theodoros DG, Gibson PG, Winkworth AL. Review series: chronic cough: behaviour modification therapies for chronic cough. *Chronic Respiratory Disease* 2007;**4**(2):89–97.

Vertigan 2011 ***{published data only}***
Vertigan A, Gibson P. Development of a brief speech pathology intervention for chronic refractory cough. *Pulmonary Pharmacology and Therapeutics* 2011;**24**(3):e5.

Vertigan 2012 ***{published data only}***
Vertigan AE, Gibson PG. The role of speech pathology in the management of patients with chronic refractory cough. *Lung* 2012;**190**(1):35–40.

Vertigan 2014 ***{published data only}***
Vertigan AE, Bone SL, Gibson PG. Development and validation of the Newcastle laryngeal hypersensitivity questionnaire. *Cough* 2014;**10**(1):1.

Vertigan 2016 ***{published data only}***
Vertigan AE, Kapela SL, Ryan NM, Birring SS, McElduff P, Gibson PG. Pregabalin and speech pathology combination therapy for refractory chronic cough: a randomized controlled trial. *Chest* 2016;**149**(3):639–48.

Vertigan 2018 ***{published data only}***
Vertigan AE, Kapela SM, Kearney EK, Gibson PG. Laryngeal dysfunction in Cough Hypersensitivity Syndrome: a cross-sectional observational study. Journal of Allergy and Clinical Immunology in Practice 2018 May 3 Epub ahead of print]. DOI: 10.1016/j.jaip.2018.04.015

Videnovic 2013 ***{published data only}***
Videnovic A. Treatment of Huntington Disease. *Current Treatment Options in Neurology* 2013;**15**(4):424–38.

Weinberger 2010 ***{published data only}***
Weinberger M. The habit cough syndrome. *Pediatric Allergy, Immunology, and Pulmonology* 2010;**23**(2):125–9.

Weinhardt 2008 ***{published data only}***
Weinhardt J, Hazelett S, Barrett D, Lada R, Enos T, Keleman R. Accuracy of a bedside dysphagia screening: a comparison of registered nurses and speech therapists. *Rehabilitation Nursing Journal* 2008;**33**(6):247–52.

Wright 2012 ***{published data only}***
Wright KA, Bravver EK, Langford VL, Brooks BR. Quantitative labial, tongue speech and swallowing rate measurements at diagnosis correlate with ALS functional rating scale-revised (ALSFRS-R) bulbar sub-score and bulbar sub-score item scores but not with ALSFRS-R total score-inter-rater reliability in speech and swallowing domains. *Amyotrophic Lateral Sclerosis* 2012;**13**(Suppl 1): 182.

Wu 2017 ***{published data only}***
Wu H-L, Tai Y-H, Wei L-F, Cheng H-W, Ho C-M. Bronchial lumen is the safer route for an airway exchange catheter in double-lumen tube replacement: preventable complication in airway management for thoracic surgery. *Journal of Thoracic Disease* 2017;**9**(10):E903–6.

Young 2008 ***{published data only}***
Young P, Finn BC, Fox ML, Emery N, Bruetman JE. Gastroesophageal reflux as a cause of vocal cord dysfunction. *Anales de Medicina Interna* 2008;**25**(7):349–52.

Zhu 2013 ***{published data only}***
Zhu SJ, Qu Y, Liu K. The curative effect of task-oriented approach in combination with articulation approach on spastic dysarthria. *Journal of Sichuan University* 2013;**44**(5): 779–82.

Zimmels 2015 ***{published data only}***
Zimmels S, Kelly A, Fleming L. Swallow aspiration and respiratory symptoms in normally developing children. *European Respiratory Journal* 2015;**46**:P3632. DOI: 10.1183/13993003.congress-2015.PA3632

Zobeiri 2011 *{published data only}*

Zobeiri M. Prevalence, risk factors and severity of asthma symptoms in children of Kermanshah, IRAN: ISAAC phase I, II. *Acta Medica Iranica* 2011;**49**(3):184–8.

Additional references

Abdulqawi 2015

Abdulqawi R, Dockry R, Holt K, Layton G, McCarthy BG, Ford AP, et al. P2X3 receptor antagonist (AF-219) in refractory chronic cough: a randomised, double-blind, placebo-controlled phase 2 study. *Lancet* 2015;**385**: 1198–205.

Altman 2000

Altman K, Mirza N, Ruiz C, Sataloff R. Paradoxical vocal fold motion: presentation and treatment options. *Journal of Voice* 2000;**14**(1):99–103.

Altman 2002

Altman K, Simpson C, Amin MR, Abaza M, Balkissoon R, Casiano RR. Cough and paradoxical vocal fold motion. *Otolaryngology Head and Neck Surgery* 2002;**127**(6):501–11.

Ando 2016

Ando A, Smallwood D, McMahon M, Irving L, Mazzone SB, Farrell MJ. Neural correlates of cough hypersensitivity in humans: evidence for central sensitisation and dysfunctional inhibitory control. *Thorax* 2016;**71**(4):323–9.

Balkissoon 2012

Balkissoon R, Kenn K. Asthma: vocal cord dysfunction (VCD) and other dysfunctional breathing disorders. *Seminars in Respiratory and Critical Care Medicine* 2012;**33** (6):595–605.

Bandura 1986

Bandura A. *Social Foundations of Thought and Action: A Social Cognitive Theory*. Englewood Cliffs, NJ: Prentice-Hall, 1986.

Belafsky 2001

Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). *Laryngoscope* 2001;**111**(8):1313–7.

Belvisi 2003

Belvisi MG. Sensory nerves and airway inflammation: role of A-delta and C-fibres. *Pulmonary Pharmacology & Therapeutics* 2003;**16**:1–7.

Belvisi 2017

Belvisi MG, Birrell MA, Wortley MA, Maher SA, Satia I, Badri H, et al. XEN-D0501, a novel transient receptor potential vanilloid 1 antagonist, does not reduce cough in patients with refractory cough. *American Journal of Respiratory and Critical Care Medicine* 2017;**196**(10): 1255–63.

Birring 2008

Birring SS, Fleming T, Matos S, Raj AA, Evans DH, Pavord ID. The Leicester Cough Monitor: preliminary validation of an automated cough detection system in chronic cough. *European Respiratory Journal* 2008;**31**:1013-8.

Blager 1988

Blager FB, Gay ML, Wood RP. Voice therapy techniques adapted to treatment of habit cough: a pilot study. *Journal of Communication Disorders* 1988;**21**(5):393–400.

Blager 1998

Blager F, Gay M, Wood R. Voice therapy techniques adapted to treatment of habit cough: pilot study. *Journal of Communication Disorders* 1998;**21**:393–400.

Blager 2000

Blager F. Paradoxical vocal fold movement: diagnosis and management. *Current Opinion in Otolaryngology and Head and Neck Surgery* 2000;**8**(3):180–3.

Boone 1993

Boone DR, McFarlane SC. A critical view of the yawn-sigh as a voice therapy technique. *Journal of Voice* 1993;**7**(1): 75–80.

Boulet 2015

Boulet LP, Coeytaux RR, McCrory DC, French CT, Chang AB, Birring SS, et al. Tools for assessing outcomes in studies of chronic cough: CHEST guideline and expert panel report. *Chest* 2015;**147**:804-14.

Canning 2006

Canning B. Anatomy and neurophysiology of the cough reflex: ACCP evidence-based clinical practice guidelines. *Chest* 2006;**129**(1):33S–47S.

Canning 2014

Canning BJ, Chang AB, Bolser DC, Smith JA, Mazzone SB, McGarvey L. Anatomy and neurophysiology of cough; chest guidelines and expert panel report. *Chest* 2014;**146** (6):1633–48.

Carney 1997

Carney IK, Gibson PG, Murree-Allen K, Saltos N, Olson LG, Hensley MJ. A systematic evaluation of mechanisms in chronic cough. *American Journal of Respiratory and Critical Care Medicine* 1997;**156**(1):211–6.

Casper 2003

Casper J, Murry T. Voice therapy methods in dysphonia. *Otolaryngologic Clinics of North America* 2000;**5**(3): 983–1002.

Chamberlain Mitchell 2019

Chamberlain Mitchell SAF, Ellis J, Ludlow S, Pandyan A, Birring SS. Non-pharmacological interventions for chronic cough: the past, present and future. Pulmonary Pharmacology & Therapeutics 2019; Vol. 56:29–38. DOI: 10.1016/j.pupt.2019.02.006

Chhetri 2014

Chhetri DK, Neubauer J, Sofer E. Posterior cricoarytenoid muscle dynamics in canines and humans. *Laryngoscope* 2014;**124**(10):2363–7.

Christopher 2010

Christopher KL, Morris MJ. Vocal cord dysfunction, paradoxic vocal fold motion, or laryngomalacia? Our understanding requires an interdisciplinary approach. *Otolaryngologic Clinics of North America* 2010;**43**(1):43–66.

Colak 2017
Çolak Y, Nordestgaard BG, Laursen LC, Afzal S, Lange P, Dahl M. Risk factors for chronic cough among 14669 individuals from the general population. *Chest* 2017;**152** (3):563–73.

Davenport 2002
Davenport P, Sapienza C, Bolser D. Psychophysical assessment of the urge to cough. *European Respiratory Review* 2002;**12**(85):249–53.

Decalmer 2007
Decalmer SC, Webster D, Kelsall AA, McGuinness K, Woodcock AA, Smith, JA. Chronic cough: how do cough reflex sensitivity and subjective assessments correlate with objective cough counts during ambulatory monitoring?. *Thorax* 2007;**62**(4):329–34.

Dunn 2015
Dunn NM, Katial RK, Hoyte FCL. Vocal cord dysfunction: a review. *Asthma Research and Practice* 2015;**1**:9. DOI: 10.1186/s40733-015-0009-z

Estill 2009
Estill J, Klimek M, Obert K, Steinhauer K. *Estill Voice Training Level One Workbook: Figures for Voice Control*. Nashville, TN: Estill Voice International, 2009.

Estill 2009a
Estill J, Klimek M, Obert K, Steinhauer K. *Estill Voice Training Level Two Workbook: Figure Combinations for Six Voice Qualities*. Nashville, TN: Estill Voice International, 2009.

Farrell 2014
Farrell MJ, Koch S, Ando A, Cole LJ, Egan GF, Mazzonne SB. Functionally connected brain regions in the network activated during capsaicin inhalation. *Human Brain Mapping* 2014;**35**(11):5341–55.

Fontana 2008
Fontana GA. Before we get started: what is a cough?. *Lung* 2008;**186**(1):2.

Forrest 2012
Forrest L, Husein T, Husein O. Paradoxical vocal cord motion: classification and treatment. *Laryngoscope* 2012; **122**(4):844–53.

French 1998
French CL, Irwin RS, Curley FJ, Krikorian CJ. Impact of chronic cough on quality of life. *Archives of Internal Medicine* 1998;**158**(15):1657-61.

Gibson 2009
Gibson PG, Vertigan AE. Speech pathology for chronic cough: a new approach. *Pulmonary Pharmacology and Therapeutics* 2009;**22**:159-62.

Gibson 2010
Gibson PG, Chang AB, Glasgow NJ, Holmes PW, Katelaris P. CICADA: Cough in Children and Adults: Diagnosis and Assessment. Australian cough guidelines summary statement. *Medical Journal of Australia* 2010;**192**(5): 265–71.

Gibson 2015a
Gibson PG, Vertigan AE. Management of chronic refractory cough. *BMJ* 2015;**351**:h5590.

Gibson 2016a
Gibson PG, Wang G, McGarvey L, Vertigan AE, Altman KW, Birring SS, et al. Treatment of unexplained chronic cough: CHEST guideline and expert panel report. *Chest* 2016;**149**(1):27–44.

GRADEpro GDT [Computer program]
McMaster University (developed by Evidence Prime). GRADEpro GDT. Version accessed prior to 6 October 2017. Hamilton (ON): McMaster University (developed by Evidence Prime), 2015.

Haines 2015
Haines J, Esposito K, Lillie S, McNamee C, Pargeter N, Robinson S, et al. Speech and language therapy in adult respiratory care - position paper. www.rcslt.org/-/media/Project/RCSLT/adults-with-respiratory-care.pdf. London, (accessed prior to 4 July 2019).

Halvorsen 2017
Halvorsen T, Walsted ES, Bucca C, Bush A, Cantarella G, Friedrich G, et al. Inducible laryngeal obstruction: an official joint European Respiratory Society and European Laryngological Society statement. *European Respiratory Journal* 2017;**50**(3):1602221.

Higgins 2011
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Hilton 2015
Hilton E, Marsden P, Thurston A, Kennedy S, Decalmer S, Smith JA. Clinical features of the urge-to-cough in patients with chronic cough. *Respiratory Medicine* 2015;**109**(6): 701–7.

Hirano 1981
Hirano M. *Clinical Examination of Voice*. New York: Springer, 1981.

Hrisanfow 2013
Hrisanfow E, Hägglund D. Impact of cough and urinary incontinence on quality of life in women and men with chronic obstructive pulmonary disease. *Journal of Clinical Nursing* 2013;**22**(1-2):97–105.

Hull 2016
Hull JH, Backer V, Gibson PG, Fowler SJ. Laryngeal dysfunction: assessment and management for the clinician. *American Journal of Respiratory and Critical Care Medicine* 2016;**194**(9):1062–72.

Irwin 1998
Irwin RS, Boulet LP, Cloutier MM, Fuller R, Gold PM, Hoffstein V, et al. Managing cough as a defence mechanism and as a symptom: a consensus report for the American College of Chest Physicians. *Chest* 1998;**114**:133S–81S.

Irwin 2006
Irwin RS, Baumann MH, Bolser DC, Boulet LP, Braman SS, Brightling CE, et al. Diagnosis and Management of Cough Executive Summary. ACCP Evidence-Based Clinical Practice Guidelines. *Chest* 2006;**129**(1 Suppl):1S-23S.

Jeyakumar 2006
Jeyakumar A, Brickman TM, Haben M. Effectiveness of amitriptyline versus cough suppressants in the treatment of chronic cough resulting from postviral vagal neuropathy. *Laryngoscope* 2006;**116**(12):2108–12.

Khalid 2014
Khalid S, Murdoch R, Newlands A, Smart K, Kelsall A, Holt K. Transient receptor potential vanilloid 1 (TRPV1) antagonism in patients with refractory chronic cough: a double-blind randomized controlled trial. *Journal of Allergy and Clinical Immunology* 2014;**134**(1):56–62.

Kotby 1993
Kotby MN, Shiromoto O, Hirano M. The accent method of voice therapy: effect of accentuations on FO, SPL, and airflow. *Journal of Voice* 1993;**7**(4):319–25.

Koufman 2011
Koufman JA. Low-acid diet for recalcitrant laryngopharyngeal reflux: therapeutic benefits and their implications. *Annals of Otology, Rhinology and Laryngology* 2011;**120**(5):281–7.

Leech 2013
Leech J, Mazzonne SB, Farrell MJ. Brain activity associated with placebo suppression of the urge-to-cough in humans. *American Journal of Respiratory and Critical Care Medicine* 2013;**188**:1069–75.

Mazzone 2007
Mazzone SB, McLennan L, McGovern AE, Egan GF, Farrell MJ. Representation of capsaicin-evoked urge-to-cough in the human brain using functional magnetic resonance imaging. *American Journal of Respiratory and Critical Care Medicine* 2007;**176**(4):327–32.

Mazzone 2011
Mazzone SB, Cole LJ, Ando A, Egan GF, Farrell MJ. Investigation of the neural control of cough and cough suppression in humans using functional brain imaging. *Journal of Neuroscience* 2011;**31**:2948–58.

Moher 2009
Moher D, Liberati A, Tetzlaff J, Altman D. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine* 2009;**6**(7): e1000097. DOI: 10.1371/journal.pmed.1000097

Morice 2006
Morice AH, McGarvey L, Pavord I. Recommendations for the management of cough in adults. *Thorax* 2006;**61**(Suppl 1):i1–24.

Morice 2007
Morice AH, Fontana GA, Belvisi MG, Birring SS, Chung KF, Dicpinigaitis PV, et al. ERS Guidelines on the assessment of cough. *European Respiratory Journal* 2007;**29** (6):1256–76.

Morice 2007a
Morice AH, Menon MS, Mulrennan SA, Everett CF, Wright C, Jackson J, et al. Opiate therapy in chronic cough. *American Journal of Respiratory and Critical Care Medicine* 2007;**175**(4):312–5.

Morrison 1999
Morrison M, Rammage L, Emami AJ. The irritable larynx syndrome. *Journal of Voice* 1999;**13**(3):447–55.

Murry 2004
Murry T, Tabee A, Aviv JE. Respiratory retraining of refractory cough and laryngopharyngeal reflux in patients with paradoxical vocal fold movement disorder. *Laryngoscope* 2004;**114**(8):1341–5.

Olin 2017
Olin JT, Deardorff EH, Fan EM, Johnston KL, Keever VL, Moore CM, et al. Therapeutic laryngoscopy during exercise: a novel non-surgical therapy for refractory EILO. *Pediatric Pulmonology* 2017;**52**(6):813–9.

Omori 2011
Omori K. Diagnosis of voice disorders. *Japan Medical Association Journal* 2011;**54**(4):248–53.

Pentax 2018
Pentax Medical Computerised Speech Lab. www.pentaxmedical.com/pentax/en/99/1/Computerized-Speech-Lab-CSL (accessed prior to 3 July 2019).

Prochaska 1982
Prochaska JO, DiClemente CC. Trans-theoretical therapy - toward a more integrative model of change. *Psychotherapy: Theory, Research and Practice* 1982;**19**(3):276–88.

Prudon 2005
Prudon B, Birring SS, Vara DD, Hall AP, Thompson JP, Pavord ID. Cough and glottic-stop reflex sensitivity in health and disease. *Chest* 2005;**127**(2):550–7.

Raj 2009
Raj AA, Pavord DI, Birring SS. Clinical cough IV: what is the minimal important difference for the Leicester Cough Questionnaire?. *Handbook of Experimental Pharmacology* 2009;**187**:311-20.

RCSLT 2008
Royal College of Speech and Language Therapists. *Speech and Language Therapy Endoscopy for Voice Disordered Patients*. London, UK: Royal College of Speech and Language Therapists, 2008.

RevMan 2014 [Computer program]
Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Rubin 2000
Rubin JS, Lieberman J, Harris TM. Laryngeal manipulation. *Otolaryngologic Clinics of North America* 2000;**33**(5): 1017–34.

Ryan 2012
Ryan NM, Birring SS, Gibson PG. Gabapentin for refractory chronic cough: a randomised, double-blind, placebo-controlled trial. *Lancet* 2012;**380**:1583–9.

Slinger 2018
Slinger C, Mehdi SB, Milan SJ, Dodd S, Blakemore J, Vyas A, et al. Speech and language therapy for management of chronic cough. *Cochrane Database of Systematic Reviews* 2018, Issue 7. DOI: 10.1002/14651858.CD013067

Smith 2005
Smith J, Johnson C, Brammer C, Kalam R, Jones S, Woodcock A. The effect of a psychological intervention on the urge to cough. American Thoracic Society International Conference; 2005 May 20-25; San Diego. 2005.

Smith 2017
Smith JA, Haines J, Yorke J. Taming chronic cough. *Thorax* 2017;**72**(2):103–4.

Solomon 2014
Solomon NP, DiMattia MJ. Effects of a vocally fatiguing task and systemic hydration on phonation threshold pressure. *Journal of Voice* 2001;**14**(3):341–62.

Song 2013
Song WJ, Morice AH, Kim MH, Lee SE, Jo EJ, Lee SM, et al. Cough in the elderly population: relationships with multiple comorbidity. *PLOS ONE* 2013;**8**(10):e78081.

Song 2014
Song WJ, Chang Y-S, Maurice A. Changing the paradigm for cough: does "cough hypersensitivity" aid our understanding?. *Asia Pacific Allergy* 2014;**4**(1):3–13.

Song 2015
Song WJ, Chang YS, Faruqi S, Kim JY, Kang MG, Kim S, et al. The global epidemiology of chronic cough in adults: a systematic review and meta-analysis. *European Respiratory Journal* 2015;**45**(5):1479–81.

Stemple 2009
Stemple J, Fry L. Voice therapy: clinical case studies. *Voice Therapy: Clinical Case Studies*. San Diego, CA: Plural Publishing, 2009.

TitzeI 2006
TitzeI IR. Voice training and therapy with a semi-occluded vocal tract: rationale and scientific underpinnings. *Journal of Speech Language and Hearing Research* 2006;**49**(2): 448–59.

Traister 2014
Traister RS, Fajt ML, Landsittel D, Petrov AA. A novel scoring system to distinguish vocal cord dysfunction from asthma. *Journal of Allergy and Clinical Immunology* 2014;**2** (1):65–9.

Vertigan 2007a
Vertigan AE, Theodoros DG, Winkworth AL, Gibson PG. Chronic cough: a tutorial for speech-language pathologists. *Journal of Medical Speech Language Pathology* 2007;**15**(3): 189–206.

Vertigan 2010
Vertigan A, Bone S, Gibson PG. Laryngeal sensory dysfunction in laryngeal hypersensitivity syndrome. *Respirology* 2010;**18**(6):948–56.

Vertigan 2013
Vertigan A, Bone S, Gibson PG. Laryngeal sensory dysfunction in laryngeal hypersensitivity syndrome. *Respirology* 2013;**18**(6):948–56.

Vertigan 2016a
Vertigan AE, Gibson PG. *Speech Pathology: Management of Chronic Refractory Cough and Related Disorders*. Kent, UK: Compton Publishing Ltd, 2016.

Vertigan 2019
Vertigan AE. The larynx as a target for treatment in chronic refractory cough. *Current Otorhinolaryngology Reports* 2019; **7**(2):129–36. DOI: 10.1007/s40136-019-00240-2

Zelcer 2002
Zelcer S, Henri C, Tewfik TL, Mazer B. Multidimensional voice program analysis (MDVP) and the diagnosis of pediatric vocal cord dysfunction. *Annals of Allergy, Asthma and Immunology* 2002;**88**(6):601–8.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Chamberlain Mitchell 2017

Methods	Multicentre, single-blinded randomised controlled trial
Participants	Treatment (PSALTI) group n = 34 (8 did not receive allocated intervention) Control group n = 41 (4 did not receive allocated intervention) • Age (median years and IQR): treatment (PSALTI) group 56 years (48 to 67 years) ; control group 61 years (53 to 67 years) • Female, n (%): treatment (PSALTI) group 26 (63%); control group 25 (71%) Trial report notes the groups were well matched at baseline, with the exception of SF-36 PCS (higher in the control group) **Inclusion criteria:** Reported as: adults with chronic cough (defined as duration > 2 months), with normal chest X-ray, minimal sputum production (< 10 mL sputum a day) with negative investigations and/or failed treatment trials for asthma, gastro-oesophageal reflux disease, and rhinitis, as per British Thoracic Society guidelines **Exclusion criteria:** Reported as: patients were excluded if they had had an upper respiratory tract infection in the past 4 weeks, were taking ACE inhibitors, were current smokers, or had a known respiratory disease (such as lung cancer, pneumonia, pulmonary fibrosis, sarcoidosis, pleural effusion, bronchiectasis). Patients were also excluded if they had vocal cord nodules, malignancy, or evidence of active aspiration
Interventions	PSALTI consisted of education, laryngeal hygiene and hydration, cough suppression techniques, breathing exercises, and psychoeducational counselling. Participants attended weekly sessions and received 1-to-1 treatment from a healthcare professional (physiotherapist or speech and language therapist) over 4 weeks. Session durations were the same as for the control group Participants in the control group attended weekly sessions and received 1-to-1 standardised healthy lifestyle advice from a healthcare professional (nurse, physiotherapist, or speech and language therapist) over 4 weeks. The control intervention was based on that used in the trial reported by Vertigan 2006. The initial session covered general advice on exercise and physical activity; the second session dietary and nutritional advice; the third session stress management; and the fourth session relaxation. The material covered in each session was based on healthy lifestyle advised by the UK Department of Health and National Health Service
Outcomes	Primary outcome(s): • Leicester Cough Questionnaire (LCQ) at week 4. Participants independently completed questionnaires at baseline, at 4 weeks (after fourth treatment session), and at 3-month follow-up. Secondary outcomes: • Leicester Cough Monitor (LCM) • Cough severity in the past 2 weeks was assessed by VAS (0 to 100 mm) as per American College of Chest Physicians guideline • The Vocal Performance Questionnaire (VPQ) (32), a 12-item tool used to assess

	patients' perceived impact on their voice, since a high prevalence of voice disorders in people with chronic cough has been reported • SF-36 • Hospital Anxiety and Depression Scale (HADS) Secondary endpoints were assessed at baseline, 4 weeks, and 3 months Capsaicin cough challenge was assessed in a subset of the participants (King's College Hospital Foundation Trust and Northumbria Healthcare NHS Foundation Trust) to measure participants' cough reflex sensitivity at baseline and at 4 weeks (after fourth treatment session)
Notes	Study conducted across 3 hospitals in the UK (King's College Hospital NHS Foundation Trust, Lancashire Teaching Hospitals NHS Foundation Trust, and Northumbria Healthcare NHS Foundation Trust). 2 further sites, Royal Brompton & Harefield NHS Foundation Trust and Guy's and St Thomas' NHS Foundation Trust, were recruitment-only sites, and participants were referred to King's College Hospital to receive the intervention. The study was undertaken between December 2011 and April 2014 Funded by: Chartered Society of Physiotherapy Charitable Trust, UK (Award PRF 10/4). Additional funding was obtained from NIHR-CRN; King's College Hospital NHS Foundation Trust; London National Institute for Health Research (NIHR)/Wellcome Trust; King's Clinical Research Facility and the NIHR Biomedical Research Centre and Dementia Unit at South London and Maudsley NHS Foundation Trust and King's College London; National Institute for Health Research Biomedical Research Centre at Guy's and St Thomas' National Health Service (NHS) Foundation Trust and King's College London; NIHR Collaboration for Leadership in Applied Health Research and Care South London (CLAHRC South London)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Reported as: Participants were block-randomised, stratified by age (above and below 50 years old) and gender by the King's Clinical Trials Unit, King's College London
Allocation concealment (selection bias)	Low risk	Reported as: Participants were registered into the randomisation service provided by the King's Clinical Trials Unit, King's College London. This prevented foreknowledge of treatment assignment for the study researchers. Group allocation was concealed from participants until they had completed the study and all postintervention assessments
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Reported as: The study was single-blinded. It was not possible to blind the treating therapist to the intervention the participant received

Chamberlain Mitchell 2017 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Reported as: Potential bias was minimised by asking participants to complete their primary outcome measures independently from the treating therapist, and participants remained blinded until after completion of the final postintervention outcome measures
Incomplete outcome data (attrition bias) All outcomes	Low risk	Reported as: 75 participants were randomised and had baseline assessments. 1 additional participant was randomised to the PSALTI group but did not attend baseline assessments. 4 participants did not receive any treatment (PSALTI group (n = 3) : myocardial infarction prior to treatment, unable to travel to hospital, and insufficient time for the study; control group (n = 1) : undisclosed illness prior to start of treatment)
Selective reporting (reporting bias)	Unclear risk	No apparent indication of selective reporting, but we did not have access to trial protocols

Vertigan 2006

Methods	Single-blinded randomised controlled trial
Participants	Treatment (SPEICH-C) group n = 43 Control group n = 44 • Age (mean years and SD): treatment (SPEICH-C) group 57.5 years (13.8); control group 61.3 years (13.2) • Female, n (%): treatment (SPEICH-C) group 35 (81%); control group 29 (66%) Trial report notes the groups were well balanced with respect to age, sex, reflux, ACE inhibitor use, allergies, asthma, postnasal drip syndrome, and smoking status **Inclusion criteria:** Reported as: chronic cough was defined as the presence of chronic coughing that persisted for 2 months following medical treatment based on the approach recommended by Irwin 1998. The severity of the cough was sufficient for patients to seek medical attention from both general practitioner and respiratory physician. Patients had undergone respiratory case history, hypertonic saline challenge, and induced sputum analysis before inclusion in the study. Significant symptoms identified during the case history were subsequently investigated and treated. A minimum age of 18 years and ability to travel to John Hunter Hospital **Exclusion criteria:** Reported as: recent upper respiratory tract infection, untreated allergy, PNDS, asthma, GER, eosinophilic bronchitis, lung pathology, abnormality on the chest radiograph, COPD, and neurological voice disorder

Vertigan 2006 (*Continued*)

Interventions	In the intervention group, participants received Speech Pathology Evaluation and Intervention for CHronic Cough (SPEICH-C). The SPEICH-C comprises 4 components including education about the nature of chronic cough, strategies to control the cough, psychoeducational counselling, and vocal hygiene education to reduce laryngeal irritation. These techniques were designed to improve the efficiency of voicing by reducing the load on the larynx while promoting adequate breath support and oral resonance. The education component emphasised the futility and negative side effects of repeated coughing, the benefits of cough suppression, and the capacity of individuals to develop voluntary control over cough. The cough suppression component required participants to anticipate when a cough was about to occur and then implement a strategy to suppress or replace the cough. The vocal hygiene component included strategies to reduce laryngeal irritation and maximise hydration in order to reduce stimulation of cough receptors. Relaxed throat breathing exercises were also provided for those participants with inspiratory dyspnoea. The psychological component was designed to facilitate internalisation of control over their cough and view the cough as something individuals do in response to irritating stimuli rather than a phenomenon outside the participant's control In the control group, participants received an equivalent course of healthy lifestyle education Participants in both groups attended 4 individual 30-minute intervention sessions scheduled over a 2-month period
Outcomes	Outcomes: • Symptom scores (including components for cough, breathing, voice, upper airway, and limitation) • The clinical outcome for each participant was rated as successful, unsuccessful, or partially successful A division between primary and secondary outcomes was not explicitly made in the trial report
Notes	Study conducted at the John Hunter Hospital, New South Wales, Australia between April 2003 and October 2004 Funded by: The Hunter Medical Research Institute

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Study randomised by random number generation.
Allocation concealment (selection bias)	Low risk	Reported as: The treating speech pathologist was not involved in the randomisation process; however, once the treatment group was allocated, the speech pathologist knew the participant's group allocation. Group allocation was concealed from participants until the postintervention symptom rating and clinical judgement of out-

Vertigan 2006 (*Continued*)

		come had been recorded
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Reported as: Because of the single-blinded design of this study and the nature of the intervention programmes, it was not possible to blind the treating speech pathologist to the type of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	As above
Incomplete outcome data (attrition bias) All outcomes	Low risk	Reported as: 1 participant in the treatment group and 4 in the placebo group did not commence their respective intervention programmes because of unexpected family responsibilities and spontaneous resolution of symptoms before treatment commenced. 3 participants in the treatment group and 2 in the placebo group discontinued intervention through failure to contact or attend appointments
Selective reporting (reporting bias)	Unclear risk	No apparent indication of selective reporting, but we did not have access to trial protocols

ACE: angiotensin-converting-enzyme; COPD: chronic obstructive pulmonary disease; GER: gastro-oesophageal reflux; IQR: interquartile range; PNDS: postnasal drip syndrome; PSALTI: physiotherapy and speech and language therapy intervention; SD: standard deviation; SF-36 PCS: the SF-36 is a generic (rather than disease-specific) 36-item, patient-reported health-related quality of life scale; 'PCS' refers to the physical component score from the instrument (and excludes data from the mental component score); VAS: visual analogue scale

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ackerstaff 1995	Not cough patients. No speech and language therapy intervention (comparison: heat and moisture exchangers intervention and no placebo)
Al-Riyami 2001	Cross-sectional study using a questionnaire. Non-randomised study. Non-interventional. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Bemanin 2015	Cross-sectional questionnaire study. Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough

(*Continued*)

Benninger 2011	Review. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Birring 2017	Review
Biswas 2015	Retrospective (non-randomised) study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Brady 2018	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Cacciari 2017	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. Interventions do not include speech and language therapy techniques (non-interventional study)
Carmel 2016	Literature review. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough and no speech and language therapy intervention
Chamberlain 2013	Review
Cholera 2016	Review. Does not relate to a diagnosis of chronic unexplained (idiopathic/refractory) cough
Dart 2003	Review. Does not relate to a diagnosis of chronic unexplained (idiopathic/refractory) cough
Faria 2014	Retrospective case control study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention and no randomisation
Fernandez 2015	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Finck 2006	Review. Not a randomised trial. Focus not on a diagnosis of chronic unexplained (idiopathic/refractory) cough
Gibson 2014	Editorial
Gibson 2015	Review
Gibson 2016	Review
Goldstein 2007	Case report. Not a randomised trial
Good 2018	Not a randomised controlled trial
Harvey 2018	Participant did not have a diagnosis of chronic cough. Single case report. Not a randomised trial
Hertegard 2002	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention for chronic unexplained (idiopathic/refractory) cough (comparison: hylan B gel with no placebo arm)
Hilgers 1996	Not a randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough

(*Continued*)

Hilgers 2003	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy (comparison: reusable, multi-magnet automatic speaking valve with no placebo arm)
Hull 2005	Retrospective case review not relating to chronic unexplained (idiopathic/refractory) cough
Hunter 2011	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Ihalainen 2015	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Irons 2010	Systematic review. Does not relate to participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough
Irwin 2010	Review. Not a randomised trial
Jensen 2013	Non-randomised study. No intervention. Not in participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough
Kapela 2019	Participants were randomised to receive either a standard speech pathology intervention or standard speech pathology intervention + supplemental pre-recorded videos to support practice at home. The comparison was therefore not speech pathology intervention versus no intervention to evaluate the effectiveness of speech and language therapy for treatment of chronic cough
Kew 2017	Systematic review. Non-randomised trial. Not in participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough
Killoran 2012	Review
Kyriakou 2018	Participants did not have a diagnosis of chronic cough, and the study was not a randomised controlled trial
Lukrafka 2010	Cross-sectional study. Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Marques 2015	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. Interventions do not include speech and language therapy techniques. Intervention is pelvic floor/hip strengthening
McGarvey 2013	Review. Not specifically examining intervention of speech and language therapy in participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough
Mellor 1998	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention (comparison: bupivacaine versus ketorolac)
Mesia 2010	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention (comparison: cetuximab platinum-fluorouracil versus platinum-fluorouracil)
Michaudet 2017	Review

(*Continued*)

Molassiotis 2010	Systematic review. Non-randomised. Not specifically examining effect of speech and language therapy in chronic unexplained (idiopathic/refractory) cough
Morice 2017	Review. Focus is not on a diagnosis of chronic unexplained (idiopathic/refractory) cough in patients who have undergone a full diagnostic workup to exclude an underlying cause, as per published guidelines or local protocols
NCT03457610	Not a randomised trial
Oner 2013	Not a randomised trial
Oskam 2013	Non-randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Park 2017	Not a randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Patterson 2007	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention (comparison: miglustat versus usual care)
Perez 2011	Non-randomised study. Not in participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough
Perez 2012	Non-randomised study. Not in participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough
Plowman 2016	Not in participants with a diagnosis of chronic unexplained (idiopathic/refractory) cough who have undergone a full diagnostic workup to exclude an underlying cause, as per published guidelines or local protocols. Interventions do not include speech and language therapy techniques (intervention is inspiratory-expiratory exercise in amyotrophic lateral sclerosis)
Pohl 2012	Review. Focus not on a diagnosis of chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention
Raggi 2016	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. Speech and language therapy intervention is on swallow rather than cough
Reverberi 2019	Participant did not have a diagnosis of chronic cough. Single case report. Not a randomised trial
Ryan 2009	Non-randomised study. No intervention. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Ryan 2010	Study not randomised
Ryan 2014	Review
Ryan 2016	Retrospective review of effect of amitriptyline on chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention. Not a randomised trial

(*Continued*)

Sauni 2013	Systematic review. Does not include participants with chronic unexplained (idiopathic/refractory) cough. No speech and language therapy intervention
Selby 2017	Non-randomised study
Shem 2012	Cross-sectional study. Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Sitoh 2000	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Smithard 1998	Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Soria 2013	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. Interventions do not include speech and language therapy techniques (interventions were aimed at dysphagia)
Soria 2013a	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Suiter 2014	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Tong 2016	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. Interventions do not include speech and language therapy techniques (comparison: Impact of expiratory muscle strength training versus sham)
Vertigan 2007	Review
Vertigan 2011	Study not randomised
Vertigan 2012	Review. Not a randomised trial
Vertigan 2014	Non-randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Vertigan 2016	Trial compares pregabalin in addition to speech pathology versus speech pathology alone and therefore does not meet our inclusion criteria
Vertigan 2018	Cross-sectional non-randomised study
Videnovic 2013	Non-randomised study. Review in Huntington's disease (not chronic unexplained (idiopathic/refractory) cough) . No speech and language therapy intervention
Weinberger 2010	Review. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Weinhardt 2008	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough. Interventions do not include speech and language therapy techniques; no specific interventions; examines agreement between nurses and speech and language therapists in swallow assessments

(*Continued*)

Wright 2012	Not a randomised study. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Wu 2017	Case report. Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Young 2008	Case report. Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Zhu 2013	Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Zimmels 2015	Not a randomised trial. Participants do not have a diagnosis of chronic unexplained (idiopathic/refractory) cough
Zobeiri 2011	Cross-sectional questionnaire study. Not a randomised trial

DATA AND ANALYSES

Comparison 1. Speech and language therapy versus healthy lifestyle advice

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Health-related quality of life (Leicester Cough Questionnaire)	1		Mean Difference (Fixed, 95% CI)	Subtotals only
2 Serious adverse events	1	75	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Objective cough counts (e.g. using the Leicester Cough Monitor)	1		Geometric Mean (Fixed, 95% CI)	Subtotals only
4 Symptoms	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Clinical improvement (as defined by trialists)	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
6 Subjective measures of cough (e.g. visual analogue scale/numerical cough scale score)	1		Mean Difference (Fixed, 95% CI)	Subtotals only
7 Capsaicin cough challenge (to induce 5 coughs)	1		Geometric Mean (Fixed, 95% CI)	Subtotals only
8 Adverse events/side effects	1	75	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 1 Health-related quality of life (Leicester Cough Questionnaire).

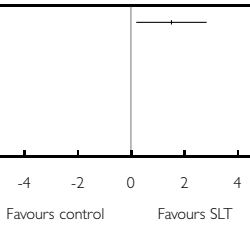
Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 1 Health-related quality of life (Leicester Cough Questionnaire)

Study or subgroup	Speech % language therapy N	Healthy lifestyle advice N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Chamberlain Mitchell 2017	31	40	1.53 (0.6735)			1.53 [0.21, 2.85]

Test for subgroup differences: Not applicable



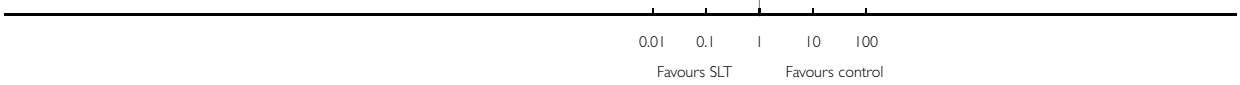
Analysis 1.2. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 2 Serious adverse events.

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 2 Serious adverse events

Study or subgroup	Speech % language therapy n/N	Healthy lifestyle advice n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Chamberlain Mitchell 2017	0/34	0/41			Not estimable
Total (95% CI)	**34**	**41**			**Not estimable**
Total events: 0 (Speech % language therapy), 0 (Healthy lifestyle advice)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Test for subgroup differences: Not applicable					

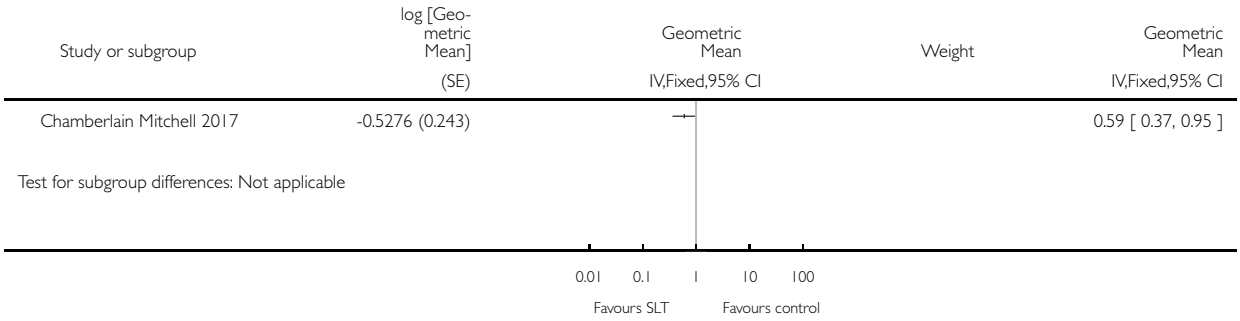


Analysis 1.3. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 3 Objective cough counts (e.g. using the Leicester Cough Monitor).

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 3 Objective cough counts (e.g. using the Leicester Cough Monitor)

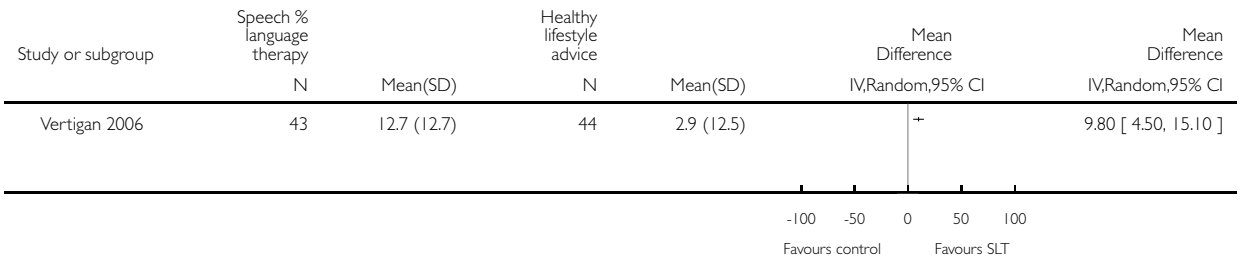


Analysis 1.4. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 4 Symptoms.

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 4 Symptoms

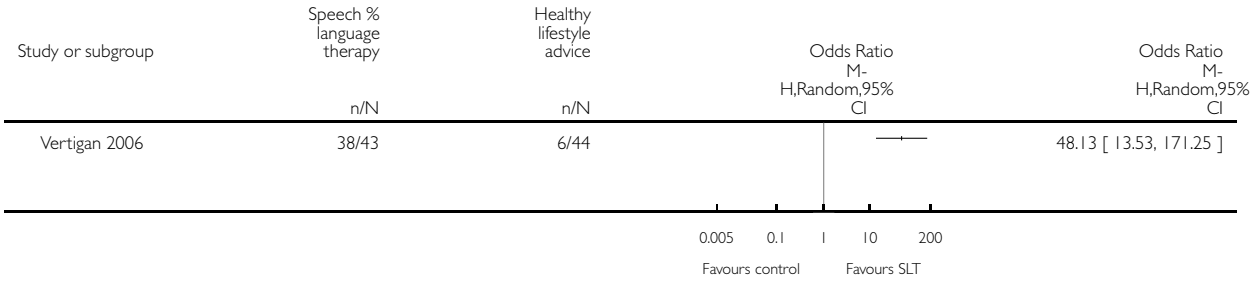


Analysis 1.5. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 5 Clinical improvement (as defined by trialists).

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 5 Clinical improvement (as defined by trialists)

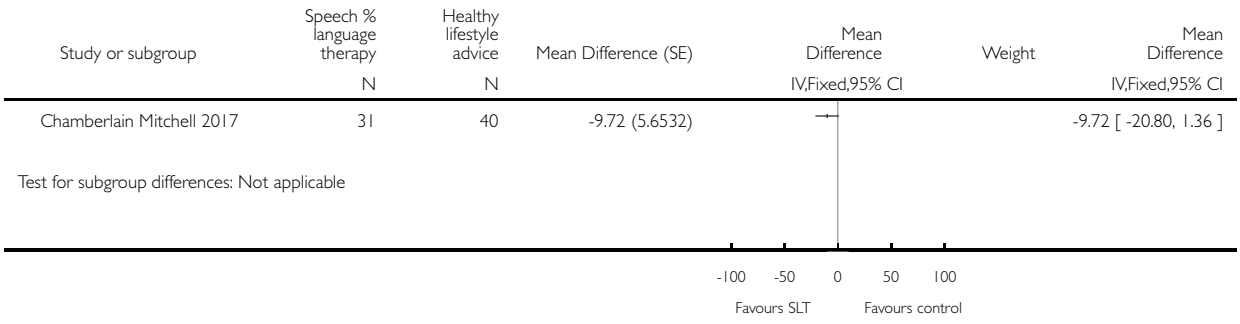


Analysis 1.6. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 6 Subjective measures of cough (e.g. visual analogue scale/numerical cough scale score).

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 6 Subjective measures of cough (e.g. visual analogue scale/numerical cough scale score)



Analysis 1.7. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 7 Capsaicin cough challenge (to induce 5 coughs).

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 7 Capsaicin cough challenge (to induce 5 coughs)

Study or subgroup	Speech % language therapy N	Healthy lifestyle advice N	log [Geometric Mean] (SE)	Geometric Mean IV,Fixed,95% CI	Weight	Geometric Mean IV,Fixed,95% CI
Chamberlain Mitchell 2017	22	27	0.1044 (0.1671)			1.11 [0.80, 1.54]
Test for subgroup differences: Not applicable						

Analysis 1.8. Comparison 1 Speech and language therapy versus healthy lifestyle advice, Outcome 8 Adverse events/side effects.

Review: Speech and language therapy for management of chronic cough

Comparison: 1 Speech and language therapy versus healthy lifestyle advice

Outcome: 8 Adverse events/side effects

Study or subgroup	Speech % language therapy n/N	Healthy lifestyle advice n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Chamberlain Mitchell 2017	0/34	0/41			Not estimable
Total (95% CI)	**34**	**41**			**Not estimable**
Total events: 0 (Speech % language therapy), 0 (Healthy lifestyle advice)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Test for subgroup differences: Not applicable					

APPENDICES

Appendix 1. Database search strategies

CENTRAL (Cochrane Register of Studies)

#1 MESH DESCRIPTOR Cough EXPLODE ALL
#2 cough*:ti,ab,kw
#3 #2 OR #1
#4 MESH DESCRIPTOR Rehabilitation of Speech and Language Disorders EXPLODE ALL
#5 ((speech* or language*) NEAR5 (therap* or treatment* or interven* or program* or train* or exercise* or rehabilit*))
#6 SLT:ti,ab
#7 #4 OR #5 OR #6
#8 #7 AND #3

Cochrane Airways Register of Trials (Cochrane Register of Studies)

#1 MESH DESCRIPTOR Cough EXPLODE ALL
#2 cough*:ti,ab,kw
#3 #2 OR #1
#4 MESH DESCRIPTOR Rehabilitation of Speech and Language Disorders EXPLODE ALL
#5 ((speech* or language*) NEAR5 (therap* or treatment* or interven* or program* or train* or exercise* or rehabilit*))
#6 SLT:ti,ab
#7 #4 OR #5 OR #6
#8 #7 AND #3

MEDLINE (Ovid)

1. Cough/
2. cough$.tw.
3. 1 or 2
4. exp "rehabilitation of speech and language disorders"/
5. ((speech$ or language$) adj5 (therap$ or treatment$ or interven$ or program$ or train$ or exercise$ or rehabilit$)).tw.
6. SLT.ti,ab.
7. or/4-6
8. 3 and 7
9. (controlled clinical trial or randomized controlled trial).pt.
10. (randomized or randomised).ab,ti.
11. placebo.ab,ti.
12. dt.fs.
13. randomly.ab,ti.
14. trial.ab,ti.
15. groups.ab,ti.
16. or/9-15
17. Animals/
18. Humans/
19. 17 not (17 and 18)
20. 16 not 19
21. 8 and 20

Embase (Ovid)

1. exp coughing/
2. cough$.tw.
3. 1 or 2
4. exp "speech and language rehabilitation"/
5. ((speech$ or language$) adj5 (therap$ or treatment$ or interven$ or program$ or train$ or exercise$ or rehabilit$)).tw.
6. SLT.ti,ab.
7. or/4-6
8. 3 and 7
9. Randomized Controlled Trial/
10. randomization/
11. controlled clinical trial/
12. Double Blind Procedure/
13. Single Blind Procedure/
14. Crossover Procedure/
15. (clinica$ adj3 trial$).tw.
16. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (mask$ or blind$ or method$)).tw.
17. exp Placebo/
18. placebo$.ti,ab.
19. random$.ti,ab.
20. ((control$ or prospectiv$) adj3 (trial$ or method$ or stud$)).tw.
21. (crossover$ or cross-over$).ti,ab.
22. or/9-21
23. exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
24. human/ or normal human/ or human cell/
25. 23 and 24
26. 23 not 25
27. 22 not 26
28. 8 and 27

CINAHL (EBSCO)

S1 (MH "Cough")
S2 cough*
S3 S1 OR S2
S4 (MH "Rehabilitation, Speech and Language+")
S5 ((speech* OR language*) n5 (therap* OR treatment* OR interven* OR program* OR train* OR exercise* OR rehabilit*))
S6 SLT
S7 S4 OR S5 OR S6
S8 S3 AND S7
S9 (MH "Clinical Trials+")
S10 randomized or randomised
S11 placebo*
S12 randomly
S13 clinical* n3 (trial* or study or studies)
S14 (single* or double* or triple*) n3 blind*
S15 S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16 S8 AND S15

ClinicalTrials.gov

Search field	Search terms
condition	cough
intervention	speech or language
Study type	interventional

WHO ICTRP

Search field	Search terms
condition	Cough
Intervention	Speech OR language

CONTRIBUTIONS OF AUTHORS

CS contributed to the Background and Methods sections; screened the titles and abstracts of the studies identified by the search and the full-text study reports of all potentially eligible studies; and spot-checked study characteristics entered into Review Manager 5 for accuracy against the study report. She also contributed to the Discussion, Authors' conclusions, and Abstract.

SBM contributed to the Background, Discussion, and Abstract.

SJM contributed to the Background and Methods sections; extracted study characteristics from included studies; independently extracted outcome data from included studies and entered the data into Review Manager 5; and independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions.* He also contributed to the Discussion, Authors' conclusions, and Abstract. In addition, he contributed to the 'Characteristics of included studies' and 'Characteristics of excluded studies' tables, the 'Summary of findings' table, and Figures.

SD contributed to the Background and Methods sections. He also contributed to the 'Characteristics of excluded studies' tables and Plain language summary.

JM contributed to the Background and Methods sections; extracted study characteristics from included studies, independently extracted outcome data from included studies and independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* . She also contributed to the Discussion and Abstract.

AV contributed to the Background and Methods sections. He also contributed to the Discussion and Abstract.

PM contributed to the Background and Methods sections and screened the titles and abstracts of the studies identified by the search and the full-text study reports of all potentially eligible studies. He also contributed to the Discussion, Authors' conclusions, and Abstract.

Contributions of editorial team

Rebecca Fortescue (Co-ordinating Editor): edited the review; advised on methodology, interpretation, and content; approved the final review prior to publication.
Chris Cates (Co-ordinating Editor) checked the data entry prior to the full write-up of the review.
Emma Dennett (Managing Editor): co-ordinated the editorial process; advised on interpretation and content; edited the review.
Emma Jackson (Assistant Managing Editor): conducted peer review; edited the Plain language summary and References sections of the protocol and the review.
Elizabeth Stovold (Information Specialist): designed the search strategy; ran the searches; edited the Search methods section.

DECLARATIONS OF INTEREST

CS: A donation, with no further requirement was provided by Breas Medical for a separate study to look at purchasing a dedicated laryngoscopy equipment to visualise the larynx during application of a cough assist device. This is to look at patterns of laryngeal behaviour when using the device, and so may help participants who initially do not tolerate it, and may help quality of life for participants with bulbar symptoms who then go onto have weak, ineffectual cough, but cannot tolerate mechanical insufflation-exsufflation. I have received honoraria payments for study days undertaken in my own time unrelated to this project, looking at laryngeal patterns and upper airways dysfunction for long-term tracheostomy weaning.

SBM: None known.

SJM: None known.

SD: None known.

JM: None known.

AV: I have had support to attend International meetings and the Winter national British Thoracic Society meeting from various Pharma groups. I have had direct payments to support GP education in asthma predominantly discussing effective assessment and inhaler therapy. These payments are unrelated to the review.

PM: Paul has accepted lecture fees and conference accommodation/fees, but these are unrelated to the current review.

SOURCES OF SUPPORT

Internal sources

- The authors declare that no such funding was received for this systematic review, Other.

External sources

- The authors declare that no such funding was received for this systematic review, Other.