Prolonged Mechanical Ventilation Weaning at Long Term Acute Care Hospitals:

Mobilization and Outcomes

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Submitted as partial fulfillment of the requirements
for the degree of Doctor of Philosophy in Nursing Sciences
in the Graduate College of the
University of Illinois at Chicago, 2018

Chicago, Illinois

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Acknowledgments

I would like to thank and acknowledge my dissertation committee, Laurie Quinn, PhD, Susan Corbridge, PhD, Kamal Eldeirawi, PhD, Mary Kapella, PhD, Alana Steffen, PhD, and Franco Laghi, MD for their assistance, valuable guidance, and patience with me throughout the completion of this dissertation. Your time is limited, I recognize and understand the commitment and dedication it has taken to mentor me throughout my doctoral education.

This work would not have been possible without the unwavering support and encouragement from my committee chair and academic advisor, Dr. Eileen Collins. It has been a great honor and privilege to work with her that last four years. Dr. Collins allowed me to pursue my research interest and her mentorship has culminated in the final dissertation research presented on the following pages. The lessons and support provided to me during my doctoral program are invaluable as I transition into post-doctoral research and academia.

I am extremely thankful and grateful to Select Medical Corporation for their support and contribution to my study. In particular, I would like to thank Amanda Dawson, PhD, Director of Research at Select Medical Corporation for her enthusiasm for student research. Without her endorsement of my research, this dissertation would not have been possible. To the staff at Select Specialty Hospital, Quad Cities, thank you for your friendship, kindness, tolerance, and cooperation. I am thankful to have received grant funding for my research from The Select Medical Corporation.

Finally, I would like to express special thanks to Dr. Blair Foreman who provided me with endless encouragement, support, and counsel while I pursued my dreams and ambitions.

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LIST OF ABBREVIATIONS

BiPap	BiLevel Positive Airway Pressure
CI	Confidence Interval
CPap	Continuous Positive Airway Pressure
CMS	The Center for Medicare and Medicaid Services
CV Surgery	Cardiovascular Surgery
GI	Gastrointestinal
HR	Hazard Ratio
IRB	Institutional Review Board
kg	Kilograms
LOS	Length of Stay
LTACH	Long-term Acute Care Hospital
μL	Microliter
mg/dL	Milligrams per Deciliter
mmHg	Millimeter of Mercury
NAMDRC	National Association for Medical Direction of Respiratory Care
PI	Principal Investigator
PMV	Prolonged Mechanical Ventilation
OR	Odds Ratio
rpm	Respirations per Minute
SD	Standard Deviation
SE	Standard Error
STACH	Short-Term Acute Care Hospital

Summary

The purpose of this doctoral dissertation research is threefold. First, examine the relationship between three specific physical therapy assisted mobilization activities of bedside dangling, stand-turn-pivot to an out-of-bed chair, and ambulation, on ventilator liberation, mortality, discharge disposition, and change in functional mobility status of patients who require prolonged mechanical ventilation (PMV) at a Midwestern Long-term Acute Care Hospital (LTACH). Second, identify and describe distinct subgroups of patients on PMV at a Midwestern LTACH as identified by grouped clinical indicators present at the time of LTACH admission. Finally, analyze subgroup differences in mortality, ventilator liberation, discharge disposition, mobilization, and changes in functional mobility status throughout the LTACH hospitalization.

The first manuscript of this doctoral dissertation, "Prolonged Mechanical Ventilation Weaning at Long Term Acute Care Hospitals: Does Mobilization influence outcomes?", examines the relationship between the physical therapy assisted mobilization activities of bedside dangling, stand-turn-pivot to an out-of-bed chair, and ambulation on ventilator liberation and mortality of PMV patients at a Midwestern LTACH. Three physical therapy assisted mobility interventions were identified and extracted from existing medical chart documentation in a retrospectively designed medical record review.

Clinically distinct subgroups of PMV patients at LTACH's have not been described. Furthermore, it is not yet known how subgroups of PMV patients at LTACHs may differ in clinically significant outcomes, or how they respond to

commonly used interventions such as mobilization activities. The second manuscript of this doctoral dissertation, “A latent class analysis of prolonged mechanical ventilation patients at a Long-Term Acute Care Hospital: Subtype differences in clinical outcomes”, examines and classifies subgroups of PMV patients at LTACH’s as identified by grouped clinical indicators present at the time of admission via latent class analysis, and analyzes for group differences in mobility, ventilator liberation, and discharge disposition amongst the subgroups. The latent class analysis was completed using retrospectively collected medical record data collected using REDCap electronic data capture tool hosted at The Center for Clinical and Translation Science at The University of Illinois at Chicago courtesy of the National Center for Advancing Translational Sciences, National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

The combined results from both analyses are significant as this is the first study to classify subgroups of PMV patients at LTACH’s as identified by grouped clinical indicators via latent class analysis. This research also reports an association between mobility and poor clinical outcome for PMV patients at LTACH’s. Differences in physical mobility and the clinical outcomes of mortality, ventilator liberation, and discharge disposition amongst the subgroups were identified. Combined with the results from the subgroup analysis, it is clear that the identified Acutely High Morbid Class 3 patients are at increased risk of immobility and death. It is this particular subgroup that needs focused and targeted interventions to improve mortality and likely, health-related quality of life for those patients who do survive.

Appendices in the final section of this dissertation included approval letters from the Institutional Review Board of the University of Illinois at Chicago and letter of support from Select Medical Corporation. The final appendix contains my curriculum vitae.

I. Prolonged Mechanical Ventilation Weaning at Long Term Acute Care Hospitals: Does Mobilization influence outcomes?

As a consequence of continual advancements in critical care technology and the capability of the medical community to prolong life, there are increasing numbers of patients who require prolonged mechanical ventilation (PMV) in the United States. Estimates are that by the year 2020 more than 625,000 patients will require PMV in the United States.[1] Long-term acute care hospitals (LTACHs) have established themselves as a primary provider of medically complex PMV care in the United States.[2-5] Patients on PMV cared for in LTACHs have a high level of clinical complexity resulting in high medical costs.[5] Expenditures by The Center for Medicare and Medicaid Services (CMS) for PMV LTACH level care between 1995 and 2012 increased from $700 million to $5.5 billion, an increase of nearly 800%.[6] Despite high costs, PMV patients cared for at LTACHs are known to have lower 30-day hospital readmission rates,[6,7] as well as functional and cognitive improvements,[5] when compared to similar patients cared for in other post-acute settings. Currently, a gap exists in the treatment of PMV patient regarding the understanding of influential factors impacting LTACH outcomes. Authors of a recent literature review found 30 studies on post-ICU ventilator weaning, but only seven were adequately powered and focused on LTACH patients.[8]

The National Association for Medical Direction of Respiratory Care has recommended an emphasis on identifying potentially reversible morbidity factors in the PMV patient, including neuromuscular pathology and subsequent immobility.[9] Consequences of prolonged immobilization, once thought necessary for the ventilated patient, are widely recognized. These include neuromuscular dysfunction, known as intensive care unit acquired weakness [10,11]; joint contracture [12]; thromboembolism [13,14]; atelectasis [14]; insulin resistance [15]; and pressure ulcers. [16] Importantly, patients with diagnosed intensive care unit-acquired neuromuscular weakness are known to require a prolonged duration of mechanical ventilation. [17,18] Recognition of these consequences has resulted in an increased effort to study interventions aimed at limiting immobility while at the same time improving mobilization.

Mobilization has been defined as an interdisciplinary, goal-directed therapy that involves energy expenditure used to facilitate movement and improve outcomes. [19] Despite support in the literature for mobility interventions of patients who require PMV, studies examining mobilization of these patients in the long-term care setting have been burdened by substantial design and methodological limitations that included small sample sizes with a lack of control groups and instrumentation reliability and validity concerns. [20,21] The effect of mobilization of patients on PMV at LTACH's on clinically significant outcomes is unknown. Furthermore, evidence regarding specific activity type, frequency, and duration of mobilization of patients on PMV is currently lacking. Therefore, the purpose of this study is to examine the relationship between the physical therapy assisted mobilization activities of bedside dangling, stand-turn-pivot to an out-of-bed chair, and ambulation on ventilator liberation and mortality of patients receiving PMV at a Midwestern LTACH.

Methods

Design

Following Institutional IRB approval, a retrospective medical record review was completed of patients receiving PMV admitted between January 1, 2008, and December 31, 2015, to a Midwestern LTACH where they were provided care as part of regular services according to institutional standards and policies. A convenience sample was collected for this study of all patients requiring PMV who met the inclusion and exclusion criteria (Table 1). A total of 352 patient charts were screened for inclusion into the study by the PI (HD), and 103 patients were eliminated for failure to meet inclusion and exclusion criteria. The remaining 249 charts were reviewed and relevant data were extracted by the PI (HD) and two trained research assistants. Study data were collected and managed using REDCap electronic data capture tools.[22,23] At the completion of primary data collection, a subsample of 55 patient charts was randomly selected and rescreened by the PI (HD) and two research assistants for calculation of inter and intra-rater reliability scores of variables used in statistical analysis. Inter and intra-rater reliability scores were calculated via intraclass correlation for ordinal and continuous level variables, and Cohen's Kappa for nominal level data, to quantify the degree of agreement between the three data extractors.[24] Cohen's Kappa for inter-rater reliability of select variables was found to range from 0.96 to 0.98, while intraclass correlation for inter-rater reliability ranged from 0.82 to 1.0. Cohen's Kappa for intra-rater reliability of select variables was found to range from 0.90 to 0.96, while intraclass correlation for intra-rater reliability ranged from 0.77 to 1.0.

Measures

Baseline demographic data extracted included: age, gender, marital status; weight measured in kilograms; underlying etiology for prolonged respiratory failure; Charlson co-morbidity score; and short-term hospital length of stay. The Charlson Co-Morbidity Index Score was computed from the data extraction retrospectively. The Charlson Co-Morbidity Index Score is a valid index of comorbid conditions and has been used extensively in retrospectively designed research studies.[25]

Mobility. Passive range of motion exercises do not require energy expenditure on the part of the patient and do not meet the definition requirements for mobilization. Also, the benefit of passive range of motion exercises in the critically ill patients is unclear in the literature.[26,27] Therefore, three active mobility activities identified from the short-term acute care literature and used for this research are: dangle at the edge of bed without back support, stand-turn-pivot to a bedside chair, and ambulation either with or without an assist device, such as a walker.[28-31] The physical and occupational therapy narrative documentation was reviewed and each occurrence of the three active mobility activities was extracted. An aggregated total was calculated for each mobility activity for the entirety of the LTACH hospitalization. Weekly averages were subsequently calculated for each patient (sum/LTACH LOS*7). Duration of the mobility activity was also extracted. Mobility duration was documented as time in minutes of edge of bed dangle, time in minutes spent in the bedside chair, and distance in feet for ambulation. Again, an aggregated total was calculated for the duration of each mobility activity for the entirety of the LTACH hospitalization, and weekly duration averages were calculated as above. Also collected from the physical therapy documentation was patient or family self-report of prior level of home function. Finally, the functional mobility status as scored by a physical therapist at LTACH admission and discharge was extracted. The LTACH physical therapists assigned a rank-ordered score, which ranged from dependent to independent, for eight different mobility-related activities including rolling in the bed, supine-to-sit-, sit-to-supine, sit-to-stand, unsupported sitting, standing balance, transfers, and ambulation. This rank order data was coded with consecutive integers from 1-8 to facilitate quantitative analysis.

Outcomes.

Ventilator liberation. Measured LTACH outcomes were ventilator liberation status including the total number of mechanical ventilation days for the entirety of the hospitalization. There is significant heterogeneity in definitions of weaning success in the published literature, ranging from complete withdrawal of mechanical ventilation that persisted until hospital discharge [32] to 48 hours of complete withdrawal of mechanical ventilation. [33] The National Association for Medical Direction of Respiratory Care has defined weaning success in patients who require prolonged mechanical ventilation weaning as complete liberation from mechanical ventilation, other than nocturnal noninvasive BiPap or CPap support, for seven consecutive days. For this study, the last day of mechanical ventilation is defined as the last day the patient received any invasive mechanical ventilator support via tracheostomy including fully assisted mechanical ventilation or pressure supportive modes that persisted until hospital discharge. Non-invasive positive pressure ventilation via face-mask is not considered invasive mechanical ventilation, and therefore, did not count as a mechanical ventilation day in this study.

Mortality. Survival status at the time of discharge and discharge disposition if discharged alive was documented. LTACH length of stay was recorded as the number of days of hospitalization.

Data Analysis

STATA Version 13.1 was used to analyze individual variables, and descriptive statistics were calculated for each variable. Tests for normality were completed and included swilk, sfrancia, sktest and visual inspection of p-plots, q-plots, and histograms. The data were cleaned using frequency distributions to identify data entry errors and bivariate relationships were examined with Pearson's correlation. Logistic regression models were used to analyze the relationship of weekly physical therapy assisted active mobilization activities, age, Charlson Co-morbidity score, and LTACH length of stay on ventilator liberation and mortality.

To compare survival amongst different levels of mobilization, survival analysis with log-rank testing and Cox Proportional Hazard regression analysis was completed. To analyze the effect of the three physical therapy assisted mobilization activities on the time to death, the frequency of each mobility activity was categorized by tertiles into low, moderate, and high frequency of occurrence per LTACH hospitalization. A 0.05 level of significance was used for all analyses.

Results

Complete data were available for analysis of 249 patients on PMV with an average age of 68.6 ±14.0 years, 122 (49%) were male, and 127(51%) were female (Table 2). The average length of short-term hospitalization before LTACH transfer was 26.4 ±17.0 days. The average LTACH hospitalization was 35.9 ±16.2 days, or 5.1 weeks (Table 3). One-hundred seventy-two patients (69%) were successfully liberated from mechanical ventilation. Sixty-four (26%) patients died during hospitalization. Liberation from mechanical ventilation did not ensure survival. Of the 172 patients who successfully weaned from the ventilator, 20 (11.6%) died prior to LTACH hospital discharge. The most common etiology of PMV was a respiratory disease, encompassing such conditions as pneumonia and COPD exacerbation, [64(25.7%)], cardiovascular surgery [52(20.9%)], and neurologic conditions such as stroke and Guillian-Barre [30(12%)].

Mobility

The average number of weekly mobility activities is presented in Table 4. Not all patients on PMV participated in active physical therapy mobilization activities. Twenty-two (8.8%) patients never progressed beyond passive range of motion therapies provided in the hospital bed. Of these 22 passive of range of motion only patients, 12 (54.4%) survived to discharge and only four (33.3%) of these 12 survivors liberated from mechanical ventilation. Of the patients who did participate in active physical therapy assisted mobilization, 206 (82.7%) participated in bedside dangling making it the most frequently occurring physical therapy assisted mobility activity, averaging between one to two times per week. While dangling, patients sat at the edge of bed for an average of 13.1 ±12.1 minutes. The least frequent physical therapy assisted mobility activity was ambulation, with 112 (45%) patients ambulating during their LTACH hospitalization. When a patient did ambulate, they did so less than once per week on average. Patients requiring PMV on average ambulated 225.6 ±289.8 feet when they participated in ambulation therapy, and usually with the assistance of a rolling walker. No patients in the study participated in any physical therapy mobility activities five times per week or more.

Outcomes

Ventilator Liberation. The results of the individual regression analyses indicate that while holding age, Charlson co-morbidity score, and LTACH LOS constant at their respective means, dangling (p <0.001), chair sitting (p<0.001), and ambulation (p<0.001) are all associated with ventilator liberation (Table 5). Specifically, for every one-day per week increase in the number of bedside dangles, the odds of successful ventilator liberation increased by 2.485 (p<0.001, CI = 1.767,3.535). Similarly, for every one-day per week increase in the frequency of sitting in a chair, the odds of successful ventilator liberation increased by 3.711 (p<0.001, CI = 2.302,5.982). For every one-day per week increase in ambulation, the odds of successful ventilator liberation increased by 3.766 (p<0.001, CI = 2.135,6.642).

The probability of ventilator liberation is highest for those patients who regularly mobilize (Figure 1). The predicted probability of liberating from mechanical ventilation is 40% if a patient requiring PMV does not dangle during their LTACH hospitalization, but increases to 96.3% if they dangle on average four times per week. The mean predicted probability of liberating from mechanical ventilation is 50% if a patient does not stand-turn-pivot to the bedside chair during their LTACH hospitalization, but increases to 99.5% if they sit in a bedside chair on average four times per week. The mean predicted probability of liberating from mechanical ventilation is 56% if a patient does not ambulate, but increases to 99.6% if they ambulate on average four times per week. Duration of mobilization activity is not associated with ventilator liberation.

Mortality. The results of the individual regression analyses indicate that while holding age, Charlson co-morbidity score, and LTACH LOS constant at their respective means, chair sitting (p= 0.002) and ambulation (p= 0.002) are associated with decreased mortality (Table 5). In contrast to ventilator liberation, dangling has no relationship with mortality (p=0.076).

Specifically, for every one-day per week increase in out of bed chair sitting, the odds of dying decreased by 0.557 (p=0.002, CI = 0.384,0.807). For each one-day per week increase in ambulation, the odds of dying decreased by 0.506 (p=0.002, CI = 0.329,0.777). The probability of death is highest for those patients who do not mobilize out of bed (Figure 2). The predicted probability of dying is 35% if a patient does not get out of bed to a bedside chair, but decreases to 4% if they sit in a bedside chair on average four times per week. Similarly, the predicted probability of dying is 33% if a patient does not ambulate, but decreases to 3% if they ambulate on average four times per week.

Ambulation distance is associated with mortality (OR 0.994, p=0.041, CI = 0.988,0.999). There is a significant reduction in mortality with ambulation up to approximately 225 feet. Ambulation beyond 225 feet was not associated with additional mortality benefit (Figure 3).

Kaplan-Meier survival estimates of the three physical therapy assisted active mobilization activities indicate a significant difference in time to death between those patients that mobilize and those who do not (Figures 5-7). Log-rank testing for equality was significant for all three mobility activities (Table 6). Cox proportional hazard regression analysis was run to provide a measure of association between ambulation and survival (Table 7). Survival appears to be the best for those PMV patients with the highest frequency of mobilization events. Estimated hazard ratios were significant for all mobility activities, at all levels of mobilization except for moderate ambulation (p=0.859). The estimated hazard ratio for moderate ambulators was not statistically different from the nonambulatory, indicating no difference in survival between these two groups. However, the hazard ratio was 0.19 between high ambulators and the nonambulatory, indicating that patients who ambulated more than four times per hospitalization had an 81% lower risk of death than those patients who did not ambulate during their hospitalization. Accounting for sampling variability, the decrease in the risk of death for high ambulators range between 92% and 56% (95% CI 0.080,0.444).

Discussion

The documented benefits of physical therapy assisted mobilization in the PMV population include reductions in duration of mechanical ventilation [34] and enhancement of overall health status with improvement in functional status, [34,35] quality of life, [36] and survival rates. [35,37] The purpose of this study was to examine the relationship of physical therapy assisted mobilization activities, as measured by three specific physical therapy assisted active mobilization activities, on ventilator liberation and mortality of PMV patients at a LTACH. Our results indicate that patients with higher frequency and duration of physical therapy assisted mobility during their LTACH hospitalizations, have a better chance of weaning from prolonged mechanical ventilation and surviving to discharge. There is an association between physical therapy assisted active mobilization therapies on the probability of ventilator liberation and survival for patients on PMV at a Midwestern

LTACH. Furthermore, infrequent mobilization is a risk factor related to poor clinical outcomes. This finding is consistent with published literature from other researchers who also have reported improvements in ventilator liberation and mortality rates amongst mobilized patients on PMV.[35,37] However, previous studies have utilized mobility intervention programs that were provided four to six times per week and averaged 20 to 40 minutes in duration per session. Subjects in our study averaged one to two active physical therapy assisted mobility events per week with an average edge of bed duration of 13 minutes (Table 4). This is an indication that clinically meaningful improvements in ventilator liberation and mortality are possible with less frequent mobility interventions. Support for less intense frequency is confirmed by the results of the survival analysis. The Kaplan-Meier curves display differences in survival between inactive/low active and even moderately active patients for both edge of bed dangling and out of bed chair sitting (Figure 5,6).

Additionally, except for the relationship between ambulation distance and mortality, it is the frequency of mobilization activities not the duration of the activity that is important. In other words, it is more important that the patient participates; how long they participate is of lesser significance. Even low frequencies of participation are impactful. For example, there is an approximate 22% increase in the probability of successful ventilator liberation when a patient on PMV dangled at the edge of the bed just once per week. Edge of the bed dangle twice per week was associated with an increase in the probability of successful ventilator liberation of approximately 40% when compared to the bedridden patient. Average mobility frequency for patients on PMV in this study was one to two times per week or less depending on activity type. While improvements in ventilator liberation and mortality were noted with lower frequency of mobilization, the predicted probabilities in the regression models indicate notable differences in outcomes amongst those who mobilize one time per week and those who mobilize four times per week. Therefore, the goal should be to increase mobilization activity frequency to multiple times per week.

Importantly, when analyzing mortality benefit, there is a frequency at which maximum benefit is reached, and additional mobilization occurrences impart no additional mortality benefit. Additional mortality benefit was not shown after three times out of bed to the bedside chair, and after two ambulatory events (Figure 3). Currently, there is no consensus on frequency, duration, or type of mobilization activity for the maximal benefit of the PMV patient in the existing literature. The discovery of a maximum frequency benefit in this study will assist with the development of physical therapy programs tailored for efficient use staff resources to maximize patient outcome.

Patients who require PMV are physically debilitated and very frequently bedridden upon admission to the LTACH. In our sample, 51.4% of patients were rated as "dependent" for transfer mobility by the physical therapy staff upon initial assessment at the time of admission. The 22 patients (9%) that never actively mobilized during their LTACH hospitalizations in our study is a reflection of the persistent and unrelenting weakened physical condition of many patients on PMV after LTACH transfer. While there are known benefits to passive range of motion activities including prevention of contractures,[38] reduction of edema,[39] and preservation of the protein architecture of muscle fibers,[40] our results indicate that the benefits of passive range of motion activities do not extend to ventilator liberation and importantly, mortality. This is consistent with findings published by Yang, et al [41] who reported a lack of improvement in ventilator liberation rates in their study where 23.7% of interventions were limited to passive range of motion exercises. In our study, of

Diaphragmatic wasting is implicated in mechanical ventilation dependence.[42] Multiple researchers have reported their efforts at improving diaphragmatic strength and have included the use of phrenic nerve pacing, [43] weighted sandbags, [44] and threshold inspiratory muscle strength training devices. [45] However, the diaphragm is not the only muscle involved in respiration. Accessory respiratory muscles include the sternocleidomastoid, the scalenes, the intercostals, the transversus muscles, pectoralis, both anterior and posterior serratus muscles, and the oblique abdominal muscles. [46] These respiratory muscles are also many of the same muscles responsible for postural control. Based on this duality of function it has been suggested that exercise programs targeting postural muscular control will benefit ventilation. In healthy volunteers, maximal inspiratory pressure is higher in the seated position than in a supine or semi-recumbent position. [47] In this study, the most common physical therapy assisted mobility activity was dangling, which is not unexpected in light of the physically weakened and dependent state of most PMV patients. Considering the physiological benefits of the upright, seated position, it is not surprising that we found an association between the frequency of upright positioning and ventilator liberation. It is interesting that the benefit of dangling did not extend to mortality. Only stand-turn-pivot to a bedside chair and ambulation were associated with a mortality benefit, indicating that patients on PMV should be progressed beyond the edge of bed dangle aggressively as ventilator liberation without ultimate hospital survival is still a poor clinical outcome.

Clinical Implications

Data presented in this study help to lay the foundation for the support of robust multidisciplinary teams of PMV caregivers. This study is an opportunity for education of the healthcare team about the multiple morbidities and complex needs of this challenging population, with the understanding that mobilization is paramount to an overall successful outcome of the LTACH patient on PMV and should be prioritized. Efforts at improving the frequency and duration of mobility activities are encouraged. This study also presents an excellent discussion point with patients and family members of patients requiring PMV in support of active and recurrent mobilization.

Limitations

This study had design limitations including retrospective design, using data collected for non-research purposes, and the use of a single LTACH site for data collection. Causal inferences about the effect of mobilization on ventilator liberation or mortality cannot be made.

Next, only physical therapy assisted mobilization was included. Organized and reliable documentation of nursing mobilization activities was not available in the medical record and as such, could not be extracted. It is highly likely that the nursing staff is assisting LTACH patients on PMV with mobilization activities such as dangle and transfer assistance to the bedside chair. As such, this analysis cannot account for any possible impact that nursing mobilization activities may have on the outcomes of interest in this study. However, researchers have previously reported that level of mobilization achieved by the physical therapist was higher than that achieved by nurses.[48]

While we can say that patients on PMV with higher levels of mobility have improved outcomes, we cannot say why these patients have higher levels of mobility. Multiple possibilities exist from differences in demographics to severity of illness differences to differences in care received at the short-stay acute care hospitals. Data regarding care received at the short-stay acute care hospitals were not collected as part of this study. Specifically, the receipt of physical therapy assisted mobility in the short-stay acute care hospitals in this patient population is not known. There is a relationship between initiation of mobility at the short-term acute care hospital and intensive care unit outcome.[49] The potentially confounding impact of care received at short-term intensive care units is not controlled for in this study. Finally, severity of illness scoring was not completed on this patient population at the time of admission and therefore, could not be controlled for in the analysis.

Recommendations for future research

Future mobility research is recommended that includes quantification of effort. While randomization of critically ill populations presents a challenge, novel technologic developments in minimally invasive ergometry monitoring opens the possibility to monitor cohorts of patient physical activity levels with increasing sensitivity.

Additionally, research to understand the differences amongst patients who mobilize frequently, and those do not, should be undertaken. Essential to improving mobilization of the PMV population is an understanding about the characteristic differences between those who do, and those who do not, mobilize. Once patients who are at risk for low mobility are identified, targeted interventions aimed at improving mobility can be developed.

Despite 82.7% of the sample participating in active mobilization therapy during their LTACH hospitalization, the frequency of documented physical therapy assisted mobilization in this study was low. Additional research into the barrier prohibiting mobility activities should be considered. The complex PMV population frequently has multiple competing medical needs, such as hemodialysis. Multidisciplinary care coordination is encouraged to ensure that all patient therapies can be completed for maximal benefit.

Finally, this study relies on the 21 days, or more, of consecutive mechanical ventilation for six or more hours a day definition of PMV that is guided by The National Association for Medical Direction of Respiratory Care and CMS. [9] However, researchers rely on a medley of definitions of PMV, with many operationalizing PMV with much shorter duration. The NAMDRC definition is now over a decade old. There is a need to standardize the definition of PMV, and consistent use among researchers and clinicians is encouraged.

Conclusion

In summary, this study found that there is a relationship between mobilization and the clinical outcomes of ventilator liberation and death of patients on PMV at LTACHs. Those patients with higher levels of physical mobility are most likely to have a desirable clinical LTACH outcome. Mobilization efforts should be a primary focus of the LTACH care of the PMV patient. While important in ventilator liberation, edge of bed dangling had no impact on mortality. Therefore, efforts to move the patient beyond the edge of the bed are encouraged.

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Tables

Table 1. Study Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Patients who have received ≥ 21 days of mechanical ventilation	Co-morbid neurologic conditions that would interfere with limb exercises: • Amyotrophic lateral sclerosis • Spinal cord injuries resulting in quadriplegia or paraplegia
Tracheostomy in place before, or placed during their LTACH hospitalization	Admission to the LTACH for home ventilator training
≥ 21 years of age at time of admission	Previous inclusion in the study from prior admission
Hemodynamically stable: • No intravenous vasopressor medications except for inotropic medication • Absence of life threatening cardiac arrhythmias	Incomplete medical record documentation with greater than 10% of data missing on variables of interest
Admitted between January 1, 2008, and December 31, 2015	A LTACH length of stay ± 2 SD greater than average LTACH length of stay

Table 2. Demographics (N=249)

Age years(±SD)	68.6(±14.0)
Gender *n*(%)	
Male	122 (49%)
Female	127(51%)
Marital Status *n*(%)	
Single	57(22.9%)
Married	116(46.6%)
Divorced	29(11.7%)
Widowed	47(18.9%)
Etiology of PMV *n*(%)	
Cardiac	27(10.8%)
CV Surgery	52(20.9%)
Respiratory	64(25.7%)
Neurologic	30(12.0%)
Trauma	21(8.4%)
Oncologic	14(5.6%)
GI	20(8.0%)
Infection/Sepsis	16(7.6%)
Renal/Endo	2(<1%)
Prior Mobility Status *n*(%)	
Independent	157(63.1%)
Cane	16(6.4%)
Walker	55(22.1%)
Wheelchair	16(6.4%)
Bedbound	2(<1%)
Admit Mobility Status *n*(%)	
Dependent	128(51.4%)
Max Assistance	28(11.2%)
Mod Assistance	29(11.7%)
Min Assistance	11(4.4%)
Supervision	7(2.8%)
Not Tested	46(18.5%)
Weight kg(±SD)	94.1(±36.6)
Charlson Score (±SD)	5.9(±2.8)
STACH LOS days(±SD)	26.4(±17.0)

Glasgow Score (±SD)	12.3(±2.9)

STACH LOS = Short Term Acute Care Hospital Length of stay

Table 3. LTACH Outcomes

LTACH LOS days(±SD)	35.9(±16.2)
Ventilator days(±SD)	20.5(±15.8)
Weaned *n*(%)	
Yes	172(69.1%)
No	77(30.1%)
Deceased *n*(%)	
Yes	62(24.9%)
No	187(75.1%)

LOS = Length of stay

Table 4. Weekly Mobility Summary Statistics

	n	**Mean**	**SD**	**Min**	**Max**
Frequency					
Dangle/week	249	1.579	1.016	0	4.148
Chair/week	249	0.979	1.130	0	4.278
Ambulation/week	249	0.766	1.094	0	4.2
Duration					
Dangle (mins)	206	13.103	12.114	0.163	63.219
Chair (mins)	141	303.304	283.897	10.244	1512.0
Ambulation (ft)	112	225.553	289.813	0.219	1472.655

n= sample size
SD = Standard Deviation

Table 5. Logistic Regression Output: Association of mobility to LTACH outcomes

	OR	SE	z	*p*-value	95% CI
			Frequency		
Ventilator Liberation					
Dangle	2.485	0.4447	5.06	<0.001*	1.747,3.535
Chair	3.711	0.904	5.38	<0.001*	2.302,5.983
Ambulation	3.766	1.090	4.58	<0.001*	2.135,6.642
Mortality					
Dangle	0.745	0.123	-1.78	0.076	0.538,1.031
Chair	0.557	0.106	-3.09	0.002*	0.384,0.807
Ambulation	0.506	0.111	-3.11	0.002*	0.329,0.777
			Duration		
Ventilator Liberation					
Dangle	1.029	0.177	1.68	0.092	0.995,1.065
Chair	1.002	0.002	1.32	0.187	0.999,1.006
Ambulation	1.008	0.004	1.90	0.058	0.999,1.016
Mortality					
Dangle	0.983	0.017	-0.97	0.334	0.951,1.017
Chair	0.997	0.002	-1.68	0.093	0.994,1.000
Ambulate	0.994	0.003	-2.04	0.041*	0.988,0.999

OR = Odds ratio
SE = Standard Error
95% CI = 95% Confidence Interval
* Significant at 0.050 level

Table 6. Survival Analysis Log-rank testing for equality

	$\chi 2$	*p*-value
Dangle	37.63	0.001*
Chair	29.10	0.001*
Ambulate	19.10	0.001*

* Significant at 0.050 level

Table 7. Cox proportional hazard regression showing effect of mobility on death

	HR	**SE**	**z**	***p*-value**	**95% CI**
Dangle					
6-10 Dangle	0.336	0.102	-3.61	0.001*	0.185,0.607
> 10 Dangles	0.166	0.58	-5.10	0.001*	0.083,0.331
Chair					
1-7 times	0.467	0.141	-2.53	0.012*	0.258,0.843
> 7 times	0.140	0.061	-4.48	0.001*	0.059,0.331
Ambulate					
1-4 times	1.064	0.372	0.18	0.859	0.536,2.113
> 4 times	0.190	0.082	-3.83	0.001*	0.081,0.444

HR = Hazard Ratio
SE = Standard Error
95% CI = 95% Confidence Interval
* Significant at 0.050 level

Figures

Figure 1. Mobility and Ventilator Liberation

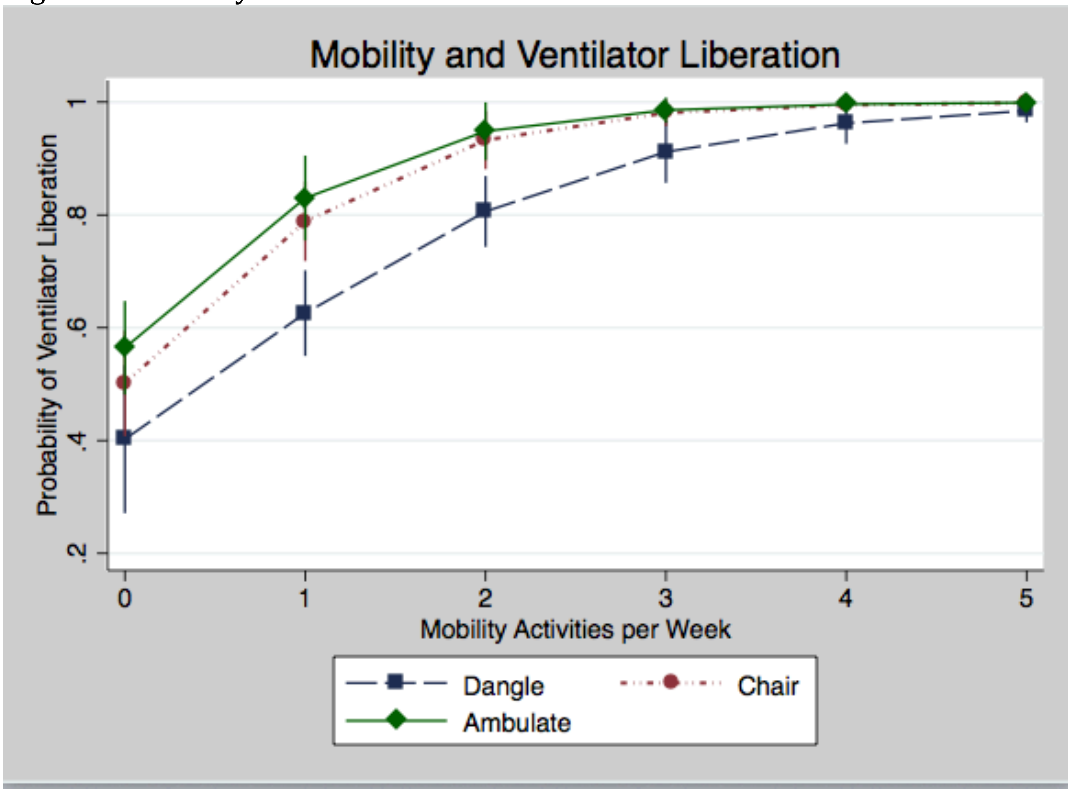


Figure2. Mobility and Mortality

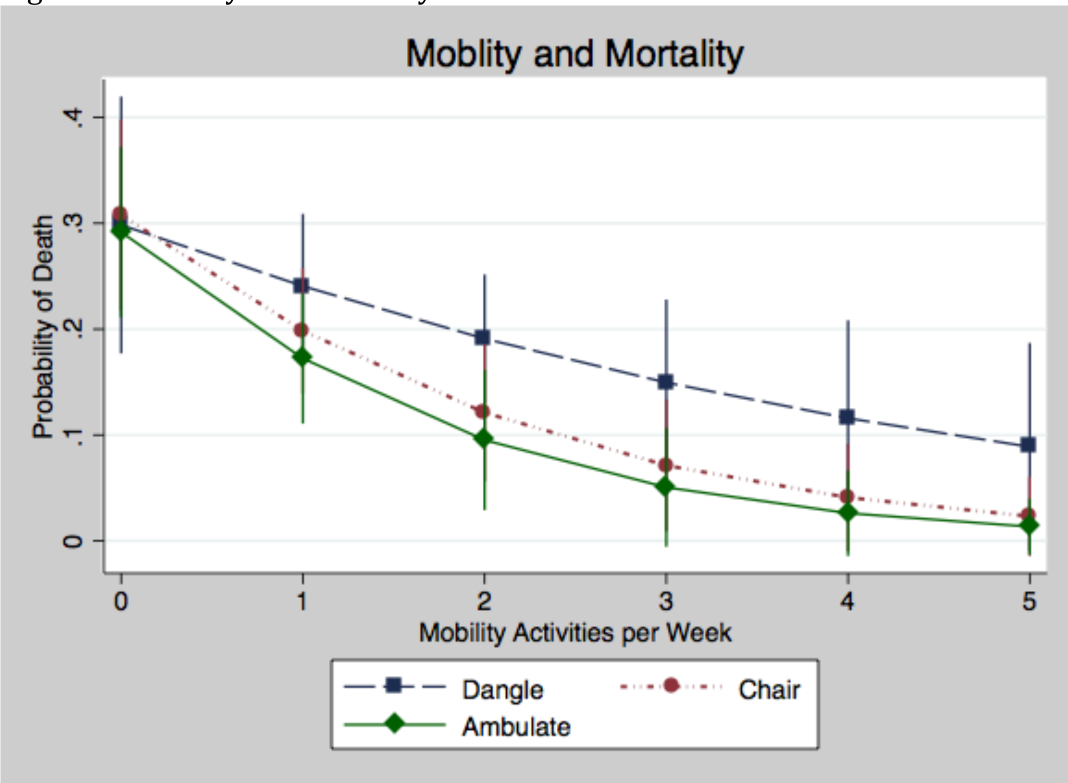


Figure 3. Ambulation Distance and Mortality

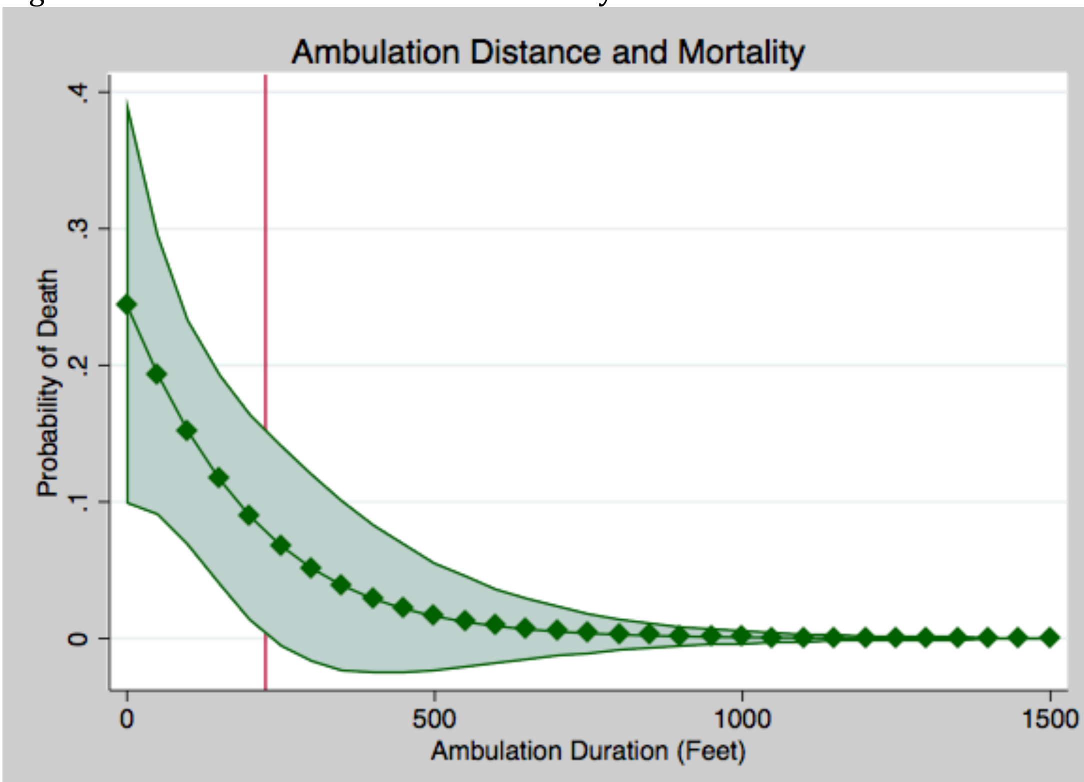


Figure 4. Kaplan-Meier Curves for Dangling Mobility Activity

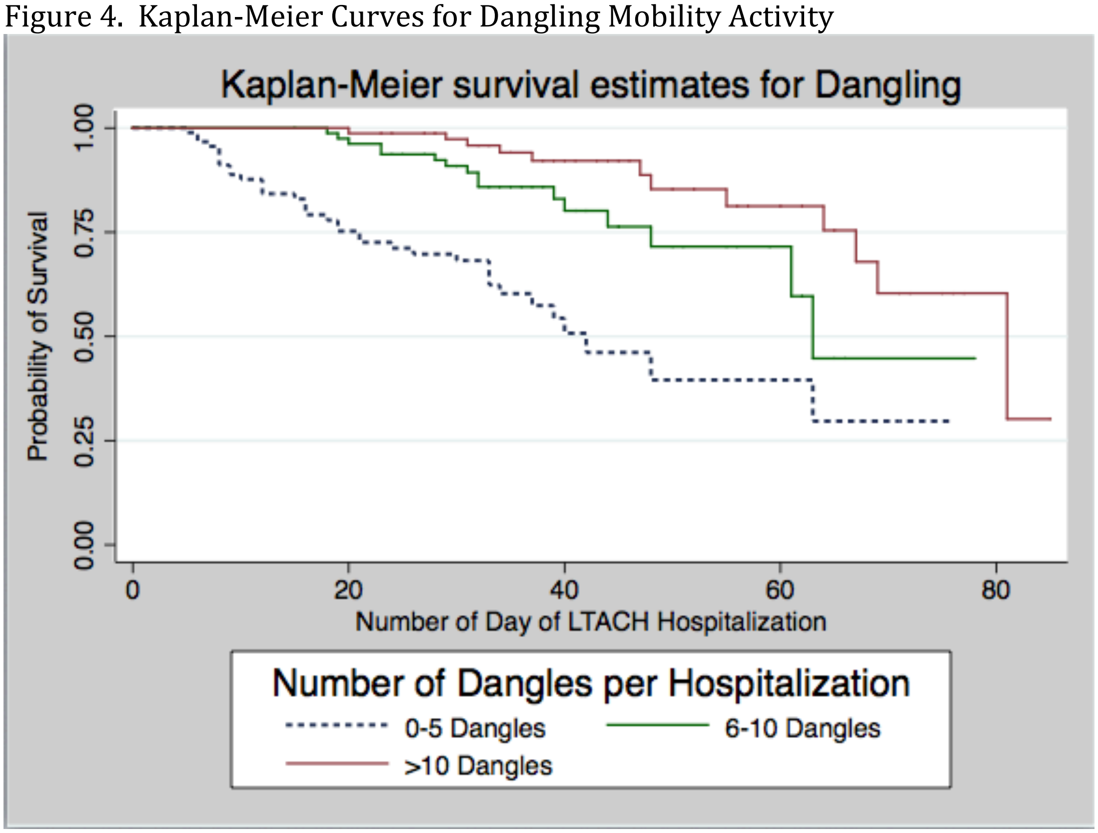


Figure 5. Kaplan-Meier Curves for Chair Mobility Activity

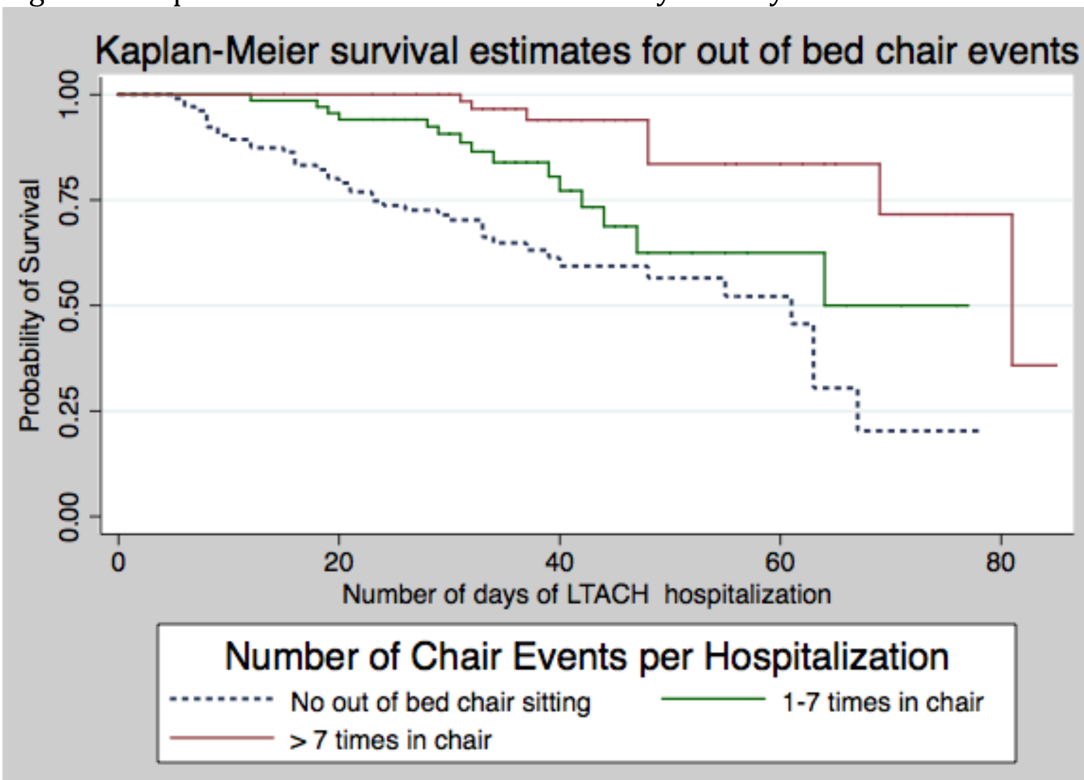
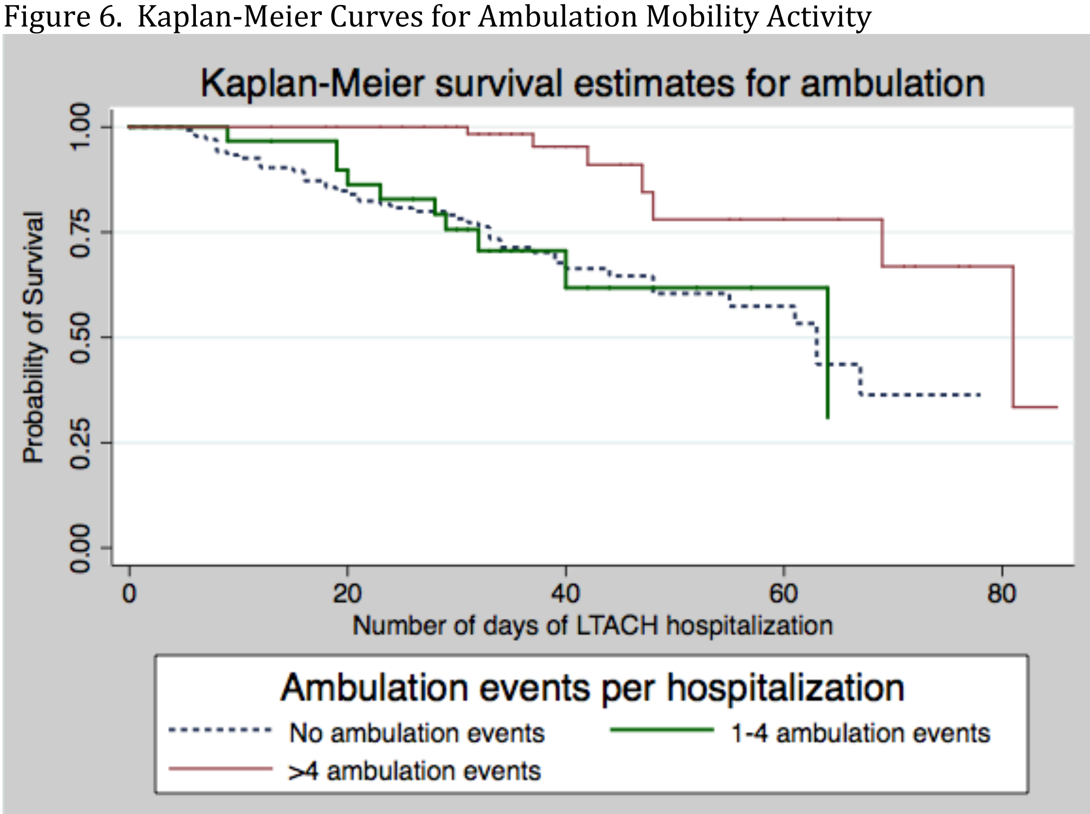


Figure 6. Kaplan-Meier Curves for Ambulation Mobility Activity



II. A latent class analysis of prolonged mechanical ventilation patients at a Long-Term Acute Care Hospital: Subtype differences in clinical outcomes

The numbers of patients who require prolonged mechanical ventilation (PMV) at U.S. hospitals are growing at an alarming rate. Recent reports indicate patients requiring PMV increased more than 5% between 2006-2008, and by the year 2020, over 625,000 patients will require PMV in the United States.[1] PMV is defined by the National Association for Medical Direction of Respiratory Care (NAMDRC) and The Center for Medicare and Medicaid Services (CMS) as the need for 21 days, or more, of consecutive mechanical ventilation for six or more hours a day.[2] Numerous concomitant comorbid factors that may contribute to ventilator dependence have been identified. The relative frequency of these factors among cohorts of PMV patients is not well defined.[2] Previous research on PMV weaning has focused on identifying and analyzing a single co-morbidity. However, patients who require PMV rarely experience a single comorbidity in isolation. It is likely that these patients experience multiple co-morbidities collectively that potentially interact, resulting in clusters of clinically distinct subgroups.

Long-Term Acute Care Hospitals

Patients who require PMV are frequently transferred from traditional intensive care units to long-term acute care hospitals (LTACHs).[3-5] LTACHs provide hospital-level medical care to patients who require extended hospitalization of typically 25 days or more.[5] LTACHs have burgeoned in response to the needs of increasing numbers of patients on PMV, representing one of the fastest growing Medicare providers in the United States. From 1995 to 2012, the number of LTACHs increased nearly 400%, from 107 to 420 hospitals.[5] Expenditures by CMS increased disproportionately as well from $700 million to $5.5 billion in the same period, an increase of nearly 800%.[6] Despite 25 years of LTACH care in the U.S., there is a paucity of research on PMV care and weaning practices. Authors of a recent literature review found 30 studies on post-ICU ventilator weaning with only seven adequately powered and focused on LTACH patients.[7]

Ventilator Liberation

Pooled data from a 2015 meta-analysis on long-term survival of PMV patients, including patients in both short-term and the long-term care environment, indicated only 50% of patients successfully liberate from mechanical ventilation.[8] There is a lack of agreement in the definition of weaning success used by researchers in the published literature, ranging from 48 hours of complete mechanical ventilation withdrawal,[9] to complete withdrawal of mechanical ventilation that persisted until hospital discharge.[10] However, NAMDRC has defined weaning success in patients who require PMV weaning as complete liberation from mechanical ventilation, other than nocturnal noninvasive BiPap or CPap support, for seven consecutive days.[2]

Discharge Outcomes

Traditionally, researchers have measured health outcomes of a clinical condition by relying on mortality data.[11] Mortality at LTACHs is high, upwards of 50% - 60% in many studies.[12-14] However, accurately measuring the mortality rate of PMV patients cared for at LTACHs is problematic. Patients who experience a life-threatening complication are often transferred out of the LTACH for higher-level care at a local short-term acute care hospital. A subsequent death would not be reported as a LTACH facility death, resulting in a possible overestimation of treatment success at LTACHs.[3] Mortality, while important, may not be a valid outcome indicator for PMV patients at LTACHs.

Researchers are shifting focus toward the assessment of functional status, studying the change in functional status of the patient on PMV from the time of admission to the time of discharge.[9,11,15-18] However, questions have been raised in these studies about the appropriateness of using assessment tools not validated in the PMV population.[19] Additionally, statistically significant improvement in functional status during hospitalization did not always translate into meaningful positive outcomes, i.e., ventilator-free survival and return to home.[20] Additional research is needed to focus on meaningful discharge outcomes including long-term quality of life in patients receiving PMV at LTACHs.

Latent Class Modeling

Statistical advances in modeling allow for identification of subgroups of patients via cluster analysis. Latent class modeling, a variant of cluster analysis, is yielding powerful improvements over traditional approaches to cluster analysis by allowing for identification of unobservable subgroups, termed a class, using observable variables.[21] Latent class models are less subject to bias as a result of relaxing the traditional statistical modeling requirements of linearity, normality, and homogeneity.[22] Additionally, analysis of latent classes can be used to identify subgroups of patients and establish potential physiologic consequences of class membership.[23] Latent class modeling lends itself well to the study of LTACH patients requiring PMV as these patients have a high prevalence of multiple physiologic co-morbidities and disparate clinical outcomes, which are all measured at different levels. Latent class modeling is considered a person-oriented approach, not a variable-oriented method, as is the case with other forms of model-based clustering algorithms.[24] Latent class analysis excels at organizing a complex array of multivariate empirical data in order to identify meaningful and scientifically interesting patterns. However, latent class analysis remains in its infancy in the PMV and LTACH literature. Therefore, the purpose of this paper is twofold: 1) to classify subgroups of patients receiving PMV at a Midwestern LTACH as identified by clinical indicators present at the time of admission and 2) examine for group differences in ventilator liberation, mobilization, and discharge disposition amongst the subgroups.

Methods

Design

After Institutional Review Board approval, a retrospective medical record review was completed of patients requiring PMV admitted between January 1, 2008, and December 31, 2015, to a Midwestern Long-Term Acute Care Hospital where they were provided care as part of regular services according to institutional standards and policies. A convenience sample of all patients requiring PMV admitted between January 1, 2008, and December 31, 2015, who met the inclusion and exclusion criteria were collected for this study (Table 1). A total 352 charts were screened for inclusion into this study; and 103 were eliminated for failure to meet inclusion and exclusion criteria. The remaining 249 charts were reviewed, and relevant data were extracted. Study data were collected and managed using REDCap research electronic data capture tools.[25,26] At the completion of primary data collection, a subsample of 50 patient charts was randomly selected and rescreened by the PI and two research assistants for calculation of inter and intra-rater reliability scores. Inter and intra-rater reliability scores were calculated via intraclass correlation for ordinal and continuous level variables, and Cohen's Kappa for nominal level data, to quantify the degree of agreement between the three data extractors.[27] Cohen's Kappa for inter-rater reliability of select variables was found to range from 0.96 to 0.98, while intraclass correlation for inter-rater reliability ranged from 0.82 to 1.0. Cohen's Kappa for intra-rater reliability of select variables was found to range from 0.90 to 0.96, while intraclass correlation for intra-rater reliability ranged from 0.77 to 1.0.

Measures

Baseline demographic data including age, gender, marital status, weight, year and month of LTACH admission, and underlying etiology for prolonged respiratory failure were extracted via medical record review.

Admission clinical indicators. Indicators of clinical status at the time of admission were extracted. These indicators include: admitting vital signs; laboratory values including basic chemistries, a complete blood count, and arterial blood gasses; short-term hospital length of stay recorded as the number of days of hospitalization; Charlson Co-Morbidity Index Score; and Glasgow Coma Scale scores. The Glasgow Coma Scale was scored by institutional protocol by nursing staff upon admission to the LTACH. The Charlson Co-Morbidity Index Score was computed by the researchers during chart review. The Charlson Co-Morbidity Index is a validated index of comorbid conditions and has been used extensively in retrospectively research studies.[28]

Outcomes.

Ventilator liberation. Indicators of ventilator weaning status were extracted and included liberation status, total number of mechanical ventilation days, and number of hours of ventilation used per day if the patient did not liberate from mechanical ventilation. For this study, the last day of mechanical ventilation was defined as the last day the patient received any invasive mechanical ventilator support via tracheostomy tube, including fully assisted mechanical ventilation or pressure supportive modes which persisted until hospital discharge. Non-invasive positive pressure ventilation via facemask was not considered mechanical ventilation in this study and therefore did not count as a mechanical ventilation day.

Mobilization. Mobility was defined using activity described in the existing short-term critical care literature and included dangle at the edge of bed without back support, stand-turn-pivot to a bedside chair, and ambulation either with or without an assistive device such as a walker. [29-32] Narrative documentation from physical and occupational therapy was reviewed for the occurrence of the three various active mobility activities. An aggregated sum was calculated for each mobility activity for the entirety of the LTACH hospitalization, which in turn was used to calculate the average number of the three various mobilization activities (sum/LTACH length of stay).

Discharge disposition. Survival status at the time of discharge and discharge disposition if discharged alive was documented. Discharge disposition was categorized into one of four options: home, inpatient rehabilitation, skilled nursing facility, or transfer to a higher-level short-term acute care hospital. LTACH length of stay was recorded as the number of days of hospitalization.

Data Analysis

SPSS Version 24 was used to analyze individual variables, and descriptive statistics were calculated for each variable. All continuous variables were expressed as mean and standard deviation. Categorical variables were presented as percentage and frequency. Tests for normality were completed and included swilk, sfrancia, sktest and visual inspection of p-plots, q-plots, and histograms. The data were cleaned using frequency distributions to identify data entry errors and bivariate relationships were examined with Pearson's correlation.

Latent Gold 5.1 was used to analyze the data for latent class analysis, identifying parsimonious classes of patients on PMV at a Midwestern LTACH using clinical indicators present at the time of admission. Models were run evaluating the relative fit from one to five classes to determine the optimal number of latent classes. Multiple approaches were used to determine the best-fitting number of classes. As the models contain continuous predictor variables, the smallest Bayesian Information Criteria value was used as the primary fit indicator to guide decision regarding model fit. Additional fit statistics taken into consideration included the following classification statistics: proportion of classification errors, pseudo R2-squared statistics, and integrated classification log-likelihood statistic. Post hoc ANOVA TUKEY or Games-Howell tests of significance were completed as appropriate to determine the significance of the parameters between the clusters. One-way analysis of variance (ANOVA) was used to determine whether significant differences existed amongst the subgroups in demographic, clinical indicators, the total number of mechanical ventilation days, and LTACH length of stay. Chi-square tests of independence were used to examine the relationship between the subgroups and nominal outcome variables of mortality and ventilator liberation status.

Results

One to five class solutions were examined using Latent Gold. Initial model development is presented in Table 8. A three-class solution was identified based on the aforementioned fit statistics. Several of the parameters in the initial model did not have significant Wald statistics, indicating that there was little variation in the specific indicator in question amongst the classes and did not discriminate in a statistically significant way.[33,34] All parameters that lacked statistical significance were removed from the initial model and the model was refit. The Bivariate Residuals were then examined for evidence of direct effect and lack of local independence amongst the indicator variables. Several were noted to be large, indicating a correlation between the associated indicator variables. Direct effects between BUN and creatinine were allowed in the model, and the model was re-fit. Again, fit statistics were analyzed for effect. The final 3-class model, with associated means and proportions by parameters, is presented in Table 9. As shown in Table 9, the three subgroups are: a young subgroup of obese patients who had low levels of clinical physiologic burden and co-morbid conditions (Class 1 Low Morbid, n=73); the oldest subgroup of patients with low levels of clincal physiologic burden but multiple co-morbid conditions (Class 2 Chronically High Morbid, n=113); and an elderly subgroup of patients with high levels of clinical physiologic burden and multiple co-morbid conditions (Class 3 Acutely High Morbid, n=71).

Demographic and Clinical Indicators

Post hoc analysis of the three latent classes revealed similarities and differences in demographic and clinical characteristics amongst the classes (Table 9). As the classes did not have equal sample sizes, tests of homogeneity of variances for each predictor variable were completed in post hoc ANOVA testing. Using Levene's test, the variance for age, weight, STACH LOS, respiratory rate, FiO2 %, pH, PaO2, BUN, creatinine, and white blood cell count were not equal. As such, Games-Howell was used as the post hoc test of significance, and confirmation was completed using Welch and Brown-Forsythe. Per Levene's testing, the variance was equal for Charlson Co-Morbidity total score and PCO2. As such, Tukey and Scheffe were used as the post hoc tests of significance for these variables.

There are many notable descriptive differences amongst the subgroups. These include age, weight, various clinical indicators particularly renal indices, Charlson Co-Morbidity scores, and etiology for prolonged respiratory failure (Tables 9 and 10). Class 1 is the youngest subgroup (58.25 years ±13.77), and class 2 is the oldest (76.64 years ±8.25). Class 1 patients are the heaviest patient subgroup (107.05kg ±52.70) but have the best overall pattern of physiologic, clinical indicators of the three subgroups. Class 3 Acutely High Morbid patients are distinguished from the other classes by several clinical, physiologic parameters. Notable amongst class 3 Acutely High Morbid patients is the highest FiO2 percentage on the ventilator (46.69 ±13.36), the highest BUN (67.36mg/dL ±29.56) and creatinine (2.64mg/dL ±1.47) measurements, and the highest white blood cell counts (13.25k/μL ±6.24). This pattern may indicate that class 3 patients are the most acutely ill.

Despite being the oldest (76.74 years ±8.25) subgroup, class 2 Chronically High Morbid patients have superior respiratory physiologic parameters with clinically normal respiratory rates (20.04 rpm ±4.48), the lowest set FiO2 percentage on the ventilator (40.41 ±4.19), and the highest measured PaO2 in arterial blood gas measurement (107.45mmHg ±37.23). In fact, the only clinical derangements amongst Chronically High Morbid Class 2 patients are a slightly alkalotic pH (7.46 ±0.05) and mild elevations in BUN measurements (39.88 mg/dL ±20.91), thus giving the impression that this subgroup may be slightly overly diuresed.

Class 1 and class 2 patients are differentiated less by clinical indicators, but to a greater extent by Charlson Co-Morbidity scores. Low Morbid Class 1 patients have the lowest number of co-morbid conditions (3.85 ±2.31), while the oldest Chronically High Morbid Class 2 patients had the highest recorded number of co-morbid conditions (6.86 ±2.57).

The subgroups can be further characterized by post hoc chi-square tests of independence of differences in underlying etiology of respiratory failure (Table 10). Class 2 is composed primarily of patients with cardiovascular surgical history (29.5%). Class 1 patients have the most extensive amount of respiratory diagnoses (37%) and neurologic diagnoses (17.8%). Class 3 also contain patients with a cardiovascular surgical history (25.4%) and respiratory diagnoses (21.1%), but interestingly is further distinguished by a substantial representation of oncology patients (9.9%).

Outcomes

Ventilator liberation. There was no difference amongst the subgroups in number of ventilator days [$F(2,246)=0.641$, $p= 0.528$]. However, there were differences in ventilator liberation amongst the classes. Acutely high morbid Class 3 patients were much less likely to wean from mechanical ventilation [$\chi 2$ (2, N= 249) = 25.478, $p< 0.001$, Cramer's V = 0.320] and more likely to die [$\chi 2$(2, N= 249) = 23.677, $p< 0.001$, Cramer's V = 0.308] than those patients in class 1 or class 2 (Tables 11 and 12).

Mobilization. There were differences amongst the subgroups in frequency of mobilization. An association between the subgroups and frequency of dangling [$F(2,246)=4.855$, $p= 0.009$], chair sitting [$F(2,246)=5.264$, $p= 0.006$], and ambulation frequency was observed [$F(2,246)=11.195$, $p< 0.001$], indicating the frequency of mobility activities was not equal amongst the subgroups. Class 3 acutely high morbid patients dangled less frequently as compared to class 1 and class 2 patients. Class 3 patients were also less likely to stand-turn-pivot to the bedside chair or ambulate as compared to the low morbid class 1 patients. There was no difference in the frequency of stand-turn-pivot to the bedside chair or ambulation frequency between the class 3 and class 2 subgroups (Table 13).

Discharge disposition. There was no difference amongst the subgroups in LTACH length of stay [$F(2,246)=2.243$, $p= 0.108$]. Although the distribution of discharge dispositions vary amongst the classes, these differences were not different from each other [$\chi 2$ (6, N=183) = 9.99, p = 0.125, Cramer's V = 0.125]. Of note, the young low morbid Class 1 patients were the most likely to discharge to home. The sick acutely high morbid Class 3 patients were more likely to transfer to a STACH for higher-level care, an important finding as the ultimate mortality rates in this subgroup were not tracked post LTACH discharge and are likely underreported in this study. Results are reported in Table 14.

Discussion

Our results demonstrate that distinct subgroups of patients receiving PMV at LTACH's exist. Analysis of the differences amongst the subgroups reveals meaningful differences beyond traditional age and gender categories. Examining differences between Class 1 and Class 2 exposes salient clinical distinction. First, there is an approximate 25kg average weight difference between these two classes. While BMI data were not collected in this study, an average weight of 107 kg likely places most patients in Class 1 in the obese weight category. This weight disparity is interesting when considering the dramatically different clinical outcomes amongst the subgroups. Those overweight/obese patients in Class 1 were approximately 11% more likely to liberate from mechanical ventilation, and 20% more likely to be discharged alive than lighter patients in Class 2. This "obesity paradox", a noted mortality benefit despite higher morbidity amongst various cohorts of the obese is a consistent finding in the critical care literature. [35-39] Consider, however, there is not a significant difference between the average weights of Class 1 and Class 3 patients. Obese patients in Class 1 were approximately 39% more likely to be discharged alive than those patients in Class 3 even though there was no difference in average weight between these two classes. Thus, the protective effect of weight does not entirely explain mortality differences between the subgroups.

Patients in Class 1 had the shortest primary short-term hospital lengths of stay before LTACH transfer (19.03 days ±8.14) as compared to patients in either Class 2 or Class 3. Patients are transferred to a LTACH only after they are stabilized and deemed appropriate for transfer by medical professionals at the sending facility [40,41]. The almost 10-day difference in stabilization and readiness for transfer amongst the subgroups is perplexing. Further examination of the etiology of respiratory failure amongst the subgroups provides useful information in analyzing the STACH length of stay differences. The etiology of respiratory failure in the majority of Class 1 patients is largely non-operative in nature and consists of respiratory diagnoses (COPD exacerbation, pneumonia, etc.) and neurologic disorders (ceberal vascular accidents, Guillian Barre Syndrom). Additionally, Class 1 also contained the lowest percentages of post-cardiac surgery patients (4.1%). In contrast, Class 2 and Class 3 both contain higher percentiles of post-cardiac surgery patients and smaller numbers of patients with a non-operative diagnosis. Previous research has suggested a negative relationship between surgical intensive care unit admissions, afterhours admission time,[43] and hospital outcome [42] This difference in outcomes between non-operative and post-operative transfer patients and afterhours admissions may continue at the LTACH level. Another possible explanation for the differences in STACH length of stay may reside in intensive care unit operational differences amongst medical versus surgical services, or possibly hospitals and health systems. This study did not attempt to analyze differences in patient characteristics and outcomes between patients on PMV transferred from university-level tertiary and quaternary care hospitals and those transferred from smaller, regional primary care hospitals. Research analyzing outcome differences amongst patients transferred to higher-level care hospitals has been mixed,[44,45] and future research analyzing differences in outcome based on previous short-term level-of-care could prove fruitful.

The Charlson-CoMorbidity total score averages amongst the classes further distinguish differences between the classes. Researchers studying intensive care unit mortality have reported that concomitant chronic health problems are associated with increased hospital mortality.[46-49] Therefore, it is not surprising that the low morbid Class 1 patients, who have the lowest average Charlson-Co Morbidity total scores, have the lowest mortality and highest discharge to home rates. In comparison, patients in Class 2 (6.86 ±2.57) and Class 3 (6.68 ±2.62) both have Charlson Co-Morbidity total scores above six. Charlson Co-Morbidity total scores above six have been shown to be an independent predictor of mortality in the critically ill, particularly in patients with acute kidney injury.[50] This co-morbidity associated mortality trend appears to continue at the LTACH level, as our findings suggest the effect of comorbidity was greatest for those with renal impairment.

The subgroups are further distinguished via clinical physiologic indicators. Examination of the blood chemistry results reveals distinctions amongst the classes. Class 2 patients have a slightly elevated pH (7.46 ±0.05) and BUN (39.88mg/dL ±20.91), values likely consistent with a metabolic alkalosis pattern and is suggestive of possible over diuresis in this subgroup. Class 3 patients have poor renal indicators despite having the lowest percentage of patients with co-morbid chronic kidney disease (2.9%), thus indicating the renal impairment seen in the acute high morbid Class 3 patients is acute. The mortality outcome of Class 3, post-cardiothoracic surgical patients with acute renal failure is not surprising as researchers have previously reported an increased risk of death in patients with acute kidney injury after cardiothoracic surgery. [51]

Further, the subgroups have different rates of ventilator liberation and mortality. For example, patients in the youngest subgroup (low morbid, Class 1) are approximately 48% more likely to be discharged alive and 57% more likely to successfully liberate from mechanical ventilation than those patients in Class 3. As discussed, the subgroups do vary on individual clinical parameters as well. The association of some of these individual clinical parameter patterns is contrary to expectations. For example, Class 2 is the oldest subgroup, has the longest short-term hospitalizations, and also has the highest Charlson Co-morbidity scores. This combination would lead a clinician to expect a high mortality rate in this subgroup. Yet, Class 2 patients have vastly superior rates of ventilator liberation and mortality when compared to Class 3 patents. Perhaps, then, it is not the individual parameters that influence ventilator liberation and mortality but the complex interplay of all of clinically significant variables combined that have meaningful impact on clinical outcomes.

Clinical Implications

This study has several implications for research and clinical practice. Identifying patients at risk for a poor clinical outcome is the first step in the development of targeted interventions aimed at improving not only survival but also health-related quality of life. Patients requiring PMV transferred to an LTACH who fit the profile for the acute, high morbid subclass should be identified upon admission as "at risk" and monitored closely throughout their hospitalizations for clinical decline.

Limitations and Recommendations for future research

To our knowledge, this is the first analysis aimed at the creation of homogeneous subgroups of patients requiring PMV transferred to a LTACH. While this is innovative and significant, there are limitations in this study. The retrospective design, using data collected for non-research purposes, is a limitation as causal inference cannot be made. Using a retrospective medical record review also limits the researcher to the data that are available in the medical record, and incomplete documentation is noted in this analysis. To offset against the effect of missing data, the latent class analysis in this study was completed with all study subjects regardless of missing data.

This study did not follow patients who were discharged alive to assess 1-year mortality rates. Longitudinal assessment of mortality amongst the clusters is recommended. Also, this study did not distinguish amongst renal failure patients requiring hemodialysis. Considering the effect of renal failure on outcome, future analysis of differences amongst dialyzed and non-dialyzed renal failure patients is encouraged.

Finally, recommendations for future research include replication studies aimed at validation of this latent class solution with similar, yet distinct data set.[52] Once the presence of subgroups within the sample is validated, development of targeted interventions aimed at improving mobility, ventilator liberation rates, and mortality outcomes in at-risk patients is encouraged.

Conclusion

We found three distinct clinical profiles of PMV patients at a Midwestern LTACH that are associated with different rates of ventilator liberation and survival. Different subgroups of LTACH patients who require PMV with varying levels of clinical indicators exist. Identification of patients at high risk for a poor clinical outcome may prove useful in ascertaining needed level of care and clinical monitoring.

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Tables

Table 8. Initial Model

Indicator Variable	Wald Statistic	p-value
Age	66.91	2.9e-15
Marital Status	10.64	0.0049
Etiology of PMV	1.72	0.42
Weight	8.02	0.018
STACH LOS	19.24	6.6e-5
Glascow total score	0.51	0.78
Tempature	0.67	0.71
Systolic Blood Pressure	1.50	0.47
Diastolic Blood Pressure	7.22	0.027
Heart Rate	4.68	0.96
Respiratory Rate	29.65	3.6e-7
FiO2%	19.95	4.6e-5
pH	26.94	1.4e-6
pO2	24.43	5.0e-6
pCO2	25.25	3.3e-6
Blood Urea Nitrogen	142.33	1.2e-31
Creatinine	88.91	4.9e-20
White Blood Cell Count	13.20	0.0014
Hemaglobin	15.64	0.0004
Hematocrit	19.94	4.7e-5
Albumin	6.50	0.039
Charlson total score	27.64	1.0e-6

Non-significant variables in initial model highlighted in grey

Table 9. Final Latent Classes

	Class 1 (n= 73)	Class 2 (n= 105)	Class 3 (n=71)	N=249
Characteristics mean (SD)				
Age	58.25(±13.77) [a,c]	76.64(±8.25) [a,b]	67.41(±13.73) [b,c]	
Weight, kg	107.05(±52.70) [a]	82.00(±20.05) [a,b]	98.68(±29.73) [b]	
STACH LOS	19.03(±8.14) [a,c]	29.89(±21.74) [a]	28.69(±12.97) [c]	
Resp Rate	23.00(±5.83) [a]	20.04(±4.48) [a,b]	24.46(±6.32) [b]	
FiO2 %	41.01(±9.51) [c]	40.14(±4.19) [b]	46.69(±13.36) [b,c]	
pH	7.44(±0.05) [a,c]	7.46(±0.05) [a,b]	7.41(±0.08) [b,c]	
PO2	84.94(±25.58) [a]	107.45(±37.23) [a,b]	88.73(±24.36) [b]	
PCO2	46.06(9.81) [a]	41.44(8.37) [a,b]	46.32(12.34) [b]	
BUN	22.00(±9.37) [a,c]	39.88(±20.91) [a,b]	67.36(±29.56) [b,c]	
Creatinine	0.76(±0.26) [a,c]	1.01(±0.40) [a,b]	2.64(±1.47) [b,c]	
WBC	10.59(±5.21) [c]	10.62(±4.05) [b]	13.25(±6.24) [b,c]	
Charlson Score	3.85(±2.31) [a,c]	6.86(±2.57) [a]	6.68(±2.62) [c]	
Gender #(%)				**Total**
Male	40(58.4%)	40(38.1%)	42(59.2%)	122(49%)
Female	65(45.2%)	33(61.9%)	29(40.8%)	127(51%)

[a] p = < 0.05 between class 1 and class 2
[b] p = < 0.05 between class 2 and class 3
[c] p = < 0.05 between class 1 and class 3

Table 10. Etiology of PMV by class*

n(%)	Class 1 (n=73)	Class 2 (n=105)	Class 3 (n=71)	Total
Cardiac	9(12.3)	9(8.6)	9(12.7)	27(10.8)
CV Surgery	3(4.1)	31(29.5)	18(25.4)	52(20.9)
Respiratory	28(38.4)	20(19)	16(22.5)	64(25.7)
Neurologic	13(17.8)	14(13.3)	3(4.2)	30(12)
Trauma	7(9.6)	8(7.6)	6(8.5)	21(8.4)
Oncologic	1(1.4	6(5.7)	7(9.9)	14(5.6)
GI	5(6.8)	11(10.5)	4(5.6)	20(8)
Infection/Sepsis	6(8.2)	6(5.7)	7(9.9)	19(7.6)
Renal/Endocrine	1(1.4)	0(0)	1(1.4)	2(0.8)

CV Surgery = cardiovascular surger
GI = Gastrointestinal
* Significant differences amongst the classes at p = < 0.05

Table 11. Ventilator Liberation by class*

#(%)				Total
Weaned Yes	61 (83.6%)	78 (74.3%)	33 (46.5%)	172(69.1%)
Weaned No	12 (16.4%)	27 (25.7%)	38 (53.5%)	77(30.9%)

* Significant differences amongst the classes at p = < 0.05

Table 12. Mortality by class*

#(%)				Total
Deceased	6 (8.2%)	27 (25.7%)	31 (43.7%)	64 (25.7%)
Alive	67 (91.8%)	78 (74.3%)	40 (56.3%)	185(74.3%)

* Significant differences amongst the classes at p = < 0.05

Table 13. Average Mobility by class

Mean (SD)				Total
Dangle	8.73(±6.83) [b]	9.01(±5.98) [c]	6.25(±5.31) [b,c]	8.14(±6.16)
Chair*	7.12 (±7.71) [b]	4.98(±5.95)	3.68(±5.74) [b]	5.24(±6.57)
Amb*	6.36(±7.11) [a, b]	3.48(±5.18) [a]	2.03(±4.40) [b]	3.91(±5.85)

[a] p = < 0.05 between class 1 and class 2
[b] p = < 0.05 between class 1 and class 3
[c] p = < 0.05 between class 2 and class 3

Table 14. Discharge Disposition by class

#(%)	Class 1	Class 2	Class 3	Total
Home	14 (20.9%)	7 (9%)	4 (10.5%)	25 (13.7%)
SNF	24 (35.8%)	40 (51.3%)	17 (44.7%)	81 (44.3%)
Rehab	23 (34.3%)	22 (28.2%)	9 (23.7%)	54 (29.5%)
STACH transfer	6 (9%)	9 (11.5%)	8 (21.1%)	23 (12.6%)

STACH = Short-term Acute Care Hospital

APPENDICES

APPENDIX A

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Approval Notice
Initial Review (Response To Modifications)

August 31, 2016

Heather Dunn, MS
Biobehavioral Health Science
845 S. Damen Avenue
Chicago, IL 60612
Phone: (563) 441-7568 / Fax: (563) 441-7665

RE: Protocol # 2016-0718
"PMV weaning at LTACH's: Does mobilization influence outcomes?"

Dear Ms. Dunn:

Your Initial Review (Response To Modifications) was reviewed and approved by the Expedited review process on August 31, 2016. You may now begin your research

Please note the following information about your approved research protocol:

Protocol Approval Period: August 31, 2016 - August 31, 2017
Approved Subject Enrollment #: 400
Additional Determinations for Research Involving Minors: These determinations have not been made for this study since it has not been approved for enrollment of minors.
Performance Sites: UIC, Select Specialty Hospital - Quad Cities
Sponsor: None
Research Protocol(s):

a) Prolonged Mechanical Ventilation Weaning at LTACH's: Does Mobilization influence outcomes?; Version 2; 08/27/2016

Recruitment Material(s):

a) No recruitment materials will be used

Informed Consent(s):

a) Waiver of Informed Consent granted [45 CFR 46.116(d)]

APPENDIX A (continued)

HIPAA Authorization(s):

a) Waiver of Authorization granted [45 CFR 164.512(i)(1)(i)]

Your research meets the criteria for expedited review as defined in 45 CFR 46.110(b)(1) under the following specific category:

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
07/13/2016	Initial Review	Expedited	07/19/2016	Modifications Required
08/29/2016	Response To Modifications	Expedited	08/31/2016	Approved

Please remember to:

→ Use your **research protocol number** (2016-0718) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the enclosure,

"UIC Investigator Responsibilities, Protection of Human Research Subjects"

(http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf)

Please note that the UIC IRB has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 413-9680. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

APPENDIX A (continued)

Sincerely,

Jovana Ljuboje
IRB Coordinator, IRB #3
Office for the Protection of Research Subjects

Enclosure(s):

1. **HIPAA Authorization(s):**
   a) Certificate of Waiver of HIPAA Authorization

cc: Mariann R. Piano, Biobehavioral Health Science, M/C 802
Eileen Collins, Faculty Sponsor, M/C 802

APPENDIX A (continued)

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Approval Notice
Amendment to Research Protocol and/or Consent Document – Expedited Review
UIC Amendment # 1

January 31, 2017

Heather Dunn, BS
Biobehavioral Health Science
845 S. Damen Avenue
Chicago, IL 60612
Phone: (563) 441-7568 / Fax: (563) 441-7665

RE: Protocol # 2016-0718
"PMV weaning at LTACH's: Does mobilization influence outcomes?"

Dear Dr. Dunn:

Members of Institutional Review Board (IRB) #3 have reviewed this amendment to your research and/or consent form under expedited procedures for minor changes to previously approved research allowed by Federal regulations [45 CFR 46.110(b)(2) and/or 21 CFR 56.110(b)(2)]. The amendment to your research was determined to be acceptable and may now be implemented.

Please note the following information about your approved amendment:

Amendment Approval Date: January 24, 2017
Amendment:
Summary:UIC Amendment #1, dated 6/25/16 and received 01/17/17, is an investigator initiated amendment for the following purposes:
The study has been altered in five ways. First, the specific aims have been altered to be more detailed and specific. The changes in the specific aims do not negatively impact the risk/benefit assessment of this proposed research. The original protocol contained three specific aims. The updated protocol contains four specific aims, with aims two, three, and four all containing sub-aims. Second, there was a very minor addition to the exclusion criteria. This protocol will now

APPENDIX A (continued)

exclude patients with total hospital length of stay greater than or less than two standard deviations from the average hospital length of stay. Third, the analysis section has been altered to better reflect the analyses required to address the specific aims as they have been rewritten. Finally, the dissertation committee has requested that a second site abstractor be added to the protocol. This second site abstractor will re-review and extract data from 80 charts to facilitate inter-rater reliability testing.

Approved Subject Enrollment #:	400
Performance Sites:	UIC, Select Specialty Hospital - Quad Cities
Sponsor:	Select Medical Corporation
PAF#:	00324868
Grant/Contract No:	Not available
Grant/Contract Title:	Select Medical Corp-084954-00001-Dunn

Research Protocol:

a) Prolonged Mechanical Ventilation Weaning at LTACH's: Does Mobilization influence outcomes?; Version 3; 01/06/2017

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
01/17/2017	Amendment	Expedited	01/24/2017	Approved

Please be sure to:

→ **Use only the IRB-approved and stamped consent document(s) and/or HIPAA Authorization form(s) enclosed with this letter when enrolling subjects.**

→ Use your research protocol number (2016-0718) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements as explained in the following, which are posted on the OPRS website (*http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/index.shtml*):
"UIC Investigator Responsibilities, Protection of Human Research Subjects" (*http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf*)

Please note that the UIC IRB #3 has the right to ask further questions, seek additional information, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact the OPRS at (312) 996-1711 or me at (312) 413-2053. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

APPENDIX A (continued)

Sincerely,

Laura Litman
IRB Coordinator, IRB # 3
Office for the Protection of Research
Subjects

cc: Eileen Collins, Faculty Sponsor, M/C 802
Mariann R. Piano, Biobehavioral Health Science, M/C 802
Privacy Office, Health Information Management Department, M/C 772

APPENDIX A (continued)

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Approval Notice
Continuing Review (Response To Modifications)

September 18, 2017

Heather Dunn, BS
Biobehavioral Health Science
845 S. Damen Avenue
Chicago, IL 60612
Phone: (563) 441-7568 / Fax: (563) 441-7665

RE: Protocol # 2016-0718
"PMV weaning at LTACH's: Does mobilization influence outcomes?"

Dear Dr. Dunn:

Your Continuing Review (Response To Modifications) was reviewed and approved by the Expedited review process on September 18, 2017. You may now continue your research.

Please note the following information about your approved research protocol:

Protocol Approval Period: September 18, 2017 - September 18, 2018
Approved Subject Enrollment #: 400
Additional Determinations for Research Involving Minors: These determinations have not been made for this study since it has not been approved for enrollment of minors.
Performance Sites: UIC, Select Specialty Hospital - Quad Cities
Sponsor: Select Medical Corporation
PAF#: 00324868
Grant/Contract No: Not available
Grant/Contract Title: Select Medical Corp-084954-00001-Dunn
Research Protocol(s):

b) Prolonged Mechanical Ventilation Weaning at LTACH's: Does Mobilization influence outcomes?; Version 3; 01/06/2017

Recruitment Material(s):

APPENDIX A (continued)

b) No recruitment materials will be used

Informed Consent(s):

b) Waiver of Informed Consent granted [45 CFR 46.116(d)]

HIPAA Authorization(s):

b) Waiver of Authorization granted [45 CFR 164.512(i)(1)(i)]

Your research meets the criteria for expedited review as defined in 45 CFR 46.110(b)(1) under the following specific category:

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
08/02/2017	Continuing Review	Expedited	08/16/2017	Modifications Required
09/06/2017	Response To Modifications	Expedited	09/18/2017	Approved

Please remember to:

→ Use your **research protocol number** (2016-0718) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the guidance,
"UIC Investigator Responsibilities, Protection of Human Research Subjects"
(http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf)

Please note that the UIC IRB has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 413-3788. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

APPENDIX A (continued)

Sincerely,

Rachel Olech, B.A., CIP
Assistant Director, IRB # 3
Office for the Protection of Research Subjects

Enclosure(s): None

cc: Holli A. Devon, Biobehavioral Health Science, M/C 802
Eileen Collins, Faculty Sponsor, Biobehavioral Health Science, M/C 802
OVCR Administration, M/C 672

APPENDIX A (continued)

Approval Notice
Amendment to Research Protocol and/or Consent Document – Expedited Review
UIC Amendment # 2

February 2, 2018

Heather Dunn, BS
Biobehavioral Health Science
845 S. Damen Avenue
Chicago, IL 60612
Phone: (563) 441-7568 / Fax: (563) 441-7665

RE: Protocol # 2016-0718
"PMV weaning at LTACH's: Does mobilization influence outcomes?"

Dear Dr. Dunn:

Members of Institutional Review Board (IRB) #3 have reviewed this amendment to your research and/or consent form under expedited procedures for minor changes to previously approved research allowed by Federal regulations [45 CFR 46.110(b)(2) and/or 21 CFR 56.110(b)(2)]. The amendment to your research was determined to be acceptable and may now be implemented.

Please note the following information about your approved amendment:

Amendment Approval Date: February 2, 2018
Amendment:
Summary: UIC Amendment #2 received on January 22, 2018: Revision of the protocol to remove the inclusion criteria of Glasgow coma scale total score of 13 or higher. After gaining access to the medical records at the site of data collection and careful review of the existing data, there was concern about the reliability and validity of the Glasgow coma scale. The Glasgow coma scale was found to have been measured inconsistently and perhaps inaccurately by the staff. For example, there were many 0's recorded when the lowest possible value is 1. Since this study is a chart review of discharged patients, there is no way to go back to obtain accurate Glasgow Coma Scale ratings on these patients. The inconsistent and potentially inaccurate documentation has led the research team to be concerned about the validity of the Glasgow coma scale scores below and also above 13. As such, a request is being made to remove the Glasgow coma score from the inclusion criteria and screen patients by all other previously existing inclusion and exclusion criteria.
Approved Subject Enrollment #: 400
Research Protocol(s):
b) Prolonged Mechanical Ventilation Weaning at LTACH's: Does Mobilization influence outcomes?; Version 4; 01/22/2018

APPENDIX A (continued)

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
01/22/2018	Amendment	Expedited	02/02/2018	Approved

Please be sure to:

→ Use your research protocol number (2016-0718) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the guidance,
"UIC Investigator Responsibilities, Protection of Human Research Subjects"
(http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf)

Please note that the UIC IRB #3 has the right to ask further questions, seek additional information, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact the OPRS at (312) 996-1711 or me at (312) 413-3788. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Rachel Olech, B.A., CIP
Assistant Director, IRB # 3
Office for the Protection of Research
Subjects

Enclosure(s): None

cc: Eileen Collins, , M/C 802
Holli A. Devon, Biobehavioral Health Science, M/C 802

APPENDIX B

August 16, 2016

University of Illinois at Chicago
Office for the Protection of Research Subjects (OPRS)
203 Administrative Office Building - M/C 672
1737 West Polk Street, Suite 203
Chicago, IL 60612

Re: Physical Mobility and the Relationship to Ventilator Liberation and Discharge Disposition: A Latent Class Analysis

To Whom It May Concern:

The purpose of this letter is to grant Heather Dunn, a graduate student at the University of Illinois at Chicago, permission to retrospectively review medical records at Select Specialty Hospital Quad Cities. Dunn's proposed project entails the collection of already extant data that characterizes a patient's characteristics, severity of illness, mobility, discharge disposition and ventilator wean status and no additional data will be collected just for the purpose of this study. As I understand it, no identifying information about the patient will be collected. As a study venue, Select Specialty Hospital Quad Cities provides a unique environment for assessing the mobilization of mechanically ventilated patients.

As Director of Research & Human Protection Administrator at Select Medical, I have reviewed Dunn's project proposal and have found the protocol to be appropriate for our patient population. I attest that individual patient data collected will be de-identified such that it will not possible to identify any individual whose data are included in the study. I support Dunn's plan and approve for her to conduct her project at Select Specialty Hospital Quad Cities.

Should you have additional questions or concerns, you may contact me at adawson@selectmedical.com or 717-920-4005.

Sincerely,

Amanda M. Dawson, Ph.D.

VITA

Heather Dunn, MS, ACNP-BC

EDUCATION

2018	PhD	Nursing, University of Illinois at Chicago, Chicago, IL: anticipated
2009	MS	Acute Care Nurse Practitioner, University of Illinois at Chicago Quad Cities Regional Program, Moline, Illinois
1998	BS	Nursing, Northern Illinois University, DeKalb, IL Cum laude Interdisciplinary minor in Gerontology

CERTIFICATIONS & LICENSES

1998 – present	Illinois Registered Nurse License # 041-309651
2005 – present	Iowa Registered Nurse License # 112885
2009 – present	American Nurse Credentialing Center Acute Care Nurse Practitioner # 2009007030
2009 – present	Iowa Advanced Registered Nurse Practitioner # L112885
2009 – present	DEA License #MD2003440
1998 – present	Advanced Cardiac Life Support Provider (ACLS)

TEACHING EXPERIENCE

2014 – 2017 **University of Illinois at Chicago – College of Nursing**
<u>Graduate Teaching Assistant</u>

2017 present **University of Illinois at Chicago – College of Nursing**
<u>Graduate Teaching Assistant for clinical instruction</u>

PROFESSIONAL EXPERIENCE

2016 – present **Kidney Specialists Inc, Bettendorf, Iowa**
<u>Advanced Registered Nurse Practitioner</u>

2014 – present **LTACH On Call**
<u>Advanced Registered Nurse Practitioner</u>

2009 – 2016 **Pulmonary Associates, Davenport, Iowa**
<u>Advanced Registered Nurse Practitioner</u>

2005 - 2009 **Genesis Medical Center, Davenport, Iowa**
<u>Registered Nurse Surgical Intensive Care Unit</u>

2004 - 2005 **Vail Valley Surgery Center, Vail, Colorado**
<u>Registered Nurse Pre-operative and Post-anesthesia Care</u>

2002 –2004 **Vail Valley Medical Center, Vail, Colorado**
Registered Nurse Patient Care Unit

2001 - 2002 **Swedish Medical Center, Englewood, Colorado**
Registered Nurse Progressive Care Unit

1999 - 2001 **Signature Physician Network, Moline, Illinois**
Registered Nurse Family Practice

1998 - 2001 **Illini Hospital, Silvis, Illinois**
Registered Nurse Medical/Telemetry

PROFESSIONAL PRESENTATIONS

2018 Needham, D. & **Dunn, H.** (2018, May). *Surviving Critical Illness: Optimizing outcomes in the post-ICU space.* Co-chair of scientific symposium session at The American Thoracic Society International Conference, San Diego, CA.

2017 **Dunn, H**. (2017, September). *Pulmonary diagnostic tests and how to interpret their findings.* Podium Presentation at The Cardiovascular Interventions and Practice Guidelines Conference, Davenport, IA.

2017 **Dunn, H.,** Laghi, F., O'Connell, S., Ryan, C., Park, C., Collins, E. (2017, May). *Differences in physical function after pulmonary rehabilitation training amongst clusters of moderate-to-severe COPD patients*. Poster Presentation at The American Thoracic Society International Conference, Washington, D.C.

2017 **Dunn, H**., Laghi, F., O'Connell, S., Ryan, C., Park, C., Collins, E. (2017, March).. *The relationship of physiologic clusters and symptom clusters as they impact physical function in patients with COPD: A latent class analysis*. Poster Presentation at The Midwest Nursing Research Society 41st Annual Research Conference, Minneapolis, MN.

2012 **Dunn, H.** & Tate, D. (July, 2012). *Care of the Ventilated Patient*. Podium Presentation at Select Specialty Hospital Professional Development Program, Davenport, IA.

VITA (continued)

RESEARCH/PUBLICATIONS (* denotes peer reviewed manuscripts)

*** Dunn, H,** Quinn, L, Corbridge, S., Eldeirawi, K., Kapella, M., & Collins, E. (2017). Mobilization of prolonged mechanical ventilation patients: An integrative review. *Heart & Lung: The journal of critical care*, 46(4), 221-233.

* **Dunn, H**, Quinn, L, Corbridge, S., Eldeirawi, K., Kapella, M., & Collins, E. (2017). Cluster Analysis in Nursing Research: An Introduction, Historical Perspective, and Future Directions. *Western Journal of Nursing Research*.

***Dunn, H**., Anderson, M. A., & Hill, P. (2010). Nighttime lighting in intensive care units. *Critical Care Nurse*, 30(3), 31-7.

RESEARCH GRANT FUNDING

2017	Select Medical Corporation Grant. $32, 012.00 total costs awarded. Principle Investigator, Prolonged Mechanical Ventilation Weaning at LTACH's: Does Mobilization Influence Outcomes?

PROFESSIONAL ASSOCIATIONS

2011 - 2016	Member, Society of Critical Care Medicine
2011 - 2016	Member, American College of Chest Physicians
2007 - present	Member, American Association of Critical Care Nurses
2006 - 2008	Member, Genesis Medical Center Intensive Care Professional Practice Counsel
1997 – present	Member, Sigma Theta Tau International, Beta Omega Chapter (1997-1998); Alpha Lambda Chapter (2015-present)
1997 - 1998	Member, Golden Key National Honor Society

HONORS

2018	Iowa Nurse Practitioner Society Membership Grant
2017	American Thoracic Society Assembly on Nursing Abstract Scholarship Award
2017	University of Illinois, Chicago College of Nursing, PhD Student Research Award
2008	Doris and Victor Day Foundation, Inc. Scholarship
1994-1998	Northern Illinois University Dean's List