

## Medical Policy



### Title: **Oscillatory Devices for the Treatment of Cystic Fibrosis and Other Respiratory Disorders**

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<b>Populations</b>	<b>Interventions</b>	<b>Comparators</b>	<b>Outcomes</b>
Individuals: • With cystic fibrosis	Interventions of interest are: • Oscillatory devices	Comparators of interest are:	Relevant outcomes include: • Symptoms

Populations	Interventions	Comparators	Outcomes
		<ul style="list-style-type: none"> <li>Standard chest physical therapy</li> </ul>	<ul style="list-style-type: none"> <li>Quality of life</li> <li>Hospitalizations</li> <li>Medication use</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With bronchiectasis</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Oscillatory devices</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Standard chest physical therapy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Symptoms</li> <li>Quality of life</li> <li>Hospitalizations</li> <li>Medication use</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With chronic obstructive pulmonary disease</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Oscillatory devices</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Standard therapy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Symptoms</li> <li>Quality of life</li> <li>Hospitalizations</li> <li>Medication use</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With respiratory conditions related to neuromuscular disorders</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Oscillatory devices</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Standard therapy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Symptoms</li> <li>Quality of life</li> <li>Hospitalizations</li> <li>Medication use</li> </ul>

**DESCRIPTION**

Oscillatory devices are alternatives to the standard daily percussion and postural drainage method of airway clearance for patients with cystic fibrosis. There are several types of devices including high-frequency chest compression with an inflatable vest and oscillating positive expiratory pressure devices, such as the Flutter and Acapella devices. Respiratory therapists and other providers may also use oscillatory devices for other respiratory conditions such as diffuse bronchiectasis, chronic obstructive pulmonary disease (COPD), and respiratory conditions associated with neuromuscular disorders.

**OBJECTIVE**

The objective of this evidence review is to determine whether oscillatory devices improve the net health outcome in patients with cystic fibrosis and other respiratory disorders.

**BACKGROUND**

Oscillatory devices are designed to move mucus and clear airways; the oscillatory component can be intra- or extra thoracic. Some devices require the active participation of patients. They include oscillating positive expiratory pressure devices, such as Flutter and Acapella, in which the patient exhales multiple times through a device. The Flutter device is a small pipe-shaped, easily portable handheld device, with a mouthpiece at one end. It contains a high-density, stainless steel ball that rests in a plastic circular cone. During exhalation, the steel ball moves up and down, creating oscillations in expiratory pressure and airflow. When the oscillation frequency approximates the resonance frequency of the pulmonary system, the vibration of the airways occurs, resulting in loosening of mucus. The Acapella device is similar in concept but uses a counterweighted plug and magnet to create air flow oscillation.

Other airway clearance techniques also require active patient participation. For example, autogenic drainage and an active cycle breathing technique both involve a combination of breathing exercises performed by the patient. Positive expiratory pressure therapy requires patients to exhale through a resistor to produce positive expiratory pressures during a prolonged period of exhalation. It is hypothesized that the positive pressure supports the small airway such that the expiratory airflow can better mobilize secretions.

High-frequency chest wall oscillation devices (e.g., the Vest Airway Clearance System) are passive oscillatory devices designed to provide airway clearance without active patient participation. The Vest Airway Clearance System provides high-frequency chest compression using an inflatable vest and an air-pulse generator. Large-bore tubing connects the vest to the air-pulse generator. The air-pulse generator creates pressure pulses that inflate and deflate the vest against the thorax, creating high-frequency chest wall oscillation and mobilization of pulmonary secretions.

All of these techniques may be alternatives to daily percussion and postural drainage in patients with cystic fibrosis, also known as chest physical therapy. Daily percussion and postural drainage need to be administered by a physical therapist or another trained adult in the home, often a parent if the patient is a child. The necessity for regular therapy can be particularly burdensome for adolescents or adults who lead independent lifestyles. Oscillatory devices can also potentially be used by patients with other respiratory disorders to promote bronchial secretion drainage and clearance, such as diffuse bronchiectasis and chronic obstructive pulmonary disease. Additionally, they could benefit patients with neuromuscular disease who have impaired cough clearance.

This evidence review addresses the outpatient use of oscillatory devices. This review does not address inpatient device use (e.g., in the immediate postsurgical period).

## REGULATORY STATUS

Several oscillatory devices have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process, including those listed in Table 1.

**Table 1. Select Oscillatory Devices Cleared by the Food and Drug Administration**

Device	Manufacturer	Clearance Date
Flutter Mucus Clearance Device	Axcan Scandipharm (for marketing in the United States)	1994
Vest Airway Clearance System	Hill-Rom	1998
Acapella device	DHD Healthcare	1999
RC Cornet® Mucus Clearing Device	PARI Respiratory Equipment	1999
inCourage® System	RespirTech	2005
Lung Flute®	Medical Acoustics LLC	2006
Smartvest Airway Clearance System	Electromed	2013

<b>Device</b>	<b>Manufacturer</b>	<b>Clearance Date</b>
AerobiKA® oscillating PEP device	Trudell Medical	2013
Vibralung® Acoustical Percussor	Westmed	2014
The Vest Airway Clearance System	Hill-Rom	2015
iPEP® system including PocketPEP® and vPEP®	D R Burton Healthcare	2016
The Monarch™ Airway Clearance System	Hill-Rom	2017
Pulsehaler™	Respinova	2021

PEP: positive expiratory pressure.

U.S. Food and Drug Administration product codes: BYI, BYT.

## **POLICY**

- A. Use of an oscillatory positive expiratory pressure (PEP) device may be considered **medically necessary** in individuals with hypersecretory lung disease (i.e., produce excessive mucus):
  - 1. who have difficulty clearing the secretions; **AND**
  - 2. who have recurrent disease exacerbations.
  
- B. High-frequency chest wall compression devices and intrapulmonary percussive ventilation (IPV) devices may be considered **medically necessary** in individuals with:
  - 1. cystic fibrosis, **OR**
  - 2. chronic diffuse bronchiectasis as determined by specific criteria (see Policy Guidelines) (including chest computed tomography scan), **OR**
  - 3. cerebral palsy with lung disease and recurrent pulmonary infections;

**AND**

  - a. standard chest physiotherapy has failed; **OR**
  - b. standard chest physiotherapy is unavailable or not tolerated.

In considering the chest wall compression and intrapulmonary percussive ventilation (IPV) devices, there should be demonstrated need for airway clearance. There should also be documented failure of standard treatments, i.e., the patient has frequent severe exacerbations of respiratory distress involving inability to clear mucus despite standard treatment (chest physical therapy and, if appropriate, use of an oscillatory PEP device) or valid reasons why standard treatment cannot be performed, such as inability of the caregiver to perform it.

- C. Other applications of high-frequency chest wall compression devices and intrapulmonary percussive ventilation devices, including, but not limited to, their use in individuals with cystic fibrosis, chronic diffuse bronchiectasis, or cerebral palsy other than as specified above, their use as an adjunct to chest physical therapy or their use in other lung diseases, such as chronic obstructive pulmonary disease or respiratory conditions associated with neuromuscular disorders, are considered **experimental / investigational**.

## **POLICY GUIDELINES**

- A. For this policy, chronic diffuse bronchiectasis is defined by
  - 1. daily productive cough for at least 6 continuous months **or**
  - 2. exacerbations more than 2 times per year requiring antibiotic therapy **and**
  - 3. confirmed by high-resolution or spiral chest CT scan.
- B. For the chest wall compression devices, a trial period to determine individual and family compliance may be considered. Those who appear to benefit most from the compression devices are adolescents and adults for whom, due to lifestyle factors, manual percussion and postural drainage (P/PD) may not be available.

- C. A trial period may also be helpful because individuals' responses to the various types of devices can be variable; the types of devices should be considered as alternative, and not equivalent, devices.

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## **RATIONALE**

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through April 18, 2022.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life (QOL), and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

## **CYSTIC FIBROSIS**

### **Clinical Context and Therapy Purpose**

The purpose of oscillatory positive expiratory pressure (PEP) therapy in patients who have cystic fibrosis (CF) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of oscillatory devices improve health outcomes in patients with CF?

The following PICO was used to select literature to inform this review.

### ***Populations***

The relevant population of interest is individuals with CF.

**Interventions**

The therapy being considered is the application of oscillatory PEP. Oscillatory PEP devices are intended to be used primarily in the home setting by patients themselves.

**Comparators**

The following therapy is currently being used: standard chest physical therapy.

**Outcomes**

The general outcomes of interest are reductions in respiratory symptoms due to airway restrictions caused by a mucous buildup in the lungs, QOL, hospitalizations, and medication use. Changes in outcomes over a minimum 3-month period should be considered meaningful.

**Study Selection Criteria**

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

**REVIEW OF EVIDENCE**

**Systematic Reviews**

A number of RCTs and a Cochrane systematic review of RCTs have evaluated oscillatory devices for treating patients with CF. The Cochrane review addressed a variety of oscillatory devices, was last updated by Morrison and Milroy (2020),<sup>1</sup> and is summarized in Table 2. Outcomes included pulmonary function, sputum weight and volume, hospitalization rate, and QOL measures. Meta-analysis was limited due to the variety of devices, outcome measures, and lengths of follow-up used. Reviewers concluded that there was a lack of evidence supporting the superiority of oscillatory devices versus any other form of physical therapy, that one device was superior over another, and that there is a need for adequately powered RCTs with long-term follow-up.

**Table 2. Characteristics of Systematic Reviews**

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Morrison et al 2020 <sup>1</sup>	Inception to July 2019	39	Patients with cystic fibrosis	1114 (4-166)	RCT and controlled studies	2 d to 2.8 y

RCT: randomized controlled trial.

**Randomized Controlled Trials**

Representative recent RCTs follow. Trial characteristics and results are summarized in Tables 3 and 4. Gaps related to relevance, study design, and conduct are summarized in Tables 5 and 6.

Mcllwaine et al (2013) published an RCT comparing high-frequency chest wall oscillation (HFCWO) with PEP mask therapy.<sup>2</sup> The primary outcome measure was the number of pulmonary exacerbations requiring an antibiotic. At the end of 1 year, patients in the PEP arm had a statistically significant lower incidence of pulmonary exacerbations requiring antibiotics compared with HFCWO group. The time to first pulmonary exacerbation was 220 days in the PEP group and 115 days in the HFCWO group (p=.02). There were no statistically significant differences in pulmonary measures, including the forced expiratory volume in 1 second (FEV<sub>1</sub>).

Sontag et al (2010) published a multicenter RCT that compared postural drainage, the Flutter device, and HFCWO.<sup>3</sup> At study termination, patients had a final assessment; the length of participation ranged from 1.3 to 2.8 years. An intention-to-treat analysis found no significant differences between treatment groups in the modeled rate of decline for percent predicted FEV<sub>1</sub> or forced vital capacity (FVC). The small sample size and high dropout rate limited the conclusions drawn from this trial.

Pryor et al (2010) evaluated 75 patients 16 years of age and older with CF from a single center in the U.K.<sup>4</sup> Sixty-five (87%) of 75 patients completed the trial and were included in the analysis. Although the study was described as a noninferiority trial, it was not statistically analyzed as such. Instead, no statistically significant differences among the regimens in the primary outcome measure of FEV<sub>1</sub> were construed as evidence for noninferiority.

Radtke et al (2018) evaluated 15 adult patients with CF using the Flutter device with moderate-intensity interval cycling exercise to measure pulmonary diffusing capacity.<sup>5</sup> The outcomes of interest included pulmonary function, sputum viscosity and volume, hospitalization rate, and QOL measures. The results yielded no differences in absolute changes in pulmonary diffusion capacity. This study is not represented in the study tables within this review.

**Table 3. Summary of Key Randomized Controlled Trial Characteristics**

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Mcllwaine et al (2013) <sup>2</sup>	Canada	12	2008 -2012	Children with CF age >6 y (N=107)	HFCWO (n=56)	PEP mask therapy (n=51)
Sontag et al (2010) <sup>3</sup>	U.S.	20	1999-2002	Adults and children with CF (N=166)	2 active Tx: flutter (n=58) and vest (n=57)	Postural drainage (n=58)
Pryor et al (2010) <sup>4</sup>	U.K.	1	NR	Patients with CF ≥16 y (N =75)	Cornet (n=15), Flutter (n=15), PEP (n=15), autogenic drainage (n=15)	Active cycle of breathing technique (n=15)

CF: cystic fibrosis; HFCWO: high-frequency chest wall oscillation; NR: not reported; PEP: positive expiratory pressure; Tx: treatment.



**Table 4. Summary of Key Randomized Controlled Trial Results**

<b>Study</b>	<b>N</b>	<b>No. of PEs Requiring Antibiotics</b>	<b>Spirometry</b>	<b>Quality of Life</b>
Mcllwaine et al (2013) <sup>2</sup>	107		Cannot confirm	Not applicable
HFCWO			Data not reported	Outcome not evaluated
n		96		
Median		2.00		
Range		1.00-3.00		
Positive expiratory pressure			Data not reported	Outcome not evaluated
n		49		
Median		1.00		
Range		0.00-2.00		
p		.007	No difference	Not applicable
Sontag et al (2010) <sup>3</sup>				
Flutter		Outcome not evaluated	Data not reported	Outcome not evaluated
Vest		Outcome not evaluated	Data not reported	Outcome not evaluated
Postural drainage		Outcome not evaluated	Data not reported	Outcome not evaluated
p			No difference	
Pryor et al (2010) <sup>4</sup>	65	Not applicable		Not applicable
Active cycle of breathing techniques		Outcome not evaluated	FEV <sub>1</sub> at 0 mo: 2.01; FEV <sub>1</sub> at 12 mo: 1.94	Small improvement (0.7) <sup>a</sup>
Autogenic drainage		Outcome not evaluated	FEV <sub>1</sub> at 0 mo: 2.68; FEV <sub>1</sub> at 12 mo: 2.64	Small improvement (0.5) <sup>a</sup>
Cornet		Outcome not evaluated	FEV <sub>1</sub> at 0 mo: 1.93; FEV <sub>1</sub> at 12 mo: 1.90	No difference (<0.5) <sup>a</sup>
Flutter		Outcome not evaluated	FEV <sub>1</sub> at 0 mo: 2.46; FEV <sub>1</sub> at 12 mo: 2.43	Moderate improvement (1.3) <sup>a</sup>
Positive expiratory pressure		Outcome not evaluated	FEV <sub>1</sub> at 0 mo: 2.17; FEV <sub>1</sub> at 12 mo: 2.02	Small improvement (0.8) <sup>a</sup>
p		Not applicable	No difference	Not reported

FEV<sub>1</sub>: forced expiratory volume in 1 second; HFCWO: high-frequency chest wall oscillation; PE: pulmonary exacerbations.

<sup>a</sup> Minimal important differences in the Chronic Respiratory Questionnaire. A change of 0.5 represents a small difference in symptoms, 1.0 a moderate difference, and 1.5 a large difference

**Table 5. Study Relevance Limitations**

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Mcllwaine et al (2013) <sup>2</sup> ,					
Sontag et al (2010) <sup>3</sup> ,					
Pryor et al (2010) <sup>4</sup> ,					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

<sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

<sup>d</sup> Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 6. Study Design and Conduct Limitations**

Study	Allocation <sup>a</sup>	Blinding <sup>b</sup>	Selective Reporting <sup>c</sup>	Data Completeness <sup>d</sup>	Power <sup>e</sup>	Statistical <sup>f</sup>
Mcllwaine et al (2013) <sup>2</sup> ,	3. Allocation concealment unclear	1. Not blinded to treatment assignment		1. Eighty-eight (82%) of 107 randomized patients completed the trial. Trial limitations were a nearly 20% dropout rate.	4. Trial stopped early without enrolling expected number of patients and might have been underpowered to detect clinically significant differences between groups	
Sontag et al (2010) <sup>3</sup> ,	3. Allocation concealment unclear	1. Not blinded to treatment assignment		1. Dropout rates were high; trial ended early: 35 (60%), 16 (31%), and 5 (9%) patients withdrew from the postural drainage, Flutter, and	4. Trial ended earlier than planned	

Study	Allocation <sup>a</sup>	Blinding <sup>b</sup>	Selective Reporting <sup>c</sup>	Data Completeness <sup>d</sup>	Power <sup>e</sup>	Statistical <sup>f</sup>
				Vest groups, respectively. Most common reasons for withdrawal after 60 days were moved or lost to follow-up (n=13) and lack of time (n=7).		
Pryor et al (2010) <sup>4</sup> ,	3. Allocation concealment unclear	1. Not blinded to treatment assignment		1. Ten of 75 randomized patients were lost to follow-up		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

<sup>b</sup> Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>d</sup>Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference

<sup>f</sup> Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### Section Summary: Cystic Fibrosis

A number of RCTs evaluating oscillatory devices have reported mixed findings and limitations (e.g., small sample sizes, large dropout rates). A systematic review identified 39 RCTs comparing oscillatory devices with other recognized airway clearance techniques; some were published only as abstracts. The study findings were not pooled due to heterogeneity in designs and outcome measures. The systematic review concluded that results from additional RCTs with adequate power and long-term follow-up would permit conclusions on the effect of oscillatory devices on outcomes for CF.

## BRONCHIECTASIS

### Clinical Context and Therapy Purpose

The purpose of oscillatory PEP therapy in patients who have bronchiectasis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of oscillatory devices improve health outcomes in patients with bronchiectasis?

The following PICO was used to select literature to inform this review.

**Populations**

The relevant population of interest is individuals with bronchiectasis.

**Interventions**

The therapy being considered is the application of an oscillatory PEP. Oscillatory PEP devices are intended to be used primarily in the home setting by patients themselves.

**Comparators**

The following therapy is currently being used: standard chest physical therapy.

**Outcomes**

The general outcomes of interest are reductions in respiratory symptoms due to airway restrictions (e.g., pulmonary exacerbations), QOL, hospitalizations, and medication use. Changes in outcomes over a minimum 3-month period should be considered meaningful.

**Study Selection Criteria**

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

**REVIEW OF EVIDENCE**

**Systematic Reviews**

Lee et al (2015) published a Cochrane review of airway clearance techniques for treating bronchiectasis, which is summarized in Table 7.<sup>6</sup> Of 7 RCTs included, 6 were crossover trials. Five trials used a PEP device, 1 used HFCWO, and 1 used postural drainage. Reviewers did not pool study findings due to heterogeneity among studies. Primary outcomes of interest were pulmonary exacerbations, hospitalizations for bronchiectasis, and QOL.

**Table 7. Characteristics of Systematic Reviews**

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Lee et al (2015) <sup>6</sup>	1966-2015	7 RCTs	Adults and children diagnosed with bronchiectasis based on plain-film chest radiography, bronchography, high-resolution computed tomography, or physician diagnosis	1107 (8-37)	1 RCT, 6 crossover RCTs	Immediate (within 24 h) and "long-term" (>24 h)

RCT: randomized controlled trial.

### Randomized Controlled Trials

Representative recent RCTs follow. Trial characteristics and results are summarized in Tables 8 and 9. Gaps related to relevance, study design, and conduct are summarized in Tables 10 and 11.

Murray et al (2009) reported on a crossover study with 20 patients. The number of exacerbations did not differ statistically at 12 weeks.<sup>7</sup> Cough-related QOL was significantly better after 12 weeks of any airway clearance technique compared with no airway clearance. Cochrane reviewers noted that the study was not blinded and that patient-reported QOL measures may have been subject to bias.

Herrero-Cortina et al (2016) reported on a crossover RCT with 31 patients.<sup>8</sup> The interventions were temporary PEP, autogenic drainage, and slow expiration with the glottis opened in the lateral position. There were no significant differences among treatments in the mean sputum clearance during the 24-hour period after each intervention, cough severity (measured using the total Leicester Cough Questionnaire score), or lung function measures (e.g., FEV<sub>1</sub>).

Livnat et al (2021) conducted a randomized trial in 51 patients with bronchiectasis that compared autogenic drainage and oscillating PEP for daily airway clearance.<sup>9</sup> Patients who had not previously performed airway clearance were included. After 4 weeks, the primary outcome (lung clearance index, calculated as the cumulative expired volume during the washout phase divided by the functional residual capacity) and FEV<sub>1</sub> did not differ between groups. Change in sputum quantity from randomization to study end did not differ between groups. The rate of exacerbations was not described, but some quality of life measures improved throughout the study in both groups.

**Table 8. Summary of Key Randomized Controlled Trial Characteristics**

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Murray et al (2009) <sup>7</sup>	U.K.	1	NR	Patients radiologically diagnosed with bronchiectasis (N=20)	Acapella Choice (n=20)	No chest physical therapy (n=20)
Herrero-Cortina et al (2016) <sup>8</sup>	Spain	1	2010-2013	Patients radiologically diagnosed with bronchiectasis (N=31)	Slow expiration with glottis opened in lateral posture (n=31) and temporary PEP (n=31)	Autogenic drainage (n=31)

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Livnat et al (2021) <sup>9</sup> ,	Israel	1	2017-2019	Patients radiologically diagnosed with bronchiectasis (N=51)	Aerobika (n=24)	Autogenic drainage (n=25)

NR: not reported; PEP: positive expiratory pressure I.

**Table 9. Summary of Key Randomized Controlled Trial Results**

Study	Total LCQ Score Difference	24-h Sputum Volume Difference, mL	No. of Exacerbations
	Median (IQR)	Median (IQR)	
Murray et al (2009) <sup>7</sup> ,	N=20	N=20	Not applicable
Acapella	1.3 (-0.17 to 3.25)	2 (0 to 6)	5
No Acapella	0 (-1.5 to 0.5)	-1 (-5 to 0)	7
p	.002	.02	.48
Herrero-Cortina et al (2016) <sup>8</sup> ,			
Autogenic drainage	0.5 (0.1 to 0.5);.01	-1.4 (5.1 to 1.2)	Not studied
ELTGOL	0.9 (0.5 to 2.1);.001	-1.6 (-4.8 to 1.0)	Not studied
TPEP	0.4 (0.1 to 1.2);.04	-2.5 (-8.6 to 0.1)	Not studied
p	See above	.01	Not applicable
Livnat et al (2021) <sup>9</sup> ,			
Aerobika	Not studied	-10	Not studied
Autogenic drainage	Not studied	-2.2	Not studied
p	Not applicable	.386	Not applicable

ELTGOL: expiration with glottis opened in lateral posture; IQR: interquartile range; LCQ: Leicester Cough Questionnaire; TPEP: temporary positive expiratory pressure.

**Table 10. Study Relevance Limitations**

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Murray et al (2009) <sup>7</sup> ,					
Herrero-Cortina et al (2016) <sup>8</sup> ,					1, 2. 24-h follow-up is not enough
Livnat et al (2021) <sup>9</sup> ,				1. No data on exacerbations	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

<sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

<sup>d</sup> Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 11. Study Design and Conduct Limitations**

<b>Study</b>	<b>Allocation<sup>a</sup></b>	<b>Blinding<sup>b</sup></b>	<b>Selective Reporting<sup>c</sup></b>	<b>Data Completeness<sup>d</sup></b>	<b>Power<sup>e</sup></b>	<b>Statistical<sup>f</sup></b>
Murray et al (2009) <sup>7</sup> ,	3. Allocation concealment unclear	1. Not blinded to treatment assignment 2. Not blinded outcome assessment 3. Outcome assessed by treating physician			3. Power not based on clinically important difference	
Herrero-Cortina et al (2016) <sup>8</sup> ,		1. Not blinded to treatment assignment 2. Not blinded outcome assessment 3. Outcome assessed by treating physician			1. Power calculations not reported 2. Power not calculated for primary outcome 3. Power not based on clinically important difference	
Livnat et al (2021) <sup>9</sup> ,		1. Not blinded to treatment assignment (participants)				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment,

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

<sup>b</sup> Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>d</sup>Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High

number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference

<sup>f</sup> Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### **Section Summary: Bronchiectasis**

A 2015 systematic review identified 7 small RCTs assessing several types of oscillatory devices; only 1 reported the clinically important outcomes of exacerbations or hospitalizations. Three reported on QOL, and trial findings were mixed. A 2016 crossover RCT did not find a significant benefit of temporary PEP compared with other airway clearance techniques.

## **CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

### **Clinical Context and Therapy Purpose**

The purpose of oscillatory PEP therapy in patients who have chronic obstructive pulmonary disease (COPD) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of oscillatory devices improve health outcomes in patients with COPD?

The following PICO was used to select literature to inform this review.

### ***Populations***

The relevant population of interest is individuals with COPD.

### ***Interventions***

The therapy being considered is the application of an oscillatory PEP. Oscillatory PEP devices are intended to be used primarily in the home setting by patients themselves.

### ***Comparators***

The following therapy is currently being used: standard therapy.

### ***Outcomes***

The general outcomes of interest are reductions in respiratory symptoms due to airway restrictions (e.g., pulmonary exacerbations), QOL, hospitalizations, and medication use. Changes in outcomes over a minimum 3-month period should be considered meaningful.

### **Study Selection Criteria**

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;



- Studies with duplicative or overlapping populations were excluded.

## REVIEW OF EVIDENCE

### Systematic Reviews

Systematic reviews have evaluated studies of airway clearance techniques in patients with COPD.<sup>10,11,12</sup> Two early reviews addressed various techniques (i.e., they were not limited to studies on oscillatory devices) while the most recent review was specific to oscillatory devices. These are summarized in Table 12. Studies included in the systematic reviews were mostly small and reviewers noted that quality of evidence was generally poor. The meta-analysis conducted by Alghamdi et al found oscillatory PEP to reduce exacerbations (odds ratio, 0.37 ; 95% confidence interval [CI], 0.19 to 0.72) and improved 6-minute walk distance (mean difference, 49.8 m ; 95% CI, 14.2 to 85.5 m), but the authors noted the need for higher-quality studies.<sup>12</sup>

**Table 12. Characteristics of Systematic Reviews**

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Ides et al (2011) <sup>10</sup> ,	1980-2008	26	Patients with COPD	659 (7-58)	Not reported	Unclear
Osadnik et al (2012) <sup>11</sup> ,	Inception to 2009 (PEDro) or 2011 (CAGR)	28	Participants with investigator-defined COPD, emphysema or chronic bronchitis	907 (5-96)	RCTs (parallel and crossover)	24 h to >8 wk
Alghamdi et al (2020) <sup>12</sup> ,	Inception to March 2020	8	Patients with COPD	381 (15-120)	RCT and crossover	5 d to 2 y

CAGR: Cochrane Airways Group Specialized Register of trials; COPD: chronic obstructive pulmonary disease; PEDro: Physiotherapy Evidence Database; RCT: randomized controlled trial.

### Randomized Controlled Trials

Representative recent RCTs follow. Trial characteristics and results are summarized in Tables 13 and 14. Gaps related to relevance, study design and conduct are summarized in Tables 15 and 16.

Chakrovorty et al (2011) reported results of a crossover RCT among patients with moderate-to-severe COPD and mucus hypersecretion.<sup>13</sup> Patients received HFCWO or conventional treatment in random order, for 4 weeks, with a 2-week washout period between treatments. The primary outcome was QOL as measured using the St. George's Respiratory Questionnaire (SGRQ). Only 1 of 4 dimensions of the SGRQ (the symptom dimension) improved after HFCWO compared with baseline, with a decrease in mean score from 72 to 64 (p=.02). None of the 4 SGRQ dimensions improved after conventional treatment. There were no significant pre- to posttreatment differences in secondary outcomes (e.g., FEV<sub>1</sub>, FVC).

Svenningsen et al (2016) reported on results of an unblinded, industry-funded, randomized crossover study.<sup>14</sup> Each intervention period lasted 21 to 28 days. In the nonsputum producers, scores differed significantly only on the Patient Evaluation Questionnaire total score. In patients who were sputum-producers at baseline, pre- versus post-PEP scores differed significantly for

FVC, 6-minute walk distance, SGRQ total score, and the Patient Evaluation Questionnaire ease of bringing up sputum and patient global assessment subscales. It is unclear if the interventions were clinically meaningful. The crossover studies had similar limitations including no between-group comparisons (i.e., outcomes after oscillatory device use vs. the control intervention), lack of intention-to-treat analysis, and short-term follow-up (immediate posttreatment period).

Goktalay et al (2013) reported on the results of a parallel-group RCT.<sup>15</sup> Patients were randomized to 5 days of treatment with medical therapy plus HFCWO (n=25) or medical therapy only (n=25). At day 5, outcomes including FEV<sub>1</sub>, modified Medical Research Council dyspnea scale scores, and the 6-minute walk distance, did not differ significantly between groups. This short-term trial included hospitalized patients who might differ from COPD patients treated on an outpatient basis.

**Table 13. Summary of Key Randomized Controlled Trial Characteristics**

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Chakrovorty et al (2011) <sup>13</sup> ,	U.K.	1	NR	Patients with at least 1 COPD exacerbation with FEV <sub>1</sub> <0.8, FEV <sub>1</sub> /FVC <0.7, and a daily wet sputum volume of >25 mL (N=38) (female, n=8; male, n=30)	SmartVest Airway Clearance System (n=22)	No SmartVest Airway Clearance System (n=22)
Svenningsen et al (2016) <sup>14</sup> ,	Canada	1	NR	COPD patients self-identified as sputum-producers or non-sputum-producers (N=32) (female, n=13; male, n=14)	Oscillatory PEP (AerobiKA device) (n=27)	No oscillatory PEP (n=27)
Goktalay et al (2013) <sup>15</sup> ,	Turkey	1	2009-2011	Patients with stage 3 or 4 COPD hospitalized for COPD exacerbations (N=50) (female, n=1; male, n=49)	HFCWO plus medical Tx (n=25)	Medical Tx only (n=25)

COPD: chronic obstructive pulmonary disease; FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity; HFCWO: high-frequency chest wall oscillation; NR: not reported; PEP: positive expiratory pressure; Tx: treatment.

**Table 14. Summary of Key Randomized Controlled Trial Results**

Study	SGRO Total Scores	BODE Index
Chakrovorty et al (2011) <sup>13</sup> ,		
SmartVest	Baseline: 63; End of treatment: 60	Not assessed

Study	SGRO Total Scores	BODE Index
No SmartVest	Baseline: 62; End of treatment:62	Not assessed
p	NS	Not applicable
Svenningsen et al (2016) <sup>14</sup> ,		
Oscillatory positive expiratory pressure	Sputum-producers: 40 (12); Non-sputum-producers: 36	Not assessed
Control	Sputum-producers: 49; Non-sputum-producers:35	Not assessed
p	.01 (sputum-producers);.64 (non-sputum-producers)	Not applicable
Goktalay et al (2013) <sup>15</sup> ,		
HFCWO plus medical treatment	Not assessed	Day 0: 7.72; Day 3: 7.00; Day 5: 6.44
Medical treatment only	Not assessed	Day 0: 7.72; Day 3: 7.48; Day 5: 7.24
p	Not applicable	Uninterpretable

BODE: body mass index, airflow obstruction, dyspnea, and exercise; HFCWO: high-frequency chest wall oscillation; NS: not significant; SGRO: St George's Respiratory Questionnaire.

**Table 15. Study Relevance Limitations**

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Chakrovorty et al (2011) <sup>13</sup> ,					
Svenningsen et al (2016) <sup>14</sup> ,					
Goktalay et al (2013) <sup>15</sup> ,					1. Not sufficient duration for benefits (short-term follow-up for 5 d)

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

<sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

<sup>d</sup> Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 16. Study Design and Conduct Limitations**

<b>Study</b>	<b>Allocation<sup>a</sup></b>	<b>Blinding<sup>b</sup></b>	<b>Selective Reporting<sup>c</sup></b>	<b>Data Completeness<sup>d</sup></b>	<b>Power<sup>e</sup></b>	<b>Statistical<sup>f</sup></b>
Chakrovorty et al (2011) <sup>13</sup> ,	3. Allocation concealment unclear	1. Not blinded to treatment assignment 2. Not blinded outcome assessment 3. Outcome assessed by treating physician		1. High loss to follow-up or missing data: 8 out of 30 withdrew due to COPD exacerbations	2. Power not calculated for primary outcome	
Svenningsson et al (2016) <sup>14</sup> ,	3. Allocation concealment unclear	1. Not blinded to treatment assignment		1. High loss to follow-up or missing data: 16% withdrew from trial	2. Power not calculated for primary outcome	
Goktalay et al (2013) <sup>15</sup> ,	1. Participants not randomly allocated 2. Allocation not concealed	1. Not blinded to treatment assignment 2. Not blinded outcome assessment 3. Outcome assessed by treating physician			1. Power calculations not reported 2. Power not calculated for primary outcome 3. Power not based on clinically important difference	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

COPD: chronic obstructive pulmonary disease.

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

<sup>b</sup> Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>d</sup> Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference

<sup>f</sup> Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2.

Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported;  
4. Comparative treatment effects not calculated.

### **Section Summary: Chronic Obstructive Pulmonary Disease**

Only a few controlled studies have evaluated oscillatory devices for the treatment of COPD, and they tended to use intention-to-treat analysis and between-group comparisons. The published studies reported mixed findings and did not support the use of oscillatory devices in COPD patients.

## **RESPIRATORY CONDITIONS RELATED TO NEUROMUSCULAR DISORDERS**

### **Clinical Context and Therapy Purpose**

The purpose of oscillatory PEP therapy in patients who have respiratory conditions related to neuromuscular disorders is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of oscillatory devices improve health outcomes in patients with respiratory conditions related to neuromuscular disorders?

The following PICO was used to select literature to inform this review.

### ***Populations***

The relevant population of interest is individuals with respiratory conditions related to neuromuscular disorders.

### ***Interventions***

The therapy being considered is the application of an oscillatory PEP. Oscillatory PEP devices are intended to be used primarily in the home setting by patients themselves.

### ***Comparators***

The following therapy is currently being used: standard therapy.

### ***Outcomes***

The general outcomes of interest are reductions in respiratory symptoms due to airway restrictions (e.g., pulmonary exacerbations), QOL, hospitalizations, and medication use. Changes in outcomes over a minimum 3-month period should be considered meaningful.

### **Study Selection Criteria**

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

## **REVIEW OF EVIDENCE**

### Systematic Reviews

A Cochrane review by Winfield et al (2014) evaluated the nonpharmacologic management of respiratory morbidity in children with severe global developmental delay treated with airway clearance techniques.<sup>16</sup> Reviewers included RCTs and nonrandomized comparative studies. They identified 3 studies on HFCWO (1 RCT, 2 pre-post) and one on PEP (pre-post), with sample sizes from 15 and 28 patients. As a result of heterogeneity, a meta-analysis was not conducted. The review is summarized in Table 17.

**Table 17. Characteristics of Systematic Reviews**

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Winfield et al (2014) <sup>16</sup> ,	Inception to Nov 2013	15	Children up to 18 y with a diagnosis of severe neurologic impairment and respiratory morbidity	Not reported	RCTs and nonrandomized comparative studies	Unclear

RCT: randomized controlled trial.

### Randomized Controlled Trials

Representative recent RCTs follow. Trial characteristics and results are summarized in Tables 18 and 19. Gaps related to relevance, study design and conduct are summarized in Tables 20 and 21.

Yuan et al (2010) reported results of a parallel-arm RCT.<sup>17</sup> Both groups were instructed to perform the assigned treatment for 12 minutes, 3 times a day for the study period (mean, 5 months). There were no statistically significant differences between groups on primary outcomes. No therapy-related adverse events were reported in either group.

Lange et al (2006) reported on the results of a parallel-arm RCT in adults with amyotrophic lateral sclerosis.<sup>18</sup> Patients were randomized to 12 weeks of HCFWO or usual care. There were no statistically significant between-group differences in pulmonary measures (FVC predicted, capnography, oxygen saturation, or peak expiratory flow). There was also no significant difference in the amyotrophic lateral sclerosis Functional Rating Scale respiratory subscale score (worsening) at 12 weeks. Of symptoms assessed as secondary outcomes, there was significantly less breathlessness and night cough in the HCFWO group than in the usual care group, and groups did not differ significantly on other symptoms, including the noise of breathing, suction frequency, suction amount, day cough, and nocturnal symptoms.

**Table 18. Summary of Key Randomized Controlled Trial Characteristics**

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Yuan et al (2010) <sup>17</sup> ,	U.S.	1	NR	Patients with cerebral palsy or neuromuscular disease attending a pediatric pulmonary clinic (N=28) (Hispanic, n=9;	HCFWO (n=12)	Standard chest physical therapy (n=11)

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
				Caucasian, n=7; Asian, n=4; African American, n=2; Pacific Islander, n=1)		
Lange et al (2006) <sup>18</sup> ,	U.S.	6	NR	Adults with amyotrophic lateral sclerosis (N=46)	HCFWO (n=22)	No treatment (n=24)

HCFWO: high-frequency chest wall oscillation; NR: not reported.

**Table 19. Summary of Key Randomized Controlled Trial Results**

Study	Hospitalization/IV Antibiotics	TDI (proportion showing worsening)
Yuan et al (2010) <sup>17</sup> ,	N=23	
HCFWO	0/12	Not assessed
Standard chest physical therapy	4/11	Not assessed
p	.09	Not applicable
Lange et al (2006) <sup>18</sup> ,	-	N=18
HCFWO	Not assessed	Functional impairment: 27.8%; Magnitude of task: 38.9%; Magnitude of effort: 27.8%
No treatment	Not assessed	Functional impairment: 43.8%; Magnitude of task: 50%; Magnitude of effort: 56.2%
p	Not applicable	Functional impairment:.331; Magnitude of task:.515; Magnitude of effort:.092

HCFWO: high- frequency chest wall oscillation; IV: intravenous; TDI:Transitional Dyspnea Index.

**Table 20. Study Relevance Limitations**

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Yuan et al (2010) <sup>17</sup> ,					
Lange et al (2006) <sup>18</sup> ,					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

<sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

<sup>d</sup> Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No

CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 21. Study Design and Conduct Limitations**

<b>Study</b>	<b>Allocation<sup>a</sup></b>	<b>Blinding<sup>b</sup></b>	<b>Selective Reporting<sup>c</sup></b>	<b>Data Completeness<sup>d</sup></b>	<b>Power<sup>e</sup></b>	<b>Statistical<sup>f</sup></b>
Yuan et al (2010) <sup>17</sup> ,	1. Allocation concealment unclear	1. Not blinded to treatment assignment 2. Not blinded outcome assessment (except chest X-rays) 3. Outcome assessed by treating physician		1. High loss to follow-up or missing data 12% missing data and all in treatment group	1, 2, 3. Trial was exploratory and was not powered to detect statistically significant findings of the primary outcomes	
Lange et al (2006) <sup>18</sup> ,	1. Allocation not concealed	1. Not blinded to treatment assignment 2. Not blinded outcome assessment 3. Outcome assessed by treating physician		1. High loss to follow-up or missing data 15% missing data at 12 wk	2. Power not calculated for primary outcome 3. Power not based on clinically important difference	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

<sup>b</sup> Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>d</sup>Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference

<sup>f</sup> Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

## Section Summary: Respiratory Conditions Related to Neuromuscular Disorders



Two RCTs and a systematic review have evaluated oscillatory devices for the treatment of respiratory conditions in neuromuscular disorders. One RCT was not powered to detect statistical significance. The other, conducted in amyotrophic lateral sclerosis patients, did not find statistically significant improvement after HCFWO compared with usual care for the primary outcomes (pulmonary function measures) or most secondary outcomes.

### **Summary of Evidence**

For individuals who have CF who receive oscillatory devices, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms, QOL, hospitalizations, and medication use. The RCTs reported mixed findings and limitations such as small sample sizes and large dropout rates. A systematic review identified 39 RCTs comparing oscillatory devices with another recognized airway clearance techniques; some were published only as abstracts. Reviewers could not pool findings due to heterogeneity in study designs and outcome measures and concluded that additional adequately powered RCTs with long-term follow-up would be needed to make conclusions about oscillatory devices for CF. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have bronchiectasis who receive oscillatory devices, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms, QOL, hospitalizations, and medication use. A 2015 systematic review identified 7 small RCTs on several types of oscillatory devices; only 1 reported the clinically important outcomes of exacerbations or hospitalizations. Only 3 RCTs reported on QOL, and findings were mixed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have COPD who receive oscillatory devices, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, QOL, hospitalizations, and medication use. Only a few controlled studies have evaluated oscillatory devices for the treatment of COPD, and they tend to have small sample sizes, short follow-up periods, and limitations in their analyses (e.g., lack of intention-to-treat analysis and between-group comparisons). Moreover, the published studies reported mixed findings and did not clearly support the use of oscillatory devices in this population. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have respiratory conditions related to neuromuscular disorders who receive oscillatory devices, the evidence includes 2 RCTs and a systematic review. Relevant outcomes are symptoms, QOL, hospitalizations, and medication use. One of the RCTs was not powered to detect statistically significant differences. The other RCT, conducted in patients with amyotrophic lateral sclerosis, did not find significant improvements after high-frequency chest wall compression devices versus usual care in primary outcomes, in pulmonary function measures, or in most secondary outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

### **SUPPLEMENTAL INFORMATION**

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

### **Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 2 academic medical centers while this policy was under review in 2008. Input indicated the available studies demonstrated that these oscillatory devices are comparable with chest physical therapy for cystic fibrosis and bronchiectasis. The most commonly mentioned clinical criteria were patients who failed or were intolerant of other methods of mucus clearance and patients who lacked caregivers to provide chest physical therapy. Input did not support the use of oscillatory devices for treatment of chronic obstructive pulmonary disease.

### **Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

### **American College of Chest Physicians**

In 2006, the guidelines from the American College of Chest Physicians recommended (level of evidence: low) that, in patients with cystic fibrosis, devices designed to oscillate gas in the airway, either directly or by compressing the chest wall, can be considered as an alternative to chest physical therapy.<sup>19</sup>

A 2018 document from the American College of Chest Physicians recommends that airway clearance strategies in children and adults with productive cough due to bronchiectasis related to any cause be individualized to the patient (ungraded, consensus statement).<sup>20</sup>

### **Cystic Fibrosis Foundation**

In 2009, the Cystic Fibrosis Foundation published guidelines on airway clearance therapies based on a systematic review of evidence.<sup>21</sup> The Foundation recommended airway clearance therapies for all patients with cystic fibrosis but stated that no therapy had been demonstrated to be superior to others (level of evidence: fair; net benefit: moderate; grade of recommendation: B).

### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

### **Ongoing and Unpublished Clinical Trials**

Some currently ongoing trials that might influence this review are listed in Table 22.

**Table 22. Summary of Key Trials**

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
<i>Ongoing</i>			
NCT04271969	Clinical Effectiveness Of High Frequency Chest Wall Oscillation (HFCWO) In A Bronchiectasis Population	100	Jun 2022
NCT05034900	Does Addition of Oscillatory Positive Expiratory Pressure (OPEP) Device to a Chest Physiotherapy Program Provide Further Health Benefits in Children With Bronchiectasis?	42	Dec 2022

NCT: national clinical trial.

## CODING

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.**

**Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.**

<b>CPT/HCPCS</b>	
94669	Mechanical chest wall oscillation to facilitate lung function, per session
A7025	High frequency chest wall oscillation system vest, replacement for use with patient-owned equipment, each
A7026	High frequency chest wall oscillation system hose, replacement for use with patient-owned equipment, each
E0480	Percussor, electric or pneumatic, home model
E0481	Intrapulmonary percussive ventilation system and related accessories
E0483	High frequency chest wall oscillation system, with full anterior and/or posterior thoracic region receiving simultaneous external oscillation, includes all accessories and supplies, each
E0484	Oscillatory positive expiratory pressure device, nonelectric, any type, each
S8185	Flutter device

<b>ICD-10 DIAGNOSES</b>	
E84.11	Meconium ileus in cystic fibrosis
E84.0	Cystic fibrosis with pulmonary manifestations
E84.19	Cystic fibrosis with other intestinal manifestations
E84.8	Cystic fibrosis with other manifestations
E84.9	Cystic fibrosis, unspecified
J47.0	Bronchiectasis with acute lower respiratory infection
J47.1	Bronchiectasis with (acute) exacerbation
J47.9	Bronchiectasis, uncomplicated

<b>REVISIONS</b>	
10-26-2010	Description section updated. In Policy section: <ul style="list-style-type: none"> <li>▪ Liberalized to the current policy language from: "There is no clinical data to show oscillatory devices provide any additional health benefit compared to conventional chest physical therapy. However, conservative therapy should be tried and failed (e.g. flutter valve) before an oscillatory device is considered medically</li> </ul>

<b>REVISIONS</b>	
	necessary in cystic fibrosis patients who lack a caregiver to perform routine percussion and postural drainage (P/PD) or are intolerant of P/PD. Other applications of oscillatory devices including their use as an adjunct to chest physical therapy or their use in diseases other than cystic fibrosis, such as bronchiectasis or COPD, are considered investigational."
	Rationale section added.
	In Coding section: <ul style="list-style-type: none"> <li>▪ Added HCPCS codes: E0481, E0484</li> <li>▪ Added Diagnosis codes: 277.01, 277.03, 277.09, 494.0, 494.1</li> </ul>
	References section updated.
03-25-2011	Rationale section updated.
	Reference section updated.
09-29-2011	Changed the policy title from "Chest Oscillation Vest" to "Oscillatory Devices for the Treatment of Cystic Fibrosis and other Respiratory Disorders."
	Added a Policy Guideline section.
	Updated the Reference section.
05-15-2012	In the Policy section: <ul style="list-style-type: none"> <li>• In Item B, inserted "or cerebral palsy patients with lung disease and recurrent pulmonary infections" to read "High frequency chest wall compression devices and intrapulmonary percussive ventilation devices may be considered medically necessary in patients with cystic fibrosis, chronic diffuse bronchiectasis, or when cerebral palsy patients with lung disease and recurrent pulmonary infections, when:"</li> </ul>
	Rationale section updated.
	Reference section updated.
06-14-2013	Rationale section updated.
	In Coding section: <ul style="list-style-type: none"> <li>▪ Added ICD-10 Diagnosis (Effective October 1, 2014)</li> </ul>
	Reference section updated.
12-31-2013	In Coding section: <ul style="list-style-type: none"> <li>▪ Added CPT code 94669 (Effective January 1, 2014)</li> </ul>
05-28-2015	Updated Description section.
	In Policy section: <ul style="list-style-type: none"> <li>▪ In Item A, removed "the FLUTTER® valve or Acapella" and added "an oscillatory positive expiratory pressure" to read, "Use of an oscillatory positive expiratory pressure device may be considered medically necessary in patients with hypersecretory lung disease (i.e., produce excessive mucus):"</li> <li>▪ Changed previous Item C to Item D.</li> <li>▪ Added new Item C, "High-frequency chest wall compression devices and intrapulmonary percussive ventilation devices are considered not medically necessary as an alternative to chest physical therapy in patients with cystic fibrosis, chronic bronchiectasis, or cerebral palsy in any other clinical situations; there are no clinical data to show that these devices provide any additional health benefit compared with conventional chest physical therapy in situations other than those specified here."</li> <li>▪ In Policy Guidelines, added "1. For this policy, chronic diffuse bronchiectasis is defined by daily productive cough for at least 6 continuous months or more than 2 times per year exacerbations requiring antibiotic therapy and confirmed by high-resolution or spiral chest CT scan." In Item 2, defined P/PD.</li> </ul>
	Updated Rationale section.
	Updated References section.
09-03-2016	Updated Description section.

<b>REVISIONS</b>	
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item B, added "as determined by specific criteria (see Policy Guidelines) (Including chest computed tomography scan)" to read "High-frequency chest wall compression devices and intrapulmonary percussive ventilation devices may be considered medically necessary in patients with cystic fibrosis, chronic diffuse bronchiectasis, or cerebral palsy patients with lung disease and recurrent pulmonary infections as determined by specific criteria (see Policy Guidelines) (including chest computed tomography scan) when:"</li> <li>▪ In Item B, added a new paragraph "In considering the chest wall compression and IPV devices, there should be demonstrative need for airway clearance. There should also be documented failure of standard treatments, i.e., the patient has frequent severe exacerbations of respiratory distress involving inability to clear mucus despite standard treatment (chest physical therapy and, if appropriate, use of an oscillatory PEP device) or valid reasons why standard treatment cannot be performed, such as inability of the caregiver to perform it."</li> </ul>
	Updated Rationale section.
	Updated References section.
08-10-2017	Policy added to the bcbsks.com website on 07-11-2017 with an effective date of 08-10-2017.
	Updated Description section.
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ Removed previous Item C, "High-frequency chest wall compression devices and intrapulmonary percussive ventilation devices are considered not medically necessary as an alternative to chest physical therapy in patients with cystic fibrosis, chronic bronchiectasis, or cerebral palsy in any other clinical situations; there are no clinical data to show that these devices provide any additional health benefit compared with conventional chest physical therapy in situations other than those specified here."</li> <li>▪ In new Item C (previous Item D), added "their use in patients with cystic fibrosis, chronic diffuse bronchiectasis, or cerebral palsy other than as specified above," and "or respiratory conditions" to read, "Other applications of high-frequency chest wall compression devices and intrapulmonary percussive ventilation devices, including, but not limited to, their use in patients with cystic fibrosis, chronic diffuse bronchiectasis, or cerebral palsy other than as specified above, their use as an adjunct to chest physical therapy or their use in other lung diseases, such as chronic obstructive pulmonary disease or respiratory conditions are considered experimental / investigational."</li> </ul>
	Updated Rationale section.
	Updated References section.
08-17-2018	Policy added to the bcbsks.com website on 07-18-2018 with an effective date of 08-17-2018.
	Updated Description section.
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item C, added "associated with neuromuscular disorders" to read, "Other applications of high-frequency chest wall compression devices and intrapulmonary percussive ventilation devices, including, but not limited to, their use in patients with cystic fibrosis, chronic diffuse bronchiectasis, or cerebral palsy other than as specified above, their use as an adjunct to chest physical therapy or their use in other lung diseases, such as chronic obstructive pulmonary disease or respiratory conditions associated with neuromuscular disorders, are considered experimental / investigational."</li> </ul>

<b>REVISIONS</b>	
	Updated Rationale section.
	In Coding section: <ul style="list-style-type: none"> <li>▪ Added HCPCS code: E0480.</li> <li>▪ Removed ICD-9 codes.</li> </ul>
	Updated References section.
01-01-2019	In Coding section: <ul style="list-style-type: none"> <li>▪ Revised nomenclature to HCPCS code: E0483.</li> </ul>
07-17-2019	Updated Description section.
	Updated Rationale section.
	Updated References section.
04-19-2021	Updated Description section.
	Updated Rationale section.
	Updated References section.
08-19-2021	Updated Description section.
	Policy section was reformatted. Position statement remains unchanged
	Updated Rationale section.
	Updated References section.
08-09-2022	Updated Description Section
	Updated Rationale Section
	Updated References Section
10-28-2022	Updated Coding Section <ul style="list-style-type: none"> <li>▪ Updated nomenclature for E0483</li> </ul>

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