

# **AEROBIKA<sup>®</sup> Oscillating PEP Therapy System**

## Study Summary

## FOREWORD

Monaghan Medical Corporation and its affiliate company Trudell Medical International have an enviable history of strong leadership in creating innovative medical devices that enhance the quality of life for people of all ages. We focus our efforts on the well-being of our employees and customers, and provide safe, valuable and easy to use devices for the American market.

The **AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP)** device is a drug-free, easy to use, hand-held device that helps people with COPD and other respiratory conditions breathe easier and live better. Clinical evaluations conducted at Robarts Research Institute (Western University, London, Canada) demonstrated use of the device could significantly improve mucus clearance, decrease cough frequency, reduce breathlessness, increase exercise tolerance and improve quality of life.

Real-world evidence evaluating the efficacy of the AEROBIKA® device demonstrated a clinically-significant 28% reduction in exacerbations, a significant reduction in the use of antibiotics and oral corticosteroids in the hospital setting (57% and 89% respectively), and exhibited significantly lower healthcare charges. This adds to the clinical evidence that shows that daily use of the AEROBIKA® device results in significant improvement in quality of life, improvement in ease of clearing mucus from the lungs, increased lung capacity, and improved exercise tolerance.

The following sections are included in the summary:

- **The Problem with Airway Maintenance in Chronic Obstructive Pulmonary Disease**

An overview of the effect structure-function decline has on the airways of patients with COPD

- **Studies Using the AEROBIKA® Device**

*In vitro* and *in vivo* studies supporting the efficacy of the AEROBIKA® device

- **Airway Maintenance in COPD, Bronchiectasis and Cystic Fibrosis**

Articles addressing the use and efficacy of Airway Clearance Techniques as part of an overall therapy program in Chronic Obstructive Pulmonary Disease, Bronchiectasis and Cystic Fibrosis

- **Guidelines**

International guidelines recommending the use of PEP and Oscillating PEP

# THE PROBLEM WITH AIRWAY MAINTENANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

## COPD READMISSIONS: ADDRESSING COPD IN THE ERA OF VALUE-BASED HEALTHCARE.

*T Shah, VG Press, M Huisinigh-Scheetz, and SR White. CHEST 2016;150(4):916-926.*

Of those patients hospitalized for an exacerbation of COPD, one in five will require rehospitalization within 30 days. Many developed countries are now implementing policies to increase care quality while controlling costs for COPD, known as value-based health care. In the United States, COPD is part of Medicare's Hospital Readmissions Reduction Program (HRRP), which penalizes hospitals for excess 30-day, all-cause readmissions after a hospitalization for an acute exacerbation of COPD, despite minimal evidence to guide hospitals on how to reduce readmissions. This review outlines challenges for improving overall COPD care quality and specifically for the HRRP. These challenges include heterogeneity in the literature for how COPD and readmissions are defined, difficulty finding the target population during hospitalizations, and a lack of literature to guide evidence-based programs for COPD readmissions as defined by the HRRP in the hospital setting. It then identifies risk factors for early readmissions after acute exacerbation of COPD and discusses tested and emerging strategies to reduce these readmissions. Finally, we evaluate the current HRRP and future policy changes and their effect on the goal to deliver value-based COPD care. COPD remains a chronic disease with a high prevalence that has finally garnered the attention of health systems and policy makers, but we still have a long way to go to truly deliver value-based care to patients.

## PHYSIOLOGIC CHARACTERIZATION OF THE CHRONIC BRONCHITIS PHENOTYPE IN GOLD GRADE IB COPD.

*AF Elbehairy, N Raghavan, S Cheng, L Yang, KA Webb, JA Neder, JA Guenette, MI Mahmoud, DE O'Donnell. Chest 2015;147(5):1235-1245.*

**Background:** Smokers with persistent cough and sputum production (chronic bronchitis [CB]) represent a distinct clinical phenotype, consistently linked to negative clinical outcomes. However, the mechanistic link between physiologic impairment, dyspnea, and exercise intolerance in CB has not been studied, particularly in those with mild airway obstruction. We, therefore, compared physiologic abnormalities during rest and exercise in CB to those in patients without symptoms of mucus hypersecretion (non-CB) but with similar mild airway obstruction. **Methods:** Twenty patients with CB ( $\geq 3$  months cough/sputum in 2 consecutive years), 20 patients without CB but with GOLD (Global Initiative for Chronic Obstructive Lung Disease) grade IB COPD, and 20 age- and sex-matched healthy control subjects underwent detailed physiologic testing, including tests of small airway function and a symptom-limited incremental cycle exercise test. **Results:** Patients with CB (mean  $\pm$  SD post-bronchodilator FEV<sub>1</sub>, 93%  $\pm$  12% predicted) had greater chronic activity-related dyspnea, poorer health-related quality of life, and reduced habitual physical activity compared with patients without CB and control subjects (all  $P < .05$ ). The degree of peripheral airway dysfunction and pulmonary gas trapping was comparable in both patient groups. Peak oxygen uptake was similarly reduced in patients with CB and those without compared with control subjects (% predicted  $\pm$  SD, 70  $\pm$  26, 71  $\pm$  29 and 106  $\pm$  43, respectively), but those with CB had higher exertional dyspnea ratings and greater respiratory mechanical constraints at a standardized work rate than patients without CB ( $P < .05$ ). **Conclusions:** Patients with CB reported greater chronic dyspnea and activity restriction than patients without CB and with similar mild airway obstruction. The CB group had greater dynamic respiratory mechanical impairment and dyspnea during exercise than patients without CB, which may help explain some differences in important patient-centered outcomes between the groups.

## CHRONIC BRONCHITIS IS ASSOCIATED WITH WORSE SYMPTOMS AND QUALITY OF LIFE THAN CHRONIC AIRFLOW OBSTRUCTION.

*P Meek, H Petersen, GR Washko, AA Diaz, V Kim, A Sood, Y Tesfaigzi. Chest 2015;148(2):408-416.*

**Background:** Chronic obstructive pulmonary disease (COPD) includes the chronic bronchitis (CB) and emphysema phenotypes. While it is generally assumed that emphysema or chronic airway obstruction (CAO) is associated with worse quality of life than CB, this assumption has not been tested. **Methods:** The present study, analyses from the Lovelace Smokers' Cohort (LSC) were validated in the COPDGene Cohort. CB without CAO (CB only) was defined by self-reported cough productive of phlegm for at least 3 months/year for 2 consecutive years and post-bronchodilator FEV<sub>1</sub>/FVC  $\geq 70\%$ . CAO without CB (CAO only) was defined by a post-bronchodilator FEV<sub>1</sub>/FVC  $< 70\%$  with no evidence of CB. Quality of life outcomes were obtained from the SGRQ and SF-36 questionnaires. A Priori Covariates included age, sex, pack-years of smoking, current smoking, and FEV<sub>1</sub>. **Results:** Smokers with CB without CAO (LSC  $n=341$ ; COPDGene=523) were younger, had a greater BMI, and less smoking exposure than those with CAO only (LSC  $n=302$ ; COPDGene=2208). Compared

to the latter group, quality of life scores were worse for those with CB only. Despite similar SGRQ Activity and SF-36 Role physical and physical functioning, SGRQ Symptoms and Impact scores and SF-36 Emotional and Social measures were worse in the CB only group, in both cohorts. After adjustment for covariates, CB only group remained a significant predictor for 'worse' symptoms, and emotional and social measures. **Conclusions:** This analysis is the first study to suggest that among subjects with COPD those with CB only present worse quality of life, symptoms and mental well-being than those with CAO only.

#### **CLINICAL ISSUES OF MUCUS ACCUMULATION IN COPD.**

*FL Ramos, JS Krahne, V Kim. International Journal of COPD 2014;9:139-150.*

Airway mucus is part of the lung's native immune function that traps particulates and microorganisms, enabling their clearance from the lung by ciliary transport and cough. Mucus hypersecretion and chronic productive cough are the features of the chronic bronchitis and chronic obstructive pulmonary disease (COPD). Overproduction and hypersecretion by goblet cells and the decreased elimination of mucus are the primary mechanisms responsible for excessive mucus in chronic bronchitis. Mucus accumulation in COPD patients affects several important outcomes such as lung function, health-related quality of life, COPD exacerbations, hospitalizations, and mortality. Nonpharmacologic options for the treatment of mucus accumulation in COPD are smoking cessation and physical measures used to promote mucus clearance. Pharmacologic therapies include expectorants, mucolytics, methylxanthines, beta-adrenergic receptor agonists, anticholinergics, glucocorticoids, phosphodiesterase-4 inhibitors, antioxidants, and antibiotics.

#### **CHRONIC BRONCHITIS IN COPD PATIENTS IS ASSOCIATED WITH INCREASED RISK OF EXACERBATIONS: A CROSS-SECTIONAL MULTICENTRE STUDY.**

*JL Corhay, W Vincken, M Schlessers, P Bossuyt, J. Imschoot. Int J Clin Pract 2013;67(12):1294-1301.*

**Background and aims:** Chronic bronchitis (CB) in chronic obstructive pulmonary disease (COPD) patients is associated with increased mortality, frequent exacerbations and faster disease progression. This study investigates the prevalence of CB in a large population of COPD patients to identify features associated with CB. **Methods:** Cross-sectional multicentre study in patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages 2-4 from Belgium and Luxembourg. **Results:** The 974 patients included were on average  $67.8 \pm 9.6$  years old; 72% were male, FEV<sub>1</sub> was  $52.5 \pm 15.8\%$  of predicted. The prevalence of CB was 64% (622/974). In patients with CB, the number of pack-years smoked and the prevalence of chronic respiratory failure, cachexia and skeletal muscle wasting were significantly higher, whereas FEV<sub>1</sub> and FEV<sub>1</sub>/VC were lower. The prevalence of CB increased with GOLD stage and was higher in patients with emphysema and those exposed to occupational risk factors. The CB group had more exacerbations, a higher percentage of patients with frequent exacerbations (37.3% vs. 14.2% of patients;  $p < 0.0001$ ), increased COPD-related, non-intensive care unit hospitalizations and all-cause hospitalisation rates. In multiple logistic regression analysis, frequent exacerbation was the most important independent variable associated with CB, followed by current smoking, chronic respiratory failure, COPD duration and age. **Conclusions:** CB prevalence in GOLD stage 2-4 COPD patients is high. CB is related to current tobacco smoking, and prevalence increases with COPD severity and duration, emphysema and age. CB could be the hallmark of a subtype of COPD easy to identify in clinical practice, associated with increased disease severity and increased risk of exacerbation.

#### **AIRWAY MUCUS FUNCTION AND DYSFUNCTION.**

*JV Fahy, BF Dickey. N Engl J Med 2010;363(23):2233-2247.*

The lungs are remarkably resistant to environmental injury, despite continuous exposure to pathogens, particles, and toxic chemicals in inhaled air. Their resistance depends on a highly effective defense provided by airway mucus, an extracellular gel in which water and mucins (heavily glycosylated proteins) are the most important components. Airway mucus traps inhaled toxins and transports them out of the lungs by means of ciliary beating and cough. Paradoxically, although a deficient mucous barrier leaves the lungs vulnerable to injury, excessive mucus or impaired clearance contributes to the pathogenesis of all the common airway diseases. This review examines the normal formulation and clearance of airway mucus, the formation of pathologic mucus, the failure of mucus clearance that results in symptoms and abnormal lung function, and the therapy of mucus dysfunction.

## REVISITED ROLE FOR MUCUS HYPERSECRETION IN THE PATHOGENESIS OF COPD.

*I Cerveri, V Brusasco. Eur Respir Rev 2010;19(116):109-112.*

Chronic obstructive pulmonary disease (COPD) is a heterogeneous and complex disease of which the basic pathophysiological mechanisms remain largely unknown. On the basis of recent results from pathological studies and large clinical trials, the presence of airway inflammation does not seem to be sufficient to explain the complexity of the disease and the relatively poor response to treatment. It is probably time to abandon the concept of COPD as a unique disease and define, identify and treat the various aspects, which may differ between individuals. Among the different phenotypic distinctions, the classical distinction “chronic bronchitis” has mucus hypersecretion as the key presenting symptom. Its role in COPD has been the subject of an ongoing debate; however, it now appears to be being re-evaluated due to findings from recent epidemiological and pathological studies. In this context, the view that chronic mucus hypersecretion plays a secondary role in the pathogenesis of COPD should be abandoned and instead, drugs targeting mucus hypersecretion should be considered as a treatment option.

## MUCUS HYPERSECRETION IN COPD: SHOULD WE ONLY RELY ON SYMPTOMS?

*PR Burgel, C Martin. Eur Respir Rev 2010;19(116):94-96. Editorial comment on 'Revisited Role for Mucus Hypersecretion in the Pathogenesis of COPD'.*

**Concluding Statement:** In conclusion, current COPD therapies have limited effects in modifying the natural history of the disease. Mucus hypersecretion occurs in all COPD subjects and increases with airflow limitation. Pathological and physiological studies suggest that chronic cough and sputum production is a manifestation of mucus hypersecretion in proximal airways, but that mucus hypersecretion in small airways is not necessarily associated with symptoms. These major findings suggest that therapies targeting mucus hypersecretion in COPD could be beneficial regardless of the presence of chronic cough and sputum production. Proof of this concept will require carefully designed clinical trials evaluating the impact of novel therapies on mucus hypersecretion and COPD relevant outcomes.

## COUGH AND SPUTUM PRODUCTION ARE ASSOCIATED WITH FREQUENT EXACERBATIONS AND HOSPITALIZATIONS IN COPD SUBJECTS.

*PR Burgel, P Nesme-Meyer, P Chanez, D Caillaud, P Carré, T Perez, N Roche; on behalf of the Initiatives Bronchopneumopathie Chronique Obstructive (BPCO) Scientific Committee. Chest 2009;135(4):975-982.*

**Background:** Epidemiologic studies indicate that chronic cough and sputum production are associated with increased mortality and disease progression in COPD subjects. Our objective was to identify features associated with chronic cough and sputum production in COPD subjects. **Methods:** Cross-sectional analysis of data were obtained in a multicenter (17 university hospitals in France) cohort of COPD patients. The cohort comprised 433 COPD subjects (65±11 years; FEV<sub>1</sub>, 50±20% predicted). Subjects with ( $n=321$ ) and without ( $n=112$ ) chronic cough and sputum production were compared. **Results:** No significant difference was observed between groups for age, FEV<sub>1</sub>, body mass index, and comorbidities. Subjects with chronic cough and sputum production had increased total mean numbers of exacerbations per patient per year (2.20±2.20 vs 0.97±1.19, respectively;  $p < 0.0001$ ), moderate exacerbations (1.80±2.07 vs 0.66±0.85, respectively;  $p < 0.0001$ ), and severe exacerbations requiring hospitalizations (0.43±0.95 vs 0.22±0.56, respectively;  $p < 0.02$ ). The total number of exacerbations per patient per year was the only variable independently associated with chronic cough and sputum production. Frequent exacerbations (two or more per patient per year) occurred in 55% vs 22% of subjects, respectively, with and without chronic cough and sputum production ( $p < 0.0001$ ). Chronic cough and sputum production and decreased FEV<sub>1</sub> were independently associated with an increased risk of frequent exacerbations and frequent hospitalizations. **Conclusions:** Chronic cough and sputum production are associated with frequent COPD exacerbations, including severe exacerbations requiring hospitalizations.

## EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND CHRONIC MUCUS HYPERSECRETION.

*Y Tesfaigzi, P Meek, S Lareau. Clinical and Applied Immunology Reviews 2006;6:21-36.*

Chronic obstructive pulmonary disease (COPD) exacerbations are an important cause of the considerable morbidity and mortality found in COPD. COPD exacerbations increase with increasing severity of COPD, and some patients are prone to frequent exacerbations leading to hospital admission and readmission. These frequent exacerbations may have considerable impact on quality of life and activities of daily living. Factors that increase the risk for COPD exacerbations are associated with increased airway inflammation caused by common pollutants and bacterial and/or viral infections. These inflammatory responses cause mucus hypersecretion and, thereby, airway obstruction and associated exacerbations.

While chronic mucus hypersecretion is a significant risk factor for frequent and severe exacerbations, patients with chronic mucus hypersecretion have a lower rate of relapse after initial treatment for acute exacerbation. The benefit of antibiotics for treatment of COPD exacerbations is small but significant. While the mechanisms of actions are not clear, mucolytic agents reduce the number of days of disability in subjects with exacerbations. Reducing mucous cell numbers in small airways could be a useful way to reduce chronic mucus hypersecretion. Our studies suggest that programmed cell death is crucial in the resolution of metaplastic mucous cells, and understanding these mechanisms may provide novel therapies to reduce the risk of COPD exacerbations.

### **COPD EXACERBATIONS • 3: PATHOPHYSIOLOGY.**

*DE O'Donnell, CM Parker. Thorax 2006;61:354-361.*

Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with increased morbidity and mortality. The effective management of COPD exacerbations awaits a better understanding of underlying pathophysiological mechanisms that shape its clinical expression. The clinical presentation of exacerbations of COPD is highly variable and ranges from episodic symptomatic deterioration that is poorly responsive to usual treatment, to devastating life threatening events. This underscores the heterogeneous physiological mechanisms of this complex disease, as well as the variation in response to the provoking stimulus. The derangements in ventilatory mechanics, muscle function, and gas exchange that characterise severe COPD exacerbations with respiratory failure are now well understood. Critical expiratory flow limitation and the consequent dynamic lung hyperinflation appear to be the proximate deleterious events. Similar basic mechanisms probably explain the clinical manifestations of less severe exacerbations of COPD, but this needs further scientific validation. In this review we summarise what we have learned about the natural history of COPD exacerbations from clinical studies that have incorporated physiological measurements. We discuss the pathophysiology of clinically stable COPD and examine the impact of acutely increased expiratory flow limitation on the compromised respiratory system. Finally, we review the chain of physiological events that leads to acute ventilator insufficiency in severe exacerbations.

### **MORTALITY IN GOLD STAGES OF COPD AND ITS DEPENDENCE ON SYMPTOMS OF CHRONIC BRONCHITIS.**

*M Ekberg-Aronsson, K Pehrsson, J Nilsson, PM Nilsson, C Löfdahl. Resp Res 2005;6:98.*

**Background:** The GOLD classification of COPD severity introduces a stage 0 (at risk) comprising individuals with productive cough and normal lung function. The aims of this study were to investigate total mortality risks in GOLD stages 0–4 with special focus on stage 0, and furthermore to assess the influence of symptoms of chronic bronchitis on mortality risks in GOLD stages 1–4. **Method:** Between 1974 and 1992, a total of 22,044 middle-aged individuals participated in a health screening, which included a spirometry as well as recording of respiratory symptoms and smoking habits. Individuals with comorbidity at baseline (diabetes, stroke, cancer, angina pectoris, or heart infarction) were excluded from the analyses. Hazard ratios (HR 95% CI) of total mortality were analyzed in GOLD stages 0–4 with individuals with normal lung function and without symptoms of chronic bronchitis as a reference group. HR:s in smoking individuals with symptoms of chronic bronchitis within the stages 1–4 were calculated with individuals with the same GOLD stage but without symptoms of chronic bronchitis as reference. **Results:** The number of deaths was 3674 for men and 832 for women based on 352,324 and 150,050 person-years respectively. The proportion of smokers among men was 50% and among women 40%. Self-reported comorbidity was present in 4.6% of the men and 6.6% of the women. Among smoking men, Stage 0 was associated with an increased mortality risk, HR; 1.65 (1.32–2.08), of similar magnitude as in stage 2, HR; 1.41 (1.31–1.70). The hazard ratio in stage 0 was significantly higher than in stage 1 HR; 1.13 (0.98–1.29). Among male smokers with stage 1; HR: 2.04 (1.34–3.11), and among female smokers with stage 2 disease; HR: 3.16 (1.38–7.23), increased HR:s were found in individuals with symptoms of chronic bronchitis as compared to those without symptoms of chronic bronchitis. **Conclusion:** Symptoms fulfilling the definition of chronic bronchitis were associated with an increased mortality risk among male smokers with normal pulmonary function (stage 0) and also with an increased risk of death among smoking individuals with mild to moderate COPD (stage 1 and 2).

### **THE NATURE OF SMALL-AIRWAY OBSTRUCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE.**

*JC Hogg, FC Chu, S Utokaparch, R Woods, WM Elliott, L Buzatu, RM Cherniack, RM Rogers, FC Scirba, HO Coxson, PD Paré. New Eng J Med 2004;350(26):2645-2653.*

**Background:** Chronic obstructive pulmonary disease (COPD) is a major public health problem associated with long-term exposure to toxic gases and particles. We examined the evolution of the pathological effects of airway obstruction in



patients with COPD. **Methods:** The small airways were assessed in surgically resected lung tissue from 159 patients — 39 with stage 0 (at risk), 39 with stage 1, 22 with stage 2, 16 with stage 3, and 43 with stage 4 (very severe) COPD, according to the classification of the Global Initiative for Chronic Obstructive Lung Disease (GOLD). **Results:** The progression of COPD was strongly associated with an increase in the volume of tissue in the wall ( $P<0.001$ ) and the accumulation of inflammatory mucous exudates in the lumen ( $P<0.001$ ) of the small airways. The percentage of the airways that contained polymorphonuclear neutrophils ( $P<0.001$ ), macrophages ( $P<0.001$ ), CD4 cells ( $P=0.02$ ), CD8 cells ( $P=0.038$ ), B cells ( $P<0.001$ ), and lymphoid aggregates containing follicles ( $P=0.003$ ) and the absolute volume of B cells ( $P=0.03$ ) and CD8 cells ( $P=0.02$ ) also increased as COPD progressed. **Conclusions:** Progression of COPD is associated with the accumulation of inflammatory mucous exudates in the lumen and infiltration of the wall by innate and adaptive inflammatory immune cells that form lymphoid follicles. These changes are coupled to a repair or remodeling process that thickens the walls of these airways.

#### **DETERMINANTS OF PROGNOSIS OF COPD IN THE ELDERLY: MUCUS HYPERSECRETION, INFECTIONS, CARDIOVASCULAR COMORBIDITY.**

*R Pistelli, P Lange, DL Miller. Eur Respir J 2003;21(40s):10s-14s.*

In this paper, the authors update the present knowledge about three risk factors for the prognosis of chronic obstructive pulmonary disease (COPD), which may be particularly relevant in elderly people: mucus hypersecretion, respiratory infections, and cardiovascular comorbidity. Chronic mucus hypersecretion (CMH) is a common respiratory symptom in old age, the relevance of which is analysed on the basis of data and collected during the first three rounds of the Copenhagen City Heart Study. In subjects aged  $\geq 65$  yrs, CMH was a strong predictor of the incidence of respiratory infections in a 10-yr follow-up period and it was also a strong predictor of death from COPD (relative risk=2.5). However, CMH was associated with consistently lower forced expiratory volume in one second (FEV<sub>1</sub>) values, but not with an accelerated decline of FEV<sub>1</sub> in this sample of an elderly population. Acute respiratory infections (ARI) are extremely common at all ages, mostly mild self-limiting illnesses at a young age, but severe often fatal illnesses in elderly people already affected by a chronic disease such as COPD. This paper summarises the present knowledge about aetiology, pathology, prognostic relevance, and prevention of ARI. Furthermore, the areas in which further research is needed are listed. Clinical cohort studies clearly support the relevance of cardiovascular comorbidity for the short- and long-term prognosis of elderly subjects affected by severe COPD. In this paper, the recently demonstrated association between particulate air pollution and cardiovascular events is reported to suggest the presence of an extremely susceptible cluster of elderly subjects in the population identified by the copresence of chronic obstructive pulmonary disease and cardiovascular comorbidity.

#### **EPIDEMIOLOGICAL STUDIES IN MUCUS HYPERSECRETION.**

*J Vestbo. 2002 Mucus hypersecretion in respiratory disease. Wiley, Chichester (Novartis Foundation Symposium 248) p 3-19.*

Respiratory mucus in epidemiology has mainly been studied using standardized questionnaires including questions on cough and phlegm. In chronic obstructive pulmonary disease (COPD) much controversy exists regarding the importance of mucus hypersecretion. From being the key element in the 'British hypothesis' it was reduced to being an innocent disorder in the 1980s but is now again recognized as a potential risk factor for an accelerated loss of lung function. Whereas early studies in mainly occupational cohorts showed no effect of chronic mucus hypersecretion on decline in lung function, such an effect has been shown in subsequent studies on general population samples. Chronic mucus hypersecretion also increases risk of hospital admission which may be due to an increased risk of lower respiratory tract infection. In severe COPD this may explain the increased mortality associated with the presence of mucus. In asthma recent findings suggest that in epidemiology chronic mucus hypersecretion may indicate lack of control which leads to an accelerated loss of lung function and increased mortality in subjects with self-reported asthma.

#### **ASSOCIATION OF CHRONIC MUCUS HYPERSECRETION WITH FEV<sub>1</sub> DECLINE AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE MORBIDITY.**

*J Vestbo, E Prescott, P Lange, Copenhagen City Heart Study Group. Am J Respir Crit Med 1996;153: 1530-1535.*

The aim of this study was to examine the association between chronic mucus hypersecretion and FEV<sub>1</sub> decline, and subsequent hospitalization from chronic obstructive pulmonary disease (COPD). We used data from The Copenhagen City Heart Study on 5,354 women and 4,081 men 30 to 79 yr of age with assessment of smoking habits, respiratory symptoms, and spirometry at two surveys 5 yr apart. Information on COPD hospitalization during 8 to 10 yr of subsequent follow-up

was obtained from a nationwide register. Chronic mucus hypersecretion was significantly associated with FEV<sub>1</sub> decline; the effect was most prominent among men, where chronic mucus hypersecretion at both surveys was associated with an excess FEV<sub>1</sub> decline of 22.8 ml/yr (95% confidence interval, 8.2 to 37.4) compared with men without mucus hypersecretion, after adjusting for age and smoking; relative risk was 5.3 (2.9 to 9.6) among men and 5.1 (2.5 to 10.3) among women. After further adjusting for FEV<sub>1</sub> at the second survey, the relative risk was reduced to 2.4 (1.3 to 4.5) for men and 2.6 (1.2 to 5.3) for women. Chronic mucus hypersecretion was significantly and consistently associated with both an excess FEV<sub>1</sub> decline and an increased risk of subsequent hospitalization because of COPD.

### CHRONIC MUCUS HYPERSECRETION IN COPD AND DEATH FROM PULMONARY INFECTION.

*E Prescott, P Lange, J Vestbo. Eur. Resp. J. 1995;8:1333-1338.*

The association of chronic mucus hypersecretion and mortality is a matter of debate. We wished to determine whether the relationship between chronic mucus hypersecretion and chronic obstructive pulmonary disease (COPD)-related mortality could be explained by proneness to pulmonary infection. We followed 14,223 subjects of both sexes for 10-12 yrs. Cases where COPD was an underlying or contributory cause of death ( $n=214$ ) were included, and hospital records were obtained where possible ( $n=101$ ). From the presence of increased mucus, purulent mucus, fever, leucocytosis and infiltration on chest radiography, death was classified as either due to pulmonary infection ( $n=38$ ), or other causes ( $n=51$ ), or unclassifiable ( $n=12$ ). Of subjects reporting chronic mucus hypersecretion at the initial examination, pulmonary infection was implicated in 54% of deaths, whereas this only occurred in 28% of subjects without chronic mucus hypersecretion. Controlling for covariates, in particular smoking habits, a Cox analysis showed a strong inverse relationship between ventilatory function and COPD-related mortality. Chronic mucus hypersecretion was found to be a significant predictor of COPD-related death with pulmonary infection implicated (relative risk (RR) 3.5) but not of death without pulmonary infection (RR 0.9). We consider that subjects with COPD and chronic mucus hypersecretion are more likely to die from pulmonary infections than subjects without chronic mucus hypersecretion. This may explain the excess mortality in subjects with COPD and chronic mucus hypersecretion found in previous studies.

## STUDIES USING THE AEROBIKA® OSCILLATING POSITIVE EXPIRATORY PRESSURE THERAPY SYSTEM

### THE USE OF FUNCTIONAL RESPIRATORY IMAGING TO INVESTIGATE THE IMPACT OF AN OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE ON LUNG DYNAMICS AND DRUG DEPOSITION.

*V Kushnarev, G Leemans, C Van Holsbeke, D Belmans, J De Backer, J Suggett. Presented at ERS 2018.*

**Background:** The AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device has previously been reported as providing benefits to Chronic Obstructive Pulmonary Disease (COPD) patients in terms of lung ventilation, lung capacity, quality of life and reduced exacerbations. This abstract reports the results of a pilot Functional Respiratory Imaging (FRI) study which attempts to provide some lung dynamics understanding following use of the device, as well as how such lung dynamics might relate to drug deposition. **Methods:** A single center, prospective study, was performed in COPD patients whereby subjects were instructed to use the AEROBIKA® device for 10 minutes, then take their standard of care medication, continuing to use the device twice daily for 15 +/- 3 days. Ten subjects were investigated: • 7 male, 3 female; mean age 67.3 ± 9.6 years; mean FEV<sub>1</sub> 55 ± 18.0% predicted. Paired inspiratory-expiratory high-resolution CT (HRCT) scans were taken before and after the start of the treatment period. Afterwards, FRI was used to evaluate changes in the lung dynamics and deposition of concomitant medication. **Results:** Analysis of individual lobes indicated a shift in internal airflow distribution (IAD) between - 7% and + 5%, significantly correlating to airway deposition of the concomitant medication. Additionally, it was observed that patients in whom the airflow was redistributed towards the lower lobes exhibited increased FEV<sub>1</sub> values. **Conclusions:** These pilot study results provide evidence supporting the theory that this specific OPEP device enables airflow redistribution and influences drug deposition patterns. Further research is required to investigate the lower lobar ventilation relationship with FEV<sub>1</sub>. The resultant airflow redistribution following use of the device may well be a contributing factor to the previously reported<sup>1,3</sup> improved clinical outcomes, and the specific nature of the redistribution might also be related to the level of clinical response observed.

<sup>1</sup>Svenningsen S, Paulin GA, Sheikh K, et al. Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. *Journal of COPD* 2016;13(1):66-74. <sup>2</sup>Stockley RA. Abstract presentations: COPD10, Birmingham, United Kingdom, 2016. *Chronic Obstr Pulm Dis.* 2017; 4(3): 225-246. doi: <http://doi.org/10.15326/jcopdf.4.3.2017.0137>. <sup>3</sup>Burudpakadee C, Seetasith A, Dunne P, et al. A real-world study of 30-day exacerbation outcomes in chronic obstructive pulmonary disease (COPD) patients managed with AEROBIKA® OPEP. *Pulmonary Therapy.* 2017;3(1):163-171. <sup>4</sup>Adapted from Svenningsen S, Paulin GA, Sheikh K, et al. Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. *Journal of COPD* 2016;13(1):66-74.



## UNDERSTANDING LUNG PHYSIOLOGICAL DYNAMICS FOLLOWING USE OF AN OSCILLATING POSITIVE EXPIRATORY PRESSURE (OPEP) DEVICE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

J Suggett, V Kushnarev, C Van Holsbeke, J De Backer, W De Backer, G Leemans. Presented at COPD11 2018.

**Background:** The AEROBIKA® OPEP device has been reported to reduce incidence of re-hospitalization following exacerbation<sup>1</sup> and improve quality of life outcomes for COPD patients with chronic bronchitis<sup>2</sup>. This abstract reports a pilot functional respiratory imaging (FRI) study which attempts to understand further the lung dynamics at play when using such as device. **Methods:** A single center, prospective study, was performed in COPD patients. Subjects were instructed to use the AEROBIKA® (TMI, London, ON) OPEP device for 10 minutes, then take their standard of care medication, continuing to use the device twice daily for 15 +/- 3 days. Paired inspiratory-expiratory HRCT scans were taken before and after the start of the treatment period. Afterwards, FRI was used to evaluate changes in the lung dynamics and deposition of concomitant medication. **Results:** Ten subjects were investigated (7M/3F, mean age 67.3±9.6 years, mean FEV<sub>1</sub> 55±18.0%predicted). Analysis of individual lobes indicated a shift in internal airflow distribution between -7% and +5%, significantly correlating to airway deposition of the concomitant medication. Additionally, it was observed that patients in whom the airflow was redistributed towards the lower lobes exhibited increased FEV<sub>1</sub> values. **Conclusions:** These pilot study results provide evidence supporting the theory that this specific OPEP device enables airflow redistribution and influences drug deposition patterns. Further research is required to investigate the lower lobar ventilation relationship with FEV<sub>1</sub>. The resultant airflow redistribution following use of the device may well be a contributing factor to the previously reported improved clinical outcomes and the specific nature of the redistribution might also be related to the level of clinical response observed.

<sup>1</sup>Burudpakdee C, Seetasith A, Dunne P, et al. A real-world study of 30-day exacerbation outcomes in chronic obstructive pulmonary disease (COPD) patient managed with AEROBIKA® OPEP. Pulmonary Therapeutics. 2017. DOI 10.1007/s41030-017-0027-5. <sup>2</sup>Svenningsen S, Paulin GA, Sheikh K, et al. Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. COPD. 2015 Oct 2:1-9.

## A REAL-WORLD EVIDENCE STUDY ASSESSING THE IMPACT OF ADDING THE AEROBIKA® OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE TO STANDARD OF CARE UPON HEALTHCARE RESOURCE UTILIZATION AND COSTS IN POST-OPERATIVE PATIENTS.

C Burudpakdee, AM Near, H Huang, D Coppolo, V Kushnarev, J Suggett. Pulmonary Therapy 2018;4(1):87-101. <https://doi.org/10.1007/s41030-018-0055-9>.

**Introduction:** The aim of this real-world study was to measure the benefit of the AEROBIKA® oscillating positive expiratory pressure (OPEP) device when added to standard of care (defined as incentive spirometry [IS]) for post-operative patients. **Methods:** Adults aged ≥ 18 years who were hospitalized for cardiac, thoracic or upper abdominal surgery between 1 September 2013 and 30 April 2017 were identified from IQVIA's Hospital Charge Detail Master (CDM) database; the index date was the date of the first hospitalization for surgery. The control cohort (IS) included patients who had ≥ 1 CDM record within 12 months prior to the index date and ≥ 1 record after discharge, evidence of IS use during index hospitalization and no evidence of use of a PEP or OPEP device at any time during the study period. The AEROBIKA® OPEP cohort was selected in a similar manner, except that patients were required to have evidence of AEROBIKA® OPEP use during the index hospitalization. AEROBIKA® OPEP patients were 1:1 matched to IS patients using propensity score (PS) matching. Hospital readmissions and costs were measured at 30 days post-discharge from the index hospitalization. **Results:** After PS matching, 144 patients were included in each cohort. At 30 days post-discharge, compared to the control (IS) cohort there were significantly fewer patients in the AEROBIKA® OPEP cohort with ≥ 1 all-cause re-hospitalizations (13.9 vs. 22.9%;  $p = 0.042$ ). The patients in the AEROBIKA® OPEP cohort also had a shorter mean length of stay ( $\pm$  standard deviation) ( $1.25 \pm 4.04$  vs.  $2.60 \pm 8.24$  days;  $p = 0.047$ ) and lower total unadjusted mean all-cause cost per patient ( $\$3670 \pm \$13,894$  vs.  $\$13,775 \pm \$84,238$ ;  $p = 0.057$ ). Adjusted analyses suggested that hospitalization costs were 80% lower for the AEROBIKA® OPEP cohort versus the IS cohort ( $p = 0.001$ ). **Conclusion:** Our results suggest that the addition of the AEROBIKA® OPEP device to standard of care (IS) is beneficial in the post-operative setting.

## COST-EFFECTIVENESS OF THE AEROBIKA® OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE IN THE MANAGEMENT OF COPD EXACERBATIONS.

S Khouidgian-Sinani, S Kowal, JA Suggett, DP Coppolo. International Journal of COPD 2017;12:3065-3073. <https://doi.org/10.2147/COPD.S143334>

**Introduction:** COPD places a huge clinical and economic burden on the US health care system, with acute exacerbations representing a key driver of direct medical costs. Current treatments, although effective in reducing symptoms and limiting exacerbations, do not adequately target the underlying disease processes that drive exacerbation development.

The AEROBIKA® oscillating positive expiratory pressure (OPEP) device has been shown in a real-world effectiveness study to lower the frequency of moderate-to-severe exacerbations during a 30-day post-exacerbation period. This study sought to determine the impact on exacerbations and costs and to determine the cost-effectiveness of the AEROBIKA® device. **Methods:** Data from published literature and national fee schedules were used to model the cost-effectiveness of the AEROBIKA® device in patients who had experienced an exacerbation in the previous month, or a post-exacerbation care population. Exacerbation trends and the impact of the AEROBIKA® device on reducing exacerbation frequency were modeled using a one-year Markov model with monthly cycles and three health states: (i) no exacerbation, (ii) exacerbation, and (iii) death. Scenario analysis and one-way sensitivity analysis (OWSA) were also performed. **Results:** When the effect of AEROBIKA® device was assumed to last 30 days, use of the device resulted in cost-savings (\$553 per patient) and improved outcomes (i.e., six fewer exacerbations per 100 patients per year) compared to no OPEP/positive expiratory pressure therapy. When the effect of the AEROBIKA® device was assumed to extend beyond the conservative 30-day time frame, the AEROBIKA® device remained the dominant strategy (21 fewer exacerbations per 100 patients per year; cost savings of \$1,952 per patient). Consistency in findings after performing OWSAs indicates the robustness of results. **Conclusion:** The AEROBIKA® device is a cost-effective treatment option that provides clinical benefit and results in direct medical cost savings in a post-exacerbation care COPD population.

## A LABORATORY ASSESSMENT INTO THE EFFICIENCY AND EFFECTIVENESS OF DIFFERENT OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICES BY MEANS OF PATIENT SIMULATED EXPIRATORY WAVEFORMS.

A Meyer, J Suggett. Presented at CHEST 2017.

**Rationale:** Oscillating Positive Expiratory Pressure (OPEP) devices can be used to manage a variety of conditions, such as CF, COPD, bronchiectasis and post-surgical recovery. OPEP devices function through a general mechanism of opening / vibrating airways and loosening mucus, however, the specific mechanism by which this is achieved differs between different devices. This investigation assesses the positive pressure oscillation waveforms of various devices and evaluates each critically in terms of consequential efficiency and effectiveness of action. **Materials and Methods:** A simulated OPEP exhalation maneuver was generated based on previous research<sup>1</sup> in which a flowmeter (TSI4040 TSI, US) was used to record the waveforms of 5 healthy adults. An average profile was then scaled so the Peak Expiratory Flow rate (PEF) was 30 L/min, thereby being more patient representative. This patient representative waveform was then used to operate, via a breathing simulator (ASL5000 IngMar, US), a range of different OPEP devices;  $n = 3$  devices, 3 replicates of each. The pressure / time waveforms were recorded (Pressure Transducer, Honeywell, USA) for each device, set at their highest resistance to enable direct comparison. In addition, various critical performance parameters were determined: percentage of exhaled breath with discernable oscillations ( $> 1.0$  cm H<sub>2</sub>O),  $t_{osc}$  [%]; average oscillation amplitude; Total Pressure Pulse Impact (TPPI) = sum of discernable pressure amplitudes in a single exhalation. **Results:** Each device waveform had its own unique pattern, as summarized in Table 1. In terms of the percentage of breath with oscillations and the average oscillation pressure amplitude, the AEROBIKA® OPEP device exhibited the highest values for both, with the vPEP<sup>+</sup> and Flutter<sup>+</sup> devices the lowest for each respectively.

**Table 1: Device Performance Comparison**

Device	$t_{osc}$ [%]	Avg Amp [cm H <sub>2</sub> O]	# of osc	TPPI [cm H <sub>2</sub> O]
AEROBIKA® Device	81%	13.9	36	495
vibraPEP <sup>+</sup>	69%	9.4	27	256
acapella choice <sup>+</sup>	67%	5.8	41	236
Flutter <sup>+</sup>	62%	3.0	46	139
vPEP <sup>+</sup>	45%	4.5	25	112

**Conclusions:** TPPI assesses both efficiency and effectiveness of the device: efficiency relates to the percentage of breath with oscillations; effectiveness relates to the number and amplitude of the oscillations. The therapeutic effectiveness of the air flow oscillations, as assessed here via the TPPI value, is considered to be dependent, in part, on the ability of the device to generate and maintain a pressure amplitude or turbulent spike throughout the maneuver.<sup>2</sup> The TPPI values showed the AEROBIKA® OPEP device to be the most effective, with double the value of the second ranking device.

<sup>1</sup>Meyer A et al, Assessment of Oscillating Positive Pressure Devices by Means of Adult Expiratory Waveforms: A Laboratory Study, Am J Respir Crit Care Med 2014; 189:A3036. <sup>2</sup>Van Fleet et al, Evaluation of Functional Characteristics of 4 Oscillatory Positive Pressure Devices in a Simulated Cystic Fibrosis Model, Resp Care 2017;62(4):451-458.

## EVALUATION OF FUNCTIONAL CHARACTERISTICS OF 4 OSCILLATORY POSITIVE PRESSURE DEVICES IN A SIMULATED CYSTIC FIBROSIS MODEL.

H Van Fleet, DK Dunn, NL McNinch, TA Volsko. *Respiratory Care* 2017;62(4):451-458. <https://doi.org/10.4187/respcare.04570>.

**Background:** Oscillatory positive expiratory pressure (OPEP) is an airway clearance therapy that delivers positive pressure and air-flow oscillations during exhalation. This study described functional characteristic differences of 4 OPEP devices during an active exhalation in a simulated model. We hypothesized peak pressure (Ppeak), positive expiratory pressure (PEP), oscillatory frequency (f), and pressure amplitude will differ, depending upon the device used, device resistance setting, and time (repeated consecutive active exhalations through the device). **Methods:** The ASL 5000 was scripted to simulate pulmonary mechanics of a pediatric cystic fibrosis patient with moderate to severe lung disease. Airway resistance was standardized at 17.1 cm H<sub>2</sub>O/L/s, pulmonary compliance at 42.1 mL/cm H<sub>2</sub>O, active exhalation at 22 breaths/min, and tidal volume at 409 mL. Resistance settings for the Acapella, RC-Cornet, Flutter, and AEROBIKA® were adjusted to low, medium, and high. Values for f, Ppeak, PEP, and pressure amplitude were recorded for 1 min and graphically displayed. Results: Significant effects for time, device, and resistance ( $P < .01$ ) were noted for Ppeak, PEP, and pressure amplitude at each resistance level, demonstrating that the devices functioned differently as more than one repetition of a series of consecutive active exhalations are performed. Significant interaction effects for device, resistance level, and time indicate inconsistent output for Ppeak ( $P < .01$ ), PEP ( $P < .01$ ), and pressure amplitude ( $P < .01$ ). Oscillatory f values fell within the respective manufacturers' operational parameters. The AEROBIKA® provided the most consistent pressure amplitude across resistance settings and produced the highest mean pressure amplitude at medium and high resistance settings. **Conclusions:** Statistically significant and clinically relevant variations in Ppeak, PEP, and pressure amplitude occurred between devices and within a device, as the resistance setting changed. The combination of device, time, and resistance settings affects OPEP device output for pressure, amplitude, and oscillatory frequency. Functional variations may impact therapeutic effectiveness, warranting additional study to determine clinical impact.

## REAL-WORLD STUDY OF 30-DAY EXACERBATION OUTCOMES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS MANAGED WITH AEROBIKA® OPEP.

C Burudpakdee, A Seetasith, P Dunne, G Kauffman, B Carlin, D Coppolo, J Suggett. *Pulmonary Therapy* 2017;3(1):163-171

**Introduction:** Oscillating positive expiratory pressure (OPEP) devices may reduce chronic symptoms in patients with obstructive pulmonary disease (COPD); however, no real-world studies have been performed to evaluate the benefits of these devices. The objective of this study was to measure the rate of early (30-day) moderate-to-severe exacerbations and related costs in COPD patients treated with AEROBIKA®, an OPEP device, vs. a matched control group in a real-world setting. **Methods:** The study utilized data from the QuintilesIMS' CDM hospital database. COPD patients treated with AEROBIKA® OPEP between 9/2013 and 8/2015 were propensity score matched to COPD patients who did not use any positive expiratory pressure device. Severe exacerbation was defined as a hospital admission with a diagnosis for chronic bronchitis or COPD. Moderate-to-severe exacerbation was defined as a hospitalization or an ED visit with a diagnosis for chronic bronchitis or COPD. Exacerbations and costs were compared between cohorts at 30 days. A generalized linear model (GLM) was used to estimate the marginal effect of AEROBIKA® OPEP on the cost of ED visits and hospitalizations due to COPD exacerbations. **Results:** A total of 405 AEROBIKA® OPEP patients were matched to 405 controls. At 30 days, 18.5% of subjects using the AEROBIKA® OPEP vs. 25.7% of controls had a moderate-to-severe exacerbation ( $p = 0.014$ ); 13.8% of subjects with AEROBIKA® OPEP vs. 19.0% of controls had a severe exacerbation ( $p = 0.046$ ). The mean per patient cost of moderate-to-severe exacerbations and severe exacerbations in the AEROBIKA® OPEP group was significantly lower than controls (\$2,975 vs. \$6,065;  $p = 0.008$ , and \$2,838 vs. \$5,871;  $p = 0.009$ , respectively). In the GLM, the per-patient cost of moderate-to-severe exacerbations in the AEROBIKA® OPEP group was 34% lower ( $p = 0.012$ ) than the control group. **Conclusions:** Study findings suggest that using AEROBIKA® OPEP as part of a treatment regimen may help reduce ED visits, hospital re-admissions and related costs in COPD patients who have a history of exacerbations.

## NONCYSTIC FIBROSIS BRONCHIECTASIS: REGIONAL ABNORMALITIES AND RESPONSE TO AIRWAY CLEARANCE THERAPY USING PULMONARY FUNCTIONAL MAGNETIC RESONANCE IMAGING.

S Svenningsen, F Guo, DG McCormack, G Parraga. *Acad Radiol* 2017;24(1):4-12.

**Rationale and Objectives:** Evidence-based treatment and management for patients with bronchiectasis remain challenging. There is a need for regional disease measurements as focal distribution of disease is common. Our objective was to evaluate the ability of magnetic resonance imaging (MRI) to detect regional ventilation impairment and response to airway clearance therapy (ACT) in patients with noncystic fibrosis (CF) bronchiectasis, providing a new way to objectively and

regionally evaluate response to therapy. **Materials and Methods:** Fifteen participants with non-CF bronchiectasis and 15 age-matched healthy volunteers provided written informed consent to an ethics board-approved Health Insurance Portability and Accountability Act-compliant protocol and underwent spirometry, plethysmography, computed tomography (CT), and hyperpolarized  $^3\text{He}$  MRI. Bronchiectasis patients also completed a Six-Minute Walk Test, the St. George's Respiratory questionnaire, and Patient Evaluation Questionnaire (PEQ), and returned for a follow-up visit after 3 weeks of daily oscillatory positive expiratory pressure use. CT evidence of bronchiectasis was qualitatively reported by lobe, and MRI ventilation defect percent (VDP) was measured for the entire lung and individual lobes. **Results:** CT evidence of bronchiectasis and abnormal VDP ( $14 \pm 7\%$ ) was observed for all bronchiectasis patients and no healthy volunteers. There was CT evidence of bronchiectasis in all lobes for 3 patients and in  $3 \pm 1$  lobes (range = 1–4) for 12 patients. VDP in lobes with CT evidence of bronchiectasis ( $19 \pm 12\%$ ) was significantly higher than in lobes without CT evidence of bronchiectasis ( $8 \pm 5\%$ ,  $P = .001$ ). For patients, VDP in lung lobes with ( $P < .0001$ ) and without CT evidence of bronchiectasis ( $P = .006$ ) was higher than in healthy volunteers ( $3 \pm 1\%$ ). For all patients, mean PEQ-ease-bringing-up-sputum ( $P = .048$ ) and PEQ-patient-global-assessment ( $P = .01$ ) were significantly improved post-oscillatory positive expiratory pressure. An improvement in regional VDP greater than the minimum clinically important difference was observed for 8 of the 14 patients evaluated. **Conclusions:** There was CT and MRI evidence of structure-function abnormalities in patients with bronchiectasis; in approximately half, there was evidence of ventilation improvements after airway clearance therapy.

### OSCILLATORY POSITIVE EXPIRATORY PRESSURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

*Svenningsen S, Paulin GA, Sheikh K, Guo F, Hasany A, Kirby M, Etemad-Rezai R, McCormack DG, Parraga G. Journal of COPD 2016;13(1):66 – 74.*

Evidence-based guidance for the use of airway clearance techniques (ACT) in chronic obstructive pulmonary disease (COPD) is lacking in-part because well-established measurements of pulmonary function such as the forced expiratory volume in 1s ( $\text{FEV}_1$ ) are relatively insensitive to ACT. The objective of this crossover study was to evaluate daily use of an oscillatory positive expiratory pressure (oPEP) device for 21–28 days in COPD patients who were self-identified as sputum-producers or non-sputum-producers. COPD volunteers provided written informed consent to daily oPEP use in a randomized crossover fashion. Participants completed baseline, crossover and study-end pulmonary function tests, St. George's Respiratory Questionnaire (SGRQ), Patient Evaluation Questionnaire (PEQ), Six-Minute Walk Test and  $^3\text{He}$  magnetic resonance imaging (MRI) for the measurement of ventilation abnormalities using the ventilation defect percent (VDP). Fourteen COPD patients, self-identified as sputum-producers and 13 COPD-non-sputum producers completed the study. Post-oPEP, the PEQ-ease-bringing-up-sputum was improved for sputum-producers ( $p = 0.005$ ) and non-sputum-producers ( $p = 0.04$ ), the magnitude of which was greater for sputum-producers ( $p = 0.03$ ). There were significant post-oPEP improvements for sputum-producers only for FVC ( $p = 0.01$ ), 6MWD ( $p = 0.04$ ), SGRQ total score ( $p = 0.01$ ) as well as PEQ-patient-global assessment ( $p = 0.02$ ). Clinically relevant post-oPEP improvements for PEQ-ease-bringing-up-sputum/PEQ-patient-global-assessment/SGRQ/VDP were observed in 8/7/9/6 of 14 sputum-producers and 2/0/3/3 of 13 non-sputum-producers. The post-oPEP change in  $^3\text{He}$  MRI VDP was related to the change in PEQ-ease-bringing-up-sputum ( $r = 0.65$ ,  $p = 0.0004$ ) and  $\text{FEV}_1$  ( $r = -0.50$ ,  $p = 0.009$ ). In COPD patients with chronic sputum production, PEQ and SGRQ scores, FVC and 6MWD improved post-oPEP.  $\text{FEV}_1$  and PEQ-ease-bringing-up-sputum improvements were related to improved ventilation providing mechanistic evidence to support oPEP use in COPD.

### ANALYSIS OF ACUTE DRUG USAGE FROM A RETROSPECTIVE COHORT STUDY ON THE IMPACT OF AN OPEP DEVICE IN COPD PATIENTS WITH CHRONIC BRONCHITIS.

*Suggett J, Carlin BW, Dunne P, Kauffman G, Coppola D. Presented at CHEST 2016.*

**Purpose:** In Chronic Obstructive Pulmonary Disease (COPD) patients with Chronic Bronchitis (CB) the AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device has been shown to significantly improve measures such as<sup>1</sup> ease-bringing-up-sputum, Forced Vital Capacity, quality of life, and 6 Minute Walk Distance. This abstract reports acute drug usage data from a real-world study over 6 months among COPD patients with CB. **Background:** Antibiotics and oral corticosteroids (OCS) are commonly prescribed drug therapies used in treatment of acute COPD exacerbations<sup>2</sup>. Antibiotic-resistant infections add considerable and avoidable costs to the already overburdened healthcare system<sup>3</sup>. **Methods:** A retrospective cohort study of the CDM hospital claims database was conducted between September 2013 and August 2015. Moderate to severe exacerbations were defined as requiring either a hospital ER visit or hospital admission. Study participants  $n=810$ ; patients who used the AEROBIKA® device  $n=405$ ; propensity score matched controls  $n=405$ ; Propensity score matches included, amongst others, demographics, history of exacerbations, comorbidities and drug usage. Inclusion Criteria included CDM record with CB diagnosis [ICD-9 491.xx] from 01/01/2011– 09/30/2015, documented



AEROBIKA® device use, newly initiated,  $\geq 1$  CDM record before and after their index date and at least  $\geq 35$  years old in the year of index visit. Exclusion Criteria included incomplete demographic data (age, gender), use of AEROBIKA® device before their index date, and use of PEP or other OPEP devices at any time during the study period. **Results:** The proportion of patients prescribed OCS and antibiotics in the hospital setting during the postindex period was significantly lower for patients using the AEROBIKA® device compared to their matched controls: Oral Corticosteroids: 1.5% vs 13.3%,  $p < 0.001$ ; Antibiotics: 14.1% vs 32.6%,  $p < 0.001$ . Decreased need for short-term drug therapies including OCS and antibiotics, may reflect better disease control. **Conclusions:** There was a significant reduction in the requirement for OCS and antibiotics in the hospital setting for patients receiving the AEROBIKA® device. These findings provide additional evidence that the drug-free AEROBIKA® device may be an effective addition to a disease management plan for COPD patients with chronic bronchitis and a history of exacerbations.

<sup>1</sup>Svenningsen S, Paulin GA, Sheikh K, *et al.* Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. COPD 2016;13(1):66–74. <sup>2</sup>Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2015. <sup>3</sup>Antibiotic Resistance Threats in the United States, 2013. US Department of Health and Human Services: Centers for Disease Control and Prevention. <sup>4</sup>Wolkove N, *et al.* Use of a mucus clearance device enhances the bronchodilator response in patients with stable COPD. CHEST 2002;121(3):702–7. <sup>5</sup>Suggett J. A Retrospective Cohort Study Demonstrating the Impact of an OPEP Device on Exacerbations in COPD Patients with Chronic Bronchitis. Presented at ERS 2016. CDM = Charge Description Master

## A RETROSPECTIVE COHORT STUDY DEMONSTRATING THE IMPACT OF AN OPEP DEVICE ON EXACERBATION RELATED HEALTHCARE COSTS IN COPD PATIENTS WITH CHRONIC BRONCHITIS.

Coppola D, Carlin BW, Dunne P, Kauffman G, Suggett J. Presented at CHEST 2016.

**Purpose:** In Chronic Obstructive Pulmonary Disease (COPD) patients with Chronic Bronchitis (CB) the AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device has been shown to significantly improve measures such as<sup>1</sup> Ease-bringing-up-sputum, Forced Vital Capacity, Quality of life and 6 Minute Walk Distance. This abstract reports moderate-to-severe exacerbation related healthcare cost data from a real-world study over 6 months among COPD patients with CB. **Background:** COPD exacerbations account for the greatest proportion of the total COPD burden on the healthcare system.<sup>2</sup> In the US, the estimated direct cost is \$30 billion and the indirect cost is approximately \$20 billion.<sup>2</sup> The US national average 30 day readmission rate for patients hospitalized with a COPD exacerbation is 23%<sup>3</sup>. The US Centers for Medicare and Medicaid Services (CMS) has introduced 30 day readmission reimbursement penalties with the goal of reducing 30 day readmission rates. COPD cases are projected to increase 155% from 2010 to 2030<sup>4</sup>. There is a predicted epidemic of COPD hospitalizations over the next 15 years<sup>4</sup>. **Methods:** A retrospective cohort study of the CDM hospital claims database was conducted between September 2013 and August 2015. Moderate to severe exacerbations were defined as requiring either a hospital ER visit or hospital admission. Study participants  $n=810$ ; patients who used the AEROBIKA® device  $n=405$ ; propensity score matched controls  $n=405$ ; Propensity score matches included, amongst others, demographics, history of exacerbations, comorbidities and drug usage. Inclusion Criteria included CDM record with CB diagnosis [ICD-9 491.xx] from 01/01/2011– 09/30/2015, documented AEROBIKA® device use, newly initiated,  $\geq 1$  CDM record before and after their index date and at least  $\geq 35$  years old in the year of index visit. Exclusion Criteria included incomplete demographic data (age, gender), use of AEROBIKA® device before their index date, and use of PEP or other OPEP devices at any time during the study period. **Results:** The mean cost of moderate-to-severe exacerbations per patient was significantly reduced in patients who used the AEROBIKA® device plus baseline care.

Length of Time	Cost Reduction		
	30 days	3 months	6 months
Mean Cost (USD)	-\$6,347	-\$6,600	-\$9,936
	( $p=0.008$ )	( $p=0.031$ )	( $p=0.018$ )

The device cost is included in the calculation; the mean cost reductions show significant savings to the healthcare system. **Conclusions:** Patients in the AEROBIKA® device cohort exhibited significantly lower costs throughout the 6 month study period. These findings provide additional evidence that the drug-free AEROBIKA® device may be an effective addition to a disease management plan for COPD patients with chronic bronchitis and a history of exacerbations.

<sup>1</sup>Svenningsen S, Paulin GA, Sheikh K, *et al.* Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. COPD 2016;13(1):66 – 74. <sup>2</sup>Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2015. <sup>3</sup>Jenks S, Williams M, Coleman E. Re-hospitalization among patients in the Medicare fee-for-service program. N Eng J Med. 2009; 360:14. <sup>4</sup>Khakban A, *et al.* Am J Respir Crit Care Med. 2016 Sep 14. [Epub ahead of print]. <sup>5</sup>Wolkove N, *et al.* Use of a mucus clearance device enhances the bronchodilator response in patients with stable COPD. CHEST 2002;121(3):702–7. <sup>6</sup>Suggett J. A Retrospective Cohort Study Demonstrating the Impact of an OPEP Device on Exacerbations in COPD Patients with Chronic Bronchitis. Presented at ERS 2016. CDM = Charge Description Master

## A RETROSPECTIVE COHORT STUDY DEMONSTRATING THE IMPACT OF AN OPEP DEVICE ON EXACERBATIONS IN COPD PATIENTS WITH CHRONIC BRONCHITIS.

Suggett J. Presented at ERS 2016.

**Rationale:** In Chronic Obstructive Pulmonary Disease (COPD) patients with Chronic Bronchitis (CB) the AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device has been shown to significantly improve measures such as Ease-bringing-up-sputum, FVC, Quality of life, and 6MWD.<sup>1</sup> To date, its effectiveness in reducing exacerbations in the real-world had not been reported in COPD patients. This abstract reports 30 day exacerbation data from real-world outcomes over 6 months among COPD patients with CB. **Background:** Acute exacerbations are the most common reason for medical visits, hospital admissions, and death in patients with COPD<sup>2</sup>. One in 5 patients hospitalized for a COPD exacerbation require re-hospitalization within 30 days<sup>3</sup>. During an exacerbation, airways are compromised by inflammation, mucus buildup, and dynamic lung hyperinflation<sup>4</sup>. Patients with compromised airways are poorly responsive to usual COPD treatments, and are at increased risk of recurrent exacerbations<sup>4</sup>. According to guidelines, the goal is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations<sup>5</sup>. **Methods:** Inclusion Criteria were CDM record with chronic bronchitis diagnosis [491.xx] from 01/01/2011 – 09/30/2015, Documented AEROBIKA® OPEP device use, ≥1 CDM record before their index date and after their index date, ≥1 CDM record of chronic bronchitis diagnosis (ICD-9 491.xx any position) on or before index date, at least ≥35 years old in the year of index visit. Exclusion Criteria included incomplete demographic data (age, gender), AEROBIKA® device use before their index date and use of PEP or other OPEP devices at any time during the study period. **Statistical Analysis:** Study participants  $n=810$ ; patients who used AEROBIKA® device  $n=405$ ; propensity score-matched controls  $n=405$ . Propensity score matching is a statistical technique that balances baseline differences between groups under non-randomized conditions. Patients who used the AEROBIKA® device were propensity score matched 1:1 to COPD patients who did not use any positive expiratory pressure device, based on demographics, exacerbation history, and treatment history. **Results:** In the AEROBIKA® cohort there was a statistically significant 28% reduction in patients with a moderate-to-severe exacerbation within 30 days (25.7% to 18.5%,  $p=0.014$ ). Results determined the Number Needed to Treat (NNT) was 14. **Conclusions:** Patients in the AEROBIKA® device cohort, experienced a significant reduction in moderate-to-severe exacerbations within 30 days (-28%,  $p=0.014$ ). This translates to a NNT of 14 which compares favorably to several drug product studies. These findings provide additional evidence that the drug-free AEROBIKA® device may be an effective addition to a disease management plan for COPD patients with Chronic Bronchitis.

<sup>1</sup>Svenningsen S, Paulin GA, Sheikh K, *et al.* Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. COPD 2016;13(1):66 – 74. <sup>2</sup>O'Donnell DE, *et al.* Can Respir J. 2007;14(Suppl B):5B-32B. <sup>3</sup>Shah T, *et al.* Chest. 2016 May 7. doi: 10.1016/j.chest.2016.05.002. [Epub ahead of print]. <sup>4</sup>O'Donnell DE, Parker CM. Thorax. 2006;61(4):354-61. <sup>5</sup>Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2015. <sup>6</sup>Marks JH. Paediatr. Respir. Rev. 2007;8:17-23. <sup>7</sup>Strickland SL. Respir. Care 2013;on line Nov 12. <sup>8</sup>Pasteur MC, Bilton D, Hill AT. Thorax 2010.65(Suppl 1):i1-i58. CDM = Charge Description Master

## QUALITY OF LIFE (QOL) RESPONDER RATE ANALYSIS FOLLOWING USE OF AN OSCILLATING POSITIVE EXPIRATORY PRESSURE (OPEP) DEVICE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): SGRQ V CAT ASSESSMENTS.

Suggett J. Presented at COPD 10, 2016.

**Background:** The AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device has been reported to improve Quality of Life outcomes for COPD patients with Chronic Bronchitis<sup>1,2</sup>. This abstract compares the responder rates from two separate studies using the same device; one with the St. George's Respiratory Questionnaire (SGRQ) and the other with the COPD Assessment Test (CAT).

### STUDY 1

**Methods:** Randomized cross-over study in 27 COPD patients for 3–4 weeks using the SGRQ<sup>1</sup>. Responder rates for clinically significant measures of improvement of greater than 4 were calculated for the COPD patients with Chronic Bronchitis.

**Results:** In Study 1, the mean SGRQ value for the 14 COPD patients with Chronic Bronchitis significantly improved from 49 to 40 ( $p=0.01$ , paired t-test) following OPEP therapy.

	Pre-AEROBIKA® Device	Post-AEROBIKA® Device
SGRQ Total Score (MCID ≤ 4)	49	40



## STUDY 2

**Methods:** Clinical assessment of 37 COPD patients over an 8 week period using the CAT<sup>2</sup>. Responder rates for clinically significant measures of improvement of at least 2 were calculated for the COPD patients with Chronic Bronchitis. **Results:** The mean CAT value for the 26 COPD patients with Chronic Bronchitis significantly improved from 19.7 to 17.4 ( $p=0.01$ , paired t-test) following OPEP therapy.

	Week 0	Week 4	Week 8
Mean CAT Scores	19.7	18.2	17.4

**Combined Outcome:** In terms of responder rate analysis, using the recognized improvement thresholds noted above, 64% of the COPD patients with Chronic Bronchitis from Study 1 showed a clinically significant improvement in Quality of Life compared to 62% from Study 2. **Conclusions:** Results from two separate studies, using different validated Quality of Life instruments, show good agreement. Nearly two thirds of COPD patients with Chronic Bronchitis exhibited clinically significant improvements in Quality of Life following self-administered treatment with the AEROBIKA® device.

<sup>1</sup>Svenningsen S, Paulin GA, Sheikh K, *et al.* Oscillatory Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. *Journal of COPD* 2016;13(1):66–74. <sup>2</sup>Suggett J. Review of Quality of Life outcomes following use of an Oscillating Positive Expiratory Pressure (OPEP) device for Chronic Obstructive Pulmonary Disease (COPD): 8 weeks field study using the COPD Assessment Test (CAT). *Am J Respir Crit Care Med* 2016;193:A6888.

## REVIEW OF QUALITY OF LIFE OUTCOMES FOLLOWING USE OF AN OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE: 8 WEEKS FIELD STUDY USING THE COPD ASSESSMENT TEST.

*Suggett J. Presented at ATS 2016.*

**Background:** Despite the multiple treatment options available, many Chronic Obstructive Pulmonary Disease (COPD) patients still suffer from a poor quality of life. We assessed the quality of life outcomes for COPD patients with chronic bronchitis following treatment with a handheld, easy-to-use Oscillating Positive Expiratory Pressure (OPEP) device, using the COPD Assessment Test (CAT) over an 8 week duration. **Methods:** A clinical assessment was undertaken in 37 COPD patients in southwestern Ontario, Canada, who received the AEROBIKA® device (Trudell Medical International) via their healthcare provider. Patients were monitored using the CAT survey over an 8 week period of daily use. The 37 patients were stable on prescribed therapy which included oxygen therapy. The CAT was administered by an attending Respiratory Therapist in their home at 0, 4 and 8 weeks of OPEP use. **Results:** 26 of the 37 COPD patients were diagnosed with Chronic Bronchitis (CB). Note: Review of the patient records of the original 37 patients identified 11 of whom had a diagnosis of emphysema, and therefore these were excluded from the analysis. The mean CAT total score for the 26 COPD patients with CB changed from 19.7 (initial) to 18.2 (4 weeks) and 17.4 (8 weeks) with a clinically (at least 2 units<sup>1</sup>) and statistically ( $p=0.011$ , paired two-tailed t test) significant reduction over the 8 weeks OPEP use. Furthermore, 62% of patients had a clinically significant improvement in their total CAT after 8 weeks. **Conclusions:** For stable COPD patients already on prescribed therapy, the addition of the AEROBIKA® device delivered a clinically and statistically significant improvement in CAT scores from baseline to 8 weeks. Notwithstanding the limitations of a relatively small study size and lack of a control, the results further support the efficacy of this device with respect to improved quality of life in these patients. Given the reported poor quality of life for many COPD patients, it is worth consideration to include an easy-to-use, drug-free OPEP device such as the AEROBIKA® device as part of the disease treatment plan for COPD patients with chronic bronchitis.

## ASSESSMENT OF A NEW PRESSURE MANOMETER FOR USE WITH AN OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE.

*Suggett J, Alizoti N, and Meyer A. Presented at ERS 2015.*

**Rationale:** Airway clearance therapy using Oscillating Positive Expiratory Pressure (OPEP) devices can be used to help mobilize and clear excess mucus secretions in the lungs. The desired therapeutic positive expiratory pressure range is often considered to be between 10 and 20 cm H<sub>2</sub>O. Confirmation of this therapeutic pressure range can be achieved using a manometer attachment with an OPEP device. This investigation assessed how a new pressure manometer incorporated onto the AEROBIKA® OPEP device might influence the frequency of oscillations. **Materials and Methods:** A new pressure manometer was assessed with the AEROBIKA® OPEP device. The manometer accessory can be attached directly to the OPEP device and is visible to the user during device use. Seven healthy volunteers were instructed to exhale through the OPEP device (without manometer attachment) according to the instructions for use (3 replicate exhalations per

subject) and the average frequency of all oscillations per breath were calculated for each subject. Pressure oscillations were recorded by means of a sensitive pressure transducer (Honeywell, Morristown, NJ) – from these profiles, oscillation frequencies in Hz could be determined. The same seven volunteers then repeated the exercise with the manometer attached to the OPEP device and were instructed to target the middle of the desired pressure range on the manometer (green zone, or 5–20 cm H<sub>2</sub>O). The relationship between pressure and frequency is independent of the user and therefore would be expected to be the same if patients were using the device rather than healthy volunteers. **Results:** The average frequencies of OPEP oscillations determined for each volunteer, with and without the manometer, are represented in the table below. A theoretical optimum frequency range is 12–15Hz (King *et al*, 1983; Silva *et al*, 2009).

Participant	Without Manometer	With Manometer
1	11.3	13.0
2	15.5	13.8
3	12.5	13.7
4	17.3	14.8
5	9.8	13.6
6	14.0	13.9
7	13.7	15.3
<b>Mean</b>	13.4	14.0
<b>SD</b>	2.3	0.7
<b>Range</b>	9.8 – 17.3	13.0 – 15.3

**Discussion & Conclusions:** The manometer attachment was able to be used quickly and effectively by all seven volunteers. With the manometer attachment connected and the instruction to target a level in the middle of desired pressure range the oscillation frequencies were more consistent, and interestingly, were even closer aligned to the reported optimum Hz range. For patients uncertain of the amount of exhalation effort to use, the OPEP with manometer attachment provided feedback as to the safe and effective positive pressure level to stay within during the therapy. The use of such a manometer may therefore be useful as part of routine therapy or as a training aid.

#### COMBINING INHALATION BY A BREATH ACTUATED NEBULIZER AND EXHALATION WITH OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE OFFERS POTENTIAL FOR SIMULTANEOUS THERAPY: A LABORATORY STUDY.

Sharpe R, Suggett J, Avvakoumova V, Schneider H, Ali R and Nagel MW. Presented at the European Cystic Fibrosis Conference 2015.

**Background:** Oscillating Positive Expiratory Pressure (OPEP) therapy is used to mobilize secretions associated with lung diseases for pulmonary rehabilitation, like Cystic Fibrosis. Traditionally, OPEP therapy has been conducted separately from aerosol therapy. **Study Purpose:** An innovative hand-held oscillatory positive expiratory pressure device (AEROBIKA® OPEP) can be connected directly to the AEROECLIPSE® II Breath Actuated Nebulizer (BAN). The patient can thereby receive aerosol therapy and secretion mobilization simultaneously. The AEROBIKA® OPEP device can also be used with any continuous nebulizer with a 22 mm adapter. *In vitro* measurements of BAN aerosol delivery performance when connected with the AEROBIKA® OPEP device. In this configuration (Inhalation), the aerosol flow path is linear with minimal restriction to mitigate internal losses caused by inertial impaction. When the patient exhales (Exhalation), the one-way valve closes, diverting the flow through the body of the OPEP device mechanically operating the vane that generates oscillatory pressure pulsations that are transmitted back to the patient. **Materials and Methods:** Measurements were made (9 replicates) of total and fine droplet mass  $\mu\text{m}$  by Next Generation Impactor (NGI) equipped with a Ph.Eur./USP induction port and operated at 15.0 L/min  $\pm$  5%. The BAN on test was operated by compressed air delivered at 50 psig and filled with 4-ml ipratropium bromide solution for nebulization (0.5 mg/mL). The BAN was initially tested connected directly to the induction port via a leak-tight fitting. The measurements were repeated with the AEROBIKA® OPEP device inserted between the BAN and induction port. The BAN on test was run to onset of sputter, and the Total Mass of ipratropium bromide ( $\text{TM}_{\text{ipr}}$ ) recovered and assayed by a validated HPLC-UV spectrophotometric method. Measurements were also made with the acapella<sup>+</sup> duet<sup>+</sup> Vibratory PEP Therapy System (Smiths Medical North America, Dublin, OH). The purpose of this arm was to examine what might happen if a clinician was to make this substitution.

## Results (mean $\pm$ SD)

	BAN Alone	BAN-AEROBIKA® device	BAN-acapella <sup>†</sup> duet <sup>†</sup>
TM <sub>IPr</sub> (μg)	582 $\pm$ 30	515 $\pm$ 28	308 $\pm$ 23
FM <sub>IPr</sub> (μg)	452	426	196

**Conclusions:** Offering the patient the opportunity to combine aerosol and OPEP therapy will reduce the overall length of treatment time. The delivery of medication from the AEROECLIPSE® II BAN is only marginally reduced by combining the BAN with the AEROBIKA® OPEP device. Substitution by devices that do not allow incoming aerosol to be transported directly to the patient, are likely to result in substantial loss of aerosol.

## REVIEW OF QUALITY OF LIFE OUTCOMES FOLLOWING USE OF AN OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COMPARISON OF SMALL N CLINICALLY CONTROLLED AND VALIDATED MEASURES TO LARGE N PATIENT SURVEY DATA.

*J. Suggett. Presented at ATS 2015.*

**Background:** Airway clearance therapy can be used to help mobilize and clear excess mucus secretions in the lungs. Excess mucus is a common complaint for Chronic Obstructive Pulmonary Disease (COPD) patients with chronic bronchitis. Contributes to breathlessness, chronic cough and difficulty performing daily tasks resulting in poor quality of life. Effective airway clearance can result in an improved quality of life. We compared the quality of life outcomes for COPD patients following treatment with a new Oscillating Positive Expiratory Pressure (OPEP) device (AEROBIKA® OPEP, Trudell Medical International, Canada), both in a cross-over clinical study using the validated St. George's Respiratory Questionnaire (SGRQ) and in a much larger non-validated patient survey. **Methods:** Randomized, 6 week cross-over study of 14 COPD (Chronic Bronchitis) patients.<sup>1</sup> Difference in SGRQ scores pre and post OPEP therapy were compared. In a separate evaluation, AEROBIKA® OPEP devices and associated surveys were supplied to non-phenotyped COPD patients in Ontario, Canada via their healthcare provider. Feedback was received from 461 patients following 1 month's use. **Results:** Clinical study results<sup>1</sup>: The mean SGRQ Total Score for the 14 COPD patients in the 6 week cross-over study changed from 45 pre-OPEP to 36 post-OPEP. A decrease in score relates to an improvement. Highlighting a statistically ( $p=0.009$ , paired two tailed t test) and clinically significant reduction of 9 points – more than 2 times the Minimum Clinically Important Difference (MCID). 97% of patients wanted to continue using the device. **Conclusions:** A highly significant improvement (both statistical and clinical) in SGRQ score was observed by patients following use of the AEROBIKA® OPEP device within the 3 week cross-over clinical study. Although the large n patient survey was in non-phenotyped COPD patients using a non-validated survey, with therefore recognized limitations, there was still a degree of correlation to the clinical study outcomes with subjective improvements related to mucus clearance, ease of breathing, quality of life and coughing reported for a large number of patients.

<sup>1</sup>Svenningsen S *et al.* Oscillating Positive Pressure Therapy in Chronic Obstructive Pulmonary Disease and Bronchiectasis. Presented at ERS 2014.

## SURVEY OF PATIENTS USING AN OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICE INDICATES IMPROVEMENT IN WELL-BEING AND COMPLIANCE TO THERAPY.

*H Harkness, C Patrick and J Lefebvre. Presented at CRC 2015.*

**Rationale:** Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death in Canada and is the only chronic condition where the affected population continues to grow. Studies have shown the AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device to have positive patient outcomes in clinical evaluations,<sup>1,2</sup> but assessment of home-based user experience was not known. A survey was undertaken with patients to determine if using the device had any impact on patient reported outcomes, compliance, and satisfaction. **Background:** Patients with COPD experience symptoms including breathlessness, chronic cough, excess mucus, and the inability to perform daily activities. COPD is characterized by a number of interrelated physiological changes in the lungs. Airflow limitation and chronic inflammation create excess mucus within the airways. Airway damage inhibits the natural ability of the lungs to clear excess mucus. Pharmacological treatments have been unable to demonstrate effect on mucus clearance.<sup>3</sup> **Method:** Patients were counselled on the proper use of the AEROBIKA® OPEP device. Each patient was asked to use the device twice daily for at least 3 weeks prior to completing the survey. Survey responses were captured via an online portal requiring a unique ID to prevent duplicate entries. **Results:** 812 unique survey responses were collected. 90% of patients had COPD (non-phenotyped). 8% had Bronchiectasis. 2% Cystic Fibrosis. Compliance to therapy was high with 97% indicating they would

continue to use the device. Patient satisfaction was 94% for the device overall with 96% it easy to use. **Conclusions:** Results from this patient feedback survey indicate that the AEROBIKA® OPEP device has a high degree of acceptance within the COPD population because it is easy to use, helps clear mucus and reduces feelings of breathlessness. Responses demonstrated a high degree of satisfaction with the AEROBIKA® OPEP device, specifically in assisting with mucus clearance and decreased breathlessness (may lead to better therapeutic benefit). The addition of the AEROBIKA® OPEP is associated with improved symptom relief.

<sup>1</sup>Svenningsen S *et al.* Hyperpolarized <sup>3</sup>He magnetic resonance imaging following oscillatory positive expiratory pressure treatment in GOLD stage II & III COPD. Presented at ATS 2013. <sup>2</sup>Svenningsen S *et al.* Oscillating Positive Expiratory Pressure Therapy in Chronic Obstructive Pulmonary Disease and Bronchiectasis. Presented at ERS 2014 (Munich, Germany). <sup>3</sup>Perry RJ *et al.* Journal of Aerosol Medicine 1990;3(3):187-196. Hogg JC *et al.* American Journal of Respiratory and Critical Care Medicine 2007;176(5):454. Burgel PR *et al.* European Respiratory Journal 2004;24(4):594- 600. Ramos FL *et al.* International Journal of COPD 2014;9:139-150. Pavia D *et al.* European journal of respiratory diseases 1983;128(Suppl):304. Hasani A *et al.* CHEST 2004;125(5):1726-1734. Baraniuk JN *et al.* Clinical & Experimental Allergy Reviews 2010;10(1):12-19. Rogers D *et al.* Annals of medicine 2006;38(2):116-125. Salathe M *et al.* CHEST 1996; 110(4):1048-1057. Poole PJ. International Journal of Chronic Obstructive Pulmonary Disease 2006;1(2):123 Rogers DF. Pulmonary Pharmacology & Therapeutics 2005;18(1):1-8. 4. Marks JH. Paediatr. Respir. Rev. 2007;8:17-23. 5 Strickland SL. Respir Care. 2013;58(12):2187-93.

## OSCILLATING POSITIVE EXPIRATORY PRESSURE THERAPY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND BRONCHIECTASIS.

*Svenningsen S, Paulin G, Wheatley A, Pike D, Suggett J, McCormack D and Parraga G. Presented at ERS 2014.*

**Background/Rationale:** Cough and sputum production are common in Chronic Obstructive Pulmonary Disease (COPD) and Bronchiectasis, both of which are associated with increased rates of mortality and other adverse clinical outcomes.<sup>1</sup> Airway Clearance Therapies (ACT) such as Oscillating Positive Expiratory Pressure (OPEP) aim to facilitate mucus transport and sputum expectoration, however clinical evidence of their efficacy is lacking.<sup>2</sup> To test the effects of daily OPEP use over a 3 week period, a hand-held device was evaluated in COPD and Bronchiectasis. **Hypothesis:** Daily use of OPEP over a 3-week period results in significantly improved mucus clearance and symptom scores in subjects with COPD and Bronchiectasis. **Research Objective:** To evaluate the safety and efficacy of four-times daily OPEP over 3 weeks in COPD and Bronchiectasis with Chronic Bronchitis/chronic sputum production. **Study Subjects and Design:** Subjects with COPD (n=14) and non-CF Bronchiectasis (n=14) were randomized to perform OPEP four-times daily in a cross-over controlled study; 3 weeks on/3 weeks off (or vice versa). Study evaluations (start/cross-over/end): Pulmonary Function Tests, Six Minute Walk Test (6MWT), St. George's Respiratory Questionnaire (SGRQ), Patient Evaluation Questionnaire (PEQ), Hyperpolarized Helium-3 Magnetic Resonance Imaging (<sup>3</sup>He MRI). **Discussion:** Following use of the OPEP device for all subjects there were statistically significant improvements in: 6MWD (p=0.02), SGRQ (p=0.02), PEQ Cough Frequency (p=0.009), PEQ Dyspnea (p=0.04), PEQ Ease in Bringing up Sputum (p<0.0001). Both COPD and Bronchiectasis subjects had improved ease in bringing up sputum. SGRQ was improved in COPD but not Bronchiectasis. 6MWD was improved in Bronchiectasis. In a subset of both COPD and Bronchiectasis subjects, ventilation defects (as measured by <sup>3</sup>He) were diminished post-OPEP. **Conclusions:** In subjects with COPD and Bronchiectasis, three weeks of OPEP therapy was well-tolerated and there was improved dyspnea, quality of life, exercise capacity and ease in bringing up sputum.

<sup>1</sup>Ekberg-Aronsson *et al.* Respir Res (2005); <sup>2</sup>van der Schans *et al.* Paediatr Respir Rev (2002).

## ASSESSMENT OF OSCILLATING POSITIVE EXPIRATORY PRESSURE DEVICES BY MEANS OF ADULT EXPIRATORY WAVEFORMS: A LABORATORY STUDY.

*J Suggett, A Meyer, S Costella, R Morton, J Mitchell. Poster presented at Presented at ATS 2014.*

**Background:** The development of the new AEROBIKA® Oscillating Positive Expiratory Pressure (OPEP) device (Trudell Medical International), required assessment of performance under realistic conditions of adult use to aid prescribing clinicians. At the same time, comparative measurements were made with other commercially available OPEP devices to gather benchmark data against which to compare the AEROBIKA® OPEP device. **Materials and Methods:** A healthy adult volunteer exhaled into the AEROBIKA® OPEP device set to the high resistance setting. The subject followed typical instructions for an OPEP device: exhale actively but not forcefully, achieve exhalation durations between 3–4 times the duration of inhalation, and replicate exhalation patterns (n=5) were recorded and the average profile was then scaled so that the Peak Expiratory Flow rate (PEF) ranged from 15 to 40 L/min. These patient representative scaled profiles were then used to operate the AEROBIKA® OPEP device by means of a programmable flow generator (modified Pulmonary Waveform Generator using Hoyt – PWG hardware). The pressure oscillations were recorded by means of a sensitive pressure transducer (Honeywell, Morristown, NJ, USA). The percentage of each simulated exhalation profile during which discernable pressure oscillations (>1.0 cm H<sub>2</sub>O) were evident (t<sub>OSC</sub>) was calculated. The procedure was repeated with

other prescribed OPEP devices (green-DM acapella<sup>†</sup>; Smiths Medical North America, Norwell, MA, USA vibratory PEP (vPEP) devices and RC-Cornet<sup>†</sup>; Curaplex, Dublin, OH, USA. **Results:** The Comparative Values of  $t_{OSC}$  at different adult PEFs for Simulated Exhalation Profiles are summarized in the Table below.

PEF (L/min)	$t_{OSC}$ (%)				
	15	20	25	30	40
<b>AEROBIKA<sup>®</sup></b>	76.0	77.0	79.5	81.0	81.5
<b>acapella<sup>†</sup> green-DH</b>	34.5	51.0	53.0	58.5	62.5
<b>RC Cornet<sup>†</sup></b>	30.0	47.0	50.0	60.5	59.0

**Conclusions:** Duration of oscillations per expiratory portion of each respiratory cycle is important as a measure of device efficiency for the clinical management of mucus secretion mobilization. Measures of  $t_{OSC}$  [% of exhalation time with oscillations] with the AEROBIKA<sup>®</sup> OPEP device were >75% at all PEF [Peak Expiratory Flow Rate] settings and were generally consistent. The other OPEP systems exhibited lower and much more variable  $t_{OSC}$  values, ranging from 30% to 63%. Duration of oscillations for AEROBIKA<sup>®</sup> OPEP was 52% to 60% greater on average compared to other devices.

### COMPARATIVE LABORATORY STUDY OF OSCILLATING POSITIVE EXPIRATORY PRESSURE WAVEFORMS FROM COMMERCIALLY AVAILABLE DEVICES USED IN AIRWAY CLEARANCE THERAPY.

*J Suggett, A Meyer, S Costella, J Mitchell. Presented at Respiratory Drug Delivery 2014.*

**Background:** Oscillating Positive Expiratory Pressure (OPEP) based treatment is becoming widely adopted in pulmonary rehabilitation as an alternative to postural drainage of mucus-based secretions for Airway Clearance Therapy (ACT). These devices are useful for patients unable to mobilize secretions by coughing alone, associated with diseases such as Chronic Obstructive Pulmonary Disease (COPD), bronchiectasis and cystic fibrosis. The AEROBIKA<sup>®</sup> hand-held OPEP device (Trudell Medical, London, Canada) has the following features: can be used by patients in any orientation, has adjustable resistance settings to enable, patients to set according to their specific requirements, can be taken apart and cleaned at home daily. With OPEP, expiratory pressure stents the airways open and helps fill under-inflated or collapsed alveoli while oscillation creates short bursts of increased expiratory airflow to thin, dislodge and move mucus to the central/upper airways where it can be coughed out. **Materials and Methods:** In order to develop exhalation breathing profiles representative of the OPEP maneuver an AEROBIKA<sup>®</sup> OPEP device ( $n=1$ ) was connected to pressure (Honeywell, Morristown, NJ) and flow (model 4000, TSI Corp., St Paul, MN) sensors. A series of exhalation flow rate waveforms as a function of elapsed time from the start of exhalation were recorded from adult volunteers ( $n=5$ ), who had been trained to use the device in accordance with instructions: exhale actively but not forcefully, achieve exhalation durations between 3 to 4 times the duration of inhalation, replicate exhalation patterns ( $n=5$ ) were recorded and the average profile was then scaled so that the Peak Expiratory Flow rate (PEF) ranged from 15 to 40 L/min. These patient representative scaled profiles were then used to operate the AEROBIKA<sup>®</sup> OPEP device by means of a programmable flow generator (MH Custom Design & Manufacturing, Midvale, UT). The percentage of each simulated exhalation profile during which discernable pressure oscillations (>1.0 cm H<sub>2</sub>O) were evident ( $t_{OSC}$ ) was calculated. The procedure was repeated with other prescribed OPEP devices (green-DM acapella<sup>†</sup>; Smiths Medical North America, Norwell, MA, USA vibratory PEP (vPEP) devices and RC-Cornet<sup>†</sup>; Curaplex, Dublin, OH, USA. Three devices of each type were each tested once. **Results:** Comparative values of  $t_{OSC}$  at different adult PEFs for simulated exhalation profiles were summarized. This range was deemed likely to encompass the achievable performance of most users of these devices. Measures of  $t_{OSC}$  with the AEROBIKA<sup>®</sup> OPEP device were >75% at all PEF settings and were generally consistent. The other OPEP systems exhibited lower and much more variable  $t_{OSC}$  values ranging from 30% to 63%. The frequencies of the oscillations for each device using the 30 L/min PEF exhalation profile were 15.2 Hz, 18.6 Hz, and 28.7 Hz for the AEROBIKA<sup>®</sup> OPEP, acapella<sup>†</sup> and RC Cornet<sup>†</sup> devices, respectively. It has been reported that a frequency range of 12-15 Hz is optimal, due to the correlation with average frequency of ciliary beating in the upper airways hence enabling easier expectoration. **Conclusions:** It is intuitive to associate higher values of  $t_{OSC}$  at a given PEF with improved efficacy of secretion mobilization. On this basis, the AEROBIKA<sup>®</sup> OPEP device performed well, especially at lower values of PEF likely to be encountered with patients having more obstructed airways. The oscillation frequencies determined for the AEROBIKA<sup>®</sup> OPEP device were closest to the reported optimum range for airway clearance. Furthermore, initial clinical studies<sup>1</sup> with COPD patients support these *in vitro* results.

<sup>1</sup>Kanhere, N, Hasany, A, Kirby, M, Suggett, J, McCormack, DG, Parraga, G: Hyperpolarized <sup>3</sup>He magnetic resonance imaging following oscillatory positive expiratory pressure treatment in GOLD Stage II and III chronic obstructive pulmonary disease, Proc Am J Respir Crit Care Med 2013, 187: A4884.



## MORE THAN DRUG DELIVERY: A NEW AIRWAY CLEARANCE THERAPY EVALUATED CLINICALLY USING MRI.

J Suggett, J Mitchell. Presented at Respiratory Drug Delivery 2014.

**Background:** The creation of Oscillating Positive Expiratory Pressure (OPEP) is a recognized Airway Clearance Therapy (ACT) to mobilize secretions associated with lung diseases in pulmonary rehabilitation, in particular in association with Chronic Obstructive Pulmonary Disease (COPD) and cystic fibrosis. Chest physiotherapy with bronchial drainage, which is the traditional method for maintaining bronchial hygiene, is very time consuming and labour intensive, so there is a strong incentive to move to more efficient techniques. With OPEP, expiratory pressure stents the airways open and helps fill under-inflated or collapsed alveoli while oscillation creates short bursts of increased expiratory airflow to thin, dislodge and move mucus to the central/upper airways where it can be coughed out. To date, there has been relatively little clinical data supporting this type of therapy in COPD, and it is also difficult to evaluate regional lung effects following ACT. A new hand-held Oscillatory Positive Expiratory Pressure device (AEROBIKA®) has been developed that can be used by patients in any orientation. We report the outcome of an *in vivo* study performed in collaboration with Robarts Research Institute and the Department of Medicine, University of Western Ontario, London, Canada, that used Magnetic Resonance Imaging (MRI) with hyperpolarized helium ( $^3\text{He}$ ) to assess the influence of the AEROBIKA® OPEP device on lung ventilation in COPD patients. **Materials and Methods:** The AEROBIKA® OPEP device was evaluated in patients with varying stages of COPD, in an 8 week, longitudinal, cross-over study design; 14 patients (ages 62-81); Group split to receive 4 weeks on OPEP therapy followed by 4 weeks off or vice versa.  $^3\text{He}$  MRI was performed at the start of the study, cross-over week and end of study. Additionally, pulmonary function testing (PFT) was performed and a validated patient evaluation questionnaire (PEQ) completed at 2 week intervals. **Results:** There were no adverse events judged related to the use of the AEROBIKA® OPEP device, nor were there any serious/severe adverse events or COPD exacerbations during the study. Given the relatively small number of patients and the fact that they were not phenotyped as an entry criteria, the focus of the study was mainly on the MRI methodology and its application to assess ACT in COPD. Notwithstanding, analysis of all patients showed a statistically significant (paired two tailed t-test) improvement in dyspnea ( $p=0.03$ ), measured as part of the PEQ, following use of the OPEP device. The MRI analysis produced both a visual regional representation as well as the ability to determine a Ventilation Defect Percentage (VDP). The VDP measurement enabled the identification of six patients exhibiting a detectable improvement ( $>2\%$ ). Analysis of this subgroup showed that following OPEP therapy there was a significant improvement in (1) Forced vital capacity ( $\text{FVC}_{\text{pred}}$ ) [ $p=0.04$ ] (2) From the PEQ, ease in bringing up sputum [ $p=0.02$ ]. The use of  $^3\text{He}$  MRI provided a clear indication of specific areas of the lungs in which ventilation is present and absent. The presence and intensity of coloration relates to ventilation, whereas no color, black, represents nonventilated areas. This methodology therefore allows identification of specific regions of the lungs in which ventilation has improved following OPEP therapy, potentially due to the removal of mucus plugs in the airways. **Conclusions:** The AEROBIKA® OPEP device was shown to be well tolerated in use with this cohort of COPD patients. There was a statistically significant improvement in dyspnea following use of the device, with additional statistically significant improvements in  $\text{FVC}_{\text{pred}}$  and ease in bringing up sputum, for a subgroup of patients demonstrating imaging improvements. The use of  $^3\text{He}$  MRI has also been shown to be a promising tool with which to interpret visually the physiological effects of ACT.

## COMBINING OSCILLATING POSITIVE EXPIRATORY PRESSURE THERAPY WITH INHALATION OF BRONCHODILATOR VIA A BREATH-ACTUATED NEBULIZER: INITIAL EVALUATION OF *IN VITRO* DATA TO DETERMINE NEBULIZER PERFORMANCE.

J Schmidt, M Nagel, H Schneider, V Avvakoumova, C Doyle, V Wang, R Ali, A Meyer, R Kopala, JP Mitchell. Presented at Respiratory Drug Delivery 2013.

**Background:** Oscillating Positive Expiratory Pressure (OPEP) is a well-established therapy to mobilize secretions associated with lung diseases in pulmonary rehabilitation, in particular in association with COPD and Cystic Fibrosis. To date, OPEP therapy has usually been given at a separate time following initial delivery of inhaled medical aerosol therapy. The most likely reason is that the former is associated with exhalation, whereas the latter can only be done effectively during inhalation. **Study Purpose:** A new hand-held Oscillatory Positive Expiratory Pressure device (AEROBIKA® OPEP, Trudell Medical International (TMI), London, Canada) can be connected directly to the AEROECLIPSE® II Breath Actuated Nebulizer (BAN, TMI). The patient can thereby receive aerosol therapy and secretion mobilization simultaneously. The AEROBIKA® OPEP device might also be used with a small volume nebulizer with a 22 mm adapter. We report the outcome of *in vitro* measurements of BAN performance as part of research into the overall capability for the new OPEP device. The medication-containing aerosol generated from the BAN upon inhalation passes through the OPEP device via a short, low resistance pathway containing an open one-way valve before being inhaled. In this configuration, the aerosol flow path is linear with minimal restriction to mitigate internal losses caused by inertial impaction. When the patient exhales, the one-way valve closes, diverting the flow through the body of the OPEP device mechanically



operating the vane that generates oscillatory pressure pulsations that are transmitted back to the patient. Initial results from a clinical study involving patients with COPD, using the AEROBIKA® OPEP device alone performed at the Robarts Research Institute, London, Canada have indicated positive findings. The to be reported data demonstrated a statistically significant improvement in dyspnea after OPEP therapy, with improvements also noted in lung ventilation defects and ease of mucus clearance. **Materials and Methods:** Measurements were made (9 replicates) of total and fine droplet mass < 5.4 µm by Next Generation Impactor (NGI) equipped with a Ph.Eur./USP induction port and operated at 15.0 L/min ± 5%. The BAN on test was operated by compressed air delivered at 50 psig and filled with 4-ml ipratropium bromide solution for nebulization (0.5 mg/mL). This product is widely used as an anticholinergic in the treatment of COPD. The BAN alone was initially tested connected directly to the inlet of the cascade impactor system via a leak-tight fitting. The measurements were repeated with the AEROBIKA® OPEP device inserted between the BAN and impactor system. The BAN on test was run to onset of sputter, and the total mass of ipratropium bromide (TM<sub>ipr</sub>), recovered and assayed by a validated HPLC-UV spectrophotometric method. Measurements were also made with the acapella<sup>+</sup> vibratory PEP device. This OPEP device is widely available for lung secretion mobilization. The purpose of this arm was to examine what might happen if a clinician was to make this substitution. Fine Particle Mass <5.4µm aerodynamic diameter (FM<sub>ipr</sub>) was evaluated. **Results:** TM<sub>ipr</sub> (mean ± SD) via the BAN alone for the AEROECLIPSE® II BAN – AEROBIKA® OPEP, and for the BAN – acapella<sup>+</sup> OPEP systems were 582±30, 515±28 and 178±21 µg respectively. These are equivalent to delivery rates of 1.9±0.1, 1.6±0.1 and 0.4±0.05 µg/s. Corresponding values of the therapeutically more important fine droplet mass < 5.4 µm for bronchodilation of the airways of the lungs (FM<sub>ipr</sub>) were 452±28, 426±27 and 177±21 µg respectively. **Conclusions:** The delivery of medication as fine particles from the AEROECLIPSE® II BAN is comparable by combining the BAN with the AEROBIKA® OPEP device, offering the patient the opportunity for combined aerosol/OPEP therapy. Substitution by OPEP devices that do not allow incoming aerosol to be transported directly to the patient, are likely to result in substantial loss of aerosol from this nebulizer that may be clinically significant.

#### **HYPERPOLARIZED <sup>3</sup>HE MAGNETIC RESONANCE IMAGING FOLLOWING OSCILLATORY POSITIVE EXPIRATORY PRESSURE TREATMENT IN GOLD STAGE II & III COPD.**

*S Svenningsen, BN Jobse, A Hasany, N Kanhere, M Kirby, J Suggett, DG McCormack, G Parraga. Presented at ATS 2013.*

**Introduction:** Airway clearance techniques are thought to help improve mucus clearance and dyspnea in chronic pulmonary diseases such as CF and bronchiectasis. The effect of positive expiratory pressure and oscillatory positive expiratory pressure (oPEP) in COPD is not well-understood. To test the effects of oPEP, a hand-held prototype device (Trudell Medical International) was evaluated in COPD ex-smokers. **Goal:** To determine the effect of oPEP on pulmonary function, imaging biomarkers of airway function, St Georges Respiratory Questionnaire (SGRQ) and a mucous clearance questionnaire. **Hypothesis:** oPEP use results in significantly improved mucous clearance and symptom scores in COPD ex-smokers. **Research Objective:** To evaluate the safety and efficacy of four-times daily oPEP over 4 weeks in COPD ex-smokers using pulmonary function tests (PFTs), hyperpolarized <sup>3</sup>He magnetic resonance imaging (MRI), six minute walk test (6MWT), the St. Georges Respiratory Questionnaire (SGRQ), and a validated symptom diary<sup>1</sup>. **Study Subjects and Design:** 17 COPD ex-smokers were randomized to 4 weeks of oPEP or no therapy in a cross-over study. Pulmonary function tests (spirometry, plethysmography, DLCO) were acquired on an EasyOne spirometer (nidd Medizintechnik AG, Zurich, CH) according to ATS guidelines. 6MWT, SGRQ, and mucous clearance symptom questionnaire were acquired at each visit. **Image Acquisition and Analysis:** MRI performed on 3T Discovery 750MR (GEHC, Milwaukee, USA) <sup>3</sup>He MRI ventilation defect percent (VDP)<sup>2</sup> generated for images acquired after a 15s breath-hold (FRC+1L). 14 subjects completed the study and two cases are presented – a single self-reported non-responder and self-reported responder. **Discussion:** In a single self-reported responder, SGRQ total score and ease of mucous clearance was improved, cough frequency was increased and FVC, RV, TLC and RV/TLC were also improved suggesting improved gas trapping and this was consistent with a very modest improvement in <sup>3</sup>He MRI VDP. In a single self-reported non-responder, there were no improvements in SGRQ, dyspnea or ease of bringing up sputum and there was no change in any PFT measurement, and <sup>3</sup>He MRI increased or worsened (15%-20%). **Conclusions:** In this pilot, proof-of-concept study, self-administered oPEP therapy over 4 weeks variably affected lung volumes, VDP and symptoms in two cases with stable advanced COPD. One COPD ex-smoker case exhibited clear improvements in spirometry and plethysmography measurements, mucous clearance and SGRQ, whereas the other case showed no or little change during the treatment period. Future work will involve careful patient phenotyping using MRI and CT to help stratify subjects to oPEP therapy and to better understand therapy responses. Results in all subjects are currently being evaluated to determine the effect of 4 weeks oPEP in 14 COPD ex-smokers who completed therapy. For two COPD ex-smokers, one a self-reported non-responder and the other a self-reported responder

to oPEP, there were changes in PFTs, <sup>3</sup>He MRI VDP, SGRQ and ease in bringing up sputum that were in agreement with self-reported response.

<sup>1</sup>Petty TL. The National Mucolytic Study: Results of a Randomized, Double-Blind, Placebo-Controlled Study of Iodinated Glycerol in Chronic Obstructive Bronchitis. *Chest*. 1990 Jan;97(1):75-83. <sup>2</sup>Kirby M *et al*. Hyperpolarized <sup>3</sup>He magnetic resonance functional imaging semi-automated segmentation. *Acad Radiol*. 2012 Feb;19(2):141-52.

## AIRWAY CLEARANCE TECHNIQUES IN COPD

### ADVANCES IN AIRWAY CLEARANCE TECHNOLOGIES FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

CR Osadnik, CF McDonald, AE Holland. *Expert Rev Resp Med*. 2013;7(6):673-685.

Techniques to promote clearance of sputum from the airways (airway clearance techniques: ACTs) have existed in clinical practice for more than a century. This review examines current evidence and clinical recommendations regarding ACTs for individuals with chronic obstructive pulmonary disease. Comparisons between this literature and reports of current practice suggest that discrepancies may exist in relation to the clinical management of sputum in individuals with COPD. The novel application of newer technologies has enhanced our ability to assess the complex physiological processes underpinning airway clearance therapy. The potential for physiologically tailored ACT prescription may, however, depend on the capacity for translation of such technology from the research setting in the clinical environment. Future directions regarding this common form of therapy will be discussed, including identification of the key research priorities to optimize evidence-based practice in this area.

### AIRWAY CLEARANCE TECHNIQUES FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

CR Osadnik, CF McDonald, AP Jones, AE Holland. *Cochrane Database Syst Rev*. 2012.

**Background:** Cough and sputum production are common in chronic obstructive pulmonary disease (COPD) and are associated with adverse clinical outcomes. Airway clearance techniques (ACTs) aim to remove sputum from the lungs, however evidence of their efficacy during acute exacerbations of COPD (AECOPD) or stable disease is unclear. **Objectives:** To assess the safety and efficacy of ACTs for individuals with AECOPD and stable COPD. **Search Methods:** We searched the Cochrane Airways Group Specialised Register of trials from inception to October 2011, and PEDro in October 2009. **Selection Criteria:** We included randomised parallel trials and randomised cross-over trials which compared an ACT to no treatment, cough or sham ACT in participants with investigator-defined COPD, emphysema or chronic bronchitis. **Data Collection and Analysis:** Two review authors independently conducted data extraction and assessed the risk of bias. We analysed data from studies of AECOPD separately from stable COPD, and classified the effects of ACTs as 'immediate' (less than 24 hours), 'short-term' (24 hours to eight weeks) or 'long-term' (greater than eight weeks). One subgroup analysis compared the effects of ACTs that use positive expiratory pressure (PEP) to those that do not. **Main Results:** Twenty-eight studies on 907 participants were included in the review. Study sample size was generally small (range 5 to 96 people) and overall quality was generally poor due to inadequate blinding and allocation procedures. Meta-analyses were limited by heterogeneity of outcome measurement and inadequate reporting of data. In people experiencing AECOPD, ACT use was associated with small but significant short-term reductions in the need for increased ventilatory assistance (odds ratio (OR) 0.21, 95% confidence interval (CI) 0.05 to 0.85; data from four studies on 171 people), the duration of ventilatory assistance (mean difference (MD) -2.05 days, 95% CI -2.60 to -1.51; mean duration for control groups seven days; data from two studies on 54 people) and hospital length of stay (MD -0.75 days, 95% CI -1.38 to -0.11; mean duration for control groups nine days; one study on 35 people). Data from a limited number of studies revealed no significant long-term benefits of ACTs on the number of exacerbations or hospitalisations, nor any short-term beneficial effect on health-related quality of life (HRQoL) as measured by the St. George's Respiratory Questionnaire (SGRQ) total score (MD -2.30, 95% CI -11.80 to 7.20; one study on 59 people). In people with stable COPD, data from single studies revealed no significant short-term benefit of ACTs on the number of people with exacerbations (OR 3.21, 95% CI 0.12 to 85.20; one study on 30 people), significant short-term improvements in HRQoL as measured by the SGRQ total score (MD -6.10, 95% CI -8.93 to -3.27; one study on 15 people) and a reduced long-term need for respiratory-related hospitalisation (OR 0.27, 95% CI 0.08 to 0.95; one study on 35 participants). The magnitude of effect of PEP-based ACTs on the need for increased ventilatory assistance and hospital length of stay was greater than for non-PEP ACTs, however we found no statistically significant subgroup differences. There was one report of vomiting during treatment with postural drainage and head-down tilt. **Authors' Conclusions:** Evidence from this review indicates that airway clearance techniques are safe for individuals with COPD and confer small beneficial effects on some clinical outcomes. Consideration may be given to the use of airway

clearance techniques for patients with COPD in both acute and stable disease, however current studies suggest that the benefits achieved may be small.

### **EFFECT OF AIRWAY CLEARANCE TECHNIQUES IN PATIENTS EXPERIENCING AN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A SYSTEMATIC REVIEW.**

*K Hill, S Patman, D Brooks. Chron Respir Dis. 2010;7(1):9-17.*

**Abstract:** Answers were sought to the following question: Are techniques, applied predominantly with the aim of clearing secretions from the airways, to patients during an acute exacerbation of chronic obstructive pulmonary disease (AECOPD), safe and effective? A systematic review was undertaken of studies that (i) were either randomized controlled or randomized cross-over trials, (ii) recruited patients during an AECOPD, (iii) reported the results of between-group analyses and (iv) investigated the effect of techniques applied primarily with the aim of clearing secretions from the airways. Studies that examined non-invasive positive pressure ventilation (NIPPV) and early rehabilitation were excluded. Data were extracted pertaining to resting lung function, gas exchange, sputum expectoration, symptoms, NIPPV use and hospital stay. Five studies were included with a mean Physiotherapy Evidence Database (PEDro) score of 4.4 +/- 1.1 (range: 3-6). The main findings were that (i) airway clearance techniques did not improve measures of resting lung function or produce any consistent change in measures of gas exchange, (ii) the application of 5 min of continuous chest wall percussion reduced forced expiratory volume in 1 second (FEV<sub>1</sub>), (iii) in people with copious secretions, mechanical vibration, and non-oscillating positive expiratory pressure (PEP) mask therapy increased sputum expectoration and (iv) in patients with hypercapnic respiratory failure, intrapulmonary percussive ventilation (IPV) and PEP mask therapy reduced the need for, and duration of, NIPPV, respectively. With the exception of continuous chest wall percussion, airway clearance techniques were safe in patients during an AECOPD. Vibration and non-oscillating PEP facilitated sputum expectoration in patients characterized by copious airway secretions. In patients with respiratory failure, techniques that apply a positive pressure to the airways may reduce either the need for, or duration of, NIPPV and hospital length of stay.

### **CHEST PHYSIOTHERAPY FOR PATIENTS ADMITTED TO HOSPITAL WITH AN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): A SYSTEMATIC REVIEW.**

*CY Tang, NF Taylor, FC Blackstock. Physiotherapy 2010 Mar;96(1):1-13.*

**Objectives:** To examine the effectiveness of chest physiotherapy for patients admitted to hospital with an acute exacerbation of chronic obstructive pulmonary disease (COPD). **Data Source:** CINAHL, MEDLINE, Embase, Cochrane, Expanded Academic Index, Clinical Evidence, PEDro, Pubmed, Web of Knowledge and Proquest were searched from the earliest available time to September 2007, using the key elements of COPD, acute exacerbation and chest physiotherapy interventions. **Review Methods:** To be included, trials had to investigate patients during admission to hospital with an acute exacerbation of COPD, and to evaluate at least one physiotherapy intervention. Two reviewers independently applied the inclusion criteria, and assessed trial quality using the PEDro scale. Results were expressed as standardised mean differences and analysed qualitatively with a best-evidence synthesis. **Results:** Thirteen trials were identified. There was moderate evidence that intermittent positive pressure ventilation and positive expiratory pressure were effective in improving sputum expectoration. In addition, there was moderate evidence that walking programmes led to benefits in arterial blood gases, lung function, dyspnoea and quality of life. No evidence was found supporting the use of any other chest physiotherapy techniques to change lung function, arterial blood gases, perceived level of dyspnoea or quality of life. **Conclusions:** Chest physiotherapy techniques such as intermittent positive pressure ventilation and positive expiratory pressure may benefit patients with COPD requiring assistance with sputum clearance, while walking programmes may have wider benefits for patients admitted with an exacerbation of COPD. Chest physiotherapy techniques other than percussion are safe for administration to this patient population.

### **EFFICACY OF PHYSICAL THERAPY METHODS IN AIRWAY CLEARANCE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A CRITICAL REVIEW.**

*R Nowobilski, T Włoch, M Płaszewski, A Szczeklik. Polskie Archiwum Medycyny Wewnętrznej 2010;120(11):468-477.*

**Abstract:** Multiplicity and variety of chest physical therapy (CPT) methods for increasing bronchial clearance in patients with chronic obstructive pulmonary disease (COPD) require an assessment of validity and reliability of the available clinical evidence. The aim of the review was to evaluate publications on CPT in COPD patients and to establish the basis (objective criteria) on which given methods and techniques are recommended or refuted. Systematic reviews, narrative reviews, and clinical practice guidelines, published in English between January 1, 2000 and July 1, 2010, were identified from the

PubMed/MEDLINE and Cochrane (DARE, CRD, The Cochrane Airways Review Group Register) databases. The PEDro and SIGN scales were used to assess the quality and grade of recommendations for selected papers. Generally, the papers that we identified were based on small studies, limited to short-term outcomes, mostly using crossover designs, and rarely including sham therapy. Recommendations from clinical guidelines were mainly grade C or D. Health-related quality-of-life analyses, including working and exercise capacity, are lacking. The evidence from the studies in patients with cystic fibrosis cannot be directly extrapolated to COPD subjects. Despite the lack of convincing evidence, clinical practice supports the value of CPT in COPD. However, when making a clinical decision, potential side effects should be considered.

## **POSITIVE EXPIRATORY PRESSURE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A SYSTEMATIC REVIEW.**

*MF Olsén, E Westerdahl. Respiration 2009;77:110-118.*

**Background:** Breathing exercises against a resistance during expiration are often used as treatment for patients with chronic obstructive pulmonary disease (COPD). Controversy still exists regarding the clinical application and efficacy. **Objectives:** The aim of this systematic review was to determine the effects of chest physiotherapy techniques with positive expiratory pressure (PEP) for the prevention and treatment of pulmonary impairment in adults with COPD. **Methods:** The review was conducted on randomised, controlled clinical trials in which breathing exercises with positive expiratory pressure were compared with other chest physical therapy techniques or with no treatment, in adult patients with COPD. A computer-assisted literature search of available databases from 1970 to January 2008 was performed. Two reviewers extracted data independently and assessed the trials systematically with an instrument for measuring methodological quality. **Results:** In total, 11 trials met the inclusion criteria, of which 5 reached an adequate level of internal validity. Several kinds of PEP techniques with a diversity of intensities and durations of treatment have been evaluated with different outcome measures and follow-up periods. Benefits of PEP were found in isolated outcome measures in separate studies with a follow-up period <1 month. Concerning long-term effects, the results are contradictory. **Conclusion:** Prior to widespread prescription of long-term PEP treatment, more research is required to establish the benefit of the technique in patients with COPD.

## **IMPROVING MUCOCILIARY CLEARANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE.**

*A Bhowmik, K Chahal, G Austin, I Chakravorty. Resp Med 2009;103:496-502.*

Patients with COPD usually experience mucus hypersecretion as a result of airway inflammation and response to noxious stimuli. These in turn lead to worsening airway resistance, impaired airflow, increased work of breathing, dyspnoea and exercise intolerance. Mucus hypersecretion may also lead to increased exacerbations and poor health related quality of life (HRQL). Institution based pulmonary rehabilitation programs incorporating airway clearance techniques have been shown to improve HRQL, reduce dyspnoea and improve exercise tolerance but are often difficult to provide due to restricted accessibility and resource implications. This review examines the current evidence base and best clinical practice in the area of airway clearance. Mechanical devices such as the flutter valves, positive end expiratory pressure and high frequency chest wall oscillation (HFCWO) may be able to provide the benefits of improved airway clearance in the patient's home potentially with reduced demands on healthcare resources.

## **USE OF MUCUS CLEARANCE DEVICES ENHANCES THE BRONCHODILATOR RESPONSE IN PATIENTS WITH STABLE COPD.**

*N Wolkove, H Kamel, M Rotaple, MA Baltzan. Chest 2002;121:702-707.*

**Study objective:** To determine whether the use of a mucus clearance device (MCD) [Flutter; Axcan Scandipharm; Birmingham, AL] could improve the bronchodilator response to inhaled ipratropium and salbutamol delivered by a metered-dose inhaler in patients with stable, severe COPD. **Patients:** Twenty-three patients with severe COPD were studied. Mean SD age was 71.7±6.3 years. Mean FEV<sub>1</sub> was 0.74±0.28 L or 34.5±12.7% predicted. **Methods:** Patients were tested in random order on 2 subsequent days after using an MCD or a sham MCD. A bronchodilator (four puffs; each puff delivering 20 µg of ipratropium bromide and 120 µg of salbutamol sulfate) was administered by metered-dose inhaler with a holding chamber after use of the MCD or sham MCD. Spirometry was performed before and after use of the MCD or sham MCD, and at 30 min, 60 min, and 120 min after the bronchodilator. Six-minute walk distance was tested between 30 min and 60 min; oxygen saturation, pulse, and a dyspnea score were recorded before and after walking. **Results:** Immediately after use of the MCD, but not the sham MCD, there was a statistically significant ( $p < 0.05$ ) improvement in FEV<sub>1</sub> and FVC (11±24% vs 1±7% and 18±33% vs 6±18%, respectively). Whether patients were pretreated with the MCD or sham MCD, there was a significant improvement in FEV<sub>1</sub> and FVC compared to baseline with combined bronchodilator therapy. At 120 min, the



change in FEV<sub>1</sub> after treatment with the MCD was greater than with the sham MCD (186±110 mL vs 130±120 mL;  $p < 0.05$ ). When comparing the MCD to the sham MCD, 6-min walk distance was greater (174±92 m vs 162±86 m;  $p < 0.05$ ), with less dyspnea before and at the end of walking. **Conclusion:** Patients with severe COPD may demonstrate a significant bronchodilator response to combined ipratropium and salbutamol delivered by metered-dose inhaler. This response may be enhanced and additional functional improvement obtained with the prior use of a bronchial MCD.

## CHEST PHYSICAL THERAPY IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC BRONCHITIS: EFFECTIVENESS [SIC] OF THREE METHODS.

A Bellone, R Lascoli, S Raschi, L Guzzi, R Adone. *Arch Phys Med Rehabil* 2000;81:558-560.

**Objective:** To compare the short-term effects of postural drainage (PD), oscillating positive expiratory pressure (using the FLUTTER device), and expiration with the glottis open in the lateral posture (ELTGOL) on oxygen saturation, pulmonary function, and sputum production in patients with an acute exacerbation of chronic bronchitis. **Design:** A prospective, randomized study. **Setting:** A clinical ward. **Patients:** Ten patients with chronic bronchitis exacerbation received PD, FLUTTER, and ELTGOL by the same respiratory therapist at about the same time of day on separate days and in random order. **Main Outcome Measures:** Oxygen saturation and pulmonary function were measured before, immediately after, and 15 minutes and 1 hour after each treatment. Improvement in sputum production was measured by total sputum wet weight immediately after and for 1 hour after treatment. **Interventions:** PD consisted of positioning the patients in a posture that allows bronchial drainage by gravity. FLUTTER is a device that is claimed to combine oscillating positive expiratory pressure with oscillations of the airflow. ELTGOL is an airway clearance technique that uses lateral posture and different lung volumes to control expiratory flow rate to avoid airway compression. The total time spent for treatments was 30 minutes. **Results:** All techniques were well tolerated, and oxygen saturation and pulmonary function did not change significantly during and after treatments. Thirty minutes after the beginning of treatment, sputum production increased significantly with all techniques, but during the 1 hour after the end of treatment, it was significantly larger with FLUTTER (from 15.0 ± 8.6g to 19.0 ± 9.3g,  $p < .01$ ) and ELTGOL (from 17.0 ± 7.0g to 20.6 ± 6.9g,  $p < .02$ ) than with PD (from 15.5 ± 4.0g to 17.5 ± 3.7g, NS). **Conclusions:** All three treatments were safe and effective in removing secretions without causing undesirable effects on oxygen saturation, but FLUTTER and ELTGOL techniques were more effective in prolonging secretion removal in chronic bronchitis exacerbation than was the PD method.

## AIRWAY CLEARANCE TECHNIQUES IN BRONCHIECTASIS

### AIRWAY CLEARANCE TECHNIQUES FOR BRONCHIECTASIS.

AL Lee, A Burge, AE Holland. *Cochrane Database of Systematic Reviews* 2013, Issue 5. Art. No.: CD008351. DOI: 10.1002/14651858.CD008351.pub2.

**Authors' conclusions:** ACTs appear to be safe for individuals (adults and children) with stable bronchiectasis, where there may be improvements in sputum expectoration, selected measures of lung function and health-related quality of life. The role of these techniques in people with an acute exacerbation of bronchiectasis is unknown. In view of the chronic nature of bronchiectasis, more data are needed to establish the clinical value of ACTs over the short and long term on patient-important outcomes, including symptoms, on physiological outcomes which may clarify the rationale for each technique and on long-term parameters that impact on disease progression in individuals with stable bronchiectasis. This is necessary in order to provide further guidance of specific ACT prescription for people with bronchiectasis. It may also be important to establish the comparative effect of different types of ACTs in people with bronchiectasis.

### INFLUENCE THAT OSCILLATING POSITIVE EXPIRATORY PRESSURE USING PREDETERMINED EXPIRATORY PRESSURES HAS ON THE VISCOSITY AND TRANSPORTABILITY OF SPUTUM IN PATIENTS WITH BRONCHIECTASIS.

EMC Ramos, D Ramos, DM Iyomasa, GL Moreira, KCT Melegati, LCM Vanderlei, JR Jardim, AS de Oliveira. *J Bras Pneumol* 2009;35(12):1190-1197.

**Conclusions:** "The fact that sputum viscosity decreased whether OPEP was performed at P15 or P25 suggests that there is no need to generate high expiratory pressure to achieve the desired result."

- "...mechanisms that promote the displacement and removal of secretions are essential to maintain the respiratory tract defenses against infections and the proliferation of bacteria."
- "...the decreased sputum viscosity after the sessions at P15 and P25 suggests a better rheological profile and greater sputum thinning after the use of the [OPEP] device."

## AIRWAY CLEARANCE TECHNIQUES IN CYSTIC FIBROSIS

### LONG-TERM MULTICENTRE RANDOMISED CONTROLLED STUDY OF HIGH FREQUENCY CHEST WALL OSCILLATION VERSUS POSITIVE EXPIRATORY PRESSURE MASK IN CYSTIC FIBROSIS.

MP McIlwaine, N Alarie, GF Davidson, LC Lands, F Ratjen, R Milner, B Owen, JL Agnew. *Thorax* 2013;0:1-6.

**Conclusions:** “The results of this study favour PEP and do not support the use of HFCWO as the primary form of AC in patients with CF.”

- “Treatment time was significantly shorter in the PEP group.”
- “There were significantly more adverse events related to the lower airways in the HFCWO group than in the PEP group (mean 2.46 vs 1.72,  $p=0.023$ ). These included increased cough, chest infection, haemoptysis, decreased lung function and chest pain”.
- “The number of hospitalisations for PE in this study was three times more in the HFCWO group than in the PEP group (19 vs 6). The cost of hospitalisation is significant for our health economy and also causes a significant burden for the family of people with CF. Thus, at a time when we are looking to reduce health costs, unless there is strong evidence to support the use of more expensive equipment we cannot justify the cost.”
- “The relatively lower PE rates and their later onset in patients performing PEP therapy compared with HFCWO supports the use of PEP as the primary ACT in patients with CF aged > 6 years.”

### ADHERENCE TO AIRWAY CLEARANCE THERAPIES BY ADULT CYSTIC FIBROSIS PATIENTS.

JS Flores, FA Teixeira, PME Rovedder, B Ziegler, PTR Dalcin. *Respiratory Care* 2013;58(2):279-285.

**Conclusions:** “Treatment recommendations and self-reported subject adherence were in best agreement when positive expiratory pressure and flutter devices were used. Healthcare professionals should consider these outcomes as potentially applicable to their own clinical practices.”

### AIRWAY CLEARANCE DEVICES IN CYSTIC FIBROSIS.

JH Marks. *Paediatric Respiratory Reviews* 2007;8:17-23.

- “Airway clearance devices as alternatives to CCPT [Conventional Chest Physiotherapy] allow CF patients to choose the therapy that best fits their lifestyle and allows greatest independence
- “Airway clearance devices are preferred by many patients compared to CCPT and may result in better adherence.”
- “PEP may be more effective for airway clearance than CCPT.”
- “Oscillating positive expiratory pressure devices and HFCWO [High Frequency Chest Wall Oscillation] appear to be at least as effective as CCPT.”

### POSITIVE EXPIRATORY PRESSURE AND OSCILLATORY POSITIVE EXPIRATORY PRESSURE THERAPIES.

TR Myers. *Respiratory Care* 2007;52(10):1308-1327.

- “In addition to enhanced secretion mobilization and elimination, the secondary objective of these airway-clearance devices is to prevent recurring infection, atelectasis, and disease progression, or to improve pulmonary mechanics and facilitate gas exchange.”
- “Oscillations reportedly decrease the viscoelastic properties of mucus, which makes it easier to mobilize mucus up the airways, and create short bursts of increased expiratory airflow that assist in mobilizing secretions up the airways.”

### PHYSIOTHERAPY AND AIRWAY CLEARANCE TECHNIQUES AND DEVICES.

M McIlwaine. *Paediatric Respiratory Reviews* 2006;7S:S220-S222.

- “Oscillation has been shown to decrease the viscoelastic properties of mucus hence making it easier to mobilize up the airways. The second effect of the oscillations is to cause short bursts of increased acceleration of the expiratory airflow which assist in mobilizing the secretions up the airways.”



## THE FLUTTER DEVICE VERSUS THE PEP MASK IN THE TREATMENT OF ADULTS WITH CYSTIC FIBROSIS.

ME Newbold, E Tullis, M Corey, B Ross, D Brooks. *Physiotherapy Canada* 2005; 57(3):199-207.

**Conclusions:** “When comparing the Flutter device and the PEP Mask in the treatment of adults with CF over a 13-month period, there were no significant differences in pulmonary function or health-related quality of life. A much larger sample would be needed to conclude with confidence that there were no between-group differences. Therefore, additional research is needed to further examine the effectiveness of the Flutter device and the PEP Mask.”

## EVIDENCE FOR PHYSICAL THERAPIES (AIRWAY CLEARANCE AND PHYSICAL TRAINING) IN CYSTIC FIBROSIS: AN OVERVIEW OF FIVE COCHRANE SYSTEMATIC REVIEWS.

JM Bradley, FM Moran, JS Elborn. *Respiratory Medicine* 2006;100:191-201.

- “Patients tended to prefer techniques that promoted independence to CCPT”
- “Single, short and longer term trials show that PEP is at least as effective as other forms of airway clearance”
- “Evidence from the Cochrane systematic reviews support current expert opinion that no one airway clearance regimen is better than another.”
- “Data are consistent that treatment factors (the duration and the complexity of the treatment) or trait factors (worry and confidence in medical practitioners) are important determinants of adherence.”
- “As current evidence suggests that physical therapy interventions are equally beneficial, treatment duration, patient preference and patient adherence may be important primary outcomes.”

## EFFECT OF HIGH-FREQUENCY ORAL AIRWAY AND CHEST WALL OSCILLATION AND CONVENTIONAL CHEST PHYSICAL THERAPY ON EXPECTORATION IN PATIENTS WITH STABLE CYSTIC FIBROSIS.

TA Scherer, J Barandun, E Martinez, A Wanner, EM Rubin. *Chest* 1998;113(4):1019-1027.

- “It is conceivable that compliance can be improved by the availability of simple, effective, and easy-to-use devices that allow independent treatment at home. Devices to apply oral airway and chest wall oscillation fit these criteria. Considering their effectiveness and their potential to reduce health-care costs by permitting self-administration, they appear to represent a useful alternative to conventional CPT.”

## GUIDELINES

### VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

*The Management of Chronic Obstructive Pulmonary Disease Working Group. Department of Veterans Affairs. Department of Defense. Version 3.0 – 2014.*

- “We suggest use of airway clearance techniques utilizing positive expiratory pressure (PEP) devices for patients with COPD exacerbations and difficulty expectorating sputum.” [p. 46]
- “In patients hospitalized for acute exacerbations of COPD, there is moderate evidence that airway clearance techniques reduce the need for invasive or non-invasive ventilatory assistance, days of ventilatory assistance, and length of hospital stay.” [p. 46]

### GUIDELINES FOR THE PHYSIOTHERAPY MANAGEMENT OF THE ADULT, MEDICAL, SPONTANEOUSLY BREATHING PATIENT.

*British Thoracic Society Physiotherapy Guideline Development Group; J Bott, S Blumenthal, M Buxton, S Ellum, C Falconer, R Garrod, A Harvey, T Hughes, M Lincoln, C Mikelsons, C Potter, J Pryor, L Rimington, F Sinfield, C Thompson, P Vaughn, J White; Thorax. 2009;64(1):i1-51.*

- “Consider the active cycle of breathing techniques (which includes the forced expiration technique), autogenic drainage and plain or oscillating positive expiratory pressure for patients with stable COPD who need an airway clearance technique to assist in the removal of secretions.”
- “Consider oscillating positive expiratory pressure devices when recommending an airway clearance technique for adults with cystic fibrosis.”

- “Consider oscillating positive expiratory pressure when recommending an airway clearance technique for adults with noncystic fibrosis related bronchiectasis.”
- “PEP and oscillating PEP devices have been shown to be equally effective as traditional chest physiotherapy in sputum clearance, and are recognised as useful techniques in the NICE guidelines on COPD. There may be a patient preference for PEP devices, with or without an oscillatory function, over traditional methods of postural drainage and manual techniques, due to the convenience they offer to the patient. No difference in benefit has been shown between devices in aiding sputum clearance.”

#### **BRITISH THORACIC SOCIETY GUIDELINE FOR NON-CF BRONCHIECTASIS – A QUICK REFERENCE GUIDE.**

*MC Pasteur, D Bilton, AT Hill. British Thoracic Society Reports 2010;2(2).*

- “The active cycle of breathing techniques (plus postural drainage) and oscillating positive expiratory devices (plus postural drainage and the forced expiration technique) should be considered when offering individuals with non-CF bronchiectasis effective airway clearance techniques.”

#### **CYSTIC FIBROSIS PULMONARY GUIDELINES: AIRWAY CLEARANCE THERAPIES**

##### **AMERICAN ASSOCIATION OF RESPIRATORY CARE (AARC).**

*PA Flume, KA Robinson, BP O’Sullivan, JD Finder, RL Vender, D Willey-Courand, TB White, BC Marshall and the Clinical Practice Guidelines for Pulmonary Therapies Committee. Respiratory Care 2009;54(4):522-537.*

- “There are no ACTs [Airway Clearance Therapies] demonstrated to be superior to others, so the prescription of ACTs should be individualized.”
- “There are advantages and disadvantages of each of the therapeutic options...and decisions regarding prescription of airway clearance may include age of the patient, patient preference, severity of disease, availability of a partner, and observed efficacy based on patient reporting (subjective measures) and objective measures (e.g., lung function).”

**Note:** GOLD, ATS and CTS Guidelines do not include Airway Clearance Therapies at time of print.

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