RESPIRATORY CARE Paper in Press. Published on November 12, 2013 as DOI: 10.4187/respcare.02704

Nonpharmacologic Airway Clearance Techniques in Hospitalized Patients: A systematic review

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Financial support: This review was funded by the American Association for Respiratory Care.

Conflict of interest:
The authors have no conflicts of interest to declare. All authors contributed input to scoping the literature search, which was performed by a professional librarian. All authors assisted with data collection and analysis, development of the report/manuscript text, and review of the manuscript prior to submission.

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Outline:

Abstract:

Nonpharmacologic airway clearance techniques are used to reduce the sequelae of obstructive secretions. We systematically reviewed comparative studies of nonpharmacologic interventions that health professionals can employ to achieve mucus clearance in hospitalized or postoperative patients without cystic fibrosis over the age of 12 months. We searched MEDLINE and other databases from 1990 to 2012 to identify relevant literature. Two reviewers independently assessed each study against predetermined inclusion/exclusion criteria. Two reviewers also independently extracted data regarding participant and intervention characteristics and outcomes and assigned overall quality ratings. The 32 studies meeting review criteria included 24 RCTs, seven crossover RCTs, and one prospective cohort study. Studies were typically small and together included a total of 2,453 subjects (mean=76/study). Studies generally examined chest physical therapy/physiotherapy (CPT) modalities in postoperative or critically ill patients or those with chronic obstructive pulmonary disease (COPD). Interventions, comparators, and populations varied considerably across studies, hampering our ability to draw firm conclusions. Interventions including conventional CPT, intrapulmonary percussive ventilation, and positive expiratory pressure typically provided small benefits in pulmonary function, gas exchange, oxygenation, and need for/duration of ventilation, among other outcomes, but differences between groups were generally small and not significant. Harms of techniques were not consistently reported, though airway clearance techniques were generally considered safe in studies that did comment on adverse effects. Further research with clearly characterized populations and interventions is needed to understand the potential benefits and harms of these techniques.

Key Words:

airway clearance techniques; chest physical therapy; breathing exercises; airway obstruction/therapy; physical therapy modalities

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Acknowledgements:

We gratefully acknowledge the contributions of the American Association for Respiratory Care (AARC) Airway Clearance Clinical Practice Guidelines Committee. Their insight into scoping the literature and reviewing studies was invaluable. The committee includes Richard Branson, MS, RRT, FAARC; Gail Drescher, MA, RRT; Carl Haas, MLS, RRT, FAARC; Dean Hess, PhD, RRT, FAARC; Ray Masferrer, RRT, FAARC; Catherine O'Malley, RRT-NPS; Bruce Rubin, MD, MEngr, MBA, FAARC; Shawna Strickland, PhD, RRT-NPS, AE-C, FAARC; Teresa Volsko, MHHS, RRT, FAARC.

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Introduction

Airway clearance techniques are intended to reduce the sequelae of obstructive secretions, which can include airflow obstruction, wheeze, respiratory infection, dyspnea, fatigue, and reduced quality of life.[1] Clearance techniques include modalities such as Active Cycle of Breathing techniques (ACBT), positive expiratory pressure (PEP) techniques such as the Flutter® device, and intrapulmonary percussive ventilation (IPV). Conventional chest physical therapy or physiotherapy (CPT) approaches are frequently used as well and include postural drainage, percussion, and vibration. Techniques may be categorized or grouped in multiple ways and are often used in concert. Airway clearance approaches may be used in individuals with impaired cough or muscle weakness,[2] impaired mucociliary clearance,[3-6] structural impairments such as bronchiectasis or asthma,[7-9] and airflow limitation as seen in chronic obstructive pulmonary disease (COPD).[7, 10-12]

The goal of the current project was to systematically review comparative studies of nonpharmacologic interventions that respiratory therapists and other health professionals can employ to achieve mucus clearance in hospitalized or postoperative patients over the age of 12 months. The American Association for Respiratory Care (AARC) commissioned the review, and AARC committee members participated in the review process. As a collaborative effort, the AARC team and the Vanderbilt Evidence-based Practice Center (EPC) developed the key questions and inclusion and exclusion criteria and engaged in identification and review of abstracts. Any AARC members involved in the work were paired with EPC staff in order to maintain rigor and protect against bias.

Methods

Literature Search Strategy

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Detailed methods for the review can be found in the full report at <URL>. Briefly, we used the search strategies provided in the online appendix to retrieve relevant research on airway clearance techniques. Our primary literature search employed the MEDLINE® (via the PubMed interface) and Cumulative Index of Nursing and Allied Health Literature (CINAHL) databases. Our search strategies used a combination of subject heading terms appropriate for each database and key words relevant to airway clearance (e.g., sputum clearance, chest physical therapy). We limited searches to literature published in English since 1990 to ensure that interventions used currently would be represented. Our searches were conducted in August 2012. We imported all citations into an electronic database and into the DistillerSR program for screening. We also manually searched the reference lists of included studies and of recent narrative and systematic reviews and meta-analyses addressing airway clearance in adults to locate citations of potential relevance.

Inclusion and Exclusion Criteria

Studies needed to include individuals over one year of age without cystic fibrosis who were receiving nonpharmacologic airway clearance therapies and who were either hospitalized (but not postoperative) or postoperative; had neuromuscular disease or respiratory muscle weakness; or who had impaired cough. We note that we excluded studies of subjects with cystic fibrosis as the Cystic Fibrosis Foundation recently published guidelines specifically related to airway clearance.[13] Studies had to report on interventions explicitly used for airway clearance and include a treatment group and an appropriate comparison group (Table 1). Comparators included other nonpharmacologic airway clearance approaches, no airway clearance intervention, or placebo. We also required that studies address one of the outcomes related to the effects of the intervention on mucus clearance outlined in Table 1. We included studies with any length of followup and in the hospital setting (i.e., not home- or outpatient clinic-based).

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Study Selection

Once we identified potential articles, we examined the abstracts to determine whether studies met our criteria. Two reviewers separately evaluated each abstract for inclusion or exclusion, using an Abstract Review Form (Online Appendix). If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it for full text assessment. Two reviewers independently assessed the full text of each included study using a standardized form (Online Appendix) that included questions stemming from our inclusion/exclusion criteria. Disagreements between reviewers were resolved by a third-party adjudicator. The group of abstract and full text reviewers included expert clinicians and health services researchers, and we required that studies be excluded by at least one clinician and one methodologist. AARC members involved in screening were paired with EPC staff in order to maintain rigor and protect against bias.

Data Extraction and Synthesis

We extracted data on study design, population characteristics (including age, underlying conditions, and need for mechanical ventilation), intervention characteristics (including type and duration of intervention and concomitant therapies), and key outcomes data into evidence tables (Online Appendix). In addition to outcomes related to airway clearance intervention effectiveness, we extracted all data available on harms of airway clearance. Harms encompass the full range of specific negative effects, including the narrower definition of adverse events. We determined that the differences among populations, interventions, controls, and outcome measures rendered meta-analysis inappropriate. Thus, analysis remains qualitative.

Quality (Risk of Bias) Assessment of Individual Studies

We assessed quality using separate tools as appropriate by study design. Tools included the

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Cochrane Risk of Bias tool for randomized controlled trials (RCTs) and the Newcastle-Ottawa scale for cohort studies. We rated the quality for key outcomes for which data were provided; if a study noted, for example, that a given was outcome was not significantly different between groups but did not provide the relevant data, we did not rate quality for that outcome. Two reviewers independently assessed quality for each study, with final decisions made via discussion to reach consensus or by third party adjudication by a senior methodologist as needed. We used the parameters outlined in Table 2 to translate quality ratings into final levels (good, fair, poor). We considered that "good" studies could not have any criteria rated as high risk of bias. For studies with "unclear" ratings, we considered the likelihood that a factor would bias a given outcome and the importance of the limitation and "downgraded" the final level as appropriate. Quality ratings for each outcome in the studies reviewed can be found in the online appendix.

Results

We reviewed 2,054 abstracts and 313 full-text papers and determined that 32 papers (comprising 32 unique studies) met inclusion criteria (Figure 1). Excluded studies can be found in the online appendices. The 32 studies meeting review criteria included 24 RCTs, seven crossover RCTs, and one prospective cohort study (Table 3). Studies were typically small and together included a total of 2,453 subjects (mean=76 individuals/study). Studies typically examined CPT modalities in postoperative or critically ill patients or those with COPD. Patients were typically assessed immediately following short-term interventions or upon hospital or ICU discharge. Five studies followed participants for one to six months post-discharge.[14-18]

The following sections summarize results of studies meeting our criteria and categorized by intervention and comparison in those studies including primarily hospitalized, non-postoperative patients (Table 4) and those focused on postoperative patients (Table 5). Several studies of ICU

populations include both postoperative patients and those hospitalized for medical therapies. We have grouped these papers with studies of hospitalized patients as their primary focus is not on the postoperative period.

Studies in Hospitalized, Non-Postoperative Patients

Studies Evaluating Chest Physical Therapy/Physiotherapy (CPT)

CPT compared to usual care or added to another treatment

Kodric and colleagues compared the "expiration with the glottis open in lateral posture" CPT technique (expiration group, n=30) with standard medical treatment (n=29) in patients hospitalized with COPD exacerbation.[16] Patients in the expiration group also received standard medical therapy and were continued on medical therapy alone after 7 days of the expiration treatment (two 30-40 minute sessions/day). Investigators analyzed patient respiratory data after 7 days of treatment, quality of life (St. George's Respiratory Quality [SGRQ] questionnaire) after one month post-discharge, and number of exacerbations and hospital admissions at six months post-discharge. The primary outcome of sputum volume was not significantly different between groups after 7 days of treatment (mean 6.8 ± 7.6 mL/day in the expiration group compared with 8.2 ± 9.4 in the medical treatment only group, p=NS) though volume changes within each group differed significantly from baseline to follow-up ($p \leq 0.001$). Dyspnea (Borg scale) was significantly reduced in the expiration group at 7 days (3.0 ± 1.8 vs. 4.3 ± 1.5, p=0.004). Length of stay (LOS) was similar between groups (mean 9.5 ± 3.2 days in the expiration group vs. 10.0 ± 2.4 in the medical treatment only group, p=NS). At one month post-discharge, quality of life scores were not significantly different between groups. Similarly, at 6-months post-discharge, COPD exacerbations and hospitalizations did not differ significantly, though only roughly 37% of patients in each group were available at the 6-month follow-up. We rated the quality for each outcome

assessed (pulmonary function, oxygenation, dyspnea, QOL, sputum volume, LOS, exacerbations) as poor.

In an RCT including mechanically ventilated ICU patients, Templeton et al. compared CPT (thoracic and pulmonary expansion; respiratory muscle exercise; secretion removal via manual hyperinflation with vibration, positioning, and suctioning) with standard ICU care.[19] Frequency and intensity of CPT could be varied at the therapists' discretion, and therapists were not blinded to patients' group allocation. Control group patients received suctioning, mobilization, and decubitus care, though all patients could receive rescue CPT as needed (45 CPT and 37 control group patients required rescue CPT at any time while ventilated, p=NS). The mean age of the 87 patients in the CPT group was 57.7 years (median APACHE II score=49), while corresponding values for the control group were 58.2 years, median APACHE II score of 41. Groups were not significantly different at baseline. Reasons for ICU admission in both groups varied and included respiratory insufficiency (n=21), intracerebral hemorrhage (n=35), and gastrointestinal causes including bleeding and perforation (n=18). The median number of days for half of patients to become ventilator free was significantly lower in the control group compared with the CPT group (11 days, range=3 to 76 vs. 15 days, range=3 to 82, p=0.045). Fourteen percent (n=12) of control patients and 12.6% (n=11) of CPT patients required re-ventilation after becoming ventilator-free (p=NS). The median length of ICU stay also did differ significantly between groups (13 days in CPT group, 12 in control). We rated the quality for the outcomes of LOS and need for and duration of ventilation as fair.

In a cohort study including mechanically ventilated ICU patients, Ntoumenopoulos evaluated CPT compared with standard care for the prevention of ventilator acquired pneumonia (VAP).[20] CPT (n=24 patients, mean APACHE II score=20.7 ± 6.9) included postural drainage or positioning for at least 20 minutes, expiratory chest wall vibration (4 sets of 6 cycles with coughing added for patients

weaned from ventilator), and suctioning (≥3 times). The control group (n=36, mean APACHE II score=18.8 ± 5.4) received sham CPT consisting of cardiopulmonary assessment and occasional musculoskeletal physical therapy plus re-positioning and suctioning as needed. Both groups received standard medical and nursing care, which included hemodynamic support, infection care, enteral nutrition, antibiotic therapy, and bronchoscopy as needed. Patients' underlying conditions included chronic obstructive airway disease (n=6 in CPT group and 11 in control), cardiomyopathy (n=1 in CPT group and 3 in control), and cardiac arrest (3 in CPT group, 5 in control). Groups were similar at baseline in terms of risk factors for VAP; however, among surgical patients, the American Society of Anesthesiologists (ASA) score was higher in the control arm (p=0.04). Significantly more patients in the control arm developed VAP (14 vs. 2 in the CPT arm, 0=0.01). The duration of ventilation, duration of ICU stay, and number with lung collapse or consolidation were also lower in the CPT group, though not significantly (median days ventilation: 4.4 vs. 5.2 in control arm, p=NS; median ICU days: 5.6 vs. 5.8 in control arm, p=NS; N with lung collapse/consolidation: 23 vs. 34 in control arm, p=NS). We rated this cohort study as good quality.

In an RCT including mechanically ventilated ICU patients between 20 and 85 years old, Chen and colleagues assessed mechanical chest vibration (via vibration pad used in supine position, 60 minutes/session, 6 times/day over 72 hours, n patients=50) and routine positioning compared with routine positioning alone (n=45).[21] Underlying conditions in both groups included sepsis (38%), respiratory failure (37%), and surgery (31%). Sixteen percent of patients had past history of COPD, and 27% had past cerebrovascular accident. Patients were not significantly different at baseline, with mean APACHE II scores of 25.4 ± 6.6 in the positioning only group and 23.1 ± 7.2 in the chest vibration group. Mean dry sputum weight (mg/24 hours) at baseline was 5.74 ± 6.23 in the vibration group and 5.42 ± 3.98 in the positioning only group. After 72 hours, sputum weight was 4.04 ± 3.43 in vibration

participants and 3.56 ± 3.10 in the positioning-only group (p=NS); however, when investigators used generalized estimating equations to address the longitudinal nature of the data and account for correlation, differences in sputum weight were significant between groups, with sputum greater in the intervention group (p=0.000). The lung collapse index of the vibration group was significantly improved compared with the positioning group at 72 hours (mean 0.96 ± 0.73 vs. 1.60 ± 0.91, p=0.000). We rated the quality for the outcome of sputum volume as poor.

Paludo et al. conducted an RCT of children (29 days to 12 years old) hospitalized with acute pneumonia and comparing twice daily CPT and standard pneumonia therapy (n=51) to standard treatment alone (n=47).[22] CPT sessions were 30 minutes in duration and included postural drainage, thoracic squeezing, chest percussion, vibration, cough stimulation, and aspiration of secretions as needed. Standard medical therapy included antibiotics, fluids, and oxygen therapy as needed. Participants were similar at baseline. There were no significant differences at follow-up in length of stay, time to normal respiratory rate or oxygen saturation, time to normal auscultation, and duration of wheezing, crackles, or chest indrawing. The CPT group had a longer median duration of coughing (5.0 days vs. 4.0 days, p=0.04) and longer duration of rhonchi (median 2.0 vs. 0.5 days, p=0.03) than the medical treatment only group. We rated the quality for the outcomes of LOS and time to normal respiratory rate and oxygenation as fair.

In an RCT assessing CPT as an adjunct to medical therapy in children with asthma, Asher and colleagues randomized patients hospitalized with acute asthma to placebo (n=19) or CPT with modalities selected at the discretion of the therapist (n=19).[23] CPT included relaxation techniques (positioning, lateral costal or diaphragmatic breathing, shoulder relaxation), secretion clearance techniques (postural drainage, coughing, FET, vibration, wing flapping), thoracic mobility exercises, and postural correction exercises.

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Each participant received a total of four treatment or placebo sessions. Placebo was defined as a 20-minute visit from a hospital volunteer who provided emotional support. CPT sessions were 20 to 30 minutes long and included modalities as described above selected by the therapist for each child. Relaxation techniques were most frequently used at the first and fourth treatment sessions (used in 95% and 84% of sessions, respectively). Secretion clearance techniques were used in 79% of the first treatment sessions and 74% of the fourth. Children received medical therapy including nebulized salbutamol, theophylline, and steroids and were similar at baseline, with a mean age of approximately 10, mean onset of asthma at roughly age 2, and mean asthma severity score of approximately 2.3 on a scale of 1 (mild) to 3 (severe). Three children (one in placebo and 2 in CPT group) completed the study twice due to readmissions. Lung function did not differ significantly between groups at baseline or follow-up. Investigators were able to measure sputum production in 26% of CPT sessions, with weights ranging from 0.7 to 10.8 grams. LOS was longer, though not significantly, in the placebo group. We rated the quality for the outcomes of LOS and pulmonary function tests as fair.

A second RCT including children with asthma (ages 4-18 years) admitted with status asthmaticus to either CPT plus standard medical therapy (n=20) or standard medical therapy alone (n=20).[24] CPT included six sessions (one each hour over 24 hours) of percussion using a pneumatic chest percussor for 20 minutes following nebulized albuterol administration. Medical therapy included inhaled beta-2 agonists and systemic steroids. Investigators measured airway resistance at baseline and follow-up using the impulse oscillometry system, and initial measurement occurred a mean of 12 ± 6 hours after admission; thus, participants had some degree of improvement before baseline measurement. Oxygen saturation did not differ from baseline to follow-up in either group while peak flow improved in both groups from baseline to follow-up ($p<0.005$). Differences in peak flow between groups were not significant. Airway resistance did not change significantly in either group from baseline to follow-up.

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Differences in airway resistance between groups as a function of time or steroid use were not significant. We rated quality for the outcome of oxygenation as poor.

CPT Compared With ACBT

The MATREX (Management of Exacerbations of COPD) RCT allocated participants hospitalized with COPD to either CPT plus ACBT or ACBT alone.[15] CPT included manual positioning, percussion during thoracic expansion, vibration upon expiration, and ACBT techniques including forced expiration. The number and duration of CPT treatments was up to the discretion of the therapist, although the CPT treatments themselves were standardized. Patients randomized to ACBT alone received advice on positioning and ACBT to mobilize sputum. Patients in both groups also received standard medical therapy. Patients were followed for 6 months after randomization, and primary outcomes were scores on the St. George Respiratory Questionnaire (SGRQ) and European Quality of Life-Five Dimensions (EQ-5D) and visual analog scales (EQ-VAS). The mean of the 258 individuals randomized to the CPT group was 69.08 ± 9.85 years, mean baseline SGRQ total score was 68.94 ± 14.66, and mean baseline EQ-VAS was 44.95 ± 21.03. The ACBT-only arm included 264 participants (mean age=69.58 ± 9.51, mean baseline SGRQ total score=69.13 ± 14.76, mean EQ-VAS-46.64 ± 21.42). Differences between groups at baseline were not significant.

CPT patients received a median of two CPT sessions (median duration=11 minutes, median 2 positions/session). At 6 months, between group differences in COPD-specific quality of life were not significant in adjusted (for baseline value and hospital site) and unadjusted intention to treat (ITT) analyses (mean SGRQ symptoms score effect size, adjusted analysis=0.04, 95% CI=-0.15 to 0.23; mean SGRQ activity score effect size, adjusted analysis=-0.02, 95% CI=-0.20 to 0.16; mean SGRQ impact score effect size, adjusted analysis=0.02, 95% CI=-0.15 to 0.18). All of the 95% confidence intervals

were within the study's predefined limits for equivalence. Similarly, quality of life ratings on the EQ-VAS (effect size 2.65, 95% CI=-2.37 to 7.65) and EQ-5D (effect size -0.01, 95% CI=-0.07 to 0.06) were not significantly different in adjusted or unadjusted ITT analyses. Length of stay was not significantly different between groups (CPT=16.02 ± 16.57 mean days, ACBT=16.85 ± 18.11 mean days). The mean number of hospital admissions during the 6-month follow-up period was 3.47 for the CPT group and 3.89 for the ACBT group (significance not reported). At 6 months the control group performed significantly better on the 6-minute walk test compared with the CPT group (mean difference=83.23, 95% CI= 13.09 to 153.37). CPT participants reported 15 adverse events including increased shortness of breath (n=5), pain (n=5), arrhythmia (n=3), bronchospasm (n=1), and thoracic hematoma (n=1). Investigators did not consider there harms to compromise patient safety. We rated quality for the outcomes of LOS, exacerbations/readmissions, and harms of airway clearance techniques as fair, and poor for dyspnea, exercise tolerance, and QOL.[15]

Syed et al. included 35 adults with bronchiectasis in a crossover RCT evaluating short term CPT compared with ACBT.[25] Investigators used a convenience sample of patients undergoing medical therapy for bronchiectasis, allocating them to either CPT (20-30 minute sessions every 3 hours; CPT included percussion and vibration in various postural drainage positions, cough and deep breathing techniques) or ACBT (huffing, deep breathing, and relaxed breathing cycles for maximum 30 minutes in various postural drainage positions). Intervention sequences were separated by 12 hours over 2 days. The mean age of the 35 participants was 45.8 ± 11.2 years, 25 were smokers, and 17 had a history of tuberculosis. The wet weight or volume of expectorated sputum did not differ significantly between treatments at follow-up (mean difference, weight=0.96 ± 17.7 ml, mean difference, volume=-1.68 ± 20.50, p weight or volume=NS). Pulmonary function tests (FVC, FEV_1, FEV_1/FVC) also did not differ between treatment sequences. Participants rated ACBT as more comfortable on a 10cm visual analog

scale (median 8 vs. 5 for CPT, p=0.004). We rated quality for the outcomes of pulmonary function and sputum volume as poor.

CPT Compared With IPV

Paneroni et al. evaluated IPV and CPT in a crossover RCT that included 22 patients with bronchiectasis.[26] The mean age of the participants was 64.4 ± 8.9 years and mean percent predicted FEV_1 was 53 ± 30. The IPV arm included three active cycles alternating high and low pressure for 30 minutes. Chest physical therapy included forced expiration, postural drainage, percussion, and vibration in three positions for a total of 30 minutes. At follow-up, there was no significant difference in mean sputum volume and wet and dry sputum weight between groups. SpO_2 also did not differ between groups. Heart rate fell significantly from baseline to follow-up in both groups ($p<.05$) but did not differ between groups. Respiratory rate decreased significantly in the IPV group from baseline, but not for CPT, and the difference between groups at the final followup was also significant (p=.047). Dyspnea improved significantly from baseline (p=.004) in the IPV group also, but between group differences were not significant. Harms were reported by both groups and included dry throat, nausea, and/or fatigue (27% of both groups). Post-treatment discomfort was lower with IPV compared with CPT (p=.03). We rated quality for the outcomes of oxygenation as good, fair for sputum volume, and poor for heart and respiratory rate, dyspnea, and harms.

Antonaglia et al. randomized patients with COPD undergoing helmet noninvasive positive pressure ventilation (NPPV) to either CPT (n=20) or IPV (n=20).[27] CPT included 25 to 30 minutes of chest percussion, mobilization, postural drainage, and expiration with the glottis open in lateral posture. IPV consisted of 25 to 30 minute sessions of mouthpiece IPV delivering high flow mini-bursts at 225 cycles/minute. Patients also received medical treatments as required. Patients in both groups were

similar at baseline (mean age-CPT group=69 ± 7 years, median APACHE II=22; mean age-IPV group=72 ± 7 years, median APACHE II=22). Twenty-seven patients in both groups were hypersecretive (≥30 ml secretions/day). Investigators assessed differences with an overall analysis of variance and included data from a historical control group in the analysis. Differences between groups at discharge were not significant for median respiratory or heart rate or mean arterial pressure. $PaCO_2$ and PaO_2/FiO_2 differed significantly between groups at discharge (mean $PaCO_2$ CPT group=64 ± 5.2 mm Hg, IPV group=58 ± 5.4, historical control group=67±4, $p<.01$; mean PaO_2/FiO_2 CPT group=218 ± 34.2, IPV=274 ± 14.8, historical control group=237±20, $p<.01$), with the IPV group demonstrating higher PaO_2/FiO_2 and lower $PaCO_2$. In both groups seven patients were required to undergo intubation and mechanical ventilation (vs. NPPV), but the IPV group required a lower median number of hours of ventilatory assistance (61 vs. 89 median hours in the CPT group, p=NR). Median length of ICU stay was also lower for the IPV group (7 days vs. 9 days for CPT, p=NR). Four patients in the CPT group and two in the IPV developed sepsis or pneumonia (p=NR). We rated quality for the outcomes of gas exchange, LOS, mean arterial pressure, and need for and duration of ventilation as fair. We rated quality as poor for the outcomes of heart rate and respiratory rate.

Clini and colleagues evaluated the effectiveness of IPV in ICU patients with tracheostomy recently weaned from mechanical ventilation.[18] The total study population (n=46) included both post-cardiac surgery patients (n=6) and those with neuromuscular disease/impairment (n=8) as well as COPD or chronic respiratory insufficiency (n=22). Groups were similar at baseline, and all participants were hypersecretive (≥40 ml secretions/day). Investigators allocated patients to either 15 days of IPV (2 sessions/day) plus CPT (n=24) or CPT alone (n=22). CPT in both groups comprised two one-hour sessions per day of postural and manual drainage followed by nebulized saline and repeat of drainage maneuvers plus suctioning. PaO_2 increased significantly in the IPV group from baseline (69 ± 8 mmHg

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to 76 ± 9 mmHg, p≤0.05) as did PaO_2/FiO_2 (238 ± 51 to 289 ± 52, p≤0.005). Maximal expiratory pressure was also significantly increased from baseline to day 15 in the IPV group (34 cmH_2O/12% to 47/1%, p≤0.005) and as compared with the CPT only group (p≤0.05). Mean differences in PaO_2/FiO_2 and maximal expiratory pressure between groups were, respectively, 21.65 (95% CI: -11.75 to 55.05, p=0.038) and 9.26 (95% CI: 1.98 to 16.54, p=0.014). At day 15, two patients in the CPT arm and one in the IPV arm had any pulmonary complications. At the one-month follow-up, no IPV patients had any complications while two in the CPT group had pneumonia (p≤0.05 for comparison of pneumonia between groups at all time points). We rated quality for pulmonary function and gas exchange as poor.

Positive expiratory pressure (PEP) modalities with and without CPT

In an RCT including 30 participants with bronchiectasis (mean age 50.7 ± 6.4 years, mean FEV_1=21%), participants received Acapella or inspiratory muscle training in a crossover fashion.[28] Acapella treatment included 10 breaths at near maximum capacity followed by breath hold, active exhalation, and coughing or huffing after every five breaths. Use of the inspiratory muscle trainer similarly included 10 breaths at maximal inspiratory effort followed by breath hold, active exhalation, and coughing/huffing after every five breaths. Treatment occurred at the same time over 3 consecutive days, with medications administered ≥ 1 hour prior to treatment. Medications include inhaled beta-agonists (n=17), inhaled corticosteroids (n=2), oral antibiotics (n=15), and oral corticosteroids (n=2). Expectorated sputum (volume in ml) was significantly greater in the Acapella group compared with muscle training (mean ± SD=7.16 ± 1.12 vs. 6.46 ± 1.08, p=0.014, mean difference=0.70 ml, 95% CI=0.13 to 1.27). Patients rated Acapella as more useful in clearing secretions but ratings of convenience, comfort, and overall performance did not differ significantly between modalities. We rated quality for the outcome of sputum volume as poor.

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In an RCT including ICU patients with COPD exacerbation, Bellone et al. evaluated 3 daily, 30-40 minute sessions of PEP plus assisted coughing compared with assisted coughing alone.[29] All patients received noninvasive mechanical ventilation until meeting weaning criteria or criteria for progressing to intubation, and all received medical therapy (nebulized salbutamol, nebulized ipratropium bromide, intravenous methylprednisolone, antibiotics). Patients were similar at baseline (PEP group, n=13 mean age=65 ± 7.8 years, mean APACHE II score=16.6 ± 1.1; coughing only group, n=14 mean age=64 ± 7.7 years, mean APACHE II= 17 ± 1.2, p=NS). Sputum production was higher in the PEP group compared with coughing-only at the end of treatment (9.6 ± 3.9 g vs. 4.7 ± 2.5 g, $p<0.01$) and continued to increase in the 60 minutes following treatment in PEP patients but not in the coughing-only group. The PEP group also required fewer days to wean from noninvasive ventilation (4.9 ± 0.8 vs. 7.0 ± 0.7, $p<0.01$). No patients in the PEP group and one in the coughing-only group progressed to intubation (p=NS). PEP-related harms included discomfort from the PEP mask reported by two patients (15.3%), neither of whom stopped treatment during the study. We rated quality for the outcomes of duration of ventilation as fair and sputum volume as poor.

In a crossover RCT including mechanically ventilated ICU patients, Unoki and colleagues compared rib cage compression (one 5 minute session) plus endotracheal suctioning to suctioning alone.[30] Intervention sequences were separated by 3 hours. Patients (mean age=56.7 ± 17.6 years, mean Simplified Acute Physiology score= 59.4 ± 10.7) were hospitalized for various causes including intracerebral hemorrhage (19%), cardiac arrest (19%), pneumonia (12%), and cerebral infarction (12%). Forty-two percent of patients had radiographic evidence of atelectasis. Sputum weight did not differ significantly between intervention periods, nor did PaO_2/FiO_2 or $PaCO_2$. The quality for the outcome of gas exchange was poor.

RESPIRATORY CARE Paper in Press. Published on November 12, 2013 as DOI: 10.4187/respcare.02704

Studies Assessing the Flutter Valve. Ambrosino and colleagues compared effects of the Flutter device and postural drainage plus percussion in 14 patients hospitalized with COPD, bronchiectasis, bronchitis, or silicosis on sputum production and patient discomfort in a crossover RCT.[31] Each patient underwent two sessions of postural drainage and manual chest percussion or breathing through the Flutter device. Each session could be conducted for up to 30 minutes at the discretion of the patient, and patients could cough and perform deep breathing as desired during each treatment. Treatments were separated by a 24-hour washout period; thus the study extended over eight days. Patients continued their standard medical therapies throughout the study. At baseline patients produced a mean of 51 ± 27 mL of sputum/day and had mean FEV_1 of 49 ± 26. Sputum production increased significantly by roughly 10mL during both treatment sequences ($p<0.001$ compared with baseline for each treatment) and was increased over baseline, though not significantly, at 60 minutes post-treatment. Patients' self-rated feelings of "chest unpleasantness due to sputum" improved significantly from baseline to 60 minutes post-treatment for both treatment sequences ($P<0.0001$). Measures of pulmonary function and oxygenation (FEV_1, forced vital capacity, peak flow, oxygen saturation) remained stable and did not differ significantly across time points. We rated quality for the outcomes of pulmonary function, oxygenation, and sputum volume as poor.

In a single-blind RCT including 15 patients hospitalized with bronchiectasis exacerbation, Tsang and Jones compared three airway clearance modalities (each delivered once/day for 15 minutes until discharge): postural drainage plus breathing and coughing exercises, Flutter and breathing/coughing and breathing/coughing alone.[32] Each group included 5 patients with mean age/group ranging from 66.8 to 64.2 years. Mean FEV_1 (% predicted) at baseline ranged from 36.10 to 48.47%. Groups were similar at baseline, though there were more smokers in the breathing/coughing alone group (4/5 compared with 1/5 in postural drainage plus breathing/coughing group and 3/5 in the Flutter group. Significance not

provided). Mean length of stay was similar among the groups—7.2 ± 3.3 days in the postural drainage plus breathing/coughing group, 6.2 ± 3.83 in the Flutter group, and 5.2 ± 0.84 in breathing/coughing alone patients (p=NS). Similarly, wet weight of sputum expectorated did not differ significantly among the groups at any time point. Pulmonary function tests (FVC, FEV_1, peak expiratory flow [PEF]) also did not differ significantly from baseline to follow-up within groups or between groups. Patient-rated scores of effectiveness were higher in the Flutter group compared with the breathing/coughing- only group at all time points (p<.0.05); effectiveness scores did not differ significantly between the Flutter and postural drainage+breathing/coughing group. We rated quality for the outcome of LOS as fair. We rated quality for the outcomes of pulmonary function and sputum weight as poor.

In a crossover RCT including 20 mechanically ventilated patients with pulmonary infection and hypersecretion in an adult ICU, Chicayaban et al. evaluated use of the Flutter valve compared with normal pressure controlled ventilation.[33] Participants were mechanically ventilated for a mean of 21.6 days, had mean APACHE II scores of 21.7, and typically (75%) had ventilator-acquired pneumonia. Participants received two 15-minute sessions of Flutter or normal ventilation, separated by a 6-hour washout period. At follow-up immediately after the intervention, secretion production was greater in the Flutter group compared with the control (5.1 ± .5 ml vs. 3.3 ± .3 ml, respectively, p<.001). Static compliance increased significantly in the Flutter group from baseline (p<.001) as did peak flow (p=.008) and expiratory flow at 75% tidal volume (p=.005). Respiratory mechanics did not change significantly in control participants. Mean airway pressure increased significantly in the Flutter group from baseline and compared with the control group (p<.05). The end tidal partial pressure of CO2 increased significantly from baseline in the control group and in Flutter participants as compared with the control group (p<.05). Oxygen saturation similarly increased significantly in the Flutter group compared with control.

($p<.05$). We rated as good the quality for the outcomes of oxygenation and arterial pressure. We rated quality of the outcomes of pulmonary function, gas exchange, heart rate, and sputum volume as fair.

Samransamruajkit and colleagues randomized children (6-16 years old) hospitalized for acute asthma to Flutter treatment (15-20 minute session) plus medical therapy or medical therapy alone.[34] Patients in the medical therapy group also had instructions to cough. Baseline age and pulmonary characteristics were similar between groups except for initial asthma score (mean=5.9 in Flutter group and 4.45 in medical treatment group, $p<0.01$) and oxygen requirement (mean=30 in Flutter and 25 in medical treatment only, $p<0.05$). At day 3 of the study, differences between groups in oxygen saturation, FiO_2, or asthma score were not significant; however, only 5 patients in each group remained at this point. Mean post-treatment asthma score did decrease significantly in the Flutter group compared with medical treatment on day 2 (1.3 ± 0.3 vs. 2.5 ± 0.3, $p=0.01$). Length of stay was not significantly different between groups, and no serious adverse events were reported in the Flutter group (harms not specified). We rated quality for the outcomes of oxygenation and LOS as fair. We rated quality for pulmonary function as poor.

Studies Evaluating Postural Drainage

Berney et al. included 20 mechanically ventilated ICU patients in a crossover RCT comparing postural drainage plus manual hyperinflation followed by ventilatory hyperinflation with postural drainage and ventilator hyperinflation followed by manual hyperinflation.[35] In both treatment conditions, the foot of the bed was elevated and patients placed in a side-lying position before undergoing six sets of six manual or ventilator hyperinflation breaths and suctioning. Patients received both treatments, separated by 2 hours, on each of 2 days. Patients (mean age=45.2 years, APACHE II score range=10 to 22) had spinal injury (n=12, 10 with quadriplegia), multiple trauma (n=4), respiratory

failure (n=1) and other indications. After the 2-day study, the mean sputum production in the manual hyperinflation group was 6.53 grams (95% CI: 5.86 to 7.20) and 6.01 grams in the ventilator hyperinflation group (95% CI: 4.83 to 7.19); weights did not differ significantly (mean difference=2.65 grams, 95% CI: 1.79 to 3.54). Both treatments significantly improved ($p<0.001$) static pulmonary compliance from baseline with a mean percentage improvement of 9.7 following manual hyperinflation (95% CI: 46.5 to 54.9) and 11.6% associated with the ventilator hyperinflation sequence (95% CI: 45.5 to 54.7). Mean arterial pressure, heart rate, and SaO_2 did not change adversely with either treatment. We rated quality for the outcome of sputum weight as poor.

Ntoumenopoulos and colleagues similarly assessed the effects of manual hyperinflation and postural drainage compared with usual care on pulmonary complications in mechanically ventilated trauma patients in an RCT.[36] Patients in the manual hyperinflation group (n=22) received six hyperinflation breaths repeated four times in postural drainage positions for 20 minutes, plus suctioning as needed between sets and routine turning. Control patients (n=24) received routine nursing care (suctioning as needed and turning twice/hour). Groups were similar at baseline (treatment group mean age=38.85 ± 16.62 years, mean APACHE II score=12.3 ± 3.8; control group mean age=41.20 ± 20.15 years, mean APACHE II= 14.1 ± 7.4). Days on mechanical ventilation, days in ICU, and level of pulmonary dysfunction (worst daily PaO_2/FiO_2 ratio) were similar between groups at follow-up. Four patients in the treatment group and eight in the control were withdrawn from the study per protocol because of suspected pneumonia; three individuals in the treatment and four in the control group were diagnosed with pneumonia (p=NS). We rated quality for the outcomes of pulmonary function, LOS, and duration of ventilation.

An RCT conducted by Krause et al. included mechanically ventilated ICU patients with atelectasis of the lower lobes and compared standard with modified postural drainage.[37] Patients were

between 13 and 85 years old and had conditions including bronchial obstruction (n=2), rib fracture or surgery (n=5), pleural effusion (n=3), pneumonia (n=3), Guillain-Barré syndrome (n=1),and pneumothorax/hemothorax (n=3). Participants received 15 minutes of either standard postural drainage (one of four positions depending on location of lung collapse, each including elevation of foot of bed,) following inhalation of mucolytics (n=9) or modified postural drainage (supine, side lying or ¼ to prone positioning, depending on location of lung collapse) following mucolytics (n=8). Both groups received percussion for five minutes and suctioning following positioning. The study does not report whether patients were statistically similar at baseline. The standard drainage group required a mean of three treatments to resolve the collapse compared with 4.5 in the modified group (p=NR). Arterial blood gas values (PaO_2, oxygen saturation, diffusion gradient, tension ratio between arterial blood and alveolar air, respiratory index, venous shunt values) improved more from baseline to the final treatment in the standard postural drainage group compared with the modified group, though differences were not significant. We rated quality for the outcome of gas exchange as fair.

Barker and Adams conducted an RCT to assess the effects of a single session of commonly used CPT modalities on pulmonary function and oxygenation in mechanically ventilated patients with acute lung injury.[38] Investigators randomly allocated participants to either supine positioning plus suctioning (Group 1, n=5, mean age=73 ± 2.6), lateral decubitus positioning plus suctioning (group 2, n=5, mean age=70 ± 7.4), or lateral decubitus positioning plus six manual hyperinflation breaths plus suctioning (Group 3, n=7, mean age=70 ± 16.3). Patients were hospitalized with sepsis (n=7), aspiration pneumonia (n=5), community acquired pneumonia (n=4), and pancreatitis (n=1); the study does not indicate if baseline differences among the groups were significant. Venous oxygenation saturation did not change significantly over time within or among groups, though it was lower in Group 2 at all time points (p=0.03). $PaCO_2$ and PaO_2/FiO_2 similarly did not differ within groups or among groups at the 60-minute

follow-up. Dynamic compliance and mean arterial pressure did not differ among the groups at follow-up. Heart rate varied significantly within and among groups over time ($p<0.05$). We rated quality for the outcome of gas exchange as fair. We rated quality for the outcomes of heart rate and mean arterial pressure as poor.

Studies Evaluating Intrapulmonary Percussive Ventilation (IPV)

Vargas et al. conducted an RCT comparing standard medical and oxygen therapy to standard therapy plus IPV via facemask in ICU patients with COPD.[39] The 16 patients in the IPV group had a mean age of 69.2 years and mean FEV_1 of 39%. Values in the standard therapy group were 70.2 years and 38%. Groups were not significantly different at baseline. IPV patients received the same medical treatment (supplemental oxygen, nebulized salbutamol or terbutaline, nebulized ipratropium bromide, subcutaneous heparin, corticosteroids, oral methylprednisolone, antibiotic, correction of electrolyte abnormalities) as the control group plus two daily 30 minute IPV sessions (mean duration of therapy=3 ± 1 days). No patient in either group received any additional airway clearance modalities. Six patients in the standard treatment group had a worsening of exacerbation and required noninvasive ventilation compared with 0 patients in the IPV group ($p<0.05$). Length of stay was also significantly longer in the standard therapy group (7.9 ± 1.3 days vs. 6.8 ± 1, $p<0.05$). Respiratory rate and $PaCO_2$ decreased significantly from baseline to the end of the first IPV session in the IPV group while PaO_2 increased ($p<0.05$); these values were not reported for the standard therapy group. We rated quality for the outcomes of pulmonary function, need for ventilation, oxygenation, and LOS as fair. We rated quality for the outcome of respiratory rate as poor.

Studies Evaluating Chest Wall Compression

RESPIRATORY CARE Paper in Press. Published on November 12, 2013 as DOI: 10.4187/respcare.02704

Mahajan and colleagues assessed hospitalized adults (≥18 years old) with physician-diagnosed acute asthma and/or COPD in an RCT sponsored by the manufacturer of the pneumatic vest evaluated.[14] Investigators randomly allocated participants to either high frequency chest wall compression via inflatable vest (The Vest® Airway Clearance System, n=25, median age 46.5 years) or sham chest wall compression, which provided a sensation of vibration without airflow oscillation (n=27, median age=50.4 years). Participants also received standardized medical treatment (albuterol, systemic or inhaled corticosteroids, supplemental oxygen, other medications as needed). Roughly 60% of patients in each group had asthma, and 40% had COPD. Baseline characteristics did not differ significantly between groups; patients in both groups had a median of one hospitalization in the year preceding the current admission.

After 60 total minutes of treatment/sham treatment (administered over two days) dyspnea was significantly improved in the treatment group compared with the sham group (median change in Borg score of -1.5 vs. 0, p=0.048). Differences in spontaneously expectorated sputum, FEV_1%, and length of hospital stay were not significant. Four patients in each group reported an acute care visit (hospitalization or ED visit) in 30-day follow-up. Patient satisfaction and adherence to both treatment and sham treatment were high. We rated quality for all outcomes (pulmonary function, dyspnea, sputum, LOS, and time to readmission) as good.[14]

Studies in Postoperative Patients

Studies Evaluating CPT

Johnson and colleagues stratified patients by degree of atelectasis in an RCT comparing CPT modalities of graduated intensity (combinations of early ambulation plus deep breathing, sustained maximal inspirations, and percussion) in post-coronary artery bypass surgery patients.[40] Investigators

RESPIRATORY CARE Paper in Press. Published on November 12, 2013 as DOI: 10.4187/respcare.02704

randomly allocated patients with minimal atelectasis on chest X-ray to either early mobilization plus deep breathing (Group 1, n=48 patients) or early mobilization plus deep breathing plus sustained maximal inspirations (Group 2, n=49). Patients with marked atelectasis were allocated to either early mobilization plus deep breathing plus sustained maximal inspirations (Group 3, n=64) or all of those modalities plus percussion (Group 4, n=63). Mobilization included graduated increases in activity; deep breathing instructions were for five deep breaths/hour daily, recorded by patients in a log. Sustained maximal inspiration comprised stacked inhalations to total lung capacity with a five-second breath hold for five repetitions and conducted once each waking hour with position changes as tolerated. Percussion sessions (3/day) consisted of one to two cupped hand percussions/second to the chest wall during the total lung capacity phase of a sustained maximal inspiration.

Patients were similar at baseline in all preoperative and pulmonary function parameters except, as per protocol, degree of atelectasis. All pulmonary function values (vital capacity, FEV_1, functional residual capacity, maximum expiratory pressure, negative inspiratory pressure, carbon monoxide diffusion) deteriorated significantly in all groups from baseline to discharge ($p<0.0001$), though discharge values did not differ significantly among groups. Length of ICU stay was significantly greater ($p<0.05$) in Group 3 (2.3 ± 0.8 days) and Group 4 (2.3 ± 0.6 days) than in Groups 1 or 2 (both groups LOS=2.0 ± 0.5 days). Length of hospital stay was similarly significantly longer ($p<0.05$) in Groups 3 (9 ± 2.7 days) and 4 (10 ± 8.5 days) than the other groups (8 ± 1.5 or 1.6 days). Eight patients in Group 1, 10 in Group 2, 14 in Group 3, and 13 in Group 4 (p=NS) met criteria for pneumonia, with an overall incidence of 12%. No patients developed respiratory failure, and none required repeat ICU admission because of respiratory complications. The authors note that percussion was associated with minor complications; however, only data for falling oxygen saturation (below 90% in 7/295 treatments) and tachycardia (12/295 treatments) was reported. None of these episodes was associated with significant

blood pressure changes. We rated quality for the outcomes of pulmonary function, LOS, and pulmonary complications as poor.[40]

In a related study, Johnson et al. randomized patients undergoing cardiac valve surgery to the same regimen of either early mobilization and deep breathing exercises plus sustained maximal inspirations (Group 1) or early mobilization, deep breathing exercises, sustained maximal inspirations, and 2 sessions of percussion/day (Group 2).[41] This study likely involved some of the same patients as Johnson's earlier study in bypass patients,[40] though the precise extent of overlap is unclear. The 41 patients in Group 1 and 34 in Group 2 were similar in most characteristics at baseline; however, patients in Group 2 were older by approximately five years (63 ± 12 years vs. 68 ± 10 years, p=0.0044). Pulmonary function values decreased in both groups from baseline to discharge, with changes in forced vital capacity, functional residual capacity, FEV_1 %, and diffusion of carbon monoxide reaching statistical significance in both groups (p<0.0001). Diffusion of carbon monoxide was significantly lower in Group 2 compared with Group 1 at discharge (15 ±5 mL/min/mmHg vs. 10 ± 2.4 mL/min/mmHg, p<0.05) as was negative inspiratory pressure (39 ± 19 cm H_2O vs. 33 ± 14 cm H_2O, p<0.05). Atelectasis scores at discharge and length of ICU stay and hospital stay were similar between groups. Two patients in each group developed pneumonia for an overall incidence of 5%. No patient progressed to respiratory failure, and none required ICU readmission for respiratory complications. We rated quality for all outcomes (pulmonary function, heart rate, LOS, pulmonary complications) as poor.

In an RCT similarly evaluating the role of CPT following cardiac valve surgery, de Charmoy and Eales allocated surgical patients to receive either coughing and mobilization instructions (n patients=14) or CPT (n patients=16) including positioning and breathing and coughing exercises with sessions twice/day on postoperative days 1-2 and once/day on days 3-4.[42] CPT patients also received assisted walking at each treatment session. Patients were similar at baseline with an overall mean age of 29.72

years (range=11-63 years). PaO_2 declined significantly in both groups from baseline but values at follow-up did not differ significantly between groups. Length of stay did not differ between groups. No patients in either group developed pulmonary complications including pneumonia. We rated quality for gas exchange and pulmonary complications as poor.

In an RCT assessing the effectiveness of deep breathing and sputum clearing techniques in reducing post-abdominal surgery pulmonary complications, Mackay et al. randomized 56 patients to either early post-surgical mobilization (n=21) or early mobilization plus deep breathing ("coached lateral basal expansion") exercises and airway clearance maneuvers (coughing huffing, FET).[43] The deep breathing group (n=29) received therapy 3 times/day on postoperative day 1, twice daily on days 3 and 4, and daily until the patient was mobile and had a clear chest assessment for 3 consecutive days. Patients were also encouraged to practice the deep breathing techniques independently during each waking hour. Early mobilization included graduated assisted and independent walking as tolerated plus leg flexion exercises performed independently. One early mobilization-only participant (who was later withdrawn from the study) was mistakenly given deep breathing exercises; investigators analyzed data for this patient by ITT and with the deep breathing group.

The mean age of the 50 study completers was 66 years, and groups were similar at baseline with 14 treatment patients and 11 early mobilization-only having a history of chronic airway limitation or pulmonary disease. Surgery types in both groups included colectomy/hemicolectomy (n=26), bowel resection (n=4), gastrectomy/esophagectomy (n=6), and abdominoperineal resection (n=3). The incidence of postoperative pulmonary complications (defined as 3 or more respiratory signs including auscultation changes, fever, chest X-ray changes, and increase or change in sputum) did not differ between groups (17% in the treatment group vs. 14% in the mobilization only group, p=NS). The absolute risk reduction was -3.0% (95% CI: -0.22 to 0.19%). Length of stay was greater in the

RESPIRATORY CARE Paper in Press. Published on November 12, 2013 as DOI: 10.4187/respcare.02704

mobilization-only group (mean 13 ± 4.5 days vs. 10.4 ± 3.0, p=0.008; difference in means=2.9, 95% CI: 0.77 to 5.03). Mean ICU days were similar between groups as was the need for mechanical ventilation (2 patients in each group required mechanical ventilation for a duration of 2 days in the control group and 0.75 day in the treatment group). We rated quality as good for LOS, pulmonary complications, and need for and duration of ventilation.[43]

In another RCT of post-abdominal surgery patients, Olsen et al. compared pre- and postoperative CPT with no CPT on the incidence of pulmonary complications.[44] Patients in the CPT group (n=174) underwent preoperative CPT (10-15 minutes of breathing exercises, huffing and coughing, education about positioning and mobilization) on the day before surgery and postoperative CPT (15-20 minute sessions conducted hourly by the patient and including deep breathing plus huffing and coughing) thereafter for an unspecified duration. Investigators also preoperatively classified patients in each group as low or high risk based on age ≥50 years plus one of the following: smoker or recent ex-smoker, BMI≥30, pulmonary disease with need for daily medication, history of other condition causing reduced ventilatory function. High risk patients in the CPT group also received PEP masks for respiratory resistance training during breathing exercises. Control group patients received no preoperative training and no postoperative CPT unless a pulmonary complication was diagnosed, at which point they received CPT plus PEP mask. Patients in each group did not differ significantly at baseline. Postoperative pulmonary complications (defined as oxygen saturation <92% or two of the following: fever, negative auscultation, radiologic evidence of pneumonia or atelectasis) were diagnosed in 10 (6%) CPT patients, 6 of whom were considered high risk, and 52 (27%, 20 considered high risk) in the control arm (p<0.001). Among obese patients, 3 CPT patients and 27 control patients developed complications (p<0.001). One CPT patient and 13 control patients were diagnosed with pneumonia (p<0.05), for an overall incidence rate of 4%. Vital capacity and peak expiratory flow declined significantly in all

patients from baseline to follow-up, but differences between groups were not significant. Duration of hospital stay was also not significantly different (mean 8.8 ± 4.5 days in CPT group, 9.0 ± 5.1 in control). The study does not indicate the duration or modalities of CPT provided to those 52 control patients with pulmonary complications who presumably received postoperative CPT per protocol. We rated quality for the outcomes of pulmonary function and complications, heart rate, and LOS as poor.

Studies Evaluating Positive Expiratory Pressure (PEP) Modalities With and Without CPT

Denehy and colleagues compared twice daily standard CPT (coughing and deep breathing including sustained maximal inspirations and FET for a minimum of 10 minutes) with CPT plus either 15 or 30 minute sessions of continuous positive airway pressure (CPAP) four times/24 hours in an RCT including post-abdominal surgery patients.[45] Investigators encouraged participants in each group to walk early and to perform deep breathing exercises independently each hour, though compliance was not tracked. Among the 50 study completers, 18 were randomized to CPT only (mean age=73.3 ± 5.8 years, mean preoperative FEV_1=2.3 ± 0.6 l), 17 to 15 minutes of CPAP (mean age=72.5 ± 6.5, mean FEV_1=2.3 ± 0.8 l), and 15 to 30 minutes of CPAP (mean age=70.5 ± 6.3, mean FEV_1=2.4 ±0.6). Patients did not differ significantly at baseline. Pulmonary function measurements (reported for 40/50 participants) included vital capacity and functional residual capacity. Pulmonary function measurements typically varied across time points in each group but did not differ significantly among groups at follow-up on postoperative day 5. Mean oxygen saturation and length of stay were also not significantly different among groups. Nearly 70% of all patients had some radiographic evidence of lung collapse or consolidation on the third postoperative day. Fourteen percent of patients across groups (4 in CPT only group, 5 in 15-minute CPAP group and 1 in 30-minute CPAP group, p=NS) had pulmonary complications (defined as fever >24 hours, chest radiograph score of 2 or more, and with elevated white

RESPIRATORY CARE Paper in Press. Published on November 12, 2013 as DOI: 10.4187/respcare.02704

cell count, altered sputum, isolation of pathogen from sputum, or need for additional antibiotics). We rated quality for the outcomes of oxygenation, pulmonary complications, and LOS as fair. We rated the quality for pulmonary function as poor.

Haeffener et al. conducted an RCT assessing the effects of incentive spirometry plus expiratory positive airway pressure compared with control techniques (coughing instructions, deep breathing exercises, early mobilization) on pulmonary function and complications in post-coronary artery bypass grafting patients.[17] The intervention group performed the spirometry protocol twice/day for 15-20 minutes; therapists gradually increased expiratory pressure to a maximum of 15cm H_2O. Spirometry patients continued the protocol at home post-discharge, with weekly phone check-ins by study staff. Lung alterations on chest X-ray (assessed at one week post-surgery) were significantly lower among spirometry patients compared with controls ($p<.0004$). At the one-month follow-up, pulmonary function improved in the spirometry group from baseline while values in the control group remained 10-26% lower than baseline. Functional capacity as assessed on the 6-minute walk test was higher in the spirometry group compared with control (data in figure only, $p<0.001$). We rated quality for the outcomes of pulmonary function, exercise tolerance, and LOS as poor.

Discussion

The 32 studies meeting our review criteria typically reported a small magnitude of treatment effect across a spectrum of interventions. Patient populations varied across studies and included individuals with COPD, bronchiectasis, asthma, as well as ICU and trauma patients. Comparators used across studies similarly varied. While studies often measured the same outcomes (e.g., length of stay, oxygen saturation), studies varied in reporting of outcomes and how they were measured (e.g., sputum weight vs. sputum volume). This heterogeneity meant that meta-analysis was not appropriate or feasible.

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Variations of CPT were the most frequently studied intervention, but there is not a standardized method for delivering CPT (Table 6) and inter-therapist variation and study technique variation may be important co-factors. Moreover, patients were often receiving critical care for more than one diagnosis, and the airway clearance outcomes and care modalities were likely not the primary determinant of the patient's condition or course of illness or recovery. Therefore, it is difficult to ascribe important clinical outcomes to the airway clearance intervention under study; and often surrogate or intermediate measures were utilized for comparison data.

We considered most studies of poor quality for the outcomes assessed (Table 7, Online Appendix). Frequently used outcome measures for airway clearance techniques are limited in their accuracy and reliability, and most are difficult to tie to the effects of airway clearance specifically.[12, 46, 47] Some measures such as sputum weight or volume have limited repeatability and specificity. Similarly, tests of pulmonary function are dependent on a patient's effort and motivation, may be variably interpreted, and may not accurately reflect the effectiveness of a given clearance modality.[46-48] We summarize study results for key outcomes below.

Summary of Results by Outcome

Sputum Weight or Volume

Studies included in the review measured sputum using both weight and volume. Measurement techniques differed, with some studies assessing dry weight, others wet weight, and some using dedicated collection pots or other techniques. Two studies of poor quality for the outcome of sputum expectorated compared CPT and standard care and found no differences between groups.[16, 21] For adults with bronchiectasis, a comparison of CPT versus ACBT, rated as poor quality, reported no significant difference in sputum volume or weight. [25] Similarly, for adults with bronchiectasis, a comparison of

CPT versus IPV, rated as fair quality, reported no significant difference in sputum volume or weight.[26] Three different studies (all poor quality) of patients with three different conditions assessed the effects of PEP versus CPT on sputum weight or in volume. Two studies reported no significant difference between PEP and the comparison.[28, 30] One small study of adult ICU patients with COPD reported more sputum in the intervention group.[29]

Three studies compared the Flutter device to a control intervention: two poor quality studies reported no significant difference.[31, 32] The third small study of adult ICU patients on a ventilator reported more sputum measured in the intervention group.[33] One poor quality study of postural drainage reported no significant difference in sputum measurements,[35] while one good quality study of chest wall compression with a vest in patients with asthma and COPD reported no significant difference in sputum between the intervention group and the sham vest group.[14]

Oxygenation and Gas Exchange

Seven studies of CPT in various populations including children with asthma,[22, 24, 34]and adults with COPD[16] or bronchiectasis,[26] and mechanically ventilated or postoperative patients[44, 45]reported no significant differences between groups in oxygenation. Studies were of good,[26] fair,[16, 22, 24, 44] or poor[34, 45] quality for this outcome. One good study of Flutter in mechanically ventilated patients and one fair study of IPV in patients with COPD reported improved oxygenation in the intervention arms.[33, 39]

Measurement of arterial blood gases, an indirect and invasive measure of effectiveness of airway clearance interventions, was evaluated in nine studies, all of which reported no significant difference in values between groups; two were fair quality and four were poor quality.[18, 30, 31, 37-39, 42] A fair quality study of the Flutter device reported better values for adult ventilated patients in the intervention group.[33]

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Finally, a fair quality study reported worse values for patients with COPD treated with CPT compared with those treated with IPV.[27]

Pulmonary Function Tests

Thirteen studies, most of poor quality for pulmonary test outcomes, reported no significant difference in values between groups.[14, 17, 23-25, 31, 32, 35, 38, 40, 41, 44, 45] Three studies reported improved results: a poor quality study of IPV + CPT versus CPT in ICU patients with COPD reported better pulmonary function tests in the intervention group,[18] and a poor quality study of spirometry plus PEP compared with standard care in postoperative CABG patients reported better pulmonary function in the intervention group.[17] A fair quality study reported that participants in the Flutter arm had better pulmonary function compared with those receiving standard care.[33]

Need for/Progression to or Duration of Mechanical Ventilation

For CPT compared to standard care in ventilated adult ICU patients, two studies of fair quality reported days on the ventilator. One reported no significant difference in the duration,[20] and the other reported a longer duration on the ventilator for the CPT (intervention) group.[19] A fair quality study in COPD patients receiving CPT or IPV reported no group difference in progression to ventilation but a shorter duration of ventilation in the IPV group.[27] Another fair quality study of IPV in COPD patients reported that fewer IPV patients progressed to ventilation,[39] while in a study of CPT in postoperative patients, progression to ventilation did not differ between groups.[43] In two fair quality studies of patients receiving noninvasive[29] or routine ventilation[36], patients receiving PEP[29] required fewer ventilator days while the duration did not differ in the study of postural drainage.[36]

Signs and Symptoms

Four studies rated poor quality for the outcome of heart rate included patients with COPD,[27] bronchiectasis,[26] and postoperative[41] or mechanically ventilated ICU patients.[38] Difference in heart rate were not significant between groups in any study. Similarly three studies assessing mean arterial pressure (one good quality evaluating Flutter vs. usual care in mechanically ventilated ICU patients, one fair quality comparing IPV with CPT in COPD patients, and one poor quality comparing CPT regimens in mechanically ventilated patients) reported no significant group differences.

In studies assessing respiratory rate, one fair quality study reported no differences in time to normal respiratory rate in children with pneumonia receiving either CPT or CPT plus usual care.[22] One study of IPV in patients with COPD reported no significant differences.[27] Patients with COPD or bronchiectasis receiving IPV did improve significantly compared with the usual care in two poor quality studies.[26, 39]

Two studies, one of poor quality comparing CPT with usual care in patients with COPD[16] and one of good quality comparing high frequency chest wall compression with placebo,[14] reported significant improvements in dyspnea in the intervention arms. Two poor quality studies comparing either IPV with CPT[26] or CPT with ACBT[15] reported no significant group differences.

Exercise Tolerance

Two studies were considered poor quality for the outcome of exercise tolerance.[15, 17] One study compared CPT plus ACBT with ACBT alone and reported significantly better tolerance among CPT patients.[15] Similarly, a small study of PEP compared with usual care in postoperative patients found improved distance walked in the PEP group.[17]

Pulmonary Complications

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For adult patients on a ventilator in the ICU, one good quality study of CPT reduced the risk of ventilator-acquired pneumonia compared to the control intervention[20] and a second fair quality study of IPV and standard care reduced the risk of ventilator-acquired pneumonia compared to standard care alone.[27] In a poor quality study of chest vibration in mechanically ventilated ICU patients, vibration resulted in less atelectasis compared with positioning. [21] While current studies report improved outcomes with intervention, the literature base is currently small, and the results imprecise. Future studies may confirm or change current estimates.

For surgical patients, pre-operative training reduced the risk of hospital-acquired pneumonia, compared to no pre-operative training in a poor quality study.[44] Four other studies of airway clearance interventions in postoperative patients reported no significant difference in complication rates; (one good, one fair, and two poor quality).[41-43, 45]

Length of Stay

Length of stay, another indirect measure of the effectiveness, was reported in nearly half of the studies. For CPT compared to standard care, five studies (three of poor quality, and two of fair quality) reported no significant difference.[16, 19, 20, 22, 23] A fair quality study reported longer LOS for patients with COPD treated with CPT compared to those treated with IPV.[27] Two studies of the Flutter device reported no significant difference in LOS compared to other standard treatments. [32, 34] A fair quality study of postural drainage and manual inflation compared to standard care reported no significant difference in LOS. [36]

A good quality study of a chest wall compression vest in patients with asthma or COPD reported no significant difference in LOS compared to a sham vest. [14] Two studies of IPV compared to standard care in ICU patients reported shorter length of stay for the patients who received IPV.[18, 39]

Three studies of airway clearance modalities in postoperative patients reported a lower LOS in the treatment groups.[40, 43, 45] Studies reporting LOS were in different patient populations, and used different interventions and comparators, and the outcome measure is indirect; therefore, the studies could not be combined meaningfully.

Exacerbations/Hospital Readmissions

Three studies (one good, one fair, one poor quality) assessing different interventions (high frequency chest wall compression or variations of CPT) in patients with COPD reported no significant group differences in the number of admissions or exacerbations.

Quality of Life

Two poor quality studies of patients with COPD, one comparing CPT with ACBT[15] and another comparing CPT with usual care[16] reported no significant group differences in quality of life as assessed on the St. George Respiratory Questionnaire and other measures.

Harms of Airway Clearance Techniques

Three studies reported harms specific to the airway clearance modalities;[15, 26, 35] one poor quality study noted a significantly lower incidence of harms in the IPV arm while the others did not assess significance.

Methodologic Considerations and Limitations

The small magnitude of treatment effects, uncertain and high risks of bias of included studies, and small number of studies using clinically meaningful outcomes significantly limits the potential impact of the review findings for individuals, guideline panels, and healthcare policy-makers. More than half of the studies were rated as having high risk of bias on the basis of allocation concealment, but this

is in the face of the fact that concealment would be a significant challenge for this type of research. Prior surgical sham studies, however, would suggest that it is possible. The complexity of care, and the fact that many other factors were more powerful drivers of important clinical outcomes, renders it difficult to tease out the specific effect of the interventions on important clinical outcomes (Table 8). Indeed the comparison is frequently poorly described or not described, and with "usual care" lacking standardization, it is challenging to assess the impact of interventions. As noted in tables throughout this report, neither the interventions nor the comparators were consistent across any subset of studies. Few controls for variation in technique, for example among therapists, were identified, and the interventions were typically poorly characterized in terms of duration and quantity. In addition, studies routinely failed to identify or capture harms of the intervention.

Nonetheless, although differences in effect were typically not significant, it is possible that effects are meaningful in terms of the patient experience and perception. It is unclear whether or not small changes in pulmonary function measured by sputum weight, sputum volume, and blood gases, translate to subjective changes in patient comfort. Few studies included any assessment of patient comfort or quality of life, and we would suggest that is an important area of further exploration. Important outcomes to consider would be exacerbations of illness and health-related quality of life.

Future Research

In building a body of evidence, initial studies should establish the effectiveness of individual interventions against placebo, and then proceed to head to head comparisons among interventions. In the absence of the first stage, head to head comparisons yielding nonsignficant results cannot be used to establish the effectiveness of either intervention. Researchers in this field should be encouraged to use standard RCT methodology with random sequence generation and to develop approaches for good

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allocation concealment. In this way, even small studies in the future would be more useful for providing a basis for guidance. However, ultimately, because of the complexity of the patient condition and the numerous modalities of care, large studies with the ability to match patient and care characteristics are essential.

The promising studies in the review should be repeated with rigorous methods, and using similar PICO (population, intervention, comparator, outcomes), thus enabling future meta-analysis to generate estimates of effect with adequate power. Elements of the intervention should be standardized and the characteristics of the comparator well described. As a field, respiratory care should consider assessing the degree to which outcomes in research are clinically meaningful and agreeing on a set of core outcomes for future work.

Conclusions

In summary, the 32 studies included in this review provide limited evidence for the effectiveness of nonpharmacologic airway clearance techniques. Evidence from this review indicates that airway clearance techniques are probably safe for patients on a ventilator in the ICU and confer zero to small beneficial effects on some clinical outcomes.[18-21, 30, 33, 35-38] Consideration may be given to the use of airway clearance techniques for patients on a ventilator in the ICU, to reduce the risk of acquiring pneumonia, based upon two studies of 76 patients.[20, 27] Based on current limited evidence, airway clearance modalities might not be recommended as routine prophylaxis to prevent postoperative pulmonary complications in adults undergoing surgery in hospital.[41-45] Similarly, in people with COPD, data from six single studies specifically targeting COPD did not provide evidence of significant short-term benefit of airway clearance modalities.[14-16, 27, 29, 39]

Our finding of limited evidence is in line with similar, recent reviews of airway clearance in patients with COPD and pneumonia, which have generally noted small benefits.[11, 12, 49, 50] Interventions,

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comparators, and populations varied considerably across studies, hampering our ability to draw firm conclusions. Interventions including conventional CPT, IPV, and PEP typically provided small benefits in pulmonary function, gas exchange, oxygenation, and need for/duration of ventilation, among other outcomes, but differences between groups were generally small and not significant. Harms of techniques were not consistently reported, though airway clearance techniques were generally considered safe in studies that did comment on adverse effects. Further research with clearly characterized populations and interventions is needed to understand the potential benefits and harms of these techniques.

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Figure Legend:

We screened the abstracts of 2054 articles identified via database searches and article reference lists. Of these, we retained 313 for review of the full text of the study and excluded 1741. We retained 32 studies, which are described in the review. The 281 excluded studies were excluded because of various reasons including not addressing outcomes, interventions, or populations of interest; study design; and setting.

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Table 1. Inclusion and exclusion criteria

Category	Criteria
Study population	• Hospitalized or postoperative patients over 1 year of age and without cystic fibrosis receiving nonpharmacologic airway clearance therapies • Patients with neuromuscular disease or respiratory muscle weakness over 1 year of age and without cystic fibrosis and receiving nonpharmacologic airway clearance therapies • Patients with impaired cough over 1 year of age and without cystic fibrosis and receiving nonpharmacologic airway clearance therapies
Time period	• 1990–2012
Publication languages	• English only

Admissible evidence (study design and other criteria)	Admissible designs
	• Controlled trials, observational studies including prospective cohort studies
	Other criteria
	• Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results
	• Patient populations must include individuals as noted above
	• Studies must address one or more of the following interventions:
	  ○ Active cycle of breathing
	  ○ Autogenic drainage
	  ○ Bronchoscopy
	  ○ Chest physical therapy/physiotherapy (percussion, vibration, positioning, postural drainage)
	  ○ Cough assist (insufflation/exsufflation, FET, device)
	  ○ Cuirass
	  ○ High frequency chest compression vest
	  ○ Intrapulmonary percussive ventilation
	  ○ Positive expiratory pressure (oscillatory PEP, Flutter, Acapella)

Admissible evidence (study design and other criteria, continued)	• Studies must provide baseline and outcome data for one or more of the following outcomes of interest:
	  ○ Time to exacerbation of disease/condition
	  ○ Need for ventilatory assistance
	  ○ Time to re-admission
	  ○ Quality of life
	  ○ Pulmonary function (FEV_1, FVC, peak flow)
	  ○ Gas exchange
	  ○ Symptoms and signs (dyspnea, cough, HR, breath sounds, retractions)
	  ○ Sputum clearance and expectoration (transport, weight, volume)
	  ○ Exercise tolerance
	  ○ Oxygenation
	Or outcome data for:
	  ○ Antibiotic use as affected by airway clearance
	  ○ Harms (including mortality) related to airway clearance interventions
	  ○ ICU or hospital length of stay
	  ○ Number of hospital admissions or hospital days
	• Studies must include extractable data on relevant outcomes, including data presented in text or tables (vs. solely in figures)
	• Study must be hospital- or inpatient-based

FET=forced expiratory technique; FEV1=forced expiratory volume in 1 second; FVC=forced vital capacity; HR=heart rate; ICU=intensive care unit; PEP=positive expiratory pressure

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Table 2. Quality rating algorithm

Low RoB criteria	High RoB criteria	Unclear RoB criteria	Quality Level
7	0	0	Good
6	0, 1	0, 1	Good or Fair
5	0, 1	1, 2	Good or Fair
5	2	0	Fair or Poor
4	0-2	0-3	Fair or Poor
0-3	0-7	0-7	Poor
0-7	3-7	0-7	Poor
0-7	0-7	4-7	Poor

RoB=risk of bias

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Table 3. Overview of included studies

Characteristic	RCT	Crossover RCT	Prospective cohort	Total Literature
N studies	24	7	1	32
Population				
Adult	18	7	1	26
Pediatric	4	0	0	4
Mixed	2	0	0	2
Underlying condition*				
Asthma	5	0	0	5
Bronchiectasis	1	3	0	4
COPD	8	2	1	11
Pneumonia or other pulmonary infection	1	3	0	4
Post-surgical/critical illness/trauma	13	3	1	17
Intervention category*				
ACBT	0	1	0	1
Chest physical therapy	19	4	1	24
High frequency chest wall compression	1	0	0	1
IPV	3	1	0	4
PEP	6	4	0	10
Country				
Asia	2	3	0	5
Australia	4	1	1	6
Europe	9	2	0	11

South America	2	1	0	3
US or Canada	5	0	0	5
Africa	2	0	0	2

*Numbers do not tally as studies may appear in more than one category; ACBT=active cycle of breathing technique; COPD=chronic obstructive pulmonary disease; IPV=intrapulmonary percussive ventilation; PEP=positive expiratory pressure; RCT=randomized controlled trial

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Table 4. Summary of key findings of studies of airway clearance in hospitalized, non-postoperative patients

Author, Year Study Design	Population characteristics	Groups, N enrollment/N final	Key Findings
CPT compared with usual care or CPT + additional treatment			
DiDario et al., 2009, [24] RCT	Children with status asthmaticus	**G1**: Mechanical percussion + standard medical therapy, 20/19 **G2**: Standard medical therapy, 20/19	• No change in airway resistance in both groups and no difference between groups over time • Normal oxygen saturation over time • Phase angle decreased (p<0.005) in both groups over time • Peak flow improved (p<0.005) in both groups and over time • All endpoints improved independent of CPT
Paludo et al., 2008, [22] RCT	Children hospitalized with pneumonia	**G1**: Postural drainage, thoracic squeezing, percussion, vibration, cough stimulation + standard pneumonia treatment, 51/47 **G2**: Standard pneumonia treatment, 47/42	• Longer median duration of coughing in intervention group (p=0.04) • No significant differences between groups in time to resolution, LOS, duration of fever, wheezing, crackles, time to normal respiratory rate or normal oxygenation saturation
Templeton et al., 2007, [19] RCT	Adult ICU patients with varied diagnoses (COPD, asthma, cardiac arrest, ICH, sepsis,	**G1**: Positioning, manual hyperinflation, drainage, 91/87 **G2**: Standard ICU care, 89/85	• Marginally significant prolongation of median time to become ventilator free among G1 (p=0.047) compared to G2 with time to become ventilator free for 50% of patients (G1: 15, G2: 11 days) • No significant differences in ICU mortality or in the time to death (G1: 11,G2:13 days) or in the

	shock, cancer), intubated and ventilated for 48hrs		median length of ICU stay (G1: 13 vs. G2: 12 days) • No significant difference between groups in time to becoming ventilator free by the time 75% of patients were weaned
Chen et al., 2009, [21] RCT	Mechanically ventilated adult ICU patients	**G1**: Positioning +chest vibration, 50/50 **G2**: Positioning only, 45/45	• Greater dry sputum weight and lower lung collapse index among patients receiving vibration • Greatest sputum expectoration in vibration group occurred in the first 24 hours post-vibration
Kodric et al., 2009, [16] RCT	Adults with acute exacerbation of COPD	**G1**: Expiration with glottis open in lateral posture + standard medical treatment , 30/30 **G2**: Standard medical treatment only, 29/29	• No significant difference in sputum volume between the 2 groups; significant reduction in both groups at 24hrs (p=0.001) • Fewer exacerbations and hospitalizations in expiration group but no significant group differences after six months (G1:n=11 G2:n=11) • Significant decrease in dyspnea score (p=0.004) in expiration group • Quality of life scores after one month were similar in both groups
Ntoumenopoulos et al., 2002, [20] Prospective cohort	Critically ill adult ICU patients, intubated and mechanically ventilated for >48 hrs	**G1**: Postural drainage, positioning, vibration, coughing, 24/24 **G2**: Control / Sham CPT, 36/36	• CPT significantly associated with a reduction in ventilator associated pneumonia (adjusted odds ratio: 0.16, 95%CI: 0.03 to 0.94) • No group differences in the length of stay in ICU or mortality • 95% developed acute lung collapse/ consolidation but no group differences
Asher et al., 1990, [23]	Children with acute severe	**G1**: CPT (positioning, lateral costal breathing,	• Lung function, sputum weight similar in both groups at the end of study

RCT	asthma	diaphragmatic breathing, shoulder relaxation, postural drainage, coughing, FET, vibration, wing flapping, percussion, thoracic mobility exercises, postural correction exercises) + medical therapy, 19/16 **G2**: "Placebo" + medical therapy, 19/18	• Placebo group had longer hospital stay compared with CPT group (p=NS)
Studies of CPT compared with ACBT			
Cross et al., 2010, [15] RCT	Adults with COPD exacerbation	**G1**: Manual chest physiotherapy with percussion, thoracic expansion exercises, vibration, periods of relaxed abdominal breathing, and forced expiration technique according to ACBT techniques, advice on positioning, 261/186 **G2**: Advice on positioning, cough and sputum mobilization according to ACBT, 266/186	• No significant differences on St George's Respiratory Questionnaire scores (symptom score, impact score, activity score) at 6 months • No significant difference in other outcome measures, including EQ-VAS score, EQ-5D score, breathlessness scale score, hospital LOS (at 6 weeks or months) • G2 walked significantly further on average at 6 months in 6 minute walk test
Syed et al., 2009, [25]	Adults with productive bronchiectasis	**G1**: ACBT, 18 **G2**: Percussion, vibration, cough and breathing	• No difference in sputum weight and volume, absolute pulmonary function tests between treatment groups

RCT--Crossover		techniques, 17 **G1**,**G2**: 35/35	• Significant difference in FEV_1/FVC % between pre-post therapy in both groups (p≤0.032) • Patients more comfortable with ACBT than CPT (VAS, p=0.004)
Studies of CPT compared with IPV			
Paneroni et al., 2011, [26] RCT--Crossover	Adults with bronchiectasis admitted to respiratory department	**G1**: Chest physiotherapy including forced expiration, postural drainage, percussion, and vibration **G2**: Intrapulmonary percussive ventilation **G1**, **G2**: 22/22	• No significant difference between groups for heart rate, SpO2, volume or wet or dry weight of sputum, dyspnea, sensation of phlegm encumbrance • Significantly greater decrease in respiratory rate with IPV • Heart rate decreased significantly in both groups • Significantly less post-treatment discomfort in IPV group, although the authors note high variability
Antonaglia et al., 2006, [27] RCT	Adult ICU patients with exacerbation of COPD	**G1**: Standard helmet-NPPV+ Percussion, postural drainage, expiration with glottis open in lateral posture, 20/20 **G2**: Helmet NPPV+ noninvasive IPV, 20/20 **G3**: Facial mask NPPV+ Percussion, postural drainage, expiration with glottis open in lateral posture (historical controls), 40/40	• At discharge, IPV group had lower $PaCO_2$ and higher PaO_2 / FiO_2, shorter duration of ventilator assistance and shorter length of ICU stay than the other 2 groups • Blood gas exchange and heart and respiratory rates improved after IPV
Clini et al., 2006 [18]	Adult inpatients with	**G1**: Chest physiotherapy (postural drainage, manual	• Significantly more patients with nosocomial pneumonia in G2; no difference between groups

RCT	tracheostomy admitted for mechanical ventilator weaning	drainage) plus IPV, 24/23 **G2**: Chest physiotherapy, 22/21	for acute hemorrhage or atelectasis. • No significant difference between groups on PaO2, PaCO2, or pH; significant improvement in PaO2/FIO2 and maximal expiratory pressure in IPV group
Studies evaluating PEP modalities			
Chicayban et al., 2011, [33] RCT--Crossover	Mechanically ventilated adult patients with pulmonary infection	**G1**: Flutter **G2**: Normal pressure controlled ventilation **G1**, **G2**: 20/20	• Flutter improved sputum production ($p < .001$) • Expiratory flow at 75% of tidal volume ($p=0.005$), arterial PO2-to-inspired oxygen concentration ratio ($p < .001$) • No change in respiratory resistance, heart rate, and mean arterial pressure ($P > .05$)
Tsang et al., 2003, [32] RCT	Adults with acute exacerbation of bronchiectasis	**G1**: Postural drainage + breathing and coughing **G2**: Flutter + breathing and coughing **G3**: Breathing and coughing alone **G1**, **G2**, **G3**: 26/15 (5 in each group)	• No significant difference in sputum production (wet weight) or lung function parameters among the 3 groups
Samransamruajkit et al., 2003, [34] RCT	Children with acute asthma (uncomplicated)	**G1**: Flutter +standard therapy, 20/20 **G2**: Standard therapy, 20/20	• G1 had more severe asthma at baseline compared with G2 • Significant increase in FVC and FEV1 in G1 vs. G2 ($p<0.05$) on the 1st and 2nd hospital days. G1 had higher FEV than G2 ($p=0.08$) • No difference in length of hospital stay between G1 and G2 ($p=0.3$) • No serious adverse effects noted in G1
Bellone et al.,	Adults with	**G1**: PEP+Assisted cough,	• Sputum production at the end of treatment was

2002, [29] RCT	acute exacerbation of COPD requiring non-invasive positive pressure ventilation in respiratory ICU	13/13 **G2**:Assited cough only, 14/14	significantly (p<0.01) higher in G1 (9.6±3.9 g) compared to G2 (4.7±2.5 g) • Mortality not significantly different in the two groups of patients • No significant change in saturated oxygen in either group • Sensation of discomfort reported with use of PEP by 2 patients (15.3%)
Ambrosino et al., 1995, [31] RCT--Crossover	Adults in-patients with high sputum >25ml/day due to diseases other than CF	**G1**: Oscillatory PEP **G2**: Postural drainage + percussion **G1**, **G2**: 14/14	• No change in expiratory flow or oxygen saturation • Similar amount of sputum production , 60min following end of treatment • No adverse effects were observed during either treatment
Unoki et al., 2005, [30] RCT--Crossover	Adult mechanically ventilated ICU patients	**G1**: Rib cage compression/Suctioning **G2**: Suctioning/Rib cage compression **G1**, **G2**: 144/31	• No improvement in oxygenation, ventilation, • or secretion clearance with rib cage compression • No significant PaO2 /FIO2 , PaCO2 differences between the 2 post-intervention periods • No significant differences in the weight of the collected sputum in the 2 periods
Studies evaluating postural drainage			
Berney et al., 2002, [35] RCT--Double crossover	Intubated, ventilated and cardiovascularly stable adult patients	**G1**: Postural drainage plus manual hyperinflation followed by ventilator hyperinflation **G2**:Postural drainage plus ventilator hyperinflation	• No significant difference in sputum wet weight between groups (p=0.11) • Pulmonary compliance improved with both types of hyperinflation techniques (p=0.001) • No adverse changes in heart rate, MAP or saturated oxygen

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		followed by manual hyperinflation **G1**, **G2**: 20	
Ntoumenopoulos et al., 1998, [36] RCT	Mechanically ventilated adult trauma patients	**G1**: Manual hyperinflation + postural drainage, 22/18 **G2**: Standard care, 24/16	• No difference in pulmonary dysfunction (worst daily PaO_2 / FiO_2) between groups • No ICU deaths reported • Days in ICU not different between groups (G1: 7.4 ± 5.7; G2: 6.8 ± 4.6) • More patients in G2 developed nosocomial pneumonia compared to G2 (p=0.017)
Krause et al., 2000, [37] RCT	Intubated teen/adult ICU patients with atelectasis (acute lobar)	**G1**: Postural drainage +percussion+suction, 9/9 **G2**: Modified postural drainage +percussion+suction, 8/8	• Oxygenation improved with G1 compared with G2 • G1 required 3 while G2 required 4.5 treatments to resolve collapse of lung • Better lung gas exchange in G1 compared with minimal changes in G2 • No statistical significance reported
Barker et al., 2002, [38] RCT	Mechanically ventilated adult ICU patients with acute lung injury	**G1**:Suction, 5/5 **G2**:Suction+positioning, 5/5 **G3**:Suction+positioning+ manual hyperinflation, 7/7	• Significant changes in $PaCO_2$ (p=0.026) over time for all 3 groups, no difference between groups (p=0.564) • PaO_2:FiO_2 ratio did not alter in any group • Significant difference between groups in Mixed venous oxygen saturation (p=0.03) • Heart rate and blood pressure statistically significantly different between groups over time (but not clinically significant) (p≤0.035)

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Studies evaluating IPV			
Vargas et al., 2005 [39] RCT	Adult ICU patients with acute exacerbation of COPD	**G1**: IPV two sessions per day plus standard medical therapy, 17/17 **G2**: Standard medical therapy (oxygen via nasal cannula with nebulized salbutamol or terbutaline, nebulized ipratropium bromide, subcutaneous heparin, corticosteroids, and antibiotic), 16/16	• Significantly less worsening of exacerbation in IPV group (G1: 0%; G2: 35.3%) • No hospital deaths occurred in either group • Significantly longer LOS in standard treatment G2 (G1: 6.8 ± 1.0; G2: 7.9 ± 1.3 p< 0.05)
Studies evaluating chest wall compression			
Mahajan et al., 2011 [14] RCT	Adult inpatients with acute asthma or COPD	**G1**: High frequency chest wall compression , 25/25 **G2**: Sham device, 27/27	• No significant difference between groups on adherence or measures of satisfaction • Significantly greater improvement in Borg score in G1 compared with G2 (71% vs. 42%, p=0.048) • No significant difference between groups for expectorated sputum, change in post-bronchodilator FEV_1 % predicted, length of stay, or use of systemic corticosteroids, acute care visits

ACBT=active cycle of breathing; CF=cystic fibrosis; CI=confidence interval; COPD=chronic obstructive pulmonary disease; ICU=intensive care unit; IPV=intrapulmonary percussive ventilation; LOS=length of stay; PEP=positive expiratory pressure; RCT=randomized controlled trial

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Table 5. Summary of key findings of studies of airway clearance techniques in postoperative patients

Author, Year Study Design	Population characteristics	Groups, N enrollment/N final	Key Findings
Studies of CPT			
Mackay et al., 2005, [43] RCT	Adults undergoing abdominal surgery	**G1:** Deep breathing, coughing, huffing, FET + mobilization, 29/29 **G2:** Mobilization only, 27/21	• No significant difference in the incidence of pulmonary complications between groups (G1:17%; G2 15%) • Significant difference in LOS (G1: 10.4 ±3 vs. G2:13.3 ± 4.5 days, p<0.008)
Denehy et al., 2001, [45] RCT	Adults admitted for upper abdominal surgery	**G1**: CPT (deep breathing exercises, sustained maximal inspiration, FET, coughing) +continuous positive airway (CPAP) pressure for 15 minutes **G2**: CPT + CPAP for 30 minutes **G3**: CPT only **G1**, **G2**, **G3**: 57/50	• Change in oxygen saturation across time was significant (p=0.0001) • No significant differences in FRC, vital capacity or SpO2 between groups • Postoperative complications occurred in all groups (G1: 11%, G2: 6%, G3:22%, p=NS) • Longer hospital stay among those with complications (p=0.021) but no difference in length of hospital stay between the groups
Charmoy et al., 2000, [42] RCT	Uncomplicated cardiac valvular surgery patients, 11-63 yrs of age	**G1**:Cough assist+breathing exercise, 16/16 **G2**: Instructions for coughing, 14/14	• None (0%) developed pulmonary complications • No difference in length of hospital stay or PaO_2 between treatment groups • Atelectasis present on day 4 postoperatively independent of treatment
Olsen et al.,	Adults	**G1:** CPT (Early	• Postoperative pulmonary complications more

1997, [44] RCT	undergoing elective open abdominal surgery	mobilization, breathing exercise, huffing, coughing, and PEP for high risk patients), 174/172 **G2:** Control (No info / treatment except for those with pulmonary complications), 194/192	frequent in G2 (27%) than in G1 (6%), p<0.001 • Improved oxygen saturation in G1 vs. G2 • No group difference in peak expiratory flow rate, forced vital capacity or duration of hospital stay
Johnson et al., 1996 [41] RCT	Adults undergoing elective cardiac valve surgery	**G1:** Sustained maximal inspiration, 41/41 **G2:** Sustained maximal inspiration + manual percussion, 34/34	• Both groups also received early ambulation and deep breathing; extent of atelectasis, reduction in FVC, FEV1 , hospital and ICU stays similar in both groups • Absolute values of diffusion of carbon monoxide and negative inspiratory pressures were lower in G2 compared with G1 (p≤0.02) at the time of discharge, decrease from baseline to discharge was similar between groups • 4 developed pneumonia , 2 in each group (overall incidence=5%), and therapy costs were higher for G2. Similar LOS in both groups
Johnson et al., 1995 [40] RCT	Adults undergoing coronary artery bypass	**G1 (minimal atelectasis):** Early ambulation+deep breathing, 48 **G2 (minimal atelectasis):**Early ambulation+deep breathing+sustained maximal inspiration**, 49** **G3 (extensive atelectasis):** Early	• Pulmonary function deteriorated from baseline to follow-up across all groups (p<0.0001) but values at followup did not differ significantly • LOS was greater in the extensive atelectasis groups • Incidence of pneumonia did not vary significantly among groups (overall incidence=12%) • Increased incidence of minor complications in G4

		ambulation+deep breathing+sustained maximal inspiration, 64 **G4 (extensive atelectasis):** Early ambulation+deep breathing+sustained maximal inspiration+manual percussion, 63	
Studies of PEP			
Haeffener et al., 2008, [17] RCT	Adults with ischemic heart disease undergoing CABG surgery	**G1:** Incentive spirometry+ expiratory positive airway pressure, 21/17 **G2:** Usual care, 22/17	• Spirometry plus positive airway pressure improved pulmonary function (forced vital capacity, forced expiratory volume ($p<0.05$), inspiratory capacity ($p<0.01$) • 6-minute walk distance ($p<0.01$) as well as a reduction in pulmonary complications after surgery ($p<0.004$) in spirometry group compared with control
Denehy et al., 2001, [45] RCT	Adults admitted for upper abdominal surgery	**G1**: CPT (deep breathing exercises, sustained maximal inspiration, FET, coughing) +continuous positive airway (CPAP) pressure for 15 minutes **G2**: CPT + CPAP for 30 minutes **G3**: CPT only **G1**, **G2**, **G3**: 57/50	• Change in oxygen saturation across time was significant ($p=0.0001$) • No significant differences in pulmonary function tests or SpO2 between groups • Postoperative complications occurred in all groups (G1: 11%, G2: 6%, G3:22%, p=NS) • Longer hospital stay among those with complications ($p=0.021$) but no difference in LOS between the groups

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CABG=coronary artery bypass grafting; CPAP=continuous positive airway pressure; CPT=chest physical therapy/physiotherapy; FET=forced expiratory technique; LOS=length of stay; PEP=positive expiratory pressure; RCT=randomized controlled trial

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Table 6. Components of CPT in studies using CPT as a treatment or comparator

Study	CPT components
Paneroni et al., 2011[26]	FET, postural drainage, percussion, vibration, coughing
Cross et al., 2010[15]	Chest percussion, vibration, assisted coughing, positioning
Chen et al., 2009[21]	Positioning, mechanical vibration
DiDario et al., 2009[24]	Mechanical percussion
Kodric et al., 2009[16]	Expiration with glottis open in lateral posture
Syed et al., 2009[25]	Postural drainage, manual percussion, vibration, coughing, diaphragmatic breathing
Paludo et al., 2008[22]	Postural drainage, thoracic squeezing, percussion, vibration, cough stimulation
Templeton et al., 2007[19]	Thoracic and pulmonary expansion, respiratory muscle exercise, manual hyperinflation, positioning, vibration
Antonaglia et al., 2006[27]	Percussion, postural drainage, expiration with glottis open in lateral posture
Clini et al., 2006[18]	Postural drainage, manual drainage
Mackay et al., 2005[43]	Deep breathing, coughing, huffing, FET
Tsang et al., 2003[32]	Postural drainage, deep breathing, coughing
Barker et al., 2002[38]	Positioning, manual hyperinflation
Berney et al., 2002[35]	Postural drainage, manual hyperinflation, ventilator hyperinflation
Ntoumenopoulos et al., 2002[20]	Postural drainage, positioning, vibration, coughing
Denehy et al., 2001[45]	Deep breathing exercises, sustained maximal inspiration, FET, coughing
deCharmoy et al., 2000[42]	Positioning, breathing exercises, coughing
Krause et al., 2000[37]	Postural drainage, percussion
Ntoumenopoulos et al., 1998[36]	Postural drainage, manual hyperinflation
Olsen et al., 1997[44]	Breathing exercises, coughing, huffing
Johnson et al., 1996[41]	Deep breathing exercises, sustained maximal inspiration, postural drainage, manual percussion
Ambrosino et al., 1995[31]	Postural drainage, manual chest percussion
Johnson et al., 1995[40]	Deep breathing exercises, sustained maximal inspiration, postural drainage,

	manual percussion
Asher et al., 1990[23]	Positioning, lateral costal breathing, diaphragmatic breathing, shoulder relaxation, postural drainage, coughing, FET, vibration, wing flapping, percussion, thoracic mobility exercises, postural correction exercises

Note: Patients typically also received suctioning, early mobilization, medical therapy, and standard turning per ICU protocols. FET=forced expiratory technique

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Table 7. Number of studies reporting key outcomes by quality rating

Outcome	Good (n studies)	Fair (n studies)	Poor (n studies)
LOS	2	9	5
Pulmonary function	1	3	11
Sputum weight/volume	1	2	8
Oxygenation	2	4	4
Gas exchange	0	5	3
Pulmonary complications	1	2	4
Duration of ventilation	1	4	0
Heart rate	0	1	4
Dyspnea	1	0	3
Harms of ACT	0	1	2
MAP	1	1	1
Respiratory rate	0	1	3
Exercise tolerance	0	0	2
QOL	0	0	2
Need for ventilation	1	3	0
Hospital readmission (Time to exacerbation)	1	1	1
TOTAL	**12**	**37**	**53**

ACT=airway clearance techniques; LOS=length of stay; MAP=mean arterial pressure; QOL=quality of life

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Table 8. Significant differences in key final outcomes by study*

Study	Arms	FEV_1	FVC	FRC	Peak flow	Lung/respiratory compliance or capacity	Maximal expiratory pressure	Sputum weight/volume	Dyspnea	Heart rate	Respiratory rate	6-minute walk test	Oxygen saturation	PaO2	PaCO2	PaO_2/FiO_2	Postoperative pulmonary complications†	Pneumonia/VAP	LOS (hospital or ICU)	Need for/progression to mechanical ventilation	Duration of mechanical ventilation	Re-admissions	Quality of life
Mahajan 2011[14]	HFCWC	0						0	+										0			0	
	Sham HFCWC	0						0	-										0			0	
Chicayban 2011[33]	Flutter				+	+		+		0			+			+							
	Standard ventilation				-	-		-		0			-			-							
Paneroni 2011[26]	IPV							0	0	0	+		0										
	CPT							0	0	0	-		0										
Naraparaju 2010[28]	Acapella							+															
	Inspiratory muscle training							-															
‡Cross 2010[15]	CPT+ACBT								0			+							0				0
	ACBT								0			-							0				0
Chen 2009[21]	CPT							+															
	Usual care							-															
Kodric 2009[16]	Expiration with glottis	0						0	+				0						0			0	0

	open in lateral posture Usual care	0						0	-				0						0			0	0
DiDario 2009[24]	CPT Usual care				0 0								0 0										
Syed 2009[25]	ACBT CPT	0 0	0 0					0 0															
Haeffener 2008[17]	Spirometry+positive airway pressure Usual care	0 0	0 0	0 0	0 0	+ -						+ -					+ -		+ -				
Paludo 2008[22]	CPT Usual care										0 0		0 0						0 0				
Templeton 2007[19]	CPT Usual care																	0 0	0 0		- +		
§Antonaglia 2006[27]	IPV CPT									0 0	0 0				0 0	0 0		0 0	0 0	0 0	0 0		
Clini 2006[18]	CPT+IPV CPT						+ -							0 0	0 0	+ -		+ -					
Unoki 2005[30]	Rib cage compression+suctioning Suctioning alone							0 0							0 0	0 0							

Vargas 2005[39]	IPV Usual care										0 0		+ -						+	+			
Mackay 2005[43]	Breathing and coughing Mobilization only																0 0		+	0 0	0 0		
Samransamruajkit 2003[34]	Flutter Usual care	+ -	+ -										0 0						0 0				
Tsang 2003[32]	Postural drainage+breathing/coughing Flutter+breathing/coughing	0 0	0 0		0 0			0 0											0 0				
	Breathing/coughing alone	0	0		0			0											0				
Barker 2002[38]	Positioning+manual hyperinflation+suctioning Lateral positioning+suctioning Supine positionng+suctioning					0 0 0				0 0 0					0 0 0								

Ntoumenopoulos 2002[20]	CPT Sham CPT																	+ -	0 0		0 0		
Berney 2002[35]	Manual hyperinflation/ventilator hyperinflation Ventilator hyperinflation/manual hyperinflation					0 0		0 0															
Bellone 2002[29]	PEP+assisted cough Assisted cough							+ -													+ -		
Denehy 2001[45]	CPT CPT+CPAP 15 mins CPT+CPAP 30 mins		0 0 0	0 0 0									0 0 0				0 0 0		0 0 0				
De Charmoy 2000[42]	CPT Usual care													0 0			0 0		0 0				
Krause 2000[37]	Postural drainage+percussion Modified postural drainage+percussion												0 0	0 0	0 0								
Ntoumenopoulos	CPT																	0	0		0		

1998[36]	Usual care																	0	0		0		
Olsen 1997[44]	CPT Usual care		0 0		0 0								0 0				+ -	+ -	0 0				
Johnson 1996[41]	Early mobilization+SMI Early mobilization+SMI+percussion	0 0	0 0	0 0						0 0								0 0	0 0				
Johnson 1995[40]	Early mobilization+deep breathing (minimal atelectasis) Early mobilization+deep breathing+SMI (minimal atelectasis) Early mobilization+deep breathing+SMI (marked atelectasis) Early mobilization+deep		0 0 0 0	0 0 0 0														0 0 0 0	+ + - -				

	breathing+SMI+percussion (marked atelectasis)																						
Ambrosino 1995[31]	CPT Flutter	0 0	0 0		0 0			0 0					0 0										
Asher 1990[23]	CPT Placebo	0 0	0 0	0 0	0 0														0 0				

+ value/change significantly better for group indicated compared with other group; - value/change significantly worse for group indicated compared with other group; 0 no significant difference between groups. Blank cell=outcomes not assessed in study.

* Note that this table reports values/change *between groups* at final follow-up only; values typically changed from baseline to followup *within each group*. Harms of ACT were also assessed in 3 studies[14, 25, 34] but significance was not typically assessed. One study[25] reported a significantly lower incidence of harms in the IPV arm. †Pulmonary complications as defined in study; ‡Number exacerbations requiring hospitalizations given but significance not reported. §Significance reported includes data for historical control group; differences between active intervention groups not clear. CPAP=continuous positive airway pressure; CPT=chest physical or physiotherapy; HFCWC=high frequency chest wall compression; IPV=intrapulmonary percussive ventilation; PEP=positive expiratory pressure; SMI=sustained maximal inspiration

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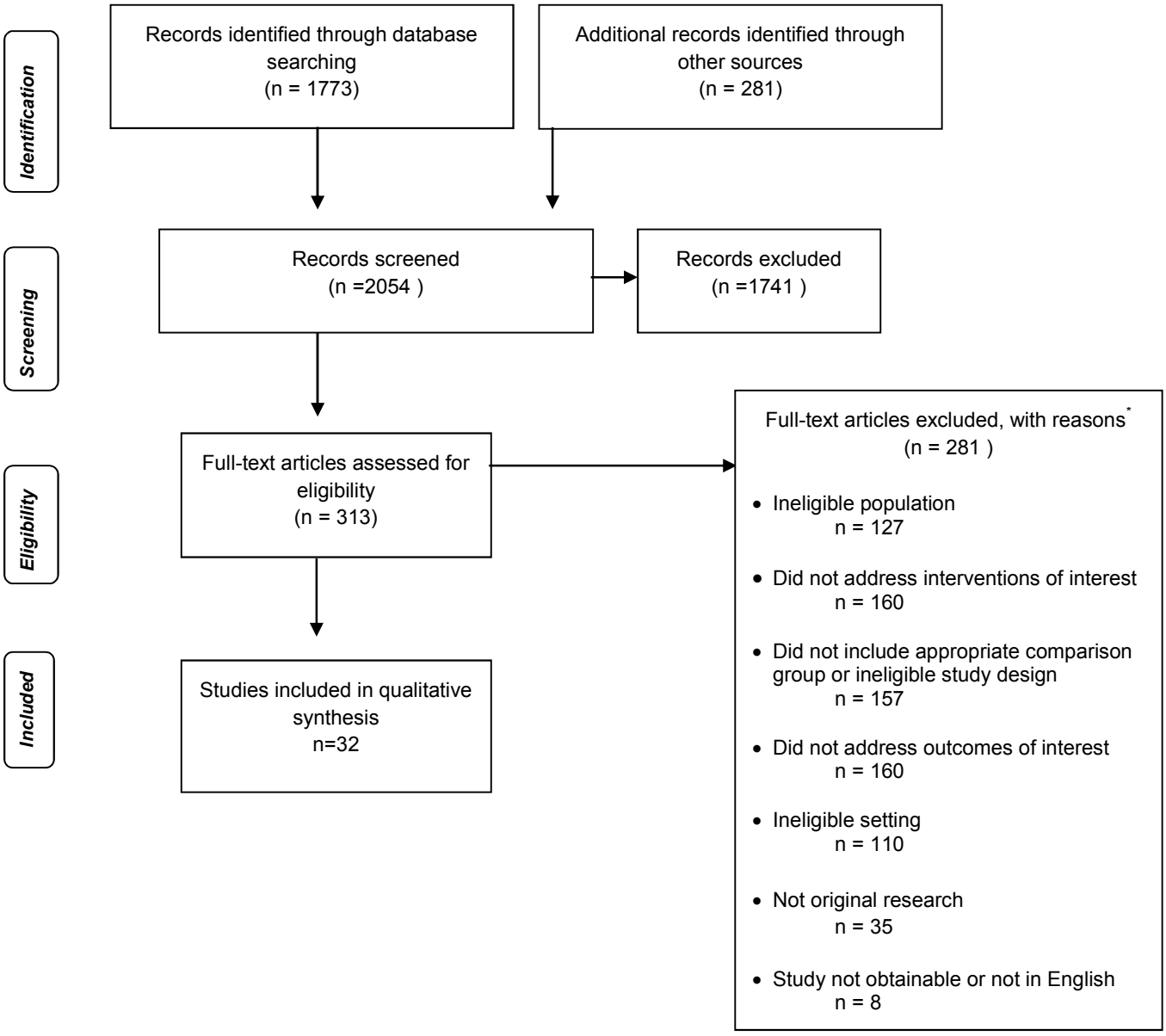
Figure 1. Disposition of studies identified for this review



* Numbers do not tally as studies could be excluded for multiple reasons.
n=number.