

Supplementary material

Table 4. Summary of Key Findings of Studies of mechanical medical devices used for airway clearance

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			Mean age, years [min-max] Gender Type of cough assistance		Efficacy	Safety	Quality of life
Bach ³⁸ <i>In-patient</i>	1993	Observational, single-center	46 subjects with NMD ► 21 ventilators users (mean-use: 22.3 hours/day) 45.7±18.0 12 Male/9 Female Cough assistance: a. Unassisted b. Air-stacking c. Manually assisted d. MI-E	Comparison of CPF with unassisted, air-stacking, manually assisted cough and MI-E in ventilators users	CPF, L/min (n=21) a. 108.6±61.8 vs b. 202.2±64.2 vs c. 256.2±77.4 vs d. 448.2±61.2 p<.001 CPF value before MI-E vs after MI-E 104.4±54 vs 109.2±52.2, p=.09	Episodes of stomach distention reported (number not mentioned) No bleeding No pneumothorax No mediastinal emphysema	Not assessed
Sivasothy ³¹ <i>In-patient</i>	2001	Randomized controlled trial, single-center	29 subjects: – 9 healthy volunteers – 8 subjects with COPD – 12 subjects with NMD (8 without scoliosis, 4 with scoliosis) Healthy volunteers: 27 [17-71] COPD: 65 [52-74] NMD - scoliosis: 63 [27-73] NMD + scoliosis: 57 [44-66] 18 Male/11 Female Cough assistance: a. Baseline b. Manually assisted cough (MAC) c. MI-E d. In combination (MIE+MAC)	Compare CPF and cough expiratory volume of subjects treated by MAC versus MI-E versus in combination	CPF, L/min [min-max] Baseline vs MAC vs MI-E vs in combination Healthy volunteers (p-value not available in the publication): a. 668 [310-700] vs b. 624 [326-700] vs c. 676 [494-695] vs d. 624 [288-695] COPD (* p<.01): a. 370 [267-483] vs b. 226 [120-315]* vs c. 288 [218-370] vs d. 245 [218-370]* NMD without scoliosis (* p<.01): a. 104 [43-188] vs b. 185 [93-355]* vs c. 156 [61-247] vs d. 248 [110-343]* NMD with scoliosis: a. 288 [175-367] vs b. 193 [185-287] vs c. 231 [148-597] vs d. 362 [218-440]	Not reported	Not assessed

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			<i>Mean age, years [min-max]</i> <i>Gender</i> <i>Type of cough assistance</i>		Efficacy	Safety	Quality of life
Mustfa ³² <i>In-patient</i>	2003	Randomized controlled trial single-center	57 subjects: – 10 healthy volunteers – 21 subjects with bulbar ALS – 26 subjects with non-bulbar ALS <i>Mean age not specified</i> <i>38 Male/19 Female</i> <i>Cough assistance:</i> a. Unassisted b. Manually c. Exsufflation with MI-E d. Insufflation with MI-E e. In-exsufflation	Evaluate pulmonary function parameters with MAC and MI-E (CPF)	CPF, L/min (% increase/unassisted) Bulbar ALS: a. 178±61 b. 197±63 (11%) p<.01 c. 225±76 (26%) p<.001 d. 188±64 (6%) e. 212±75 (19%) p<.05 Non-bulbar ALS: a. 217±84 b. 244±83 (13%) p<.001 c. 279±87 (28%) p<.001 d. 226±86 (4%) e. 264±73 (21%) p<.001	Not reported	Not assessed
Chatwin ³³ <i>In-patient</i>	2003	Comparative study, single-center	22 subjects with NMD 19 age-matched controls <i>25±13 [10-56], median 21</i> <i>16 Male/6 Female</i> <i>Cough assistance:</i> a. Unassisted-cough b. Physiotherapist-assisted cough c. Non-invasive ventilator-assisted cough d. Exsufflation-assisted cough e. In-exsufflation assisted cough	CPF and strength of cough, distress and comfort (rated by subject)	CPF, L/min Treated group vs age-matched group, <i>Mean (95% CI)</i> a. 169 (129-209) vs 578 (508-648) b. 188 (146-229) vs 587 (512-663) c. 182 (147-217) vs 565 (495-635) d. 235 (186-284) vs 633 (570-695) e. 297 (246-350) vs 629 (565-603) Variance analysis for intervention: treated group p<.001 and age-matched group p<.001 Strength of cough (visual analogue scale in cm) Treated group vs age-matched group, <i>Mean (95% CI)</i> a. 5.4 (5.2-6.7) vs 7.0 (6.4-7.7) b. 5.9 (5.2-6.7) vs 7.7 (7.1-8.3) c. 5.8 (4.8-6.8) vs 7.2 (6.5-7.9) d. 6.9 (5.3-7.0) vs 7.9 (7.3-8.5) e. 7.3 (6.6-8.0) vs 8.1 (7.5-8.6) Variance analysis for intervention: treated group p<.001 and age-matched group p<.001	No adverse event observed	Comfort and distress Authors reported no significant change from baseline in results for comfort or distress of intervention on the VAS (No data reported in the publication, no p-value available)

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			Mean age, years [min-max] Gender Type of cough assistance		Efficacy	Safety	Quality of life
Miske ³⁹ <i>Out-patient</i>	2004	Observational, retrospective data, single-center	62 children with NMD <i>Range of ages at introduction of MI-E use: 0.25-28.6, median 12.6 years</i> <i>34 Male/28 Female</i> <i>Cough assistance: MI-E</i>	Description criteria	Reported by caregivers 5 children experienced reduction in the frequency of pneumonia 4 subjects experienced improvement in chronic atelectasis	6 subjects discontinue treatment: - 1 on parent advice - 2 chose to use other devices (1 with tracheostomy thought it contributed to her chronic abdominal pain, other chest discomfort) - 3 subjects thought that the device was ineffective or unpleasant No episode of pneumothorax or pulmonary hemorrhage No episode of symptomatic reflux One subject experienced premature ventricular contractions (initial use)	Not assessed
Winck ³⁶ <i>In-patient</i>	2004	Comparative, single-center	29 subjects - 7 subjects with NMD - 13 subjects with ALS - 9 subjects COPD <i>NMD: 29 [26-49] ALS: 55 [47-68] COPD: 69 [54-73]</i> <i>21 Male/8 Female</i> <i>Cough assistance: MI-E</i>	Tolerance and effect on breathing pattern (CPF, oxygen saturation, ...)	CPF, L/min <i>baseline vs MI-E 40 cmH₂O</i> NMD: 180 [150-275] vs 220 [190-300] p<.05 ALS: 170 [128-300] vs 200 [170-352] p<.001 COPD: 250 [173-288] vs 275 [195-315] (no p-value available in the publication) S_{po2}, % <i>baseline vs MI-E 40 cmH₂O</i> NMD: 94 [92-96] vs 98 [97-98] p<.001 ALS: 94 [94-95] vs 98 [97-98] p<.001 COPD: 92 [91-94] vs 97 [95-97] p<.02	Subject declaration No abdominal distention or vomiting No blood-streaked sputum No chest pain	Subject declaration No discomfort
Vianello ⁴⁰ <i>In-patient</i>	2005	Observational, single-center (historical comparison)	11 subjects with NMD 16 subjects with NMD (historical comparison group) <i>34.91±17.28 39.75±21.56</i> <i>7 Male/4 Female 12 Male/4 Female</i> <i>Cough assistance: a. MI-E b. conventional chest physical treatment</i>	Treatment failure defined by: administration of cricothyroid, minitracheotomy or endotracheal intubation	Treatment failure, n <i>MI-E vs conventional chest physical treatment</i> 2 vs 10 p=.047 Hospital stay, days <i>MI-E vs conventional chest physical treatment</i> 20.5±20 vs 19.8±17, p=.93	1 stomach distension episode in 1 subject 1 mild nasal bleeding in 1 subject	Not assessed

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			Mean age, years [min-max] Gender Type of cough assistance		Efficacy	Safety	Quality of life
Fauroux ⁴¹ <i>In-patient</i>	2008	Observational, single-center	17 children with NMD [5-18] 12 Male/5 Female Cough assistance: MI-E	Pulmonary function parameters Tolerance	SNIP, cm H₂O Baseline vs MI-E 40 cm H ₂ O 29±19 vs 31±20 p=.046 CPF, L/min Baseline vs MI-E 40 cm H ₂ O 162±97 vs 192±99 p=.02 P_{icCO₂}, mmHg Baseline vs MI-E 40 cm H ₂ O 39.9±3.8 vs 37.8±4.7 p<.001 Vital capacity, L Population vs MI-E 40 cm H ₂ O 1.04±1.13 vs 1.87±1.04 (no p-value available)	No abdominal distension No gastroesophageal reflux No chest pain or discomfort	Respiratory comfort VAS/100 73±21 vs 83±19, p=.02
Chatwin ³³ <i>In-patient</i>	2009	Randomized controlled trial, single-center	8 subjects with NMD <u>Group 1:</u> day 1 morning without MI-E and afternoon with MI-E day 2 morning with MI-E and afternoon without MI-E <u>Group 2:</u> day 1 morning with MI-E and afternoon without MI-E day 2 morning without MI-E and afternoon with MI-E 22.25 [4-44] 6 Male/2 Female Cough assistance: MI-E + standard airway clearance	Compare current respiratory physiotherapy practice without MI-E to current respiratory physiotherapy practice with MI-E on pulmonary function parameters (S _{pO₂} , P _{icCO₂}) Subject satisfaction	No difference in mean heart rate, S _{pO₂} et P _{icCO₂} (no data reported in the publication) Treatment time, min [min-max]: Before MI-E vs after MI-E 30 [0-27] group 1 vs 47 [0-35] group 2 p=.03	Not assessed	Fatigue, VAS cm The lower the score the more favorable the outcome Before MI-E vs after MI-E 3.2±2.2 group 1 vs 5.1±2.6 group 2 p=.005 No statistical difference in comfort breathlessness or mood is reported in the publications (data available on figure in publication)

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			Mean age, years [min-max] Gender Type of cough assistance		Efficacy	Safety	Quality of life
Senent ³⁷	2011	Comparative, single-center	16 subjects with ALS 9 bulbar vs 7 non-bulbar 63 [57-68] 12 Male/4 Female Cough assistance: Cough manual techniques: a. Unassisted cough b. Coached unassisted cough c. Coached unassisted cough with abdominal thrust. Cough instrumental techniques d. Abdominal thrust + air-stacking e. Abdominal thrust + subject's bi-level pressure ventilator with its usual settings f. Abdominal thrust + subject ventilator IPAP of +30 cm H ₂ O g. In-exsufflator	CPF responses of bulbar and non-bulbar subjects Perception of techniques by subjects and physiotherapists	<u>CPF (min-max), L/min</u> a. 84 (35-118) b. 79 (36-142) c. 104 (80-140) d. 284 (146-353) e. 212 (99-595) f. 233 (100-389) g. 488 (243-605) Difference between manual techniques and instrumental techniques: p<.001 No different between each instrumental technique No different between each manual techniques No different between bulbar and non-bulbar group (no actual p-value available in publication)	<u>Six months follow-up:</u> 3 subjects developed pneumonia and 1 died (subjects were in group e) 1 subject died in palliative care	Not assessed

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			Mean age, years [min-max] Gender Type of cough assistance		Efficacy	Safety	Quality of life
Moran ⁴² <i>Out-patient</i>	2013	Observational, retrospective data, single-center	10 children with NMD 9.87 [1.4-18.1] 7 Male/3 Female Cough assistance: MI-E	Effects of home MI-E on admission rates, admission details, length of stay and ventilation requirements Impact of MI-E on the life-style of child and family	<p>Time in hospital (days) (95% CI) <i>Before MI-E vs after MI-E</i> 6 months: 39.0±30.7 vs 9.3 ±10.9 (95% CI 2.8-56.6) p=.04 12 months: 43.7±35.6 vs 13.3±12.6 (95% CI 4.7-56.2) p=.03</p> <p>Hospital admission respiratory (n) (95% CI) <i>Before MI-E vs after MI-E</i> 6 months: 1.6±1.5 vs 1.1±1.2 (95% CI -0.9-1.7) p=.45 12 months: 2.0±1.8 vs 1.7±1.8 (95% CI -1.4-1.9) p=.69</p> <p>Time in intensive care unit (days) (95% CI) <i>Before MI-E vs after MI-E</i> 6 months: 17.7±19.1 vs 2.1±4.8 (95% CI -1.1-32.3) p=.06 12 months: 19.9±22.3 vs 4.6±7.3 (95% CI -1.0-31.6) p=.06</p> <p>Invasive ventilation time (hours) (95% CI) <i>Before MI-E vs after MI-E</i> 6 months: 128.2±165.6 vs 0 (95% CI -24.9-281.4) p=.09 12 months: 170.8±256.6 vs 18.2±48.2 (95% CI -46.4±351.6) p=.11</p> <p>Non-invasive ventilation time (hours) (95% CI) <i>Before MI-E vs after MI-E</i> 6 months: 276.5±268.9 vs 56.5±94.4 (95% CI -57.9±497.9) p=.10 12 months: 278.0±267.9 vs 82.8±102.4 (95% CI -58.4-448.8) p=.11</p>	No adverse event observed	Caregivers reported size and awkwardness of the device and its inability to run from battery power
Lacombe ³⁴ <i>In-patient</i>	2014	Randomized controlled trial, single-center	18 subjects with NMD 32.8 [21-68] 13 Male/5 Female Cough assistance: a. MI-E b. MI-E+MAC c. IPPB+ MAC	Compare CPF using three techniques that combine inspiratory and expiratory support: MI-E+MAC, MI-E and IPPB+MAC, Comfort and effectiveness evaluated with a visual analog scale	<p>CPF L/min highest with IPPB+MAC than with MI-E+MAC (p=.01) or MI-E alone (p=.030)</p> <p>(data not available, represented on figure in publication)</p> <p>Effectiveness (VAS cm) <i>MI-E vs IPPB+MAC vs MI-E+MAC</i> 6.4 (4.8-8.2) vs 8.3 (7.2-9.0)* vs 8.5 (6.2-9.0)* * p<.05 compared to MI-E alone</p>	Not assessed	Comfort (VAS cm): <i>MI-E vs IPPB+MAC vs MI-E+MAC</i> 6.4 (5.5-7.0) vs 7.0 (6.0-8.5) vs 6.6 (5.8-8.0) (not significant, no actual p-value reported in the publication)

First Author	Year	Study design	Population	Objectives and outcome measures	Key findings		
			Mean age, years [min-max] Gender		Efficacy	Safety	Quality of life
			In-patient/out-patient Type of cough assistance				
MI-E = Mechanical in-exsufflation IPPB = Intermittent Positive Pressure Breathing MAC = Manually assisted cough CPF = Cough peak flow ALS = Amyotrophic lateral sclerosis COPD = Chronic obstructive pulmonary disease NMD = Neuromuscular disease							

Table 5. Research strategy

1 – Bibliographics databases

Study type / subject Terms used		Period	Number of references
LUNG EXPANSION			
Recommendations		No limit – 10/2014	11
Step 1	(Intermittent Positive-Pressure Breathing OR Insufflation/instrumentation OR Inhalation/instrumentation)/de OR (insufflator* OR exsufflator* OR insufflator-exsufflator*)/ti,ab OR (airway clearance/ti,ab AND (positive expiratory pressure OR PEP OR IPPB OR intermittent positive pressure breathing)/ti,ab) OR airway clearance*/ti,ab OR IPPB/ti		
AND			
Step 2	Health Planning Guidelines/de OR (practice guideline OR guideline OR Consensus Development Conference OR Consensus Development Conference, NIH)/pt OR (recommendation* OR guideline*)/ti		
Systematic reviews and meta-analysis		No limit – 10/2014	26+3
Step 1			
AND			
Step 3	(metaanalys* OR meta-analys* OR meta analysis OR systematic review* OR systematic overview* OR systematic literature review* OR systematical review* OR systematical overview* OR systematical literature review* OR systematic literature search)/ti OR meta-analysis/pt OR cochrane database syst rev/ta		
Randomized controlled trial		No limit – 10/2014	72+3
Step 1			
AND			
Step 4	(random*/ti OR (randomly OR randomized OR placebo)/ti,ab OR (Random Allocation OR Double-Blind Method OR Single-Blind Method OR Cross-Over Studies)/de OR (randomized controlled trial OR controlled clinical trial)/pt		
Comparatives studies		No limit - 10/2014	51
Step 1			
AND			
Step 5	(clinical trial* OR comparative stud* OR versus)/ti OR clinical trial/pt OR comparative study/pt		
Observational studies		No limit – 10/2014	42
Step 1			

AND

Step 6 (observational* OR cohort* OR longitudinal stud* OR follow-up stud* OR prospective stud* OR retrospective stud*)/ti OR (Cohort Studies OR Longitudinal Studies OR Follow-Up Studies OR Prospective Studies OR Epidemiologic Studies OR Retrospective Studies)/de

COUGH ASSISTANCE

Recommendations

No limit – 10/2014 3+1

Step 7 ((Cough/de OR cough*/ti,ab) AND ((Respiratory Paralysis OR Paralysis OR Spinal Cord Diseases OR Spinal Cord Injuries OR Neurodegenerative Diseases OR Nervous System Diseases)/de OR paralyzed OR paralised OR paraly* OR palsy OR palsies OR spinal cord* OR neurodegenerative* OR neurologic* OR nervous system*)/ti)) OR (cough assistance OR cough assist therap* OR mechanical insufflation* OR in exsufflation* OR cough capacity OR cough respiratory therapy OR mechanically assisted cough*)/ti,ab OR MIE/ti

AND

Step 2

Systematic reviews and meta-analysis

No limit – 10/2014 3

Step 7 AND Step 3

Randomized controlled trial

No limit – 10/2014 29

Step 7 AND Step 4

Comparatives studies

No limit – 10/2014 23

Step 7 AND Step 5

Observational studies

No limit – 10/2014 92

Step 7 AND Step 6

de : descriptor ; ti : title ; ab : abstract ; * truncation; ! : explosion; pt: publication type

2 – Visited websites

Last consultation: 10/01/2014

Bibliothèque médicale Lemanissier

Catalogue et index des sites médicaux francophones – CISMeF

Comité d'Evaluation et de Diffusion des Innovations Technologiques – CEDIT

Evaluation des technologies de santé pour l'aide à la décision (Fédération hospitalière de France) – ETSAD

Expertise collective INSERM

Société française de médecine générale – SFMG

Société française de pneumologie de langue française – SPLF

Adelaide Health Technology Assessment – AHTA

Agency for Healthcare Research and Quality – AHRQ

Alberta Heritage Foundation for Medical Research – AHFMR

Alberta Medical Association

American Association for Respiratory Care –AARC

American College of Physicians – ACP

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical

American Thoracic Society

Blue Cross Blue Shield Association – BCBS - Technology Evaluation Center

BMJ Clinical Evidence

British Thoracic Society

California Technology Assessment Forum – CTAF

Canadian Agency for Drugs and Technologies in Health – CADTH

Canadian Task Force on Preventive Health Care

Canadian Thoracic Society

Centers for Disease Control and Prevention

Centre fédéral d'expertise des soins de santé – KCE

Centre for Clinical Effectiveness – CCE

Centre for Reviews and Dissemination databases

Clinical Practice Guidelines Portal

CMA Infobase

Cochrane Library

College of Physicians and Surgeons of Alberta – CPSA

Cystic Fibrosis Foundation

Cystic Fibrosis Trust

Euroscan

Guideline Advisory Committee – GAC

Guidelines and Protocols Advisory Committee – GPAC

Guidelines International Network – GIN

Health Services Technology Assessment Text – HSTAT

Australia and New Zealand Horizon Scanning Network

Institut national d'excellence en santé et en services sociaux – INESSS

Institute for Clinical Evaluative Sciences – ICES

Institute for Clinical Systems Improvement – ICSI

Institute for Health Economics Alberta – IHE

Medical Services Advisory Committee – MSAC

Minnesota Department of Health – Health Technology Advisory Committee (to 2002) – HTAC

National Coordinating Centre for Health Technology Assessment – NCCHTA

National Guideline Clearinghouse – NGC

National Health and Medical Research Council – NHMRC

National Horizon Scanning Centre – NHSC

National Institute for Health and Clinical Excellence – NICE

New Zealand Guidelines Group – NZGG

New Zealand Health Technology Assessment – NZHTA

NHS Evidence

Ontario Health Technology Advisory Committee – OHTAC

Public Health Agency of Canada - Diseases Prevention and Control Guidelines

Scottish Intercollegiate Guidelines Network – SIGN

Singapore Ministry of Health

Thoracic Society of Australia and New Zealand

Tripdatabase

U.S. Preventive Services Task Force

Veterans affairs, Dep. Of Defense Clinical practice guidelines

West Midlands Health Technology Assessment Collaboration – WMHTA

3 – Literature monitoring

A literature monitoring was performed until December 2015 on the websites listed above and in the Medline database.

Table 6. List of full-text articles excluded, with reasons

Author	Date of publication	Reason for exclusion
Aiello M	2008	WI
Andrews J	2013	WI
Ann Intern	1983	WPP
Bach JR	2002	WI
Bach JR	1995	UR
Bach JR	1997	WI
Bach JR	2000	WO
Bach JR	2004	UR
Bach JR	2007	UR
Bach JR	2010	WO
Berlowitz D	2013	WI
Choi WA	2012	WI
Cleary S	2013	WI
Elkins MR	2006	WI
Estenne M	1989	WI
Felix E	2014	WI
Flume PA	2009	WI
Garuti G	2013	UR
Gomez-Merino E	2002	UR
Goncalves MR	2012	WPP
Gosselink R	2008	WPP
Gregoretti C	2013	UR
Guerin C	2010	WO
Ishikawa Y	2011	UR
Kang SW	2006	UR
Khirani S	2013	WI
Konstan MW	2010	WI
Kulnik ST	2014	WI
Lemoine TJ	2012	WI
Lester MK	2009	WI
McKim DA	2012	UR
Mckoy NA	2012	WI
Mellies U	2005	WSD
Miske LJ	2013	WO
Murray JF	1974	WSD
Niranjan V	1998	UR
Osadnik C	2014	WI
Oskoui M	2007	WI

Ottonello G	2011	WI
Pelissier J	2001	WI
Pryor JA	2010	WI
Sancho J	2003	WSD
Servera E	2005	WO
Silverman EP	2006	WI
Simonds AK	1989	UR
Toussaint M	2009	UR
Tzeng AC	2000	UR
van Der Schans CP	2000	WI
Vianello A	2011	WO
Winfield NR	2014	WPP

WSD Wrong study design
WPP Wrong patient population
WO Wrong outcome
WI Wrong intervention
UR Unclear reporting