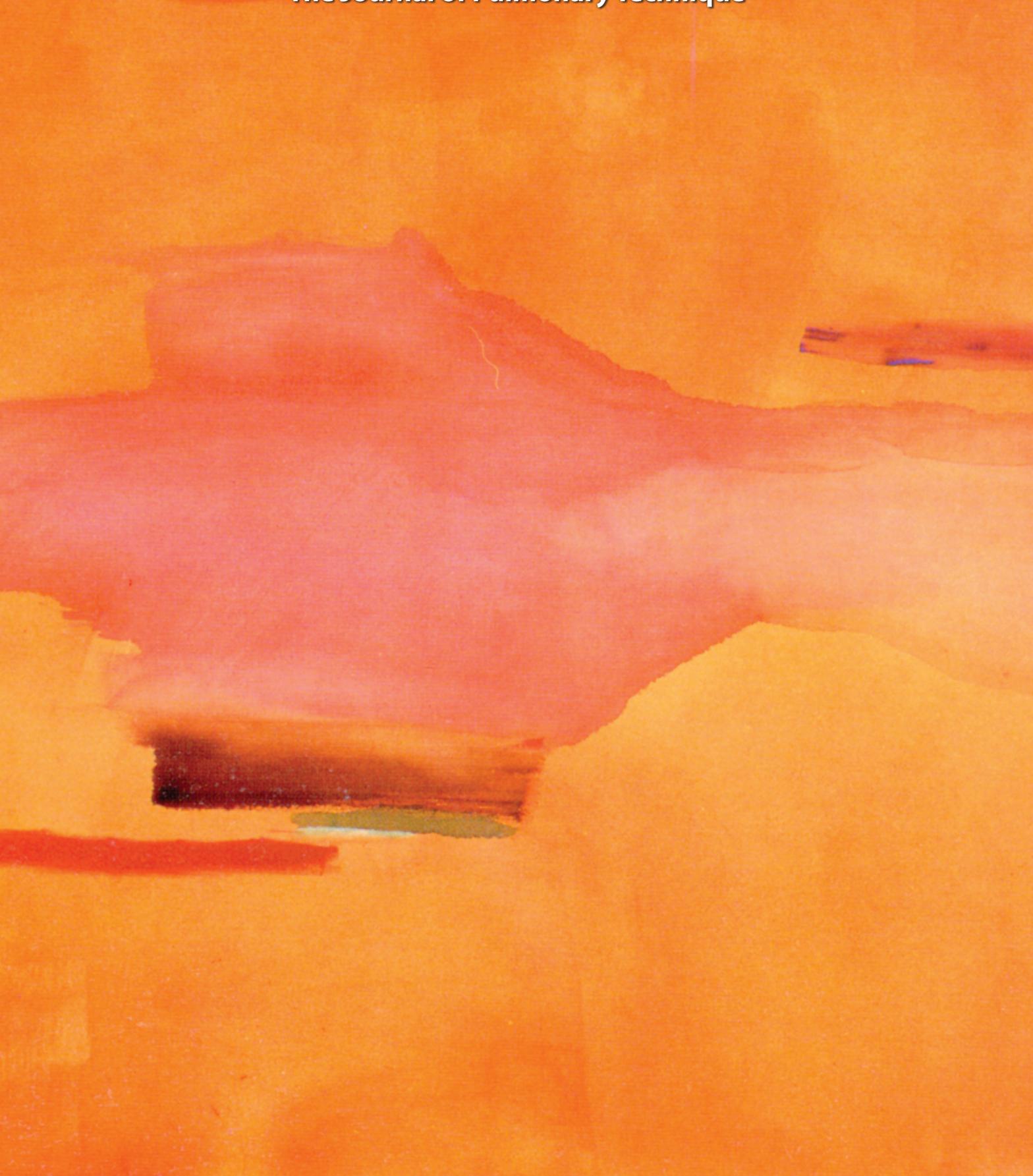


Volume 14 Number 4 Fall 2019

# Respiratory Therapy<sup>TM</sup>

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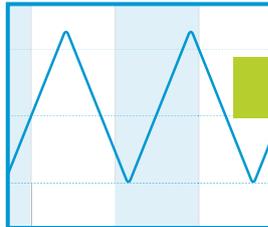


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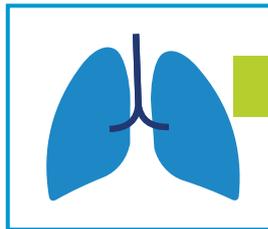
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1. Milla CE, Hansen LG, Weber A, Warwick WJ. High frequency chest compression: effect of the third generation waveform. Biomed Instrum Technol 2004; 38:322-328. Note: 8 CF comparing triangular waveform vs. sine waveform technology.
2. Data from RespirTech’s bronchiectasis patient outcomes program. Methodology: As of 6/30/19, self-reported data from over 16,000 bronchiectasis patients.

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## Capsule Acquires Company

Capsule Technologies, Inc., a leader in medical device integration and non-critical care patient monitoring solutions, announced it has acquired Bernoulli Health. The acquisition includes Bernoulli One, a real-time clinical surveillance solution that gives care teams contextual information on a patient's condition that can facilitate early intervention, improve patient safety and enable better clinical outcomes. The acquisition grows Capsule Technologies' leadership position by extending the reach of its clinical platform into additional use cases by adding patient data visualization to the platform's existing data management and connectivity capabilities. Today, hospital clinical leadership is focusing on more direct ways to improve patient safety by increasing continuous surveillance on patients throughout their entire course of stay in the hospital. Bernoulli Health's clinical surveillance solution provides early detection of critical events so care teams can intervene before deterioration occurs. The addition of this capability furthers Capsule Technologies' focus on improving patient safety by providing clinicians with tools that simplify clinical workflow and provide data-driven insights at the point of care. "Capsule Technologies' success is built on our vendor-neutral approach, giving hospitals the flexibility and freedom to deploy almost any medical device," said Kevin Phillips, Capsule Technologies' vice president of product management. "Our customers are assured that we can connect to their devices, process data on the fly, and integrate normalized relevant physiologic and treatment data to any downstream clinical system that best meets their needs. Integrating Bernoulli Health's clinical surveillance solution into our medical device integration platform provides yet another option for those customers who want a tightly connected turnkey experience."

"Bernoulli Health and Capsule Technologies have a shared vision to unlock the power of medical device data to provide better clinical insights across all levels of patient acuity," said Janet Dillione, chief executive officer of Bernoulli Health. "With the emergence in the market of clinical surveillance, predictive

analytics and real-time healthcare, we are confident that bringing together these two organizations will be highly beneficial to all our stakeholders and especially customers."

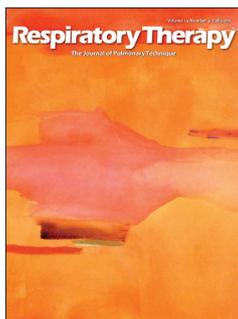
## New Analysis Shows Sleep Apnea More Common than Previously Thought

ResMed revealed roughly 170 million people across North and South America have sleep apnea, according to a study it presented at the annual SLEEP meeting hosted by the American Academy of Sleep Medicine (AASM) and the Sleep Research Society. The study, a deeper analysis of ResMed's 2018 finding that 936 million people worldwide have sleep apnea, concludes that:

- 170 million people in North and South America (37 percent of adults) have sleep apnea, based on the AASM 2012 criteria — a "conservative" estimate.
- 3 countries with the highest number of cases are the United States (54 million), Brazil (49 million), and Colombia (11 million). Sleep apnea is a chronic disease in which people stop breathing for 10 seconds or more throughout the night, repeatedly waking to breathe and prevent suffocation. While sufferers rarely remember waking up, the disruptive cycle causes chronic sleep deprivation, which is linked to daytime fatigue, increases the risk in road and workplace accidents, and is common among people with other diseases like heart failure, high blood pressure, obesity, and type 2 diabetes. "Previous estimates stated 100 million worldwide have sleep apnea. Now we know it's nearly double that in just the Americas alone," said study coauthor and ResMed Chief Medical Officer Carlos M Nunez, MD. "Given how common sleep apnea is, especially among people with other common diseases, doctors should screen their high-risk patients and help those who are diagnosed get onto life-changing treatment as soon as possible." The gold standard treatment for sleep apnea is a positive airway pressure (PAP) device that prevents the intermittent suffocation associated with sleep apnea by blowing a mild stream of air into the upper airway to keep it open and maintain breathing during sleep. PAP devices that are cloud-connectable, enabling remote and self-monitoring, have shown to raise adherence rates above 80 percent, compared to roughly 50 percent on non-cloud connected devices. "Digital health can show patients how well they're doing on treatment, coach them on how to improve, and motivate them by celebrating milestones they've reached," Nunez said. "These features all help drive patient adherence, which is critical if we're going to help millions reduce the short- and long-term risks associated with sleep apnea."

## Asthma Self-management Support Studied

Mount Sinai was part of the largest clinical trial for asthma self-management support in older patients, which resulted in improved control and quality of life, and fewer emergency department visits. Asthma affects 7 percent of Americans older than 65 and causes more symptoms and hospitalizations in this age group than in younger patients with asthma. While experts have called for interventions specifically targeting this population, few relevant studies have been reported. Mount Sinai and other institutions tested the effect of a comprehensive, patient-tailored asthma self-management support intervention for older adults on clinical and self-management outcomes. This is the largest study ever conducted for an intervention to improve outcomes in older adults with asthma. It is also the first study to screen patients for barriers to control of their asthma, including social determinants of health, and target only



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the identified barriers for intervention. The intervention resulted in improved asthma control and quality of life, and led to fewer emergency department visits. Additionally, very few studies involve systematic evaluation of social determinants of health with actions linked to the data that are collected. In this randomized trial that included 391 adults, intervention patients had significantly better asthma control, quality of life, medication adherence, and inhaler technique than control patients. The proportion of intervention patients with an emergency department visit for asthma was 6 percent vs 12 percent, a significant difference. Older adults receiving a patient-tailored self-management support intervention for asthma, whether in the home or clinic, achieved meaningful improvements in asthma control and quality of life, self-management behaviors, and reductions in ED visits compared to patients in usual care. By specifically targeting social determinants of health and other drivers of health-related behaviors, the intervention is a promising model of self-management support and disease control for older adults with asthma, and possibly other chronic diseases. This was a group effort of: Division of General Internal Medicine, Icahn School of Medicine at Mount Sinai, New York; Division of General Internal Medicine, Feinberg School of Medicine, Northwestern University, Chicago; Department of Psychology, The Graduate Center, City University of New York; City Health Works, New York; Institute for Family Medicine, New York; Little Sisters of the Assumption Family Health Service, New York; Department of Psychology, Hunter College, City of New York.

Mount Sinai's Dr Federman said of the research: "Health systems, insurers, and policymakers are increasingly recognizing the powerful influence of social factors on health and outcomes of health like hospitalizations and health care spending. Despite gaining more attention, few studies have tested ways of providing health care that address these social determinants of health. This newly developed approach is helping people with complex health problems, in this case older adults with asthma. By screening patients for barriers to controlling their asthma and addressing the barriers that were identified, the new program helped these older adults take their medications regularly, improve their control of asthma, and reduce their visits to emergency departments by more than 50 percent."

### FDA Approves Supplemental New Drug Application

Merck announced that the US Food and Drug Administration (FDA) has approved Merck's supplemental New Drug Application (sNDA) for the use of ZERBAXA (ceftolozane and tazobactam) for the treatment of patients 18 years and older with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by the following susceptible Gram-negative microorganisms: *Enterobacter cloacae*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Serratia marcescens*. The sNDA for ZERBAXA had previously been designated Priority Review status by the FDA. To reduce the development of drug-resistant bacteria and maintain the effectiveness of ZERBAXA and other antibacterial drugs, ZERBAXA should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. This expanded use is based on results of the pivotal Phase 3 ASPECT-NP trial that compared ZERBAXA 3g (ceftolozane 2g and tazobactam 1g) intravenously every 8 hours to meropenem (1g intravenously every 8 hours) for 8 to 14 days for the treatment of adult patients with HABP/VABP. ZERBAXA is contraindicated in patients with known serious hypersensitivity to the components of ZERBAXA (ceftolozane/tazobactam), piperacillin/tazobactam, or other members of the beta-lactam class. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterials. Additionally, *Clostridium difficile*-associated diarrhea (CDAD), ranging from mild diarrhea to fatal colitis, has been reported with nearly all systemic antibacterial agents, including ZERBAXA. See Important Safety Information below. "Pneumonia in ventilated patients remains a significant clinical challenge and is associated with substantial morbidity and mortality," said Dr Andrew Shorr, head of pulmonary, critical care and respiratory services, Medstar Washington Hospital Center, Washington, DC. "The need to cover diverse pathogens including *Pseudomonas aeruginosa* and certain *Enterobacteriaceae* adds to the challenge." According to a recent publication by the Foundation for the National Institutes of Health Biomarkers Consortium, ventilated patients with HABP have a higher rate of mortality

(39%) than those with VABP (27%). In addition, *Pseudomonas aeruginosa* is the most common Gram-negative pathogen in HABP/VABP and is becoming increasingly difficult to treat. “We are grateful to all of the patients who participated in the studies which led to the approval of ZERBAXA for the treatment of HABP/VABP,” said Dr Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories. “This approval reflects Merck’s longstanding commitment to helping alleviate the burden of infectious diseases, including serious infections caused by Gram-negative pathogens.”

A total of 726 adult patients hospitalized with HABP/VABP were enrolled in a multinational, double-blind study (NCT 02070757) comparing ZERBAXA 3g (ceftolozane 2g and tazobactam 1g) intravenously every 8 hours to meropenem (1g intravenously every 8 hours) for 8 to 14 days of therapy. All patients had to be intubated and on mechanical ventilation at randomization. Efficacy was assessed based on all-cause mortality at Day 28 and clinical cure, defined as complete resolution or significant improvement in signs and symptoms of the index infection at the test-of-cure (TOC) visit which occurred 7 to 14 days after the end of treatment. The

analysis population was the intent-to-treat (ITT) population, which included all randomized patients. Of the 726 patients in the ITT population, the median age was 62 years and 44% of the population was greater than or equal to 65 years of age, with 22% of the population greater than or equal to 75 years of age. The majority of patients were white (83%), male (71%) and were from Eastern Europe (64%). The median APACHE II score was 17 and 33% of patients had a baseline APACHE II score of greater than or equal to 20. All patients were on mechanical ventilation and 519 (71%) had VABP. At randomization, the majority of patients

had been hospitalized for greater than or equal to 5 days (77%) and were in an ICU (92%), with 49% of patients ventilated for greater than or equal to 5 days. At baseline, 36% of patients had creatinine clearance (CrCl) less than 80 mL/min. Of these, 14% had CrCl less than 50 mL/min. Approximately 13% of patients were failing their current antibacterial drug therapy for HABP/VABP, and bacteremia was present at baseline in 15% of patients. Key comorbidities included diabetes mellitus, congestive heart failure, and chronic obstructive pulmonary disease at rates of 22%, 16% and 12%, respectively.

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### Pressure-Support Ventilation Better for Weaning Trials

Pressure-support appears to be better than T-piece ventilation for spontaneous-breathing trials, a randomized trial suggests. Spontaneous-breathing trials (SBT) are used to evaluate the readiness of patients receiving mechanical ventilation for extubation and liberation from ventilatory support. Pressure-support ventilation (PSV) and T-piece ventilation lasting 30 minutes to two hours are the most common modes of SBT, but it remains unclear which is the optimal method. Dr Carles Subira of Althaia Xarxa Assistencial Universitaria de Manresa, in Spain, and colleagues at 18 intensive care units in that country compared two weaning

strategies: one more demanding for patients (T-piece for two hours) versus one less demanding for patients (8-cm H<sub>2</sub>O PSV for 30 minutes). Successful extubation (ie, remaining free of mechanical ventilation 72 hours after the SBT) occurred in 473 patients (82.3%) in the PSV group and 428 patients (74%) in the T-piece group (P=0.001), the team reported June 11 in JAMA. Significantly more patients were extubated after the first SBT in the PSV group (92.5%) than in the T-piece group (84.1%), with no difference in need for reintubation within the next 72 hours. “These findings support the use of a shorter, less demanding

ventilation strategy for SBTs,” the researchers conclude. The results are consistent with those of a 2014 Cochrane review comparing the two approaches. The researchers also found that hospital mortality rates were significantly lower in the PSV group (10.4%) than in the T-piece group (14.9%,  $P=0.02$ ), as was 90-day mortality (13.2% vs. 17.3%,  $P=0.04$ ). Dr Timothy D Girard of the University of Pittsburgh School of Medicine, in Pennsylvania, who co-authored an accompanying editorial, told Reuters Health by email, “Though exciting and intriguing, this result is surprising because it’s not apparent why this would be the case. None of the other secondary outcomes seemed to be affected by the type of SBT used, so more research is needed to determine whether the mortality benefit is real and, if so, what mechanism underlies it.” “Given the size of the trial and its results, I anticipate that future guidelines will recommend the less demanding (30-minute PSV) SBT be used during a patient’s first SBT,” he said. “The trial, however, doesn’t give us guidance about a subsequent SBTs after a patient fails their first SBT since such patients were no longer managed according to the trial protocol.” “We as critical-care clinicians need to proactively identify patients who are ready to be liberated from mechanical ventilation,” Dr Girard said. “This trial shows that shorter, less demanding SBTs are safe when first assessing a patient’s readiness, so using a more demanding SBT at that time is not only unnecessary but potentially dangerous because it may inappropriately delay extubation.” Dr Jan Friedrich from Saint Michael’s Hospital and the University of Toronto, Canada, who has researched various SBT methods, said by email that the trial “strengthens the current weak recommendation to preferentially use pressure support rather than T-piece spontaneous-breathing trials.” “There may be select patients where clinicians may still want to use T-piece spontaneous breathing trials (which provide less support) in cases where the risks of reintubation are particularly high and the clinicians want to be more sure that the patient can be successfully extubated,” he said. “However, there is a lack of randomized-controlled-trial evidence identifying any particular type of patient where such a strategy may be beneficial.”

### **Results Presented on Safety of Treatment for Adults with Ventilated Nosocomial Pneumonia**

Merck announced the first presentation of results from ASPECT-NP, a randomized, double-blind, multi-center Phase 3 clinical trial evaluating the efficacy and safety of ZERBAXA (ceftolozane and tazobactam) for the treatment of adult patients with ventilated nosocomial (hospital acquired) pneumonia. The results demonstrated non-inferiority of an investigational dose of ZERBAXA to meropenem, the active comparator, in the primary and key secondary endpoints. Based on these results, Merck has submitted supplemental new drug applications to the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) seeking regulatory approval for ZERBAXA for this potential new indication. The FDA Prescription Drug User Fee Act (PDUFA) date is June 3, 2019. Detailed findings of the ASPECT-NP Phase 3 trial are scheduled to be presented at the 29th European Congress of Clinical Microbiology & Infectious Diseases (ECCMID). “ASPECT-NP is unique among registration trials for nosocomial pneumonia, as all patients were intubated and mechanically ventilated and nearly all were treated in the intensive care unit,” said Dr Marin Kollef, director of Medical Critical Care and Respiratory Care Services of Barnes-Jewish Hospital and the Golman Professor of Medicine at Washington University School of Medicine, St. Louis, MO. “This is a disease state with a high mortality rate, and Merck’s commitment to this trial provides meaningful evidence

that helps expand our understanding of the management of this patient population.” In the US, ZERBAXA is currently indicated for the treatment of adult patients with complicated urinary tract infections, including pyelonephritis, caused by certain susceptible Gram-negative microorganisms, and is indicated, in combination with metronidazole, for the treatment of adult patients with complicated intra-abdominal infections caused by certain susceptible Gram-negative and Gram-positive microorganisms. To reduce the development of drug-resistant bacteria and maintain the effectiveness of ZERBAXA and other antibacterial drugs, ZERBAXA should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

### **New Catheter Securement Product Unveiled**

Dale Medical Products, Inc., the company known for its high quality, patient-friendly medical device securement solutions, is expanding its offering with its new Hold-n-Place Catheter Securement Products. Like the Dale Hold-n-Place General Purpose Securement Devices, the new catheter securement products are Engineered Stabilization Devices (ESD) and feature a soft, comfortable, flexible design with no hard plastic parts. No skin prep is required for application, and no alcohol is required for removal. Hold-n-Place Catheter Securement Devices are available in two sizes: one for IV, arterial and mid-line catheter securement and another for CVC, PICC and arterial sheath securement. Either device is available by itself, with a transparent dressing, or with a PrevaHex Antimicrobial Transparent Film Dressing by entrotech life sciences, inc. Hold-n-Place is the first and only catheter ESD available with the PrevaHex dressing. Together, the two products combine the effectiveness of an ESD with the first and only CHX chlorhexidine dressing cleared by the FDA with complete antimicrobial protection throughout the transparent areas, and with the adhesive strength and transparency clinicians are looking for in a seven-day securement solution. “Clinicians tell us they appreciate the safety and security of Dale Hold-n-Place products,” says John Brezack, President of Dale. “We are pleased to expand the offering with our new catheter securement devices.” For more information about Dale’s new Hold-n-Place Catheter Securement line, or to request a product sample, please visit <https://www.dalemed.com/product/hold-n-place-catheter-securement/> or call 800-343-3980.

*Continued on page 28...*

## **AARC PREVIEW**

### **Aerogen**

Booth #827

#### **What products will you be presenting at AARC?**

Aerogen will be presenting our high-performance aerosol drug delivery system comprised of the Aerogen Solo and the Aerogen Ultra.

#### **Are there any new products you wish to emphasize?**

Aerogen technology is dramatically changing how pediatric and adult asthmatic patients are dealt with in the hospital. Visit booth 827 to find out how the Aerogen Ultra has transformed the care pathways for asthmatic patients in all areas of the hospital.

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Disposable BiLevel CPAP System

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PRODUCT**

Flow-Safe II+<sup>®</sup> is the first Disposable BiLevel & CPAP System in ONE!

Everything clinicians need is now available for delivering CPAP or BiLevel therapy in one Disposable Flow-Safe II+ System.

This includes a deluxe full face mask with adjustable headstrap and manometer for verifying CPAP and BiLevel IPAP and EPAP pressures. Ideal for transport and easy to set-up – just attach the oxygen tubing to an oxygen source for delivering your choice of CPAP or BiLevel therapy.

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To Learn More Visit Mercury Medical in New Orleans at AARC Booth #226

[www.mercurymed.com](http://www.mercurymed.com)

### **Discuss Educational/training materials you'll be offering.**

Aerogen will be sharing breakthrough data on the impact of Aerogen technology on respiratory patients, in particular pediatric asthmatic patients.

### **Why should AARC participants visit your display?**

Don't miss booth #827 this year! Aerogen is presenting breakthrough clinical evidence on pediatric and adult asthma patients. This data will dramatically impact how you think about treating severe asthmatics of all ages.

## **D-R Burton**

Booth #316

### **What products will you be presenting at AARC?**

The iPEP system by D-R Burton Healthcare uniquely combines OPEP and Incentive Spirometer therapies to address all three respiratory needs: lung expansion, treatment of atelectasis, and secretion clearance. The iPEP takes the mystery out of secretion clearance by providing patients and healthcare providers with feedback that measures the patient's inspiratory capacity during OPEP therapy. The iPEP system includes a palm-sized PocketPEP, a compact OPEP device ideal for patients to use at home to help prevent pulmonary-related readmissions. The PocketPEP is also available separate from the iPEP.

## **Dale Medical Products**

Booth #433

### **What products will you be presenting at AARC?**

Dale Tracheostomy and Endotracheal Tube Holders.

### **Discuss educational/training materials you'll be offering.**

Dale Medical Products is the proud sponsor of Perspectives in Nursing, a source of free, quality CEUs for clinicians for the past 15 years. Perspectives is committed to providing timely and relevant information on postoperative recovery strategies. Articles focus on the continuum of care from hospital to home. Perspectives strives to provide pertinent, pragmatic information, continuing education, and guidelines to maximize clinicians' ability to enhance patient outcomes and minimize secondary (iatrogenic) problems.

### **Why should AARC participants visit your display?**

Visit to see our trusted quality Tracheostomy and Endotracheal tube holders. Learn about and request samples of all our holders.

## **Draeger**

Booth #122

### **What products will you be presenting at AARC?**

Evita V800, Babylog VN800, Seattle PAP plus Bubble CPAP System, BabyFlow plus Nasal CPAP System

### **Are there any new products you wish to emphasize?**

Evita V800, Babylog VN800, Seattle PAP plus Bubble CPAP System.

### **Discuss educational/training materials you'll be offering.**

Learn and Earn. Visit our A Breath Ahead educational online

portal to learn some of the latest in clinical practices while earning needed CRCE's. We have over 20 complimentary courses on various topics — focused on different patient populations for you to view.

### **What speakers or papers will you be featuring?**

We will be offering a free pre-Congress education session on APRV through an unrestricted educational grant to SUNY Upstate Medical Center. It will take place on Friday, November 8, 2019 from 1-5:30 p.m. For more information or to join this session and earn CRCEs, please email Ed Coombs at edwin.coombs@draeger.com. As one of the developers of Dräger's new bubble CAP system — Seattle PAP, Rob DiBlasi, Research/QI Manager, Respiratory Care and Principle Investigator at Seattle Children's Hospital, will be speaking in our booth about the new developments made to bubble CPAP that could have a substantial impact on reducing the work of breathing in infants with respiratory distress.

### **Why should AARC participants visit your display?**

Stop by our booth to see how our new product offerings are Improving Critical Care through protective therapies, connected technologies, care-centered workplaces, and comprehensive data-driven services. You will have the chance to receive an ACCU-VOLUME Measuring Tape (while supplies last).

## **Electromed**

Booth #1327

### **What products will you be presenting at AARC?**

Electromed will present the SmartVest SQL Airway Clearance System at AARC congress 2019. The SmartVest system uses high frequency chest wall oscillation (HFCWO), a proven therapy prescribed for people with impaired airway clearance, that helps clear the lungs of excess mucus, reducing the risk of respiratory infections and hospitalizations. The SmartVest system consists of an inflatable garment connected to a programmable air pulse generator. During therapy, the SmartVest garment delivers a rapidly repeating pulse of air, alternately squeezing and releasing the upper body. Each squeeze simulates a "mini cough," which acts to loosen, thin and propel mucus toward major airways, where it can be more readily expectorated or suctioned away.

### **Are there any new products you wish to emphasize?**

Electromed's SmartVest SQL with SmartVest Connect wireless technology is a personalized HFCWO therapy management portal for patients with impaired airway clearance. The SmartVest SQL with wireless technology features built-in cellular connectivity, offering healthcare teams and patients access to treatment information to better collaborate in making patient-centered care decisions. SmartVest Connect is available online at <https://connect.smartvest.com> using a wirelessly enabled SmartVest SQL system. SmartVest Connect enables patients to track progress of their therapy plan and includes a real-time SmartVest Score and easy-to-read goal reports that provide an in-depth look at performance. Created to encourage patient engagement, SmartVest Connect provides feedback for patients to take an active role in their HFCWO therapy, fostering improved therapy adherence. Additionally, SmartVest SQL with SmartVest Connect is simple, intuitive, and designed to automatically update following completion of a therapy session: just plug it in.

# How long will the oxygen last at this flowrate?



Praxair's *Grab 'n Go® Digital* portable medical oxygen system now features an easy-to-read "time remaining" display, with audible and visual alerts. These alerts are designed to activate if the cylinder pressure drops below 300 psig. With no need to estimate oxygen supply, transports can be more efficient with reduced human error.

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of Your Cylinder Needs Today at  
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### What speakers or papers will you be featuring?

A first-of-its-kind independent study was recently published in BMC Pulmonary Medicine revealing that early use of HFCWO therapy with the SmartVest system as part of a treatment algorithm significantly decreased exacerbations requiring hospitalization and antibiotic use among non-cystic fibrosis bronchiectasis patients.

The study is the first to report “stabilization of key lung function parameters” as a result of HFCWO use. This suggests that early bronchiectasis treatment with HFCWO may significantly slow the otherwise normal progression of the disease.

### Why should AARC participants visit your display?

Feel the SmartVest difference and learn firsthand what makes the SmartVest system a preferred choice for HFCWO therapy through a hands-on demonstration. The microfiber material, ergonomic fit, and 360° oscillation coverage provides a more comfortable fit as well as the SmartVest’s pressure relief that allows patients to breathe easier during therapy. Managing symptoms like chronic cough, shortness of breath and stopping the cycle of recurrent respiratory infections with the SmartVest system can significantly reduce healthcare utilization and associated costs.

## Fisher Paykel

Booth #308

### What Products will you be presenting at AARC?

Respiratory products for both the Adult and Infant continuums:

- **Adult:** Humidity is critical to human respiratory health and well-being. We promote optimal outcomes for clinicians and patients by restoring natural balance across the adult respiratory care continuum.
- **Infant:** World-leading respiratory care for precious neonates and pediatrics, with innovative solutions across the infant care continuum.

### Are there any new products you wish to emphasize?

Our featured products will be focused on Adult Nasal High Flow:

- **AIRVO 2 Humidified High Flow System** – At a flow range of 2 to 60 L/min, the AIRVO 2 can be used across the entire care continuum, from the ED and the ICU to the floors and in the home.
- **Optiflow+ Nasal Cannula** – The leading-edge design of the Optiflow+ cannula originates from Fisher & Paykel Healthcare’s dedication to improve care and outcomes, giving clinicians confidence in the comfortable delivery of Nasal High Flow.
- **AirSpiral Breathing Tube** – With 93% less condensate\* may reduce interruptions to therapy.

### Other products presented:

- **F&P Nivairo NIV Full Face Mask** – A portfolio of full face NIV masks with easy to use comfort features including four mask sizes and a new, vented single-limb setup to help you deliver quality care with ease.
- **Optiflow Junior 2 Nasal Cannula** – Optiflow Junior 2 nasal cannula is the next generation of care for neonates, infants and children. It retains all the existing benefits of the original Optiflow Junior and now includes a XS and XXL sized cannula and better prong stability than ever before.

### Discuss educational/training materials you’ll be offering.

#### **Sunrise Symposium, Sunday November 10 at 7am**

**Advocating High Flow Therapy:** RT Driven Change across the Hospital Description – Advocating for practice change with nasal high flow across the hospital can be challenging. Using real world examples and practical approaches related by a key physician and RT leadership, you will learn how to drive practical implementation by focusing on data driven outcomes and cross-functional relationships.

#### **Optiflow Symposium, Sunday, November 10 at 4pm**

Conducted at an offsite location after the congress closes, this session will walk attendees through the latest data on nasal high flow across the hospital continuum with special emphasis on the practical application of the therapy.

### Why should AARC participants visit your display?

The F&P booth will feature a unique opportunity to experience nasal high flow firsthand and learn how it can be used for a variety of applications in the ED, ICU, general floor and other locations.

\*When compared with the 900PT501 AIRVO tube in internal Fisher & Paykel Healthcare testing

## IngMar Medical, LLC

Booth #201

### What products will you be presenting at AARC?

We will be featuring our RespiSim System as well as the ASL 5000 Lung Solution, both of which are designed for ventilator management training and built around the world’s most realistic breathing simulator, the ASL 5000. Use the RespiSim System to conduct high-fidelity training in anesthesia, critical care, emergency medicine, pulmonology, and respiratory care. The Lung Solution was developed in collaboration with Laerdal Medical and is designed to integrate the world’s most realistic breathing simulator with the SimMan 3G, SimMan Essential, and SimMan 3G Trauma, as well as the new SimBaby.

### Are there any new products you wish to emphasize?

Yes! We are ecstatic to preview the latest version of our RespiSim System software—version 4.0. This new software is designed to be more user-friendly, intuitive, and robust for the end user. We are also proud to showcase the latest addition to the ASL 5000 Lung Solution—Laerdal’s new SimBaby.

### Discuss educational/training materials you’ll be offering.

We will be conducting hands-on demonstrations of both the RespiSim System and the ASL 5000 Lung Solution with a focus on live patient-ventilator interactions created by the ASL 5000. We would like to give attendees a glimpse into what is possible with high-fidelity ventilation simulation.

### Why should AARC participants visit your display?

We will be playing the game “Guess the Patient-Ventilator Interaction”—with the chance to win an Apple iPad!

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*Product availability may vary from country to country and is subject to varying regulatory requirements.*

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- RAPIDPoint® 500 Blood Gas System
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Now you can customize, without compromise.

[siemens-healthineers.us/bloodgas](https://www.siemens-healthineers.us/bloodgas)

## Instrumentation Industries

Booth #1007

### What products will you be presenting at AARC?

We will be presenting our complete line of Inline MDI Adapters, as well as Silicone Connectors, Barbed Tubing Adapters ("Christmas Tree Connectors"), Instant Flow Valves, Pilot Tube Repair Kit, Cuff Pressure Monitors, Vacuum/Pressure Gauges, and NIF Meters to name just a few of the items we will have on display at our Booth.

### Are there any new products you wish to emphasize?

Our latest Inline Adapter, the RTC 26-C. This adapter joins our family of other Inline Adapters. The RTC 26-C now allows the Combivent Respimat Inhaler to be administered in line through a Ventilator Circuit.

### Discuss educational /training materials you'll be offering.

We will have product information sheets as well as the actual products at our booth for participants to have a hands-on experience. The RTC 26-C adapter will be at our booth for hands on demos.

### Why should AARC participants visit your display?

We have everything needed to make Respiratory Therapy work for you. With our selection of Connectors and Adapters, accessories and Ventilator products, you will be able to make any connection easily. We have many difficult to find parts that are essential to do your job. "We're your connection!"

## Instrumentation Laboratory

Booth #137

### What products will you be presenting at AARC?

GEM Premier ChemSTAT system with Intelligent Quality Management (iQM), GEM Premier 5000 blood gas testing system with (iQM2), GEMweb Plus 500 Custom Connectivity.

### Are there any new products you wish to emphasize?

GEM Premier ChemSTAT system.

### Discuss educational/training materials you'll be offering.

Werfen Academy, hands-on demonstrations.

### What speakers or papers will you be featuring?

Clinical poster handouts regarding pleural fluid testing on GEM Premier 5000 blood gas analyzer.

### Why should AARC participants visit your display?

To see the latest in whole-blood analyzer technology, including our newest system, the GEM Premier ChemSTAT with iQM, designed for rapid basic metabolic panel (BMP) testing at the point of care, primarily in hospital Emergency Departments (EDs) and Clinical Laboratories. And our leading blood gas testing system, the GEM Premier 5000 with iQM2.

## Sil.Flex™ TC Pad

### Innovative pad stabilizes trach flange and absorbs pressure at stoma sites

Stoma sites may become sensitive or compromised due to constant pressure or movement of the tracheostomy tube and flange against tender tissue. The Sil.Flex™ TC Pad is designed to cushion the area between the flange and the stoma site, reducing movement and pressure at the site. The contoured surface of the Stoma Pad provides a stable, comfortable interface between the flange and the patient's neck.

Early use of the use of the TC Pad may assist in reducing irritation and tissue breakdown at the stoma site as well stabilizing the tracheostomy tube. Use of the TC Pad may decrease the air leak around the stoma site during trach weaning or during speech therapy by improving the seal between pad and stoma site.

Email us at [information@respiralogics.com](mailto:information@respiralogics.com) to use Sil.Flex for your trach patients.



#### FEATURES

Available in two sizes, accommodating small infants through large adults

Contoured surface rests against the neck and reduces flange contact with stoma site

Hypo-allergenic, latex free, medical-grade silicone gel pad



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# Mercury Medical

Booth #226

## What products will you be presenting at AARC?

Mercury will be displaying and demonstrating a number of innovative clinical solutions such as the First & ONLY ONE Disposable Flow-Safe II+ BiLevel & CPAP system. It is the only available disposable device in the global market that combines both BiLevel and CPAP in one complete single-patient use system with integrated manometer for verifying pressures. The lightweight disposable feature allows for easy CPAP or BiLevel CPAP therapy set-up and delivery during transport. Flow-Safe II+ is ideal for situations where backup BiLevel CPAP equipment is scarce or unavailable. Clinicians can now deliver BiLevel and CPAP therapy with just ONE disposable device. Coupled with Flow-Safe II+, Mercury Medical will be showing Flow-Safe II EZ<sup>®</sup> CPAP & Nebulizer system with unparalleled advantages. Flow-Safe II EZ delivers consistent CPAP pressure while providing an integrated nebulizer using only one oxygen source. Additionally, it has an on/off switch that controls the nebulizer only, not the CPAP pressure. CPAP pressure is still controlled by the flow meter. Compared with other systems that require two O<sub>2</sub> lines, Flow-Safe II EZ consumes less oxygen. Also featured is the latest Neo-Tee disposable infant T-piece resuscitator with higher PEEP (orange knob). This newest addition offers approximately 8-10 cm H<sub>2</sub>O PEEP with less flow, saving on oxygen consumption especially during transport. The Neo-Tee product family was the first disposable T-piece on the market and has gained global acceptance. All Neo-Tees are MR conditional and DEHP-Free. Neo-Tee's sister product, Resusa-Tee Adult/Child T-piece resuscitator will be displayed along-side Neo-Tee for those

patients above 10 kg. Delivering proper tidal volume at the proper pressure and rate are key elements for providing successful manual resuscitation. Mercury will be featuring the CPR-2 small adult manual resuscitator with LiteSaver Manometer and PEEP valve. This is an award-winning manual resuscitator combination for any facility with a Protective Lung Strategy Program. The CPR-2 small adult manual resuscitator with LiteSaver Manometer helps to reduce over inflation and breath stacking. This product is truly a "LiteSaver."

## Are there any new products that you wish to emphasize?

Mercury's new products mentioned previously (Flow-Safe II+, Flow-Safe II EZ, Neo-Tee with higher PEEP (orange knob) and CPR-2 Small Adult Manual Resuscitator with LiteSaver Manometer all improve patient outcomes at an economical cost. Discuss what educational/training materials you'll be offering? Full product training will be provided at the booth by Mercury Medical Product Specialists. We will provide product information brochures, wall charts/posters with specifications, training videos via the Mercurymed.com website and offer free samples. The samples will be provided by fully trained Mercury Medical sales representatives who can answer your product questions and help fulfill your facility's clinical needs.

## Why should AARC participants visit your display?

Mercury is a leading manufacturer of respiratory products and is highlighting several key industry first disposable products that provide value and improve patient outcomes at the same time. Mercury is the ONLY ONE company that has introduced the unique concept of a disposable BiLevel and CPAP device. An alternative when expensive equipment is not

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available at the right time. Additionally, Mercury was the very first company to bring a completely disposable infant T-piece system to market and the latest Neo-Tee version with higher PEEP (orange knob) continues the trend of improving patient outcomes at an economical cost for the NICU, L&D, ED and transport.

With respect to NRP, Mercury strives to create products that help clinicians meet industry guidelines. RT Directors, NICU Respiratory Specialists and nurses who visit our display will find resuscitation devices that meet NRP and AHA guideline requirements. For instance, the disposable Neo-Tee T-Piece Resuscitator offers more consistent inspiratory and expiratory pressure than other types of resuscitators. It is affordable for use at every NICU, L&D and ED bedside. Furthermore, NRP recommends using a colorimetric CO<sub>2</sub> Detector on the OETT for intubated patients or supraglottic airway connector to ensure proper placement with rapid color change. Mercury provides the ONLY ONE disposable CO<sub>2</sub> Detector solution for premature infants below 1 kg with the Neo-StatCO<sub>2</sub> <Kg — and it works for 24 hours. NRP also requires clinicians to use the right size mask for infants. With that in mind, Mercury recently introduced the ONLY ONE anatomical silicone preemie masks to help solve the issues of masks covering the baby's eyes, or having to intubate when the smallest sizes are not available. These preemie masks are not only soft and flexible but they are ergonomically designed which offers a tighter seal and reduction in mask leakage. The anatomical silicone preemie masks will also be exhibited in the Mercury booth. In summary, clinicians should visit the Mercury display to get a first-hand view of our products and advantages.

## MGC Diagnostics

Booth #419

### What products will you be presenting at AARC?

MGC Diagnostics will display recent product developments and technology advancements, including systems for pulmonary function testing and gas exchange testing. Pulmonary Function Testing systems include: The Platinum Elite body plethysmograph and the Ultima Series cardiorespiratory diagnostic systems. Both have RTD real time diffusion technology, which delivers clinically significant graphic data and immediate results. Gas Exchange Testing systems include: The Ultima CPX metabolic stress testing system, CCM Express indirect calorimeter and the Ultima Cardio<sub>2</sub> gas exchange analysis system with integrated 12-Lead ECG. Our latest version of cardiorespiratory diagnostic software incorporates HIPAA – HITECH Security Safeguards to protect your patient's Identifiable Health Information. We will also be showcasing the CPFS/D USB spirometer – a full function, portable spirometer and Resmon PRO FULL FOT (Forced Oscillation Technique) device.

### Are there any new products you wish to emphasize?

MGC Diagnostics will be highlighting the release of Ascent cardiorespiratory diagnostic software for our pulmonary function line of products. Ascent software has been designed from the ground up, resulting in the most advanced testing software platform available. Designed to function with today's hardware and with an eye on future innovations, Ascent software guides the user through the software to ensure an effective patient outcome. We will also be featuring the new Meridian



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Series cardiorespiratory diagnostic systems for exercise or metabolic testing. The Meridian Series offers a highly accurate compact system that is perfect for the university setting, cath lab or exercise lab. Designed for today's modern lab, the Meridian Series offers solutions for your testing needs.

**Discuss educational/training materials you'll be offering.**

Managing the MGC Diagnostics exhibit will be our best-in-class clinical, sales and support staff available to answer not only your product questions, but provide expert consultation for your clinical application and cardiorespiratory business needs.

**Why should AARC participants visit your display?**

MGC Diagnostics delivers diagnostic solutions for detection, classification and management of cardiorespiratory patients worldwide. This singular focus guides our strategy and defines our commitment to customers, employees and shareholders. These attributes make us uniquely qualified to solve today's challenges and uncover solutions for tomorrow's opportunities.

## Nova Biomedical

Booth #1206

**What products will you be presenting at AARC?**

Nova will be showing the Stat Profile Prime Plus blood gas/critical care analyzer that offers the broadest test menu of any blood gas/critical care analyzer. With up to 20 tests on board, fast, economical critical care results, and the industry's best overall user satisfaction, Nova's products are the best value in blood gas/critical care testing. Stat Profile Prime Plus is a comprehensive, whole blood critical care analyzer that offers blood gases, electrolytes, hematology, metabolites, co-oximetry, and 32 calculated results in a simple, compact device. Prime Plus combines maintenance-free, replaceable cartridge technology for sensors and reagents with patented, new, maintenance-free and non-lysing whole blood co-oximetry technology. Test menu includes pH, PCO<sub>2</sub>, PO<sub>2</sub>, Na, K, Cl, iCa, iMg, Glucose, Lactate, Urea, Creatinine, Hct, Hb, SO<sub>2</sub>%, and Co-Ox. Prime Plus uses a small 135µL sample, produces rapid results—a complete 20-test panel in about one minute—and offers automated quality control with real-time, supplement quality monitoring of each sample analysis, calibration, and quality control analysis.

**Are there any new products you wish to emphasize?**

Prime Plus is the newest blood gas/critical care analyzer from Nova Biomedical. Prime Plus received FDA clearance in November 2018 and is our emphasis product for the Respiratory Care market.

**Discuss educational/training materials you'll be offering.**

Immediately following analyzer installation, training of operators is provided by Nova training and applications staff. Correlation studies are included as part of the training process. We maintain a highly skilled and experienced technical support "hotline" staff to answer calls 24/7/365, as well as one-day on-site service by a trained Nova representative. Nova's library of on-demand webinars on timely topics such as point of care testing, critical care, clinical practice and regulatory updates, and common conditions including sepsis and hyperglycemia allow RTs to obtain critical knowledge and training from experts at their own pace.

**Why should AARC participants visit your display?**

Visit the Nova booth to see the new, maintenance-free Stat

Profile critical care blood gas analyzers that can provide up to 20 tests including blood gases, electrolytes, metabolites, hematology and maintenance-free and non-lysing whole blood co-oximetry. With applications in respiratory care and critical care areas throughout the hospital, Prime Plus provides the comprehensive test menu needed to address the rapid, point-of-care diagnostic support of critically ill patients including those with sepsis, respiratory distress, burns, shock, DKA and trauma. Prime Plus analyzers play an important role in providing expanded whole blood tests that are needed for these patients. With Prime Plus, RTs improve patient care by providing more critical care tests from a single sample using fewer resources and generating faster results. Nova analyzers feature fully automated operation and analysis of user-selected test menus with just a touch of a button. They perform an automated two-point calibration at pre-set intervals to assure that the instrument is ready for analysis at all times. Automated, on-board, true liquid quality control eliminates the steps involved in manually performing QC, thereby dramatically reducing labor costs. Snap-in MicroSensor™ cards and reagent cartridges are maintenance free and replaced in minutes.

**Discuss your R&D process, including clinical user input.**

Kubtec's business is built upon digital X-ray and nothing else. Our institutional knowledge base is deep, and we can truly say that we are the experts in our clearly defined chosen field: neonatal and women's imaging.

Our approach is to identify unmet needs in the market and to move quickly to provide solutions to clinicians, patients and providers.

Our concepts are often derived from consultations with our broad customer base and are tested with neonatal physicians, technicians and administrators at tradeshow, hospitals and workshops. Product concepts pass through a stage gate process and are continually tested against user requirements and quality standards prior to release.

## Passy Muir

Booth #1200

**What products will you be presenting at AARC? Pediatric Anatomical Demonstration and Teaching Model**

—the latest addition to the Passy Muir line of anatomical teaching models, Tracheostomy P.A.M. (Pediatric Airway Model) is designed for use by healthcare practitioners to educate students, families, patients, and clinicians about tracheostomy in the pediatric airway and the proper application of the Passy Muir Valve. Conveniently sized, Tracheostomy P.A.M. illustrates the approximate anatomy of a toddler (ages 2-4). Consistent with the anatomy of a toddler, the larynx is positioned higher, the hyoid bone is more anterior, and the tongue fills the oral cavity.

P.A.M. is packaged with helpful educational accessories to enable clinicians to provide a wide variety of education related to tracheostomy. The kit includes three demonstration Passy Muir® Valves, a cuffed tracheostomy tube, and a syringe for cuff deflation. The kit allows for education and practice related to use of a speaking valve. A nasogastric tube is provided for the display of nasogastric placement. A customized

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Tracheostomy P.A.M. product package is provided for easy storage and transport of the entire P.A.M. kit. Passy Muir has prepared helpful instructional videos for use of the Tracheostomy P.A.M. (Pediatric Airway Model), available online and in the provided Educational Toolkit Flash Drive, and the clinical staff at Passy Muir is available to answer any questions regarding assembly or to provide suggestions on how to use the Tracheostomy P.A.M. Pediatric Airway Model for teaching purposes. For more information, or to purchase, visit [www.passymuir.com](http://www.passymuir.com).

**Toby Tracheapuppet Therapy Hand Puppet** – A therapist's best companion and a child's best friend, the Toby Tracheapuppet plush therapy hand puppet is ideal for interaction with young patients, facilitating vocalization, and therapeutic play. Featuring a pediatric tube and a Passy Muir Valve for demonstration and education, Toby Tracheapuppet provides therapists and caregivers with a lighthearted method to introduce children to tracheostomy and the Passy Muir Valve. For more information, or to purchase, visit [www.passymuir.com](http://www.passymuir.com).

**TRACHTOOLS Communication App v1.3** – Now in English and Spanish, this tracheostomy patient-friendly app for iPhone, iPad, and Android, enables communication at the touch of a button. With useful resources for patients, families, and clinicians, the app features an intuitive menu, user-defined voice options, easy to use navigation, and helpful links to tracheostomy care information. Patients and clinicians can cross language barriers with the translation feature for the prerecorded phrases. The app is perfect for clinicians, patients, families, and caregivers. Available free from the App Store or Google Play. At Passy Muir, better communication means better care.

### **Are there any new products you wish to emphasize?**

Our complete line of Tracheostomy Education Models. Our updated family of tracheostomy education models provide healthcare practitioners with an easy way to educate students, families, patients, and clinicians about airway anatomy and tracheostomy. Packaged with helpful educational accessories to enable clinicians to provide a wide variety of education related to tracheostomy, these kits include demonstration Passy Muir Valves, cuffed tracheostomy tube, a syringe, and nasogastric tube. Conveniently sized, these models are perfect for demonstration and education and feature new customized packaging to provide easy storage and transport.

The PMV-AD1522 and PMV-AD22 Adapters – Available wherever you purchase other Passy Muir products, these versatile adapters are designed to provide a secure connection between the Passy Muir Valve and a tracheostomy tube, ventilator tubing, closed suction systems, or other adapters. Each adapter is latex free, color coded for easy identification, and provided in re-sealable, multiple unit packaging. The PMV-AD1522 is a step-down adapter designed to connect the PMV 007 (Aqua Color) to a T-piece type closed suction system. The flexible PMV-AD22 adapter is designed for use with the PMV 2001 (Purple Color). All Passy Muir products are proudly made in the USA.

Visit our newly updated website, with both English and Spanish language options. Featuring an intuitive and easy-to-navigate interface, [www.passymuir.com](http://www.passymuir.com) provides an extensive wealth of helpful information and resources for clinicians and patients. With informative clinical animations and videos, patient stories, evidence-based resources, product information, online

education, therapy information, FAQs, and much more, our new site provides visitors with a comprehensive source for all things related to tracheostomy and the Passy Muir Valve.

### **Discuss education/training materials you'll be offering:**

Icon-based reference bibliography with citations of up-to-date research specific to tracheostomy. Colorful icons make it easy to quickly find a reference by category and application.

**Passy Muir Pocket Guide.** Handy pocket-sized Assessment, Placement, Accessories; Connections guide featuring useful information pertaining to patient selection, airway assessment, and Passy Muir Valve placement. Includes information regarding ventilator connections, clinical benefits, care and cleaning, and therapeutic techniques.

**Aerodigestive Health.** Written by clinical professionals for clinical professionals, the publication features papers and research by respiratory therapists, speech-language pathologists, physicians, and other healthcare professionals on the latest clinical information for working with patients with tracheostomy and the Passy Muir Valve. If interested in contributing an article, or to learn more about how you can be involved in the journal, please email [aerodigest@passymuir.com](mailto:aerodigest@passymuir.com). Passy-Muir, Inc. is committed to improving the quality of life for patients with tracheostomy or ventilator-dependence. To meet this mission, we provide free education through on-line self-study webinars and onsite in-services tailored to meet the needs of your facility. These educational opportunities are free and provide CEUs for respiratory therapy, speech pathology, and nursing. Visit [www.passy-muir.com/education](http://www.passy-muir.com/education) for more information.

We also offer a national seminar at a nominal cost which provides 8 CEUs, delivers state-of-the-art education from both an RRT and SLP through didactic lecture, patient videos, hands-on instruction, specialized training in ventilator application and dysphagia management, and case studies to synthesize all the information. Visit our website for 2019 opportunities still available, and stay tuned for a 2020 seminar near you — with dates and places to be announced soon. Visit [www.passymuir.com](http://www.passymuir.com) for more information.

### **Why should AARC participants visit your display?**

Visiting our display provides attendees an opportunity to participate in interesting hands-on activities and gain helpful insights from our expert clinical professionals. Visitors can check out our products and educational teaching models, the Toby Tracheapuppet therapy hand puppet, explore the bi-lingual TRACHTOOLS communication app, and learn about our exciting new seminars and educational offerings.

## **Precision Medical, Inc.**

Booth #320

### **What products will you be presenting at AARC?**

Precision Medical will be presenting the industry's only freestanding Helium-Oxygen Blender and discussing the clinical applications using the modular system. With both low-flow and high-flow blender options, these units are easily paired with the optional cylinder clamp and pole thus reducing set up times and tank changes. The assortment of modular accessories gives clinicians the ability to fully customize the Heliox System across varied clinical settings and increasing patient safety. Our hospital sales team will also be showcasing a sampling of Precision Medical products that are Joint Commission compliant. Each



## The Intelligent Analyzer.

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product meets EC.02.04.03 EP 8 standards such as labeling that designates the appropriate gases for which they are intended. Other safety innovations will be presented such as our Trach Guard that prevents obstruction of the tracheostomy tube and does not allow accidental incorrect connections.

### Why should AARC participants visit your display?

At this year's AARC, participants will be able to see first-hand Precision Medical's rebranding which includes a more modern company logo and other key visual updates allowing us to better communicate with our customers. The gradual rebranding will be seen across product labels and packaging. We are also launching our new website giving customers increased visibility of Precision Medical products. Founded in 1982, Precision Medical continues to provide our valued customers with high quality, made in the USA respiratory care equipment. After more than 35 years, we continue to design and manufacture in the USA. The difference is precision.

## Radiometer

Booth #217

### What will you be presenting at AARC?

Come to booth #217 to learn about LIVE Connect: Radiometer's platform for current and future digital services. Through LIVE Connect, Radiometer Service Personnel can help you maintain uptime with a suite of digital services. Analyzer performance data is shared via a one-way communication with authorized Radiometer personnel. Neither patient nor operator data is ever shared, so you can rest assured that your patients' data is secure.

## VORTRAN Medical Technology

Booth #1238

### What products will you be presenting at AARC?

We will be presenting our PercussiveNEB 2.0 (airway clearance device), VCI (ETT cuff inflator) GO2VENT (gas-operated resuscitator), APM-Plus (airway pressure monitor), IPPB, and Manometer.

### Are there any new products you wish to emphasize?

This year we have released the new version of our VORTRAN APM (Airway Pressure Monitor), called the APM-Plus. It can monitor resuscitators, ventilators, and bubble CPAP while also providing adjustable alarm settings. We also released a new model of our GO2VENT; GO2VENT Model 6001 is cost-saving for any customer who doesn't require the 50% FiO2 entrainment feature on our main GO2VENT 6123 Model. Lastly is the GO2VENT EMS Pack, which is a specially packaged GO2VENT designed for the needs of EMS responders.

### Discuss educational/training materials you'll be offering.

At our table, we will have all of our products set up to simulate real-life usage. All visitors are free to visit for the opportunity to get hands-on experience. Our trained staff will be able to answer any questions and guide you as to the correct way to use the devices. Our main feature will be an intubation manikin—practice intubating and properly inflating the cuff using our VORTRAN Cuff Inflator. Then connect our GO2VENT to ventilate the patient and set the proper airway alarms using our APM-Plus.

### What speakers or papers will you be featuring?

Our PercussiveNEB 2.0 will be featured in an abstract written by researchers at the University of South Alabama. "Comparison of PercussiveNEB 2.0 and Metaneb Using a Bench Top Mechanical Ventilation Design" measures the distance of mucus movement to compare how effective each device is at secretion clearance. Both devices were shown to be effective.

### Why should AARC participants visit your display?

VORTRAN Medical has been providing respiratory devices for over 30 years. With the rising costs of health care, we aim to create devices that are not only effective life-saving and treatment devices, but cost-effective as well. Please visit our booth for a fun hands-on experience and a chance to win samples of our products.

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# The Benefits of an Automatic Resuscitator Over Manual

In this feature, *Respiratory Therapy* interviews clinicians and healthcare providers about the actual application of specific products and therapies. Participating in the interview is Robert Kohler EMT-P, Stamford Emergency Medical Service.

**Respiratory Therapy:** What are the reasons for choosing an automatic resuscitator (like the VORTRAN GO2VENT) over manual (eg bag-valve-mask)?

**Robert Kohler:** All the various respiratory functions in the body are dependent on a narrow range of pH in which they can operate. Ventilation has a profound effect on the pH of the blood stream. Although in the field we don't know what the exact pH is, if we automate the ventilation process we will provide a stable value the body's buffer system can map to and compensate for if necessary.

Resuscitation is a two-person function. You the practitioner and the patient. While you don't know the patients pH the patients buffer system does. Give the patient a consistent target which cannot be achieved through the use of a BVM and let their own buffer system do the rest.

Whether it is the GO2VENT or some other automated process, automation is the key. The GO2VENT is brilliantly simple in its design. It uses less oxygen than a BVM and it is lightweight, inexpensive and durable. With minimal training it is very easy to deliver effective, consistent ventilations across the wide variety of situations found in the pre-hospital environment. Furthermore it is just as easy to disconnect from the system and go back to a BVM should you run out of oxygen, as it requires no special adaptors.

**RT:** What makes the VORTRAN GO2VENT unique for EMS providers?

**RK:** The compact size, weight and durability of the GO2VENT are exceptional for the capability it provides. The GO2VENT has brought a new level of care to the street

**RT:** How has the VORTRAN GO2VENT changed your ability to resuscitate patients?

**RK:** Yes and realize resuscitation in the pre-hospital environment is much different than in hospital. To put it bluntly, it is chaotic at best. Remember the GO2VENT is used when a patient is literally fighting for their life and needs to be sedated in order to properly be ventilated. The GO2VENT offers the option of one less pair of hands needing direction from you the Paramedic. Just set it and GO! Now you can step back and look at the bigger picture. The patient!

**RT:** The VORTRAN GO2VENT has been stockpiled in many disaster preparedness services, how would you recommend they utilize them?

**RK:** In short, any time a Bag Valve Mask would be used it should be replaced with a GO2VENT. The GO2VENT can even be configured to continue ventilation in an MRI!

**RT:** What are the risks and benefits of using the VORTRAN GO2VENT?

**RK:** Minimal risk that I can see, certainly nothing you would not have using a BVM. The benefits I explained earlier.

**RT:** When setting up the VORTRAN GO2VENT, what are some of the common mistakes?

**RK:** Initially starting the GO2VENT with too much oxygen is the biggest one. You should start using only 10 liters per min. Secondly people don't wait and let the vent work. You should back out the rate knob a half turn at a time over about 10 seconds until ventilation starts. Understandably this is an eternity when your patient has stopped breathing in the back of your ambulance but given the chance your patient will fare better.

**RT:** In your experience as trainer/educator for EMS, what is the biggest challenge in adapting the VORTRAN GO2VENT?

**RK:** The management style of the service it is used in. There are few Paramedics both young and old that embrace change. If management does not believe in the science and encourage its use through policy there is little hope that Paramedics will pick it up on their own.

**RT:** What areas of improvement are needed regarding EMS emergency ventilation?

**RK:** Realize Ventilation is the prime directive. Your job is to make sure this patient continues to breathe and breathe effectively.

**RT:** What recommendations would you make to any EMS services that are not utilizing automatic resuscitation?

**RK:** Reevaluate their priority's and realize we once used to use MAST trousers and Long Spine Boards on the ambulance but things have changed.

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If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at [s.gold4@verizon.net](mailto:s.gold4@verizon.net).

## IMPACT BE: A New Airway Clearance Resource to Help Educate the Non-CF Bronchiectasis Patient

In this feature, Respiratory Therapy interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Steve Robins and Carol Capece, founders and partners of the SPARK Group.

**Respiratory Therapy:** Tell us a little about yourself and the SPARK consulting group

**Steve, Carol:** We launched SPARK Healthcare 10 years ago with the clear mission of identifying unmet needs in disease states we felt strongly about and creating evidence-based solutions which address those needs. We've created programs to help children with cystic fibrosis (CF) transition from pediatric to adult care, empower people with gastrointestinal disease to improve treatment adherence, and provide physicians with the information they need to more efficiently identify and diagnose patients with non-CF bronchiectasis. We're proud of the fact that our work has been published in a number of medical journals and that it's featured in quality improvement initiatives in clinics around the country.

We've always had at least one foot in the pulmonary care category, partnering with healthcare providers, researchers, patient opinion leaders, and advocacy groups to develop unique program solutions in CF, non-CF bronchiectasis, asthma, and beyond. We're thrilled to partner with the team at International Biophysics Corporation, manufacturer of the AffloVest, to create "IMPACT BE" (Individual Management of Patient Airway Clearance Therapy) to support people that have been diagnosed with non-CF bronchiectasis, a severely underserved patient population.

**RT:** What is the IMPACT BE program and how did this get started?

**S, C:** IMPACT BE provides a structured toolset that non-CF bronchiectasis patients and healthcare providers can use together to help assess, evaluate, and educate on airway clearance treatment (ACT) options.

From the literature and from our interactions with pulmonary care professionals, we knew there was a paucity of support resources for the non-CF bronchiectasis patient community. The diagnosis can take 2 years or more and, even then, there are no approved medications to treat the disease. We wanted to do something that could make a difference in this community. In speaking with pulmonary care team members around the

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SPARK is strategic consultancy that develops public health educational programs focusing on improving treatment adherence, improving the clinician/patient relationship, and driving clinic efficiencies to achieve better patient health outcomes. If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at [s.gold4@verizon.net](mailto:s.gold4@verizon.net).

country, we knew these patients could benefit – both in terms of improved lung function and quality of life – from adopting an airway clearance routine. Our own research with care teams suggested there was no structured approach to introduce airway clearance to non-CF bronchiectasis patients, to get them off on the right foot, and ensure they were sticking with it. When we discussed this issue with the team at International Biophysics and the IMPACT Advisory Team, we began to brainstorm ideas that led to the creation of IMPACT BE.

**RT:** What is the primary clinical need being addressed by this project?

**S, C:** The majority of non-CF bronchiectasis patients have a difficult time clearing mucus, and the resulting buildup of material in their large and small airways creates an ideal environment for bacteria to get trapped and grow which can lead to inflammation, infection, etc. These patients are hospitalized frequently due to persistent lung infections and associated complications. Treatments at home and in-hospital often consist of various courses of antibiotics. Airway clearance, while considered a standard part of the treatment regimen, is seldom discussed in detail, and care team members representing large and small pulmonary programs across the country agreed that a structured approach to discussing all airway clearance options with their non-CF bronchiectasis patients would be highly valued.

**RT:** What are the primary objectives of the program for the clinician and the patient?

**S, C:** IMPACT BE is a structured toolkit for non-CF bronchiectasis patients and healthcare providers that:

1. Brings structure and efficiency to how airway clearance is discussed in the clinic
2. Proactively addresses patient knowledge and skill gaps around airway clearance, and
3. Improves patient adherence to airway clearance therapies and health outcomes

**RT:** Can you tell us who is involved with project?

**S, C:** To ensure we were developing a solution that meets the needs of the non-CF bronchiectasis community, we assembled the IMPACT Advisory Team. This team is comprised of a multi-disciplinary team of researchers who have deep experience in non-CF bronchiectasis and represent centers of various sizes and geographies. We'll also be soliciting feedback on the program resources directly from non-CF bronchiectasis patients through market research and the pilot program.

**RT:** How will the program be rolled out?

**S, C:** We're getting input from the IMPACT Advisory Team and patients at key project milestones, but we know that what we're creating will need refinement before it's ready for national rollout. With this in mind, we're planning a 10-clinic pilot program that will begin in the fall of 2019. During the pilot, we will measure program uptake and adoption, assess the feasibility of implementation in the clinic setting, and gain qualitative feedback from patients and healthcare providers on the program tools. We will then incorporate feedback from the pilot centers and prepare for a national rollout. Once the program is finalized, "Peer Coaches" will be available to train care teams across the country and instruct them on how to use the program, best practices that grew out of the pilot, and how they can measure success.

**RT:** What are the major components of the program?

**S, C:** We'll develop a series of clinic-based tools that will be administered by care teams. The goal is to actually save clinic time by bringing structure to discussions around the various airway options, the importance of treatment adherence, etc. The clinic-based materials will be available in print and digital formats. We'll also produce an educational wall poster, an easy-to-use take home reference resource and a website ([www.IMPACT-BE.com](http://www.IMPACT-BE.com)) where the educational materials and instructional videos will live.

**RT:** What are the anticipated benefits of the program?

**S, C:** The program will be available at no cost to care teams, and they'll be trained by a trusted colleague who will offer a series of best practices from his/her own experience with the program.

Again, our hope is that IMPACT BE will simply bring structure to discussions that may already be happening with bronchiectasis patients around airway clearance. And if they aren't already happening, we're hoping to make them as efficient as possible in the clinical setting by providing a series of easy-to-use tools that we hope will facilitate the conversations and allow patients and care teams alike to take a more proactive approach to gaining better health outcomes.

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# The Efficacy of High-Flow Oxygen Therapy in Infants with Bronchiolitis

Chris Campbell

Bronchiolitis is the most common cause of hospital admissions for infants worldwide. This acute lower airway lung disease has a significant impact on the global healthcare system. In the United States alone, \$1.7 billion of healthcare spend can be attributed to bronchiolitis related admissions.<sup>1,2</sup> Severe bronchiolitis is characterized by small airway inflammation resulting in hypoxemia, hypercarbia, and increased work of breathing,<sup>1</sup> all of which respond to the provision of positive pressure. However, respiratory support involving CPAP and mechanical ventilation has traditionally only been available in the Pediatric Intensive Care (PICU) setting.

Observational and physiological studies suggest that NHF at appropriate flow rates may decrease work of breathing, improve oxygenation, and reduce rates of intubation.<sup>17,18</sup> NHF is the delivery of heated and humidified blended air and oxygen delivered through nasal cannulae.<sup>14,15</sup> As such, Nasal High Flow (NHF) therapy is being increasingly used to manage bronchiolitis across the hospital, despite limited high quality evidence demonstrating safety and efficacy beyond the PICU.

In 2018, the largest NHF trial to date was published in the prestigious *New England Journal of Medicine* by Donna Franklin et al, to answer the question of whether the early use of NHF in the Emergency Department (ED) and pediatric wards would result in fewer treatment failures leading to the escalation of care.

## The Study

1472 patients younger than 12 months old with bronchiolitis and a requirement for supplemental oxygen were recruited from 17 EDs and general wards across Australia and New Zealand. Patients received either heated and humidified NHF therapy (flow rate of 2L/kg/min) or standard oxygen therapy (maximum flow rate of 2L/min). Infants who met the therapy failure criteria in the standard oxygen group received rescue NHF therapy, whereas infants in the NHF group who met the treatment failure criteria were escalated to the PICU. NHF was delivered with the Optiflow™ Junior system (Fisher and Paykel Healthcare)\*.

The primary outcome of treatment failure was defined as meeting ≥3 of 4 clinical criteria: persistent tachycardia, tachypnea, hypoxemia, and medical review triggered by a hospital early-warning tool. Secondary outcomes included duration of hospital stay, duration of oxygen therapy, and rates

of transfer to a tertiary hospital, ICU admission, intubation, and adverse events.

## Study Results

The use of NHF in the ED and general wards resulted in significantly fewer infants in the NHF group requiring escalation of care, compared to those receiving standard oxygen therapy. 12% (87 of 739) of infants in the NHF group required escalation of care, compared to 23% (167 of 733) in the standard-therapy and rescue NHF group (risk difference, -11 percentage points; 95% confidence interval, -15 to -7;  $P < 0.001$ ). Among the 167 infants in the standard-therapy group who had treatment failure, 102 (61%) responded to rescue NHF and did not require further escalation.

No significant differences were observed in the duration of hospital stay or the duration of oxygen therapy. In addition, there was no significant between-group difference in the incidence of adverse events. In each group, one case of pneumothorax (<1% of infants) occurred. There was no evidence of a shorter duration of oxygen therapy, lower rate of ICU admission, or shorter duration of hospital stay in infants receiving NHF therapy than in those receiving standard oxygen therapy.

## Conclusion

Based on the study's results, the authors concluded that, "In conclusion, our randomized, controlled trial involving infants with bronchiolitis showed a significantly lower rate of escalation of care due to treatment failure when high-flow oxygen therapy was used early during the hospital admission than when standard oxygen therapy was used."

\*Fisher and Paykel Healthcare provided equipment and consumables for all the trial sites. The company had no involvement in the design and conduct of the trial, the analysis of the data, or in the preparation of the manuscript or the decision to submit it for publication.

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Chris Campbell is the Senior Editor of Respiratory Therapy.

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*News...continued from page 8*

### **Device Earns Hot Products Award**

Mercury Medical and JEMS (Journal of Emergency Medical Services) are proud to announce the selection of Flow-Safe II+ Disposable BiLevel CPAP device and the WoundClot Next Generation Hemostatic Agent as winners of the Hot Products Award from the JEMS EMS Today Conference and Exposition, which was held February 20-22 in National Harbor, MD. Mercury Medical was the only company to win multiple awards. Flow-Safe II+ and WoundClot were selected after a panel of judges consisting of emergency medical services (EMS) product specialists, physicians, educators, managers and paramedics reviewed a host of product contenders designed to not only improve the ability to deliver optimal emergency medical care to sick and injured patients, but also allow EMS agencies to do it safely, more efficiently and with enhanced comfort for the patient. Products were evaluated based on four distinct categories: 1) Originality; 2) Functionality; 3) Ease of use; and 4) Need in the EMS setting. Flow-Safe II+ and WoundClot were two of only 14 products selected as Hot Products after the EMS Today Hot Products team reviewed and rated dozens of products submitted by a number of companies. Mercury Medical CEO and President John M Gargaro, MD said, "We were delighted to be a multiple winner of the 2019 Hot Product Award at the recent JEMS EMS Conference and Exposition. This speaks volumes about our employees at the Company and their continuous focus on nurturing and developing leading edge products in the markets we serve." Flow-Safe II+ is the first disposable Bilevel CPAP system in the United States. This customized system provides clinicians every item needed for delivering BiLevel CPAP and CPAP therapy. Flow-Safe II+ is a single patient use device that includes an adjustable full-face mask and manometer that provides verifiable CPAP and BiLevel IPAP and EPAP pressures which are critical in delivering timely and continuous therapy. This third-generation system uses 50% less oxygen than the original Flow-Safe CPAP System. In addition, it eliminates the need for costly capital equipment maintenance and helps prevent the potential cross contamination from patient to patient from the typical expensive respiratory capital equipment in hospitals, surgery centers and pre-hospital environments. WoundClot, the Next Generation Hemostatic Agent is a patented advanced bleeding control hemostatic gauze that will prove to be a game-changer in immediate and life-saving use situations by providing for the temporary stoppage of severe blood loss. This, for example, will enable EMS providers and the ER at hospitals the capability to address accident victims' wounds whether they be punctures, lacerations or abrasions. Once WoundClot comes into contact with blood, the solid gauze converts to an expanding gel and can absorb 2,500% its' weight, quickly and effectively stopping severe blood loss. The biodegradable gauze is non-exothermic and contains proprietary molecular groups created in the manufacturing process which then work directly with the body's own repair process to form a natural clot in the wound. Once the patient reaches definite treatment, the gelatinous membrane is easy to remove. Mercury Medical is the exclusive distributor of WoundClot Hemostatic Gauze. JEMS Editor-in-Chief and EMS Today Conference Chairman A.J. Heightman said, "There were an amazing group of Hot Product submissions for our reviewers to review and rate this year. All of the products reviewed were extremely innovative and well designed for the EMS industry, showing that our

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# Long-Term Effects of Oxygen-Enriched High-Flow Nasal Cannula Treatment in COPD Patients with Chronic Hypoxemic Respiratory Failure

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**Background:** This study investigated the long-term effects of humidified high-flow nasal cannula (HFNC) in COPD patients with chronic hypoxemic respiratory failure treated with long-term oxygen therapy (LTOT).

**Patients and methods:** A total of 200 patients were randomized into usual care ± HFNC. At inclusion, acute exacerbation of COPD (AECOPD) and hospital admissions 1 year before inclusion, modified Medical Research Council (mMRC) score, St George's Respiratory Questionnaire (SGRQ), forced expiratory volume in 1 second (FEV<sub>1</sub>), 6-minute walk test (6MWT) and arterial carbon dioxide (PaCO<sub>2</sub>) were recorded. Patients completed phone interviews at 1, 3 and 9 months assessing mMRC score and AECOPD since the last contact. At on-site visits (6 and 12 months), mMRC, number of AECOPD since last contact and SGRQ were registered and FEV<sub>1</sub>, FEV<sub>1</sub>%, PaCO<sub>2</sub> and, at 12 months, 6MWT were reassessed. Hospital admissions during the study period were obtained from hospital records. Hours of the use of HFNC were retrieved from the high-flow device.

**Results:** The average daily use of HFNC was 6 hours/day. The HFNC group had a lower AECOPD rate (3.12 versus 4.95/patient/year,  $p < 0.001$ ). Modeled hospital admission rates were 0.79 versus 1.39/patient/year for 12- versus 1-month use of HFNC, respectively ( $p < 0.001$ ). The HFNC group had improved mMRC scores from 3 months onward ( $p < 0.001$ ) and improved SGRQ at 6 and 12 months ( $p = 0.002$ ,  $p = 0.033$ ) and PaCO<sub>2</sub> ( $p = 0.005$ ) and 6MWT ( $p = 0.005$ ) at 12 months. There was no difference in all-cause mortality.

**Conclusion:** HFNC treatment reduced AECOPD, hospital admissions and symptoms in COPD patients with hypoxic failure.

**Keywords:** COPD, high-flow heated and humidified oxygen, HFNC, exacerbation, AECOPD, modified Medical Research Council score, mMRC score, 6-minute walk test, 6MWT

## Introduction

In advanced COPD, long-term oxygen therapy (LTOT) is an

established treatment for patients with chronic hypoxemic respiratory failure. LTOT has been shown to increase the survival in patients with severe resting hypoxemia, with optimal use of  $\geq 15$  hours/day.<sup>1,2</sup> The prevalence of LTOT in COPD is 40-48/100,000 patients and is increasing.<sup>3,4</sup> Adherence to optimal treatment has proved difficult.<sup>5</sup> Despite improved survival when treated with LTOT, life expectancy is limited when in need of LTOT, in part due to concomitant comorbidities and hypercapnic failure,<sup>3,6,7</sup> although it has been indicated that LTOT stabilizes the partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>).<sup>8</sup> Moreover, patients are susceptible to acute exacerbation of COPD (AECOPD),<sup>9</sup> with poor outcomes in terms of mortality and recurrence of AECOPD.<sup>10</sup>

In addition, patients are highly symptomatic,<sup>11</sup> have impaired quality of life (QoL)<sup>12</sup> and limited walking distances, none of which improve with LTOT.<sup>13</sup>

Humidified high-flow nasal cannula (HFNC) with optional supplementary oxygen delivery has evolved in recent years, with a growing body of evidence of reduced respiratory resistance, decreased work load of breathing, improved pulmonary compliance, recruitment and mucus clearance in adults.<sup>14-16</sup> HFNC is primarily established in acute and critical care settings for treating mild-to-moderate acute hypoxic failure<sup>17</sup> and ventilator weaning.<sup>18</sup> However, there is increasing evidence that HFNC is beneficial in chronic respiratory diseases. Recent studies have shown increased time to first exacerbation and forced expiratory volume in 1 second (FEV<sub>1</sub>) in patients with obstructive lung diseases and mucus retention challenges,<sup>19</sup> in addition to a reduction in respiratory rate,<sup>20</sup> PaCO<sub>2</sub><sup>21</sup> and increased exercise performance<sup>22</sup> in advanced COPD patients and patients with chronic hypoxemic respiratory failure. However, knowledge about the long-term effect of HFNC is sparse.

Thus, we hypothesize that in COPD patients with chronic hypoxemic respiratory failure, long-term HFNC may reduce AECOPD rate, dyspnea and mortality as well as increase exercise performance. The aim of this study was to investigate the effects of long-term HFNC in conjunction with usual care, including LTOT, with the primary outcome being the rate of AECOPD, and, as secondary outcomes, hospital admissions; dyspnea, assessed by modified Medical Research Council (mMRC) score; QoL, assessed by St George's Respiratory Questionnaire (SGRQ); PaCO<sub>2</sub>; all-cause mortality and exercise performance, measured by 6-minute walk test (6MWT).

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## Patients and methods

In this randomized, prospective trial a total of 200 patients were included from 4 outpatient clinics in the North Jutland Region of Denmark between December 2013 and July 2015 (Figure 1). Inclusion criteria were COPD with chronic hypoxemic respiratory failure (ie, 3 arterial blood gases [ABGs] during stable conditions demonstrating hypoxemia)<sup>23</sup> and previously prescribed LTOT by a pulmonary medicine specialist, at least 3 months prior to the start of the study. Exclusion criteria were malignant disease, terminal nonmalignant disease, unstable psychiatric disease and home treatment with noninvasive ventilation (NIV). A change in smoking habits during the study period would lead to exclusion. All patients received personalized inhaled medicine according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines,<sup>24</sup> had previously undergone pulmonary rehabilitation and were in specialized care in connection with LTOT treatment, according to the GOLD recommendations.<sup>25</sup> Change of medication and attending rehabilitation were allowed, if recommended by the patients' usual caregivers.

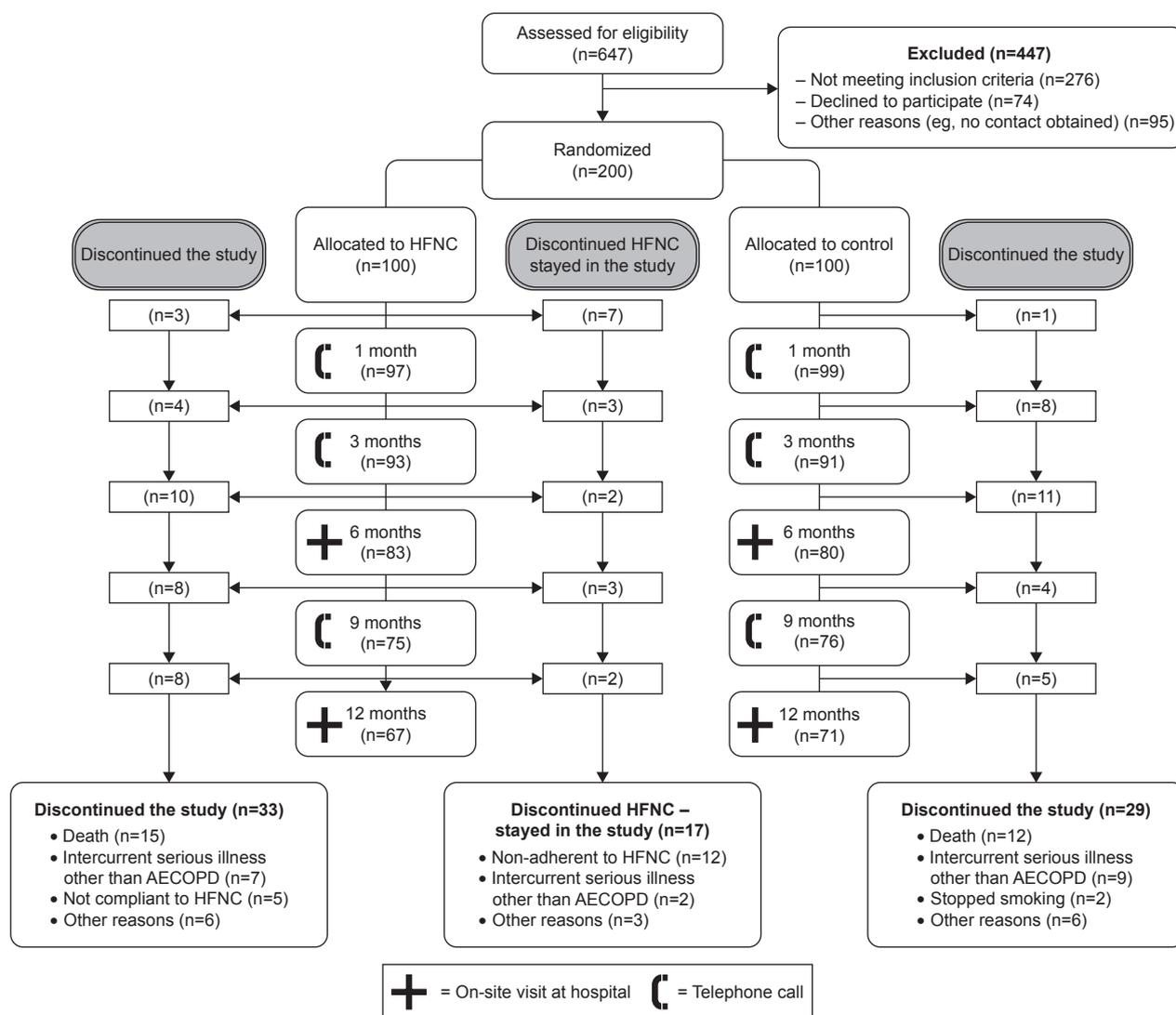
## Inclusion

By the use of numbered sealed envelopes containing group

allocations, patients were randomly assigned to either LTOT (controls) or LTOT plus HFNC home treatment delivered by Airvo™ via Optiflow™ nasal cannula (both; Fisher & Paykel Healthcare, Auckland, New Zealand). A recommended 20 L/min flow rate was decided upon after an unpublished pilot test determined that this was comfortable and allowed high compliance during sleep. Starting at 15 L, flow was titrated over 30 minutes at the baseline visit. Patients were instructed in use of the device, received a written quick guide to the device and were recommended to use HFNC for 8 hours/day, preferably at night; however, there were no restrictions in the duration of use nor time of day.

At inclusion, age, sex, body mass index (BMI), smoking status including pack-years, number of AECOPD events during the previous year, months treated with LTOT prior to inclusion and administered LTOT (L/min) flow was recorded. Dyspnea was evaluated by mMRC score, and QoL was assessed using SGRQ.

Spirometry was performed (Spida spirometry PC software/MicroMedical SpiroUSB™; CareFusion, San Diego, CA, USA) according to the American Thoracic and European Respiratory



**Figure 1** Enrollment, inclusion, follow-up and discontinuation of HFNC-treated patients and controls. **Abbreviations:** AECOPD, acute exacerbation of COPD; HFNC, high-flow nasal cannula.

Societies' criteria.<sup>26</sup> FEV<sub>1</sub>, forced vital capacity (FVC) in the percentage of expected value and the FEV<sub>1</sub>/FVC ratio were recorded.

ABG analysis was performed in all patients during the administration of usual supplementary oxygen<sup>27</sup> (ABL 800 Flex blood gas analyzer; Radiometer, Copenhagen, Denmark). pH, PaCO<sub>2</sub>, partial pressure of oxygen (PaO<sub>2</sub>) and arterial oxygen saturation (SaO<sub>2</sub>) were recorded. The supplementary oxygen flow rate was kept unaltered during HFNC treatment unless SaO<sub>2</sub> <88% was detected. Hypercapnic failure was defined as PaCO<sub>2</sub> >6.0 kPa.

A 6MWT was performed,<sup>28</sup> with patients using usual oxygen flows and use of walkers if needed. Initial oxygen-pulsed saturation (SpO<sub>2</sub>), heart rate (HR, beats/min) as well as minimum SpO<sub>2</sub> and maximal HR, walking distance and BORG score at the end of 6MWT were recorded.

Both the HFNC and control groups received medical care by their usual health care providers during the study period, including treatment for AECOPD. Patients were instructed to keep diary cards for registration of number of AECOPD events treated outside hospital.

The usual providers of LTOT homecare for both the treatment and control groups, AGA, Linde Healthcare, Dronninglund, Denmark, delivered and serviced the HFNC system during regular home visits. Re-instruction in use of the device was given by the technical staff at home delivery of HFNC. All patients used the HFNC device with oxygen-enriched air.

## Follow-up

Follow-up is shown in Figure 1. During the 1-year trial period, 2 Aalborg University Hospital study nurses conducted phone interviews at 1, 3 and 9 months and in-clinic visits at 6 and 12 months for both HFNC-treated patients and controls. Study nurses did not perform home visits.

AECOPD was defined as worsening of symptoms (worsening of dyspnea, cough and sputum production) for >2 consecutive days leading to treatment with systemic glucocorticoids or antibiotics.<sup>25</sup> Diary cards for AECOPD were read at each contact. If in doubt, patients were instructed to consult the study nurse in addition to scheduled phone interviews, where all registered AECOPDs on diary cards were recorded in the study file. In conjunction, the number of hospital admissions (at least 24-hour inpatient contact) due to AECOPD (primary diagnosis of COPD [ICD-10: DJ44], or a combination of either acute respiratory failure [DJ96] or pneumonia [DJ13-18] with COPD as a secondary diagnosis) was evaluated at the end of the study period from patients' hospital case records.

mMRC score and smoking status were evaluated at each contact.

Lung function and BMI were measured, and SGRQ was evaluated at 6- and 12-month visits.

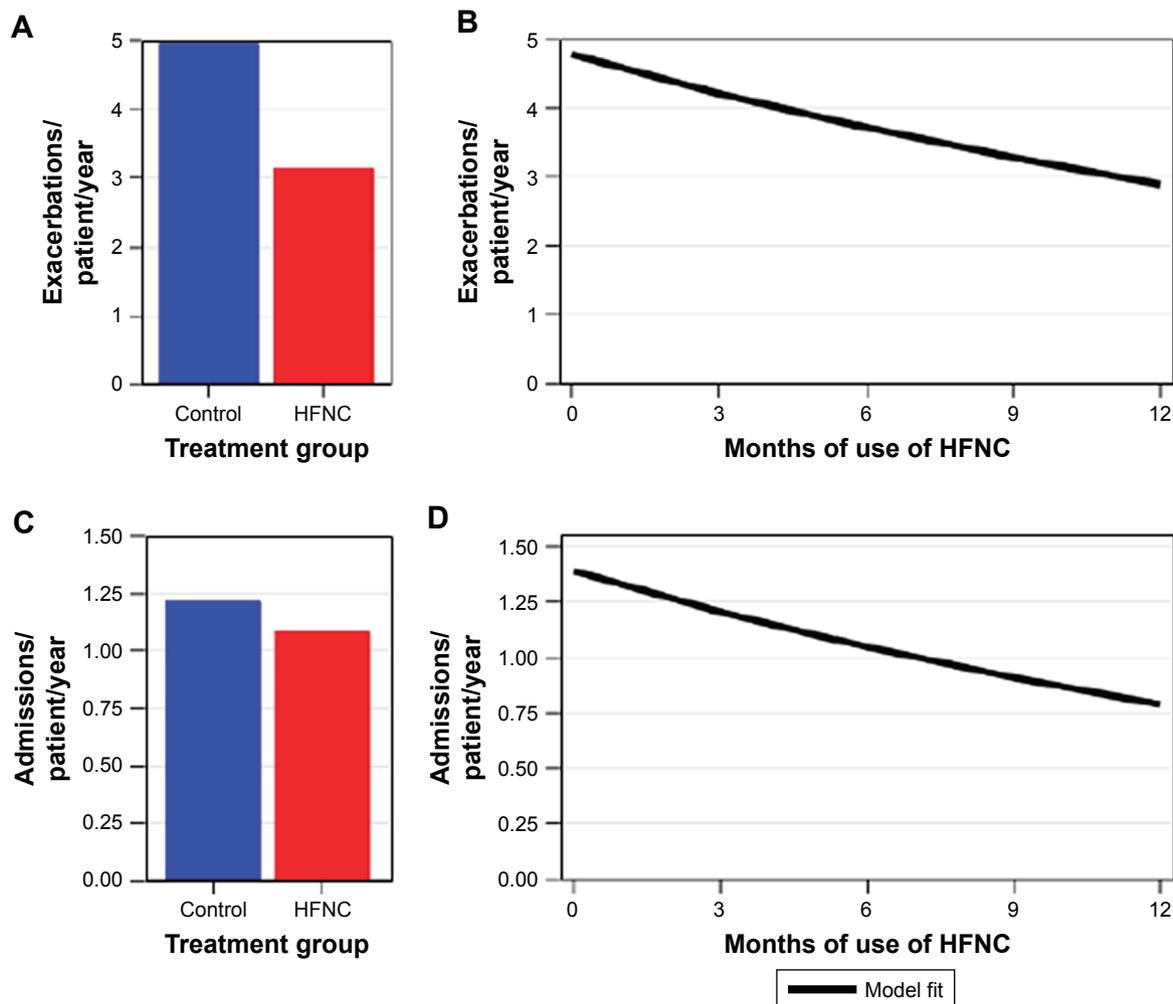
ABGs were drawn while patients were on usual LTOT at 6- and 12-month visits. After 30 minutes of HFNC treatment in patients who were allocated to treatment, ABG analysis was repeated. The need to change oxygen levels during the use of HFNC was evaluated at each visit.

**Table 1** Background information on the randomized study population, humidified HFNC-treated patients and controls at baseline

Variables at baseline	HFNC-treated patients (n=100)	Controls (n=100)	p-value for group difference
Sex, % female	56	63	NS
Age, years	71.0 (8.2)	70.4 (9.0)	NS
Treated with LTOT prior to inclusion, months	28.9 (32.6)	33.5 (30.6)	NS
BMI, kg/m <sup>2</sup>	25.0 (6.4)	25.4 (6.0)	NS
Smoking status, N, never/present/former	1/14/85	0/26/74	NS
Pack-years	41.7 (17.8)	40.5 (19.5)	NS
mMRC score	3.3 (0.9)	2.9 (0.9)	0.008
Exacerbations in the preceding year	3.23 (3.1)	2.9 (2.8)	NS
Current oxygen flow, L	1.6 (0.7)	1.6 (0.8)	NS
pH	7.41 (0.04)	7.41 (0.02)	NS
PaCO <sub>2</sub> , kPa	6.5 (1.3)	6.4 (1.0)	NS
PaO <sub>2</sub> , kPa*	9.9 (1.8)	9.9 (1.7)	NS
SaO <sub>2</sub>	95 (3.1)	95 (2.7)	NS
FEV <sub>1</sub> , %	29.8 (12.6)	31.8 (12.9)	NS
FVC%	64.1 (18.2)	63.9 (19.0)	NS
FEV <sub>1</sub> /FVC	37.5 (11.1)	40.2 (10.3)	NS
6MWT (N), m	(91) 254.6 (89.2)	(96) 245.2 (85.0)	NS
Borg score, end of test	6.3 (2.3)	6.2 (2.3)	NS
HFNC flow, L	20 (1.1)		
Oxygen supply with HFNC, L	1.75 (0.8)		
pH after 30 minutes of HFNC	7.42 (0.03)		
PaCO <sub>2</sub> after 30 minutes of HFNC, kPa	6.2 (1.2)		
PaO <sub>2</sub> after 30 minutes of HFNC, kPa	8.9 (1.2)		
SaO <sub>2</sub> after 30 minutes of HFNC, kPa	94 (2.6)		

**Notes:** Results are presented as mean (SD) unless otherwise stated. \*ABG on usual supplementary oxygen supply.

**Abbreviations:** ABG, arterial blood gas; BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; HFNC, high-flow nasal cannula; LTOT, long-term oxygen therapy; mMRC, modified Medical Research Council; 6MWT, 6-minute walk test; NS, nonsignificant; Pa, arterial partial pressure; Sa, arterial saturation.



**Figure 2** Fitted exacerbation rates (combined reported exacerbations and hospitalized exacerbations) (**A, B**) and hospital admission rates (**C, D**). **Notes:** In (**A** and **C**), blue (control) and red (HFNC) bars show rates per group as randomized (intention-to-treat analysis). In (**B** and **D**), the regression line for exacerbations (**B**) and admissions (**D**) relates actual device use, zero for the control group and 12 months for the study completers, with withdrawal subjects ranging in between (per-protocol analysis) to the number of events per patient, showing longer actual use giving lower rates of exacerbation and admission. **Abbreviation:** HFNC, high-flow nasal cannula.

The 6MWT was repeated at 12 months with recording of BORG score and HR.

In the HFNC group, patients reported their daily hours of HFNC therapy and diurnal pattern of use at each contact. In conjunction, the technical staff read operating hours from the HFNC device every second month and the average use (hours/day since the last reading) was calculated.

### Ethics

The study was approved by the North Jutland Ethical Committee (N-20110057), the Danish Data Protection Agency (2008-58-0028), and registered at ClinicalTrials.gov (NCT 02731872). All patients were informed according to the Declaration of Helsinki, and written informed consent was obtained prior to inclusion in the study.

### Statistical analysis

Sample sizing was based on AECOPD rate being reduced by 20% from an historical estimate of 3.80/patient/year. Group size of 93 gives 80% power with a 2-sided 5% level of significance, which was increased to 100 to be conservative. Patients were encouraged to remain in the study for assessments even if HFNC was no longer used (Figure 1).

The analysis population was defined as all subjects randomized to treatment and who had no major protocol deviations affecting efficacy data, giving 100% inclusion of all 200 subjects enrolled. As such, data were included on patients who discontinued the study or paused treatment and those who discontinued HFNC but stayed in the study, in the HFNC group (intention-to-treat).

Background and pretreatment information is provided as mean and SD.

Normally distributed data were analyzed in the general linear model framework with the simplest model of treatment group augmented by covariates of age and sex and, where available, baseline value of the dependent variable. Poisson regression modeling of both AECOPD and hospital admissions per patient was completed with the length of time in the study used to give estimated rates per year per treatment group with the same explanatory model as mentioned earlier. Analyses using the 2 groups as randomized are akin to intention to treat. The extra analyses where the 2 groups of treatment were replaced by 1 continuous explanatory variable of actual days of the use of HFNC are akin to per protocol. Fitted values from modeling were used to assess the treatment effect adjusted for other model terms.

## Results

### Background

Baseline information of the study population is reported in Table 1.

HFNC-treated patients and controls were comparable at baseline, apart from mMRC score, where HFNC-treated patients had a higher mMRC score. Concomitant hypercapnic failure was seen in 60% of controls and 52% of HFNC-treated patients. Average days in the study were 309 days for HFNC-treated patients, comparable to controls at 311 days. Mean oxygen flow during LTOT remained unaltered at 12 months in both groups (1.6 L/min in the HFNC group and 1.7 L/min in the control group).

### HFNC

Overall, on average, HFNC was used for 248 days, 6 hours/day, throughout the study period (readings from the HFNC device). Within the first month, 14% of HFNC-treated patients stopped using the device, including 3% who left the study entirely. The remaining 86% used HFNC for 286 days, 7 hours/day on average, throughout the study period. HFNC was used at night by 53% of the patients; during the day by 32% and both at night and day by 15%. Patients using HFNC at night, or both night and day, used the device significantly longer than those using only during daytime ( $p < 0.003$ ). By the end of study, 33% of the HFNC group had left the study, compared to 29% of the control group (Figure 1). Reasons for leaving the study or discontinuing HFNC are shown in Figure 1.

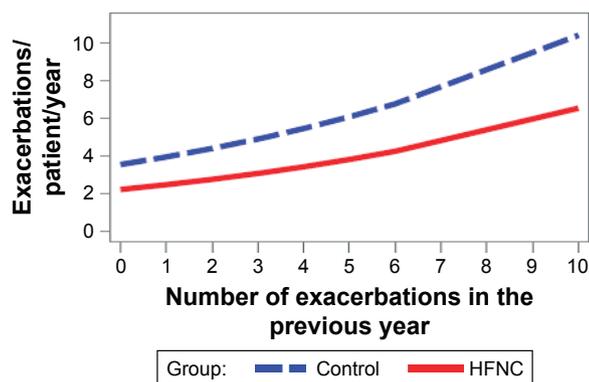
No adverse or serious adverse events were recorded.

### Exacerbations and hospital admissions

AECOPD rates were significantly lower in the HFNC group than the control group, 3.12 versus 4.95/patient/year,  $p < 0.001$  (Figure 2A).

A reduction in AECOPD is also seen with increasing use of HFNC ( $p < 0.001$ ), using the actual number of days of the use of HFNC as an explanatory continuous variate (eg, zero for the control group; Figure 2B). This predicts an AECOPD rate of 4.78/patient/year for zero use and 2.89/patient/year for 1 year of use for the average patient with 3 AECOPDs in the previous year.

There was no significant group difference in hospital admission rates (placebo: 1.22/patient/year, HFNC: 1.08/patient/year,



**Figure 3** Fitted values, based on number of exacerbations in the year prior to study, of the expected number of exacerbations with zero use (blue dashed) and the HFNC-treated (red solid).

**Abbreviation:** HFNC, high-flow nasal cannula.

$p = 0.373$ ; Figure 2C). However, using the actual number of days of the use of HFNC as an explanatory continuous variate (eg, zero for the control group; Figure 2D), a reduction in hospital admissions was seen (using previous year admissions as baseline covariate), which predicts an admission rate of 1.39/year for zero use and 0.79/year for 1 year of use for the average patient with 1 admission in the previous year ( $p > 0.001$ ).

Figure 3 shows, in a fitted model, how the study year exacerbation rates relate to the previous year's exacerbations,  $p < 0.001$ , by the treatment group.

### mMRC score

Fitted change in mMRC score for HFNC-treated patients and controls over the 12-month period is shown in Figure 4A. At 3 months, HFNC-treated patients had improved mMRC scores ( $p < 0.05$ ), and from 3 months onward they had lower mMRC scores compared to controls ( $p < 0.001$ ).

### QoL

Changes in SGRQ total score are shown in Figure 4B. HFNC-treated patients were stable, while controls had a clinically significant deterioration of 4.38 over 12 months. As such, HFNC-treated patients had better SGRQ at both 6 ( $p = 0.002$ ) and 12 months ( $p = 0.033$ ) compared to controls.

### PaCO<sub>2</sub>

Fitted means for PaCO<sub>2</sub> are plotted in Figure 4C. Over 12 months, PaCO<sub>2</sub> for HFNC-treated patients decreased while it increased for controls, resulting in a significant difference between groups at 12 months ( $p = 0.005$ ). At baseline, a 0.29 kPa reduction in PaCO<sub>2</sub> was seen after 30 minutes of HFNC treatment. Similar reductions were seen at 6 (0.28 kPa) and 12 months (0.26 kPa).

### 6MWT

Fitted means for 6MWT are shown in Figure 4D with a significant difference at 12 months,  $p = 0.005$ , excluding non-walkers. No differences were seen in Borg score or HR.

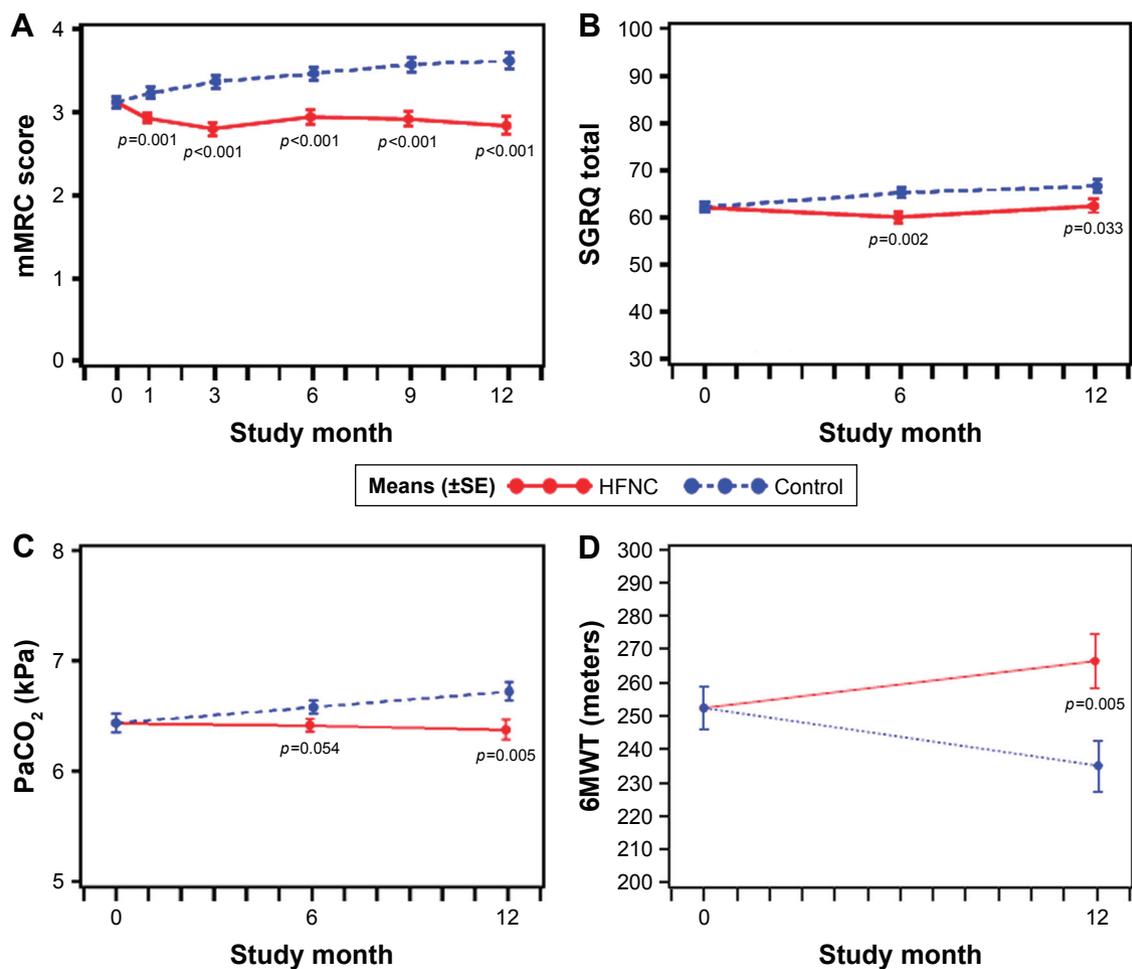
### Lung function, oxygen levels and BMI

A tendency toward increased FEV<sub>1</sub> in HFNC-treated patients at 6 and 12 months was seen relative to controls ( $p = 0.084$  and  $p = 0.056$ , respectively). A minority of HFNC-treated patients required LTOT oxygen flow rates to be increased. At baseline, this was 15 patients (1.0 ± 0.5 L/min), at 6 months 11 patients (1.2 ± 1.0 L/min) and at 12 months 9 patients (1.2 ± 1.1 L/min). The decrease in the number of patients requiring increased oxygen flow on HFNC was mainly due to dropout.

There were no significant differences in baseline-adjusted changes in FVC%, FEV<sub>1</sub>/FVC, pH, PaO<sub>2</sub> or SaO<sub>2</sub> between the groups at 6 or 12 months. A significant increase in BMI in HFNC-treated patients compared to controls was seen at 6 months (25.7 versus 25.3, respectively,  $p = 0.04$ ). However, this was no longer present at 12 months.

### Mortality

There was no difference in all-cause mortality between treatment groups; 15% for HFNC-treated patients and 12% for controls ( $p = 0.636$ ; Figure 1). In the HFNC group, 4 out of 15 patients discontinued treatment prior to and not in connection to death. No association was found between all-cause mortality and exacerbations.



**Figure 4** Fitted data on mMRC score (A), SGRQ (B), arterial partial pressure of CO<sub>2</sub> (C) and 6MWT (D), in high-flow, humidified, nasal cannula delivered oxygen (HFNC) patients (red solid line) or controls (blue dashed lines) during the study.

**Notes:** Dots represent assessment times. p-values show differences between the HFNC and control groups.

**Abbreviations:** HFNC, high-flow nasal cannula; mMRC, modified Medical Research Council; 6MWT, 6-minute walk test; SE, standard error; SGRQ, St George's Respiratory Questionnaire.

## Discussion

This is the first study reporting on 12 months of treatment of LTOT-treated COPD patients using HFNC in a home setting.

In this study, for COPD patients who were prescribed LTOT, consistent use of HFNC significantly reduced AECOPD and hospitalization. Furthermore, HFNC significantly reduced mMRC score and preserved SGRQ and 6MWD, while the control group measures deteriorated. A reduction in PaCO<sub>2</sub> was seen in HFNC-treated patients with significant differences in PaCO<sub>2</sub> levels at 12 months compared to controls. Finally, no significant difference was seen in all-cause mortality between the 2 groups.

The significant reduction in AECOPD in HFNC-treated patients compared to controls is in agreement with a previous study by Rea et al,<sup>19</sup> where HFNC significantly increased time to first exacerbation. However, Rea et al's study differs in 2 important ways from this study. First, the study population; Rea et al's study included a mixed population of patients with obstructive lung diseases with better lung function and few with hypoxic failure compared to those included in this study. AECOPD is known to be the strongest predictor for future exacerbations,<sup>29,30</sup> and patients with chronic hypoxemic respiratory failure are known to be even more susceptible to AECOPD than normoxic patients,<sup>29,31</sup> consistent with the control group in this study where the number of AECOPD events increases over time. However,

HFNC significantly reduced the risk of AECOPD, with the risk reducing with increasing with HFNC treatment time. In our opinion, this strongly supports the preventive effect of HFNC treatment on exacerbations, even in very severe COPD patients. HFNC may therefore prove to be a novel and an effective non-pharmacological treatment adjunct for this group of very severely ill patients.

Second, in Rea et al's study, HFNC was only used 1-2 hours/day, compared to the current study with an average use of 6-7 hours/day. While Rea et al's study did not find a significant reduction in exacerbations, this study did. This indicates that the duration of the use of HFNC is important for the reduction in AECOPD. However, this needs further scientific substantiation.

In this study, mMRC score improved significantly throughout the study period in HFNC-treated patients in contrast to controls, where a deterioration was observed. Even when following recommended medical treatment, dyspnea is one of the most common symptoms of severe COPD with a large impact on patient lives.<sup>32,33</sup> The most effective treatment of dyspnea is rehabilitation,<sup>34</sup> yet adherence is difficult in more severely ill patients.<sup>35</sup> In a recent Cochrane review, the effect of oxygen treatment on dyspnea proved to be modest.<sup>36</sup> The observed effect of HFNC on symptoms is therefore notable and substantiates the role of HFNC treatment in COPD chronic care.

This study provides a rare and thorough description of the development in clinical features and patho-physiological findings in advanced COPD patients with hypoxic failure. Despite the control group receiving the recommended treatment for this patient group, they still experienced increased hypercapnia, decreased lung function, walking distance and QoL. This is consistent with previous findings and is associated with poor prognosis.<sup>37</sup> This study demonstrates that the long-term HFNC treatment decelerates disease progression, as seen with 6MWD, QoL and PaCO<sub>2</sub>. The significant difference in PaCO<sub>2</sub> between the HFNC-treated and controls after 12 months is consistent with a recent study by Nagata et al,<sup>38</sup> despite only half the patients being hypercapnic at inclusion. In comparison, in a recent meta-analysis on nocturnal NIV, an alternative add-on treatment for severe COPD patients with hypercapnic failure, there were no significant differences between the treatment and control groups in 6MWD, QoL or PaCO<sub>2</sub> after 12 months of treatment.<sup>39</sup> This suggests that HFNC may be superior to NIV in slowing disease progression, although further investigation is required to substantiate this. The physiologic mechanism behind these improvements is as follows: as a flow of 20 L/min provides a positive expiratory pressure (PEP) of less than 2 cm H<sub>2</sub>O,<sup>17</sup> the PEP effect is possibly of lesser importance. Despite providing open circuit ventilation, HFNC has been shown to increase inspiratory tidal volume in COPD, especially when used during daytime use,<sup>40,41</sup> whereas nighttime use has been shown to relieve respiratory load.<sup>41</sup> Clearance of anatomical dead space is probably important for the reduction in PaCO<sub>2</sub>.<sup>42</sup> However, the most important effect in COPD chronic care is most likely improved mucociliary clearance, driven by the humidification of the air delivered by high flow to distal airways.<sup>17</sup> This may enhance recruitment, improve alveolar ventilation and reduce patients' respiratory workload. All these mechanisms together would decrease the patients' sensation of dyspnea and thereby increase physical ability and, as previously indicated, reduce exacerbations.<sup>19,43</sup> As such, this study suggests that HFNC should be a treatment used in conjunction with LTOT in COPD patients with hypoxic failure to reduce exacerbations and maintain health status in general.

The daily duration of the use of HFNC increased when patients included nighttime use. Recommended flow was based only on the experience of patients' tolerability; therefore, further investigation is needed. However, based on this study, we recommend that the use should preferably be during sleep, with a flow of at least 20 L/min.

This study has some limitations. A randomized blinded study could have been wished for, however, blinding the patients against the flow, the heat and the humidity is not realistic. Data on active hours of use of LTOT may have been interesting; however, oxygen delivery device actual use is not currently available, and patients' self-report usage is inaccurate.

Recall bias is possible for AECOPD, and patients' activities, such as rehabilitation, could influence results if not evenly distributed within the 2 groups. Differences in prescribed medicine and participation in rehabilitation could also potentially influence results. However, as patients were randomly allocated to the HFNC and control groups, were all treated according to guidelines, including referral to vaccination and rehabilitation according to national guidelines<sup>44</sup> and received the same standard of care and visits from the LTOT homecare company, we expect this to be similar between the 2 groups.

The recommendation of 8 hours of the use of HFNC has no real scientific background. The only previous long-term study recommended 2 hours of use per day, resulting in 1.6 hours of use on average. Studies on LTOT compliance have showed that mobility is important to obtain compliance, and this study shows that daytime users use HFNC significantly less than nighttime users. An average use of HFNC in patients including nighttime use close to the recommended 8 hours does tell us that this is applicable. However, further studies are needed to decide the duration of optimal use. Furthermore, this study allowed both day- and nighttime use of HFNC. The physiological mechanisms of HFNC have previously been suggested to be different at day- and nighttime, however, this study was performed in healthy individuals and the population therefore not necessarily comparable to our study population.<sup>41</sup> A comparison of the effect of day- and nighttime use would be ideal, but was not performed in this study as differences in duration of use also occur between day- and nighttime use.

One-seventh of the HFNC group ceased treatment within the first month, although only 3% left the study population completely, while 44% of the study population discontinued the use of HFNC during the observation period. However, more than one-quarter of those who discontinued died during the study. This is substantial, but consistent with prospective studies of NIV on comparable patient populations with similar treatment durations in the home.<sup>45,46</sup> There is of course a risk that those who were non-adherent were patients who did not feel any physical amelioration, or even felt worse, using HFNC. However, as results from the treatment group also included those who discontinued use of HFNC but stayed in study and as overall study time was similar between the treatment groups and controls this is not a likely explanation. Retention rates on this study were similar, but by definition, patients remained in the control arm longer than in the HFNC arm. Therefore, group comparisons were as randomized and more in line with an intent-to-treat paradigm. The analyses of exacerbations and admissions using actual days of the use of HFNC (eg, zero for the control group) were closer to a per-protocol paradigm.

The choice of included variables is always contentious. As such, the use of other established symptom scores, eg, the COPD assessment test, could have substantiated and elaborated description of patients' symptoms. In addition, the clinical relevance of some of the changes, ie, PaCO<sub>2</sub>, is arguable. The changes did not lead to significant changes of pH; perhaps patients were able to compensate. However, PaCO<sub>2</sub> levels have previously been shown to affect the outcome of AECOPD in patients with chronic hypoxemic respiratory failure,<sup>47</sup> even when the PaCO<sub>2</sub> values were lower than those demonstrated in this study. Therefore, the reduction in PaCO<sub>2</sub> could have clinical benefit.

## Conclusion

This study shows that in COPD with hypoxic failure treated with LTOT, adjunct HFNC therapy reduces exacerbations, admissions and symptoms. In addition, HFNC stabilizes the clinical condition of advanced COPD patients, but does not improve all-cause mortality. In future, HFNC should therefore be considered a beneficial adjunct to the recommended treatment of COPD patients with chronic hypoxemic respiratory failure.

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### Author contributions

Line Hust Storgaard participated in conception and design, data collection and drafting the manuscript for important intellectual content. Hans-Ulrich Hockey participated in conception and design, analysis and interpretation and drafting the manuscript for important intellectual content. Birgitte Schantz Laursen participated in conception and design and drafting the manuscript for important intellectual content. Ulla Møller Weinreich participated in conception and design, data collection, analysis and interpretation and drafting the manuscript for important intellectual content. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

### Disclosure

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# These RT Students Overcame Incredible Obstacles on their Paths to Graduation

Jim Bierl RRT-NPS

In my long career as respiratory therapist and educator, I have met many wonderful students who have gone on to make formidable professional careers. Many have a unique reason or story behind why they wanted to become a respiratory therapist and many have overcome great obstacles along the way.

This spring our program will graduate two young ladies whose unique stories are an inspiration. The obstacles they have endured and how they overcame them to lead them to this point have been a lesson in strength and courage for all of us.

## Brianna's Story

It was the fall of 2014 when Brianna was diagnosed with a simple case of mononucleosis. She had been ill for only a short time, but it seemed she was getting worse very quickly. She was rushed to the ER when it was discovered her spleen had ruptured. From there she was quickly transported to the Woman's Children Hospital of Buffalo.

She continued to deteriorate over the next couple of days and became septic and was going into multi-organ-system failure. Now intubated and on mechanical ventilation, her doctors wanted to place her on ECMO. Her parents had never heard of ECMO and were told that it was her only option. Scared and nervous, they made the decision and consented to the procedure.

“Because of ECMO and the incredible staff at Children's Hospital, Brianna survived.”

Even though they were told of the risks involved, they were not prepared for all that came with it. During the procedure Brianna went into cardiac arrest, not once but twice and had to be resuscitated.

“I will never forget the first time they allowed us to see Brianna. Her body was traumatized. It had ballooned three to four times her normal size. Her left eye was purple and swollen shut. This was not our beautiful, athletic, strong, healthy daughter. How could this be happening.”

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Jim Bierl RRT-NPS, Program Director, Respiratory Care Program, Erie Community College.

Brianna was trached and remained on ECMO for 2-1/2 weeks.

She was eventually discharged 2 months later and transferred to a nearby facility for rehabilitation. She lost vision in her one eye but grew stronger in time. She has little memory of everything she went through, but her parents do remember. They are grateful to the doctors, nurses, respiratory therapists and staff for the wonderful care she received.

“Because of ECMO and the incredible staff at Children's Hospital Brianna survived.”

Incredibly, Brianna came to see me the summer after her experience. Being 18, she wanted to get back on track and started looking at careers. She came across the Respiratory Therapy profession, she knew it sounded familiar, but she could not remember why. She soon realized that Respiratory Therapists had helped her during her hospital stay. There were in the ICU and manned her ECMO pump as well. She did a little more digging into the program and soon applied.

I remember the day she first came to see me about the program. She told me her story and I soon realized she was someone special.

Brianna started taking classes and began our program in fall 2017. She graduated in the spring of 2019.

Over the last several years, Brianna and her family have acted as advocates and even counselors for other families facing similar decisions. They continue to work with the hospital and share their experiences and offer hope to other families facing the same decisions they did. One such dad told me that Brianna and her mom came to see them in the hospital just prior to his young daughter being placed on ECMO. “They came at my darkest hour and gave me hope.”

Brianna's strength and determination will serve her well in the future. She will bring a high level of empathy and compassion to the patients she treats.

I know what it is like to be on the other side. I can relate when the patient needs to use the bathroom or what it's like to be woken up at night to receive care, the uncomfortable feeling of being suctioned and how it feels to not have a visitor and feeling alone.

## Emma's Story

Emma's story is very different, but her strength and courage are equally remarkable.

Born in 1992, she was immediately intubated, mechanically ventilated, then transported to the Children's Hospital of Buffalo. Within a couple of months, she was trached and diagnosed with congenital central hypoventilation syndrome.

Upon discharge, she had 24-hour nursing care for the first several months. Her parents became actively involved, learning trach care and began taking care of her during daytime. When she began school, a nurse attended until 4th grade. After that, school nurses had to be trained on trach care.

To say her childhood was not a normal one would be an understatement. Like other children she would get sick but because of her diagnosis, she would get hospitalized often and sometimes for long periods.

When Emma was 10 years old, her dad began our Respiratory Care Program. When we met, he told me he wanted to become a therapist so he could continue to care for his daughter. Her dad graduated in 2004 and continues to practice today. Emma continued to grow and thrive thanks to the wonderful care she received from her parents.

When Emma was 15 years old, she and her parents made the decision to decannulate and go on BIPAP. She began a 3-month trial of BIPAP with a capped tracheostomy tube. This decision was considered risky at the time, but she and her family wanted to normalize her life as much as they could. The emergence of new and better technology made this more possible and her father understood that.

“As a respiratory patient, I know what it feels like to be suctioned, to be vented, to have your trach changed, to wear a mask every night and to be a child experiencing these things.”

In 2011 she had a pacemaker placed for precautionary reasons when genetic testing found she was predisposed to cardiac pauses after experiencing fainting spells during childhood.

After high school she began college as an English major, but her interest in sciences and particularly to the respiratory system brought her to our program.

“I wanted to know the normal function of breathing and how mine was different. I wanted to know how my vent worked, what the settings meant, what exactly was being suctioned out of my trach and what they were listening for with the stethoscope.”

Emma eventually decided she not only wanted to know more about the respiratory system, she wanted to help those living with pulmonary diseases.

Emma started our Respiratory Care Program in 2017 and plans to graduate with Brianna this past May. She has been a great addition to our program, as we have often learned from her.

“As a respiratory patient, I know what it feels like to be suctioned, to be vented, to have your trach changed, to wear a mask every night and to be a child experiencing these things. I only want to make the best out of these experiences, to draw from them for greater empathy towards my patients and share my knowledge to assure them and perform every treatment and task with patient comfort in mind.”

I will be proud to see these young ladies receive their diplomas this spring. I know both will bring a genuine sense of empathy and understanding to wherever they end up and especially to all the people they care for. Their experiences are an invaluable asset as they begin their journey into the profession.

# The 9 Nevers of Nasal Suctioning Protocol and Suction Catheter Induced Nasal Trauma (SCINT)

Nicholas Pastron, CEO, NJR Medical Inc.

Many clinicians use Nasotracheal (NT) & Nasopharyngeal (NP) suctioning for patients having difficulty with secretion clearance.<sup>1</sup> NT & NP suctioning can help avoid intubations, keep your extubated patients extubated and also ensure your end-of-life care patients breath more comfortably.<sup>1-5</sup> Most clinicians are familiar with NT & NP suctioning because it is commonly done in the critical care area.<sup>1</sup> But many are not familiar with the dangerous incidents and sentinel events that have occurred due to the nasal suctioning of contraindicated patients.<sup>6-12</sup>

Implementing “The 9 Nevers of Nasal Suctioning Protocol” into your existing suctioning protocol will help you:

1. Educate and raise awareness of contraindications to nasal suctioning
2. Implement a pre-procedural screening tool using “The 9 Nevers of Nasal Suctioning” to identify contraindicated patients
3. Flag contraindicated patients to prevent nasal suctioning on them
4. Provide an alternate route to nasal suctioning, using a No-Bite V™ (suction catheter introducer for oropharyngeal and oral airway suctioning)
5. Prevent incidents and sentinel events related to nasal suctioning

## The 9 Nevers of Nasal Suctioning:

1. **Suction Catheter Induced Nasal Trauma (SCINT)**<sup>1,6,8,13-15</sup>
  2. **Anticoagulation**<sup>1,2,5</sup>
  3. **Coagulopathy Issues**<sup>1,2,5</sup>
  4. **Colonization in Nares (MRSA)**<sup>16</sup>
  5. **Recent Nasal/Sinus Trauma, Fracture or Surgery**<sup>1,5,6</sup>
  6. **Facial or Head Trauma/ Basal Skull Fracture**<sup>1,5,6,17</sup>
  7. **Transsphenoidal Neurosurgery**<sup>12,17</sup>
  8. **End-of-Life Care**<sup>1,6,8,13-15,18</sup>
  9. **Occluded Nasal Passages/Deviated Septum**<sup>1,5</sup>
- If answered yes to any of the above 9, flag patient, by placing a sign above bed: **DO NOT NASAL SUCTION**
  - **Avoid NT & NP suctioning altogether**
  - **Use The No-Bite V™ (suction catheter introducer for the oral airway) as an alternative to nasal suctioning**



**Figure 1.** Photos from a SCINT case in a CA hospital where the patient was NT suctioned for aspiration pneumonia. He was on Aspirin, bled for 90 mins, lost approximately 700 ml of blood and required a blood transfusion. This incident required an ENT physician to perform an emergent nasal packing procedure at bedside.

## 1. SCINT – Suction Catheter Induced Nasal Trauma

SCINT is usually due to frequent NT or NP Suctioning, but can also be caused by just 1 suctioning experience. Nasal Suctioning can cause irritation, inflammation, mucous membrane breakdown and pain.<sup>1,6,8,13-15</sup> This can ultimately result in severe nasal trauma & bleeding.<sup>1,6,8,13-15</sup>

### SCINT – Contributing Factors & High-Risk Patients

#### I. Frequent Suctioning Needs

Patients with frequent suctioning needs receive more nasal friction and ultimately can develop mucous membrane breakdown.<sup>6,15</sup>

Conditions that may require frequent suctioning are:

- a. Pneumonias and other Respiratory Infections
- b. Dysphagia & Chronic Aspiration Patients
- c. ALS – Amyotrophic Lateral Sclerosis

**Inspiration** is credited to the amazing RT's and RN's at The Cleveland Clinic, NYU Langone Health, RWJ–Barnabas Health, Kaiser Permanente San Jose, Rush University Medical Center, Banner Health–University Medical Center Tucson, Ascension Via Christi Hospital–St. Francis & Nationwide Children's Hospital.

We could not have created this protocol without your knowledge and many years of experience using the No-Bite Suction. We are constantly learning from you all.

Thank You,  
Nicholas Pastron, CEO  
NJR Medical Inc.

- d. CF – Cystic Fibrosis
- e. CVA – Strokes with Dysphagia
- f. MND – Motor Neuron Diseases
- g. MS – Multiple Sclerosis
- h. MD – Muscular Dystrophy
- i. TBI – Traumatic Brain Injury
- j. ID – Intellectual Disability

## II. Fragile

To no fault of any clinician, another main cause of SCINT is the “fragility of the patient”. There are many documented cases of patients that developed nasal trauma, bleeding and pain following nasal suctioning.<sup>1,6,8,13-15</sup>

Although any patient classified under **The 9 Nevers of Nasal Suctioning** may be considered fragile, we found it necessary to label the below populations as **High-Risk SCINT Patients**:

- a. Cancer Patients – who have received Chemotherapy or Radiation
- b. Long-Term Steroid Patients
- c. FTT Elderly – Failure To Thrive
- d. Chronically Ill
- e. Terminally Ill

## III. Coiling Suction Catheters

Another contributing factor to SCINT is coiling of suctioning catheters upon insertion, leading to multiple additional attempts via the nares. Anatomical anomalies of the nares exist and can cause the occurrence of coiling suction catheters.<sup>1,5</sup>

On semi-awake patients, a cough reflex can be triggered and the patient can coil the suctioning catheter by coughing it out.

## IV. Uncooperative Patients

Uncooperative patients, sometimes unaware of their surroundings, can purposely tongue-out the suction catheter. Whether confused or sedated, patients may resist suctioning because they do not understand what is happening. Patients may become very difficult to suction, receive sedation or even require a second clinician for restraining.

**Key Point** – Look for signs and symptoms of SCINT. If you see SCINT, STOP nasal suctioning and consider The No-Bite V™ Suction.

## 2. Blood Thinners

Bleeding complications are a common concern of any patient on anticoagulants or platelet inhibitors. Many recommend these patients do not blow their nose too hard,<sup>19</sup> let alone insert a suction catheter into their nose.

The two most common types of blood thinners are Anticoagulants and Antiplatelets.

- **Anticoagulants:** These medicines increase the time it takes for a blood clot to form. These medicines include:<sup>19</sup>
  - a) Warfarin (Coumadin or Jantoven)<sup>19</sup>
  - b) Heparin<sup>19</sup>
  - c) Dabigatran (Pradaxa)<sup>19</sup>

- d) Rivaroxaban (Xarelto)<sup>19</sup>
- e) Fondaparinux (Arixtra)<sup>19</sup>
- f) Enoxaparin (Lovenox)<sup>19</sup>
- g) Dalteparin (Fragmin)<sup>19</sup>
- h) Apixaban (Eliquis)<sup>19</sup>
- i) Edoxaban (Savaysa)<sup>19</sup>

- **Antiplatelets:** These medicines prevent the platelets in your blood from sticking together and forming a blood clot. These medicines include:<sup>19</sup>

- a) Aspirin<sup>19</sup>
- b) Clopidogrel (Plavix)<sup>19</sup>
- c) Ticagrelor (Brilinta)<sup>19</sup>
- d) Ticlopidine (Ticlid)<sup>19</sup>
- e) Prasugrel (Effient)<sup>19</sup>
- f) Pletal (Cilostazol)<sup>19</sup>

**Key Point** – Find out if your patient is on blood thinners. Check your patient’s labs for elevated PT, INR, & PTT levels. Also, if your patient on blood thinners has not had their labs checked recently, we recommend avoiding nasal suctioning in the event the labs are elevated.

## 3. Coagulopathy Issues

- a. Thrombocytopenia-low platelet count – below 150,000 platelets per microliter (mcl)<sup>20</sup>
  - Aplastic Anemia<sup>20</sup>
  - Vitamin B-12 Deficiency<sup>20</sup>
  - Folate Deficiency<sup>20</sup>
  - Iron Deficiency<sup>20</sup>
  - Viral infections, HIV, Epstein-Barr and Chickenpox<sup>20</sup>
  - Chemotherapy, Radiation, or Toxic Chemical Exposure<sup>20</sup>
  - Liver Cirrhosis secondary to Chronic Alcoholism or Hepatitis C<sup>20</sup>
  - Leukemia<sup>20</sup>
  - Myelodysplasia<sup>20</sup>
  - Platelet Destruction – Autoimmune vs Medication Side Effect<sup>20</sup>
  - Heparin Induced Thrombocytopenia (HIT)<sup>20</sup>
  - Disseminated Intravascular Coagulation (DIC)<sup>20</sup>
- b. Hemophilia A & B (clotting factor deficiency)<sup>21</sup>
- c. Factor II, V, VII, X, or XII deficiencies (clotting factor deficiency)<sup>21</sup>
- d. Von Willebrand’s Disease (Von Willebrand factor deficiency)<sup>21</sup>

**Key Point** – Check your patient’s history for blood disorders and low platelet counts. Also look for elevated lab levels of PT, INR, & PTT.

## 4. MRSA Colonization in Nares

NT or NP suctioning a patient with a nasal MRSA colonization is contraindicated because most patients who develop MRSA infections will have been colonized prior to infection.<sup>16</sup> Many hospitals are systematically nasal swabbing all patients for MRSA upon admission. Nasally inserting a suction catheter could advance nasal MRSA down into the trachea or lungs, which could lead to a MRSA respiratory infection.<sup>16</sup>

Methicillin resistant *Staphylococcal aureus* (MRSA) infection continues to be a leading cause of morbidity and mortality among hospitalized patients, especially in those who are critically ill.<sup>16</sup> In the most recent National Healthcare Safety

Network (NHSN) report spanning the years 2009-2010, MRSA was the most commonly isolated (18%), and was the number one pathogen causing Ventilator-associated pneumonias (VAP) and surgical site infections (SSI).<sup>16</sup> MRSA has become endemic in health care institutions worldwide, with up to 70% of invasive *S. aureus* infections caused by resistant strains.<sup>16</sup>

Although the health field has yet to completely understand it, some MRSA Colonization Risk Factors are:

- a. Patients with previous admissions to hospitals<sup>16</sup>
- b. Presence of chronic wounds<sup>16</sup>
- c. Patients from nursing homes<sup>16</sup>
- d. Long term stays at other healthcare facilities<sup>16</sup>
- e. Previous use of urinary or intravenous catheters<sup>16</sup>

**Key Point** – Check your patient’s history and labs for a MRSA (+) positive Nasal Swab.

## 5. Recent Nasal Trauma/Fracture/Sinus or ENT Trauma/ Surgery

Due to a high risk of inflicting trauma, NP and NT suctioning is contraindicated in any patient with:<sup>1,5,6</sup>

- a. Nasal trauma<sup>1,5,6</sup>
- b. Nasal fracture<sup>1,5,6</sup>
- c. Nasal surgery<sup>1,5,6</sup>
- d. Sinus infection<sup>1,5,6</sup>
- e. Sinus surgery<sup>1,5,6</sup>
- f. Disorders involving the sinuses<sup>1,5,6</sup>

**Key Point** – Check your patient’s history for nasal or sinus issues.

## 6. Facial or Head Trauma/Basal Skull Fracture

Auto accidents are a frequent cause of basilar skull fractures. Other causes include assaults and violence, motorcycle accidents, bicycle accidents, slip and fall accidents, or any other direct blow to the head. Occurring in 4% of severe head injury patients, you may provide care for basal skull fracture patients.<sup>1,5,6,17, 22,23</sup>

### Signs and symptoms

- a. Battle’s sign — ecchymosis behind the ear<sup>22,23</sup>
- b. Raccoon eyes — periorbital ecchymosis ie “bilateral black eyes”<sup>22,23</sup>
- c. Cerebrospinal fluid rhinorrhea – A patient experiencing a CSF leak may state they taste a “metallic taste” or “salty taste”<sup>22,23</sup>
- d. Cranial nerve palsy – limited eye movement, double vision, dilated pupils, droopy eyelids<sup>22,23</sup>
- e. Bleeding from the nose and ears<sup>22,23</sup>
- f. Hemotympanum – presence of blood behind eardrum<sup>22,23</sup>
- g. Conductive or perceptive deafness, nystagmus, vomitus<sup>22,23</sup>
- h. Optic nerve entrapment causing irregularities in vision<sup>22,23</sup>

**Key Point** – Check your patient’s history for facial or head trauma. Also look for the above signs and symptoms of potential Basal Skull Fracture.

## 7. Transsphenoidal Neurosurgery

Transsphenoidal surgery is a type of surgery in which surgical instruments are inserted into part of the brain by going through the nose and drilling out the sphenoid bone (a butterfly-shaped bone at the base of the skull).<sup>12,17</sup> Transsphenoidal surgery is used to remove tumors of the

pituitary gland and is usually patched up with a piece of fat from the abdomen.<sup>12,17</sup> With an average of about 5,500 patients undergoing transsphenoidal operations every year in the US, you may provide care to transsphenoidal surgery patients, especially if your hospital has a neurosurgery program.<sup>12,17</sup>

Transsphenoidal surgery patients are always considered contraindicated to NP or NT suctioning. A catheter can easily pass through the fat plug and enter the intracranial space. In 2014, this exact incident was documented, ultimately leading to the patient’s death.<sup>12</sup>

**Key Point** – Check your patient’s history for Transsphenoidal Neurosurgery or any mention of pituitary gland surgery.

## 8. End-of-Life Care

End-of-Life Care is a term that encompasses Comfort Care, Terminal Weaning, Palliative Care and Hospice. The general thought is that clinicians should try to avoid NT or NP suctioning when possible due to the potential pain and nasal trauma that can easily be caused in End-of-Life Care.<sup>1,6,13-15</sup> Dying patients can become especially fragile and causing nasal trauma goes against the sole purpose of comfort care.

In certain instances, secretions can build up and the family may perceive the patient sounding like they are “drowning to death” in their own secretions.<sup>18</sup> This is usually referred to as the “Death Rattle” and can be a very unnerving experience for the family.<sup>18</sup> Clinicians usually apply medication patches to dry up the secretions in this population.<sup>18</sup> But if the patient had an existing pneumonia with copious secretions, medications may not work and suctioning may be needed.<sup>18</sup>

In the above situations, The No-Bite V™ (suction catheter introducer) has been proven to be a more comfortable suctioning experience compared to nasal suctioning.<sup>18</sup>

**Key Point** – NT & NP suctioning of End-of-Life Care patients should be avoided due to the additional pain and trauma that nasal suctioning can cause.

## 9. Occluded Nasal Passages/Deviated Septum<sup>1,5</sup>

Sometimes a patient may list a history of deviated septum or occluded nasal passages, but many times they may not even know. This leaves you with a trial and error approach, which is not the most ideal situation.

**Key Point** – Check your patient’s history for deviated septum or occluded nasal passages. And if you are in a situation where you are performing NT or NP suctioning and feel an obstruction or resistance, stop the procedure.

## Implementation Of Protocol

1. Add “The 9 Nevers of Nasal Suctioning Protocol” to your existing NT & NP suctioning protocol.
2. Implement a pre-procedural screening tool to identify contraindicated patients. Use our Screening Tool by simply cutting it out and making copies for your staff.
3. Flag contraindicated patients to prevent nasal suctioning on them, by placing signage above their head of bed, stating, “DO NOT NASAL SUCTION”.
4. Provide an alternate route to nasal suctioning, using a

No-Bite V™ (suction catheter introducer for oral airway suctioning).

### Implementing The No-Bite V™ in your Facility

Coordinate an in-service with NJR Medical. A clinical specialist will provide education on “The 9 Nevers of Nasal Suctioning” Protocol as well as technique of the device. Return demonstrations will be allotted for your RT & RN staff on an anatomically correct mannequin head.

### Note from the Author

The 9 Nevers of Nasal Suctioning Protocol is not a complete list of **ALL** NT suctioning contraindications. It is intended to identify patients with nasal route suctioning contraindications that can still be deep suctioned via the oral route with the No-Bite V™.

According to the AARC Guideline: Nasotracheal Suctioning 2004, there are other suctioning contraindications in which a patient should not be deep suctioned by any method:<sup>24</sup>

### Contraindications to deep suctioning by any method

1. Epiglottitis or Croup<sup>1,5,24</sup>
2. Laryngospasms,<sup>1,5,24,25</sup> Bronchospasms<sup>6,24</sup>
3. Irritable Airway<sup>1,24</sup>
4. Upper Respiratory Tract Infections<sup>1,24</sup>
5. Neck or Tracheal Injury/Surgery<sup>5,24</sup>
6. Gastric Surgery with High Anastomosis<sup>5,24</sup>
7. Myocardial Infarction (MI)<sup>5,24</sup>
8. Acute Head or Neck Injury with risk of increasing Intracranial Pressure<sup>1,5,6, 24-32</sup>

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# Improving Home COPD Monitoring Through Statistical Process Control (SPC)

Alex Stenzler

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a group of progressive lung diseases that obstruct airflow. It is the third leading cause of death in the United States, affecting 16 million Americans and millions more who are not aware they have the disease.<sup>1</sup> The American Lung Association (ALA) states that there may be as many as 24 million American adults living with COPD.<sup>2</sup> Over 800,000 hospitalizations each year in the U.S. are related to COPD. In 2015, 3.2 million people died from COPD worldwide, an increase of 11.6 % compared with 1990. During that same time period, the global prevalence of COPD increased by 44.2 % to 174.5 million individuals.<sup>3</sup>

Integral to the management of patients with COPD is the development of new and effective treatments, as well as the monitoring of these patients to identify exacerbations and enable early intervention. The burden of COPD on US healthcare systems has been moving these patients back to their homes earlier, which increases the need for technology that is able to monitor these patients at home. This home monitoring has increased the need for hospital laboratory quality lung function monitoring collection from patients without onsite technical assistance, so that meaningful and actionable data can be used to intercede early when pulmonary degradation is identified.

Forced Vital Capacity measurements (Forced Spirometry) are the standard for evaluating dynamic lung function in COPD. It requires that patients take a maximum inhalation to Total Lung Capacity and then forcefully blow out all the air in their lungs as hard and as fast as they can, for at least six seconds and frequently longer. To perform this correctly, all of their respiratory muscles, including their diaphragm, abdominal and internal intercostals muscles must provide a maximum level of sustained contraction. Patients are expected to meet the ATS/ERS criteria for reproducibility, including three measurements

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that meet ATS/ERS standards for acceptability and two measurements where the FEV1 and FVC are within 150 mL of each other.<sup>4</sup> To meet these criteria, a patient may be requested to perform up to 8 measurements. Understandably, for most COPD patients the extended contraction of these muscles can be fatiguing.

The potential for fatigue during Forced Spirometry is well known and is usually occur whenever patients are required to perform serial spirometry measurements either within a short time frame, or very frequently. Fatigue is usually associated with bronchial provocation challenges, serial measurements in response to a drug dose, as well as when daily monitoring patients at home with respiratory dysfunction is required.

The major risks associated with fatiguing patients with COPD are that they either become unwilling to perform additional measurements to attain repeatability or that the fatigue of their muscles reduces their ability to perform maximum-effort measurements correctly when required to perform multiple measurement. In the worst situation the patient refuses to perform any measurements in anticipation of the fatigue from the FVC measurement. With the ability to monitor COPD patients being so important, adherence to frequent testing is the rate critical step to collecting the data and providing effective care.

## Monitoring Patients through Statistical Process Control

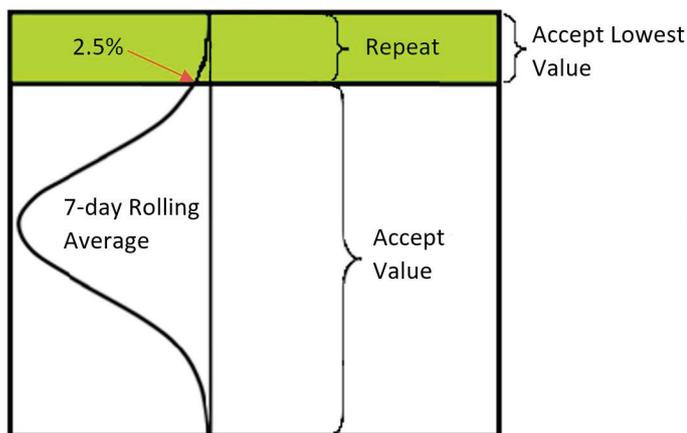
Statistical Process Control (SPC) is a set of statistical methods based on the theory of variation that enables the detection of changes in measurements following an extended period of collecting baseline data.<sup>5</sup> It can be used to detect, early on, whether any changes have occurred, long before results from larger evaluations are available and the modeling fits well with patient-centered medical home programs.

In 2013, Sirichana, Patel, Taylor, et al, presented work on a Statistical Process Control (SPC) algorithm approach for monitoring patients with COPD at home.<sup>6</sup> This SPC process enables patients to perform tests on a “daily” basis and not be either fatigued or annoyed at having to perform multiple measurements at each session.

The statistical process control (SPC) algorithm maintains a short history of past spirometry data (typically a seven-day rolling average from sessions of home monitoring or data from baseline testing). When a new measurement is collected, it is compared

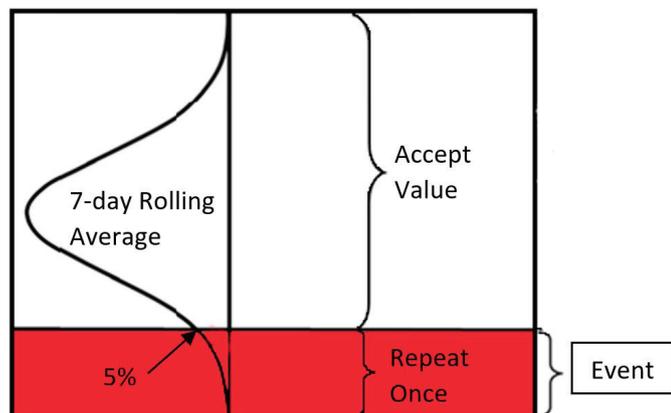
to the past data rolling average. If the new test data is within a Z-Score of 1.645 below to 1.96 above the previous data, the patient is done with a single measurement for that day or that session. Only if the data falls outside those limits is the patient required to perform additional test maneuvers. The higher cut-off value identifies the highest 2.5% of normally distributed values ( $P=0.975$ ). If the measured values are higher than this, subjects are asked to repeat the maneuver to assure that there was not a technical error. On the repeat measurement, the lowest of the two measures are accepted as the daily “Best” for inclusion in the rolling average (technical acceptability). (See figure 1).

**Figure 1.** This identifies measurements greater than 97.5% of all other measurements that might reflect a technical error that requires confirmation.



The lower cut-off value identifies the lowest 5% of normally distributed values ( $P=0.050$ ). If the measured values are lower than this, subjects are asked to repeat once. If the repeated value is above the threshold, then that value is accepted as the daily “Best” for inclusion in the rolling average. If lower again, a clinical event is identified. Lower limit events on two consecutive days can be considered as a marker of a potential exacerbation requiring further investigation by a healthcare professional (clinical event detection). (See figure 2).

**Figure 2.** This identifies measurements below 95% of all other measurements that might reflect a significant fall in function that also requires confirmation.



Sirichana enrolled 13 COPD patients in this pilot study with a mean (SD) age of 70.4 (7.3) years. Baseline FEV1 was 52.0% predicted (15.5%). The patients were initially monitored using ATS/ERS spirometry criteria, followed by a change to the

SPC algorithm criteria. They collected a total of 1,999 days of monitoring including 1,358 days of conventional monitoring using ATS/ERS spirometry criteria and 641 days of monitoring using the SPC algorithm. During the conventional monitoring (ATS) period, patients performed an average of 4.5 (0.5) maneuvers per day (range 3-5) as compared to 1-2 maneuvers per day during the SPC algorithm period. The time required of the patients for performing the spirometry tests was 13:05 (5:23) minutes per day with a 55.1% adherence during the ATS monitoring period as compared with only 6:37 (2:82) minutes per day but with an 85.6% adherence during the SPC algorithm period. (See table 1).

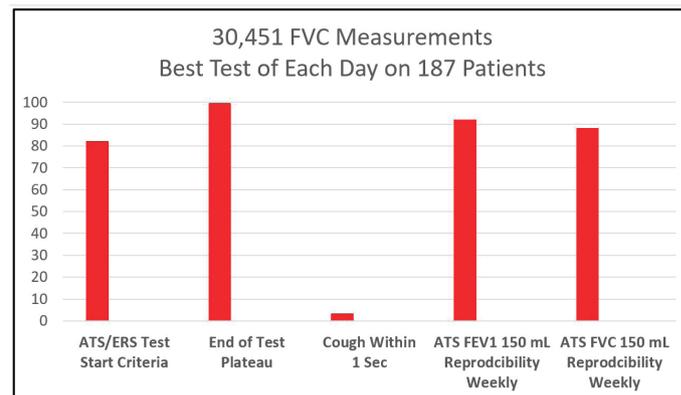
**Table 1.** Testing Time and Adherence to Forced Spirometry Monitoring (SD)

	ATS/ERS Criteria	SPC Algorithm
Number of Days Monitored	1358	641
Time per day (minutes)	13.05 (5.23)	6.37 (2.82)
Adherence	55.1%	85.6%

The group mean (SD) for FEV1 from the ATS/ERS maneuver period was 1.00 (0.45) L, which was comparable to that from SPC maneuver period, 0.99 (0.47) L ( $P = 0.995$ ). They detected 0.16/patient-year exacerbations during ATS/ERS monitoring compared to 1.01/patient-year during SPC monitoring.

In 2017, Taylor incorporated statistical process control into the spirometry monitoring platform of Monitored Therapeutics, Inc. (MTI) as part of the introduction of Avatar-Assisted-Technology to collect hospital laboratory quality spirometry from patients at home ([www.monitoredrx.com](http://www.monitoredrx.com)). A review of 30,451 forced spirometry measurements collected by MTI from patients at home with an analysis of the best measurement of each day, demonstrated that 82% met ATS/ERS criteria for start of effort including time to peak flow and back extrapolated volume and 99.5% of the measurements met end-of-test plateau. (See figure 3). A secondary analysis was performed of weeks where patients performed at least 3 measurements. There were 2,705 weeks when more than three measurements were performed (30,272 total measurements). In 92% of the weeks, the ATS/ERS 150 mL reproducibility requirements were met for FEV1 and 88% for FVC.

**Figure 3.** Home Monitoring Performance



## Conclusion

The use of a Statistical Process Control approach for monitoring  
*Continued on page 47...*

# Bag-Valve-Mask Tidal Volume and Lung Protective Ventilation Strategies

Steve LeCroy, MA, CRT, EMTP

In 2017 the “Resuscitation Academy Blog” touched on a High-Performance CPR program (HP-CPR) that was developed by the Resuscitation Academy. The Academy offers a week-long training program developed from resuscitation protocols created by Seattle and King County. The program has the following performance measures:

1. Depth of chest compressions (2.0-2.4 inches for an adult)
2. Ventilation volume (300-400 mL per ventilation)
3. Decompression (allow the chest to 100% recoil)
4. Chest compression rate of 100-120 per minute

Measures 1, 3 & 4 are standard measurements supported by significant research. However, measurement number 2, ventilation volume, is less clear and creates controversy over what size manual resuscitator should be used with adult patients. Does it make sense to use the same volume for all adult patients? Do respiratory arrest patients get the same volume as cardiac arrest patients? Everyone seems to agree that the standard adult manual resuscitator (1500-1600 mL) is too big and is one of the leading causes of over-ventilation. To compound the bag size problem there is no consistency across manufacturers regarding bag description and bag size. For example, Mercury Medical's® Child bag is 501 mL while Ambu's® Spur® II pediatric bag is 683 mL (Ambu® does not offer a child bag).

The HP-CPR guidance document does not mention the size of the patient. The question then becomes does patient size matter? For example, if the patient weights 100 kgs (220 lbs) the tidal volume would still be 300 to 400 mL per ventilation. In contrast for the same patient the International Liaison Committee on Resuscitation (ILCOR) resuscitation guideline recommends 6-7 mL per/kg or 600 to 700 mL per ventilation. The weak link is using predicted body weight as the key measurement. Predicted body weight is based on the patient's height and gender, a practice that has been proven to be highly unreliable. I believe the lower tidal volume is based on implementing a Lung Protective Ventilation Strategy (LPVS) and to protect the airway by reducing gastric insufflation that may lead to vomiting and aspiration.

## Lung Protective Ventilation Strategies

LPVS goes beyond just reducing the tidal volume. The mainstays for LPVS is (1) limit tidal volume to prevent volutrauma; (2) limit end-inspiratory (peak) pressure to prevent barotrauma; (3)

provide adequate PEEP to keep alveoli open; (4) limit the oxygen percentage or FiO<sub>2</sub>. The idea for Lung Protective ventilation was developed to prevent injury and increase oxygenation when a patient was placed on a ventilator. If LPVS is good for ventilators, then the same strategy should be used with a manual ventilator.

## Limiting Tidal Volume and Pulmonary Physiology Low tidal volume and dead space

Dead space represents the volume of ventilated air that does not participate in gas exchange. Effective ventilation must provide adequate CO<sub>2</sub> removal and oxygen saturation while not exposing the patient to excessive airway pressures (barotrauma) or tidal volumes (volutrauma). If CO<sub>2</sub> is not removed efficiently it will convert to an acid lowering the patient's pH (acidosis). Patients that become acidotic have a higher mortality rate.

“Maintaining adequate pH should be weighed against the need to provide safe MV (mechanical ventilation) settings and safe airway pressures.”

– Brian J. Wright, MD

Even though the above quote is regarding mechanical ventilation, I believe it also applies to manual ventilation.

A lower tidal volume may work for smaller patients or patients in a low cardiac output states such as when CPR is being performed but may be totally ineffective for patients in respiratory arrest with relatively normal cardiac output. There must be a balance between CO<sub>2</sub> production and elimination. Some medical conditions such as Acute Respiratory Distress Syndrome (ARDS), advanced COPD and pulmonary embolism can have an increase in dead space requiring greater minute volume (tidal volume X ventilation rate). If the tidal volume is fixed or limited the only option to increase minute volume is to increase the ventilation rate. Unfortunately, fast respiratory rates with small tidal volumes only impact the dead space and does not improve ventilation. In addition, higher rates reduce exhalation time causing the patient to stack breaths increasing auto PEEP. The higher the auto PEEP the harder it is to ventilate a patient. The clearance of CO<sub>2</sub> depends on the relationship between CO<sub>2</sub> production and alveolar ventilation. It's important

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to point out that the average adult has approximately 150 mL of dead space in their airway, using the HP-CPR numbers would only leave 150-250 mL of usable air for adult patients.

### Reducing gastric insufflation

The volume of air used with a manual resuscitator is important but it's only part of the story. Clinicians must be aware of the increase in pressure when the bag is squeezed too rapidly. When providing ventilations with a mask, as opposed to an advanced airway, air can go either towards the lungs or towards the stomach. Under optimal conditions the air will enter the lungs most likely due to resistance in the esophagus caused by the closing of the lower sphincter muscle. However, the lower esophageal sphincter can open with a small amount of pressure (20-25 cmH<sub>2</sub>O) resulting in gastric distention. It only takes a few breaths to fill the stomach and people tend to vomit when the stomach fills with air. Additionally, a distended stomach compresses the diaphragm making it more difficult to expand the lungs.

When it comes to manual ventilation the ideal manual resuscitator bag size is still a mystery. But here's what we do know:

1. 1500-1600 mL bag is too big
2. Lung Protective Ventilation Strategies improves patient outcomes
3. There is no consistency in bag sizes by manufacturer
4. Determining tidal volume by patient height and gender is a guess at best
5. Barotrauma and Volutrauma are bad
6. It's doubtful that one size bag will fit all adult patients
7. Manual resuscitator effectiveness relies on the skill of the user
8. Good ventilation depends on the relationship between CO<sub>2</sub> production and alveolar ventilation
9. ILCOR resuscitation guideline for ventilation recommends 6-7 mL per kg

### Summary

In respect to the HP-CPR guideline of 300-400 mL ventilation volume, I have been unable to find any supporting research for a standard volume for all adults or a calculated tidal volume in the range of 3-4 mL/per kg. The American Heart Association still recommends a tidal volume of 6-7 mL/kg. Currently, a perfect solution does not exist when it comes to manual resuscitator bag size for adult patients. The best solution to safely ventilate (manually) the greatest portion of the adult population is a skilled provider using a 1000 mL bag (functional volume of 750 mL) that incorporates a manometer, PEEP valve and pressure pop-off.

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*Improving Home COPD Monitoring...continued from page 45*  
COPD patients has been shown to significantly shorten the time each day for testing in patients at home, reduce patient fatigue, and increase adherence with testing. For patients undergoing serial measurements, it assures that measurements that don't meet ATS/ERS quality criteria are not accepted for a single measurement requirement and yet minimizes the number of attempts to assure meaningful data. It should be recommended by the ATS Pulmonary Function steering committee that Statistical Process Control should be the standard for home monitoring of patients with COPD if an effective monitoring program is the intended use of spirometers.

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# Enabling Continuous Surveillance for Ventilated Patient Populations

## How the Hospital for Special Care drives continuous surveillance, automation and alarm management for enhanced patient safety

Pamela Held, M.Ed, RRT

The Hospital for Special Care (HSC) is the fourth-largest long-term acute-care hospital in the United States, and one of only two in the nation that serves both adults and children. With locations in New Britain and Hartford, CT, the non-profit health system is nationally recognized for advanced care and rehabilitation in pulmonary care, acquired brain injury, medically complex pediatrics, neuromuscular disorders, spinal cord injury, comprehensive heart failure and comprehensive inpatient and outpatient treatment for children and adolescents with autism spectrum disorder.

### The Challenge

The respiratory therapy department at HSC manages more than 100 ventilators—each with its own set of alarms—at patients' bedsides across the hospital, including:

- The Pediatric Unit, a 30-bed, four-team unit that offers rehabilitation therapies, as well as learning programs that focus on building patients' physical, cognitive and social abilities.
- The Respiratory Care and Respiratory Step-Down Units, 36- and 38-bed units, respectively, for patients requiring intensive nursing and respiratory care, including intravenous medication and non-invasive respiratory monitoring.
- The Close Observation Unit, a 12-bed, interdisciplinary team-based unit that focuses on weaning adult patients from mechanical ventilation.

For many years, the number of ventilators and the complicated layout of the units forced the hospital's respiratory therapists to spend much of their shift racing from room to room responding to hundreds of non-actionable alarms.

As a long-term care and rehabilitation facility, HSC is committed to patient quality of life and clinicians encourage patients to remain active, which is typically good for their recovery process; however, the number of false alarms blaring daily was distracting to clinical staff and disruptive to patients.

The critical nature of ventilators as life-support devices and the volume of alarms they produced were major drivers in HSC selecting a solution that would enable HSC's team of respiratory therapists to provide continuous surveillance monitoring of

patients, while reducing non-actionable alarms and enhancing patient safety.

HSC needed a technology platform to capture and distribute real-time data from more than 100 ventilators and pulse oximeters and filter out alarms that were not clinically actionable.

### The Impact

The critical nature of ventilators as life-support devices and the volume of alarms they produced were major drivers in HSC's use of a solution to provide continuous surveillance capabilities in addition locations and facilitating automation of numerous administrative processes.

**Continuous Clinical Surveillance.** The application allows HSC's team of respiratory therapists real-time access to vital patient information and intervene before a situation becomes critical.

Traditional patient monitoring, including vital-sign spot checks and single-parameter device monitoring, is insufficient to support the typical RT's workflow. Even if additional devices, processes or redundancies were leveraged as a kind of stop-gap measure, the essential problem of patient monitoring is actionable data.

Continuous surveillance, on the other hand, allows RTs to discern the signal from the noise through real-time, continuous data flow from multiple sources that can be filtered and intelligently analyzed for significant trends and prospective intervention.

With real-time access to patient data and alarms, health systems can begin to anticipate patients trending toward distress—and intervene before costly rescues and escalations are required. The respiratory therapy team at HSC was able to see the condition of any patient in the unit and respond appropriately.

Notably, since the implementation of clinical surveillance application, HSC has not experienced a single serious patient safety event related to ventilators. The typical response time to a clinically relevant alarm is under 34 seconds.

**Automation.** The solution removed the manual processes associated with vent checks. The solution captures all the measured parameters (peak airway pressures, volumes, etc.) and settings, eliminating the risk of transcription errors. The automated process also means that respiratory therapists spend

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less time performing menial documentation tasks and spending more time assessing, treating and engaging with patients.

The application also automatically integrates ventilator data to HSC's Allscripts electronic medical record system, which has decreased documentation errors and improved accuracy. The application also automated HSC's Admissions, Discharges, and Transfers (ADT) feed for automatic patient admitting.

**Alarm Management.** Non-actionable alarms were a particularly acute problem at HSC. A typical critical care ventilator can alarm for approximately 135 different reasons. The ventilator population at HSC comprised primarily of alert and active patients, which increased incidents of nuisance alarms, such as a patient coughing or a sensor coming loose.

Prior to implementing the application, the number of ventilators and the complicated layout of the units forced the hospital's respiratory therapists to spend much of their shift racing from room to room responding to more than 4,800 ventilator device alarms per day. Hospital leadership was concerned that alarm fatigue could become a serious and chronic problem due.

Devices tethered to patients ostensibly to alert RTs that an intervention is required are rarely actionable. For example, many long-term care and rehabilitation facilities encourage patient mobility as part of the recovery process. However, moving around or talking or coughing can easily set off device alarms.

Since implementation, the number of ventilator alarms has been reduced by 80 percent. When actionable alarm conditions occur the respiratory therapist is alerted by pager, overhead audible alarm, visual alerts through desktop/laptop computers and an overhead scrolling message bar.

**Data Distribution.** Continuous surveillance eliminates the need for individual recollections and faulty memories for the completion of management and audit committee reports. Clinical surveillance capabilities empower every RT with a clear, evidence-based picture of every event. The data aggregated from ventilator devices can be used to assess performance and identify potential areas of need. Additionally, because clinical surveillance automates processes that were previously done manually, such as manual ventilator checks, RTs can focus more on the patient rather than the ventilator.

HSC has reader boards in addition to the laptops on the roll stands, and then the workstations at the central station. Networked laptop and desktop computers as well as scrolling message bars running the application have been deployed at key locations, providing respiratory therapists with access to data and alarms from all ventilated patients. In addition, ventilator alarms were routed through pagers to the specific respiratory therapists assigned to each patient.

**Accountability.** The real-time data collected is leveraged by Respiratory Care Services in reporting to the Performance Management Audit Committee, which monitors ventilator management performance by the RTs, and also helps identify improved performance and potential areas of need. An additional benefit is helping them refine related protocols.

The system also automates processes that were previously done manually, such as manual ventilator checks, which frees up the

respiratory therapist to focus on the patient. Reduce or eliminate non-actionable alarms while simultaneously providing triage and distribution of relevant alarms, allowing respiratory therapists to focus on patients. Analyze objective, comprehensive clinical data after any patient incident to assess response processes and preventative measures.

## Conclusion

Respiratory therapists (RT) are presented with a unique opportunity to assume a position of leadership in the development and implementation of comprehensive, reliable and scalable patient safety initiatives.

Health systems are under significant pressure from regulatory bodies, such as the Joint Commission and the Centers for Medicare & Medicaid Services (CMS), to enhance overall patient safety and mitigate adverse events in both acute care and intensive care units. For example, CMS' Hospital-Acquired Conditions Reduction Program (HACRP) penalizes health systems for high rates of ventilator-associated injuries and other hospital-acquired illnesses.<sup>1</sup>

In addition to regulatory factors, patient safety is a multi-faceted challenge that counts clinical communication, technology, insufficient monitoring practices, workflow and even facility design among its primary pain points.

Addressing these challenges requires the ability to capture a holistic, real-time picture into the patient's condition and where it is trending over time, and route actionable information to the respiratory therapists and other member of the clinical team. Fortunately, continuous surveillance checks all of these boxes for the respiratory therapist.

Continuous surveillance is capable of safely managing patient populations across the enterprise, reducing the cost of care, aligning with reimbursement and regulatory incentives, enhancing clinical workflow and decision making and closing many of the workflow inefficiencies and patient observation gaps inherent in traditional monitoring protocols.

Patient safety in the modern hospital system is complex and fraught with known and unknown risks. Clinical surveillance presents a game-changing opportunity to help RTs practice clinical excellence at the top of their license, and help hospitals align with the standards, regulations and expectations of modern patient safety initiatives.

# Possibilities and Opportunities for Subglottic Air Insufflation in Patients with Tracheostomies – More Than Just Above Cuff Vocalisation (ACV)

Norbert Niers

## Abstract

For patients, in whom a deflation of the cuff and reconnection of the upper and lower airways is not justified or not possible, the retrograde flow of air with above cuff ventilation offers a low-risk therapeutic option, which, in addition to enabling patient participation, increases patient autonomy and improves the quality of life.

Tracheostomy counts as one of the most frequent procedures in intensive care. It is estimated that some 24% of patients on intensive care units have a tracheostomy (Mehta and Mehta 2017 in Schneider-Stickler and Kress, published 2018).<sup>6</sup>

This artificial airway has certain advantages, as mechanical ventilation is easier than with endotracheal intubation. Pulmonary hygiene for the management of secretions can be achieved more easily with the possibility of endotracheal suction. One considerable advantage over an endotracheal tube is that the patient can be awake and, in most cases, will not require any sedation.

Interdisciplinary, therapeutic patient care consists of ensuring that the inserted cannula not only meets the indication for a tracheostomy tube, but also maintains the patient's existing resources and unaffected abilities (eg in the management of secretions, breathing, speaking or swallowing) without hindering or even eliminating them.

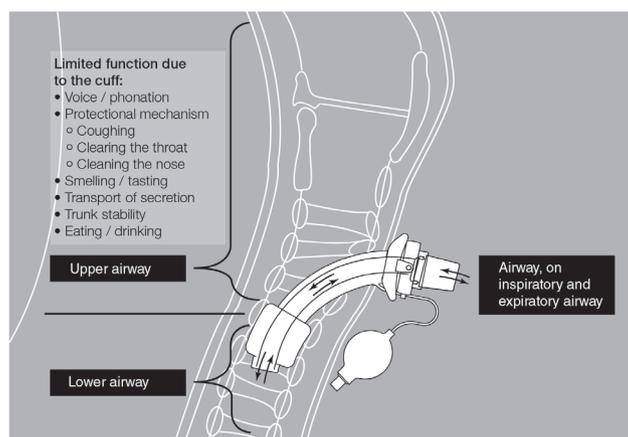


Figure 1. The restrictions of an inflated cuff

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One important therapeutic goal is to reconnect the upper and lower airways, in order to promote oropharyngeal sensitivity with the flow of air through the larynx and enable the patient to speak. The classic way is the successively prolonged deflating time of the cuff.

With some patients, it is not possible to deflate the tracheostomy tube cuff, especially in the early stages. For example, high pressure ventilation may be required to prevent atelectasis and this cannot be sufficiently achieved without an inflated cuff. The risk of aspiration is also increased with uncuffed tubes and deflated cuffs.

For aspiration prophylaxis, it is advisable to remove the above-accumulated secretion by means of a subglottic suction — even with an inflated cuff.

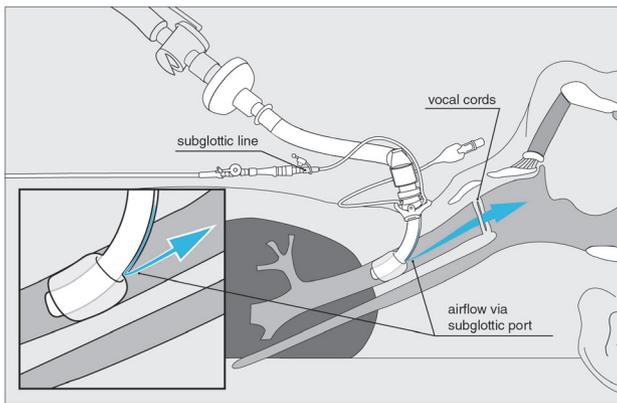
Various studies have provided evidence of the protective effects of regular subglottic suction on the lungs, especially in the prevention of nosocomial ventilation-associated pneumonia (VAP). The Robert Koch Institute (RKI), the German Commission for Hospital Hygiene and Infectious Disease Prevention in Berlin, recommends the suction of subglottic secretions, if the duration of mechanical ventilatory support is likely to be more than 72 hours. This is a category IA recommendation.<sup>10</sup>

Tracheostomy tubes made for subglottic suctioning have an additional lumen that ends in a hole immediately above the cuff and allows secretions to be removed through the subglottic port.

Besides the possibility of removing secretions, the subglottic line ending in the subglottal region also provides the option for air insufflation by offering the patient an air flow for vocalisation. **It is a close imitation of cuff deflation.** The patient is able to produce an audible voice using the *above cuff vocalisation (ACV)* technique.<sup>2,3</sup> Air insufflation may also have a positive impact on laryngeal function and early or long-term rehabilitation.

The term *above cuff vocalisation (ACV)* coined for this procedure by McGrath et al<sup>2,3</sup> puts the focus firmly on vocalisation (phonation), which can be achieved in many cases by means of this airflow. Restoring the voice is a great motivation for the patient and also strengthens their autonomy.

However, there are essential, far-reaching and complex prerequisites for vocalisation:



**Figure 2.** Air insufflation via the subglottic port

- intact laryngeal function, in particular, of the vocal cords (vocalis muscle and recurrent laryngeal nerves)
- the intent and drive to speak (with the required degrees of wakefulness and strength)
- the necessary speech motor function (no serious dysarthrophonia)
- the necessary systematic language (no serious aphasia)
- the necessary speech coordination (no serious apraxia)

But even without achieving phonation, laryngeal flow provides valuable therapeutic and physiological support. Laryngeal flow has a higher-order role in the therapeutic setting, also for the support of passive or even comatose patients. The flow of air almost automatically restores or regenerates sensitivity, with far-reaching effects.

In practice, it has been shown time and again that a flow of air (via the subglottic line) leads to increased spontaneous activity of the swallowing reflex and the patients start to make an effort to control the supraglottic space by trying to clear the throat and swallowing.

#### Laryngeal flow accounts for more than 'just phonation', as it:

- exploits sensorimotor possibilities with dysphagia (swallowing reflex and clearing of secretions)
- prevents complications (reduces pooling of secretions above the cuff)
- activates the patient (wakefulness, motor activation) through stimulation by the air (contact with and reaction to the flow)
- prepares the patient for a later deflation of the cuff, improves the situation with respect to secretions and increases sensitivity
- improves the quality of life by enabling or optimising communication

Accurate observation of the patient's reactions to the flow of air is crucial. Positive reactions such as swallowing activity and the start of efforts to clear the throat are of high therapeutic benefit and should not be overlooked. The stimulation of swallowing, appropriate changes in posture and supportive measures such as the jaw control grip give the patient further encouragement.

#### Social aspects

Impact on quality of life during treatment — less stress, frustration and anxiety with:

- increased patient autonomy

- involvement in their own treatment, expression or verbal manifestation of the patient's will
- opportunities for communication
- motivation to participate in rehabilitation
- improved compliance during the weaning process

Even though, as mentioned previously, a large number of the patient clientele could benefit from this option, there are still a number of prerequisites and contraindications to take into consideration.

#### Prerequisites

- Tracheostomy tube with subglottic line in situ
- A metered compressed air or oxygen supply must be available
- Clear upper respiratory tract
- Sufficiently stabilised tracheostomy and the possibility to remove the secretion via subglottic line
- Possible contraindications
- Upper airway obstruction
- Recent tracheostomy (do not attempt until at least five days old)
- A vulnerable, severely inflamed stoma
- Severe air leak between stoma and tracheostomy tube, with or without secretion
- A heavily sedated patient

#### ACV procedure

After the **patient has been fully informed** about the procedure, a **subglottic suction** is performed to remove the secretions.

The patient's **posture or position** is then optimised.

The **compressed air is connected** through a line that should have the option for **fingertip occlusion**. Once the initial trial phase is over and the appropriate flow rate has been determined, this accessory will allow the patient to regulate vocalisation as required.

#### The air supply starts at a rate of 1 litre/minute for the patient to become accustomed to the flow and is gradually increased up to 3-6 litres/minute.

The irritation experienced at the beginning (as a result of hypersensitivity following the possibly long absence of flow) can be alleviated by initially introducing the air insufflation **only during expiration**.

It must be remembered that subglottic pressure regulation by the abdominal muscles, which is important for phonation, cannot occur with an inflated cuff. The patient only has laryngeal (and articulatory) control options.

By altering the air supply to vary the flow, the subglottic pressure that causes the vocal cords to vibrate can be determined — this may take several attempts. Depending on the conditions, considerably higher flow rates may be required to restore the voice.

Once phonation has been achieved, the flow should be reduced as much as possible to prevent mucosal irritation and lower the noise level.

If vocalisation is not possible, the oropharyngeal flow of air will at least ensure the articulation of non-vocal sounds. This would allow to better understand the patient than it is possible

## Troubleshooting

Problem	Cause / Possible solution
Subglottic suction not successful	<ul style="list-style-type: none"> <li>• Suction line blocked by viscous secretions</li> <li>• The opening of the subglottic line is blocked by its proximity to the tracheal wall: smaller tracheal cannula or more flexible tracheal cannula</li> </ul>
No oral / nasal flow can be produced	<ul style="list-style-type: none"> <li>• Change the patient's position, paying particular attention to symmetry/alignment</li> <li>• Try briefly increasing the flow</li> <li>• If necessary, seal a parastomal leak</li> <li>• <b>Stop the air insufflation</b></li> </ul>
Irritation due to the flow, with persistent cough	<ul style="list-style-type: none"> <li>• Reduce the flow</li> <li>• Flow introduced only during expiration at first</li> <li>• Inform the patient that irritation usually only occurs at the beginning</li> <li>• The opening of the subglottic line lies directly on the tracheal wall:               <ul style="list-style-type: none"> <li>◦ Change the position of the head and/or trunk; tube with smaller outer diameter, more flexible tracheal cannula, variation in length or angle</li> </ul> </li> <li>• Irritation due to dry air: humidify air with a booster</li> <li>• Diagnostic imaging</li> </ul>
No phonation	<ul style="list-style-type: none"> <li>• Try briefly increasing the flow</li> <li>• Voice therapy with phonation aids</li> <li>• Change the patient's posture/position</li> <li>• Diagnostic imaging: endoscopy / radiology</li> </ul>



**Figure 3.** Subglottic air supply with fingertip occlusion for self-regulation

with lipreading alone. The use of the ACV technique is therefore worthwhile even without achieving phonation.

### Summary and Outlook

Even though the subglottic air insufflation technique

- is easy to perform
- may contribute to better verbal communication
- has positive effects on the ability to swallow and the management of secretions
- and helps to prepare for weaning and decannulation
- it is rarely used in routine clinical practice

Irrespective of the patient's communicative performance, this method allows a very early initiation of therapy to alleviate, for example, disorders of swallowing.

The acronym **ACV** should therefore stand for *above cuff ventilation* instead of *above cuff vocalisation*, in order to reflect the holistic aspects of this therapeutic option more accurately and not restrict it solely to phonation.

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# Volunteer Validation Study Looks at the Future Use of Oxygen Reserve Index

Chris Campbell

Monitoring a patient who is under anesthesia is crucial to a successful surgery. Medical teams have standard practices when it comes to monitoring patients during surgical procedures. Pulse oximetry is one such standard method when it comes to keeping track of a patient's oxygen status. But is there a more effective method available when it comes to tracking that oxygen status? One study—entitled Oxygen Reserve Index: Validation of a New Variable—talks about the limitations of pulse oximetry.

“There is no doubt that monitoring a patient's oxygen status during anesthesia using pulse oximetry is essential and is considered standard care in the perioperative setting,”<sup>1,2</sup> the authors wrote. “Nevertheless, monitoring oxygenation using pulse oximetry has its limitations, because during normoxia and hyperoxia, oxygen saturation (SpO<sub>2</sub>) is >97% in the typical patient, especially in those patients receiving supplemental oxygen. Meanwhile, actual partial pressure oxygen dissolved in arterial blood (PaO<sub>2</sub>) can vary substantially ranging from normoxia (80-100 mm Hg) to extreme hyperoxia (≈500-600 mm Hg). Hence, SpO<sub>2</sub> monitoring gives little information on PaO<sub>2</sub> under such circumstances, necessitating arterial blood gas analysis (BGA), which is both invasive and gives intermittent information on oxygenation only. In addition, it is associated with additional costs and time delay, blood loss when performed repeatedly, and occurrence of puncture-related complications.”<sup>3</sup>

The authors talk about the recent introduction of Oxygen Reserve Index (ORi) and set out to see if it reflects oxygenation during moderate hyperoxia by conducting a prospective validation intervention study.

“This study is the first prospective validation study in human volunteers systematically investigating the relationship between ORi and oxygen status at multiple standardized inspiratory oxygen concentrations,” the authors wrote.

The study was led by a team of researchers (Jaap Jan Vos, MD, PhD, Cornelis H. Willems, MD, Kai van Amsterdam, MSc, Johannes P. van den Berg, MD, Rob Spanjersberg, Michel M. R. F. Struys, MD, PhD, FRCA, and Thomas W. L. Scheeren, MD, PhD) with the Department of Anesthesiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; and Department of Anesthesia and Perioperative Medicine, Ghent University, Gent, Belgium.

The authors say that ORi, a new relative indicator of PaO<sub>2</sub>, is “derived from noninvasive multiwavelength pulse co-oximetry (Rainbow SET; Masimo, Irvine, CA). ORi is based on technology as published before<sup>4-6</sup> and uses wavelengths of light to collect optical absorbance information in the moderate hyperoxic range and resolves extremely small differences in absorbance into a unitless index (range, 0.00-1.00). The ORi algorithm is optimized for detecting changes in PaO<sub>2</sub> during mild-to-moderate hyperoxia, that is, in the range of 100-200 mm Hg (“ORi-sensitive range”). Previously,<sup>7</sup> a positive correlation between intraoperative values of ORi and PaO<sub>2</sub> was found over a wide range (62-534 mm Hg) of PaO<sub>2</sub> values. In another study, ORi monitoring provided an advance warning of an impending hypoxic state, with a median (range) detection of impending desaturation of 31.5 seconds (19-34 seconds) before changes in SpO<sub>2</sub> actually occurred.<sup>4</sup> There are no data systematically comparing PaO<sub>2</sub> with ORi within its sensitive range as of yet. Therefore, this prospective interventional validation study in healthy volunteers was set up to validate ORi by comparing it with whole blood references of arterial blood. By exposing subjects to standardized oxygen concentrations via a tight-fitting face mask, the hypothesis was tested that ORi reflects PaO<sub>2</sub> within the ORi-sensitive range. Additionally, the validity of ORi for PaO<sub>2</sub> values outside its designated, sensitive range was regarded equally important. Therefore, subjects were additionally exposed to oxygen concentrations beyond the ORi-sensitive range, aimed to induce mild hypoxia (fraction of inspired oxygen [FiO<sub>2</sub>] = 0.14) and extreme hyperoxia (FiO<sub>2</sub> = 1.0).”

## The Study

In this prospective validation intervention study, 20 healthy volunteers were breathing standardized oxygen concentrations ranging from mild hypoxia (fraction of inspired oxygen = 0.14) to hyperoxia (fraction of inspired oxygen = 1.0) via a tight-fitting face mask. ORi was measured noninvasively by multiwavelength pulse co-oximetry using 2 finger sensors. These ORi values (unitless scale, 0.00-1.00) were compared with measured PaO<sub>2</sub> values. Repeated-measurements correlation analysis was performed to assess the ORi/PaO<sub>2</sub> relationship. ORi trending ability was assessed using a 4-quadrant plot. The area under the receiver operating characteristics curve was calculated to assess the prediction of hypoxia (low-ranged PaO<sub>2</sub>, <100 mm Hg).

## What The Authors Discovered

In the “discussion” section of the study, the authors described the “positive correlation” between PaO<sub>2</sub> and Ori.

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Chris Campbell is the Senior Editor of Respiratory Therapy.

“Within the ORi-sensitive range (PaO<sub>2</sub>, 100-200 mm Hg), we found a strong positive correlation between PaO<sub>2</sub> and ORi, with a good ORi trending ability with respect to PaO<sub>2</sub> changes ‘within’ this range,” the authors wrote. “Hence, ORi monitoring might be considered a potential noninvasive tool for assessing oxygenation in patients receiving supplemental oxygen. Additionally, sensitivity and specificity of ORi for detecting low-ranged PaO<sub>2</sub> values (<100 mm Hg)—outside its designated sensitivity range—was good, suggesting that ORi monitoring potentially allows for predicting impending hypoxia at a stage when SpO<sub>2</sub> values are still at maximum (≥97%). We observed a strong positive correlation between PaO<sub>2</sub> and ORi within the ORi-sensitive range, being slightly higher compared to the correlation found in the only available study up to now.<sup>7</sup> In this retrospective study in surgical patients (n = 106), an r<sup>2</sup> value of 0.536 (R = 0.73) was found for the linear PaO<sub>2</sub>–ORi correlation for PaO<sub>2</sub> values between 62 and 240 mm Hg. Our study was set up to obtain a substantial number of ORi values for PaO<sub>2</sub> between 100 and 200 mm Hg, considering this the ORi-sensitive range. Hence, we restricted our correlation analyses to the values obtained within this range. These data suggest that ORi provides a reasonable estimation of PaO<sub>2</sub> under moderate hyperoxia. Importantly, we observed that, within volunteers, substantial differences can exist between the absolute values of simultaneously measured ORi values from sensors placed at different sites on the subject.”

## Conclusion

The authors concluded the study by discussing how ORi can be successfully used.

“In conclusion, in healthy volunteers, ORi provides reasonable trending information of PaO<sub>2</sub> around the moderate hyperoxic range of PaO<sub>2</sub> for which its use is intended. Also, changes in PaO<sub>2</sub> are well reflected by changes in ORi, with good concordance. The trend in ORi can be used to track changes in PaO<sub>2</sub> levels in the moderate hyperoxic region, and absolute values should not be interpreted for PaO<sub>2</sub> levels.”

## Disclaimer

Oxygen Reserve Index (ORi) has obtained CE Marking. ORi has not received FDA 510(k) clearance and is not available for sale in the United States.

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# Spirometry Quality, Alarming Results and the Path Forward

Amanda K Clark, RRT

Spirometry is defined as an objective and quantifiable measurement of lung function<sup>1</sup> and is considered a lab exam. As with any lab test, a quality-control process or procedure should be established to ensure accurate measurements are reported. When assessing the quality assurance and quality control (QA/QC) of a spirometry program there are several points to be considered such as device maintenance, adherence to American Thoracic Society (ATS) guidelines, and technical skill level of the end user performing the test. High-quality spirometry requires both an accurate device and clear patient instruction from competent end users. The objective of this article is to unpack these fundamental issues so that corrective action can be implemented.

## Device Maintenance

Device maintenance for any diagnostic tool is essential. Routine maintenance can be device specific for which the manufacturer's instructions should be noted. General maintenance of a spirometer device includes disassembling and deep cleaning of the flow head, manufacturer recommended guidelines should be followed. For infection control, in any setting, the device should be wiped down between patients and used with a bacterial viral filter to protect the flow head from particles exhaled from the patient (ATS 2005).<sup>6</sup> Daily verification of calibration is performed to verify volume measured at variable flow rates (ATS 2005).<sup>6</sup> This should not be confused with calibration adjustments, but rather to assess and document that the device is measuring within  $\pm 3\%$  of assessed volume (typically 1 or 3L) daily.<sup>1,6,10</sup> Yes, daily! Confusion has been introduced to the market by manufacturers claiming their device does not require such verification.<sup>4,5</sup> However, such messaging is clearly not aligned with practice standards. Lastly, annual preventive maintenance should be scheduled and performed by the manufacturer.<sup>6,10</sup> The annual pm assesses the overall integrity of the device and internal calibration adjustment can be made as needed.<sup>6</sup> Unfortunately, many of these critical steps have been ignored or miscommunicated in the marketplace. This mixed messaging leads to a decline in quality-control processes, which ultimately lead to mismanagement of the patient, or at best, duplicate testing due to questionable results. In a study performed by Hegewald et al of Intermountain Medical Center, states office spirometers are

shown to be accurate when tested under ideal laboratory conditions.<sup>5</sup> However, when evaluating devices in a "real world" setting (i.g., spirometers in primary care offices) most were not accurate.<sup>5</sup> Inaccuracies noted in his study likely could have been prevented. Ignorance of simple maintenance routines can miss critical warning signs that something may have altered the integrity of the device. Continuing to use a device in variable condition brings into question results collected and reported.

## ATS Guidelines

Adherence to guidelines has been an ongoing challenge for many. Barriers to adherence exist since guidelines are perceived as complex.<sup>4,5</sup> Often QA/QC plans are not viewed as necessary for a successful program. This could be because there is confusion over the definition of quality assurance and quality control. Simply defined:

**QA** is more process oriented, aimed at preventing defects; making sure that the data reported provides confidence, thus meeting minimal ATS reporting standards.

**QC** is a process that is device related to verify that measured parameters of flow and volume are acceptable and correct.

Quality control from ATS at a glance:

1. Maintain a log of daily calibration verification results
2. Document any repairs made
3. Document dates of software and hardware changes

Table 1 helps to break down what, when, and how to check for spirometry QC.

On the other hand, QA adhering to ATS guidelines is a bit more complex to establish. It requires an organization to put a defined review process in place. One method to accomplish this task is to utilize peer-to-peer review of tests reported from a lab or institution. A second would be to establish a program in conjunction with the quality department and pulmonary providers for over-read coordination. This approach was successful in studies demonstrated in the UK, for example, White<sup>7</sup> found that remote electronic reporting of primary care-based spirometry is a useful QA tool. Regardless of method, this is not a small task to take on. Success will be prevalent if there are specific objectives tied to end user feedback and re-training if necessary.

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**Table 1.** Modified from ATS Summary of Equipment QC (2005)<sup>6</sup>

Variable to Test	Frequency	How to Check
Volume (Referred to as "Daily Cal Check")	Daily	Calibration verification with 3L syringe to within $\pm 3\%$ (2.90-3.09) <i>actual steps may vary with software, see device manual</i>
Syringe Leak	Daily	Pull syringe all the way out, put in stopper, apply $\sim 3\text{cmH}_2\text{O}$ constant pressure for one minute. (note, the syringe will not move if no leak is present)
Volume Linearity	Monthly	1L increments with 3L Syringe over entire volume range
Flow Linearity	Weekly	Check three variable flow ranges
Time	Quarterly	Verify time measured via stopwatch
Software	PRN/ Annual	Log any change to software versions as updates arrive. Note this at least annually

### Technical Skill

The final critical piece to any successful spirometry program at its core is technical skill level of the end user(s) performing the test. It can be difficult to embed confidence and skill with only limited training. Rather, this must be reinforced over time. For example, the NIOSH CDC spirometry training course, designed for occupational testing and required for end users testing Occupational Safety and Health Administration (OSHA) and Mine Safety and Health Administration (MSHA) workers, is approximately 16 hours in total over 2-3 days.<sup>9</sup> Ongoing training is reinforced by a 5-year renewal in the program.<sup>9</sup> While this may seem out of reach for many clinicians, an alternative path could be through annual competency/skills assessments. Combining competency and an ongoing peer review process ensures that skill levels remain proficient and feedback is useful for building confidence. Such a practical approach quickly addresses common reasons that results reported fail to meet ATS standards. In Hegewald (2016)<sup>5</sup> study on quality spirometry, 153 tests were reviewed, 40% of those did not meet ATS minimal guidelines for reporting. Of that 40%, the primary reason for failure was not meeting end of test criteria (defined as 6 seconds of exhalation or plateau of flow whichever is greater),<sup>5,6</sup> accounted for 61% of failed tests results while 44% from poor repeatability.<sup>5</sup> Sadly, such results are quite common in many office practices.<sup>2,3,4</sup> However, a QA competency program could identify and correct such issues in real time, thus increasing overall quality.<sup>7</sup> The example listed in Table 2 is a practical tool to get you started with the skills competency portion of your QA program.<sup>8,10</sup>

**Table 2.** Example of core competencies for spirometry end-user evaluation

Skills to Master	Proficiency Achieved
Ability to follow process and procedure set forth	Yes/No
Communicate clear and effective instructions to the patient	Yes/No
Demonstration of maneuver for the patient	Yes/No
Troubleshoot and correct technique issues in real time	Yes/No
Identify what results meet or do not ATS guidelines	Yes/No
Provides useful comments for the interpreting provider noting patient effort and technical quality	Yes/No

If skill proficiency is not achieved by an end user, a written pathway to ensure achievement should be put in place to include additional training necessary for achievement.

While this brief article is packed with many nuggets, it contains the framework to begin quality processes. It is imperative that we as respiratory therapists take the initiative to work with outpatient facilities and physician practices within our organizations to promote quality spirometry.

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# Introductory Clinical Research Practicum for RT Sophomores

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## Abstract

**Introduction:** Establishing an entry-level baccalaureate degree for registered respiratory therapists (RRTs) remains a paramount objective for the respiratory therapy (RT) profession. Graduates with a baccalaureate degree (BD) in RT typically possess research training needed for advanced clinical practice. During the anticipated lengthy process of universally implementing the baccalaureate as the entry-level degree in the RT profession, associate degree (AD) programs should consider adding formal research training in the form of an introductory, clinical research practicum (CRP), which would provide graduating sophomores with essential research methods and skills in preparation for upper-level academic work and advanced RT clinical practice. The current study revealed that sophomores improved their research knowledge and skills as a result of participating in a CRP prior to graduating from an AD program.

**Methods:** RT students ( $N=26$ ) participated in a CRP consisting of 4 days of didactic sessions plus 2 days of hospital-based practice. Gains in clinical research knowledge were evaluated by pre- and post-CRP quizzes, while gains in clinical research skills were evaluated by a validated CRP skills inventory.

**Results:** Post-CRP quiz score (mean  $\pm$  SD = 73.08  $\pm$  12.17) was significantly ( $p = 0.0001$ ) greater than pre-CRP quiz score (mean  $\pm$  SD = 51.92  $\pm$  11.14) and post-CRP quiz score was a significant ( $p = 0.016$ ) predictor of post-CRP skills inventory score (mean  $\pm$  SD = 93.46  $\pm$  6.75).

**Conclusion:** RT sophomores who participated in an introductory CRP, gained fundamental clinical research knowledge and skills prior to graduation and possibly enhanced their preparation for upper-level academic work and advanced clinical practice.

**Keywords:** clinical research practicum; undergraduate clinical research experience; associate degree; baccalaureate degree; respiratory therapy education; registered respiratory therapist; clinical research knowledge; clinical research skills; advanced clinical practice.

## Introduction

The US healthcare system continues to change rapidly and dramatically as a result of the need to improve quality of care and reduce costs of care.<sup>1</sup> As a result, the respiratory therapy (RT) profession, along with other healthcare disciplines, has been taking steps to significantly improve cardiopulmonary care. In 2007, the American Association for Respiratory Care (AARC) established a task force to functionally define emerging roles and responsibilities for RRTs.<sup>2</sup> Over the course of 3 subsequent task force conferences, it was determined that the imperative to improve health care quality and reduce health care costs could most efficiently be achieved by improving prevention and management of disease, increasing the use of clinical transdisciplinary teams<sup>3</sup> and significantly expanding the use of evidence-based diagnostics and interventions.<sup>4</sup> Attendees at the second AARC task force conference identified 73 competencies in 7 major areas that would be needed by RRTs for advanced RT practice. Two of the 7 major areas were: 1) understanding evidence-based medicine and 2) designing and/or implementing RT clinical protocols, both of which require RRTs who are well versed in clinical research.<sup>2</sup>

Evidence-based protocol-guided care has become the most accepted way to deliver RT.<sup>5</sup> Daily practice for RRTs is increasingly characterized by the need to systematically translate innovative research findings into evidence-based protocol-guided practice.<sup>4</sup> As RT practice evolves and becomes more complex, there will be a greater need for RRTs who are not only conversant with the best available scientific findings but also understand methods and materials used to generate those findings. Hence, RRTs will need to critically assess scientific studies to ascertain whether results from those studies are pertinent to a given clinical case and if so, how those results should be used in the clinical decision-making process.<sup>6,7</sup> The ability to optimally function in an advanced RT clinical practice environment requires knowledge of research methods and the ability to apply research skills.

The third AARC task force conference addressed professional education enhancements that would be needed to achieve emerging competencies and dispositions in the profession. RRTs often function as contributing members of clinical transdisciplinary healthcare teams<sup>2,3</sup> that customarily employ evidence-based methods to deliver health care in and out of the hospital.<sup>1</sup> On such teams, intensivist RRTs typically demonstrate their specialized, clinical expertise by helping other members of the team to appreciate the complexity of integrated mechanical

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ventilator systems and clinical monitoring systems that are just two of the many information nodes in modern intensive care units. The current environment requires an advanced clinical RRT with sophisticated knowledge of cardiopulmonary physiology and the ability to make recommendations and base decisions on the best available scientific evidence.

Emerging RT roles and responsibilities require a significant educational commitment to research training for RT students. Transitioning to an entry-level baccalaureate degree (BD) in RT is the single most important step that can be taken to enable RRTs to achieve the level of research erudition required to practice at the top of their license. Therefore, the American Association for Respiratory Care (AARC) has targeted 2020 as the date by which 80 percent of respiratory therapists (RTs) should possess a baccalaureate or be working toward one.<sup>5</sup> RRTs with a BD in RT, typically possess research training needed to undertake advanced RT clinical practice.

The ability to practice evidenced-based protocol-guided RT is central to delivering safe, efficacious and cost-effective cardiopulmonary care; therefore, the need for advanced RRTs with a background in scientific research is expected to increase significantly. Given that most RT academic programs currently award the associate degree (AD) and will probably continue to do so for some time, and given that RT research training is usually not part of the typical AD curriculum,<sup>1</sup> the time has come to include this training. AD programs in the process of educationally transitioning to BD programs or currently establishing articulation agreements with BD-granting academic institutions can also take steps to prepare their graduating sophomores for upper-level academic work and advanced clinical practice by offering an introductory clinical research practicum (CRP). The CRP described in this study is designed for temporally, spatially and financially constrained AD programs, and is only one example of such a practicum. It is offered as an AD-based example for 2-year programs seeking preliminary ideas for developing and implementing their own customized CRP.

Previous educational research has shown that undergraduate RT clinical research can be successfully undertaken by credentialed sophomores with advanced standing in an AD program.<sup>8</sup> Additionally, a recent study<sup>9</sup> demonstrated that a cohort of traditional RT sophomores in an AD program, successfully undertook undergraduate clinical research that was modeled after research training provided to undergraduates in bioscience programs.<sup>10</sup> It has been known for some time that undergraduates who participate in structured research experiences in bioscience, are more likely to complete a baccalaureate degree in bioscience.<sup>11,12</sup> We hypothesized that establishing an introductory CRP in an AD program in RT would enable graduating sophomores to acquire fundamental research knowledge and skills needed to prepare for upper-level academic work toward a BD and to prepare to use scientific research findings to inform advanced RT clinical practice.

## Methods

The CRP described herein was designed for sophomore students during Clinic IV, the next-to-last clinical rotation prior to graduation from a 2-year RT program. During this clinic, sophomores typically rotate through multiple instructor-led clinical specialty practica that last either two or four days and include: NICU, sleep lab, PICU, catheterization lab, PFT, hyperbaric chamber, neurorespiratory rehabilitation, and clinical

research. Each clinical specialty practicum is designed to fully immerse RT students in clinical environments that enable them to further enhance their psychomotor skills. A significant part of students' didactic preparation for the CRP involved understanding specific research concepts plus becoming familiar with the clinician-scientist's professional disposition, before undertaking the two-day hands-on practicum. Students were periodically reminded that this undergraduate clinical research experience was intended to prepare them for entry into BD programs in RT and advanced RT clinical practice.

Prior to commencing the CRP, sophomores completed a proctored, validated pre-CRP quiz consisting of 20 multiple-choice questions (5 points per question) to evaluate baseline knowledge of selected, fundamental research concepts and methods. This was followed by four full-day didactic sessions plus two days of hospital-based practice during which students implemented an established affiliate-specific evidence-based clinical protocol.<sup>13</sup> Students provided patient care, performed clinical measurement, collected data, employed statistical modeling and made recommendations for re-design of clinical protocol. At the end of two days of hospital-based practice, a faculty clinical facilitator used a validated semi-quantitative CRP research skills inventory to evaluate gains in research skills according to five learning objectives<sup>10</sup> (see Table 1).

**Table 1.** CRP research skills inventory

1	Student explained rationale for participation in hospital-based CRP.
2	After reading a previously unstudied RT scientific poster in hospital, student explained poster's introduction, method, result, discussion and conclusion sections.
3	After reading a previously unstudied RT scientific article, student identified the study as a randomized controlled trial, identified control and experimental groups, identified independent and dependent variables, explained p value, explained conclusion and explained how findings could be used to design or modify the hospital's clinical protocol.
4	At bedside, student measured and recorded selected cardiopulmonary parameters using NM3 volumetric capnography monitor.
5	Student recommended modifications for hospital's evidence-based protocol.

Students who exceeded a given learning objective earned 20 points, those who met a learning objective earned 15 points and those who did not meet a learning objective earned 5 points. Exceeding all five learning objectives earned a maximum of 100 points. Earning at least 85 points was deemed evidence that students had acquired fundamental research skills. Research concepts presented during the four-day didactic learning sessions were aligned with research skills evaluated during the subsequent two-day hospital-based practicum. After completing the two-day hospital-based practicum, students completed a post-CRP quiz (identical to the pre-CRP quiz) to measure gains in research knowledge. Scores for sophomore participants were entered into a SPSS 25 data spreadsheet for paired samples t-test and multiple regression statistical modeling. Statistical significance was established at  $p < 0.05$ .

## Results

Mean age of sophomore participants ( $N = 26$ ) was 27 years, majority (77%) were female and none had previous AD or higher level academic degree(s). Post-CRP quiz scores (mean  $\pm$  SD =

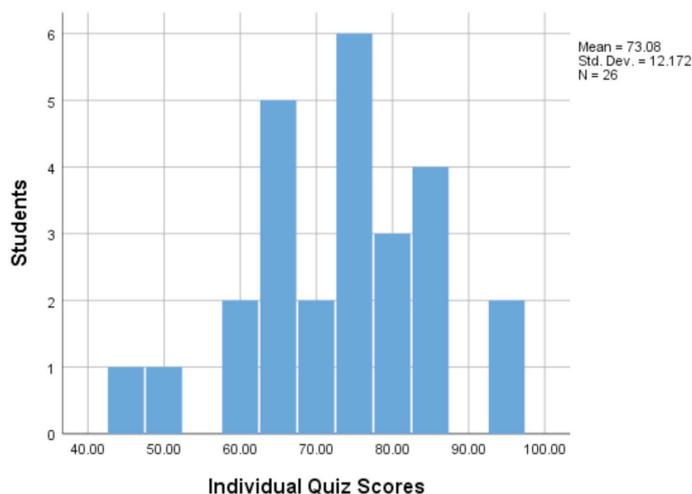


Figure 1. Post-CRP quiz scores

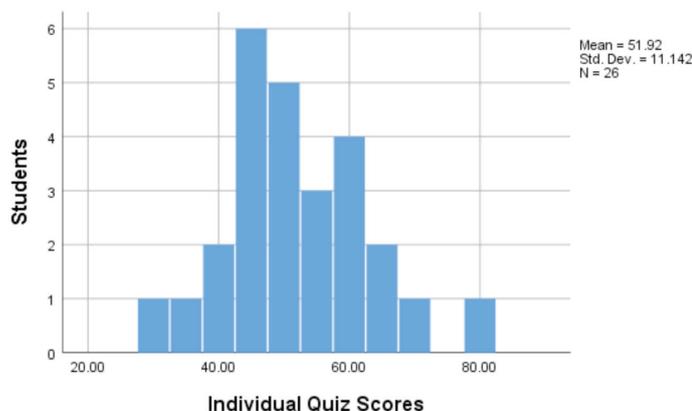


Figure 2. Pre-CRP quiz scores

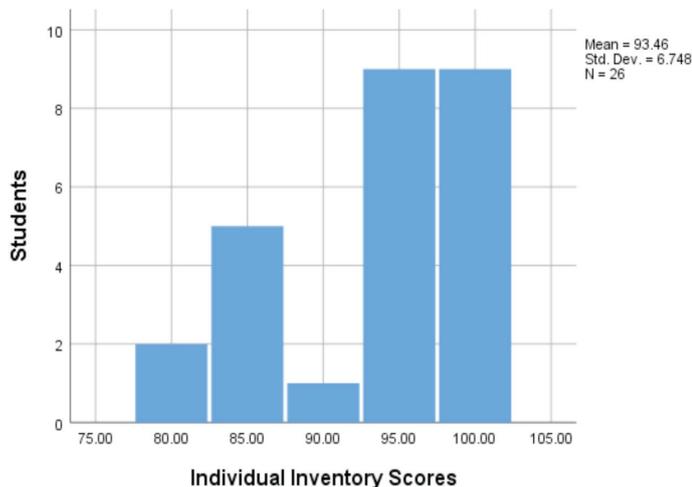


Figure 3. Post-CRP skills inventory scores

73.08 ± 12.17) were significantly ( $p = 0.0001$ ) greater (see Figure 1) than pre-CRP quiz scores (mean ± SD = 51.92 ± 11.14) (see Figure 2). Additionally, multiple regression analysis revealed that post-CRP quiz scores (mean ± SD = 93.46 ± 6.75) were significant ( $p = 0.016$ ) predictors of post-CRP skills inventory scores (see Figure 3).

## Discussion

Studies of academic programs in respiratory therapy have shown that research competencies are more often taught in BD than in AD programs.<sup>2</sup> A group survey of RT academic program directors revealed that most AD programs do not typically teach concepts pertaining to evidence-based medicine, implementation of clinical protocols, critical evaluation of scientific research findings, or statistical evaluation of research findings, whereas most BD programs teach these concepts.<sup>12</sup> These concepts are the foundation for emerging roles and responsibilities that RRTs increasingly play as professional members of the transdisciplinary healthcare team. If RRTs are now expected keep up professionally and to be conversant with clinical research evidence and to recommend care for cardiopulmonary patients based on the best available evidence, then graduates from AD programs should have a fundamental understanding of research methods and skills that enables them to fulfill their roles and responsibilities as new RRTs on the path toward becoming professionals. During the current educational transition to the entry-level BD, it would seem prudent for AD programs to establish a collaborative educational relationship with upper-level academic programs, clinical affiliates and commercial vendors to support an introductory clinical research experience for their graduating sophomores.

Although the typical AD curriculum is burgeoning with coursework, there is nevertheless an unmet need to teach sophomores introductory research knowledge and skills. The challenge of teaching these additional competencies will be placed on AD program educators who are adept at working under pressure to perennially prepare their students for emerging roles and responsibilities.<sup>1</sup> Educators' readiness to accept this new mission may catalyze an immediate positive transformation of RT clinical practice at the local level. RT sophomores engaged in patient clinical rounds during an ICU clinical practicum, have reported that many of their RT clinical instructors are not only expected to contribute to the bedside discussion of patients' clinical therapeutic objectives but are expected to bolster their bedside clinical recommendations by referencing scientific evidence that supports those recommendations.

The current study showed that a 2-year RT program with the usual temporal and spatial curricular constraints, established a CRP that improved students' research acumen. Our findings suggest that 4 days of didactic presentations plus 2 days of a hospital-based clinical research practicum is sufficient time for introductory research training given acknowledged AD curricular constraints.<sup>8</sup> In addition to experiencing significant gains in clinical research knowledge and skills, an exit survey administered to sophomores after the CRP, found that 95% of students strongly agreed with the statement that their introductory clinical research experience had made them more interested in working toward a BD in RT.

A clinical research experience such as the one described herein would be expected to facilitate students' academic pathway from AD to BD program by giving them a sample of the type of academic work they would probably encounter in an upper-level academic program as well as the type of advanced clinical work they would probably undertake as newly-minted professional, RRT clinician-scientists. An undergraduate clinical research experience would also help sophomores hone critical thinking skills and clinical decision making capabilities.<sup>14,15</sup> More broadly,

a formal, clinical research initiative begun in a given AD program could become the leading edge of a clinical research network that includes BD programs, graduate-level programs, clinical affiliates and other healthcare institutions and serves to accelerate translation of scientific innovations to advanced RT practice.

There is a need for RT clinical research mentors to assist research efforts at the local RT clinical community level. Establishing local RT clinical research networks<sup>15</sup> could catalyze RT professional development by starting collaborative clinical research projects, by delivering in-service clinical research training for current RT practitioners, by assisting with acquisition of research grants and by serving as a clearinghouse for standardizing multi-center evidence-based protocol-guided clinical RT practice.<sup>5</sup> Embracing and promoting clinical RT research would serve as evidence to RT educators, RT students, RT clinical practitioners, non-RT clinical practitioners, patients, political stakeholders and others, that RT clinical research is part of our professional DNA and is expressed daily as value-added evidence-based protocol-guided clinical practice that improves healthcare quality and reduces costs.

An important limitation of this study was its small sample size. In an effort to redress this, we intend to repeat this study annually, adding additional sophomore participants as part of a continuing CRP educational research program. The program will continue evaluating clinical research erudition of each sophomore graduating class, monitoring sophomore BD completion rates and monitoring effects of RRT clinical research knowledge and skills on advanced RT clinical practice at the local RT community level.

## Conclusion

Graduating sophomores participated in an introductory CRP prior to graduating from an AD program in RT. Participation was associated with significant gains in clinical research knowledge and skills that may facilitate preparation of sophomores for entry into BD programs and for advanced clinical practice as professional RRTs.

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# Utilizing Vacuum Pressure Swing Adsorption to Create a More Reliable Portable Oxygen Concentrator

Philip Geanacopoulos

## Fundamentals of Operation in Portable Oxygen Concentrators (POC)

Oxygen concentrators produce an oxygen-rich gas mixture by drawing in room air and stripping nitrogen from air. Air is comprised of 20.946% oxygen, 78.084% nitrogen and 0.977% other trace gases. If 100% of nitrogen gas molecules are removed from room air ( $20.946/(20.946+0.977)$ ), what remains is 95.54% oxygen and 4.46% inert gases. Therefore, the best possible performance a POC can deliver to long-term oxygen therapy users is 95.54% oxygen.

## Separating Nitrogen Gas

Removing nitrogen from air typically requires a two-sieve bed system. The process involves separating air into its constituent components by means of adsorption. While under pressure, nitrogen gas molecules bind with a molecular sieve as air passes through the sieve bed. The molecular sieve, which is synonymous with desiccant, attracts and holds nitrogen molecules on the surface of the sieve bead. The outside surface area of lithium-based sieve bead accounts for approximately 1% of the total surface area of the bead. Most POC manufacturers accomplish the adsorption process one of two ways — Pressure Swing Adsorption (PSA) and Vacuum Pressure Swing Adsorption (VPSA).

## How the Adsorption Cycles Work

Working as a two-sieve bed system, air is drawn through the POC's air inlet filters by a small compressor. During the adsorption phase, the pressurized air enters the sieve tube where nitrogen is captured by the zeolite sieve material. Nitrogen molecules are continuously adsorbed by the sieve material while under pressure, thus separating oxygen molecules from nitrogen molecules. Before the sieve material is fully saturated with nitrogen, the system switches ("swings") over to the other sieve bed. At the discharge side of the adsorber, therapeutic oxygen flows into the POC product tank and delivered to the oxygen user through a cannula during inspiration.

## VPSA and Purging Nitrogen

The entire VPSA process consists of adsorption (oxygen product), desorption (purging), and repressurization (pressure build up). In a POC utilizing VPSA, the second sieve bed is regenerated during every swing cycle by opening a valve which is connected to a vacuum pump. During the adsorption phase, the pump draws out nitrogen and moisture in the opposite

direction of the oxygen flow. Then, the nitrogen and moisture are purged back into the atmosphere through the POC's air outlets. This results in the sieve beds being regenerated constantly, thus extending the useful life of the sieve material. As each new swing cycle begins, the regenerated sieve is as good as it can possibly be. VPSA systems outperform PSA systems as they are designed to achieve higher oxygen purity by purging nitrogen and residual moisture each and every cyclical swing.

## Conclusion

Therapeutic oxygen is critical to long-term oxygen therapy patients. A POC utilizing vacuum is the most efficient method to desorb nitrogen from air. VPSA technology delivers high oxygen purity to patients for the longest period of time as residual nitrogen and water vapor are constantly purged from the sieve beds. This fundamental technology creates a more reliable and efficient POC.

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# COPD Treatment—Where Do Pulmonary Rehabilitation and Non-Invasive Ventilation Fit In?

Graham T Atkins, MD, Pulmonologist, Eileen Saenz CRT

COPD is estimated to affect around 16 million Americans (6.4%), and millions more who are not yet aware that they have it.<sup>1</sup> Common symptoms include cough and dyspnea — the feeling of breathlessness, particularly with activities such as walking. Dyspnea is an unpleasant sensation and can significantly limit some patients with COPD. Patients with severe COPD find themselves short of breath with any activity and things like walking from one room to another, making a meal or doing the laundry become challenging. This lack of functional ability can limit patients with severe COPD who often remain housebound and unable to do the activities they enjoy. Isolation and depression are common.

In many patients with COPD, dyspnea is driven by emphysema-related dynamic hyperinflation of the lungs and resultant diaphragmatic muscle fatigue. Treatment for COPD aims to improve lung function by helping patients empty air from their lungs, decreasing hyperinflation and improving diaphragmatic function. Inhaled bronchodilators, pursed lip breathing technique and pacing when walking can all help reduce dynamic hyperinflation and decrease dyspnea with activity. Pulmonary rehabilitation, typically an 8-week outpatient program involving exercise training, education and self-management intervention, has been shown to significantly reduce dyspnea.<sup>2</sup>

For some patients with severe COPD, particularly those with chronic hypercapnic respiratory failure, non-invasive ventilation (NIV) can relieve dyspnea and improve exercise capacity.<sup>3</sup> Multiple large studies have shown that for COPD patients with persistent day time hypercapnia, long term use of NIV has been associated with reduced hospitalization and improved quality of life.<sup>4</sup>

## Case Study

Clint Burdette is a 65-year-old man with very severe COPD (GOLD stage 4). His pulmonary function testing is notable for FEV<sub>1</sub> 0.93L (28% predicted), hyperinflation (TLC 109%), air trapping (RV 197%) and severe diffusion impairment. He requires continuous supplementary oxygen at 2L/minute via nasal cannula and despite treatment with appropriate inhaled bronchodilator therapy was very dyspneic with activity. He is

a keen wood worker and was struggling to keep going in his wood shop. He was seen in the Dartmouth-Hitchcock pulmonary clinic by Dr James Carroll, Dr Graham Atkins and Heidi Pelchat RT. They recommended pulmonary rehabilitation and the Life2000 non-invasive ventilator, both of which led to significant improvements in his dyspnea and quality of life.

## Pulmonary Rehabilitation

The Dartmouth-Hitchcock Pulmonary Rehabilitation program includes exercise and educational classes for individuals with respiratory disorders, such as COPD. The goal of the program is to decrease and manage respiratory symptoms, increase the



ability to do everyday activities, identify and modify respiratory risk factors, and improve cardiopulmonary fitness.

For Clint, the program was life changing. He improved his 6-minute walk distance, a measure of exercise capacity, by 35%. He felt better too, his UCSD dyspnea score improved by 47% and all quality of life metrics improved. He felt less isolated,

found a support network of patients who exercise together regularly and continued in the maintenance exercise program and the pulmonary patient support group.

## Life2000® Non-invasive ventilator

Having improved substantially after pulmonary rehabilitation, Heidi Pelchat, RT, wondered whether Clint might benefit from non-invasive ventilation. He had been hypercapnic during previous hospital admissions. Clint was evaluated in the pulmonary clinic and wore the Life2000 non-invasive ventilator while exercising on a treadmill. Wearing the device, he felt less short of breath and found he could walk faster with less dyspnea and a shorter recovery period after exercise.

The Life2000 uses Proportional Open Ventilation® (POV®) technology to deliver a tidal volume to the patient. To accomplish this, the Breathe interfaces use the Venturi effect to

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add to the output volume of the Life2000 Ventilator by entraining ambient air. The amount of entrained air is proportional to the patient's breathing effort and lung mechanics. This proportional response typically results in the patient feeling nonrestrictive, particularly during activity, when the patient's effort and ventilatory drive is greatest. Studies utilizing Breathe® ventilators with POV® technology have demonstrated reductions in dyspnea,<sup>5</sup> work of breathing,<sup>6</sup> and CO<sub>2</sub> levels,<sup>7</sup> while increasing SpO<sub>2</sub>,<sup>5</sup> exercise endurance,<sup>5</sup> and the ability to perform ADLs.<sup>8</sup>



Life2000 therapy helped Clint exercise for longer in pulmonary rehabilitation and regain his ability to participate in activities he had previously given up on.

He is back to woodworking, does some yoga and is now the Activities Director at his community center.

### Conclusions

Pulmonary rehabilitation is a highly recommended, evidence-based program that significantly reduces dyspnea for patients with moderate or severe COPD.

Non-invasive ventilation can relieve dyspnea for patients with severe COPD and chronic hypercapnic respiratory failure.

The Life2000 non-invasive ventilator can be worn during day-to-day activities and for this patient improved dyspnea, exercise capacity and quality of life.

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# Eosinophilic and Non-Eosinophilic Asthma: Understanding Phenotypes and Endotypes

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Approximately 26 million or 1 in 13 Americans have asthma (CDC, 2018). Of these, 5-10% are classified as severe. Severe asthma is associated with poor symptom control, unresponsiveness to treatment, and increased mortality (CDC, 2016). The subset of patients with severe disease serves as a stimulus for improving phenotypic identification and personalization of asthma care. It is now believed that by classifying asthma based on specific phenotypes and endotypes, better outcomes may be realized (GINA). Significant advances have been made in understanding the eosinophilic asthma phenotype, which is the focus of this paper.

Asthma is a common but complex chronic disorder of the airways affecting pediatric, adult, and geriatric individuals in all races, and both sexes. Asthma's varied disease manifestation, or heterogeneity, is increasingly being defined by phenotypes and endotypes. A disease **phenotype** refers to an observable characteristic of a disease. Examples of clinical asthma phenotypic characteristics may include asthma that is induced by exercise, infection, or linked with obesity (Bostantzoglou C, Delimpoura V, Samitas K, 2015). **Endotypes** describe the various underlying cellular and molecular mechanisms that cause phenotypic expression. Respiratory Therapists should understand the growing body of evidence clarifying the need for personalizing asthma care to address the specific phenotypic and endotypic characteristics of individual patients.

Expert guidelines have been developed to provide clinical guidance for asthma care including those from the National Asthma Education and Prevention Program (NAEPP) and Global Initiative for Asthma (GINA). The goal of these asthma care guidelines is to promote disease control or optimize the degree to which the manifestations of asthma are minimized. Asthma control includes two domains: current impairment and future risk. Impairment refers to the frequency and intensity of symptom expression. Risk approximates the likelihood of future exacerbations or of progressive loss of pulmonary function.

Asthma treatment primarily involves two categories of medications, controllers and relievers. The backbone of controller medications includes combinations of inhaled corticosteroids (ICS) and long acting beta<sub>2</sub> agonists. Short acting beta agonists (SABAs) provide acute relief from bronchospasm. Expert guidelines direct a "stepwise approach" in order to achieve control of symptoms and to minimize risk of exacerbations and untoward medication side effects.

The mainstay of asthma control evaluation is spirometry (Chhabra, 2015). Spirometry assessment provides an objective and reproducible measure of airflow limitation. Forced expiratory volume in 1 second (FEV<sub>1</sub>) <60% of predicted is understood to be an independent predictor of future risk of exacerbation (Barrett, 2004). However, patients with fixed airflow obstruction have accelerated lung function decline compared with asthmatic patients fully reversible with bronchodilator therapy. Spirometry alone cannot be used to fully determine control due to disease complexity.

Validated questionnaires have been created to assist in determining a patient's specific level of asthma control. One questionnaire used to evaluate symptom control, the Asthma Control Test (ACT), is a five-question health survey used to measure asthma control. Three levels of asthma control are possible with this tool. A score of 25 indicates full control, 24 to 20 partial control, and 19 to 5 uncontrolled asthma. However, ACT scores are a more effective means of excluding rather than of confirming exercise induced bronchospasm even when used appropriately for patients 12 years and older. Also, the predictive value of the tool decreases in younger patients (Tripodi, Barreto, 2016).

In cases of severe asthma, phenotypic and endotypic assessment is increasingly utilized to evaluate control and personalize care. Each asthma phenotype may have one or more endotypes driving their clinical presentation. Type 2 and Non-Type 2 inflammatory endotypes are the best understood. Identification may involve the use of inflammatory biomarkers in sputum, blood, bronchial tissue, or exhaled gas.

## Type 2 (Eosinophilic) Asthma

Eosinophilic inflammation correlates with asthma severity. Allergens, through the actions of thymic stromal lymphopoietin, stimulate Type 2 helper T cells (Th<sub>2</sub>) to release cytokines. Those cytokines, secreted by Th<sub>2</sub> cells, have an influence on other cells including mast cells, eosinophils, bronchial cells, and airway

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smooth muscle cells. Measurable substances or biomarkers indicative of Type 2 asthma include increased fraction of exhaled nitric oxide (FeNO) and sputum eosinophils levels.

### Type 2 Cytokines Include

Cytokines	Airway Response
Interleukin 4	IgE production and activation of mast cells
Interleukin 5	Activation of eosinophils
Interleukin 13	Hyperresponsiveness, mucus production, smooth muscle constriction & hypertrophy

Interleukin 5 (IL-5) promotes the recruitment of eosinophils into the circulation from bone marrow. Eosinophils normally comprise less than 5% of the leukocytes in peripheral blood. Elevated levels of eosinophilia plays an important role in airway hyperresponsiveness and remodeling. Several recent pharmacological biologic approaches for improving asthma control are related to reducing eosinophilia. Once confirmed, eosinophilic asthma may be considered allergic or non-allergic. The allergic asthma phenotype usually presents with an early onset and is associated with other atopic disease including eczema, allergic rhinitis, and food allergy. Immunoglobulin E (IgE) is elevated in this phenotype.

### Biologic therapies that target IL-5

Monoclonal Antibody	Administration & Considerations
Reslizumab (Cinqair)	The recommended dosage is 3 mg/kg once every 4 weeks administered by intravenous infusion over 20-50 minutes
Mepolizumab (Nucala)	Fixed 100-mg dose. Subcutaneous 1-mL injection into the upper arm, thigh, or abdomen once every 4 weeks
Benralizumab (Fasenera)	30 mg administered once every 4 weeks for the first 3 doses, and then once every 8 weeks thereafter by subcutaneous injection into the upper arm, thigh, or abdomen.

Interleukin 4 (IL-4) promotes the development of allergic inflammation. It is associated with secretion of IgE by B lymphocytes. IgE-dependent mast cell stimulation resulting from IL-4 activity has an essential role in the development of allergic reactions. IL-4 also contributes to airway obstruction through promotion of mucus hypersecretion (Steinke, J. Respiratory Research. 2001; 2(2): 66–70).

Interleukin 13 (IL-13) has been shown to cause an increase goblet cell differentiation, activation of fibroblasts, bronchial hyperresponsiveness, and switching of B cell antibody production from IgM to IgE (Corren, 2013). Each of these responses may contribute to the pathogenesis of asthma.

### Biologic therapies that target IL-4 and IL-13

Monoclonal Antibody	Administration & Considerations
Dupilumab (Dupixent)	Initial 400 or 600 mg dose in moderate-to-severe asthma patients. Dual inhibitor of IL-4 and IL-13 signaling

Anti-IgE therapy has been shown to reduce eosinophils in the airway and the blood. Exposure to aeroallergens may cause

sensitization and production of Th2-dependent antibodies, including IgE. IgE signals mast cells to release biologically active mediators including histamines, prostaglandins, and leukotrienes. The symptomatology may be expressed as allergic rhinitis and allergic asthma. Allergens prompt their untoward effects in a two-step process. In the first step the immunologically naïve person is sensitized to the allergen. The second step requires a second exposure to the allergen to provoke the disease response. The importance of allergen avoidance cannot be over stated in sensitized patients. The biologic Omalizumab has also proven effective in treating this phenotype (Nielsen, 2002).

### Biologic therapies that directly target IgE

Monoclonal Antibody	Administration & Considerations
Omalizumab	Dosing is based on pretreatment serum total IgE level from 30 up to 700 IU/mL and body weight of 66 to 330 lb.

### Non-allergic Eosinophilic Asthma

The phenotypic expression of non-allergic eosinophilic asthma is often of later onset with normal IgE levels. Specific IgE levels of common aeroallergens may be better markers of atopy than total IgE levels. Many patients with asthma have normal IgE levels but may have elevated specific IgE levels. In this case, the ratio of specific-IgE to total IgE is more predictive of response than the total IgE (Mahesh, 2017).

Nasal polyps and aspirin sensitivity are more commonly seen in these individuals. The underlying endotypic mechanism includes the release of TSLP, IL-25, and IL-33 from airway epithelium in response to stimuli including air pollutants, glycolipids, and microbes (Brusselle G., 2013).

### Non-Type 2 (Non-eosinophilic)

The non-eosinophilic severe asthma phenotype is a recognized patient population that is inadequately responsive to corticosteroid therapy. These patients have airway inflammation linked to neutrophilic predominance rather than eosinophilic. Neutrophilia may be due to corticosteroid administration and delayed neutrophil apoptosis (Thomson, 2016). In other words, in cases of asthma where neutrophil-dominated inflammation is predominating, treatment with corticosteroids can promote neutrophil life span. This may amplify the consequences of neutrophilic inflammation.

Macrolide antibiotics, specifically azithromycin has demonstrated some benefit in this category of asthmatics due in part to immunomodulatory and anti-inflammatory effects (Nirula, 2016). Endotypic evaluation reveals activated Type 17 helper T cells (Th17) to release IL-17 which drives neutrophil recruitment. The IL-17 antagonist Brodalumab is approved by the FDA to treat psoriasis, however additional studies are required to determine the potential role in the treatment of asthma.

In summary, severe asthma is difficult to treat. The complex and heterogenous nature of severe asthma has spurred research into specific phenotypes and their corresponding endotypes. Understanding new treatment approaches may assist the respiratory therapist to personalize and improve asthma care.

*Continued on page 71...*

# Adaptive High Frequency Chest Wall Oscillation (HFCWO) Therapy for Maximum Patient Adherence: A Patient-Centered Approach

Pritesh K Pandya, PhD; Gary Hansen, PhD; Sarah Daignault; Billy Kasper, RRT, MHA; Nereida A Parada, MD

## Abstract

For over 20 years, the standard prescription for high frequency chest wall oscillation (HFCWO) has been 30 minutes twice per day. The history of this choice was based on the similarity to manual chest physiotherapy and may not have any relevance to what patients actually need. The time commitment for HFCWO therapy can be considerable, so long-term success depends on balancing the intensity and duration of the treatment with the patient's own tolerance and life style. No therapy can work if patients do not use it, and it has become clear that not all patients require the full "30-minute rule" therapy. To promote a patient-centered approach to treatment, clinicians should consider adding flexibility in the prescription for HFCWO therapy and not feel constrained to the standard prescription. Here, we propose *adaptive HFCWO therapy*, where the patients are empowered to understand their symptoms and adapt the duration of treatment to their own personal needs in coordination with their healthcare team. Symptom tracking and adherence monitoring can provide important feedback to both patients and their healthcare teams. This regimen is intended to provide an optimal amount of therapy without unduly adding to treatment burden.

## Discussion

High frequency chest wall oscillation (HFCWO) is a well-established airway clearance approach that has been demonstrated as a therapy to help clear the lungs of secretions in patients with different types of lung disease (eg, cystic fibrosis (CF), bronchiectasis, and COPD) or in certain neurodegenerative disease states in patient populations who are unable to clear secretions from the lungs (eg ALS, Parkinson's Disease).<sup>1</sup> Although many of these chronic disease states cannot be cured and treatment plans depend on the severity of the symptoms, airway clearance is a critical part of the treatment regimen and solution. The goal of HFCWO is to loosen mucus that has pooled in the airways so patients can cough it up more easily. The need for airway clearance is one of the 'treatable traits' of these disease states that HFCWO therapy can address.<sup>2</sup> Originally developed by Warwick and Hansen,<sup>3,4</sup> HFCWO devices

were designed to address the challenges faced by CF patients and has become an integral part of the standard of care.<sup>5</sup> It has been reported to be equally effective<sup>6-13</sup> or superior<sup>3,14-17</sup> to other airway clearance therapies. While originally used in CF patients, HFCWO has been gaining in use for patients with bronchiectasis (BE).<sup>18,19</sup>

Unfortunately, low adherence is a major challenge in the treatment of chronic respiratory conditions.<sup>20,21</sup> For example, in CF it has been reported that adherence is 50% or less for pulmonary medications, airway clearance, and enzymes.<sup>22,23</sup> Factors associated with poor adherence include barriers such as treatment burden, time management difficulties, patient fatigue, and limited perceived health benefit.<sup>24</sup> The negative consequences linked to poor adherence are profound and include higher health care costs, reduced quality of life, increased exacerbations, and earlier mortality.<sup>20,25</sup> It is increasingly recognized that effective treatment leads to better adherence<sup>26</sup> while low adherence leads to suboptimal outcomes such as reduced health and well-being, lower productivity, disease relapse/exacerbation, and unscheduled use of more expensive health care resources.<sup>27,28</sup> The number and length of required treatments certainly adds to the patient perception of treatment burden, though it is possible that familiarity with the treatment will increase the patient's acceptance of the required time commitment and improve adherence.<sup>26</sup> Additionally, treatment needs in many chronic respiratory conditions may ebb and flow in response to changing patient conditions, and calls for an adaptive strategy for HFCWO care. These, in turn, may lead to decreased health and added treatment burden down the line. The time burden for therapy is often high, and is a particular issue for HFCWO.<sup>24,29</sup> Data from a large registry study in bronchiectasis show that optimal outcomes and response to vest therapy requires a period of time for patients to acclimatize and report the benefits of treatment.<sup>30</sup>

The prescription or dosage recommended for HFCWO is often fixed at two times a day for 30 minutes. It is interesting to note that this '30 minute rule' was originally recommended to approximate the time used in manual chest physiotherapy,<sup>31</sup> which is a very time-consuming and resource-intensive treatment. Moreover, in the early development of HFCWO techniques, pioneering studies found that each individual had a pressure-frequency combination that worked optimally.<sup>32</sup> All current systems available on the market incorporate multiple frequencies over the course of a treatment session, which can require considerable time. Successful treatment balances the

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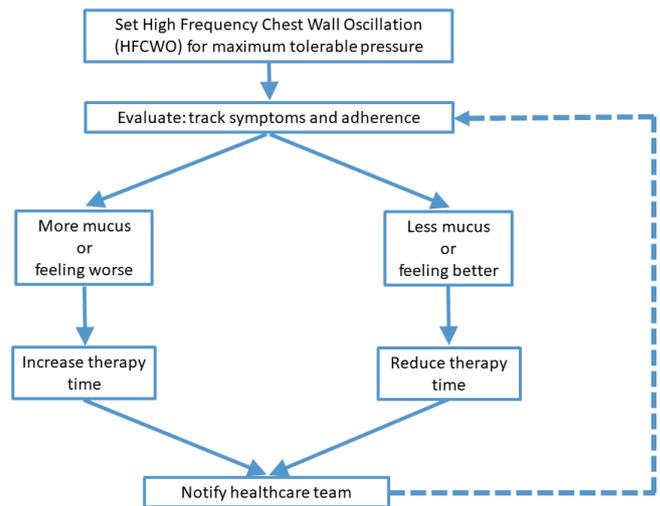
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need for time spent in therapy with the individual patients' capacity to meet this need. Even when the need is great, patients lead busy lives and often struggle to find time to be adherent with all of their therapies. In patients using HFCWO therapy, the result may be a substantial burden of treatment, or else significant non-adherence.<sup>27</sup>

Despite over two decades of experience with HFCWO, there has been remarkably little change in the recommended dosage for this airway clearance technique. A 'one size fits all approach' to dosing is unlikely to be the most appropriate way to approach airway clearance with vest therapy given the increased understanding we have of chronic lung disease states and patient behaviors. In this paper, we suggest a more tailored patient-centric approach intended to help this long-standing problem. Interventions that seem burdensome, are scheduled too frequently, or require too much patient effort will often result in non-adherence.<sup>27</sup> More is not necessarily better if it increases the patient burden. To facilitate positive patient outcomes, *the optimal dose for an intervention should be considered as the regimen which results in maximum adherence (at the maximum tolerable time and pressure) at minimum treatment burden.* As we enter the era of personalized care, prescribers should consider the concept of *adaptive HFCWO treatment* to better balance treatment burden and adherence to achieve the desired outcomes.

Although not a new idea, the adaptive treatment strategy is a patient-centered approach that tailors HFCWO treatment delivery in a dynamic way that meets the patients' changing needs/symptoms and addresses their immediate treatable traits.<sup>33</sup> The adaptive process alters the duration and/or magnitude of the treatment based on how the patient is actually feeling. Chronic lung conditions are not static and patient symptoms evolve as a function of the disease state as well as a function of the treatment itself. Treatment burden in a majority of chronic conditions changes over time in response to disease severity and comorbidities. The underlying assumption of this proposal is that optimal dosing will change over time and treatment plans that do not adjust to the patient's needs may unnecessarily lead to patient overburden or treatment fatigue.

A schematic flow of the adaptive HFCWO treatment approach is illustrated in Figure 1. From a clinical perspective, the adaptive approach should be based on two pillars. The first pillar is based on the patients' self-reported symptoms, principally their sputum production and cough. The second pillar is the patients' index of their overall sense of well-being (eg their overall energy level, difficulty breathing, etc.). In a condition when sputum production is low and their sense of well-being is high, the patient should be empowered by a more flexible prescription to reduce the number of sessions per day or to reduce the duration of each treatment to 15 minutes per session rather than the default 30 minute recommendation. The patient could possibly continue on this dosing regimen for one week and then monitor or reassess their symptoms and state of well-being to determine if there has been any notable change to report to their healthcare team. If they are stable or are experiencing improvement, the patient (with guidance and coaching from their healthcare team) could then elect to either keep their therapy time and pressure settings the same or reduce the treatment duration even further as long as their condition is stable. When sputum production is high or their sense of well-being is low, they could increase the number of sessions to two per day and increase the duration



**Figure 1.** Schematic Flow of Adaptive High Frequency Chest Wall Oscillation (HFCWO) Therapy

back up to at least 30 minutes. For example, if the patient reports that they 'feel it in my chest and I can't bring it up', this indicates a low sense of well-being and calls for a change in treatment. If the patient is reporting that their chest is full, are experiencing shortness of breath, and lack energy, then the treatment need is higher and they should increase the dosage of the treatment at the maximum tolerable pressure. Alternatively, as treatment starts to take effect and they feel more energetic and report that lung secretions are effectively being cleared, they could opt to decrease their therapy time. The adaptive HFCWO treatment approach would be enabled by a more flexible prescription provided by the healthcare provider. There will of course be a dynamic balance between when to use the device more and when to use the device less at different stages of the disease. But in general, patients should set the HFCWO device to highest tolerable pressure setting and then alter the therapy time as needed.

Promoting patient action and positive healthy behaviors is a guiding principle in chronic respiratory care. Such an adaptive approach personalizes care and has several potential benefits. In addition to reducing the perceived burden of treatment, a dynamic adaptive dosing strategy enables the patient to establish a feedback loop with their own body thereby promoting self-efficacy. An adaptive approach to dosing and treatment also fosters increased dialogue and engagement with the healthcare team and empowers the patient to make reason-based decisions on their own treatment. The opportunity to facilitate patient engagement with their own treatment and with their healthcare team is an important goal of an integrated adaptive titration approach. With a tailored approach, the patients become actively engaged not only in their own treatment, but also in self-awareness of their own symptoms. Symptom tracking is urged, allowing the patient to take ownership of the therapeutic process. Importantly, this process may be used by the healthcare team to foster conversations and better treatment. Clinicians recognize that adherence to therapy requires clear and coherent communication between the patient and healthcare team to ensure that treatments are maximally effective. Providers rely on patients carrying out health/treatment recommendations as directed, to optimize patients' health outcomes and improve health-related quality of life. The benefit of this approach is that it enables new partnerships, collaborative discussions,

cooperative efforts, helps alleviate treatment burden, and tailors treatment regimens to the realities of people's daily lives.

The future of chronic care of respiratory conditions is evolving rapidly. Personalized and patient-centered approaches are not new in pulmonary medicine and rehabilitation. In fact, adaptive approaches to respiratory care and HFCWO therapy were suggested early on in the care of CF patients. However, dosing recommendations for HFCWO therapy have changed little during this time. As next generation digital technologies to monitor patient symptoms and recent developments in connected care approaches are being integrated into HFCWO devices and treatment of chronic respiratory diseases, we are entering an exciting era of HFCWO treatment and pulmonary rehabilitation for chronic respiratory conditions. Understanding adherence patterns in patients using noninvasive vest therapy will likely provide a way to deliver more person-specific interventions. The tools and platforms implemented in new HFCWO devices that include monitoring will allow objective measurement of critical elements of treatment burden such as the number of treatments and time of administration. Digital data with symptom trackers and time of device use data will revolutionize the ability of respiratory healthcare system stakeholders (patients, providers, healthcare team members) to make data-driven treatment decisions and clinical recommendations. Objective data of targeted interventions based on personal adherence patterns may be cost-effective and result in considerable cost-savings. For research, the ability to log individual patient data from large numbers of patients anonymously may also enable modeling studies to document the utility of personalizing doses between patients in heterogeneous respiratory diseases. We predict that with the next developments in technology, significant progress will be made in further improving and optimizing HFCWO therapy to enhance overall patient outcomes.

## Conclusion

Our current proposal on adaptive HFCWO therapy is based on prior experience, increased knowledge, and clinical experience. It is time to fit personalized and connected care approaches for treatment of chronic respiratory conditions in the evolving healthcare ecosystem. It is our hope that these innovative tools in conjunction with clinically relevant data-driven modifications will address the barrier of adherence and facilitate the uptake of HFCWO therapy for patients who need them.

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# Tracheostomy Tube Cuff Considerations: Purpose, Practice, and Impact

Michael S Harrell, BS, RRT and Kristin A King, PhD, CCC-SLP

Care of patients with a tracheostomy has become a frequent topic of discussion in the medical industry and publications. Due to this focus, details related to the care plan of such patients are of concern and must be considered. One significant aspect of patient care is the safety and efficacy of proper cuff management, especially when using a bias-closed position, no-leak Valve.

## Purpose of a Cuff

The purpose of the inflated tracheostomy tube cuff is to direct airflow through the tracheostomy tube and into the airway when the cuff is inflated. This occurs typically during mechanical ventilation, as a closed ventilator circuit allows control and monitoring of ventilation for the patient. Frequently, the patient has a more seriously compromised system than patients who are not on a ventilator. The inflated cuff also may be important in cases of gross emesis or reflux when gross aspiration may occur; the cuff may assist in limiting the penetration of aspirated material into the lower airway.

However, the definition of aspiration is when any food, liquid, or other matter passes below the vocal folds. Therefore, the cuff cannot prevent aspiration as it also is located below the vocal folds (see Figure 1). When neither mechanical ventilation nor a risk of gross aspiration is present, the cuff should be deflated. Another consideration is to change the patient to a cuffless tracheostomy tube.

## Practice: Cuff Inflation

The inflated cuff should be avoided whenever possible because it has the potential to cause multiple complications, such as:

- 1) Increased risk of tracheal injury, including mucosal injury, stenosis, granulomas, and more;
- 2) Diminished ability to use the upper airway, leading to disuse atrophy over time; and
- 3) Restriction of laryngeal movement (laryngeal tethering) which may impact swallowing negatively.

If a patient requires an inflated cuff, then the manner in which it is being inflated should be considered. The complications that have been reported with tracheostomy tube cuffs may be avoided by ensuring proper management. Three methods which are commonly used to inflate a tracheostomy tube cuff are a cuff

manometer (cufflator), minimal occlusion volume, or minimal leak technique. While some guidelines provide that cuff pressure should be between 20-25 cmH<sub>2</sub>O, others suggest 15-30 cmH<sub>2</sub>O.<sup>1</sup> The disparity that exists between resources makes it imperative that healthcare professionals understand the potential impact and how to manage a cuff properly. Using the pilot balloon or pushing air into the cuff by syringe and without a stethoscope places the patient at high risk of an improperly inflated cuff which may cause damage or impairment. Dikeman and Kazandjian (2002) recommended that cuff inflation always occur with the use of manometer or stethoscope.<sup>2</sup>

## Practice: Cuff Deflation

Deflating the tracheostomy tube cuff, when appropriate, has been shown to have multiple patient benefits, including:

- 1) Reducing the risk of potential tracheal mucosal damage;
- 2) Returning the patient to a more normal physiology, including closing the system by using a bias-closed position, no-leak Valve;
- 3) Restoring speech and improving communication;
- 4) Allowing for the possible improvement of the swallow;
- 5) Potentially lowering the risk of aspiration;
- 6) Allowing rehabilitation to begin as early as possible; and
- 7) Decreasing the time to decannulation.

Cuff deflation is recognized as an important step in the care plan for a patient with a tracheostomy.<sup>3</sup> The benefits of cuff deflation can be safely and effectively extended to a patient with mechanical ventilation, when appropriate assessment and patient selection is performed.<sup>4</sup> This early cuff deflation may decrease delays in the rehabilitation process and potentially avoids the negative consequences related to the inflated cuff. The earlier that a patient has their cuff deflated, the earlier the patient may be weaned or decannulated. When decannulation is not a possible goal, cuff deflation may still accommodate the benefits outlined above on a long-term basis.

## Impact of Cuffs on Swallowing

Another reason for closely monitoring tracheostomy tube cuff status is that it may have a negative impact on swallowing. While a consensus does not exist in the research, it has been reported that an inflated cuff may impinge upon swallowing by tethering the larynx and reducing hyolaryngeal excursion during the swallow. Another reported impact is that an over-inflated cuff may impinge on the esophagus, causing reflux of ingested substances. However, research has shown that use of a Passy Muir® Valve improves swallowing and reduces aspiration more

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often and more significantly than cuff deflation alone (Suiter et al., 2003).<sup>5</sup>

Amathieu, Sauvat, Reynaud, Slavov, Luis, Dinca, ... Dhonneur (2012) conducted a study looking at incremental increases in cuff pressure for patients with tracheostomy and measured the impact on the swallow reflex.<sup>6</sup> They found that as the cuff pressure increased, the swallow reflex became increasingly more difficult in both latency and magnitude. Their findings indicated that any pressure above 25 cmH<sub>2</sub>O has a significant risk of negatively affecting swallowing. This finding becomes even more significant when considering the role that swallowing function plays in weaning a patient from both mechanical ventilation and from a tracheostomy tube.

A study by Ding and Logemann (2005) investigated swallowing in both cuff inflated and cuff deflated conditions.<sup>7</sup> They found that the frequency of reduced laryngeal elevation and silent aspiration were significantly higher in the cuff-inflated condition as compared to the cuff-deflated condition. Significant swallow physiology changes also were found to be significantly different among various medical diagnostic categories. The researchers suggested that these findings indicate a need to test both conditions during a swallow study.

In a recent systematic review, Goff and Patterson (2018) analyzed multiple studies and concluded that patients should be evaluated for possible swallowing impairment regardless of cuff condition.<sup>8</sup> They also suggested that patients should be seen and evaluated on a case-by-case basis to determine the safety of swallowing for return to oral nutrition. These recommendations were suggested because the research to date has not reached a consensus in order to establish a standard of care for tracheostomy and cuff management as they relate to swallowing.

### Impact of Team Management

The complexity of this patient population lends itself to being managed by a multidisciplinary team (MDT). It has been demonstrated that a team of appropriately trained professionals armed with evidence-based guidelines significantly improves care and reduces negative outcomes for the patient with tracheostomy.<sup>3,9</sup> A team approach assists with continuous monitoring, proper cuff management, and the patient care plan.

Working with patients following tracheostomy and with mechanical ventilation takes a multidisciplinary team (MDT) approach to ascertain that the needs of the patient are well met. Because of the complex nature of working with these patients, having the involvement of different disciplines provides perspective on various aspects of care. Typically, these patients are followed by both the respiratory therapist (RT) and the speech-language pathologist (SLP). However, many other healthcare professionals are trained and involved with the tracheostomy and use of the Passy Muir® Valve. To initiate an MDT approach, it takes multiple healthcare professionals, including the physician, nursing, dieticians, physical therapists, occupational therapists, and with the patient at the center of it all.

In a study conducted by Fröhlich, Boksberger, Barfuss-Schneider, Liem, & Petry (2017), they investigated best practice for early intervention with use of the Passy Muir Valve as a standard of care in the ICU following tracheostomy and mechanical ventilation.<sup>10</sup> Their findings demonstrated that

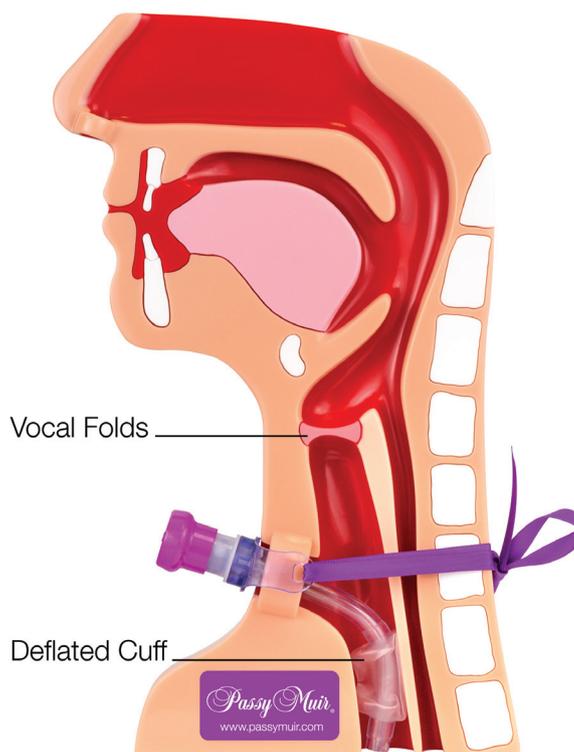


Figure 1. Cuff location in relation to the vocal folds

patients improved with voicing and swallowing more quickly than those without MDT intervention. However, since the authors were able to follow the patients over a period of time, which included up to 51 trials with the PMV®, they also reported how the implementation of a team approach had a positive impact on potential adverse events, with none occurring. The researchers attributed this to the multidisciplinary team approach and suggested the findings support the idea that two professionals should be at the bedside to provide assessment and intervention with the PMV in-line with mechanical ventilation.

Santos, Harper, Gandy, & Buchanan (2018) also investigated the impact of team management on the post-tracheostomy care of patients.<sup>11</sup> Their findings concur with Fröhlich, et al (2017) and suggest that having the involvement of an MDT allows the patient to progress faster in multiple areas.<sup>10</sup> The parameters addressed in their study were time in the ICU, total hospital days, days to Valve use, days to verbal communication, oral intake, and decannulation. The group receiving team management were found to have improved care in all areas measured. Patients who received the Valve with the MDT did so earlier in their care and had restored voicing, communication, and the ability to participate in their care. The positive impact of an MDT on the care of patients and the ability to achieve earlier voicing cannot be understated in its clinical significance. As with any medical procedure or device, thorough education is important in achieving the desired outcomes. Providing the education, and competency verification necessary, is the duty of the organization providing healthcare services.

It is the responsibility of healthcare professionals to provide the best possible care to their patients. Proper cuff management, including cuff deflation, contributes significantly to the best practice plan of care for the patient with a tracheostomy. Proper cuff management also leads to earlier intervention for communication and swallowing. The safety and efficacy of the

plan depends largely on the education and competency of the team caring for these individuals, as well as a commitment from the healthcare facility to a multidisciplinary tracheostomy team approach for patient care.

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industry is keeping pace with the current science of emergency medicine and developing or upgrading their products to stay out in front of the science and technology curve.”

## Data to be Presented at Thoracic Conference

Sunovion Pharmaceuticals Inc. said it would be presenting data from its portfolio of treatments for chronic obstructive pulmonary disease (COPD) at the American Thoracic Society International Conference 2019 in Dallas, Texas. “Several of Sunovion’s presentations at ATS 2019 focus on the importance of comorbidities, including anxiety and depressive symptoms and metabolic syndrome, on physiological and symptomatic responses in patients with moderate-to-very severe COPD who participated in the LONHALA MAGNAIR clinical program,” said Thomas H Goodin, PhD, Senior Director of Clinical Development at Sunovion. “COPD is a serious and complex medical condition that affects millions of Americans. Patients with COPD often present in the clinic with significant medical and psychiatric comorbidities. Therefore, it is important to provide these data from post hoc analyses to healthcare practitioners that evaluate the effectiveness and tolerability of a COPD therapy in the presence of other relevant medical conditions to help support individualized patient care.” Lonhala Magnair (glycopyrrolate) Inhalation Solution (25 mcg twice daily) was the first nebulized long-acting muscarinic antagonist (LAMA) approved for the treatment of COPD in the US LONHALA is administered by oral inhalation exclusively through the MAGNAIR Nebulizer System, which uses eFlow technology developed by PARI Pharma GmbH. The MAGNAIR Nebulizer System is a virtually silent, portable, closed system nebulizer that is designed to administer the medication in two to three minutes, as people breathe normally. Sunovion received approval from the US Food and Drug Administration (FDA) for LONHALA MAGNAIR in December 2017, and it became available to patients in April 2018.

## FDA OKs Wearable Device for In-Home Monitoring of Vital Signs

The US Food and Drug Administration (FDA) has approved the Current device from Current Health for in-home monitoring of vital signs for patients with heart failure, chronic obstructive pulmonary disease, and other chronic illnesses, the company has announced. The Current device received Class II FDA clearance for use in hospitals earlier this year. When used at home, the device has led to fewer readmissions and emergency department visits, the company says. Worn on the upper arm, the wireless, artificial-intelligence-powered device passively and continuously monitors a patient’s respiration, pulse, oxygen saturation, temperature, and mobility, delivering updates and alerts to the health provider via their mobile devices or electronic health record. This allows healthcare providers to intervene preventively and proactively, the company says. “As healthcare providers transition from a hospital-centric to a community-centric model of healthcare, they face new challenges. When patients leave the hospital doors, visibility on their health reduces to near zero. Oftentimes, an issue is not discovered until the patient presents to the emergency department and is readmitted,” Current Health CEO Christopher McCann writes in a blog post. The device’s algorithms “continuously analyze data, along with relevant contextual patient information, to offer actionable and proactive insights into the wearer’s health,” said McCann. It also integrates with third-party devices to capture additional metrics to develop patient-specific digital therapeutics and recommendations. The device monitors and tracks more vital signs than any other all-in-one wearable device on the market today, and “with ICU-level accuracy,” he added. Through a “chatbot,” patients can report symptom information and connect with their care team through video or secure text messaging.

# Mechanical Ventilation Enhances Extrapulmonary Sepsis-Induced Lung Injury: Role of WISP1- $\alpha$ v $\beta$ 5 Integrin Pathway in TLR4-Mediated Inflammation and Injury

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## Abstract

**Background:** High tidal volume ventilation of healthy lungs or exacerbation of existing acute lung injury (ALI) by more moderate mechanical ventilation (MTV) produces ventilator-induced lung injury. It is less clear whether extrapulmonary sepsis sensitizes the lung to MTV.

**Methods:** We used a two-hit model of cecal ligation and puncture (CLP) followed 12 h later by MTV (10 ml/kg; 6 h) to determine whether otherwise noninjurious MTV enhances CLP-induced ALI by contrasting wildtype and TLR4<sup>-/-</sup> mice with respect to: alveolar-capillary permeability, histopathology and intrapulmonary levels of WNT-inducible secreted protein 1 (WISP1) and integrin  $\beta$ 5; plasma levels of cytokines and chemokines (TNF- $\alpha$ , IL-6, MIP-2, MCP-1) and intrapulmonary neutrophil infiltration; and other inflammatory signaling via intrapulmonary activation of JNK, p38 and ERK. A separate cohort of mice was pretreated with intratracheal neutralizing antibodies to WISP1, integrin  $\beta$ 5 or IgG as control and the presented phenotyping repeated in a two-hit model; there were 10 mice per group in these first three experiments. Also, isolated peritoneal macrophages (PM) from wildtype and TLR4<sup>-/-</sup>, MyD88<sup>-/-</sup> and TRIF<sup>-/-</sup> mice were used to identify a WISP1-TLR4-integrin  $\beta$ 5 pathway; and the requisite role of integrin  $\beta$ 5 in WISP1-induced cytokine and chemokine production in LPS-primed PM was examined by siRNA treatment.

**Results:** MTV, that in itself did not cause ALI, exacerbated increases in alveolar-capillary permeability, histopathologic scoring and indices of pulmonary inflammation in mice that previously underwent CLP; the effects of this two-hit model were abrogated in TLR4<sup>-/-</sup> mice. Attendant with these findings was a significant increase in intrapulmonary WISP1 and integrin  $\beta$ 5 in the two-hit model. Anti-WISP1 or anti-integrin  $\beta$ 5 antibodies

partially inhibited the two-hit phenotype. In PM, activation of TLR4 led to an increase in integrin  $\beta$ 5 expression that was MyD88 and NF- $\kappa$ B dependent. Recombinant WISP1 increased LPS-induced cytokine release in PM that was inhibited by silencing either TLR4 or integrin  $\beta$ 5.

**Conclusions:** These data show for the first time that otherwise noninjurious mechanical ventilation can exacerbate ALI due to extrapulmonary sepsis underscoring a potential interactive contribution of common events (sepsis and mechanical ventilation) in critical care, and that a WISP1-TLR4-integrin  $\beta$ 5 pathway contributes to this phenomenon.

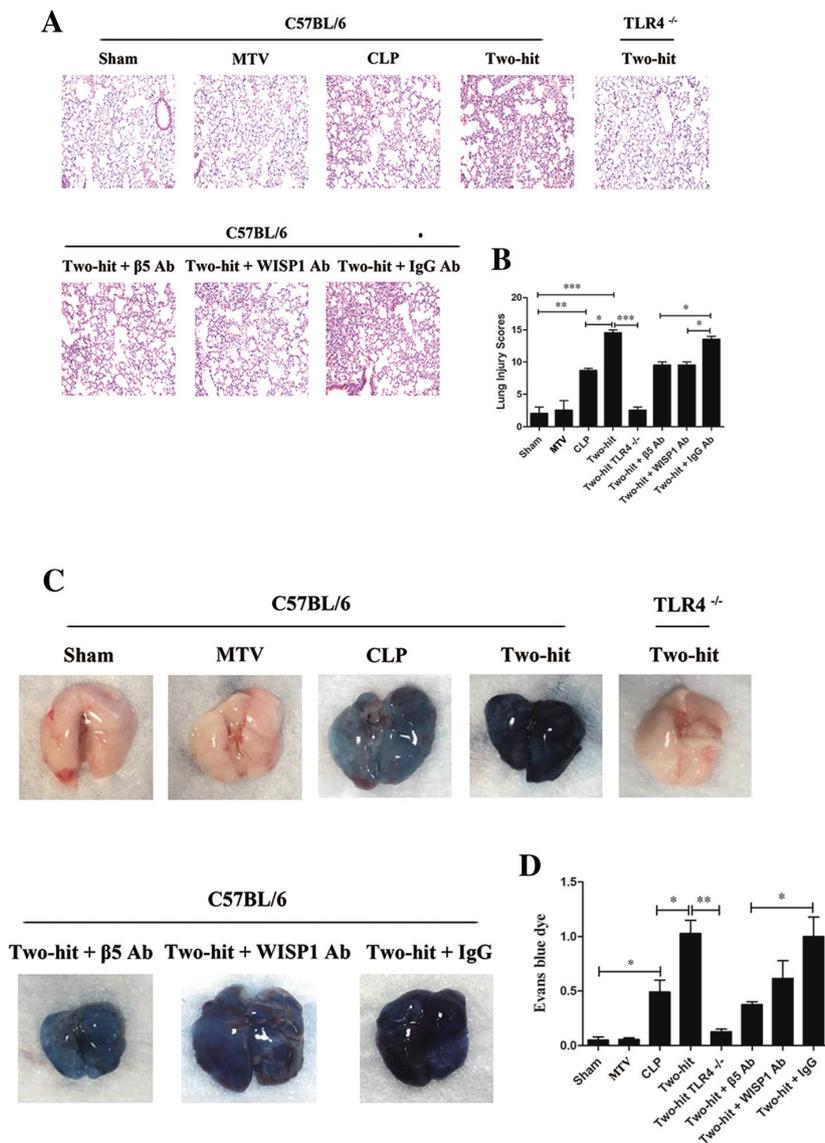
## Introduction

Mechanical ventilation (MV) is well known to cause an iatrogenic syndrome of ventilator-induced lung injury (VILI). The pathophysiology of VILI includes intrapulmonary inflammatory cell infiltrates, increased vascular permeability and pulmonary edema, and it may occur in ventilation of a healthy lung or worsening of preexisting and coexisting injury.<sup>1</sup> Sensitization of VILI secondary to pre-existing acute lung injury (ALI) due to pneumonia,<sup>2,3</sup> intratracheal endotoxin<sup>4-7</sup> or sterile injury<sup>8-10</sup> has provided preclinical evidence of a two-hit model.

Although extrapulmonary endotoxemia combined with noninjurious mechanical ventilation leads to VILI,<sup>11,12</sup> evidence of such a two-hit phenomenon in experimental extrapulmonary bacterial sepsis is less clear. Ventilating rodents after polymicrobial sepsis due to cecal ligation and puncture (CLP)<sup>13-15</sup> has produced equivocal results regarding sensitization to VILI. Mechanical ventilation with injurious high VT (30-40 ml/kg) exacerbated 48 h of CLP-induced lung injury in rats;<sup>16</sup> shorter periods of CLP were not associated with subsequent exacerbation of VILI in mice<sup>17</sup> or rats<sup>9,18</sup> although such overall injury was accelerated in the latter. Lower VT (15-20 ml/kg) did not exacerbate CLP-induced ALI in intact rats<sup>9</sup> or isolated perfused rat lungs.<sup>19</sup> Since both CLP and VILI have a common TLR4-mediated pathway to inflammation and injury<sup>5,20-22</sup> it seems plausible that mechanical ventilation could exacerbate CLP-mediated events within the lung and thus differences are likely to be secondary to variables in experimental protocols (degree of preexisting lung injury, volume and duration of ventilation) as suggested by Yehya et al.<sup>18</sup>

In the current study, we examined the effect of prolonged (6 h), otherwise noninjurious<sup>4</sup> moderate VT ventilation (MTV) in mice with preexisting mild ALI after CLP (12 h). We focused

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**Fig. 1** MTV enhances CLP-induced lung damage via TLR4-dependent WISP1–integrin β5 pathway. As shown in Additional file 1: Figure S1, mice lung tissue samples in eight mice groups were fixed and stained with hematoxylin–eosin for histological analysis (a) and lung injury score (b). Gross lung image in each group (c) and vascular permeability evaluated by Evans blue dye (d). Mice receiving combination of CLP + MTV (two-hit model) compared to mice subjected to CLP alone for 18 h or sham operation followed by 6 h of MTV. Two-hit model in wildtype mice compared to subgroup of TLR4<sup>-/-</sup> mice or wildtype mice that received intratracheally neutralizing antibodies to either integrin β5 (β5 Ab) or WISP1 (WISP1 Ab) or a control antibody (IgG Ab) during mechanical ventilation. \**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001. CLP cecal ligation and puncture, MTV moderate tidal ventilation, TLR4 toll-like receptor 4, WISP1 WNT1 inducible secreted protein

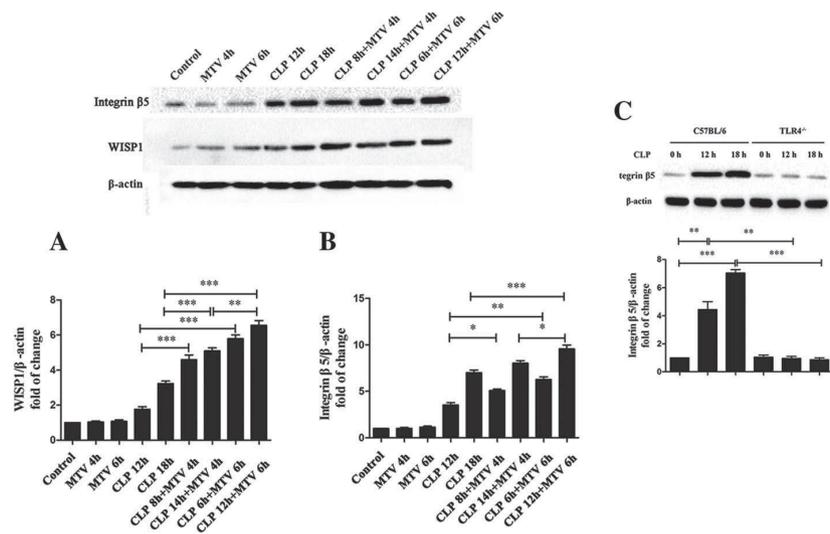
on a novel WNT1 inducible secreted protein (WISP1 or CCN4; also referred to as WNT1 inducible signaling protein-1)–integrin β5 pathway of TLR4-mediated pulmonary inflammation and injury in this two-hit model as we previously noted key roles for WISP1 and beta integrins in VILI<sup>21</sup> and CLP<sup>22,23</sup> mediated ALI. The mechanism by which WISP1 acts in CLP and/or VILI remains unclear. WISP1 appears, however, to be a modulator of TLR4–CD14 signaling and is known to signal through integrins<sup>24</sup> although the precise integrin is unclear. Although several integrins are important in ALI,<sup>25</sup> integrin β5 is a central regulator of increased permeability in VILI<sup>26</sup> and CLP.<sup>27</sup>

Thus, the overall hypotheses of this study were that: prolonged ventilation with otherwise noninjurious moderate VT exacerbates ALI in extrapulmonary sepsis; WISP1 and integrin β5 contribute to this two-hit model (ie, CLP + MTV); and TLR4 is central to the WISP1–TLR4–integrin β5 proinflammatory pathway.

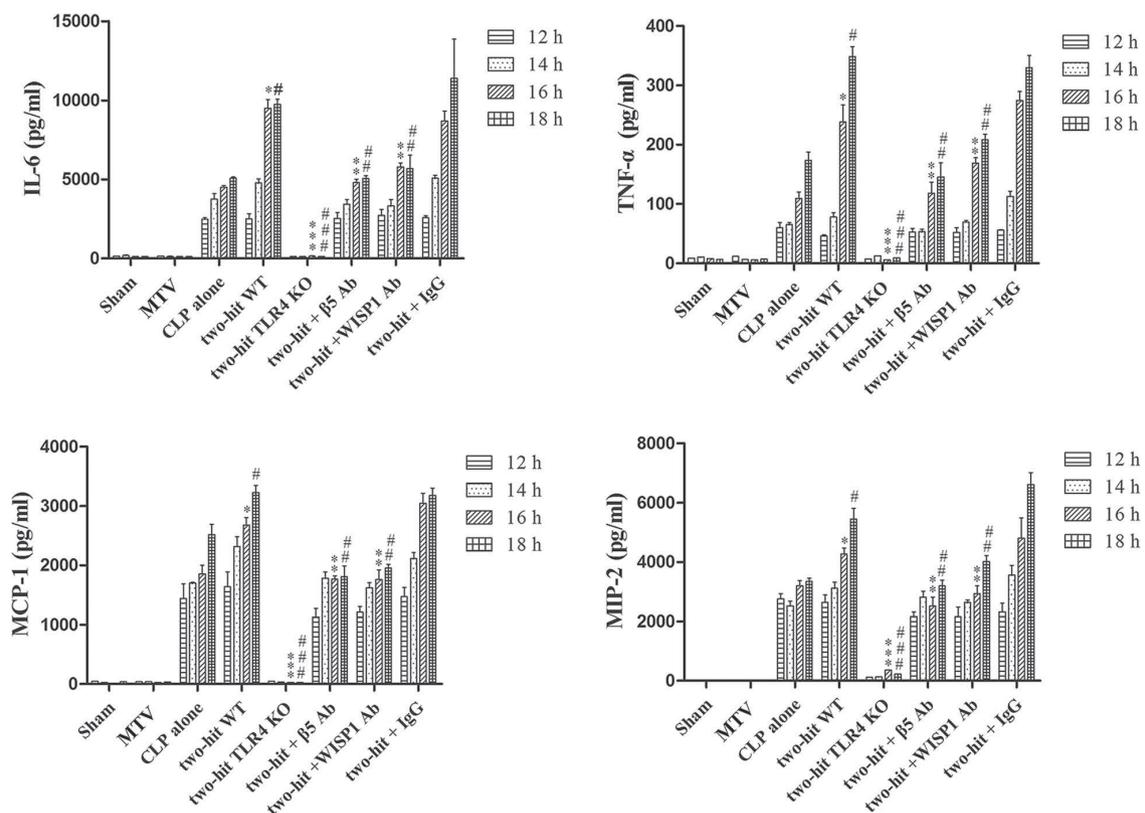
## Methods

### Experimental protocols

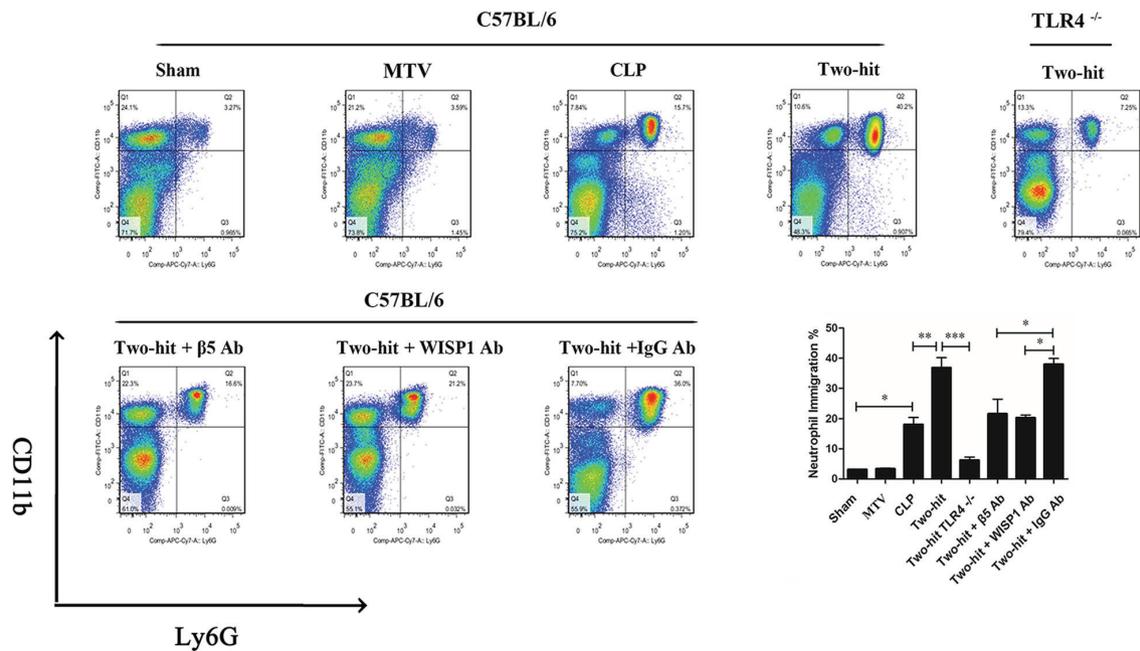
Animal protocols were approved by the Animal Care and Use Committee and experiments were performed in strict adherence to NIH Guidelines and followed current guidelines for preclinical models in research. Details of materials and methods are provided in Additional file 8: Materials and Methods) and experimental protocols are outlined for intact mice (Additional file 1: Figure S1) and cultured PM (Additional file 2: Figure S2) including: MTV and CLP-induced lung damage via TLR4-dependent, WISP-1 and integrin β5 contributory fashion in two-hit lung damage; MTV and CLP-induced changes in circulating levels of cytokines and chemokines, and an association with increased neutrophil infiltration of the lungs of intact mice; other inflammatory signaling (pJNK, p38, pERK) pathways in lungs of mice after CLP and MV; the mechanism of upregulation of integrin β5 in LPS-treated PM isolated from wildtype, TLR4 null, Myd88<sup>-/-</sup> and TRIF<sup>-/-</sup> mice; and the requisite role of integrin β5



**Fig. 2** MTV enhances CLP-induced WISP1 and integrin  $\beta 5$  expression via TLR4-dependent pathway. WISP1 protein level (a) and integrin  $\beta 5$  expression (b) in lungs from each group of mice shown by western blot. MTV did not affect both levels and CLP led to small increases but two-hit model increased very significantly. Integrin  $\beta 5$  expression in lungs induced by CLP demonstrated in time-dependent fashion from wildtype mice (C57BL/6) but not TLR4<sup>-/-</sup> mice (c). Corresponding actin identified for normalizing densitometry. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . CLP cecal ligation and puncture, MTV moderate tidal ventilation, TLR4 toll-like receptor 4, WISP1 WNT1 inducible secreted protein



**Fig. 3** MTV increases circulating levels of cytokines and chemokines. Cytokines (TNF- $\alpha$  and IL-6) and chemokines (MIP-2 and MCP-1) in plasma detected by ELISA. Mice receiving combination of CLP + MTV (two-hit model) compared to mice subjected to CLP alone or sham operation followed by MTV. Two-hit model in wildtype mice compared to subgroup of TLR4<sup>-/-</sup> mice (TLK4 KO) or wildtype (WT) mice that received intratracheally neutralizing antibodies to either integrin  $\beta 5$  ( $\beta 5$  Ab) or WISP1 (WISP1 Ab) or a control antibody (IgG) followed with CLP 12, 14, 16 and 18 h and MTV 0, 2, 4 and 6 h, respectively. CLP alone induced expected increase in circulating cytokines and chemokines but not induced by MTV alone. Two-hit model (CLP + MTV) increased cytokines and chemokines by MTV in time-dependent manner whereas deletion of TLR4 prevented these increases and inhibition of WISP1 or integrin  $\beta 5$  with neutralizing antibodies also blocked increases induced by MTV. \* $P < 0.05$  compared with CLP alone at 16 h; \*\* $P < 0.05$  compared with two-hit WT at 16 h; \*\*\* $P < 0.05$  compared with two-hit WT; # $P < 0.05$  compared with CLP alone at 18 h; ## $P < 0.05$  compared with two-hit WT at 18 h; ### $P < 0.05$  compared with two-hit WT at 18 h. CLP cecal ligation and puncture, IL interleukin, MCP-1 monocyte chemoattractant protein-1, MIP-2 macrophage inflammatory protein-1, MTV moderate tidal ventilation, TLR4 toll-like receptor 4, TNF- $\alpha$  tumor necrosis factor alpha, WISP1 WNT1 inducible secreted protein



**Fig. 4** MTV increases PMN infiltration in lungs of septic mice. Neutrophil immigration in lung detected by flow cytometry. Mice receiving combination of CLP + MTV (two-hit model) compared to mice subjected to CLP alone for 18 h or sham operation followed by 6 h of MTV. Two-hit model in wildtype mice compared to subgroup of TLR4 null mice or wildtype mice that received intratracheally neutralizing antibodies to either integrin  $\beta 5$  ( $\beta 5$  Ab) or WISP1 (WISP1 Ab) (or control antibodies (IgG Ab)). Neutrophil influx by quantifying percent of CD11b<sup>+</sup> and Ly6G<sup>+</sup> cells in CD45<sup>+</sup> cell population isolated from lung homogenates. CLP significantly increased percent of PMN while MTV had no impact on percent PMN in lung; CLP and MTV (two-hit model) significantly further increased neutrophil immigration in lung whereas TLR4 deletion completely prevented change in percentage of PMN induced by CLP + MTV compared to this two-hit model in wildtype mice. Blocking either WISP1 or integrin  $\beta 5$  partially prevented increase in percentage of PMN induced in two-hit model compared to combined CLP and MTV in mice receiving control IgG antibody. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . CLP cecal ligation and puncture, MTV moderate tidal ventilation, TLR4 toll-like receptor 4, WISP1 WNT1 inducible secreted protein

in WISP1-induced cytokine and chemokine production in LPS-primed PM.

### In-vivo experimental animal model

C57BL/6 mice (8-10 weeks old, male) were purchased from Jackson Laboratory and TLR4<sup>-/-</sup> mice were used as described previously.<sup>21,22</sup> Forty wildtype mice were prospectively randomized to one of four groups (n = 10 per group): spontaneous breathing (sham control), spontaneous breathing with CLP; mechanical ventilation; or CLP and MTV. Mild sepsis was induced by CLP<sup>13,14</sup> as modified by Ding et al<sup>23,28</sup> and MTV (10 ml/kg; 150/min, zero positive end-expiratory pressure) was performed in anesthetized mice alone or after CLP (12 h). A cohort (n = 20) of TLR4<sup>-/-</sup> mice underwent sham and spontaneous breathing (n = 10; control) or CLP and MTV as already described (n = 10). In separate cohorts, mice were intratracheally administered anti-WISP1 (n = 10), anti-integrin  $\beta 5$  (n = 10) or serum IgG (n = 10; 0.5  $\mu$ g/g in 50  $\mu$ l PBS) after CLP but before MTV. Phenotypic changes due to CLP, MTV or their combination included histopathology (scored by a pathologist blinded to experiments), alveolar-capillary permeability (Evans Blue albumin<sup>21</sup>) and inflammation as assessed by plasma levels of cytokines and chemokines, neutrophil immigration in the lung (flow cytometry) and intrapulmonary MAP kinase activation (phosphorylation status of JNK, ERK and p38).

### In-vitro studies

Isolation and culture of peritoneal macrophages (PM) from wildtype, TLR4<sup>-/-</sup>, MyD88<sup>-/-</sup> or TRIF<sup>-/-</sup> mice was performed as described previously.<sup>21,22</sup> Cells were treated with LPS and/or costimulated with recombinant WISP1 (rWISP1) and cytokine production was assessed in conditioned medium of wildtype

cells or after transfection with 50 nM small interfering RNA (siRNA) for integrin  $\beta 5$  (sc-35681; Santa Cruz) or scrambled siRNA. The role of TLR4 signaling was assessed by comparing the response of PM isolated from wildtype vs TLR4<sup>-/-</sup>, Myd88<sup>-/-</sup> or TRIF<sup>-/-</sup> mice.

### Histological examination

Lung tissue samples were fixed in 4% paraformaldehyde in PBS overnight at 4°C and processed as described previously<sup>22</sup> including semiquantitative histopathology (H&E; light microscopy) by a pathologist blinded to the experimental group.

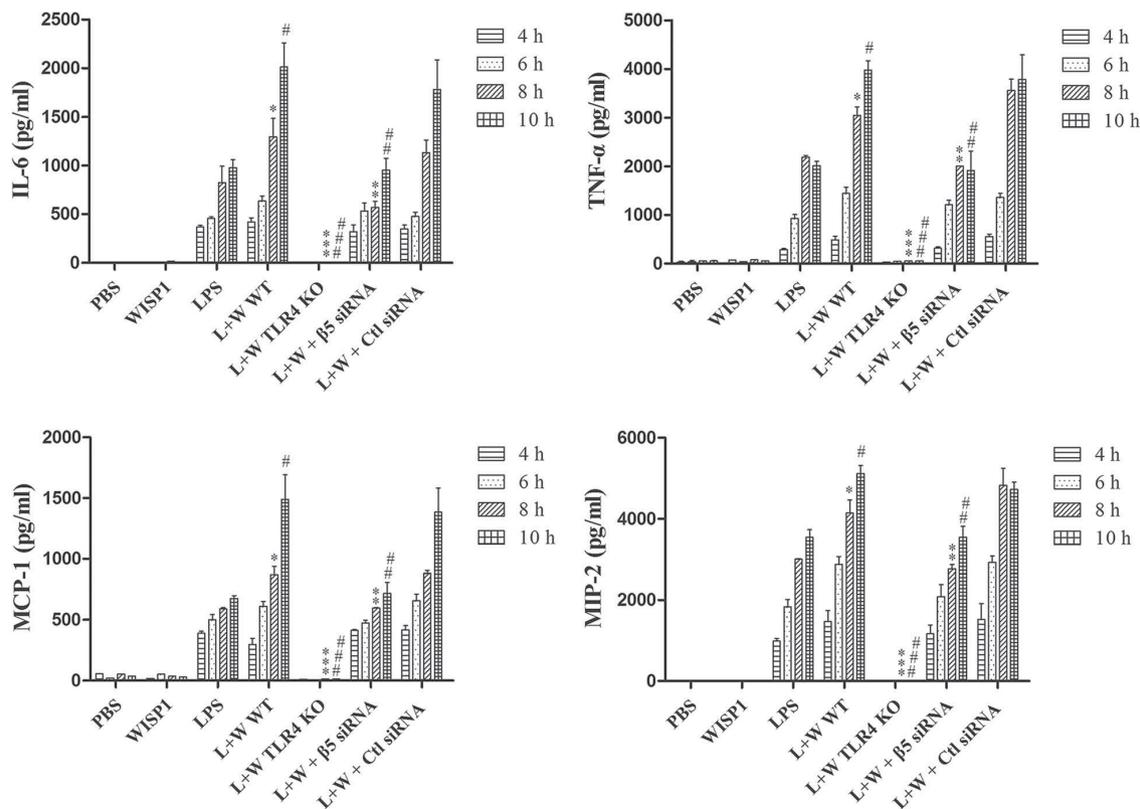
Western blot analysis of WISP-1 and integrin  $\beta 5$  was performed as described previously.<sup>21,22</sup> Plasma or conditioned medium were assayed for cytokines and chemokines using commercially available ELISA reagents for TNF- $\alpha$ , IL-6, MIP-2 and MCP-1.

### Flow cytometry

The lung was enzymatically digested and mechanically dissociated (MACS dissociator) and single cell suspensions were isolated by passing the suspension through a 70- $\mu$ m filter. Cells were stained with mAbs specific to Fixable Viability Dye eFluor<sup>®</sup> 506, CD45, CD11b, Ly6G for 30 min at 4°C and fixed with 2% paraformaldehyde for 10 min at 4°C. An LSR II (Becton Dickinson) was used for flow cytometry and data were analyzed with FlowJo software.

### Alveolar-capillary permeability

Evans blue albumin (EBA; 0.5%, 25 mg/kg body weight) was injected into the internal jugular vein 1 h before euthanasia and lung harvesting. Blood samples and lung tissue were obtained and processed as described previously<sup>21,22</sup> and the



**Fig. 5** WISP1-induced cytokine and chemokine production in LPS-primed peritoneal macrophages requires integrin  $\beta 5$ . Peritoneal macrophages (PM) treated with LPS (0.1  $\mu\text{g/ml}$ ) followed by WISP1 (10  $\mu\text{g/ml}$ ) exposure at 4 h. Supernatants collected at 2 h intervals from 4 to 10 h following WISP1 stimulation. Cytokines (TNF- $\alpha$  and IL-6) and chemokines (MIP-2 and MCP-1) in supernatant detected by ELISA. PM receiving combination of LPS + WISP1 (L + W) from wildtype mice (WT) compared to PM from subgroup of either TLR4<sup>-/-</sup> mice or wildtype mice receiving integrin  $\beta 5$  siRNA transfection (or control siRNA) subjected to LPS or WISP1. LPS-induced increases in IL-6, TNF- $\alpha$ , MIP-2 and MCP-1 evident within 4–10 h and addition of WISP1 induced further increases in all four mediators. Suppression of integrin  $\beta 5$  expression prevented WISP1-induced enhancement of LPS induction in four mediators. \* $P < 0.05$  compared with LPS alone at 8 h; \*\* $P < 0.05$  compared with L + W WT at 8 h; \*\*\* $P < 0.05$  compared with L + W WT; # $P < 0.05$  compared with LPS alone at 10 h; ## $P < 0.05$  compared with L + W WT at 10 h; ### $P < 0.05$  compared with L + W WT at 10 h. Ctl, control; IL interleukin, KO knockout, LPS lipopolysaccharide, MCP-1 monocyte chemoattractant protein-1, MIP-2 macrophage inflammatory protein-1, PBS phosphate buffered saline, siRNA small interfering RNA, TNF- $\alpha$  tumor necrosis factor alpha, WISP1 WNT1 inducible secreted protein

EBA permeability index was calculated by dividing pulmonary EBA absorbance at 620 nm/g of lung tissue by plasma EBA absorbance at 620 nm.

### Immunofluorescence staining of cells and fluorescence microscopy

PM were cultured for a defined time period, fixed in 4% paraformaldehyde in PBS for 15 min. Cells were washed in PBS, permeabilized using 0.1% Triton X-100, blocked with 5% BSA for 45 min and sequentially administered primary antibody and secondary antibody (Alexa-488-conjugated donkey anti rabbit secondary antibody). Nuclei were stained with DAPI (Thermo Fisher Scientific) and cells were examined and recorded using EVOS FL fluorescence microscopy (immunofluorescence analysis; Thermo Fisher Scientific).

Reagents are described in Additional file 8: Materials and Methods.

### Data analysis and statistics

Data are presented as the mean  $\pm$  SEM of the indicated number of experiments and analyzed using one-way and two-way ANOVA; post-hoc testing was performed using the Bonferroni modification of the t test. The individual studies performed throughout this work represent five independent studies. Power analyses were performed by using type I error probability of 0.05, with a power of 0.9, to determine the sample size necessary

to reject the null hypothesis. All statistical analyses were carried out using the GraphPad Prism 5 program.  $P < 0.05$  was considered statistically significantly.

### Results

CLP alone led to modest lung injury as demonstrated by histology (Fig. 1a, b) and a significant increase in alveolar-capillary permeability (Fig. 1c, d). MTV alone had no impact on lung injury or permeability, but when applied after CLP it markedly enhanced both the lung injury score and alveolar-capillary permeability. The histopathologic and permeability changes in the two-hit model were completely abrogated in TLR4<sup>-/-</sup> mice and partially (but significantly) reduced in cohorts of mice receiving antibodies to either WISP1 or integrin  $\beta 5$ . In wildtype mice, we noted that: MTV did not affect intrapulmonary levels of either WISP1 or integrin  $\beta 5$ ; CLP led to small but significant increases in either WISP1 or integrin  $\beta 5$ ; and the two-hit model increased either of these molecules 2–3 $\times$  more than CLP alone (Fig. 2a, b). We previously noted that high VT ventilation increases in WISP1 were abrogated in TLR4<sup>-/-</sup> mice<sup>21</sup> and we now note (Fig. 2c) that CLP-induced increases in integrin  $\beta 5$  are abrogated in TLR4<sup>-/-</sup> mice.

CLP increased circulating cytokines and chemokines whereas MTV alone did not; the combination of MTV and CLP, however, caused levels of all four mediators to progressively rise above levels measured with CLP alone (Fig. 3). Deletion of TLR4

prevented increases in cytokines and chemokines in the two-hit model and inhibition of WISP1 or integrin  $\beta 5$  blocked further increases induced by MTV (Fig. 3).

CLP significantly increased neutrophil influx in the lung while MTV had no impact; CLP and MTV further significantly increased neutrophil immigration (Fig. 4) that was abolished in TLR4 null mice. Blocking WISP1 or integrin  $\beta 5$  partially prevented the increase in the percentage of PMN induced in the two-hit model compared to combined CLP and MTV in mice receiving control IgG antibody.

We sought further evidence that MTV directly enhanced inflammation in the lungs of septic mice by measuring levels of activated JNK, p38 and ERK MAP kinase. Six hours of MTV had no effect on MAP kinase activation but significantly promoted MAP kinase activation in mice previously subjected to CLP (Additional file 3: Figure S3). TLR4 deletion prevented the increases in MAPK activation in CLP-treated and CLP + MTV-treated mice. Blocking WISP1 or integrin  $\beta 5$  also prevented the increase in MAP kinase phosphorylation induced by MTV in CLP mice.

To explore the mechanism of integrin  $\beta 5$  upregulation by TLR4, we exposed peritoneal macrophages (PM) to LPS and found that ultrapure LPS induced a time and concentration-dependent increase in surface integrin  $\beta 5$  expression (Additional file 4: Figure S4). The increase in integrin  $\beta 5$  expression was TLR4 and MyD88 dependent, but TRIF independent (Additional file 5: Figure S5). We also found that integrin  $\beta 5$  upregulation by LPS was NF- $\kappa$ B dependent (Additional file 6: Figure S6).

LPS-induced increases in IL-6, TNF- $\alpha$ , MIP-2 and MCP-1 in medium of isolated PM were evident within 4-10 h and the addition of rWISP1 induced further increases in all four mediators (Fig. 5). No increase in any of the mediators could be seen in PM from TLR4<sup>-/-</sup> mice. Suppression of integrin  $\beta 5$  expression with siRNA (Additional file 7: Figure S7) prevented the WISP1-induced enhancement of LPS-induced IL-6, TNF- $\alpha$ , MIP-2 and MCP-1 released by PM (Fig. 5).

## Discussion

In the current study, MTV did not cause ALI, but exacerbated CLP-mediated increases in alveolar-capillary permeability and indices of pulmonary inflammation (histopathology, cytokines, chemokines, neutrophil influx and activation of MAPK) in wildtype mice: the effects of this two-hit model were completely abrogated in TLR4 null mutants and partially inhibited by neutralizing antibodies to either WISP1 or integrin  $\beta 5$ . In PM, activation of TLR4 led to an increase in integrin  $\beta 5$  expression and rWISP1 increased LPS-induced cytokine release in PM that could be inhibited by silencing either TLR4 or integrin  $\beta 5$ . Collectively, these data show: that prolonged MTV ventilation exacerbates ALI caused by extrapulmonary sepsis; and an important positive feedback role for the WISP1-integrin  $\beta 5$  pathway in TLR4-mediated exacerbations to this two-hit model.

Mechanical ventilation with high VT is well known to injure healthy lungs and a consensus from experimental and clinical conditions supports the hypothesis that mechanical ventilation can worsen injury in previously damaged lungs.<sup>1,11,29-31</sup> Although systemic<sup>11</sup> endotoxin interacts with mechanical ventilation in producing ALI,<sup>16</sup> there is a lack of consensus from studies directed at identifying extrapulmonary bacterial sepsis as a

sensitizing condition to VILI. CLP remains the gold standard of experimental polymicrobial sepsis<sup>15</sup> but ventilating rodents after CLP has produced equivocal results regarding sensitization to VILI.<sup>9,18,19</sup> Nin et al<sup>16</sup> reported that mechanical ventilation aggravated CLP-induced multiorgan dysfunction in rats but the investigators used prolonged CLP (24-48 h) and high VT (35 ml/kg). Others have used lower VT ventilation after CLP and did not observe worsening of lung injury.<sup>9</sup> Uematsu et al<sup>17</sup> noted that high VT ventilation (40 ml/kg) after CLP increased mediator release but did not affect pulmonary function. Yehya et al<sup>18</sup> showed that high VT (30 ml/kg) accelerated lung injury secondary to previous CLP in rats but the endpoints of injury (lung compliance, pulmonary edema, oxygenation and computed tomography of micro-CT scans) reached the same pathophysiology as from CLP alone. These authors highlighted subtleties in the degree of initial injury with CLP and the magnitude and duration of mechanical ventilation, and speculated that prolonged ventilation with lower VT may indeed enhance lung injury after CLP. In this regard, we unequivocally note that otherwise noninjurious MTV for a prolonged (6 h) time exacerbated underlying CLP-induced ALI. Indeed, whether CLP in itself causes ALI in mice is conjectural. Iskander et al<sup>32</sup> clearly showed that pulmonary injury after CLP in mice cannot be considered the etiology of death in the acute phase. The authors did note that a severe model of sepsis with significant mortality could show signs of lung injury. We reported previously<sup>22,23,28</sup> that the current model of CLP was associated with 80% mortality in 72 h and this presumably accounted for the modest but significant ALI noted at the earlier time period in the current study. Furthermore, we noted that 6 h of MTV (10 ml/kg) without PEEP was void of significant lung injury. In this regard, our model of effects of mechanical ventilation reproduces previous experience of lack of injury with MTV (10 ml/kg, zero PEEP),<sup>4,28</sup> and was somewhat similar to the results from Hegeman et al<sup>33</sup> who noted little evidence of ALI in mice after 5 h of mechanical ventilation with 7 ml/kg and 3 cmH<sub>2</sub>O of PEEP or 5 h of MV with 15 ml/kg and zero PEEP. These authors did report VILI under both conditions at a longer time period (12 h).<sup>33</sup>

We<sup>21,34</sup> and others<sup>5,35</sup> have noted the important role of TLR4 in experimental VILI. We also noted<sup>22,23,28</sup> that a considerable component of patho-physiology, inflammation and injury of CLP was due to TLR4 activation (and CD14). The injury, neutrophil sequestration and inflammation due to combined effects of CLP and MTV in the current study were all abrogated in TLR4 null mice.

WISP1 is a secreted matricellular protein involved in cell adhesion, migration, differentiation, proliferation and survival.<sup>36</sup> From an unbiased haplotype association mapping in inbred strains of mice, we identified WISP1 as a candidate gene associated with VILI.<sup>21</sup> We subsequently identified a role for WISP1 in CLP-induced ALI.<sup>22,23</sup> WISP1 was first noted in the lung to be a component of bleomycin-induced lung injury and fibrosis,<sup>37</sup> and subsequently has been reported to be important in epithelial-mesenchymal transition,<sup>38</sup> airway remodeling<sup>39</sup> and proliferation of fibroblasts in the context of lung fibrosis.<sup>40</sup> In-vitro mechanical stretch of type II epithelial cells activated innate immunity and increased WISP1 expression, providing fundamental support for its involvement in VILI.<sup>41</sup> We noted that intrapulmonary WISP1 is elevated in VILI,<sup>21</sup> CLP,<sup>22,23</sup> combined poly(I:C) and mechanical ventilation,<sup>42</sup> and in the current report in combined CLP and MTV; neutralizing antibodies to WISP1 partially reduced lung injury and inflammation in all of these conditions. The potential convergence of WNT/ $\beta$ -catenin

signaling and WISP1 adds to its importance in VILI<sup>43</sup> as well as WNT-mediated lung epithelial cell repair.<sup>44</sup>

The mechanism by which WISP1 acts in CLP and/or VILI remains unclear. It appears, however, to be a modulator of TLR4–CD14 signaling and is known to signal through integrins.<sup>24</sup> WISP1 coimmunoprecipitated with active, glycosylated TLR4 in lungs of mice subjected to high VT ventilation and rWISP1 augmented LPS-induced TNF- $\alpha$  release in a TLR4–CD14-dependent fashion in PM.<sup>21</sup> The RGD peptide-sensitive response of intact mouse lungs to CLP and the coimmunoprecipitation of WISP1–integrin  $\beta 6$  in lungs of these mice<sup>23</sup> suggested the presence of the WISP1–integrin  $\beta 6$  pathway in mediating TLR4-dependent inflammation and injury. We noted an obligatory role for integrin  $\beta 3$  in WISP1-mediated release of TNF- $\alpha$  in PM<sup>22</sup> and an important role for integrin  $\beta 3$  in polymicrobial sepsis and combined injury from poly I:C instillation and mechanical ventilation.<sup>42</sup> In the current study we noted that siRNA to integrin  $\beta 5$  reduced WISP1-mediated release of multiple cytokines in PM and integrin  $\beta 5$  contributed to lung inflammation and injury with CLP and MTV. Identifying the precise integrin  $\beta$  subunit involved in complex lung injury and signaling in isolated macrophages is complicated by: the multitude of  $\beta$  subunits; the nondiscriminatory inhibition by RGD peptides; and the promiscuity of WISP1 regarding interactions with  $\alpha V\beta$  integrin subunit receptors.<sup>45</sup> We focused on the interaction of WISP1 and integrin  $\beta 5$  because: others noted that WISP1 induces IL-6 production through integrin  $\beta 5$  receptor in human synovial fibroblasts;<sup>46</sup> and although several integrins are important in ALI,<sup>25</sup> integrin  $\beta 5$  is a central regulator of increased permeability in VILI<sup>26</sup> and CLP.<sup>27</sup>

We limited our phenotyping of lung injury to inflammation, alveolar-capillary permeability and histopathologic changes, and did not assess lung mechanics or evolution of changes in gas exchange. As such, fundamental issues of alveolar overdistension and physiologic consequences in the current study remain conjectural. It is noteworthy, however, that we recently reported<sup>28</sup> that low VT (6 ml/kg; 6 h) mechanical ventilation was protective after CLP (6 h). We relied on neutralizing antibodies to assess the role of WISP1 and integrin  $\beta 5$  in a two-hit model and partial effects noted in the study may have been secondary to incomplete deletion. For pragmatic reasons, we used PM as a surrogate for the likely cell of interest (alveolar macrophage) and future studies validating these observations with alveolar macrophages, a more challenging cell to isolate in sufficient number, are necessary.

## Conclusion

In the current study, we provide evidence that mild lung injury secondary to extrapulmonary sepsis can sensitize intact mouse lung to subsequent prolonged MTV. This two-hit model is TLR4 sensitive and has important proinflammatory contributions from both WISP1 and integrin  $\beta 5$ . In isolated PM, we further defined the nature of WISP1 signaling and identified a requisite TLR4-dependent activation of integrin  $\alpha V\beta 5$  and MyD88–NF- $\kappa B$  pathway inflammatory mediator biosynthesis. This two-hit model provides relevant new information regarding unresolved issues of a common risk factor for ARDS (systemic sepsis) and sensitization to often-used MTV.

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# PARTNERING FOR BRONCHIECTASIS SOLUTIONS



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