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Airway Clearance Techniques for Patients With Stable Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

M Wang

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, the Evidence Development and Standards branch and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

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List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
ACT	Airway clearance technique
COPD	Chronic obstructive pulmonary disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to determine the effectiveness of airway clearance techniques (ACT) for patients with stable chronic obstructive pulmonary disease (COPD) in the community or home setting.

Clinical Need and Target Population

Chronic obstructive pulmonary disease encompasses a group of conditions characterized by irreversible airflow limitation from lung tissue damage. These conditions affect more than 1.5 million Canadians (1) and are a major cause of both morbidity and mortality, with patients often experiencing shortness of breath (dyspnea), decreased exercise capacity, and impaired quality of life. One of the symptoms of COPD is increased sputum production, which over time can obstruct the airways and has been shown to be associated with increased risk of hospitalization and infections of the lower respiratory tract. (2-4) Thus, removing mucus from the airway may be an important target for COPD therapy.

Technology/Technique

Airway clearance techniques promote the removal of pulmonary secretions and are usually performed by patients themselves. A wide array of techniques are used, including manual therapies and mechanical interventions.

Manual therapies are based on the assumption that applying external force to the chest can loosen mucus, or that using effective and productive coughing or breathing methods along with proper gravitational positioning can aid in airway mobilization and clearance. Specific techniques in this group include postural drainage, autogenic drainage, percussion, vibration, shaking, deep breathing, directed coughing, active breathing techniques, and forced expiratory technique. Mechanical interventions involve the use of additional devices to open the airways and loosening of the remaining trapped mucus higher, or to produce turbulence in the airways to enable mucus to separate from the airway walls to aid in its removal. Devices and techniques include positive expiratory pressure mask, oscillating positive expiratory pressure, high-frequency chest wall oscillation, and intrapulmonary percussive ventilation.

A previous rapid review by Health Quality Ontario found limited evidence of benefit from ACTs for patients with acute exacerbations of COPD. (5) While patients often perform or receive ACTs, the benefits of these techniques are unclear, especially in a population with stable COPD.

Rapid Review

Research Question

What is the effectiveness of airway clearance techniques for patients with stable COPD in the community or home?

Research Methods

Literature Search

Search Strategy

A literature search was performed on April 8, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations and EBM Reviews, for studies published from January 1, 2009, to April 8, 2014. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2009, and April 8, 2014
- systematic reviews and meta-analyses on airway clearance techniques for stable (non-hospitalized) COPD patients

Exclusion Criteria

- randomized controlled trials, editorials, case studies, observational studies, or commentaries
- comparison of different methods of airway clearance techniques

Outcomes of Interest

- COPD exacerbations
- hospitalizations
- health-related quality of life

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the

methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (6)

Rapid reviews of systematic reviews normally examine the quality of the body of evidence for each outcome using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (7) Where this is not possible due to the limited number of studies available for the outcomes of interest, we assess the quality of the evidence using a risk of bias assessment of the individual studies in a systematic review, including allocation concealment, blinding, accounting of patients and outcome events, selective reporting bias, and other limitations. (8)

Results of Rapid Review

The database search yielded 396 citations published between January 1, 2009, and April 8, 2014 (duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Five systematic reviews examining airway clearance techniques for non-acute exacerbations of COPD were identified (Table 1). (9-13) The reference lists of the included studies were hand-searched to identify other relevant studies but none were found. Only the systematic review by Osadnik et al (13) separated acute exacerbations of COPD from the stable COPD population. Based on its relevant focus and high quality (AMSTAR rating of 11; Appendix 2, Table A1), it was chosen for this analysis.

Table 1: Systematic Reviews of Airway Clearance Techniques for COPD

Author, Year	Description of Systematic Review
Ides et al, 2011 (9)	Systematic review of airway clearance techniques for COPD
Langer et al, 2009 (10)	Clinical practice guideline for the physiotherapy management of COPD based on systematic review of the evidence, which includes improving airway mucus clearance
Nowobilski et al, 2010 (11)	Systematic review of systematic reviews, narrative reviews, clinical practice guidelines, and secondarily, primary studies on chest physical therapy for COPD
Fagevik Olsén and Westerdahl, 2009 (12)	Systematic review of chest physiotherapy techniques with positive expiratory pressure for COPD
Osadnik et al, 2012 (13)	Systematic review for AECOPD and stable COPD

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease.

The systematic review included 19 studies of airway clearance techniques for stable COPD (see Appendix 3 for study characteristics), 6 of which were randomized controlled trials and the remaining being randomized cross-over trials. (13) We could not perform the typical analysis using GRADE to assess the quality of evidence for each outcome of interest as only a few studies analyzed the specified outcomes. None of the studies were done in a home setting, and other study settings were identified as either hospital, outpatient clinic or research institute. Since it was not always clear if the hospital setting was outpatient-based, the results of this rapid review focused on the patient population of stable COPD regardless of setting.

Two studies examined subsequent exacerbations (both with nonsignificant findings), 2 studies examined hospitalization (with inconsistent findings), and only 1 study looked at health-related quality of life (with a finding of improvement). (13) Table 2 summarizes the heterogeneity in airway clearance techniques examined in these studies and the significance of results for the 9 outcomes examined by Osadnik et al. (13)

The included studies were in general of low quality with small numbers of study participants, inadequate or no mention of randomization/allocation and blinding, and short length of follow-up (Appendix 2, Table A2). Most studies involved comparison with usual care; a few examined comparisons with sham therapy. A variety of techniques were examined (positive expiratory pressure mask, forced expiratory technique, vibration, postural drainage, breathing techniques, percussion, directed coughing) with co-interventions such as standard COPD bronchodilator therapy. For 4 studies, only the abstract was available and additional details of the results could not be extracted by the authors, and 2 studies were noted to be without full English translation.

Due to study heterogeneity and differences in reporting study outcomes, the data could not be meta-analyzed for a summary effect measure for specific outcomes, nor could data be subgrouped by technique. In addition, 11 of the 19 studies were published before 2000, potentially limiting the ability to generalize their findings for current techniques, particularly recent advancements in mechanical airway clearance techniques. Although the remaining 8 studies were more recent, no study published within the last 5 years examined a population with stable COPD.

Findings for the secondary outcomes in the systematic review (pulmonary function, gas exchange, symptoms, sputum clearance, exercise tolerance, antibiotic use) were also inconsistent among studies. For pulmonary function, only 4 of 13 studies reported significant improvement. No studies (0 of 7) found an improvement in gas exchange. Airway clearance techniques showed potential benefit for exercise tolerance and sputum clearance (3 of 3 studies and 6 of 8 studies, respectively). Finally, 1 of 3 studies examining antibiotic use found a significant reduction, and 4 of 7 studies found improved symptoms. In total, considering all the included studies for any type of airway clearance technique for stable COPD patients, 13 of the 19 studies reported an improvement in at least 1 of the 9 study outcomes examined.

From the current evidence, uncertainty still exists about the clinical effectiveness of airway clearance techniques for patients with stable COPD; however, they may be clinically beneficial based on low quality studies.

Table 2: Summary of Airway Clearance Techniques for Stable COPD and Reported Outcomes in Included Systematic Review

Author, Year	Intervention	Primary Outcomes of Interest			Secondary Outcomes					
		Exacerbations	Hospitalization	HRQOL	Pulmonary Function	Gas Exchange	Symptoms	Sputum Clearance	Exercise Tolerance	Antibiotic Use
Cegla et al, 1997	PEP (Cornet, Flutter)				NS	NS				
Cegla et al, 2001	PEP (Cornet)				✓					
Cegla et al, 2002	PEP (Cornet)		✓		✓					✓
Christensen et al, 1990	PEP (mask with PEEP valve)	NS	NS		NS	NS	NS			NS
Christensen and Dahl, 1991	PEP mask	NS			NS		✓			NS
Christensen et al, 1991a	PEP mask				NS		✓			
Martins et al, 2006	ELTGOL							✓		
Martins et al, 2007	ELTGOL							✓		
May and Munt, 1979	CCPT				NS	NS		✓		
Morsch et al, 2008	PEP (Flutter +/- FET)							NS		
Oldenburg et al, 1979	CCPT; physical exercise				NS			✓		
Pavia et al, 1976	mechanical vibration						NS	NS		
Rasmussen and Juul, 2001	PEP valve							✓		
Rivington-Law et al, 1984	breathing; breathing + CPPT				NS	NS				
van Hengstum et al, 1988	PEP mask; breathing + CPPT				NS			✓		
Weiner et al, 1996	PEP (Flutter)				NS	NS	✓		✓	
Wolkove et al, 2002	PEP (Flutter)				✓	NS	✓		✓	
Wolkove et al, 2004	PEP (Flutter)			✓	✓	NS	NS		✓	

Abbreviations: CCPT, conventional chest physiotherapy; COPD, chronic obstructive pulmonary disease; ELTGOL, slow expiration with glottis open in the lateral position; FET, forced expiratory technique; HRQOL, health-related quality of life; NS, not significant; PEEP, positive end-expiratory pressure; PEP, positive expiratory pressure.
Note: Check mark denotes significant finding(s), and where described by the systematic review, those that are clinically meaningful. The results of the Hasani et al study (abstract only) were not explicitly mentioned in the included systematic review.
Source: Osadnik et al, 2012. (13)

Conclusions

- One systematic review was included that examined airway clearance techniques for patients with stable COPD.
- The 19 studies (4 of which were only available as abstracts) were generally of low quality, based on risk of bias assessment; due to the heterogeneity in study design, interventions, and reporting, the evidence could not be analyzed using GRADE for our specific outcomes of interest.
- Thirteen of the 19 studies showed potential improvement through the use of airway clearance techniques for patients with stable COPD for the following outcomes: exacerbations, hospitalizations, health-related quality of life, pulmonary function, gas exchange, symptoms, sputum clearance, exercise tolerance, or antibiotic use; but there were considerable study limitations and differences in techniques examined.
- Further well-designed studies are required to determine with certainty the effectiveness of airway clearance techniques for patients with stable COPD.

Acknowledgements

Editorial Staff
Amy Zierler, BA

Medical Information Services
Corinne Holubowich, BEd, MLIS

Health Quality Ontario's Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients

Panel Members	Affiliation(s)	Appointment(s)
Co-Chairs		
Dr Chaim Bell	Mount Sinai Hospital University of Toronto	Clinician Scientist Associate Professor
Lisa Droppo	Ontario Association of Community Care Access Centers (OACCAC)	Chief Care Innovations Officer
Primary Care		
Dr Kenneth Hook	Ontario College of Family Physicians STAR Family Health Team	Past-President Senior Physician
Dr Alan Kaplan	Family Physicians Airway Group of Canada	Chair, Family Physicians Airway Group of Canada
Dr Peter Selby	Department of Family and Community Medicine & Psychiatry and Dalla Lana School of Public Health University of Toronto Ontario Tobacco Research Unit	Associate Professor Principal Investigator
Respirology		
Dr Samir Gupta	St Michael's Hospital	Adjunct Scientist, Keenan Research Centre
Dr Roger Goldstein	West Park Health Centre Toronto Rehabilitation Institute	Respiratory Division Head Associate Medical Staff Professor of Medicine
Respiratory Therapy		
Ivan Nicoletti	Erie St. Clair CCAC	Care Coordinator
Sara Han	Ontario Lung Association Mount Sinai Hospital	PCAP Provincial Coordinator Certified Respiratory Educator
Miriam Turnbull	ProResp Inc	General Manager
Madonna Ferrone	Erie St. Clair LHIN	Project Manager ARGI, Lung Health Collaboratist
Nursing		
Cheryl Lennox	South West Community CCAC, Intensive Home Care Team	Nurse Practitioner-Primary Health Care

Panel Members	Affiliation(s)	Appointment(s)
		Certified Respiratory Educator
Andrea Roberts	Toronto Central CCAC	Rapid Response Transition Nurse
Mary-Jane Herlihey	ParaMed Home Health Care Ottawa	Clinical Consultant
Suzy Young	St. Mary's General Hospital	Nurse Practitioner Primary Health Care SWCCAC Intensive Health Care Team Certified Respirator Educator

Appendices

Appendix 1: Literature Search Strategy

Databases: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to February 2014>, EBM Reviews - ACP Journal Club <1991 to March 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <January 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <1st Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2014>, Ovid MEDLINE(R) <1946 to March Week 4 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <April 08, 2014>

Search Strategy:

#	Searches	Results
1	exp Patient Discharge/	19503
2	exp Aftercare/ or exp Convalescence/	10124
3	"Continuity of Patient Care"/ or exp "Recovery of Function"/	47225
4	((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab.	37339
5	exp Stroke/	87237
6	exp brain ischemia/ or exp intracranial hemorrhages/	130703
7	(stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*)).ti,ab.	199089
8	exp Heart Failure/	90534
9	(((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab.	132170
10	exp Pulmonary Disease, Chronic Obstructive/	37292
11	exp Emphysema/	10805
12	(copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab.	57323
13	(chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab.	35566
14	exp Pneumonia/	75197
15	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab.	139396
16	or/1-15	764570
17	exp Physical Therapy Modalities/	134218
18	exp "Physical and Rehabilitation Medicine"/	19795
19	exp Respiratory Therapy/	92927
20	exp Breathing Exercises/ or Percussion/ or Intermittent Positive-Pressure Ventilation/ or Vibration/	26337
21	(((physiotherap* or physio-therap* or physical ther* or kinesiotherap*) adj2 (respirat* or chest* or lung* or pulmonar* or percussion* or humidification or breath* or COPD or airway* or thora*)) or (active cycle adj2 breath*) or ((lung or pulmonary) adj2 hygien*) or incentive spirometr* or acapella* or ((airway or secretion* or sputum or bronchopulmonar* or	31480

	tracheobronch* or mucus or chest*) adj2 clear*) or (sputum adj2 (clear* or mobili*)) or ((postural or autogenic or gravity assist*) adj2 drainage*) or positive expiratory pressure* or thoracic expansion exercise* or chest percussi* or percussive ventilat* or forced expir* technique* or chest wall oscillat* or draining technique* or clapping or vibration or flutter*).ti,ab.	
22	or/17-21	283800
23	16 and 22	30512
24	Meta Analysis.pt.	47150
25	Meta-Analysis/ or exp Technology Assessment, Biomedical/	56209
26	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	201233
27	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	2762
28	or/24-27	217647
29	23 and 28	920
30	limit 29 to (english language and yr="2009 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	463
31	case reports/ or comment.pt. or editorial.pt. or letter.pt. or congresses.pt.	2882301
32	30 not 31	450
33	remove duplicates from 32	396

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Scores of Included Systematic Review

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Osadnik et al, 2011 (13)	11	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al, 2007. (6)

Table A2: Risk of Bias Among Randomized Controlled Trials for Airway Clearance Techniques for Stable COPD Patients

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Cegla et al, 1997	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[d]
Cegla et al, 2001	Limitations[e]	Limitations[b]	No limitations	No limitations	No limitations
Cegla et al, 2002	Limitations[e]	Limitations[b]	No limitations	Limitations[c]	Limitations[f]
Christensen et al, 1990	Limitations[a]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
Christensen and Dahl, 1991	Limitations[a]	Limitations[b]	Limitations[g]	No limitations	No limitations
Christensen et al, 1991a	Limitations[e]	Limitations[b]	No limitations	No limitations	Limitations[h]
Hasani et al, 1995	Limitations[e]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
Martins et al, 2006	Limitations[i]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
Martins et al, 2007	Limitations[i]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
May and Munt, 1979	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[j]
Morsch et al, 2008	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Oldenburg et al, 1979	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Pavia et al, 1976	Limitations[i]	Limitations[b]	No limitations	No limitations	No limitations
Rasmussen and Juul, 2001	Limitations[e]	Limitations[b]	Limitations[g]	Limitations[c]	Limitations[h]
Rivington-Law et al, 1984	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[k]
van Hengstum et al, 1988	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Weiner et al, 1996	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[d]
Wolkove et al, 2002	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Wolkove et al, 2004	Limitations[l]	Limitations[b]	No limitations	No limitations	No limitations

[a]Randomization said to be done, but method was not described. No information on allocation concealment.
[b]No information or insufficient information provided; study not likely to have been adequately blinded.
[c]Data not available for some patients or outcomes.
[d]Full English translation not available.
[e]No information or insufficient information provided for random sequence generation and allocation concealment methods.
[f]Unclear why participants were randomly excluded.
[g]Incomplete or inadequate data for patients or outcomes.
[h]Washout period unclear.
[i]Random sequence generation mentioned, but no mention of allocation concealment.
[j]Unclear why some participants received the intervention while others did not.
[k]Unclear which group excluded patients were from.
[l]Random sequence generation methods not mentioned, but study had adequate allocation concealment.
Source: Osadnik et al, 2012. (13)

Appendix 3: Randomized Controlled Trials for Stable COPD in the Included Systematic Review

Table A3: Characteristics of Included Studies for Airway Clearance Techniques in Stable COPD

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Cegla et al, 1997	90	56.0 (10.4)	RCT	Outpatient pulmonary clinic	Presumed stable COPD Tracheobronchial instability Productive sputum < 65 years of age	COPD pharmacotherapy and oxygen	1) Same as control + Cornet (5 min, 4x/day for 7 days) 2) Same as control + Flutter (5 min, 4x/day for 7 days)	7 days
Cegla et al, 2001	35	65.0 (10.0)	RXT	Pulmonary research institute	Stable COPD Tracheobronchial instability Non-smoker in last 5 years	COPD pharmacotherapy	Same as control, but exhalation via Cornet	2 days
Cegla et al, 2002	81	63.4 (9.2)	RCT	Pulmonary research institute	Stable severe COPD Tracheobronchial instability	COPD pharmacotherapy	Same as control + Cornet (≥ 5 min, 3x/day whenever dyspnea or mucus was noticed)	2 years
Christensen et al, 1990	60	65 (median)	RCT	Outpatient chest clinic	Stable severe COPD Chronic mucus hypersecretion	PEP mask, with PEEP valve at 0 cm H_2O (≥ 15 min, 3x/day)	Same as control, but PEP mask, with PEEP valve at 10 cm H_2O	6 months
Christensen and Dahl, 1991	30	64	RCT	Hospital	Stable COPD Any smoking status	COPD pharmacotherapy via spacer connected to PEP mask at 0 cm H_2O (10 tidal breaths, 2x/day)	Same as control, but PEP of 10–20 cm H_2O	4 weeks
Christensen et al, 1991a	10	54.4 (16.6)	RXT	Outpatient clinic	Stable COPD Daily cough, expectoration, and dyspnea, requiring daily COPD pharmacotherapy	COPD pharmacotherapy with PEP mask at 0 cm H_2O (3x/day for 2 weeks)	1) Same as control, except 10–15 cm H_2O 2) Same as control, except 1 placebo medication	3 x 2 weeks

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Hasani et al, 1995 (Abstract only)	24	69 (8.5)	RXT	Thoracic medicine department	Asthma, bronchiectasis, stable COPD	Resting	1) 6 coughs/min x 5 cycles with 1 min rest in between 2) 6 forced expiratory techniques/min x 5 cycles with 1 min rest in between	1 day
Martins et al, 2006 (Abstract only)	5	N/A	RXT	Physiotherapy/nuclear medicine department	Mild-moderate COPD Daily excessive sputum expectoration	Rest for 20 min Only spontaneous coughing allowed	Expiration with glottis open in lateral posture for 20 min (10x slow and deep expirations followed by 2 min rest x 3 sets in right lateral position	1 week
Martins et al, 2007 (Abstract only)	12	45–75 (Range)	RXT	Physiotherapy/nuclear medicine department	Mild-moderate stable COPD Daily excessive sputum expectoration	Rest for 20 min Only spontaneous coughing allowed	Expiration with glottis open in lateral posture for 20 min (10x slow and deep expirations followed by 2 min rest x 3 sets in right lateral position	1 week
May and Munt, 1979	35	59	RXT	Hospital	Stable COPD History of productive cough and obstructive defect on spirometry	30 min chest heat lamp therapy (10 min heat in side-lying, 10 min rest supine no heat, 10 min heat side-lying alternate side)	1) 90 sec manual percussion followed by vibrations, assisted coughing and brief rest in 7 different postural drainage positions 2) Directed, unassisted coughing every 5 min x 30 min	2 days
Morsch et al, 2008	20	64.9 (6.8)	RCT	Outpatient pulmonology clinic	Stable stage III COPD	7 min induced sputum via ultrasonic nebulizer	Same as control + Flutter (5 min calm, prolonged exhalations through Flutter followed by vigorous coughing)	1 day
Oldenburg et al, 1979	8	62.1 (4.4)	RXT	Hospital clinic	Stable, simple and obstructive COPD	Upright resting	1) 5 x 4 min cycle ergometry, with 4 min rest 2) 5 x 6 min postural drainage, with 1 min rest 3) Coughing once/min x 5 min, with 3 min rest	5–10 days

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Pavia et al, 1976	10	65.3 (5.9)	RXT	Hospital chest clinic	Stable COPD Productive cough, shortness of breath, difficulty expectorating phlegm	1 hour rest in reclined position Inactive vibration pad	Same as control + active vibration	N/A
Rasmussen and Juul, 2001	25	66.6	RXT	Hospital	Stable COPD	Self-administered PEP valve therapy at 0 cm H_2O, 2x/day for 4 days	1) Same as control, but PEP at 5 cm H_2O 2) Same as control, but PEP at 12.5 cm H_2O 3) Same as control, but PEP at 20 cm H_2O	4 x 4 days
Rivington-Law et al, 1984	14	66	RXT	N/A	Stable COPD Crackles on auscultation	15 min rest with hands on chest	1) Same as control, except followed by 15 min deep breathing 2) Same as control, except followed by 15 min deep breathing + manual chest wall vibrations	3 days
van Hengstum et al, 1988	8	63	RXT	Hospital	Presumed stable COPD	Rest with spontaneous coughing only	1) PEP mask in forward leaning sitting position (10–15 cm H_2O for 2 min, followed by abdominal breathing and 2 maximal huffs and coughs x 5 cycles 2) 6 positions of postural drainage with diaphragmatic breathing, thoracic expansion exercises, diaphragmatic breathing, 2 huffs interspersed with relaxed diaphragmatic breathing and coughs	≥ 12 days

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Weiner et al, 1996	20	63.3 (9.5)	RCT	Medical centre	Stable COPD Bronchial hypersecretion	Flutter (with steel ball removed) x 10 breaths followed by 30 sec rest x 4–8 sets, daily for 3 months	Same as control, but with steel ball	3 months
Wolkove et al, 2002	23	71.7 (6.3)	RXT	Hospital	Stable severe COPD	Flutter for 10 min (steel ball removed), followed by COPD pharmacotherapy	Same as control, but with steel ball	3 days
Wolkove et al, 2004 (Abstract only)	15	71 (10)	RXT	Outpatient clinic	Stable COPD ≥ 10 pack-year smoking history	Flutter for 10 min (steel ball removed), 4x/day prior to usual COPD pharmacotherapy for 1 week	Same as control, but with steel ball	22 days

Abbreviations: COPD, chronic obstructive pulmonary disease; MRC, Medical Research Council; min, minute(s); N/A, not available; PEEP, positive end-expiratory pressure; PEP, positive expiratory pressure; RCT, randomized controlled trial; RXT, randomized cross-over trial.

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Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: EvidenceInfo@hqontario.ca
www.hqontario.ca