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CASE REPORT
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ABSTRACTS
Poster Abstracts from the 2017 Conference of the Canadian Society of Respiratory Therapists
54th CSRT Annual Education Conference
Westin Bayshore, VANCOUVER, BC
May 24-26, 2018

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ISSN 1205-9838 (Print), 2368-6820 (Online). Date of issue: July 2017.

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Stewarding our community’s journal

Andrew West, EdD(c), RRT, FCSRT

Over the past decades the Canadian Journal of Respiratory Therapy has grown remarkably. Its evolution to its current status as an internationally respected scientific publication that serves to inform the practice of respiratory therapists has occurred alongside a drive for scholarship that has been maturing more widely within our profession.

It has always been the role of the editorial board to steward and safeguard the Canadian Journal of Respiratory Therapy as an important component of the architecture of our growing community. To that end the Journal maintains an editorial board membership that represents the breadth of the profession’s areas of practice and, importantly, offers the Journal a range of perspectives and insights into the practice of scientific publication.

Currently, the editorial board of this Journal is embarking on a strategic planning process that will extend its current momentum over the near and long term. Of specific interest to the board will be strategies that serve to enhance the applicability of the publication to an expanding audience. There are many exciting initiatives already in the works that we believe will make important advances in this direction.

With unfortunate widespread evidence of irresponsible publishing practices and rising retraction rates over recent years, the important role of editorial boards in ensuring the quality of published information sources has been heightened [1].

Respiratory therapy represents a relatively small community where national leadership is often provided by dedicated volunteers who caringly contribute to our shared advancement. This too is the case with respect to the editorial leadership of this Journal. Consequently, throughout our professional lives we are often called upon to contribute in a variety of ways, often requiring us to undertake several roles concurrently. This, coupled with the interaction and strong bonds that have historically existed between respiratory therapists and our industry partners, professional associations, and academic institutions, it is easy to conceive how competing interests may arise at these intersections.

In the context of scientific publishing, it is incumbent upon editorial boards to implement stringent measures to manage any conflicting interests. Typically we think of conflicts of interest that may surface with respect to an author or group of authors relative to their published works. This could, for example, include undisclosed financial gain for an author emanating from the published works—potentially undermining the integrity of a publication. As the financial ties of authors have been demonstrated to be associated with more favourable clinical outcomes in trials [2], this illustration highlights the need for robust editorial safeguards. Accordingly, the editorial processes of this Journal have been designed to equip the editorial board to deal with such instances. For example, disclosure of potential conflicts are required to be reported by as potential authors for review by the editorial board who appraise the risk of such conflict to the integrity of the publication [3].

Similarly, it is important to note that editorial boards themselves are not immune from potential conflicts of interest. The occurrence of such conflict may be most evident when considering the case of an editorial board member publishing within the journal on which editorial board they serve. This is not uncommon in professional communities the size of respiratory therapy and, in fact, arises with some regularity. Again, the editorial processes of the Canadian Journal of Respiratory Therapy are carefully and rigorously enacted to mitigate these conflicts of interest and have always ensured that every editorial board member regularly disclose all real or perceived conflicts of interest. In general terms, when making editorial decisions such real or perceived conflicts are carefully scrutinized and, whenever necessary, individual board members (including the Editor-in-Chief) are promptly excluded from the editorial process and any decisions related to that point of conflict. It is worth noting that these publication safeguards are entirely consistent with those recommended by the International Committee of Medical Journal Editors (ICMJE), the most widely accepted and endorsed publishing guidelines globally. As is the practice of this Journal, it is important for editorial board members who make final decisions about manuscripts to excuse themselves from decision-making where they may have personal, professional, or financial involvement in any of the issues they might judge [4].

The need for reflection on the potential impacts of holding dual roles has recently become personally pertinent as I prepare to undertake a position later this year as the Chief Executive Officer of the Canadian Society of Respiratory Therapists, the proprietary organization of this Journal. Engaging in these dual operational and editorial roles requires transparency and special attention to maintaining our rigorous publication standards. In the interest of optimizing the long-term operational and editorial effectiveness of the Canadian Journal of Respiratory Therapy over the long term, I plan to step aside from my current role to be best positioned to contribute in new ways. To that end, a search for a new Editor-in-Chief of this Journal is currently underway. In the meantime, our exemplary editorial team and robust editorial standards position us well to continue on with business as usual—informing the practice of respiratory therapists with high-quality published literature.

As always, we welcome thoughts and feedback from our readership on the articles in this issue or on the topic of conflict, either in general or pertaining specifically to our board. Please consider submitting a letter to the editor (editor@csrt.com) for publication so we can continue the conversation.

Andrew West, EdD(c), RRT, FCSRT, Editor-in-Chief

REFERENCES

Correspondence: Andrew West, 201 – 2460 Lancaster Road, Ottawa, ON, K1B 4S5, email editorinchief@csrt.com

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Noninvasive ventilation in life-threatening asthma: A case series

Andrew Miller BSRT, RRT-ACCS, RRT-NPS, Dean A VanHart BSRT RRT, Michael A Gentile RRT FAARC

Background: The use of noninvasive ventilation (NIV) in severe acute asthma is controversial. A pH < 7.25, PaCO₂ > 60 mmHg, and altered mental status have been described as contraindications to NIV in acute asthma. We hypothesized that NIV was safe and effective in asthma patients with a pH < 7.25 or PaCO₂ > 60 mmHg.

Methods: Following institutional review board approval, the medical records of subjects who received NIV for acute asthma in the emergency department between January 2010 and July 2012 were reviewed. Subjects were included if they had a pH < 7.25 or PaCO₂ > 60 mmHg on either an arterial or venous blood gas. Primary outcome was need for endotracheal intubation. The use of noninvasive ventilation (NIV) in severe acute asthma is controversial. A pH < 7.25, PaCO₂ > 60 mmHg, and altered mental status have been described as contraindications to NIV in acute asthma. We hypothesized that NIV was safe and effective in asthma patients with a pH < 7.25 or PaCO₂ > 60 mmHg.

Results: Sixty-two subjects received NIV for asthma, with 20 (mean age 42 ± 12 years, 62% male) meeting the inclusion criteria. Intubation was avoided in all 20 subjects, including nine (45%) with prior history of intubation due to asthma, eight (40%) who were obtunded, and three (15%) who were unresponsive upon arrival. Results are described as medians (ranges). Initial blood gas (80% venous) results were: pH 7.16 (6.89–7.27), PaCO₂ 77 (65–144) mmHg, and HCO₃⁻ 27 (20–32) mmol/L. Repeat blood gases (45% venous) performed a median of 117 minutes later were: pH 7.31 (7.22–7.45), PaCO₂ 48 (31–63) mmHg, and HCO₃⁻ 33 (19–31). Vomiting occurred in one patient; no other adverse events were noted.

Conclusion: We identified a small series of asthmatic patients with severe respiratory acidosis or altered mental status in whom NIV was safe and effective.

Key Words: noninvasive ventilation; asthma; status asthmaticus; NIV; respiratory acidosis; emergency department

INTRODUCTION

An estimated 2 million patients visit emergency departments (EDs) in the United States for asthma exacerbations each year [1]. Data from the National Ambulatory Care Reporting System in Canada indicate that there were 1,000 cases of severe, acute asthma required resuscitation in 2015 and 2016 (National Ambulatory Care Reporting System Quick-Stats, Accessed May 8, 2017). In the ED, asthma exacerbations are typically treated with frequent inhaled bronchodilators (beta₂-agonists and anticholinergics), systemic corticosteroids, and oxygen. Adjunctive therapies used in severe or life-threatening exacerbations include epinephrine, methylxanthines, ketamine, intravenous (IV) magnesium, heliox, and mechanical ventilation (invasive and noninvasive) [2]. There is substantial morbidity and mortality (as high as 20%) associated with invasive mechanical ventilation in asthma [3]. ED treatment is focused on maximizing therapy to avoid endotracheal intubation. Airway manipulation during attempts at endotracheal intubation in asthma patients may cause worsening bronchospasm and the subsequent increase in intrathoracic pressure post intubation can cause cardiovascular collapse, including cardiac arrest [3].

The use of noninvasive ventilation (NIV) in asthma is controversial due to lack of high-level data from randomized, controlled trials. A Cochrane review concluded that despite promising initial results, there is a lack of data to support the use of NIV in status asthmaticus [4]. A clinical practice guideline published by the Canadian Medical Association in 2011 was unable to make recommendations on NIV in asthma due to lack of data [5]. To date, no randomized trials on the use of NIV in acute asthma have enrolled patients with abnormal gas exchange. However, despite the lack of evidence from randomized trials, the use of NIV in asthma in clinical practice is increasing, with a concurrent decrease in the use of invasive mechanical ventilation [6]. For asthma patients with respiratory failure, expert reviews have recommended a pH < 7.25 [7, 8], arterial partial pressure of CO₂ (PaCO₂) > 60 mmHg [9], and altered mental status (AMS) [3, 7–10] to be contraindications to NIV. The successful use of NIV in patients with blood gas values below these thresholds has been described, including recent reports describing successful use of NIV in an asthma patient presenting with an initial pH of 6.95 and PaCO₂ of 125 mmHg [11] and a series of 17 asthma patients who received NIV with a mean initial pH of 7.18, PaCO₂ 78 mmHg, and GCS of 14 prior to NIV. These reports have raised question regarding the limits of NIV in severe asthma exacerbations [12]. We hypothesized that NIV was safe and effective in asthma patients with a pH < 7.25 or PaCO₂ > 60 mmHg.

METHODS

Following institutional review board approval, all adult (>18 years of age) patients who received NIV in the ED between January 2010 and July 2012 were retrospectively identified through a search of electronic medical records as part of a larger review of NIV use in our ED. Subjects who were intubated without receiving NIV and those with abnormal gas exchange who did not receive NIV were unable to be identified. Subjects were screened for a history of asthma, as determined from physician notes, and were followed for their entire hospital stay. Subjects with chronic obstructive pulmonary disease (COPD), congestive heart failure, renal failure requiring dialysis, and suspected or known vocal cord dysfunction were excluded. Subjects were included if initial blood gas (arterial or venous) revealed they had a venous or arterial pH < 7.25 or PaCO₂ > 60 mmHg. Venous blood gases are utilized routinely in our emergency department in the assessment of acid–base balance. The decision to send arterial or venous blood gases was at the discretion of the treating physician and done per departmental standards. We considered venous blood gas analysis to be an adequate surrogate for arterial blood gas analysis as a venous PaCO₂ of 50 mmHg or greater has been shown to be 100% sensitive for the detection of hypercapnia (defined as a PaCO₂ > 45 mmHg) [13]. Oxygenation was measured via continuous pulse oximetry in all subjects. Mental status was determined from clinical documentation and subjects were considered to have AMS if there was any specific mention of lethargy, obtundation, or if the clinical context clearly indicated the presence of AMS.
Subject demographics, home medication regimen, medical history, vital signs, blood gases, NIV settings, need for intubation, disposition, ED length of stay, and hospital length of stay were extracted from the medical record by the primary author (AGM) and a registered respiratory therapist (DAV). Data on epinephrine, methylxanthines, ketamine, and heliox use were not recorded. Extracted data were entered into a standardized Microsoft Excel (Seattle, WA) spreadsheet and analyzed with Graphpad statistics software. Repeated measurements of the means for pH, CO₂, HCO₃⁻, and lactate were compared using the paired t test with an alpha set at 0.05.

NIV settings were titrated based on institutional protocol designed to optimize triggering, target tidal volume 4–8 mL/kg of predicted body weight, and decrease accessory muscle use while maintaining a total inspiratory pressure ≤20 cmH₂O. NIV was delivered by critical care ventilator (Carefusion Vela) or dedicated NIV machine (Respironics Vision or V-60). Only initial NIV settings were recorded. Vital signs included heart rate, respiratory rate, blood pressure, pulse oximetry (SpO₂), and fraction of inspiratory oxygen (FiO₂). Bedside spirometry or peak expiratory flow rate were not performed in any subjects. Primary outcomes were needed for intubation at any point during their hospital stay; secondary outcomes were disposition from the ED and hospital length of stay. Disposition was determined by the attending ED physician in consultation with the admitting service. In our institution, adult asthma patients requiring continuous bronchodilator therapy or NIV are required to be admitted to the intensive care unit (ICU).

RESULTS
A total of 943 subjects received NIV in our ED during the study period. Sixty-two patients received NIV for acute asthma and 20 (median age 43 years, range 23–65 years, 65% male) met the inclusion criteria. Zero of 20 subjects required intubation during their hospital stay. Demographic variables are summarized in Table 1.

AMS was present in nine (45%) subjects. Of these, eight (40% of all subjects) were noted to be lethargic or obtunded, including three (15%) who were unresponsive, and one (5%) who had significant agitation. Glasgow coma scale was documented to be 8 in one unresponsive subject; specific measures of responsiveness were not documented in the other subjects. Two (10%) subjects received bag valve mask ventilation via emergency medical services personnel during transport to the ED.

Blood gas results and NIV settings for all subjects are summarized in Table 2. Results for lethargic/obtunded subjects are summarized in Table 3. Venous blood gases were obtained initially in 16 (80%) subjects, repeat blood gases were performed in 18 subjects and of these, 11 (55%) were arterial blood gases. Eighteen (90%) subjects received continuous albuterol (50% at 40 mg/h, 39% at 20 mg/h, and 11% at 30 mg/h); 19 (95%) received IV magnesium, 19 (95%) received IV corticosteroids, and 5 (25%) received benzodiazepines.

Pre-NIV vitals are summarized in Table 2. Six (30%) subjects were admitted to the ICU; 12 (60%) to a regular bed, one (5%) was discharged home, and one (5%) signed out against medical advice. Of the eight obtunded patients, three (38%) were admitted to the ICU, four (50%) to the floor, and one (13%) signed out against medical advice. Total time spent in the ED was 327 (97–1400) minutes for all subjects and 269 (118–1400) minutes for obtunded subjects. The median (range) hospital length of stay was 2 (0–4) days and 1.5 (0–4) days for obtunded subjects, with all 20 subjects being discharged to home. Vomiting occurred in one patient with no concern for acute aspiration. No other complications (including pneumothoraces) related to NIV were noted.

DISCUSSION
In our series, no subjects required endotracheal intubation, including those presenting with AMS. To our knowledge, this is the first case series of NIV in the emergency setting in acute asthma that included severe acidosis, hypercapnia, and AMS as entry criteria. Previous reviews have included severe acidosis and AMS to be contraindications to NIV in acute asthma; however, our results indicate NIV was safe and efficacious in our cohort as indicated by no significant adverse events, rapid improvement in blood gas values, low rate of ICU admission, and short hospital stay [3, 7–10].

There have been a few small case series (enrolling between 17 and 22 subjects) on the use of NIV in asthma patients with respiratory acidosis. These studies have been done in the ICU, not the ED [12, 14, 15]. Studies done in the ED environment have enrolled patients with normal gas exchange [16–21]. Meduri et al. [14] reported a case series of 17 (mean pH 7.25, PaCO₂ 65 mmHg) subjects treated with NIV in their ICU with a subsequent intubation rate of 12%. Fernandez et al. [15] reported the use of NIV in 22 subjects with a pre-NIV pH of 7.28 and PaCO₂ 63 mmHg who failed to respond to aggressive initial management in the ED. Their blood gases worsened prior to NIV initiation (mean pH decreased from 7.26 to 7.24 and PaCO₂ increased from 53 to 63 mmHg) but improved within 6 hours of NIV initiation to a mean pH of 7.32 with a PaCO₂ 51 mmHg following NIV. Three (14%) patients were intubated, two due to AMS and one due to mask intolerance [15]. Our study adds to these prior studies as the accumulation of data from different centers demonstrates the use of NIV in acute asthma and respiratory acidosis is a safe practice that is associated with low intubation rates.

The study enrolling subjects most similar to ours was that of Murase et al. [12], who reported the use of NIV in 17 asthma subjects treated in their ICU following the introduction of NIV into their clinical practice. They included patients who were confused in whom mental status rapidly normalized, except for one patient who required intubation. Their cohort who received NIV had a mean pre-NIV pH of 7.18 with a PaCO₂ of 77 mmHg and found an intubation rate of 12%. One patient was intubated due to mask intolerance and the other after 72 hours of NIV due to worsening blood gases [12]. Compared with our cohort, the patients in their study were older (55 vs 42 years of age), more likely to be female (82% vs 38%) and had a longer hospital length of stay (8.4 vs 2 days). They did not report the amount or frequency of bronchodilator treatments, making comparison difficult. Both of these studies indicate NIV can be safely delivered to patients with AMS, provided they are in a closely monitored area with a team experienced in providing NIV. In patients with mask intolerance, we administer low dose benzodiazepines to reduce anxiety and allow improved treatment tolerance.
Our results indicate venous blood gases may have a potential role in the assessment of acute asthma, either as a screening tool or as the primary assessment of acid–base status. Venous blood gases can easily be obtained using existing IV lines or upon IV placement. Investigation into the role of venous blood gases in acute asthma is warranted. Aggressive therapy focused on the maximization of bronchodilatation through the use of continuous bronchodilator therapy and IV magnesium may also have played a role in our success, as both therapies have been shown to improve airflow in severe asthma [22, 23].

Consistent with prior reports, the use of NIV in acute asthma appears to be a safe practice that can be used even in patients who present with severe respiratory failure and AMS. NIV in this type of patient should only be initiated by experienced teams in well-monitored areas in which practitioners and equipment needed for emergency intubation are available. In our facility, the RT does not leave the bedside of patients with AMS receiving NIV. The feasibility of performing a randomized trial in asthma patients presenting respiratory failure is questionable, as many clinicians may feel withholding NIV would be unethical, and consenting subjects with AMS would be extremely challenging given the window between identification and initiation of some form of respiratory support. Any future trial of NIV in asthma should be multi-center with a well-defined protocol for NIV settings/titration, continuous bronchodilator therapy delivered via vibrating mesh nebulizer, IV magnesium, and strict criteria for NIV failure. While intubation is a logical primary outcome, studies should also examine the effect of NIV on need for ICU admission, hospital/ED length of stay, or time to clinical improvement.

The use of NIV in patients with AMS is controversial; however, the successful use of NIV in hypercapnic encephalopathy due to COPD has been described when delivered by an experienced team in a closely monitored environment where invasive mechanical ventilation was readily available [24–26]. Of the eight obtunded patients in our series, none required endotracheal intubation and only 38% required ICU admission. Given the rapid resolution of acidosis in our study, a trial of NIV in severe asthma may be warranted, as long as the patient is in a well-monitored environment. When a patient with AMS was placed on NIV during the study period, an RT stayed at the bedside with the patient until their mental status improved. Rapid-sequence induction medications and intubation equipment were also kept readily at the bedside.

The role of external PEEP in acute asthma is unclear; however, its use may facilitate bronchodilation, improve gas exchange, and improve ventilation/perfusion mismatching [8, 9, 27]. The optimal method to determine inspiratory positive airway pressure (EPAP)/PEEP during NIV in acute asthma is unknown. Our results indicate that a moderate amount of expiratory positive airway pressure (EPAP)/PEEP during NIV in severe asthma may be warranted, as long as the patient is in a well-monitored environment. When a patient with AMS was placed on NIV during the study period, an RT stayed at the bedside with the patient until their mental status improved. Rapid-sequence induction medications and intubation equipment were also kept readily at the bedside.

There are many limitations in our study. The nature of the study limited us to data available in the electronic medical record. Changes to our electronic medical record resulted in a shortened timeframe as we were no longer able to reliably track subject location. There was no control group and we were unable to identify asthma patients who were intubated without a trial of NIV or patients with severe acidosis who did not require NIV. The terms lethargic and obtunded were not explicitly defined and relied on clinical documentation. The decision to place a subject on

### TABLE 2

Blood gas results and NIV settings for all 20 subjects

<table>
<thead>
<tr>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.13 ± 0.10</td>
<td>7.16</td>
</tr>
<tr>
<td>PCO₂ (mmHg)</td>
<td>82 ± 18</td>
<td>65–144</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td>27 ± 2.8</td>
<td>27–20–32</td>
</tr>
<tr>
<td>Lactate† (mmol/L)</td>
<td>2.9 ± 2.3</td>
<td>1.9–0.9–9.3</td>
</tr>
</tbody>
</table>

### TABLE 3

Lethargic or obtunded subjects, n = 8

<table>
<thead>
<tr>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.05 ± 0.10</td>
<td>7.07</td>
</tr>
<tr>
<td>PCO₂ (mmHg)</td>
<td>94 ± 22</td>
<td>91–144</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td>26 ± 2.3</td>
<td>26–22-29</td>
</tr>
<tr>
<td>Lactate* (mmol/L)</td>
<td>4.2 ± 2.9</td>
<td>3.9–0.9–9.3</td>
</tr>
</tbody>
</table>

Note: Paired t-test performed to compare means, arterial, and venous blood gas results combined for analysis.

*Available for eight subjects, repeat measurement available for three subjects.

NIV, noninvasive ventilation; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; RR, XXXXX; BP, blood pressure.

*Available for 6 subjects.
†Available for 19 subjects.
NIV, NIV settings, medication administration, and disposition were not based on standardized criteria. It is possible that our results are attributable to selective application of NIV to patients who are likely to succeed. Likewise, the initial decision to place a patient on NIV may have biased clinicians against intubating patients or admitting to ICU settings (incorporation bias). The higher proportion of arterial blood gases in repeat analysis may have overestimated the improvement in gas exchange. Venous blood gases have not been validated in patients with asthma. Disposition was determined by the treating physician in consultation with the inpatient team without formal criteria for ICU admission. The lack of a control group may make any reduction in endotracheal intubation rate highly speculative; however, it is likely many of our subjects would have required intubation without NIV. It is unlikely that subjects with this degree of illness will be enrolled in randomized controlled trials in the future as their illness severity makes it unlikely informed consent could be obtained from the patient or legal representative before treatment is initiated. Thus, case series and observational data remain, for now, the best source of evidence for NIV in severe acute asthma with respiratory acidosis.

CONCLUSION

In conclusion, we identified a series of patients presenting to our ED with severe asthma exacerbations as measured by severe respiratory acidosis or altered mental status in whom NIV was safe and effective.

REFERENCES


Comparison of the accuracy of classification models to estimate healthcare use and costs associated with COPD exacerbations in Saskatchewan, Canada: A retrospective cohort study

John Paul Kuwornu PhD1, Gary F. Teare PhD1,2, Jacqueline M. Quail PhD1,2, Evelyn Forget PhD1, Saman Muthukumarana PhD3, Xiaoyun E. Wang MSc2, Meric Osman MA2, Lisa M. Lix PhD1,2


Objective: COPD is a high-cost disease and results in frequent contacts with the healthcare system. The study objective was to compare the accuracy of classification models with different covariates for classifying COPD patients into cost groups.

Methods: Linked health administrative databases from Saskatchewan, Canada, were used to identify a cohort of newly diagnosed COPD patients (April 1, 2007 to March 31, 2011) and their episodes of healthcare encounters for disease exacerbations. Total costs of the first and follow-up episodes were computed and patients were categorized as persistently high cost, occasionally high cost, and persistently low cost based on cumulative cost distribution ranking using the 75th percentile cutoff for high-cost status. Classification accuracy was compared for seven multinomial logistic regression models containing socio-demographic characteristics (i.e., base model), and socio-demographic and prior healthcare use characteristics (i.e., comparator models).

Results: Of the 1182 patients identified, 8.5% were classified as persistently high cost, 26.1% as occasionally high cost, and the remainder as persistently low cost. The persistently high-cost and occasionally high-cost patients incurred 10 times ($12,449 vs $1263) and seven times ($9334 vs $1263) more costs in their first exacerbation episode than persistently low-cost patients, respectively. Classification accuracy was 0.67 for the base model, whereas the comparator model containing socio-demographic and number of prior hospital admissions had the highest accuracy (0.72).

Conclusions: Costs associated with COPD exacerbation episodes are substantial. Adding prior hospitalization to socio-demographic characteristics produced the highest improvements in classification accuracy. Accurate classification models are important for identifying potential healthcare cost management strategies.

Key Words: chronic obstructive; cost analysis; healthcare costs; logistic models; longitudinal studies; pulmonary disease

INTRODUCTION

Patients with chronic obstructive pulmonary disease (COPD) are responsible for more than one-quarter of all hospitalizations and emergency department (ED) visits, and more than one-fifth of ambulatory visits [1]. Previous studies have shown that COPD exacerbations, periods in the disease course that are characterized by worsening patient symptoms, require follow-up care [2], and are therefore major contributors to the total healthcare costs associated with the disease treatment and management. Annual costs are estimated to be 10 times higher among COPD patients who experience exacerbations than among those who do not [3]. The average cost of a severe COPD exacerbation was estimated at $9557, with the overall economic burden to the Canadian healthcare system projected in the range of $646-$736 million per annum [4].

COPD exacerbations often require an ED visit or hospitalization [5, 6]. Patients may also receive follow-up care from their primary care provider or a specialist and might require additional medications [7]. Accordingly, an exacerbation episode may require multiple contacts with different healthcare providers and services. Comprehensive information about costs associated with COPD exacerbations can benefit from an episode-of-care data system, which aggregates healthcare services related to the treatment of the condition [8]. The episode of care provides a clinically meaningful unit for measuring healthcare costs [9] and allows for a detailed analysis of the treatment processes that generate the costs [10].

The phenomenon of a very few individuals, usually the top 5%-15% of healthcare users, accounting for more than 50% of healthcare costs has been consistently reported in the literature [11]. However, recent analyses have also revealed that these high-cost patients are a heterogeneous subgroup, with some patients persistently incurring high costs while others only occasionally incur high-cost services [12]. Understanding this dynamic nature of healthcare expenditures could potentially benefit the development of cost-management strategies. Given that the prevalence of COPD is projected to increase in the future and place even greater economic burden on the healthcare system [4], developing models to predict high-cost groups in early episodes could contribute to the development of timely interventions. The study objectives were to use linked population-based administrative health data to estimate healthcare resource use and costs associated with episodes of COPD exacerbations and to compare the accuracy of classification models with different covariates for classifying patients into cost groups.

METHODS

Data sources: We used administrative health data from the province of Saskatchewan, Canada, which has a population of approximately 1.1 million according to the 2011 Statistics Canada Census. Like all Canadian provinces, Saskatchewan has a universal healthcare program, which means that virtually all residents are eligible for health insurance coverage.

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Episodes of care for COPD were constructed using databases that capture primary, emergency, and acute care service, for all provincial health insurance beneficiaries, including physician billing claims, ED visit records, hospital discharge abstracts, and prescription drug dispensation records. A hospital discharge abstract is completed when a patient is discharged from an acute care facility. Up to 25 diagnoses are recorded using the International Classification of Diseases, 10th Revision, Canada (ICD-10-CA) codes on each admission record. Information on emergency care is collected in the ED database, which captures up to 16 diagnoses on each record using ICD-10-CA. Physician billing claims contain information submitted by physicians providing care to patients in outpatient settings. A single diagnosis is recorded on each claim using three-digit ICD-9 codes. Prescription drug dispensation records contain information on drugs dispensed in outpatient settings, including the date of dispensation and national drug identification numbers. The population registry and vital statistics registry were also used in the study. They contain demographic information, as well as dates of health insurance coverage and death.

Data were accessed and analyzed at the provincial Health Quality Council in accordance with a standing data-sharing agreement between the organization and the provincial Ministry of Health. Ethics approval for the research was received from the University of Saskatchewan Biomedical Research Ethics Board.

Study design and cohort selection

The study adopted a retrospective cohort design. The cohort was composed of adults (35+ years old) who were newly diagnosed with COPD between April 1, 2007 and March 31, 2011 and were residents of Saskatoon health region (SHR) and Regina Qu’Appelle health region (RQHR), two of 12 health regions in Saskatchewan at the time of the study and the only ones for which ED data were available. Both SHR and RQHR are the only health regions that contain major urban centers (population > 200 000 in each center) and together account for just over half of the provincial population.

We used the following validated case definition to identify individuals with COPD: (i) one or more hospitalizations with a diagnosis of COPD in any diagnosis field or (ii) one or more physician visits with a diagnosis of COPD [14]. This case definition had a sensitivity of 85.0% and a specificity of 78.4% when compared with clinical evaluations by a physician [1]. The index date for COPD diagnosis was the date of the earliest hospitalization admission or physician visit for COPD. Cases were identified from hospital discharge abstracts using the following ICD-10-CA codes: J41, J42, J43, or J44; cases in physician billing claims were identified with ICD-9 codes 491, 492, or 496.

To increase the likelihood that cohort members were newly diagnosed COPD cases, we used a look-back period of 5 years from the index date to determine whether a patient had a prior COPD diagnosis. We selected this duration of time based on previous research [15], which showed that most adults with clinically significant COPD will contact the healthcare system at least once in this period. The cohort was limited to individuals who had continuous provincial health insurance coverage from five years prior to their index date until death or March 31, 2012, whichever came first. This restriction allowed us to identify incidence COPD cases and also capture all insured healthcare contacts during the episode. We restricted the cohort to an incident cohort to study changes in healthcare utilization and costs as the condition progresses. Finally, the study considered only the index (i.e., first) and follow-up episodes among patients who experienced at least two episodes following their COPD diagnosis date.

Defining episodes of care for COPD exacerbations

All episodes of care for COPD exacerbations following the index diagnosis were defined using the healthcare services that initiated, continued, and ended them. We identified episodes of care based on a method developed by the Canadian Institute for Health Information (CIHI), a national nonprofit organization that provides standardized methods and data sources for health services research, for ascertaining exacerbations [16]. Hospital- or ED-initiated episodes had: (i) a COPD diagnosis in the most responsible diagnosis field or (ii) a diagnosis of an acute lower respiratory tract infection in the most responsible diagnosis field and a diagnosis of another COPD (ICD-10-CA code J44) in the second diagnosis field. Physician visit initiated episodes were identified by an ICD-9 code for COPD or respiratory infection and had to be accompanied by the dispensation of a drug used to treat acute exacerbations of COPD, including antibiotics, systemic corticosteroids, short-acting beta agonists (SABAs), and SABAs combined with anticholinergics within two days of a physician visit.

An episode continued if there were respiratory-related hospitalizations or ED, family practitioners (FP), or specialist visits that followed the initiating service within a 30-day period. All respiratory-related outpatient prescription drugs dispensed during this period were also included in the episode.

An episode ended after either the occurrence of a 30-day clean period, in which there were no respiratory-related healthcare contacts, or death. All patients were followed for at least one year from their index date until March 31, 2012, or death, whichever occurred first. All ongoing episodes at the end of the observation period were excluded to ensure we had complete information to estimate cost of all exacerbation episodes included in the study.

Episode of care costs

The total cost of an episode of care was the sum of all costs associated with healthcare utilization related to respiratory diagnoses incurred between the episode start and end dates. Inpatient hospital costs were estimated based on a standard methodology developed by CIHI [17]. Briefly, inpatient hospital costs were computed by multiplying the resource intensity weight (RIW) of a hospital stay with the cost per weighted case (CPWC). An RIW is a relative value that describes the expected resource consumption of a patient based on: (i) their case mix group; (ii) factors known to affect resource utilization and length of stay including age, comorbidity, hospital-based interventions; and (iii) atypical length of stay such as patients who are transferred between facilities and palliative cases. The CPWC represents the cost of an average patient’s hospital stay. We used CPWC figures estimated for Saskatchewan. For the ED cost component, total annual expenditures were obtained from the Ministry of Health and total annual number of visits was extracted from the ED database; these were used to estimate an average cost per visit. The cost of a physician visit was the amount billed by the physician to the provincial Ministry of Health, as recorded in the physician billing claims. Prescription drug costs were based on prices of the active substance plus a dispensing fee, as recorded in the dispensation records.

Episode costs were adjusted for inflation using the health and personal care component of the Saskatchewan consumer price indices [18] and expressed in 2011–2012 constant dollars. All costs were estimated from the perspective of the public payer; individual out-of-pocket expenditures such as co-payments were not included in this study.

Study measures

Outcomes: Using the ranked distribution of cumulative total costs in the index and follow-up episodes, we identified high-cost status using the 75th percentile cutoff. Patients were categorized into three cost groups: persistently high cost (i.e., those whose costs were at the 75th percentile and above in the first and subsequent episode), occasionally high cost (i.e., those whose costs were at the 75th percentile and above in either of the episodes), and persistently low cost (i.e., those whose costs were below the 75th percentile in both episodes). The choice of a cutoff point is largely empirically driven [19]; previous studies have used different cutoffs to define high-cost patients including the top 5% [20, 21], the top 10% [22, 23], the top 20% [24], the top 25% [25], or the top tertile [26]. For our data, using more stringent cutoffs such as top 10% would have resulted in sample sizes that were too small to...
provide stable estimates in regression models [22]. We also estimated the time between the index and follow-up episode for each cost group.

Health services utilization measures: For each patient, we tracked the number and duration of use of various healthcare services in each episode (see Table A1 in the appendix for the definitions of these utilization variables). These included visits to EDs, FPs, and specialists as well as hospital admissions to general wards and specialized care units (SCUs). The number of dispensed drugs was calculated using the American hospital formulary service pharmacologic-therapeutic classification system by summing the number of different four-digit drug classifications for each cohort member.

Patient and disease characteristics: The patient and disease characteristics included in the analysis were guided by the Andersen healthcare utilization model [27]. Andersen proposed that an individual’s healthcare use is influenced by three broad groups of factors, namely predisposing, enabling, and need. The predisposing factors were sex (i.e., male or female) and age group (i.e., 35–54, 55–74, or 75+). The enabling factor was residence location (i.e., urban or rural); urban residents were those whose postal codes were in a census metropolitan or agglomeration area (i.e., 10,000+ population). Finally, the need factor examined in this study was the level of comorbidity, which was defined using the Charlson comorbidity index [28]. This index was based on diagnoses in the hospital discharge abstract and the physician billing claims data. The index score for each individual in the study cohort was categorized as 0, 1, 2, or ≥ 3. The Charlson comorbidity index has previously been used to predict healthcare utilization in Saskatchewan [29]. We also included the fiscal year of COPD diagnosis (i.e., 2007–2008, 2008–2009, 2009–2010, or 2010–2011) in the model, as this may influence follow-up care patterns. All variables were defined as of the index date of COPD diagnosis except for the Charlson comorbidity index score, which was calculated using data for the 365-day period prior to the index date.

Statistical analysis

We described overall and individual cost components of episodes of COPD exacerbations with means and standard deviations (SDs). The χ² statistic was used to test for differences in patients’ healthcare encounters in the three cost groups. All hypothesis tests were conducted using two-tailed tests at the significance level of 0.05. We plotted the duration (in days) of healthcare utilization measures during the episodes of care.

A multinomial logistic regression model was fit to the data to predict cost group membership using information on patients’ age, sex, residence location, comorbidities, and fiscal year of COPD diagnosis (i.e., base model). A previous study [21] has shown that including the number of previous healthcare services would enhance a model’s ability to predict future high-cost patients. To evaluate the improvement in classification accuracy, we included the number of times different healthcare services were utilized in the index episode. To the base model, these subsequent models added: number of hospital admissions (model 1), number of ED visits (model 2), number of FP visits (model 3), number of specialist visits (model 4), number of types of drugs dispensed (model 5), and all five healthcare utilization measures (model 6). We added each of the five healthcare services to the base model one at a time to construct models 1 to 5, whilst model 6 comprised of the base model and all five healthcare services.

To evaluate model performance, we used measures of goodness-of-fit (i.e., the log-likelihood and Bayesian information criterion, BIC) and classification accuracy. Classification accuracy was evaluated by comparing the proportional-by-chance accuracy rate of the data with each model’s classification accuracy rate [30]. The proportional-by-chance accuracy rate is calculated by summing the square of the proportions of the categories of the dependent variable (i.e., proportion of cohort in each cost group). Models with at least 25% improvement over the proportional-by-chance accuracy rate were accepted as having adequate classification accuracy [30]. To compare our results with previous studies [31, 32], we conducted two pairwise logistic regression models using the same predictors as discussed above, comparing the c statistic from these models. The first model compared the persistently high-cost group with the
RESULTS

Cohort selection and characteristics
A total of 12,543 COPD cases were identified between April 1, 2007 and March 31, 2011. After exclusion criteria were applied (i.e., previous healthcare utilization with a COPD diagnosis within a 5-year look-back period (38.0%), and not having continuous provincial health insurance coverage (5.4%)), a total of 7,099 individuals were eligible for study inclusion. During an average follow-up time of 3.7 years, 2,659 individuals had a total of 53,485 episodes. The final cohort (n = 1,182) was comprised of all individuals with at least two COPD episodes of care during the follow-up period.

Based on the 75th percentile cutoff of the cumulative total episode cost distribution, 100 (8.5%) patients were classified as persistently high cost, 309 (26.1%) as occasionally high cost, and 773 (65.4%) as persistently low cost. The average time between the last date of the index episode and the first date of the follow-up episode was longer for the persistently high-cost patients (374.2 days; SD = 361.8 days) than for the occasionally high-cost (351.2; SD = 325.0) and persistently low-cost (341.9; SD = 313.9) patients. In general, patients in the persistently high-cost group were older (74.6 years; SD = 11.7 years) than those in the occasionally high-cost (71.8 years; SD = 12.0 years) and persistently low-cost (65.5 years; SD = 12.5 years) groups. The persistently high-cost group was composed of 52.0% males, and this percentage was similar to the occasionally high-cost (71.8 years; SD = 12.0 years) and persistently low-cost group (71.8 years; SD = 12.0 years). The average time between hospitalizations for the persistently high-cost group (309 days) was much longer than that of patients in the persistently low-cost group (77 days) and the occasionally high-cost group (83 days).

Health services utilization during episodes
The number of hospital admissions, SCU admissions, ED visits, FP visits, and specialist visits were significantly different among the three cost groups in both episodes (p < 0.001 for all services) (Table 2). All patients in the persistently high-cost group were admitted to hospitals during both episodes, whilst lower percentages of patients in the occasionally high-cost and persistently low-cost groups were hospitalized during these episodes. Similarly, a higher percentage of patients in the persistently high-cost group was admitted to SCUs during their hospitalizations and had ED and specialist visits more than patients in the other two groups. However, a higher percentage of patients in the persistently low-cost group utilized more FP services and outpatient drug dispensations than patients in the two high-cost groups.

Patients in the persistently high-cost group had the longest hospital and SCU stays, followed by the occasionally high-cost group and then the persistently low-cost group (Figure 1). The average number of days in EDs was similar among the cost groups. Overall, the average number of days in episodes was higher in the persistently high-cost group than in the other two cost groups.

Multinomial logistic regression results
In the multinomial logistic regression models (Table 3), compared with patients who were 75+ years of age, those in age group 35–54 years (odds ratio (OR) = 0.19, 95% CI [0.09–0.41]) or age group 55–74 years (OR = 0.53, 95% CI [0.33–0.85]) were much less likely to be in the persistently high-cost group than the persistently low-cost group. Also, compared with those with no comorbid conditions, patients with a Charlson comorbidity score of 1 (OR = 2.68, 95% CI [1.51–4.77], 2 (OR = 2.28, 95% CI [1.17–4.42]), or ≥3 (OR = 4.29, 95% CI [2.30–8.00]) were more likely to be in the persistently high-cost group than the persistently low-cost group.

Table 2

<table>
<thead>
<tr>
<th>Frequency of healthcare services utilization by episode cost group</th>
<th>Persistent high cost (n = 100)</th>
<th>Occasionally high cost (n = 309)</th>
<th>Persistently low cost (n = 773)</th>
<th>Persistent high cost (n = 100)</th>
<th>Occasionally high cost (n = 309)</th>
<th>Persistently low-cost (n = 773)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of hospital admissions*</td>
<td>0</td>
<td>25.2</td>
<td>77.2</td>
<td>42.4</td>
<td>88.6</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>68.3</td>
<td>22.8</td>
<td>50.8</td>
<td>11.4</td>
<td>8.0</td>
</tr>
<tr>
<td></td>
<td>2+</td>
<td>6.5</td>
<td>0.0</td>
<td>6.8</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>No. of SCU admissions*</td>
<td>0</td>
<td>93.5</td>
<td>98.7</td>
<td>93.8</td>
<td>99.2</td>
<td>98.9</td>
</tr>
<tr>
<td></td>
<td>1+</td>
<td>6.5</td>
<td>1.3</td>
<td>6.2</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>No. of ED visits*</td>
<td>0</td>
<td>61.8</td>
<td>83.3</td>
<td>61.2</td>
<td>81.7</td>
<td>62.3</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>31.4</td>
<td>15.7</td>
<td>32.4</td>
<td>15.8</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td>2+</td>
<td>6.8</td>
<td>1.0</td>
<td>4.6</td>
<td>2.5</td>
<td>2.9</td>
</tr>
<tr>
<td>No. of FP visits*</td>
<td>0</td>
<td>31.0</td>
<td>15.7</td>
<td>24.9</td>
<td>12.7</td>
<td>25.9</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>24.0</td>
<td>43.6</td>
<td>33.3</td>
<td>48.9</td>
<td>37.9</td>
</tr>
<tr>
<td></td>
<td>2+</td>
<td>45.0</td>
<td>40.7</td>
<td>41.8</td>
<td>38.4</td>
<td>40.7</td>
</tr>
<tr>
<td>No. of specialist visits*</td>
<td>0</td>
<td>51.8</td>
<td>77.1</td>
<td>54.7</td>
<td>81.4</td>
<td>72.6</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>11.7</td>
<td>13.0</td>
<td>16.2</td>
<td>10.2</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
<td>2+</td>
<td>36.5</td>
<td>11.9</td>
<td>29.1</td>
<td>8.4</td>
<td>28.5</td>
</tr>
<tr>
<td>No. of different drugs</td>
<td>Mean (SD)</td>
<td>7.1 (74)</td>
<td>4.7 (63)</td>
<td>8.6 (185)</td>
<td>4.3 (50)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Note: *Utilization distributions in the three cost groups are significantly different using a χ² test at p < 0.001. SCU, special care unit; ED, emergency department; FP, family practitioner; SD, standard deviation.
Similarly, patients in age groups 35–54 or 55–74 years were less likely to be in the occasionally high-cost group than the persistently low-cost group compared with patients aged 75 years and above. Again, compared with those with no comorbid conditions, patients with Charlson comorbidity scores of 1, 2, or ≥ 3 were more likely to be in the occasionally high-cost group than the persistently low-cost group. The associations of sex, residence location, and fiscal year of the COPD diagnosis with cost group membership were not statistically significant.

Models’ prediction performance

Model 1 (i.e., the model containing patients’ demographic and disease characteristics as well as the number of hospital admissions in the first episode) had the best fit to the data based on the BIC (Table 4). Although the classification accuracy differed substantially across the multinomial logistic regression models, each of the models provided more than 25% improvement over the proportional-by-chance accuracy rate of 0.50 for our data. Thus, all the models had adequate classification; but model 1 had the highest classification accuracy rate. The c statistic from the logistic regression models ranged from 0.74 to 0.88 for the models comparing persistently high cost with persistently low cost, and from 0.68 to 0.83 for the models comparing occasionally high cost with persistently low cost.

DISCUSSION

In this study, we estimated the healthcare costs associated with episodes of COPD exacerbation and examined high-cost persistence using population-based administrative health data from Saskatchewan, Canada. By using the episode of care as the unit of analysis, our study uniquely characterizes the critical link between utilization patterns and healthcare costs. The episode-of-care approach reveals how the use of different services are related during COPD exacerbations. This provides a comprehensive understanding of the key drivers of overall episode-of-care costs associated with COPD exacerbations.
TABLE 3
Baseline characteristics of the study cohort and ORs from the multinomial logistic regression models

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Persistently high-cost patients (n = 100)</th>
<th>Occasionally high-cost patients (n = 309)</th>
<th>Persistently low-cost patients (n = 773)</th>
<th>All (n = 1182)</th>
<th>Persistently high-cost patients (n = 100)*</th>
<th>Occasionally high-cost patients (n = 309)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–54</td>
<td>9 (9.0)</td>
<td>45 (14.6)</td>
<td>250 (32.3)</td>
<td>304 (25.7)</td>
<td>0.19 (0.09–0.41)*</td>
<td>0.35 (0.23–0.52)*</td>
</tr>
<tr>
<td>55–74</td>
<td>37 (37.0)</td>
<td>129 (41.80)</td>
<td>317 (41.0)</td>
<td>483 (40.9)</td>
<td>0.53 (0.33–0.85)*</td>
<td>0.71 (0.52–0.96)*</td>
</tr>
<tr>
<td>75+</td>
<td>54 (54.0)</td>
<td>155 (43.7)</td>
<td>206 (28.7)</td>
<td>395 (33.4)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>52 (52.0)</td>
<td>148 (47.9)</td>
<td>375 (48.5)</td>
<td>575 (48.7)</td>
<td>1.25 (0.81–1.93)</td>
<td>1.03 (0.78–1.36)</td>
</tr>
<tr>
<td>Male</td>
<td>48 (48.0)</td>
<td>161 (52.1)</td>
<td>398 (51.5)</td>
<td>607 (51.4)</td>
<td>ref</td>
<td>161 (52.1)</td>
</tr>
<tr>
<td>Residence location</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Urban</td>
<td>21 (21.0)</td>
<td>77 (24.9)</td>
<td>191 (24.7)</td>
<td>893 (75.5)</td>
<td>1.33 (0.79–2.25)</td>
<td>1.05 (0.76–1.45)</td>
</tr>
<tr>
<td>Rural</td>
<td>79 (79.0)</td>
<td>232 (75.1)</td>
<td>562 (75.3)</td>
<td>209 (24.5)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>0</td>
<td>42 (42.0)</td>
<td>155 (50.2)</td>
<td>567 (73.4)</td>
<td>764 (64.6)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>1</td>
<td>22 (22.0)</td>
<td>70 (22.7)</td>
<td>91 (11.8)</td>
<td>183 (15.5)</td>
<td>2.68 (1.51–4.77)*</td>
<td>2.43 (1.68–3.52)*</td>
</tr>
<tr>
<td>≥3</td>
<td>15 (15.0)</td>
<td>40 (12.9)</td>
<td>66 (8.4)</td>
<td>121 (10.2)</td>
<td>2.28 (1.17–4.42)*</td>
<td>1.83 (1.17–2.86)*</td>
</tr>
<tr>
<td>Fiscal year of COPD diagnosis</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>2007–2008</td>
<td>27 (27.0)</td>
<td>90 (29.1)</td>
<td>266 (34.4)</td>
<td>383 (32.4)</td>
<td>ref</td>
<td>ref</td>
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<tr>
<td>2008–2009</td>
<td>29 (29.0)</td>
<td>87 (28.2)</td>
<td>194 (25.1)</td>
<td>310 (26.2)</td>
<td>1.22 (0.68–2.16)</td>
<td>1.18 (0.82–1.69)</td>
</tr>
<tr>
<td>2009–2010</td>
<td>24 (24.0)</td>
<td>84 (27.2)</td>
<td>158 (20.4)</td>
<td>266 (22.5)</td>
<td>1.45 (0.79–2.64)</td>
<td>1.56 (1.07–2.25)</td>
</tr>
<tr>
<td>2010–2011</td>
<td>20 (20.0)</td>
<td>48 (15.5)</td>
<td>155 (20.1)</td>
<td>223 (18.9)</td>
<td>1.12 (0.60–2.11)</td>
<td>0.85 (0.56–1.29)</td>
</tr>
</tbody>
</table>

Note: *Statistically significant at α = 0.05. OR, odds ratio; COPD, chronic obstructive pulmonary disease.
*Reference group was persistently low-cost patients.

TABLE 4
Comparison of goodness-of-fit and classification accuracy between models

<table>
<thead>
<tr>
<th>Performance metric</th>
<th>Base model</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodness-of-fit, multinomial models</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>−2 Log-likelihood</td>
<td>1842.98</td>
<td>1455.33</td>
<td>1762.55</td>
<td>1835.90</td>
<td>1711.69</td>
<td>1833.55</td>
<td>1429.88</td>
</tr>
<tr>
<td>BIC</td>
<td>1998.64</td>
<td>1625.13</td>
<td>1932.33</td>
<td>2005.70</td>
<td>1881.49</td>
<td>2003.35</td>
<td>1656.28</td>
</tr>
<tr>
<td>Classification accuracy, multinomial models</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>PBCAR*</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
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<tr>
<td>Model classification accuracy</td>
<td>0.67</td>
<td>0.72</td>
<td>0.66</td>
<td>0.67</td>
<td>0.69</td>
<td>0.67</td>
<td>0.71</td>
</tr>
<tr>
<td>% improvement over PBCAR</td>
<td>34.0</td>
<td>44.0</td>
<td>32.0</td>
<td>34.0</td>
<td>34.0</td>
<td>34.0</td>
<td>42.0</td>
</tr>
<tr>
<td>Logistic regression comparing persistently high-cost with persistently low-cost (n = 873)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c statistic</td>
<td>0.74</td>
<td>0.87</td>
<td>0.80</td>
<td>0.75</td>
<td>0.85</td>
<td>0.76</td>
<td>0.88</td>
</tr>
<tr>
<td>Logistic regression comparing occasionally high-cost with persistently low-cost (n = 1082)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c statistic</td>
<td>0.68</td>
<td>0.82</td>
<td>0.73</td>
<td>0.69</td>
<td>0.74</td>
<td>0.68</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Notes: Base model = age, sex, residence, Charlson comorbidity index; Model 1 = base model + no. of hospital admission in index episode; Model 2 = base model + no. of emergency department visits in index episode; Model 3 = base model + no. of family practitioner visits in index episode; Model 4 = base model + no. of specialist visits in index episode; Model 5 = base model + no. of drugs dispensed in index episode; Model 6 = base model + no. of all the above healthcare services in index episode. BIC, Bayesian information criterion; PBCAR, proportional-by-chance accuracy rate.

*PBCAR = (100/1182)² + (309/1182)² + (773/1182)² = 0.50.

The average episode of care costs for the persistently high-cost patients were between 10 and 22 times higher than that of the persistently low-cost patients in the baseline and follow-up episodes, respectively. Similarly, the average episode costs for the occasionally high-cost patients were between 7 and 12 times higher than that of the persistently low-cost patients in the baseline and follow-up episodes, respectively. Although overall average cost was lower in the follow-up episode for the entire cohort, this cost increased for the persistently high-cost patients by 29.3%. The increase in costs among persistently high-cost patients is likely due to the increase in hospital length of stay (i.e., number of days in hospital) as well as the number of days spent in specialized units during hospitalizations in the follow-up episode.

Previous studies [19] showed that older patients are more likely than younger ones to be in the persistently high-cost group. We found that older age (75+ years) was associated with both persistently high-cost and occasionally high-cost groups. Although long-term care is expensive and usually places its users in the high-cost group, this care setting is deemed the most appropriate for the frail elderly, who are typically not the focus of intensive case management interventions [20]. Instead of including home care or long-term care costs in the total episode costs, we rather calculated the proportion of patients who were users of these services before or during their episodes of care and found that only 11.0% of the persistently high-cost patients used these services. Thus, it is likely that the great majority of the persistently high-cost patients might be suitable candidates for case management interventions.

Being able to predict whether individual patients will continue to incur high healthcare costs over time is useful for understanding patterns of healthcare utilization and identifying individuals for case management interventions [33]. We found that each of the multinomial logistic regression models compared in our study had more than 25% improvement over the proportional-by-chance accuracy rate, demonstrating that each of these models had adequate classification accuracy. However, model 1 (i.e., the model containing patient demographic and disease characteristics as well as the number of hospital admissions in the previous episode) had the highest classification accuracy rate and should be preferred over the other models. Unlike our study, previous studies
have developed logistics regression models to predict patients who might become high-cost users in the future, with c statistics ranging from 0.81 to 0.85 [31, 32]. For comparison purposes, we also developed logistic regression models and found that the models that predicted persistently high-cost patients had c statistics ranging between 0.74 and 0.88, whilst those that predicted occasionally high-cost patients had c statistics ranging from 0.68 to 0.83. One of the key differences between the c statistic reported in our study and those in the cited studies is that the cited studies did not distinguish between persistently high-cost and occasionally high-cost patients. Our results indicate that predictions of the persistently high-cost group, the group more likely to benefit from case management interventions, are more accurate compared with the occasionally high-cost group.

The study has some limitations. First, a common limitation of studies that use administrative health data to construct episodes of care is the inability to make distinctions between scheduled and unscheduled visits to healthcare providers; this information is not routinely collected in some databases such as ED databases [34]. A second potential limitation of the study is that we only considered a clean period of 30 days to distinguish one episode from another, although this is a common approach to defining episodes of care [35]. Scheduled visits beyond 30 days may be counted as part of a new episode. However, recommended practice [7] suggests that follow-up visits be scheduled within two to four weeks of discharge from acute care; hence, the possibility of scheduled visits distorting our episode construction may be minimal. Third, we used simple average costs for some cost components such as ED costs. This did not take acuity or complexity of patients’ conditions into account. However, hospitalization, which was the major component of episode costs, was based on a standard methodology developed by CIHI to reflect variations in resource utilization. Fourth, the prediction accuracy of the models compared in this study was based on the model building dataset only. There is the need to validate these models in independent datasets. Fifth, our study did not include all potential confounders such as smoking status, physical activity, and body mass index. Our inability to account for these variables, because they were not routinely collected in the data sources used in our study, may possibly have led to spurious findings. Future research should consider including these potential confounders.

Sixth, there was the possibility of underestimating healthcare utilizations and costs if patients sought treatment outside the two health regions included in the study. However, given that these health regions contained the major urban centers with the main healthcare facilities, the likelihood of patients receiving treatment outside these regions may be minimal. Seven, there was the possibility of survival bias in our study, which could bias the results toward the null, particularly among the elderly age group. Lastly, the generalizability of the findings is limited to the health regions included in our study.

Despite these limitations, this study demonstrates a practical approach to link various administrative health databases to characterize healthcare costs of patients with a complex health condition. Healthcare costs have been increasing at an unsustainable rate in many jurisdictions, and some governments are currently instituting cost-controlling provider costs if patients sought treatment outside the two health regions included in the study. However, given that these health regions contained the major urban centers with the main healthcare facilities, the likelihood of patients receiving treatment outside these regions may be minimal. Seven, there was the possibility of survival bias in our study, which could bias the results toward the null, particularly among the elderly age group. Lastly, the generalizability of the findings is limited to the health regions included in our study.

Despite these limitations, this study demonstrates a practical approach to link various administrative health databases to characterize healthcare costs of patients with a complex health condition. Healthcare costs have been increasing at an unsustainable rate in many jurisdictions, and some governments are currently instituting cost-controlling provider reimbursement reforms such as bundled payment, which pays providers for an entire episode of care [36, 37]. Understanding healthcare costs based on the episodes of care, as demonstrated in our study, is important for adopting new provider payment schemes.

CONCLUSION
The costs associated with episodes of COPD exacerbations are substantial; some patients incur high healthcare expenditures persistently. Adding prior hospitalizations to socio-demographic characteristics produced the highest improvements in classification accuracy of patients into their respective high-cost groups. Being able to identify persistently high-cost patients is important for implementing strategies to manage costs and improve quality of life.

REFERENCES


APPENDIX

TABLE A1

Definitions of healthcare utilization variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>Analysis in which variable was included</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of hospital admissions</td>
<td>The number of times a patient was admitted to hospital during episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of days in hospital</td>
<td>Total number of days a patient spent in hospitals during episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of SCU admissions*</td>
<td>The number of times a patient was admitted to SCUs during hospital stays in the episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of days in SCUs*</td>
<td>Total number of days a patient spent in SCUs during hospital admissions in the episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of ED visits</td>
<td>The number of times a patient visited EDs during episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of days in ED</td>
<td>Total number of days a patient spent in EDs during episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of FP visits</td>
<td>The number of times a patient visited FPs during episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of specialist visits</td>
<td>The number of times a patient visited specialist physicians during episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of different drugs</td>
<td>The number of different types of outpatient drugs dispensed during the episode</td>
<td>√</td>
</tr>
<tr>
<td>No. of days in episode</td>
<td>The total number of days the episode covered, starting from the first date of the episode to the last date</td>
<td>√</td>
</tr>
</tbody>
</table>

Notes: *These variables were defined for only those who had hospital admission. √ = variable was included in the specified analysis; SCU, special care units; ED, emergency department; FP, family practitioner.
**CASE REPORT**

**Pulmonary rehabilitation after lung transplantation with severe complications: A case report**

Guo-Qiang Jing¹, Jie Li MS RRT NPS ACCS²,³, Bing Sun MD³, Huiwen Chu³, Haichao Li³, Xue Wang³, Xiao Tang MD³

Lung transplantation is an effective treatment for end-stage lung disease [1]. However, a recent meta-analysis demonstrated that pretransplant patients who were underweight had 1.36 times higher risk for post-transplant mortality than patients with a normal body mass index (BMI) [2]. Patients with poor nutrition had higher in-hospital mortality rates after lung transplant due to a higher rejection rate and a higher rate of infectious episodes [3, 4]. Thus, a nutritional disorder is considered as a relative contraindication for a lung transplant [1].

According to a recent study by Hadem et al. [5], the need for postlung transplantation mechanical ventilation for more than 21 days is commonly required in 13.8% (95/690) of cases. Prolonged mechanical ventilation increases the possibility of acquiring infection and ventilator-induced diaphragm dysfunction, which worsens weaning difficulties [5]. However, with early intervention, multidisciplinary teams—including respiratory therapists (RTs)—can help lung transplant patients' rehabilitation and accelerate weaning [6].

In the case presented here, pursuant to the American Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation [7], a rehabilitation plan was made and implemented by RTs in conjunction with a multidisciplinary team for a patient after lung transplantation. A variety of movement exercises in the statement were applied to the plan, which included interval strength and endurance training for upper and lower extremities as well as inspiratory muscle training. Moreover, bronchial hygiene was utilized to improve secretion clearance and reduce airway resistance as well as to minimize work of breathing for this particular case due to his muscle weakness and surgical injury. As for ventilator management, careful progressive attempts at weaning were the key to the success. It should be noted that most hospitals in mainland China do not have RTs [8], therefore, the participation of an RT in our team plays a very important role in this patient’s rehabilitation.

Ethical approval was sought for this case study through Beijing Chaoyang Hospital's institutional review board and it was deemed unnecessary (06/02/2017).

**INTRODUCTION**

Lung transplantation is an effective treatment for end-stage lung disease [1]. However, a recent meta-analysis demonstrated that pretransplant patients who were underweight had 1.36 times higher risk for post-transplant mortality than patients with a normal body mass index (BMI) [2]. Patients with poor nutrition had higher in-hospital mortality rates after lung transplant due to a higher rejection rate and a higher rate of infectious episodes [3, 4]. Thus, a nutritional disorder is considered as a relative contraindication for a lung transplant [1].

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**CASE PRESENTATION**

A 59-year-old male with a BMI of 14.36 kg/m² (40/1.67²) was admitted to the hospital for a lung transplant in March 2014. He was diagnosed with interstitial lung disease, pneumoconiosis, and severe pulmonary hypertension five prior to admission. One year prior, he started home oxygen (nasal cannula) and his six-minute walk distance was less than 100 m. On admission, his pulmonary function was very weak. His upper limbs could not defend against resistance by the examiner, and his lower extremities could move, but not against gravity. Echocardiography showed mild to moderate systolic tricuspid valve regurgitation, with systolic pulmonary artery pressure (sPAP) of 93 mm Hg. Before surgery, he was placed on veno-arterial extracorporeal membrane oxygenation (VA-ECMO) with settings of 2531 rpm/min, blood flow 1.89 L/min, and oxygen flow 2 L/min to assist with the bilateral lung transplant. Three hours after surgery, the patient returned for a second thoracotomy surgery to stop the bleeding.

On the first postop day, sPAP was 26 mm Hg and hemoglobin was 84 g/L. ECMO was weaned 34 hours later. However, the attempt to switch ventilator mode from pressure-assist control (PAC) to pressure support ventilation (PSV) failed. Electrical activity of the diaphragm showed weak neuromuscular drive. A chest computed tomography (CT) scan found bilateral collusive pneumothorax (Figure 1). Percutaneous tracheotomy was performed at the bedside on postop day five.

The patient’s muscle strength decreased after surgery (muscle strength grade 2) due to immobility for a period of time (Figure 2). Passive limb functional exercise was initiated, followed by combined passive and active limb exercises four times a day. Daily therapeutic bronchoscopy was performed to help clear the copious amount of secretions. Ventilator settings were carefully titrated based on vital signs and subjective complaint. Eight days later, he was placed on Optiflow via a T-piece with FiO² 0.60 and flow 50 L/min. However, his PaCO² gradually increased from 35 mm Hg to 66 mm Hg in the following three days. He also felt short of breath and was diaphoretic and was then placed back on the ventilator with PA/C. A chest CT showed some improvement in the right-side pneumothorax, but worsening consolidation and a...
persistent left-side pneumothorax (Figure 1). Five days later, the T-piece with Optiflow was again attempted intermittently. However, on day three the patient became drowsy, with diminished and coarse breath sounds in the left lung. Arterial blood gas (ABG) showed hypercapnia (pH 7.279; PaCO₂ 85.7 mmHg; PaO₂ 206.9 mmHg). He then was placed back on mechanical ventilation with PSV: PS 16 cm H₂O, positive end-expiratory pressure (PEEP) 6 cmH₂O, FiO₂ 30%.

Nutritional support was reevaluated and adjusted, and a percutaneous gastrointestinal ostomy was performed at bedside on week six. Slight suction pressure was connected with a left chest tube to help drain gas and his paradoxical breathing gradually improved. His cough ability was still weak, but the need for bronchoscopy decreased. We initiated as aggressive bronchial-hygiene therapy as he was able to tolerate, such as postural drainage and chest percussion three to four times a day. He was mobilized to the chair at bedside and given active resistance muscle exercises. Ventilator settings were gradually reduced, and he was intermittently switched from the ventilator to the T-piece with Optiflow, and his ABG became stable.

The patient was able to sit on a chair without assistance and stand up at bedside on week eight (limb muscle strength grade 4). At week 10, he was able to perform assisted walking with ventilator support. Ventilator settings were adjusted based on his vital signs and subjective complaint. A chest CT on week 11 displayed no presence of pneumothorax, and consolidation in the right lower lobe had improved. However, a bronchoscopy showed copious secretions in the right main bronchus. Chest wall oscillation was used to clear secretions. During this time, the patient started exhibiting insomnia and anxiousness. An antidepressant and sleep medication were prescribed by a consulting psychologist. The patient was weaned intermittently from the ventilator to the T-piece (FiO₂ 24%–28%) on week 13. Finally, a cuffless tracheostomy tube was placed on week 14 and capped 5 days later. He was decannulated with 2 L/min nasal cannula on week 15, and discharged from the intensive care unit with a BMI of 16.06 kg/m².

DISCUSSION
This patient was a poor candidate for a lung transplant due to severe malnutrition, advanced age, the need for ECMO support during surgery, and the need for long-term mechanical ventilation after the transplant. Additionally, this patient had numerous complications immediately after the transplant, such as bleeding and bilateral collusive pneumothorax. Pulmonary rehabilitation has a vital role in the treatment of lung transplantation patients [7]. After a full evaluation of this case, the multidisciplinary team listed and prioritized 5 key treatable problems: secretion retention, respiratory dysfunction, skeletal muscle weakness, malnutrition, and psychological anxiety. A multidisciplinary rehabilitation program was created specifically for this difficult patient.

Secretion retention
Tomkiewicz et al. [9] reported that ciliary function, or mucus properties, were significantly altered in a canine model of single lung autotransplantation, and that this abnormality lasted four months postoperatively. Our case was also found to have secretion retention, especially in the early phase postoperation. Esguerra-Gonzales et al. [10] found that...
four daily bronchial hygiene treatments provided to lung transplant patients improved peak expiratory flow from 205 L/min to 225 L/min as well as improving patients’ dyspnea scores and oxygenation. For this patient, chest percussion combined with postal drainage and high-frequency chest wall oscillation were provided to help mobilize secretions; cough assist and bronchoscopy were also used to assist with secretion clearance.

Respiratory dysfunction
The possibility of weaning this patient from the ventilator was monitored closely, and weaning was progressively attempted. Physical signs, symptoms, and subjective feelings were utilized to evaluate the patient’s tolerance and to determine the next step in weaning attempts.

Skeletal muscle weakness
For this specific patient, physical therapy was introduced early, immediately after the patient was removed from ECMO. Passive exercises were provided when his muscle strength was low and active exercises were initiated as he was gaining muscle strength. To encourage the patient to exercise, ventilator support was increased during exercise to provide sufficient ventilation and oxygen delivery. Ventilator settings were carefully titrated by the RT, based on the patient’s progress. At the late phase, the RT walked the patient with the ventilator and adjusted settings for the patient. Every time the patient was doing exercises, the RT always stayed aside and made decisions on when to discontinue and when to resume exercises.

Malnutrition
Nutrition disorder is one of the major issues in this individual case, as malnutrition limited his rehabilitation. After a full assessment by the physician, different ways of feeding (intravenous and enteral nutrition support) were utilized in different phases of recovery. A nutrition plan was evaluated and revised daily. Also, a high-protein, high-fat, and low-carbohydrate diet was given to reduce carbon dioxide production along with oxygen consumption on the metabolic process.

Psychological anxiety
Psychological counseling helps lung transplant recipients improve rehabilitation and their life quality [11]. When the patient reported insomnia and anxiousness, a psychologist was consulted, and an antidepressant was prescribed. When the patient reported insomnia and anxiousness, a psychologist was consulted, and an antidepressant was prescribed. When the patient reported insomnia and anxiousness, a psychologist was consulted, and an antidepressant was prescribed. When the patient reported insomnia and anxiousness, a psychologist was consulted, and an antidepressant was prescribed. When the patient reported insomnia and anxiousness, a psychologist was consulted, and an antidepressant was prescribed.

CONCLUSION
This case demonstrated that careful evaluation and an individual systematic rehabilitation program from a multidisciplinary team with early intervention may help lung transplanted patients’ rehabilitation and accelerate weaning. Most hospitals in China do not have access to the services of RTs. This novel case study importantly records the role of the RT within the evolving context of Chinese healthcare and rehabilitation systems. The RTs involved in this case demonstrated their ability to provide a unique and indispensable role within the team, including careful evaluation, airway clearance, breathing exercises, early mobility, and physical intervention.

ACKNOWLEDGEMENTS: We thank J. Brady Scott MSc RRT-ACCS FAARC and Tyler Weiss MSc RRT-ACCS AE-C for reviewing the manuscript.

REFERENCES
Poster Abstracts from the 2017 Conference of the Canadian Society of Respiratory Therapists

We are pleased to present abstracts from the posters that were displayed at the CSRT Annual Education Conference in Halifax, Nova Scotia, on 11-13 May 2017. Over the course of the conference, posters were displayed in the exhibit hall in two separate competitions: one for respiratory therapists (RTs) and one for students.

The winning RT poster was from Julie Brown et al., “Does an E-learning Module Improve Health Science Students’ Venipuncture Skills?” The winning student RT poster was from Susan Abdo from Dalhousie University, School of Health Science, Respiratory Therapy, for her poster, “A Selective-Binding Agent in Replacement of Anticholinesterase Inhibitors for the Reversal Neuromuscular Blockade.” Congratulations to everyone who participated!

As evidenced by the abstracts reproduced below, the work of our colleagues in 2017 highlighted current research and practice innovations led by RTs. The editorial board looks forward to receiving these manuscripts for consideration for publication in the Canadian Journal of Respiratory Therapy. Please note that these abstracts have not been peer-reviewed.

RESPIRATORY THERAPY POSTER

COMPETITION ABSTRACTS

WINNER

DOES AN E-LEARNING MODULE IMPROVE HEALTH SCIENCES STUDENT’S VENIPUNCTURE SKILLS?
TJ Lindenmaier, J Flook, J Brown, A Mitchell, L Ranieri,
H Harrison, D Steary, E Lorusso
Fanshawe College, London, ON, Canada
jbrown@fanshawec.ca

The development of psychomotor skills and the confidence associated with performing professional tasks are key milestones for health sciences students. Traditionally, these students are provided with lectures, readings, and limited simulated lab time in the didactic component of their education. Due to heavy course loads it is difficult to provide one-on-one training for all students and to ensure that this training translates into strong professional competence. We have therefore created an E-learning module to be used in conjunction with traditional didactic education for a common healthcare skill: venipuncture. There is limited research on the effectiveness of E-learning modules in developing psychomotor skills for health sciences students and practitioners; our goal is thus to evaluate the effectiveness of our supplementary module in traditional didactic programs. Students from these programs at Fanshawe College will be recruited and randomly assigned to a control or a study group. Students will be scored based on three main components: (1) psychomotor skills, (2) level of confidence, and (3) academic competence. We hypothesize that the study group will outperform the control group in all three areas of evaluation. Overall, this work will provide insights into the utility of E-learning in helping students achieve key competencies required in their future professions.

DOES THE DELIVERY OF VARIOUS FLOW RATES FROM A HIGH-FLOW NASAL CANNULA DECREASE PEAK INSPIRATORY FLOW RATES MEASURED AT THE AIRWAY OPENING OF HEALTHY ADULT SUBJECTS?
T Fournier, J Annear, J Doucet
New Brunswick Community College, Saint John, NB, Canada
tammie.fournier@nbcc.ca

High-flow nasal cannula (HFNC) can improve oxygenation due to small increases in end-expiratory pressure and fixed inspired oxygen fractions. Pressurized metered dose inhalers (pMDIs) improve aerosol deposition when combined with valved holding chambers (chambers). Anecdotal observations suggest some patients receiving HFNC cannot produce efforts necessary to open chamber one-way valves; however, removing HFNC for pMDI may cause alveolar derecruitment and oxygen desaturation. In an independent, observational correlational study, a relationship between HFNC and peak inspiratory flow rate (PIFR) through the mouth was sought. Post baseline PIFRs, HFNC was applied, PIFR was then repeated at 10, 30, and 60 L/min HFNC. American Thoracic Society (ATS) standards were used; goal for in-test reproducibility of PIFR was set at 5%; average attained was 2.9%, (SD = 0.025). Numerical data disprove our hypothesis that flow from HFNC would have a dampening effect on PIFR (findings revealed average PIFRs at baseline were lower than at 60 L/min); however, less data were collected as HFNC flow rates increased. Spirometer error occurred with some subjects; specifically, the “Perform Maximal Inspiration at Any Time” error message was produced and inspiratory flow/volume would not be measured during FIVC. Prior to HFNC application, all (n = 31) completed baseline FIVC maneuvers without error; error occurred with HFNC only. Subjects who could not be measured at any given flow rate were female (n = 13) and, on average, were shorter in height than those who didn’t error (n = 18). Researchers believe the frequent error indicated that...
flow/pressure from HFNC was sensed by the pneumotach on the subject side (where a valved chamber would be) rendering FIVC unmeasurable. As HFNC flows increased, observations of air leaving the mouth increased. While significance of observations are unclear, further investigation is warranted; guidelines for HFNC in combination with pMDI do not exist. Anecdotal observations suggest their combination may be ineffective.

VENTILATOR ASSOCIATED EVENTS IN A PEDIATRIC INTENSIVE CARE UNIT: APPLYING THE 2013 CENTERS FOR DISEASE CONTROL AND PREVENTION VAP DEFINITIONS

A Gionfriddo, C Lee
Hospital for Sick Children, Toronto, ON, Canada
Ashley.gionfriddo@sickkids.ca

BACKGROUND: Ventilator associated pneumonia (VAP) is a common hospital-acquired infection. In 2013, the CDC introduced new VAP criteria providing a more objective approach to defining VAP. The criteria were amended for adults but not for the pediatric population. OBJECTIVE: To identify if patients admitted to SickKids diagnosed with VAP using established pediatric CDC definitions would fulfill VAP criteria according to newly introduced 2013 CDC VAE algorithm. To compare how this categorization effects clinically relevant outcomes. METHODS: A retrospective chart review of children diagnosed with VAP from January 2006 to December 2015. Subjects identified from an infection control database included patients from a cardiac and general pediatric ICU. Patients were excluded if on high frequency ventilation, ECMO support, or re-intubated 24 hours following extubation. Primary outcome: proportion of subjects who fulfilled the updated VAP criteria. Secondary outcome; comparison of length of stay (LOS) in ICU, hospital and length of mechanical ventilation (MV). Student t test was used for between group comparisons.

RESULTS: A total of 325 subjects were identified with 279 meeting eligibility for review. Forty six subjects were excluded. According to the VAE algorithm n = 58 (21%) met VAC; n = 53 (19%) met IVAC; n = 52 (19%) met VAP and n = 5 (2%) met the VAE criteria. Failure to fulfill the new definitions was based on inadequate increase in positive end expiratory pressure or fraction of inspired oxygen. An independent t test showed no significant difference in ICU and hospital LOS and length of MV between those with the established definition and the new CDC criteria.

CONCLUSION: Only a minority of children with VAP diagnosis under the established pediatric criteria met the updated, adult-based diagnostic criteria. The updated criteria also failed to provide stronger associations with clinically relevant outcomes. This work suggests that additional studies are required before new definitions for VAP are introduced for children.

THE HYPOXIC DRIVE MYTH

O Jarvis
Concordia Hospital, Winnipeg, MB, Canada
japo@mts.net

INTRODUCTION: The Hypoxic Drive Theory started in 1949, when Davies and Mackinnon wrote an article describing the neurological effects of patients with emphysema who were given high concentrations of oxygen. Since then many health care workers live in fear of patients with the hypoxic drive. Should they? That depends on if you still believe in the hypoxic drive. If you do, it prompts some questions; why don’t all retainers stop breathing when given high levels of oxygen, why are do some people believe retainers don’t exist, why do some people give them too much oxygen no matter what? These are questions addressed in this literature review.

OBJECTIVES: To understand the relationships of the neurological basis of breathing, chemoreceptors, ventilation perfusion mismatch and the Haldane effect. To explain the physiology of patients who are chronically hypercapnic and their response to breathing 100% oxygen. To offer explanations as to why some patients who are chronically hypercapnic become more hypercapnic.

METHODS: The literature was reviewed for articles on “COPD and hypoxic drive”, and “COPD and oxygen-induced hypercapnia”. Studies were reviewed if they looked at the response of retainers breathing 100% oxygen, while not receiving any assisted ventilation.

RESULTS: Four articles were found looking at patients who are chronically hypercapnic and their response to breathing 100% oxygen. All four studies showed PCO2 increased when patients were asked to breathe 100% oxygen. The studies noted inconsistent response of minute ventilation, respiratory rate and P0.1. All studies found at the end of the exposure to 100% oxygen that the changes in the above parameters were not significant enough to explain the rise in PCO2.

CONCLUSIONS: Research since 1980 has shown that when patients who are chronically hypercapnic are given 100% oxygen to breathe their drive to breathe remains intact. These articles do not support the explanation that patients who are chronically hypercapnic are given 100% oxygen to breathe will have a decreased drive to breathe. Thus, the explanation for hypercapnia must be due to another mechanism that causes the buildup of CO2 and interferes with the ability of a retainer to remove CO2. Therefore, these patients are considered to have Oxygen-Induced Hypercapnea, not a loss of hypoxic drive.

DOES TIMING OF TRACHEOSTOMY INFLUENCE OUTCOMES IN THE CRITICALLY ILL?

C Nkwonta
University of Manitoba College of Medical Rehabilitation – Respiratory Therapy, Winnipeg, MB, Canada
umnkwonc@myumanitoba.ca

BACKGROUND: Tracheostomy is one of the most commonly performed interventions on critically ill adults; however, optimal timing for tracheostomy in this patient population remains controversial.

OBJECTIVE: To investigate whether mortality rates and the incidence of ventilator-associated pneumonia are decreased with early tracheostomy as compared to late tracheostomy.

METHODS: A systematic search was conducted on databases Pubmed and CINAHL in adherence with PRISMA guidelines for randomized controlled trials that evaluated and compared patients managed with early versus late tracheostomy. Data were obtained on outcomes of interest: mortality rates and VAP.

RESULTS: Out of 67 studies identified in the initial search, five studies were included in the systematic review including a total of 2314 patients. There was no significant reduction in 30 to 90-day mortality between early versus late tracheostomy patients. No effective conclusions could be made on the incidence of VAP in early versus late tracheostomy patients.

CONCLUSION: Early tracheostomy performed within 7 days of the initiation of mechanical ventilation was not associated with a reduction in mortality rate as compared to late tracheostomy performed between days 8 and 15. The effect of tracheostomy timing on the incidence of VAP varied between individual studies and therefore, no definite conclusions were drawn. Based on the results within individual studies the ideal timing for tracheostomy remains challenging to determine.

A SOCIO-CULTURALLY INFORMED INSTRUCTIONAL DESIGN FRAMEWORK FOR CLINICAL SIMULATION IN RESPIRATORY THERAPY

A West1, B Kim1, G Parchoma2

1Werkund School of Education, University of Calgary, Calgary, AB, Canada
2College of Education, University of Saskatchewan, Saskatoon, SK, Canada
Andrew.West@ucalgary.ca

BACKGROUND: Socio-cultural perspectives on learning suggest that instructional design in clinical simulation should maintain focus on supporting learner cognition with technology-enhanced learning strategies
rather than expecting that learning occurs as a result of any particular technology. While existing instructional design frameworks in respiratory therapy often encompass a variety of complex environmental design factors, they do not fully address the integrated nature of learning, technology, and the environment. Moreover, technologically oriented conceptualizations of fidelity continue to emerge in clinical simulation practice and research, without considering socio-cultural theories of learning in complex learning environments.

OBJECTIVE: Adopting the perspective that a shift in theoretic lens from individualistic to a more socio-cultural orientation may better support our understanding of learning through simulation in respiratory therapy education, we propose an enhanced instructional design framework.

DESCRIPTION OF INNOVATION: Building on the conceptual framework for instructional design developed by the Canadian Network for Simulation in Healthcare (Chiniara et al., 2013), this enhanced framework incorporates the attributes of the learners’ experience with the technology, addressing the physical, semantical, and phenomenal aspects of fidelity. This enhanced instructional design framework recognizes the joint learning relationship that exists between learners and simulation environments, and highlights how designs that foster this relationship can enhance simulation fidelity. A practical implementation algorithm of the framework is provided to assist simulation practitioners in taking socio-cultural perspective into their educational designs.

IMPACT: This enhanced instructional design framework is augmented by a socio-cultural definition of fidelity and informed by educational theory on knowledge-building in technology-enhanced learning environments. The framework will be useful in fostering the relationships that support an effective clinical simulation learning environment. This will be of particular value to instructional designers, researchers, theorists, and practitioners in the clinical simulation-based respiratory therapy education field.

STUDENT POSTER COMPETITION ABSTRACTS

WINNER

A SELECTIVE-BINDING AGENT IN REPLACEMENT OF ANTICHOLINESTERASE INHIBITORS FOR THE REVERSAL NEUROMUSCULAR BLOCKADE

S Abdo
School of Health Science, Respiratory Therapy, Dalhousie University, Halifax, NS, Canada
ss356264@dal.ca

BACKGROUND: Post-operative residual curarization (PORC) occurs in 60% of anesthetized patients. The morbidly obese undergoing neuromuscular blockades for surgical procedure are at a higher risk of undergoing post-operative complications like PORC attributed to insufficient reversal of induced paralysis. New emerging agents for the reversal of neuromuscular blockade, such as the selective binding agent, sugammadex, may prove to be more efficient in providing a faster and more permanent reversal of paralytics than traditional anticholinesterase inhibitors such as neostigmine.

RESEARCH QUESTION: Does sugammadex, a selective relaxant-binding agent, have a faster reversal time than, neostigmine, a cholinesterase inhibitor, on morbidly obese patients on rocuronium as neuromuscular blockade?

METHODS: A systematic review of the literature was conducted across the databases: PubMed, EMBASE, and Cochrane. Only English randomized controlled trials (RCTs), clinical trials, and systematic reviews published during the last 10 years were included.

RESULTS: Three RCTs, six SRs, and two CPGs were included (14 total). Three studies were excluded as they did not meet the inclusion criteria. Two RCTs, four SRs, and one CPG showed IS to be as effective as DB&C. One RCT, two SRs, and two CPGs showed IS to be less effective than DB&C. We were unable to find any high level evidence showing IS to be more effective than DB&C.

CONCLUSION: High level of evidence (RCT or greater) was found that supports IS as being more effective than DB&C at preventing PPCs. The results demonstrate that IS, at its best, is only as effective as DB&C. These findings suggest the role of IS in the clinical environment is due for re-evaluation.

WHAT ARE THE LONG-TERM PULMONARY EFFECTS OF SMOKING SHISHA?

M Al-Alazzi
University of Manitoba, Winnipeg, MB, Canada
maryamabd@yahoo.com

BACKGROUND: The desire to smoke shisha is stimulated by its captivating exotic look, joy experienced as it is a social activity, and the assumption of its harmlessness. Its use is escalating tremendously being a re-emerging global epidemic. Unique population health challenges are posed by the hazardous indoor air quality, second- and third-hand smoke, and its prevalence among youth, university students, and certain ethnic backgrounds. The main objective of this study was to investigate the long-term pulmonary effects of smoking shisha on relation to forced vital capacity (FVC), forced expired volume in 1 second (FEV1), FEV1/FVC, and diffusion capacity of lung for carbon monoxide (DLCO).

Methods: A systematic review was conducted by searching the databases PubMed and Scopus. Shisha has different names throughout the world;
hence, different search terms were utilized. Language restriction was applied to only English and Arabic. Five observational studies were critically appraised, which were published between January 2007 and January 2017.

RESULTS: Two of the three studies that compared shisha smokers to nonsmokers, found a significant ($p < 0.001$) decrease in FVC values, whereas one study found no difference ($p = 0.351$). However, when comparing shisha smokers to cigarette smokers, one study found FVC, FEV1, and FEV1/FVC to be significantly higher ($p < 0.05$) in shisha smokers, whereas another study found the same values significantly lower ($p < 0.001$). Also, a negative correlation was found in shisha smokers’ PFT values, in relation to the amount, duration, and total amount smoked.

CONCLUSION: Although it is not clear if shisha smoking is more harmful than cigarette smoking, it was found to have a serious impact as it is associated with declined pulmonary function. In particular, deep inhalation and duration of shisha smoking could deteriorate long-term health. Given the unique socio-cultural contexts in which shisha is used, there is a necessity for a culturally proficient, client-centered, focused approach on prevention, control and shisha-smoking cessation. Since the current research on shisha smoking convey distinctive, but also inconclusive pulmonary effects, longitudinal, evidence-based research will help us in understanding this mode of smoking as we continue to evolve in the trends of the 21st century.

CONTAMINATION OF HEALTH CARE PROVIDERS WITH THE USE OF PPE – A REVIEW

B Babiarz
The Minchener Institute of Education at UHN, Markham, ON, Canada
14bb1@michener.ca

INTRODUCTION: Personal protective equipment (PPE) has become a widely used and accepted method of protecting health care workers from potential disease. Health care providers (HCPs) provide care to a variety of patients and are potentially exposed to organisms or infectious disease that could be hazardous to themselves or other patients. There is a wide range of infection control practices that differ based on the organization, increasing confusion on the proper practices for infection control. With differences in practices, HCPs develop habits for their use of PPE that may not be the most effective and may lead to an increase of self-contamination. The effectiveness of PPE is dependent on HCP compliance, organizational policies and procedures, and training.

OBJECTIVE: To identify limitations and common errors in the use of PPE in clinical practice. Identify areas for improvement through investigation of available literature.

METHODOLOGY: PubMed and Cochrane library databases were used to compile studies that explored the effectiveness of PPE practices used in clinical practice in North America.

RESULTS: Results from literature review were unanimous. Two studies and 1 systematic review that studied contamination with PPE use in HCPs found that a large portion of users self-contaminated with PPE use, specifically during the removal process. These studies indicate that poor technique/improper use, rushed removal, and gaps in following infection control recommendations lead to remarkably high levels of contamination. Lack of education and training has been highlighted in other studies examining adherence to infection control measures. Clearer signage on the removal of PPE has also been suggested in addition to signage on isolation precautions to improve standardization of PPE doffing.

CONCLUSION: There is an overwhelming amount of literature showing contamination of HCPs even with the use of PPE through improper use. Most HCPs surveyed in studies indicate there is very minimal training in the use of PPE. Standardized protocols for the use, preparation, and removal of PPE need to be established and enforced to improve clarity of isolation practices. More strategic training regimens could be implemented for all clinical and non-clinical staff, reducing different practices between different staff.

THE EFFECTIVENESS OF PROPHYLACTIC ANTIBIOTICS IN PREVENTING AECOPD

S De Los Santos
Bachelor of Respiratory Therapy Program at the University of Manitoba, Winnipeg, MB, Canada
sheilaredslds@gmail.com

BACKGROUND: Recent studies have predicted that by 2030, chronic obstructive pulmonary disease (COPD) will become the 3rd leading cause of death worldwide. COPD is both a treatable and preventable disease, which affects mostly those who currently smoke or have a history of smoking. Acute exacerbations of COPD (AECOPD) will occur on average of 1.4 times per year per patient, which will likely send these patients to the hospital resulting in an increased cost of health care as well as a decline in the patient’s quality of life and lung function. The use of prophylactic antibiotics to prevent AECOPD is a growing interest; however, they are not standardized in the treatment of COPD in conjunction with current medication therapy.

OBJECTIVES: To determine whether or not the use of prophylactic antibiotics is effective in preventing acute exacerbations in patients with COPD.

METHODS: A systematic literature search was conducted in January 2017 using the following computerized databases: PubMed and Ovid Medline. Randomized controlled trials (RCTs) were the only publications of interest in the search. A secondary search was performed by reviewing the citations of relevant publications.

RESULTS: Twenty-five publications were identified in total after conducting the primary and secondary search. After applying inclusion and exclusion criteria and screening the abstract and full-text articles, two RCTs were included in the present literature review. Both RCTs reviewed in the present literature review were double-blind, placebo-controlled studies, which were interested in the frequency of AECOPD during the study trial. One study showed evidence that prophylactic antibiotics reduced the frequency of AECOPD and improved quality of life at the expense of possibly acquiring antimicrobial resistance. In contrast, one study showed no evidence of the emergence of antimicrobial resistance; however, the use of antibiotics did not significantly reduce the frequency of AECOPD.

CONCLUSIONS: Each study conducted showed a reduction in hospital admissions; however, they both lacked data that proved the safety and effectiveness after one year.

B2 ADRENERGIC AGONIST TACHYPHAXIS

DJ Early
SAIT Polytechnic, Calgary, AB, Canada
davidjohnearly@gmail.com

RTs are often peripherally aware that B2 adrenergic agonists, such as salbutamol, have diminishing returns but don’t realize the extent. This is troubling as salbutamol is our frontline medication for the treatment of acute asthma exacerbations, both in the hospital and self-administered in the community. This poster explores current literature to establish the effects and scope of chronic B2 agonist use, including B2 adrenergic receptor desensitization, airway hyper-reactivity to inhaled allergens, bronchial cell changes, and patient outcomes. Current literature suggests that the bronchodilatory effects of salbutamol are reduced by as much as 30% with just 2 weeks of chronic B2 adrenergic agonist use. Additionally, airway hyper reactivity that is selective for allergens has been noted. Possible explanations for these effects are explored, including immune system destabilization, and intracellular movement of B2 receptors. Data examined reveals that salbutamol monotherapy and LABA use correlate with poor patient outcomes. In light of the data examined, there seems to be great potential for a positive feedback loop to develop. As patients become desensitized to B2 adrenergic agonists they will need to use higher doses to achieve the desired effect, which in turn will lead to further desensitization and greater airway reactivity in response to allergens. In light of this, recommendations are made to improve patient education, change the way we think about asthma treatment,
IS THE USE OF ULTRASOUND EFFECTIVE IN DIAGNOSING PNEUMONIA IN CHILDREN?
J Fang
University of Manitoba, Winnipeg, MB, Canada
Jfang338@gmail.com

BACKGROUND: Pneumonia is an acute respiratory infection that causes inflammation of the alveoli, causing the lungs to fill with fluid and purulent material. It is one of the single largest infectious causes of death in children (WIHO, 2016). Chest radiography (CXR) is the most common diagnostic tool to visualize signs of pneumonia. Lung ultrasound (LUS) is a noninvasive tool that is said to have a greater accuracy in detecting pneumonia and may serve as an alternative to CXR; however, LUS is currently not included in the guidelines for diagnosing sublingual immunotherapy.

OBJECTIVES: The objective of this systematic review was to determine the accuracy ultrasound in diagnosing pneumonia in children.

METHODS: A systematic literature search was conducted in October 2016 using PubMed and Scopus. Randomized controlled trials and clinical trial studies were the only publications included in the search. A secondary search was conducted by reviewing the references of relevant publications.

RESULTS: A total of 58 publications were identified after conducting the primary and secondary search. A total of five publications were included in the present systematic review.

DISCUSSION: The primary outcomes measured in each of the studies were the rates of diagnosis for pneumonia in the participants from LUS findings in comparison with rates of diagnosis from CXR findings. Detection and diagnosis of pneumonia in the subjects with ultrasound were higher in comparison with CXR.

CONCLUSIONS: Lung ultrasound is a simple and reliable diagnostic tool that can be used by clinicians on those with suspicion of pneumonia. Although the publications included in the present review displayed higher detections rates or pneumonia with the use of LUS compared with CXR, further randomized controlled trials with a larger sample size are required for better statistical analysis.
anatomy, including the upper and lower respiratory tracts, and cardiac anatomy. Both respiratory students, who did not have any hands-on experience with cadavers prior to the event, and medical students benefited from the anatomy laboratory session. Tangible anatomy helped to create a better understanding of the human body. The RT students were able to make connections between in-class content of cardiopulmonary anatomy and clinical scenarios. The medical students who ran the session gained a better understanding of the role of the respiratory therapist and the extent of anatomy taught in the RT curriculum. Overall, students were satisfied with the session. Both parties developed skills in communication and professionalism, and earned the value of interprofessional health education at any point in one’s professional career. A reciprocal IPHE event instructed by RT students is anticipated for the future. The session will include respiratory care topics relevant to a medical student’s curriculum.

SHOULD OXYGEN BE USED IN A MYOCARDIAL INFARCTION?
R O’Neill
Dalhousie University, Halifax, NS, Canada
cr258889@dal.ca

BACKGROUND: The use of oxygen in normoxemic patients having an acute myocardial infarction (MI) remains a debate. Recently, the 2015 Advanced Cardiac Life Support (ACLS) guidelines updated their recommendations on the use of oxygen in normoxemic patients as emerging evidence has suggested it may be harmful to the patient.

RESEARCH QUESTION: For normoxemic adults having an acute MI, does receiving room air pre-hospital decrease myocardial injury (decreased infarct size, decreased troponin and creatine kinase) compared with those receiving supplemental oxygen prehospital?

METHODS: Four databases were reviewed (CINAHL, PubMed, Cochrane, EMBASE) for research within the last 10 years using keywords "myocardial infarction," "infarct size," and "oxygen." Studies were excluded when oxygen or room air was not started prehospital. Endpoints of interest were myocardial infarct size and peak troponin and creatine kinase (CK) levels.

RESULTS: Two randomized control trials (RCT) and one systematic review (SR) were included in the review of the literature. When comparing the oxygen to air groups, one RCT reported a significant increase in CK and infarct size and no significant increase in troponin. The other RCT did not find any significant increase in infarct size or peak troponin in the oxygen groups. The SR on the use of oxygen or air in a MI found existing evidence too weak to evaluate.

CONCLUSION: Existing evidence of the role of oxygen in normoxemic myocardial infarction patients is limited and conflicting. There is some evidence to suggest it may cause cardiac damage but larger studies will need to be done to confirm this.

VENTILATOR-INDUCED LUNG INJURY: PROTECTING THE LUNGS VS. THE ALVEOLI: ARE WE OPTIMIZING OUR VENTILATION STRATEGIES?
J Gould, J Jaikaran, V Vijayakumar, CA Yip
Fanshawe College, London, ON, Canada
v_vijayakumar@fanshaweonline.ca

Ventilator-induced lung injury (VILI) is an iatrogenic consequence that can lead to physiological complexities such as acute respiratory distress syndrome (ARDS), or may occur secondary to pre-existing ARDS. VILI further complicates the clinical course and interventional strategy for affected patients, and although unavoidable at times, it should be better prevented by using appropriate ventilation parameters and strategies individualized for each patient. The breath-mechanical profile has been used to describe alveolar dynamics during breathing and identify the three major mechanisms of VILI: static overdistension, alveolar recruitment/de-recruitment, and stress concentration. Current strategies to prevent VILI focus on using low tidal volumes and optimal positive end-expiratory pressure (PEEP), however low tidal volumes may still have potential to cause alveolar trauma based on the mechanisms of VILI, and methods of finding optimal PEEP may be restricted as per capabilities between clinical sites. Exploring the use of already existent cost-effective strategies such as: stress-indices (derived from pressure-time curve of constant inspiratory flow), deadspace fraction (calculated from volumetric capnography), and time-controlled PEEP (optimizing expiratory flow-cycling to maintain intrinsic PEEP) may provide much value in improving safe lung-protective mechanical ventilation practice.

BIOMARKERS AND PATHOPHYSIOLOGY OF ARDS: FUTURE DIRECTIONS OF DIAGNOSIS, PROGNOSIS AND TREATMENTS
L Wang
SALT, Calgary, AB, Canada
limei.wang@sait.ca

Acute Respiratory Distress Syndrome (ARDS) is defined as an acute-onset, progressive, hypoxic condition with bilateral lung infiltration and diffuse alveolar damage. An investigation revealed that overall ICU hospital mortality of ARDS patients is higher than 40% in adults, and ARDS accounts for up to 30% of all pediatric ICU mortality. The incidence of ARDS almost doubled during last 23 years and is expected to rise continuously. Our understanding of the pathology of ARDS is still incomplete, and it is necessary to re-evaluate our clinical translation of diagnostic, preventive, and therapeutic strategies. A grasp of the cellular and molecular mechanisms of ARDS is essential for developing effective therapies. Recent studies demonstrate that biomarkers of acute lung injury and ARDS in plasma and bronchoalveolar lavage fluid provides a hope to better elucidate pathophysiological mechanisms of ARDS and to identify the severity and prognosis and potential effective treatments. The purpose of this paper is to review and summarize the current knowledge on biomarkers of ARDS, provide important insights into the pathophysiological mechanisms, and identify the future directions of diagnosis, prognosis and treatment of ARDS. The important biomarkers of ARDS, including biomarkers of exudative phase and biomarkers of fibroproliferative phase, will be listed and discussed in this paper.

DOES THE USE OF PRONE POSITIONING IMPROVE SURVIVAL IN PATIENTS WITH ARDS?
L Yankech, C Campbell
University of Manitoba, Winnipeg, MB, Canada
yankech@myumanitoba.ca

INTRODUCTION: Prone positioning has potential to be an effective treatment to improve oxygenation in patients with ARDS due to changes in lung physiology. This research intends to investigate the use of prone positioning to improve survival in adult patients with ARDS, and to provide a fuller outlook on the research conducted on prone positioning and ARDS.

METHODOLOGY: A systematic literature search was conducted in October 2016, using the databases PubMed and Ovid. A total of five articles were included in the qualitative synthesis process after primary abstract screening and secondary full text reviews. Randomized control trials comparing prone to supine positioning were included in this review. All participants in the included studies are adult patients (over 16 years of age) who had been diagnosed with ARDS within 36–72 hours. The primary outcome measured in the studies are mortality (28–90 day mortality) and PaO2/FiO2 ratios.

RESULTS: In four of the five studies reviewed, ICU mortality was the primary outcome. The other study’s primary outcome was PaO2/FiO2 ratio. Four out of the five studies supported the use of prone positioning, whereas one did not.

CONCLUSION: Only two of the studies had sufficient sample sizes to reach statistical significance. Based on these two studies, prone positioning appears to be an effective treatment strategy for ARDS when applied early and for long periods of time. However, the treatment needs to be applied with caution as complications are common. More research in this area is required to determine how efficacious prone positioning is in treating ARDS, how early it should be applied to be efficacious, and for how long prone sessions should last.
EXPLORATION OF MEDICAL ASSISTANCE IN DYING IN CANADA: USE FOR PATIENTS DIAGNOSED WITH AMYOTROPHIC LATERAL SCLEROSIS
K Yuill
SAIT Respiratory Therapy Program, Calgary, AB, Canada
kelly.yuill@yahoo.ca

This paper will explore the journey Canada has taken to allow patients access to Medical Assistance in Dying (MAID) and the reasons why this change in legislature is a positive advancement in the Canadian healthcare system for the terminally ill, specifically those with amyotrophic lateral sclerosis (ALS). On 6 February 2015, the Supreme Court of Canada (SCC) decriminalized the use of MAID. The following year, Bill C-14 was implemented throughout Canada on 17 June 2016. This new regulation contains specific MAID safeguards to allow for continuity and fluidity nationwide. To understand the diversity from patient case to case, the arguments in favour of the legalization and use of MAID, such as the right to self-determination and relief from suffering, and the arguments in opposition, such as religious, ethical, and moral reasons, will be examined. Furthermore, this paper will look in detail at the MAID systems and regulations already in place in Alberta. Additionally, examination of research regarding the use of MAID for those patients diagnosed with ALS in other jurisdictions will help highlight the importance of this new end of life options in Canada. Seeing as MAID is so recent to the Canadian legislature, more research needs to be conducted and more education to all Canadians is required to allow for nationwide implementation.
Indications and clinical use:
BREO® ELLIPTA® (fluticasone furoate/vilanterol) 100/25 mcg and BREO® ELLIPTA® 200/25 mcg are indicated for the once-daily maintenance treatment of asthma in patients aged 18 years and older with reversible obstructive airways disease.

BREO® ELLIPTA® is not indicated for patients whose asthma can be managed by occasional use of a rapid onset, short duration, inhaled beta2-agonist or for patients whose asthma can be successfully managed by inhaled corticosteroids along with occasional use of a rapid onset, short duration, inhaled beta2-agonist. BREO® ELLIPTA® is not indicated for the relief of acute bronchospasm.

Contraindications:
- Patients with severe hypersensitivity to milk proteins.
- In the primary treatment of status asthmaticus or other acute episodes of asthma.

Most Serious Warnings and Precautions:
ASTHMA-RELATED DEATH: Long-acting beta2-adrenergic agonists (LABA), such as vilanterol, increase the risk of asthma-related death. Physicians should only prescribe BREO® ELLIPTA® for patients not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid, or whose disease severity clearly warrants initiation of treatment with both an inhaled corticosteroid and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and do not use BREO® ELLIPTA® for patients whose asthma can be adequately controlled on low- or medium-dose inhaled corticosteroids.

Other Relevant Warnings and Precautions:
- BREO® ELLIPTA® should not be used for the relief of acute symptoms of asthma (i.e., as rescue therapy for the treatment of acute episodes of bronchospasm).
- Patients who have been taking a rapid onset, short duration, inhaled bronchodilator on a regular basis (e.g., q.i.d) should be instructed to discontinue the regular use of these drugs and use them only for symptomatic relief if they develop acute symptoms while taking BREO® ELLIPTA®.
- BREO® ELLIPTA® should not be initiated in patients with acutely deteriorating asthma, which may be a life-threatening condition.
- Exacerbations may occur during treatment. Patients should be advised to continue treatment and seek medical advice if symptoms remain uncontrolled or worsen after initiation of therapy.
- BREO® ELLIPTA® should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medicines containing a LABA, as an overdose may result.
- Caution in patients with cardiovascular disease: vilanterol can produce clinically significant cardiovascular effects in some patients as measured by an increase in pulse rate, systolic or diastolic blood pressure, or cardiac arrhythmias such as supraventricular tachycardia and extrasystoles. In healthy subjects receiving steady-state treatment of up to 4 times the recommended dose of vilanterol (representing a 10-fold higher systemic exposure than seen in patients with asthma) inhaled fluticasone furoate/vilanterol was associated with dose-dependent increases in heart rate and QTcF prolongation. Use with caution in patients with severe cardiovascular disease, especially coronary insufficiency, cardiac arrhythmias (including tachyarrhythmias), hypertension, a known history of QTc prolongation, risk factors for torsade de pointes (e.g., hypokalemia), or patients taking medications known to prolong the QT interval.
- Effects on Ear/Nose/Throat: localized infections of the respiratory tract; chronic or insufficiency have occurred during and after transfer to less systemically available inhaled corticosteroids.
- Bone effects: decreases in BMD have been observed with long-term administration of products containing inhaled corticosteroids.
- Effect on growth: orally inhaled corticosteroids may cause a reduction in growth velocity when administered to children and adolescents.
- Monitoring recommendations: serum potassium levels should be monitored in patients predisposed to low levels of serum potassium. Due to the hyperglycemic effect observed with other beta-agonists, additional blood glucose monitoring is recommended in diabetic patients. Monitoring of bone and ocular effects (cataract and glaucoma) should be considered in patients receiving maintenance therapy. Patients with hepatic impairment should be monitored for corticosteroid effects due to potentially increased systemic exposure of fluticasone furoate.
- Use with caution in patients with convulsive disorders or thyrotoxicosis and in those who are unusually responsive to sympathomimetic amines.
- Hematologic effects: may present with systemic eosinophilic conditions; with some patients presenting clinical features of vasculitis consistent with Churg-Strauss syndrome. Physicians should be alerted to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients.
- Hypersensitivity effects: immediate hypersensitivity reactions have occurred after administration, and patients should not be re-challenged with BREO® ELLIPTA® if it is identified as the cause of the reaction. There have been reports of anaphylactic reactions in patients with severe milk protein allergy with other inhaled dry powder drug products containing lactose.
- Immune effects: greater susceptibility to infections. Administer with caution and only if necessary in patients with active or quiescent tuberculosis infections of the respiratory tract; chronic or
Hypersensitivity effects: immediate hypersensitivity reactions, including anaphylaxis, may occur with inhaled corticosteroids. One should avoid re-challenging patients with these medications after a hypersensitivity reaction. ELLIPTA® patients should not be re-challenged with BREO®.

Hematologic effects: may present with suppression of bone marrow function, including neutropenia and agranulocytosis, or with a history of increased intraocular pressure, and cataracts. Close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts.

Respiratory effects: paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with a rapid onset, short duration inhaled bronchodilator. BREO® ELLIPTA® should also be discontinued immediately, the patient assessed, and alternative therapy instituted if necessary. The incidence of pneumonia in patients with asthma was uncommon. Patients with asthma taking BREO® ELLIPTA® 200/25 mcg may be at an increased risk of pneumonia compared with those receiving BREO® ELLIPTA® 100/25 mcg or placebo.

Drug interactions: caution should be exercised when considering coadministration with inhibitors of cytochrome P450 3A4; inhibitors of P-glycoprotein (P-gp); sympathomimetic agents; beta-adrenergic receptor blocking agents; non-potassium sparing diuretics (i.e., loop or thiazide diuretics); drugs that prolong the QTc interval (e.g., monoamine oxidase inhibitors and tricyclic antidepressants); xanthine derivatives; and acetylsalicylic acid.

No dosage adjustment is required in patients over 65 years of age, or in patients with renal or mild hepatic impairment.

Caution should be exercised when dosing patients with hepatic impairment as they may be more at risk of systemic adverse reactions associated with corticosteroids. Patients should be monitored for corticosteroid-related side effects. For patients with moderate to severe hepatic impairment, the maximum daily dose is 100/25 mcg.

For More Information:
Please consult the Product Monograph at gsk.ca/breo/en for important information relating to adverse reactions, drug interactions, and dosing information, which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-387-7374. To report an adverse event, please call 1-800-387-7374.

Adverse Events:
Adverse reactions reported at a frequency of ≥1% and more common than placebo in one clinical study of BREO® ELLIPTA® 100/25 mcg included: nasopharyngitis, oral candidiasis, upper respiratory tract infection, headache, dysphonia, oropharyngeal pain, epistaxis. Adverse reactions reported at a frequency of ≥1% in another clinical study of BREO® ELLIPTA® 200/25 mcg and BREO® ELLIPTA® 100/25 mcg also included the following additional adverse reactions: influenza, bronchitis, sinusitis, respiratory tract infection, pharyngitis, cough, rhinitis allergic, abdominal pain upper, diarrhea, toothache, back pain, pyrexia, muscle strain.

Dosing Considerations:
For optimum benefit, advise patients that BREO® ELLIPTA® must be used regularly, even when asymptomatic.

Once asthma control is achieved and maintained, assess the patient at regular intervals and do not use BREO® ELLIPTA® for patients whose asthma can be adequately controlled on low- or medium-dose inhaled corticosteroids.
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A safe, easy, natural way to thoroughly clean and sanitize CPAP equipment

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As Rated By CPAP Users

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