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Mechanical insufflation-exsufflation and available funding for Canadian adult patients. A Canadian Thoracic Society Position Statement

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ABSTRACT

Many neuromuscular disease patient populations suffer from a weak, inadequate cough, which may lead to respiratory tract infections, respiratory failure, and increased mortality. Hospitalized neuromuscular disease patients are often treated with a mechanical insufflation-exsufflation (MI-E) machine to improve lung volume, promote mucociliary clearance and improve their respiratory health. Many of these patients require MI-E within their homes to maintain the benefits achieved in hospitals. Currently, a resource paper that outlines provincial funding avenues for home MI-E machines does not exist. Accordingly, Canadian Respiratory Health Professionals (CRHP) Leadership Council members formed a working group to propose and collate recommendations and resources for using MI-E in neuromuscular populations at home.

RÉSUMÉ

De nombreuses populations de patients atteints de maladies neuromusculaires souffrent d'une toux faible et inadéquate, ce qui peut entraîner des infections des voies respiratoires, une insuffisance respiratoire et une mortalité accrue. Les patients hospitalisés atteints d'une maladie neuromusculaire sont souvent traités avec un appareil d'insufflation- exsufflation mécanique (IE-M) pour améliorer leur volume pulmonaire, favoriser la clairance mucociliaire et améliorer leur santé respiratoire. Un grand nombre de ces patients ont besoin d'IE-M à domicile pour maintenir les bienfaits obtenus dans les hôpitaux. À l'heure actuelle, il n'existe pas de document de référence décrivant les possibilités de financement provincial pour les appareils d'IE-M à domicile. Par conséquent, les membres du Conseil de direction des Professionnels canadiens en santé respiratoire (PCSR) ont formé un groupe de travail pour proposer et assembler des recommandations et des ressources pour l'utilisation de l'IE-M chez les populations neuromusculaires à domicile.

SUMMARY OF KEY MESSAGES

1) Consensus machine settings for the mechanical insufflation-exsufflation (MI-E) are variable in the literature for adult patient populations. We recommend that clinicians titrate parameters to achieve an increased insufflation time and greater expiratory flow to produce a peak cough flow (PCF) of \geq 270 L/min, which produces an effective cough. We suggest combining MI-E with manually assisted cough techniques to increase PCF further if required. 2) Patients with amyotrophic lateral sclerosis who present with a weak cough (PCF <270 L/min) should be administered MI-E to effectively achieve a PCF that is strong enough to clear secretions. However, the application of MI-E may not be effective in bulbar amyotrophic lateral sclerosis due to the risk of upper airway collapse. 3) MI-E use in patients with Duchenne Muscular Dystrophy is recommended to improve the short-term sense of breathlessness and helps prevent the need for hospitalization, intubation and tracheostomy. 4) The use of MI-E in individuals with spinal cord injury may be beneficial for improving PCF. The addition of manually assisted cough may further increase cough strength. More research on the applicability of MI-E in this population is needed. 5) The use of MI-E in generalized neuromuscular disorder patients has been shown to improve PCF and vital capacity compared to other methods of assisted cough. The addition of a manually assisted cough further improves PCF. The use of MI-E also suggests the prevention of hospitalizations in generalized neuromuscular disorder patients. 6) We recommend using home MI-E by non-professional caregivers with generalized neuromuscular disorder patients as it is found to be safe and effective with adequate training. The precise amount and nature of training are unclear. 7) We recommend using MI-E in mechanically ventilated adult patients (> 18 years) to increase the volume of secretions expectorated compared to standard sterile suctioning techniques. 8) We strongly recommend that Canadians have equitable access to MI-E which requires provinces to prioritize available funding for home MI-E. Currently there are large gaps in funding sources throughout the country.

KEYWORDS

Cough assist; mechanical insufflator-exsufflator; secretion clearance; neuromuscular diseases; cough; insufflation; respiratory insufficiency; artificial respiration CONCLUSION: Available evidence supports the use of MI-E for multiple neuromuscular patient populations with a weak cough to prevent respiratory complications, including intubation, tracheostomy and hospitalizations. Such patients should have access to home-based MI-E.

Background

Cough is a vital reflex that protects the airways and lungs. A cough is triggered by an irritant, which leads to a cascade of coordinated events to clear the airway.¹ The pattern of the cough includes three phases. The first is the inspiratory phase that increases the lung volume to prepare for a cough. The second phase is the compression phase, which involves the closing of the larynx and increasing intrathoracic pressure due to abdominal muscle contraction. The final phase of the cough, the expiratory phase, starts with the glottis opening and air flowing at a high rate out of the lungs, intending to remove mucus or other debris.¹ It is necessary to have the coordination and participation of all factors involved in the cough to be as effective as possible. When this is not the case, looking for ways to supplement this vital reflex is necessary. The mechanical insufflator-exsufflator (MI-E) is one option.^{2–4}

A MI-E device is designed to help patients simulate a cough by applying a gradual positive pressure (insufflation), followed by a rapid switch over to negative pressure (exsufflation). The shift between the positive and negative pressure is quick and mimics a cough to move sputum upward and outward.⁴ The MI-E machine can be applied to many different types of patients using a facemask, mouthpiece or adapted to a patient's endotracheal or tracheostomy tube.⁴⁻⁶

The MI-E is one available tool within an arsenal of mechanical mucociliary clearance techniques. Benefits of regular MI-E use include more effective secretion clearance,⁷ reducing the risk of requiring a tracheostomy or endotracheal intubation when combined with manual chest physiotherapy compared to manual chest physiotherapy alone⁸ and an overall improvement in lung function.⁹ MI-E has been shown to clear secretions from the peripheral airways. This ability to mobilize deeper secretions is a limitation of traditional suctioning maneuvers because traditional methods only remove mucous from the central airways.⁴ Even though some authors argue against regular MI-E use in patients with neuromuscular disorders based on a lack of robust empirical evidence^{10,11} many national guidelines recommend using MI-E devices.^{11–13}

There is also debate surrounding the ideal settings for MI-E machines, ranging from manufacturer's parameters to population-specific protocols.^{3,14,15} Despite the debates regarding standardized clinical use and set parameters, many clinical services throughout the health care system use the MI-E with documented success. These settings include intensive care units, general medical and/or surgical units, rehabilitation units, long-term ventilation and weaning units.⁶

Less empirical evidence exists regarding the use of MI-E when patients are discharged into the community. Home MI-E is an option for many patients and is associated with a reduction in health service utilization,¹⁶ including

decreased hospitalizations and cost-savings.¹⁷ One consideration for routine home MI-E is the dedication of care providers that are required. This scenario can be labour intensive, especially during recurrent upper respiratory tract infections.¹⁸ Currently, MI-E usage varies across Canada, and MI-E machines are not widely available in hospitals or for home use.⁶ Often, MI-E is predominantly used in intensive care units and medical and/or surgical units. Improving education and expertise on a national scale might improve MI-E usage and promote consistent MI-E use.⁶ It was also identified that the provision of equipment was a limitation for expanding further use of MI-E.4,15 Finally, there is a scarcity of literature outlining what resources exist to support patients in the process of obtaining a MI-E for home use. The purpose of this article is to review the literature regarding MI-E benefits and risks, to provide recommendations for its use, and collate resources regarding provincial funding for home MI-E. The research question guiding this review is what publicly available information exists regarding the process to obtain a MI-E at home and what criteria need to be met by adult (>18 years of age) home care patients in each Canadian province or territory.

Methods

Two members of the Canadian Respiratory Health Professionals (CRHP) Leadership Council and a representative of the Saskatchewan cough assist task force comprised the team conducting a narrative review of the MI-E literature to address the issues regarding the use of MI-E in the community and identify potential funding sources for community MI-E machines for neuromuscular populations. The review focuses on disease processes that benefit from home MI-E, including any articles that discussed the cost of any part of the MI-E. Additionally, the working group completed an environmental scan, including publicly available web resources and professional networks, to identify any supplemental relevant information regarding costs and available funding from both government and non-government sources. Narrative reviews provide a broad overview of a topic to offer a scholarly critique of the literature to deepen one's understanding of a topic.¹⁹ Because this was not a systematic review, an evaluation of the included articles' methodological quality was not conducted, and a preferred reporting item for systematic review and meta-analysis (PRISMA) is not required. ^{20,21}

The working group focused on the following questions:

- 1. What is MI-E?;
- 2. Which specific adult disorders have evidence supporting a benefit from using a MI-E either for secretion clearance or improving lung volume?;

- What are the costs associated with community use of MI-E?;
- 4. What are the Canadian funding sources available to help cover the cost of community provision of a MI-E?; and
- 5. Are the gaps in funding likely to result in less effective treatment of the patient populations identified in question 2?

Results

What is MI-E?

The most commonly used MI-E machines in Canada are the CoughAssist (Philips Respironics, Pennsylvania) and the Pegaso (Dima Italia, Bologna, Italy). The MI-E's circuit consists of an antibacterial/antiviral filter, wide-bore tubing, male 22 mm connection and either a catheter mount for invasive connection (eg, tracheostomy), an oral facemask or a mouthpiece. The MI-E is set to either manual or automatic mode. Automatic mode is the preferred option in home settings without the presence of a trained health care professional. The machine can also have the settings locked to minimize accidental setting changes that could have safety implications for the patient.

There is debate surrounding the most appropriate parameters for the MI-E. Existing research indicates that increasing pressure above the manufacturer's recommended settings is safe and effective.¹⁴ A Canadian cross-sectional survey of Canadian units (eg, intensive cares, weaning centers) and concluded that the average inspiratory and expiratory pressures were 31 cmH₂O and -32 cmH₂O, respectively.¹⁵ Other resources have cited optimal pressures to be +/-35-40 cmH₂O using an interface at the mouth/nose.³ Other interfaces, such as one connected to artificial airways (eg, endotracheal and tracheostomy tube), require higher MI-E pressure as bench research indicates the more narrow the artificial airway's inner diameter is, the lower the peak expiratory flow for a given expiratory pressure.⁵ The goal of optimal MI-E pressures is to achieve a peak cough flow (PCF) ≥270 L/ min, which is considered the lowest threshold for effective secretion clearance in preventing respiratory morbidity.¹⁸ PCF is defined as the maximum airflow generated during a cough.⁴ Optimized insufflation time should be considered when targeting greater expiratory flows since allowing a deeper inspiration has been proposed to generate greater expiratory flow. It has recently been shown that a higher expiratory flow bias (expiratory flow greater than inspiratory) is more effective at moving airway secretions.²² MI-E machines can also be timed with manually assisted cough techniques, such as an abdominal thrust, to further increase peak cough flow and effectiveness of the overall airway clearance.^{2,4} MI-E machine also avoids airway damage that can be associated with suctioning, thus offering a non-invasive procedure to manage airway secretions.^{2–4}

Key Message 1:

Consensus machine settings for the MI-E are variable in the literature for adult patient populations. We recommend that clinicians titrate parameters to achieve an increased insufflation time and greater expiratory flow to produce a PCF of \geq 270, which produces an effective cough. We suggest combining MI-E with manually assisted cough techniques to increase PCF further, if required.

Which specific adult disorders have evidence supporting benefit from using a MI-E either for secretion clearance or lung volume recruitment?

Amyotrophic lateral sclerosis (ALS)

ALS is associated with degeneration of both upper and lower motor neurons, resulting in progressive weakness of the bulbar, thoracic, abdominal and limb muscles.²³ The weakening of the bulbar innervated musculature results in issues with swallowing, speech and airway protection. The involvement of cervical and thoracic segments results in weakness of the abdominal muscles and diaphragm.²⁴ Weak respiratory and bulbar innervated musculature results in an inability to clear pulmonary secretions, the potential for aspiration pneumonia or other severe respiratory complications. The European Federation of Neurological Societies has recommended the use of MI-E in ALS for clearing bronchial secretions, particularly during an acute chest infection.²⁵

In one study, MI-E increased PCF in stable patients with ALS to above the threshold of 2.7 L/s (162 L/min), the level agreed to by consensus of the study authors to effectively clear secretions.²⁶ In contrast, those with severe bulbar symptoms (described as having a maximum insufflation of >1 L and a PCF of less than 2.7 L/s [162L/min]) could not increase their PCF above the 2.7 L/s (162 L/min) clinical threshold, likely due to the collapse of the upper airways during MI-E exsufflation phase.²⁶ This collapse potentially renders the use of MI-E ineffective in this sub-population of individuals with ALS. MI-E is also not indicated in patients with a PCF of >4 L/min (as defined by the study authors) with a maximum insufflation by lung volume recruitment via a bag/valve interface. For these patients, cough flows are already strong enough to clear secretions effectively with manually assisted coughing alone.²⁶

MI-E has been compared to breath stacking (ie, the technique in which patients breathe in slow intervals, stacking one breath on top of the other) with a lung-volume recruitment bag in a randomized control trial with the primary outcome as patients' chest infection rates requiring the use of antibiotics and/or hospitalization.²⁷ No statistically significant difference was found between these two groups, which may indicate that the MI-E may not be superior in the prevention of respiratory infections in those with ALS. However, the breath stacking group subjects had a significantly higher baseline PCF compared with the MI-E group. The preexisting difference in PCF between groups may be responsible for the lack of a significant difference in preventing respiratory infections.

In hospitalized ventilator-dependent ALS patients with a cuffed tracheostomy admitted for a chest infection, the combination of tracheal suctioning and MI-E suggests superiority compared to tracheal suctioning alone. The combination of tracheal suctioning and MI-E showed improvements in saturation (S_pO_2), and lower peak inspiratory pressure and mean airway pressure measured by the mechanical ventilator.⁷ MI-E was also reported to be more comfortable than tracheal suctioning when clearing secretions.⁷

While other forms of assisted coughing have also been shown to be effective in improving PCF to >270 L/min (eg, breath stacking with a lung-volume recruitment bag with or without abdominal thrusts), using MI-E is often rated as being the most comfortable way to clear secretions in patients with both bulbar and non-bulbar ALS.²⁸ When compared to abdominal thrusts alone and spontaneous coughing alone, the use of MI-E is far superior in achieving a PCF considered to be effective for secretion clearance.²⁸ Additionally, certain MI-E machines have the option to add high-frequency oscillations to the inspiratory and expiratory phases. This option contributes no changes (increase or decrease) to the PCF beyond what is already occurring without the oscillations.²⁹

Key Message 2:

Patients with ALS who present with a weak cough (PCF <270 L/min) should be administered MI-E to effectively achieve a PCF that is strong enough to clear secretions. However, the application of MI-E may not be effective in bulbar ALS due to the risk of upper airway collapse.

Duchenne muscular dystrophy (DMD)

Patients with DMD initially present with progressive weakness of the axial skeletal muscles, with weakness extending into the muscles of respiration, resulting in an ineffective cough and respiratory complications. These complications are a major source of morbidity and mortality in the DMD population.³⁰ Short, single treatments of MI-E in stable patients with DMD indicates no changes in unassisted PCF but does decrease respiratory rate and improved rapid shallow breathing.³¹ The result suggests that MI-E usage may help to improve the subjective sensation of shortness of breath in patients with DMD.³¹

Another cohort study of DMD patients compared the natural course DMD between invasive and non-invasive ventilation (NIV) management and compared the causes of death in various management approaches. In the group which received NIV, MI-E as needed, and cardioprotective medications once left ventricular ejection fraction was $\leq 45\%$ (eg, beta-blockers, angiotensin-converting enzyme inhibitors) resulted in significantly longer survival when compared to the group receiving invasive ventilation. ^{32,33} This same study reported that using NIV combined with MI-E decreased the need for tracheostomy. ³²

Using MI-E in DMD patients allows them to be able to continue oral intake safely while preventing respiratory complications from potential aspiration events.³⁴ In this study, the MI-E was used 3-5 times daily and for emergencies in patients with PCF < 270 L/min. This protocol usage may help prevent the need for intubation and/or tracheostomy, thereby improving the quality of life in these patients with DMD.³⁴ Overall, MI-E is effective in preventing hospitalizations, pulmonary morbidity and avoiding the need for a tracheostomy in DMD patients requiring NIV.^{18,32}

Key Message 3:

MI-E use in patients with DMD is recommended to improve the short-term sense of breathlessness and helps prevent the need for hospitalization, intubation and tracheostomy.

Spinal cord injury (SCI)

Patients with SCI, especially those with quadriplegia (cervical level of injury), are at risk for respiratory secretion retention for various reasons. Patients with a higher level of SCI are at higher risk because of a complete or partial loss of innervation to the diaphragm and the abdominal muscles and respiratory accessory muscles.³⁵ Patients who retain a normally innervated diaphragm but have absent or partial innervation to the abdominal muscles may also be at risk because of a weakened cough.³⁶ The weakness of the respiratory musculature could lead to a poor ability to inspire and an ineffective cough, resulting in atelectasis and secretion retention.

MI-E, combined with movement therapies (eg, stretching, strengthening, joint mobilization), was found to help increase unassisted PCF, vital capacity and forced expiratory volume in the first second (FEV₁) in a cervical SCI patient population.³⁵ These results were compared to a control group with similar characteristics. However, even in the treatment group, the unassisted PCF after MI-E use was below the 270 L/min threshold (188 L/min).³⁵ Additionally, MI-E has improved peak expiratory flow in a cervical SCI population with a tracheostomy compared to traditional manual secretion clearance techniques.³⁷

The use of MI-E in SCI patients has also been investigated to prevent acute care admissions for respiratory complications. A retrospective cohort study found that SCI patients with cervical spine injury at C5 or higher may have had fewer admissions for respiratory tract infections when prescribed a MI-E for home use.³⁶ This trend did not quite reach statistical significance except when examined in those subjects with a significant smoking history. This study had a relatively small number of participants; therefore, statistical power may have been a factor in the lack of statistical significance achieved.

The availability of MI-E machines for SCI patients has been studied as well. Approximately half of the respondents to a practice questionnaire sent to health care professionals treating SCI individuals reported that they used a MI-E within their hospitals.³⁸ The same respondents reported that they were satisfied with using the MI-E machine because it was effective in helping to clear secretions. The main barrier identified to the use of MI-E was a lack of knowledge of its existence.³⁸ A lack of knowledge of the applicability of a MI-E in the SCI population may be responsible for its underutilization.

Key Message 4:

The use of MI-E in individuals with SCI may be beneficial for improving PCF. The addition of manually assisted cough may further increase cough strength. More research on the applicability of MI-E in this population is needed.

General neuromuscular disease (NMD)

The NMD category includes many individual diagnoses. Specific diagnoses may include ALS, a variety of muscular dystrophy forms, poliomyelitis, post-polio syndrome, spinal muscular atrophy, spinal cord injury, multiple sclerosis, cerebral palsy and Ulrich syndrome. A commonality amongst these diseases is that they tend to impact cough strength and the ability to achieve adequate inspiration. An ineffective cough may be due to weakness of the muscles of respiration, deformities in the thoracic cavity secondary to muscle imbalance or a combination of the two.³⁹ The use of MI-E has been demonstrated to produce a higher PCF than voluntary coughing alone and manually assisted cough in both adult and pediatric NMD populations.⁹

Some individuals with NMD require home mechanical ventilation secondary to their respiratory muscle weakness. In a four-year observational study, the daily use of MI-E in NMD patients helped to decrease the use of emergency services and prevent hospitalizations due to chest infection.⁴⁰ The same study also found that having non-professional trained caregivers provide the MI-E to the participants was safe and effective when expert physiotherapists and nurses appropriately trained caregivers.

In a randomized crossover trial, Kim and colleagues measured the PCF of NIV dependent patients with NMD without a respiratory tract infection. Patients had a more effective PCF when using MI-E compared to either a spontaneous cough or a maximal inspiratory capacity maneuver (with manual resuscitation bag) plus abdominal thrust.⁴¹ Adding an abdominal thrust to MI-E generated the highest PCF in NMD patients. However, in a similar population, MI-E was found not to be beneficial in those with a PCF > 300 L/min using insufflation by NIV along with a manually assisted cough. However, the use of MI-E alone or in addition to manually assisted cough was found to be significantly better than no cough intervention.⁴²

Both adults and children with NMD receiving nocturnal NIV and admitted to hospital with an acute respiratory tract infection can benefit from the use of MI-E for secretion clearance compared to those who receive standard physio-therapy treatment for secretion clearance.⁴³ Patients tolerated the treatment well, resulting in shorter treatment times when using the MI-E. Similar volumes of secretion were cleared in both groups, although using the MI-E was associated with higher levels of fatigue.⁴³

The use of MI-E in NMD patients admitted to the ICU with an impaired cough was found to improve the PCF, quantity of sputum and ease of sputum expulsion when compared to those receiving traditional physiotherapy interventions for secretion clearance.⁴⁴ This group included both patients with NMD and others with impaired cough (eg, COPD, cystic fibrosis, bronchiectasis). Additionally, using MI-E in hospitalized patients with NMD was found to prevent treatment failure (ie, requiring intubation) compared to traditional physiotherapy for secretion clearance.⁸ MI-E was also found to be well-tolerated by the participants in this study.⁴⁴

The effect of MI-E on the vital capacity of NMD patients has also been studied. Using MI-E can significantly improve

vital capacity in NMD patients when used twice daily for over a year.³⁹ Its continued use past the first year will help to maintain this improvement in vital capacity. This improvement is crucial in NMD patients since structural changes within the thoracic cavity can severely restrict lung expansion, and therefore, vital capacity, one of the biggest predictors for mortality in NMD.⁴⁵

Key Message 5:

The use of MI-E in generalized NMD patients has been shown to improve PCF and vital capacity compared to other methods of assisted cough. The addition of a manually assisted cough further improves PCF. The use of MI-E also suggests the prevention of hospitalizations in NMD patients.

Key Message 6:

We recommend using home MI-E by nonprofessional caregivers with generalized NMD patients as it is found to be safe and effective with adequate training. The precise amount and nature of training are unclear.

Mechanical ventilation

MI-E has recently been applied to the generalized mechanical ventilated (MV) population indicating preliminary benefits. Individuals receiving MV have impaired airway mucus clearance because endotracheal intubation inhibits the mechanisms for effective coughing.⁴⁶ Ineffective coughing is compounded by sedative use in MV patients, which further exacerbates airway mucous clearance. The standard methods for airway clearance in MV patients include a combination of respiratory physiotherapy (eg, positioning and manual techniques) and direct suctioning with a sterile catheter through the endotracheal tube to withdraw mucus located in the proximal airways.⁴⁷ Standard methods are also associated with complications, including mucosal trauma, pain, and transient respiratory and hemodynamic instability.^{48,49}

MI-E machines have the option to change the interface to support invasive connections (via endotracheal or tracheostomy tube) to mobilize secretions. Currently, small studies have outlined specific protocols, small benefits and negligible adverse events. Sánchez-García and colleagues⁵⁰ report 13 cases who had MI-E applied with an insufflation of +50 cmH₂O for 3 seconds and exsufflation of -45 cmH₂O for 4 seconds, 26 times during their course of recovery. The procedure was safe, well-tolerated and effective in visibly producing secretions in the proximal segment of the endotracheal tube.⁵⁰

More rigorous, randomized studies indicate similar results. Ferreira de Camillis and colleagues⁵¹ performed a parallel, randomized trial to assess the effectiveness of combining a MI-E with respiratory physiotherapy. The authors chose to apply pressures of $+40 \text{ cmH}_2\text{O}$ and $-40 \text{ cmH}_2\text{O}$ for insufflation and exsufflation for three sets of 10 cycles. The authors concluded that the addition of MI-E increased the mean weight of secretions removed with no complications.⁵¹ Nunes and colleagues⁵² performed a similar

randomized cross-over design with 4 sets of 4 respiratory cycles with MI-E pressures of either +30/-30 cmH₂O plus endotracheal suctioning (30S protocol), +50/-50 cmH₂O plus endotracheal suctioning (50S protocol), or endotracheal suctioning only. There were no adverse events or changes in physiological parameters (eg, peak airway pressure, heart rate, blood pressure). Using the 50S protocol removed the greatest volume of secretions.⁵² Preliminary research literature indicates the use for MI-E in the intensive care context. The use of MI-E on critically ill patients seems reasonably safe. This tool may be of value to health care professionals involved with critically ill, MV patients.

Key Message 7:

We recommend using MI-E in mechanically ventilated adult patients (> 18 years) to increase the volume of secretions expectorated compared to standard sterile suctioning techniques.

What are the costs associated with the community use of MI-E?

Several reports indicate that the use of MI-E may reduce health care costs.^{8,26,53,54} Despite these benefits, a minimal amount of peer-reviewed literature exists that describes the expenses, cost savings, reimbursement potential or reimbursement process for MI-E in home care patients in any context. A single study in the United-States and Italy population sought to establish an on-demand, cost-effective telephone-accessed MI-E feedback program in ALS patients.¹⁷ The authors described that MI-E rentals in 2010 cost an average of CAD \$22.06 (USD \$21.71, €16.33) per day and Medicare reimbursement of CAD \$406 (USD \$424, €301) (no time frame provided). However, the authors did not elaborate on any other specifications about the reimbursement process. Another article identified in this review also stated that MI-E rentals cost CAD \$13.51 (USD 13.29, €10 per day).⁴⁰ Additionally, costs and reimbursement practices cannot be extrapolated to other locations. The legislations and processes differ provincially and nationally. These discrepancies further exacerbate the notion that MI-E costs/ reimbursement practices are a major limitation in the widespread use of MI-E technology.⁴

The most common MI-E device in Canada is the Philips Respironics CoughAssist E70TM. As of April 2020, this machine retailed for approximately CAD \$5000 and can be obtained through several Canadian respiratory equipment vendors. The authors of this review directly contacted vendors to obtain information regarding the cost of required equipment; the costs reported are approximations as the prices are subject to change. The cost of an external battery (for increased mobility) is an additional CAD \$400. However, the battery is not required to operate the machine. There are also disposable items required for the MI-E. These include a bacteria filter (changed every 6 months), 6 feet of corrugated, reusable tubing, a 15 mm connector, and either an appropriately fitted mask, mouthpiece or the connector that directly attaches to the tracheostomy tube.

Table 1.	Cost	breakdown	of MI-E	device	Cough-Assist	E70	and related produ	ucts.

Cost (CAD)
COST (CAD)
\$5,000
\$400
\$18
\$2.67 (262 pieces for \$700)
\$55
\$55
\$6228

Abbreviations: MI-E, mechanical insufflation-exsufflation.

Replacing the disposables depends on the frequency of use, the volume of respiratory secretions expectorated, and the interface required (mask vs tracheostomy interface). Other add-on items can be purchased, including a stand for the machine and a foot pedal to operate the device on manual mode while keeping the hands free to do abdominal thrusts or other manual tasks. The approximate cost per item, per person, can be found in Table 1 and may vary by vendor.

Additional hidden costs to consider is that of external care providers to perform in-home MI-E, adapting the patient's home environment or the lost wages incurred by having a trained family member perform MI-E.55,56 Home care rates depend on the service provider's qualifications and will often depend on the patient's income. Depending on the frequency of the home-care visits, the costs could compound quickly. Currently, no study exists that specifically outlines costs related to home MI-E; however, many of these patients will require some form of ventilation for which caregiver cost has been researched. The overall cost of home MV was assessed in a Canadian longitudinal prospective observational cost analysis study.⁵⁷ Nonoyama and colleagues sought to determine private and public health care utilization and costs for home MV. The overall monthly median healthcare cost was CAD \$5275 (\$2291-\$10, 181) with \$2410 (58%) publicly funded; \$1609 (39%) family caregiving; and \$141 (3%) out-of-pocket (<1% third-party insurance). These results indicate that caregivers play a major financial role in ventilating patients 57 and, potentially, subsequent MI-E requirements. There is a minimal amount of published research on the costs associated with the community use of MI-E. Anecdotal information obtained from vendors suggests a heavy burden of cost for individuals not qualifying for coverage for a MI-E.

What are the available funding sources in Canada to help cover the cost of community provision of a MI-E?

The use of MI-E across Canada may be influenced by the costs associated with the machine and the required disposable equipment. The authors searched publicly available web resources and contacted professional colleagues to identify relevant information. The resulting information indicated that funding for MI-E machines varies between provinces and with the individual diagnosis. Table 2 outlines the details regarding the availability of provincial/territorial funding.

There are other sources of funding for MI-E available at a national level. Many of these are dependent on diagnosis

Province or Territory	Is MI-E provincially funded?	Who can prescribe?	Name of the funding program	Diagnoses that are funded	Other Criteria
British Columbia	Yes	Respirologist	Provincial Respiratory Outreach Program	NMD or chest wall restriction with hypercapnia, stable condition, normal PCO ₂ but does have cor pulmonale, nocturnal hypoventilation, severe supine dyspnea, or symptoms of alveolar hypoventilation (requirements for program qualification)	Require home ventilation or BiPAP
Alberta	No				
Saskatchewan	Yes	Respirologist, Physiatrist, Pediatrician, Neurologist, Rheumatologist	Saskatchewan Aids to Independent Living	Neuromuscular conditions, post-polio, SCI, or condition with weak respiratory muscles	Either ventilator dependent or at risk of becoming ventilator dependent. PCF of <270 L/min with LVR or manually assisted cough, and not be a resident of a special care home or acute care facility
Manitoba	No				
Ontario	Yes, but client is only given an annual grant and will need to pay any extra costs	Physician (preferably a Respirologist)	Ontario's Ventilator Equipment Pool	NMD, post-polio, SCI or a condition with weak respiratory muscles or paralysis	Individuals who qualify for the Assistive Devices Program, applicant is at risk of becoming ventilator dependent or is ventilator dependent, and has a PCF of <270 L/min with LVR or manually assisted cough
Québec	Yes, if they qualify	Respirologist, Neurologist, Respiratory Therapist, (Under PNAVD collective order)	Programme national d'assistance ventilative à domicile (PNAVD)	NMD, Kyphoscoliosis, Post-Polio Syndrome, SCI	Require home ventilation or BiPAP PCF <270 L/min Inability to perform LVR
Newfoundland/ Labrador	No				
Nova Scotia	Yes, if they qualify for social assistance.	Any. (Preferably Respirologists, Neurologists, Physiatrists)	Nova Scotia Department of Community Services	ALS/ MD/ MS	Restrictive pattern and PCF <270L/min
Prince Edward Island	No				
New Brunswick	Yes, if they qualify for social assistance	Physician. Preferably respirologist, intensivist or physiatrist	New Brunswick Social Development Health Services program	ALS / Motor Neuron Disease, DMD, SCI / Tetraplegia, Central Hypoventilation, Kyphoscoliosis, Polio / Post-Polio, Spinal Muscular Atrophy, Other degenerative NMD	PCF <200 L/min
Yukon	No				
Northwest Territories					
Nunavut	No				

as they are available through charitable organizations specific to a disease process (eg, ALS Society of Canada, Muscular Dystrophy Canada). Other funding sources include Workers' Compensation Board and provincial motor vehicle insurance providers for individuals who require the MI-E due to an injury from a work-related accident or motor vehicle collision, respectively. Individuals who have served in the Canadian Forces can also qualify for coverage through Veterans Affairs Canada. For Canadians who have treaty status, a MI-E can be obtained through Non-Insured Health Benefits. Other local charitable organizations have also provided funding for MI-E through their own application processes. Each of these organizations has criteria for funding, which may be subject to change. Some Canadians who have private insurance coverage may have (at least a proportion of) the MI-E covered. Still, coverage for a MI-E is quite variable depending on the insurance provider and the level of coverage purchased. It may require a prescription from a general physician or a specialist physician (eg, respirologist). Of note, just because these sources of funding exist does not mean that a patient would automatically qualify as each of these programs also has its own set of criteria for funding a MI-E.

It is important to understand that none of the identified funding sources for the MI-E machines cover the disposable equipment cost. Patients who require a home MI-E must purchase the disposable equipment themselves or seek reimbursement from a private health insurance company if their policy includes disposable equipment coverage. The lack of coverage for disposable equipment may encourage individuals to use the products for longer than recommended, leading to potentially increased risk of respiratory infection secondary to bacteria in the filter, tubing, or mask/tracheostomy interface. The integrity of the disposables may also become compromised over time due to frequent cleaning. This loss of integrity may result in a loss of pressure in the circuit and, therefore, less efficient overall treatment. There is inconsistency in available government funding for MI-E across Canada. There are other potential sources of funding for specific patients, but there still appear to be large gaps in the availability of coverage.

Key Message 8:

We strongly recommend that Canadians have equitable access to MI-E which requires provinces to prioritize available funding for home MI-E. Currently there are large gaps in funding sources throughout the country

Are the gaps in funding likely to result in less effective treatment of the patient populations identified as benefiting from MI-E?

Currently, no empirical literature exists to identify the number of patients who qualify for MI-E in Canada through the various sources identified. Additionally, no literature exists to quantify how many individuals have attempted to access funding sources (whether they were eligible or not). During the preparation of this manuscript and through the conversations with professional colleagues who provide MI-E treatment to patients, anecdotally, they report that they often do not attempt to apply MI-E with patients due to the minimal available funding. The literature focusing on MI-E use in Canada is limited to MI-E usage in acute care facilities rather than in the community or home. Additionally, the use of MI-E in acute care is variable within the geographical areas where it was studied.^{6,15} Further investigation into the community use of MI-E (eg, whether the availability of funding impacts influence prescribing trends of MI-E) is essential to understand better whether Canadians with impaired cough effectiveness are having their needs met for secretion clearance.

The available literature outlined in this narrative review supports the use of MI-E in many neuromuscular populations in both acute care and in the community. Therefore, having more consistent funding for MI-E machines across Canada is essential to ensure optimal care. Specifically, MI-E for home use in many neuromuscular patient populations may be important for preventing respiratory complications that result in high rates of hospitalization and potential mortality. Only six out of 13 Canadian provinces/territories have some government funding for community use of MI-E. The cost of the disposable equipment, potentially hiring of support staff to administer the MI-E and/or training of family, is not included in this funding, making the home use of MI-E very cost-prohibitive for those areas who do not have access to funding.

This review identified some other available sources of funding across Canada. These funding sources are mostly variable and not uniformly inclusive of all patients. Charitable lung health organizations, individuals who would benefit from the use of MI-E and health care professionals interested in secretion clearance in neuromuscular populations may need to lobby their provincial or territorial governments to create a funding program where they do not already exist. This document may be used in support of such lobbying efforts. There are provincial programs that have been developed with criteria for funding already laid out, which could be applied in other geographic areas of the country that do not already have funding sources available.

Limitations

The limitations of this paper are driven by the lack of available peer-reviewed literature regarding cost and access to MI-E for home care of neuromuscular disease patient populations. The researchers relied on their professional contacts to outline the process of obtaining a MI-E and its associated costs. Another limitation of this narrative review is that the search strategy is not exhaustive compared to a systematic review. However, our purpose was to select relevant literature to provide a broad overview of the topic and identify relevant information regarding costs for individuals and/or health care professionals.

Conclusion

The purpose of this article is to review the literature regarding MI-E and provide a collated resource regarding provincial funding for home MI-E. The results of this review outlined many disease processes that benefit from the continuous use of MI-E as they transition from hospitalization back to the community. The results of this review indicated that the process to obtain a MI-E for home use is difficult, and it is unclear what the cost of MI-E is to the individual since coverage varies across Canada. We hope this review may serve as a support for health care professionals and individuals to lobby efforts to mandate provincial funding for home MI-E.

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KH, LNP, and MZ report no conflicts of interest. Please reach out to the authors of this paper if you are interested in support to create a MI-E funding program in your provincial/territorial government.

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References

- Polverino M, Polverino F, Fasolino M, et al. Anatomy and neuro-pathophysiology of the cough reflex arc. *Multidiscip Respir Med.* 2012;7(1):5 doi:10.1186/2049-6958-7-5.
- Bach JR. Mechanical insufflation-exsufflation. Comparison of peak expiratory flows with manually assisted and unassisted coughing techniques. *Chest.* 1993;104(5):1553–1562. doi:10.1378/ chest.104.5.1553.
- Homnick DN. Mechanical Insufflation-Exsufflation for Airway Mucus Clearance. *Respir Care*. 2007;52(10):1296–1305.
- Chatwin M, Toussaint M, Goncalves MR, et al. Airway clearance techniques in neuromuscular disorders: A state of the art review. *Respir Med.* 2018;136:98–110. doi:10.1016/j.rmed.2018.01.012.
- Guerin C, Bourdin G, Leray V, et al. Performance of the coughassist insufflation-exsufflation device in the presence of an endotracheal tube or tracheostomy tube: a bench study. *Respir Care*. 2011;56(8):1108–1114. doi:10.4187/respcare.01121.
- Prevost S, Brooks D, Bwititi P. Mechanical insufflation-exsufflation: Practice patterns among respiratory therapists in ontario. *Can J Respir Ther.* 2015;51(2):33–38.
- Sancho J, Servera E, Vergara P, et al. Mechanical insufflationexsufflation vs. tracheal suctioning via tracheostomy tubes for patients with amyotrophic lateral sclerosis: a pilot study. *Am J Phys Med Rehabil*. 2003;82(10):750–753. doi:10.1097/01.PHM. 0000087456.28979.2E.
- Vianello A, Corrado A, Arcaro G, et al. Mechanical insufflationexsufflation improves outcomes for neuromuscular disease patients with respiratory tract infections. *American Journal of Physical Medicine and Rehabilitation*. 2005;84(2):83–88. doi:10. 1097/01.PHM.0000151941.97266.96.
- 9. Chatwin M, Ross E, Hart N, et al. Cough augmentation with mechanical insufflation/exsufflation in patients with

neuromuscular weakness. Eur Respir J. 2003;21(3):502–508. doi: 10.1183/09031936.03.00048102.

- Morrow B, Zampoli M, van Aswegen H, et al. Mechanical insufflation-exsufflation for people with neuromuscular disorders. *Cochrane Database Syst Rev.* 2013;(12):CD010044. doi:10.1002/ 14651858.CD010044.pub2.
- Auger C, Hernando V, Galmiche H. Use of Mechanical Insufflation-Exsufflation Devices for Airway Clearance in Subjects With Neuromuscular Disease. *Respir Care*. 2017;62(2): 236–245. doi:10.4187/respcare.04877.
- McKim D, Road J, Avendano M, Canadian Thoracic Society Home Mechanical Ventilation Committee, et al. Home mechanical ventilation: A Canadian Thoracic Society clinical practice guideline. *Can Respir J.* 2011;18(4):197–215. doi:10.1155/2011/139769.
- Strickland SL, Rubin BK, Drescher GS, et al. AARC clinical practice guideline: effectiveness of nonpharmacologic airway clearance therapies in hospitalized patients. *Respir Care*. 2013;58(12): 2187–2193. doi:10.4187/respcare.02925.
- Gomez-Merino E, Sancho J, Marin J, et al. Mechanical insufflationexsufflation: pressure, volume, and flow relationships and the adequacy of the manufacturer's guidelines. *Am J Phys Med Rehabil.* 2002;81(8):579–583. doi:10.1097/00002060-200208000-00004.
- Rose L, Adhikari NK, Poon J, et al. Cough Augmentation Techniques in the Critically Ill: A Canadian National Survey. *Respir Care*. 2016;61(10):1360–1368. doi:10.4187/respcare.04775.
- Mahede T, Davis G, Rutkay A, et al. Use of mechanical airway clearance devices in the home by people with neuromuscular disorders: effects on health service use and lifestyle benefits. *Orphanet J Rare Dis.* 2015;10:54 doi:10.1186/s13023-015-0267-0.
- Vitacca M, Paneroni M, Trainini D, et al. At home and on demand mechanical cough assistance program for patients with amyotrophic lateral sclerosis. *Am J Phys Med Rehabil.* 2010; 89(5):401–406. doi:10.1097/PHM.0b013e3181d89760.
- Bach JR, Ishikawa Y, Kim H. Prevention of pulmonary morbidity for patients with Duchenne muscular dystrophy. *Chest.* 1997; 112(4):1024–1028. doi:10.1378/chest.112.4.1024.
- Greenhalgh T, Thorne S, Malterud K. Time to challenge the spurious hierarchy of systematic over narrative reviews? *Eur J Clin Invest*. 2018;48(6):e12931 doi:10.1111/eci.12931.
- Jahan N, Naveed S, Zeshan M, et al. How to Conduct a Systematic Review: A Narrative Literature Review. *Cureus*. 2016; 8(11):e864 doi:10.7759/cureus.864.
- 21. Ferrari R. Writing narrative style literature reviews. *Medical Writing*. 2015;24(4):230–235. doi:10.1179/2047480615Z.00000000329.
- 22. Volpe MS, Naves JM, Ribeiro GG, et al. Airway Clearance With an Optimized Mechanical Insufflation-Exsufflation Maneuver. *Respir Care*. 2018;63(10):1214–1222. doi:10.4187/respcare.05965.
- Andersen T, Sandnes A, Brekka AK, et al. Laryngeal response patterns influence the efficacy of mechanical assisted cough in amyotrophic lateral sclerosis. *Thorax*. 2017;72(3):221–229. doi:10. 1136/thoraxjnl-2015-207555.
- Bach J, Upadhyaya N. Association of Need for Tracheotomy With Decreasing Mechanical In-Exsufflation Flows in Amyotrophic Lateral Sclerosis. Am J Phys Med Rehabil. 2018; 97(4):e20–e22. doi:10.1097/PHM.000000000000755.
- Andersen PM, Abrahams S, Borasio GD, EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis, et al. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)-revised report of an EFNS task force . Eur J Neurol. 2012;19(3):360–375. doi:10.1111/j.1468-1331.2011.03501.x.
- 26. Sancho J, Servera E, Diaz J, et al. Efficacy of mechanical insufflation-exsufflation in medically stable patients with amyotrophic lateral sclerosis. *Chest.* 2004;125(4):1400–1403. doi:10.1378/chest. 125.4.1400.
- 27. Rafiq MK, Bradburn M, Proctor AR, et al. A preliminary randomized trial of the mechanical insufflator-exsufflator versus breath-stacking technique in patients with amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Frontotemporal Degener*. 2015; 16(7-8):448–455. doi:10.3109/21678421.2015.1051992.

- Senent C, Golmard JL, Salachas F, et al. A comparison of assisted cough techniques in stable patients with severe respiratory insufficiency due to amyotrophic lateral sclerosis. *Amyotroph Lateral Scler.* 2011;12(1):26–32. doi:10.3109/17482968. 2010.535541.
- Sancho J, Bures E, de La Asuncion S, et al. Effect of High-Frequency Oscillations on Cough Peak Flows Generated by Mechanical In-Exsufflation in Medically Stable Subjects With Amyotrophic Lateral Sclerosis. *Respir Care.* 2016;61(8): 1051–1058. doi:10.4187/respcare.04552.
- Camela F, Gallucci M, Ricci G. Cough and airway clearance in Duchenne muscular dystrophy. *Paediatr Respir Rev.* 2019;31: 35–39. doi:10.1016/j.prrv.2018.11.001.
- Cesareo A, LoMauro A, Santi M, et al. Acute Effects of Mechanical Insufflation-Exsufflation on the Breathing Pattern in Stable Subjects With Duchenne Muscular Dystrophy. *Respir Care.* 2018;63(8):955–965. doi:10.4187/respcare.05895.
- Ishikawa Y, Miura T, Ishikawa Y, et al. Duchenne muscular dystrophy: survival by cardio-respiratory interventions. *Neuromuscular Disorders*. 2011;21(1):47–51. doi:10.1016/j.nmd.2010.09.006.
- Ishikawa Y, Bach JR, Minami R. Cardioprotection for Duchenne's muscular dystrophy. Am Heart J. 1999;137(5): 895–902. doi:10.1016/S0002-8703(99)70414-X.
- Miura T, Takami A, Makino M, et al. Rate of oral intake and effects of mechanical insufflation-exsufflation on pulmonary complications in patients with duchenne muscular dystrophy. J Phys Ther Sci. 2017;29(3):487–490. doi:10.1589/jpts.29.487.
- Lee Y, Kim J, Jin Y. The efficacy of pulmonary rehabilitation using a mechanical in-exsufflator and feedback respiratory training for cervical cord injured patients. *J Phys Ther Sci.* 2012;24(1): 89–92. doi:10.1589/jpts.24.89.
- Crew J, Svircev J, Burns S. Mechanical insufflation-exsufflation device prescription for outpatients with tetraplegia. J Spinal Cord Med. 2010;33(2):128–134. doi:10.1080/10790268.2010.11689687.
- Pillastrini P, Bordini S, Bazzocchi G, et al. Study of the effectiveness of bronchial clearance in subjects with upper spinal cord injuries: examination of a rehabilitation programme involving mechanical insufflation and exsufflation. *Spinal Cord.* 2006; 44(10):614–616. doi:10.1038/sj.sc.3101870.
- Schmitt J, Stiens S, Trincher R, et al. Survey of use of the insufflator-exsufflator in patients with spinal cord injury. J Spinal Cord Med. 2007;30(2):127–130. doi:10.1080/10790268.2007. 11753923.
- Stehling F, Bouikidis A, Schara U, et al. Mechanical insufflation/ exsufflation improves vital capacity in neuromuscular disorders. *Chron Respir Dis.* 2015;12(1):31–35. doi:10.1177/1479972314562209.
- Bento J, Gonçalves M, Silva N, et al. Indications and Compliance of Home Mechanical Insufflation-Exsufflation in Patients with Neuromuscular Diseases. Archivos de Bronconeumología (English Edition). 2010;46(8):420–425. doi:10.1016/S1579-2129(10)70100-2.
- Kim SM, Choi WA, Won YH, et al. A Comparison of Cough Assistance Techniques in Patients with Respiratory Muscle Weakness. *Yonsei Med J.* 2016;57(6):1488–1493. doi:10.3349/ymj. 2016.57.6.1488.
- 42. Lacombe M, Del Amo Castrillo L, Bore A, et al. Comparison of three cough-augmentation techniques in neuromuscular patients: mechanical insufflation combined with manually assisted cough, insufflation-exsufflation alone and insufflation-exsufflation

combined with manually assisted cough. *Respiration*. 2014;88(3): 215–222. doi:10.1159/000364911.

- Chatwin M, Simonds AK. The addition of mechanical insufflation/exsufflation shortens airway-clearance sessions in neuromuscular patients with chest infection. *Respir Care*. 2009;54(11): 1473–1479.
- 44. Saghebi S, Sharafeh S, Kharabian S, et al. The effectiveness of mechanical insufflator/exsufflator in sputum discharge among intensive care unit admitted patients. *Arch Crit Care Med.* 2017; In Press (In Press):e60468. doi:10.5812/accm.60468.
- 45. Phillips MF, Quinlivan RC, Edwards RH, et al. Changes in spirometry over time as a prognostic marker in patients with Duchenne Muscular Dystrophy. Am J Respir Crit Care Med. 2001;164(12):2191–2194. doi:10.1164/rccm2103052.
- Smina M, Salam A, Khamiees M, et al. Cough peak flows and extubation outcomes. *Chest.* 2003;124(1):262–268. doi:10.1378/ chest.124.1.262.
- Nakagawa N, Franchini M, Driusso P, et al. Mucociliary clearance is impaired in acutely ill patients. *Chest.* 2005;128(4): 2772–2777. doi:10.1378/chest.128.4.2772.
- Jongerden I, Rovers M, Grypdonck M, et al. Open and closed endotracheal suction systems in mechanically ventilated intensive care patients: a meta-analysis. *Crit Care Med.* 2007;35(1): 260–270. doi:10.1097/01.CCM.0000251126.45980.E8.
- 49. Puntillo K, Max A, Timsit J, et al. Determinants of procedural pain intensity in the intensive care unit. The Europain® study. *Am J Respir Crit Care Med.* 2013;189(1):131126070246006– 131126070246047. doi:10.1164/rccm.201306-1174OC.
- 50. Sánchez-García M, Santos P, Rodriguez-Trigo G, et al. Preliminary experience on the safety and tolerability of mechanical "insufflation-exsufflation" in subjects with artificial airway. *Intensive Care Med Exp.* 2018;6(1):8 doi:10.1186/s40635-018-0173-6.
- Ferreira de Camillis ML, Savi A, Goulart Rosa R, et al. Effects of Mechanical Insufflation-Exsufflation on Airway Mucus Clearance Among Mechanically Ventilated ICU Subjects. *Respir Care*. 2018; 63(12):1471–1477. doi:10.4187/respcare.06253.
- Nunes L, Rizzetti R, Neves D, et al. Mechanical insufflation/ exsufflation improves respiratory mechanics in critical care: Randomized crossover trial. *Respir Physiol Neurobiol*. 2019;266: 115–120. doi:10.1016/j.resp.2019.05.008.
- Bach JR. Continuous noninvasive ventilation for patients with neuromuscular disease and spinal cord injury. Semin Respir Crit Care Med. 2002;23(3):283–292. doi:10.1055/s-2002-33037.
- Winck J, Goncalves M, Lourenco C, et al. Effects of mechanical insufflation-exsufflation on respiratory parameters for patients with chronic airway secretion encumbrance. *Chest.* 2004;126(3): 774–780. doi:10.1378/chest.126.3.774.
- Dale CM, King J, Nonoyama M, CANuVENT group, et al. Transitions to Home Mechanical Ventilation: The Experiences of Canadian Ventilator-Assisted Adults and Their Family Caregivers. Ann Am Thorac Soc. 2018;15(3):357–364. doi:10. 1513/AnnalsATS.201708-663OC.
- Siewers V, Holmøy T, Frich JC. Experiences with using mechanical in-exsufflation in amyotrophic lateral sclerosis. *European Journal of Physiotherapy*. 2013;15(4):201–207. doi:10.3109/ 21679169.2013.834513.
- 57. Nonoyama ML, McKim DA, Road J, et al. Healthcare utilisation and costs of home mechanical ventilation. *Thorax*. 2018;73(7): 644–651. doi:10.1136/thoraxjnl-2017-211138.