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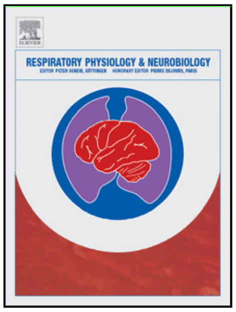

Title: Non-pharmacological techniques for the extremes of the cough spectrum

Author: Arietta Spinou

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Title Non-pharmacological techniques for the extremes of the cough spectrum

Author names and affiliations:

Arietta Spinou, MSc, PhD

Health Sport and Bioscience, University of East London

Corresponding Author:

Dr Arietta Spinou

School of Health Sport and Bioscience

University of East London

Stratford Campus

Water Lane, Stratford

London E15 4LZ

United Kingdom

Tel: +44 (0)20 8223 4520

Email: a.spinou@uel.ac.uk

Highlights

- Cough is a protective reflex, an airway clearance mechanism and a common respiratory disease symptom. Humans are able to partially supress cough or perform it on demand.

- Cough can be seen as a continuum or spectrum, where the middle area represents normal and effective cough. The extremes of this spectrum represent upregulated or downregulated cough, although, the cut-off points of these areas are unclear.
- A variety of non-pharmacological techniques is available for managing both extremes of the cough spectrum. Patients who present reduced or weak cough could receive cough augmentation techniques, whilst those with increased cough sensitivity or frequency could receive training for cough control techniques.

Abstract

Cough can be viewed as a continuum where extremes represent disease phenotypes. Under this unified concept, non-pharmacological treatment for the extremes of the cough spectrum includes both cough augmentation and cough control techniques. Supporting the cough motor output and exercising the cognitive control on coughing are the main directions of these techniques. Cough augmentation can be provided to patients who present low ability to generate adequate peak cough flows, with the aim to develop the sheering forces that are essential for effective airway clearance. On the other hand, individuals with high cough sensitivity or frequency can practice techniques for cough control, which incorporates a combination of education, retraining and psychological support. These techniques aim to empower patients to increase their supramedulary control on cough. Although hypotheses that are generated by the physiology of cough can support most non-pharmacological techniques, their exact mechanisms of effectiveness remain unclear.

Keywords cough management; cough augmentation; cough control; physiotherapy; speech and language therapy

The wide spectrum of cough

The word cough describes a protective respiratory reflex and airway clearance mechanism, a symptom of respiratory diseases, and a voluntarily controlled movement. Cough can be initiated by a variety of stimuli but humans can also perform it on demand or partially suppress it. Clinicians and researchers usually work on distinct aspects of cough, representing upregulated or downregulated presentations. This potentially facilitates clinical specialisation and communication. However, seen cough presentations as a continuum along with managing the problems stemming from the extremes of its spectrum, could facilitate our holistic understanding of cough. The aim of this review is to summarise our current knowledge on the physiology of cough and present the non-pharmacological techniques that are available for addressing both extremes of the cough spectrum.

Cough as a reflex

Cough is a complex protective reflex that removes irritant material or excessive secretions from the airways (Irwin et al., 1998). For instance, cough could be a response to environment insults, temperature changes and exposure to stimuli such as cigarette smoke (Morice, 2013). Its neural pathway is not fully understood in humans, and current knowledge derives mainly from studies on animal models. The vagus nerve contains most of the nerve fibres controlling cough, as vagal denervation can eliminate coughing (Canning et al., 2004). This also explains the occurrence of cough following irritation of the external ear, an area innervated by a small branch of the vagus nerve (Tekdemir et al., 1998). However, other nerves are also involved, as cough can be initiated from areas that do not have vagal innervation e.g. the pharynx in the upper airway cough syndrome. Cough can be initiated from the larynx, trachea and larger bronchi, particularly on the airway bifurcations, but not from stimulation of smaller bronchi, bronchioles and alveoli. This could be evolutional, as the luminal airflows and velocities that are able to be generated in smaller airways would be too low to produce turbulent flow and shear forces for effective airway clearance (Kim et al., 1986b; Widdicombe, 2008). The neuronal bodies of the neurons that can initiate the cough are located in the nodose and jugular ganglia, and travel to the brainstem and more specifically to Nucleus Tractus Solitarius (NTS) (Canning et al., 2004). Subsequently they synapse with second order neurones to the areas of control for cough, respiration and skeletal muscle tone (Mutolo et al., 2008).

The stimulus and the area of the respiratory tract that is stimulated, affect the afferent component of cough. Cough can be induced by mechanical or chemical stimulation, and mechanosensors and chemoreceptors are involved (Mazzone, 2004). The mechanosensors are myelinated fibres that are categorised into Rapidly Adapting Receptors (RARs) and Slowly Adapting Receptors (SARs), based on their adaptation pattern to lung inflation (Mazzone, 2005; Widdicombe, 2003). They are located in the intrapulmonary airways and lung parenchyma and respond primarily to mechanical stimuli or change in pH (Grace et al., 2013; Mazzone, 2004). Studies in guinea pigs also discovered a third type of low pressure mechanosensors, the cough receptors, which are predominantly located in the extrapulmonary airways (Canning et al., 2004). Mechanical stimuli include lung deflation, vibration, bronchoconstriction, smooth muscle contraction, vasodilation, oedema, and foreign bodies (Mazzone, 2005; Widdicombe, 2003). Chemosensors, are unmyelinated fibres primarily sensitive to chemical stimuli. They are mainly located in the extrapulmonary airways, though a few of them are intrapulmonary (Mazzone, 2004; Ricco et al., 1996; Tatar et al., 1988). Stimuli to chemosensors include inflammatory mediators, environmental irritants, alerted mucus secretion, acid and responses to temperature (Grace et al., 2013; Mazzone, 2005; Widdicombe, 2003). Overall, it is possible that the most important nerve fibres for cough are the cough receptors, C-fibres and indirectly RARs, but other nerves are also involved (Mazzone, 2004; Widdicombe, 1995). SARs are responsible for the Hering-Breuer reflex and controlling the breathing pattern, thus it is likely that they facilitate the cough reflex (Schelegle and Green, 2001).

Based on the cough reflex, a rather uncommon classification of cough is according to the grades of eutussia (normal), hypertussia (sensitised), hypotussia (desensitised), dystussia (pathological) and atussia (absent), although this assumes the recognition of distinct characteristics for normal and abnormal cough (Chung et al., 2009). Cough reflex sensitivity is assessed using provocation tests, with the inhalation of a tussive substance such as capsaicin, citric acid, and tartaric acid, or by the inhalation of ultrasonic distilled water (fog). Nevertheless, increase response to challenge test substances can be within normal range, thus overlap with normal cough (Morice, 2013). Therefore, cough challenge tests have a role in the experimental assessment of cough reflex sensitivity changes within individuals, rather than been used for diagnosis. Most studies show that women have a lower cough reflex threshold, although some researchers have found similar sensitivity across both sexes (Dicpinigaitis and Rauf, 1998; Fujimura et al., 1996; Kastelik et al., 2002; Morice, 2013). The reason of these differences is unclear, but might be attributed to height, pulmonary function, hormonal factors, amount and activity of receptors and membrane channels, laryngeal hypersensitivity and dysfunction, or even social, behavioural and environmental factors (Dicpinigaitis and Rauf, 1998; Fujimura et al., 1996; Kavalcikova-Bogdanova et al., 2016; Plevkova et al., 2017). Clinically, women present more frequently with chronic cough than men, particularly when they are in postmenospausal ages (Plevkova et al., 2017).

Cough as a voluntary movement

There is evidence demonstrating a supramedullary control on cough, as cough in humans can be voluntarily produced and partially suppressed (Lee et al., 2002). In healthy individuals, voluntary coughing activates cortex areas that are also activated on voluntary breathing (Simonyan et al., 2007). Functional brain imaging revealed that several brain regions are activated during voluntary or cognitive components of cough and cough suppression (Mazzone et al., 2011). The same study indicated that the capsaicin-induced cough is not solely a brainstem-mediated reflex but requires facilitation by cortical regions (Mazzone et al., 2011). Moreover, individuals report a sensation of urge to cough that they can voluntarily ignore and consciously suppress, thus does not necessarily result in coughing (Davenport et al., 2009; Dicpinigaitis et al., 2012; Leech et al., 2013; Mazzone et al., 2007). In support of this supramedullary control, many studies have reported the placebo effect of antitussive medications and even tussive agents (Eccles, 2002; Leech et al., 2012). Additionally, cough can be inhibited or abolished in anaesthesia (Nishino et al., 1990).

Cough as a mechanism of airway clearance

The motor output of cough can be defined as a movement sequence of inspiratory, compressive and expulsive phases (McCool, 2006). Some authors have supported the presence of an additional phase that follows the expiratory and is called the cessation or relaxation phase (Leith et al., 2011), but this is rarely used. In the inspiratory phase the laryngeal abductors open the glottis and the inspiratory muscles contract to expand the thorax and generate a high inspiratory volume (McCool, 2006). The expansion of thorax lengthens the fibres of the expiratory muscles and creates a good length-tension relationship for their contraction. In the compressive phase, the ventricular folds adduct, and the epiglottis covers the laryngeal inlet for 0.2 seconds (Rubin, 2010; Sant'Ambrogio et al., 1997). During this phase, the expiratory muscles contract almost isometrically and increase the subglottic, intra-abdominal, intrathoracic and intra-alveolar pressures (Addington et al., 2008; Poletto et al., 2004). In the expulsive phase (expiratory), the arytenoid cartilages rapidly abduct the glottis open (0.2-0.4 seconds), the expiratory muscles contract and dynamically compress the airways, and the air that passes from the trachea, larynx and vocal cords produces the characteristic cough sound, which also acts as a voiceprint (Widdicombe, 2008). This movement generates a high velocity of expiratory airflow that can reach 28,000 cm per second (85% the speed of sound) (McCool, 2006).

The theories of mucus mobilisation through coughing are mainly based on mechanical principles, *in vitro* and animal models. The effectiveness of cough to remove airway secretions is attributed to both generating adequate expiratory airflow and dynamically compressing the airways. Airflow transfers kinetic energy to the mucus layer of the airways and under specific conditions can generate mucus movement in the airflow's direction (Benjamin et al., 1989; Clarke et al., 1970; Kim et al., 1986a; Kim et al., 1987; Kim et al., 1986b; Ntoumenopoulos, 2008; Volpe et al., 2008). The interaction between the airflow and mucus follows the two-phase gas-liquid interaction from fluid mechanics, which is, in theory, influenced by the Reynolds number (Equation 1) (Fontana, 2008). According to *in vitro* studies, the cephalic mobilisation of mucus, and therefore the effectiveness of cough, requires a Peak Expiratory Flow (PEF) to Peak

Inspiratory Flow (PIF) ratio (PEF:PIF) ≥ 1.1, or an Expiratory Flow (EF) minus Inspiratory Flow (IF) difference (EF-IF) ≥ 17 L/min (Kim et al., 1986b; Volpe et al., 2008).

$$Re = \frac{2V\rho}{\pi r \eta}$$

Equation 1. The Reynold’s number (Re) (dimensionless).

Rate of the airflow (V), gas density (ρ), mucus viscosity (η), airway radius (r), constant (π).

The compression of the airways also influences the expiratory airflow. According to the wave speed theory, during expiration the pressure that is generated in the alveoli decreases downstream (towards the mouth) within the airways due to airway resistance (friction loss). In the level where the intrabronchial pressure equals the intrapleural pressure, an equal pressure point is reached. Downstream (towards the mouth) of the equal pressure point the airways tend to collapse, while upstream (towards the alveoli) the airways are distended (Pedersen and Butler, 2011). During the expiratory phase of cough and as the air volume decreases, the equal pressure point moves downstream. The decrease of the upstream pressure equals the elastic recoil of the lungs and governs the flow rate for the upstream segment (Equation 2) (Fontana, 2008). When the maximum expiratory flow is achieved, any additional expiratory effort or increase in pressure does not change the flow of the upstream segment but further dynamically compresses the downstream segment. Although the highest shearing forces develop in this area of airway compression and the maximum flow can be estimated (Equation 3), this is a dynamic process and its actual value cannot be determined.

$$V = \frac{P_{el}}{R_{us}}$$

Equation 2. The rate of expiratory airflow (V) of the upstream segment.

Expressed as a function of the elastic recoil of the lungs (Pel) and resistance of the upstream segment (Rus).

$$V = A\left[\rho^{-0.5}\left(\frac{A\delta P}{\delta A}\right)\right]^{0.5}$$

Equation 3. The maximum expiratory airflow (V).

Expressed as a function of gas density (ρ), airway cross sectional area (A) and the specific elastance of the airway wall (AδP/δA).

Nevertheless, intrinsic factors also affect mucokinesis (Houtmeyers et al., 1999). The mucus can mobilise from airways of the tenth airway generation and higher (Kim et al., 1986a; Kim et al., 1986b; Scherer, 1981), when the mucus layer thickness is 10-15% of the airway diameter (Kim et al., 1986b), and according to the orientation of the airways (Kim et al., 1987). Moreover, mucus of lower viscosity moves with a lower airflow compared to mucus of higher viscosity (Clarke et al., 1970; King et al., 1989; Rubin, 2002; Trout et al., 1998; Volpe et al., 2008) and mucus of a given viscosity mobilises easier from lower-compliance lung areas to higher-compliance ones (Soland et al., 1987; Volpe et al., 2008). Although these mechanical principles derive from models and cannot directly apply to *in vivo* situations, they do support the generation of hypothesis about the mechanisms of effectiveness for some non-pharmacological cough techniques.

Cough as a symptom

Cough is an important and common respiratory symptom worldwide and its impact on the healthcare systems and individuals is profound (Morice, 2008). The prevalence of cough varies according to environmental factors, genetic factors, and co-morbidities (Morice, 2008). Based on an interview-led survey with 18,277 respondents (20-48 years old), Dublin, Ireland, had the highest prevalence of productive cough (27.4%) and Cambridge, UK, the lowest (3.8%) compared to cities from 16 countries (Janson et al., 2001). In another community-based study across 36 general practices at Yorkshire, UK, 12% of individuals reported that they had coughing bouts daily or weekly within the preceding two months (Ford et al., 2006). Cough is the most common reason for visiting general practitioners (Niimi, 2007) and the majority of the individuals who consult a general practitioner about cough are prescribed medications and have at least one hospital specialist visit (Everett et al., 2007). In 2002, the market of over the counter cough medications was £92.5 million in the UK and $328 million in the USA (Morice, 2002). Effects to individuals are also important. An internet survey conducted by the European Lung Foundation in 29 European countries, showed that cough lasting for >8 weeks impacted the quality of life and the ability of individuals to undertake activities (Chamberlain et al., 2015).

Distinct types of cough categorisation have been suggested. The classification of cough as a symptom based on its duration is common (Irwin et al., 2017), although the duration thresholds are arbitrary selected (McGarvey, 2008). According to this, acute cough lasts <3 weeks, sub-acute cough lasts 3-8 weeks, and chronic cough lasts >8 weeks in duration (Irwin and Madison, 2000). Still, a literature review identified that most studies about chronic cough use the threshold of ≥3 months (n=55), less frequently they use ≥8 weeks (n=3), or the duration is not recorded (n=11) (Song et al., 2016). Cough is also clinically classified as dry or wet, where wet or productive cough is accompanied by production of sputum (McGarvey, 2008). However, measuring sputum volume is challenging, as the amount that is swallowed cannot be assessed (McGarvey, 2008). Other ways of clinically assessing cough as a symptom include cough frequency, intensity, severity and associated impact on the patient's life (Birring and Spinou, 2015).

Non-pharmacological management

The role of cough augmentation

Cough is a vital mechanism for the expectoration of airway secretions in the presence of mucociliary dysfunction, phlegm or excessive amounts of mucus (Foster, 2002; Houtmeyers et al., 1999). Individuals who present impaired and ineffective cough are at high risk of respiratory infection and respiratory failure (Bach and Saporito, 1996; Dohna-Schwake et al., 2006). Patients with decreased respiratory airflows, such as those with respiratory muscle weakness, neuromuscular disease (e.g. amyotrophic lateral sclerosis or Duchenne muscular dystrophy), spinal cord injury, or patients who are intubated and mechanically ventilated, can require assistance for effective airway clearance (Gregoretti et al., 2013; Schroth, 2009). Moreover, neurological conditions such as Parkinson's disease, stroke, and multiple sclerosis might also present reduced cough, due to motor output impairment or sensory issues (Aiello et al., 2008; Ebihara et al., 2003; Ishii and Mashimo, 2017). These individuals have higher risk of aspiration and resulted pneumonia, whilst objective airflow measures of voluntary cough can be used to estimate their aspiration risk (Pitts et al., 2010).

Cough effectiveness can be described as the ability of cough to promote airway secretions and noxious particles downstream (towards the mouth). In the expiratory phase of cough, the initial peak expiratory flow influences the effectiveness of airway clearance (McCool, 2006). Assessment of the peak expiratory flow during coughing, known as Peak Cough Flow (PCF), has been commonly used to measure the effectiveness of cough. Healthy adults generate a peak expiratory flow of 360-840 L/min (Bach and Saporito, 1996; Fontana et al., 1997; Smith et al., 2012), whilst the PCF of 160-180 L/min is the proposed threshold for effective airway clearance (Bach and Saporito, 1996). Successful extubation also correlates with the PCF, although its exact cut-off points present small variations amongst studies (range from 35 to 70 L/min) (Beuret et al., 2009; Duan et al., 2016; Salam et al., 2004). Furthermore, the risk of pneumonia in acute stroke reduces with higher PCF on voluntary cough and to a lesser extent with higher PCF on cough reflex (Kulnik et al., 2016).

Cough augmentation techniques

Cough augmentation could be beneficial for patients who cannot generate adequate expiratory airflows to exceed the proposed PCF threshold for effective airway clearance. There is a variety of cough augmentation techniques (Table 1), which are usually applied by physiotherapists or trained carers. Their aim is to increase the initial inspiratory volume, the expiratory flow, or improve all the components of cough.

Manual or mechanical hyperinflation

Hyperinflation uses the manual or mechanical delivery of positive airway pressures during inspiration via a non-resuscitation bag (manual hyperinflation, bagging, air stacking) or positive pressure ventilator (mechanical hyperinflation or insufflation), respectively. The aim of the hyperinflation is to increase the inspiratory volume during the initial phase of the cough and consequently improve the expiratory flow at the expulsive phase. Therefore, hyperinflation techniques could be appropriate for patients presenting reduced vital capacity or weak inspiratory muscles. Studies show that patients with neuromuscular disease, amyotrophic lateral sclerosis, Duchenne muscular dystrophy and spinal cord injury present higher PCF when using hyperinflation compared with unassisted cough (Kang et al., 2005; Kang et al., 2006; Sarmento et al., 2017; Toussaint et al., 2009).

Manually assisted cough

The manually assisted cough is a group of techniques that involve manual pressure being applied to the patient’s chest and/or abdominal wall. According to the area of the force application, the manually assisted cough is generally categorised into three types: thoracic compression or anterior chest wall compression, abdominal compression or thrust, and the combination of thoraco-abdominal compression. The physiological rationale of the manually assisted cough is that it produces an external mechanical force that can partly substitute the pressure generation of the expiratory muscles and increase the PCF. Hence, an expiratory flow bias is generated, which results to mucus mobilisation and secretion clearance via the two-phase gas-liquid interaction. Manually assisted cough can be applied to patients with expiratory muscle weakness who generate decreased intra-abdominal and intrathoracic pressures and consequently low PCF values. It can be used both alone and in combination with other techniques. Most studies show that it can successfully increase PCF compared to unassisted cough in patients with respiratory muscle weakness, neuromuscular disease, amyotrophic lateral sclerosis, Duchenne muscular dystrophy and spinal cord injury (Bach, 1993, 2004; Mustfa et al., 2003; Toussaint et al., 2009; Trebbia et al., 2005). However, there is no improvement when patients also have scoliosis (Chatwin et al., 2003; Sivasothy et al., 2001). The benefits seem greater for individuals who present lower unassisted PCF values and when this technique is combined with higher inspiratory volume prior to the manoeuvre (Mustfa et al., 2003; Sivasothy et al., 2001).

Mechanical insufflation-exsufflation / Hyperinflation and manually assisted cough

The mechanical insufflation-exsufflation resembles the full cycle of cough, by initially delivering positive airway pressure (insufflation), controlling a pause (compression), and then applying negative airway pressure (exsufflation). A combination of hyperinflation and manually assisted cough can also be used with the aim to improve both the inspiratory and expulsive phases of cough. In patients with respiratory muscle weakness and neuromuscular disease, the mechanical insufflation-exsufflation produces higher PCF compared to unassisted cough and other cough augmentation techniques (Bach, 1993; Bach et al., 1993; Kim et al., 2016; Morrow et al., 2013; Mustfa et al., 2003; Sancho et al., 2017). Interestingly, some evidence indicate higher effectiveness from the combination of the mechanical insufflation-exsufflation with manually assisted cough, whilst other show that PCF does not significantly increase for patients who generating PCF of 300 L/m with a hyperinflation technique and manually assisted cough (Kim et al., 2016; Lacombe et al., 2014). This limitation during exsufflation could occur if the patient's cough effort and manually assisted cough exceeds the vacuum capacity of the pressures from the delivery device, thus transiently decrease the PCF potential (Lacombe et al., 2014).

Abdominal electrical stimulation and abdominal binding

Direct electrical stimulation of the abdominal muscles during expiration aims to improve the expulsive phase of cough. The additional stimulation can theoretically improve the contraction of abdominals, therefore increase the PCF and cough effectiveness. This technique has been used in patients with amyotrophic lateral sclerosis and spinal cord injuries. In patients with spinal cord injury, coughs with superimposed electrical stimulation of the abdominals increase PCF values and in some cases are approximately as effective as manually assisted cough (Butler et al., 2011; Jaeger et al., 1993; Laghi et al., 2017). Following the same physiological rational, a fixed abdominal binding, has been used in a few studies on patients with spinal cord injuries (Bodin et al., 2005). However, the binding is applied throughout all cough phases, thus it seems unlikely that a fixed pressure to abdominals could result in significant flow changes in a highly dynamic motor event such as coughing. Indeed, the effectiveness of abdominal binding is questionable. Wearing an abdominal binder did not improve the stimulated cough flows or respiratory pressures (Butler et al., 2011; Lin et al., 1998), although a study on patients with spinal cord injury showed that the triple-strap abdominal binders produced significantly higher compared to single-strap abdominal binders (Julia et al., 2011). The combination of binding and electrical stimulation also showed a significant increase on cough effectiveness (Lin et al., 1998). However, relevant studies include small sample sizes and electrical stimulation was associated with some adverse effects, such as transient inconsequential lower extremity spasms (Laghi et al., 2017).

Respiratory muscle training

Respiratory muscle training uses threshold resistance devices to improve the inspiratory or expiratory muscle strength and endurance, and therefore the corresponding cough phase. Using this type of training could theoretically increase the PCF and cough effectiveness. Patients with Parkinson's disease who underwent training of expiratory muscles showed significant improvements in maximum expiratory pressures and safe swallowing (Troche et al., 2014). Despite respiratory muscle training showing increase to the maximum expiratory pressures of patients with multiple sclerosis and spinal cord injury, the PCF was not significantly different to unassisted cough (Tamplin and Berlowitz, 2014; Westerdahl et al., 2016), or increase was limited to multiple sclerosis patients with moderate and not mild levels of disability (Chiara et al., 2006). Furthermore, a randomised control pilot showed that the muscle function and PCF improve with time in patients following acute stroke, irrespective of the additional training (Kulnik et al., 2015).

The role of cough control

Asthma, bronchitis, gastro-oesophageal reflux disease, and the upper airway cough syndrome are frequent causes of cough in patients with normal chest X-ray (Irwin et al., 2017). In the cases where there is no identifiable cause, cough is called idiopathic or refractory (Morice, 2013). However, a variety of respiratory diseases present cough as a cardinal symptom, such as the common cold, bronchiectasis, pulmonary fibrosis and interstitial lung diseases. The concept of cough hypersensitivity syndrome was proposed to represent high cough sensitisation, where the causes of chronic cough cannot be explained by the presence of clearly stated underlying diagnosis (Morice, 2013). For patients with refractory cough, cough control techniques could be a treatment option. These techniques have been recently investigated.

Cough control techniques

Non-pharmacological cough control techniques are groups of combined techniques that are tailored to the patient needs. They involve a mixture of patient education, voluntary control of cough, laryngeal hygiene and psycho-educational counselling (Table 1) (Vertigan et al., 2006), with the aim to activate or restore a possible dysfunctional inhibitory control of cough. There are small variations to the professionals who deliver the treatments, usually being trained physiotherapists or speech and language therapists (Chamberlain Mitchell et al., 2017; Vertigan et al., 2006). More specifically, patients receive education about their condition and cough reflex hypersensitivity, the ability to volitional control cough and the benefits of avoiding repeated coughing (Chamberlain Mitchell et al., 2017; Vertigan et al., 2006). Awareness, identification and avoidance of the triggers of cough and practicing controlling the urge to cough are based on the cough supramedulary control. Education also includes improvement on understanding and anticipation of urge to cough, and implementing cough control techniques using suppression or replacement (Vertigan et al., 2006). Distraction techniques such as swallowing, drinking small amounts of water and sucking sweets, change the sensory input, therefore could result in cough inhibition. In experimental studies, healthy adults who rinsed their mouth with sucrose solution (sweet) or inhaled menthol vapor significantly increased the cough threshold to capsaicin (Wise et al., 2012). It is possible that sweet taste stimulation has analgesic effects, triggers salivation and affects its composition, or affects airway secretion (Wise et al., 2014). Vocal cords hygiene reduces laryngeal irritation and improves hydration, thus decreases stimulation of the receptors of cough located in the larynx. Correcting the dysfunctional breathing by adopting a nose breathing pattern, relaxed throat breathing, pursed lips breathing, and vocal cord exercises could be appropriate for patients with dyspnoea. Psychological support focusses on improving the acceptance of a behavioural method. This can also increase the motivation to modify behaviours of over-awareness and reduce stress and anxiety. Additionally, setting realistic goals and practice has been suggested to influence the success of the treatment (Vertigan et al., 2006). Evidence from randomised controlled trials support a significant reduction of cough severity, cough frequency, and cough reflex sensitivity, and improvement in quality of life in patients with chronic cough who received treatment for cough control (Chamberlain Mitchell et al., 2017; Ryan et al., 2010; Vertigan et al., 2006).

Conclusion

Researchers and clinicians often isolate the extreme presentations of cough rather than seeing cough as a continuum. This review combines both the lower and upper extremes of the cough spectrum and for the first time comprehensively presents the non-pharmacological management of cough augmentation and cough control. Physiology indicates that some of the techniques could be beneficial in specific groups of patients and the hypothesised mechanism for their effectiveness is discussed. Most of the evaluations of the cough augmentation techniques showed an increase in the PCF compared to unassisted cough. However, most studies were cross-sectional and non-randomised, where the usual sequence of cough techniques (unassisted cough, hyperinflation, manually assisted cough and then mechanical insufflation-exsufflation) could have resulted in a high risk of bias. Additionally, most studies did not assess clinical outcomes such as survival, frequency of exacerbations and hospitalisation, or duration of hospital stay. These are important outcome measures that require further investigation. Fewer studies, but of higher quality, support the use of cough control in patients with chronic refractory cough, by utilising supramedulary control. These studies showed improvements in quality of life, cough frequency and other clinical outcomes (Chamberlain Mitchell et al., 2017; Ryan et al., 2010). Still, future studies need to investigate the potential mechanisms of effectiveness of these techniques and assess the contribution of individual components to overall effectiveness. In conclusion, non-pharmacological management of cough is an option to consider alongside medications or as a stand-alone treatment in managing the extremes of the cough spectrum.

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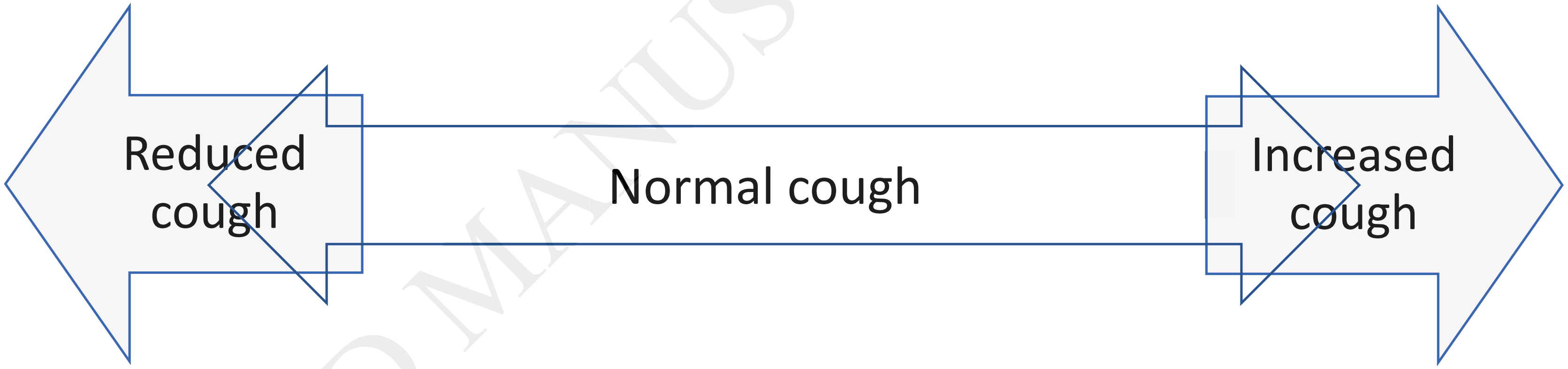

Figure 1. Diagram presenting the theoretical concept of cough as a spectrum.

There is an overlap between normal cough and its extremes, whilst these thresholds are not clearly defined.

Table 1. Non-pharmacological cough management techniques and their hypothesised mechanism of effectiveness.

Cough management technique	Hypothesised mechanism of effectiveness
Cough augmentation	
Manual or mechanical hyperinflation	Inspiratory phase
Manually assisted cough	Expiratory phase
Mechanical insufflator-exsufflator	Inspiratory and expiratory phase
Hyperinflation and manually assisted cough/exsufflator	Inspiratory and expiratory phase
Electrical stimulation	Expiratory phase
Respiratory muscle training	Inspiratory or expiratory phase (according to muscle group)
Cough control	
Education	Understanding of physiology and ability for voluntary control
Vocal cords hygiene and avoidance of irritant stimuli	Reduction and avoidance of cough sensory input
Breathing pattern retraining and other exercises	Distraction and alteration of sensory input
Psychological support and psycho-educational counselling	Improve motivation and facilitate realistic goals