

THE RELATIONSHIP BETWEEN SELF-REPORT AND PERFORMANCE-  
BASED MEASURES OF PHYSICAL FUNCTION FOLLOWING AN INTENSIVE  
CARE UNIT STAY

BY

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## **LIST OF ABBREVIATIONS**

ADLs: Activities of Daily Living

APACHE III: Acute Physiologic and Chronic Health Evaluation III

ARF: Acute Respiratory Failure

ExP: Exercise Program

FPI: Functional Performance Inventory

FPI-SF: Functional Performance Inventory-Short Form

ICU: Intensive Care Unit

SF-36pfs: 36-Item Short Form Medical Outcomes Survey Physical Function

Subscale

SPPB: Short Physical Performance Battery

SoC: Standard of Care

## **ABSTRACT**

**PURPOSE:** The relationship between self-report and performance-based measures of physical function has not been addressed in ICU patients. The purpose of this study was to examine this association in these patients.

**METHODS:** 300 ICU patients were randomized into an exercise program (ExP) or standard of care (SoC). Self-report (SF-36 Physical Function Subscale (SF-36pfs), Functional Performance Inventory-Short Form (FPI-SF)) as well as performance-based (Short Physical Performance Battery (SPPB), skeletal muscle strength) measures were taken at hospital discharge, 2, 4, and 6 months post-enrollment. Partial correlations between self-report and performance-based measures of physical function in each group were calculated. Covariates included age, APACHE III score, and gender. Alpha was set at  $p < 0.05$ .

**RESULTS:** At hospital discharge, a significant, but weak, correlation ( $r = 0.32$ ) was found between the SF-36 and SPPB in the SoC group. At 2 months, weak to moderate correlations were found between self-report and performance measures in both groups. In the SoC group, the SF-36 was significantly correlated with the SPPB ( $r = 0.47$ ) and muscular strength ( $r = 0.34$ ); the FPI was significantly correlated with the SPPB ( $r = 0.64$ ) and muscular strength ( $r = 0.52$ ). In the ExP group, the SF-36 was significantly correlated with the SPPB ( $r = 0.61$ ) and muscular strength ( $r = 0.42$ ); the FPI was significantly correlated with the SPPB ( $r = 0.54$ ) and with muscular strength ( $r = 0.28$ ). A similar pattern was seen at 4 and 6 months in both groups. **CONCLUSION:** Self-report and performance-based measures of physical function appear to assess different constructs at

hospital discharge. Following recovery from an ICU stay, these measures become complementary, but indicate different constructs are being assessed.



## **INTRODUCTION**

Acute respiratory failure (ARF) can be defined as an acute cardiopulmonary dysfunction requiring mechanical ventilation<sup>1-3</sup>. ARF results from one of four different origins: 1) neuromuscular dysfunction, 2) an acute/chronic respiratory disease, 3) cardiogenic and noncardiogenic pulmonary edema and pneumonias, and finally 4) various vascular diseases<sup>3</sup>. The instances of Intensive Care Unit (ICU) admittance due to ARF are greater than any other organ dysfunction/failure, with 56% of ICU patients suffering from ARF during a stay<sup>4,5</sup>. Furthermore, ICU stays resulting from ARF are frequently longer in duration and result in significantly greater morbidity and mortality rates with approximately one third of these individuals dying during their stay in the ICU<sup>4,5</sup>. Additionally, data suggest that longer ICU stays are associated with greater skeletal muscle weakness and dysfunction upon discharge, a condition known as ICU acquired skeletal muscle weakness<sup>6,7</sup>.

In addition to ICU length of stay, the duration of mechanical ventilation has been shown to be an independent predictor of ICU acquired skeletal muscle weakness as well as survival rates<sup>8,7</sup>. Treatments complementary to mechanical ventilation aim to reduce the inflammation associated with an ICU stay and to limit voluntary respiration so as not to conflict with mechanical ventilation. As a result, pharmaceutical interventions in the form of antibiotics, corticosteroids, and neuromuscular blocking agents may also be administered<sup>9,10</sup>. It is postulated that

the use of corticosteroids and neuromuscular blocking agents could contribute to the loss of skeletal muscle and the associated weakness<sup>7,11,12</sup>.

Mechanical ventilation and the subsequent pharmacological interventions all contribute to the immobilization of ARF patients in the ICU. Furthermore, this immobilization has been shown to amplify the deleterious effect of pharmaceutical interventions in relation to ICU acquired muscle weakness and skeletal muscle atrophy<sup>13</sup>. Collectively immobilization, mechanical ventilation, and utilization of pharmaceuticals are risk factors for, and contribute to, skeletal muscle atrophy and weakness, and are associated with deconditioning and dyspnea in ARF patients<sup>7,14,15</sup>. As a result of ICU acquired weakness, ARF patients experience declines in physical function which can be assessed subjectively using a variety of questionnaires and objectively using performance-based tests<sup>7,16,17</sup>. It has been reported that approximately half of all ARF patients leaving the ICU have difficulty with at least one activity of daily living (ADL), and approximately 25 percent of patients report needing more help with ADLs post-hospitalization versus pre-hospitalization<sup>18</sup>. Furthermore, ICU survivors report decreased levels of physical function when compared to normal healthy controls upon hospital discharge and for as much as two years out from discharge<sup>15</sup>. Due to the association between physical function and ADLs<sup>19,20</sup> it stands to reason that providing ICU patients with interventions that enhance physical function could improve post-ICU discharge outcomes. A number of recent studies

supports the use of physical therapy or similar exercise interventions to bolster these post-ICU outcomes<sup>21-23</sup>.

Ultimately, identifying changes in any of these outcomes depends on the type of instrument and the condition of patients when measurements are obtained.

Currently, both self-report and performance-based instruments are utilized in determining physical function of critically ill individuals<sup>24-26</sup>. However, there is currently no data regarding the strength of the relationship between these two methods of measurement in this population. If differences between self-report and performance-based measures do exist, then by elucidating these differences researchers and clinicians may have a better understanding of which instrument to administer under which circumstances. Furthermore, it is unknown what effects a physical therapy and or exercise intervention may have on these relationships, nor is it known what effect time from hospital discharge may have on altering this relationship. Further research is needed to determine the effect of a rehabilitation program and time on the relationship between self-report and performance-based measures of physical function. Therefore, the purpose of this study was to examine the relationships between self-report and performance-based measures of physical function at hospital discharge and follow-up points of 2, 4 and 6 months post enrollment, in a sample of ARF patients who were exposed to either standard of care (SoC) or an exercise rehabilitation program (ExP).

## **REVIEW OF LITERATURE**

### *Critical Care Medicine*

Critical care medicine is a multidisciplinary field where practitioners deliver care based on the technology and intellectual insights from different subspecialties<sup>27</sup>. In the United States, between the years 1985-2000, there was a steady increase in both costs and use of critical care medicine. In the year 2000, the number of critical care medicine beds (87,400 beds) was 13.4% of total hospital beds and the associated costs accounted for 13.3% of total hospital costs (approximately 55.5 billion dollars; 0.56% of US GDP)<sup>28,29</sup>. In the subsequent 5 years, these numbers rose by 6.5% and 44.2% equaling a total of 93,955 beds and approximately 81.7 billion dollars respectively<sup>30</sup>. This financial change represented an increase of 44.2%, and accounted for 0.66% of the US GDP due to direct costs alone<sup>30,31</sup>. As 90% of all critical care medicine beds fall within one of three intensive care unit (ICU) categories—intensive, premature/neonatal, and coronary care, the increase in critical care medicine usage and costs likely depicts increases within the ICU itself<sup>30</sup>.

The overall demographic shift within the United States further reflects a population in need of ICU care. An outcome of an ever-aging baby boom generation (estimated at approximately 78 million people) is an overall increase in the mean age of the population. Numerous sources report that the majority of ICU patients are 65 years or older<sup>32,33</sup>. As the population age and ICU admittance both increase, it makes sense that associated mortality would

increase as well. Although variable, overall ICU mortality rates have been reported between 10 and 29%<sup>31,34,35</sup>.

One primary reason patients are admitted to an ICU is for acute respiratory failure (ARF)<sup>36</sup>. Acute respiratory failure results in over 1.1 million ICU admissions per year<sup>31,33</sup>. Not only are ARF patients admitted to the ICU in greater numbers, but their ICU length of stay and daily costs have been found to be significantly greater in comparison to non-ARF patients<sup>5,37,38</sup>.

#### *Acute Respiratory Failure*

Acute respiratory failure is a clinical condition which results in the respiratory system failing to meet the metabolic, oxygenation, and ventilatory demands of the patient<sup>39</sup>. Pathologies that cause ARF include neuromuscular conditions, consequences of acute or chronic obstructive airway diseases, pulmonary edema and pneumonia, or a pulmonary embolism<sup>3</sup>. Arising from these conditions are impairments to the various components of the respiratory and musculoskeletal system including: alveolar tissue, blood vessel endothelium, the muscles of respiration, neurological components involved in respiration, as well as skeletal muscle mass<sup>3,27,40–42</sup>. Damage to any of the respiratory components may lead to an increase in fluid and a build-up of pro-inflammatory cytokines including tumor necrosis factor-alpha. Subsequently, a reduction in surfactant production further decreases respiratory muscle function affecting respiratory rate, rhythm, and depth. These changes lead to a ventilation/perfusion mismatch

that results in the characteristic dyspnea, exercise intolerance, and decreased physical functioning that ARF patients experience<sup>3,27,40,41</sup>.

ICU acquired skeletal muscle weakness has been reported in 25%-33% of ARF patients who have been mechanically ventilated for 4-7 days<sup>43</sup>, and is another negative outcome for ARF patients surviving an ICU stay<sup>7,44</sup>. Patients with ICU acquired muscle weakness have longer periods of hospitalization, decreased ability to accomplish ADLs, reduced exercise capacity, as well as increased need for prolonged care, and mortality<sup>7,45</sup>. While the exact cause of ICU acquired muscle weakness is unknown, in actuality, it is thought to have a variety of contributing etiologies: neuropathies of the somatic motor neurons (critical illness polyneuropathy), skeletal muscle myopathies (critical illness myopathy), or a combination (critical illness neuromyopathy). Risk factors for ICU acquired skeletal muscle weakness include ICU related medications<sup>8</sup>, deconditioning due to immobilization<sup>46</sup>, increased age<sup>47</sup>, and/or sepsis or inflammation during hospitalization<sup>48</sup>. Whatever the cause ICU acquired skeletal muscle weakness results in reduced physical function.

A large amount of research has gone into examining the effect of pro-inflammatory cytokines, particularly tumor necrosis factor-alpha, on skeletal muscle in a variety of populations and models<sup>49-52</sup>. In 1995 Meduri et. al., utilized assays of bronchoalveolar lavage fluid to check for the presence of tumor necrosis factor-alpha and other pro-inflammatory cytokines in patients with early

and late stage ARF. Findings indicated that non-survivors had a significantly, and persistently, greater concentration of tumor necrosis factor-alpha and interleukins 1 beta, 2, 4, 6, and 8 than survivors<sup>53</sup>. Similarly, findings in human models demonstrate that protein synthesis rates negatively correlate with tumor necrosis factor-alpha expression<sup>54</sup>, as well as the presence of other cytokines<sup>55</sup>. In 2000, Oberholzer and colleagues reported findings in animal models that overexpression of tumor necrosis factor-alpha may cause skeletal muscle myopathy and endothelial dysfunction. This dysfunction causes a cascade of events leading to loss of muscle mass and subsequent weakness<sup>56</sup>. Structural and functional changes associated with increases in these pro-inflammatory cytokines may result in the use of corticosteroids, the need for mechanical ventilation, or an ICU stay and the associated immobility and bed rest<sup>8,14,27,40,57-59</sup>

Advanced age may also play a role in the development of ICU acquired skeletal muscle weakness. It is well documented that atrophy of muscle fibers occurs as one ages<sup>60-62</sup>. This same sarcopenic phenomenon is present in patients with COPD and other pulmonary related diseases<sup>63</sup>. Collectively this loss of skeletal muscle, due to pathology or age, results in decreased strength and physical function, and is associated with the onset of disability<sup>64-66</sup>. Reports have shown reduced physical function to be associated with both ICU and post-hospital-discharge morbidity and mortality rates<sup>7,18</sup>.

### *Physical Function in ARF Patients*

Herridge and colleagues evaluated 109 ARF survivors at different time points: 3, 6, and 12 months after ICU discharge<sup>7</sup>. Patients submitted to pulmonary function and six-minute walk (6MW) testing, a quality of life evaluation, and an interview. Of those included in the analysis 11 percent (12 patients) died during the one-year follow-up; 9 of these patients died in the first 6 months—indicating a 6 month post-discharge mortality rate of 75%. Over the course of the follow up period, Herridge found that those individuals who survived their ICU stay were severely ill, with median Acute Physiologic And Chronic Health Evaluation (APACHE) II scores of 23 (scored from 0-71, higher scores indicate greater illness), and a median ICU length of stay of 25 days. While in the ICU, patients lost 18 percent of their baseline body weight. Patients reported functional limitations post ICU stay due to muscle weakness and fatigue. This was exemplified by the fact that during periods of exercise, 6 percent of patients had an O<sub>2</sub> saturation below 88 percent. At 12 months, the median SF-36 physical domain score increased to 25, up from the 3 month measured score of 0. However, this score was still far below the population norm of 84. Median 6MW distances increased from 281 meters at 3 months to 422 meters at 12 months. These values were also lower than predicted. Together the SF-36 and 6MW scores indicate below average self-report and performance-based physical function levels. Finally, Herridge reported that, in ICU patients, the absence of systemic corticosteroid treatment and ICU acquired illness, as well as a rapid



resolution of lung injury and multiorgan dysfunction was associated with better functional status during the one-year follow-up.

In 2011, Herridge et. al. evaluated 83 of the 109 ARF patients from her previous study at 2, 3, 4, and 5 years post-ICU discharge<sup>67</sup>. At 5 years, minor improvements in median 6MW (436 m; 76% of predicted distance) and the physical domain of the SF-36 (41 up from 25 at 12 months) were seen. Younger patients were found to have an improved rate of recovery when compared to older patients; however, at 5 years post discharge both groups had lower than normal predicted levels of physical function. Interestingly, pulmonary and respiratory function was normal to near-normal in all patients at 3-5 years.

Building on Herridge's findings, Garland analyzed a cohort of 1,722 ARF patients from the Study to Understand Prognosis and Preferences for Outcomes and Risks of Treatment (SUPPORT) study<sup>18</sup>. Thirty-eight percent (650) of those initially enrolled did not survive hospitalization. Interviews aimed to assess functional capacity and quality of life were conducted at a median of 5 months after hospital discharge. At this time, 48% of survivors reported needing help with at least one activity of daily living (ADL), while 27% rated their quality of life as poor or fair. Over the 5 year follow-up Garland reported a mortality rate of ~36% in those patients. Cox proportional hazard regression identified older age, male gender, preexisting comorbid conditions, and worse pre-hospital functional status as factors associated with shorter survival times.

Collectively, these data show that survivors of ARF, recovering from an ICU stay, experience decreased physical function. Both physical and pulmonary sequela, i.e., muscle wasting and weakness and ventilator/perfusion mismatch at pre-admission and post-discharge, can influence physical disability and elevate mortality. Due to the direct impact that ARF has on physical function, it is important to understand how physical function is defined and the associated methods of assessment.

### *Physical Function*

The PROMIS (Patient Reported Outcomes Measurement Information System) initiative is a project funded by the National Institutes of Health with the aim of utilizing measurement science to develop a state-of-the-art protocol for assessing health<sup>68</sup>. PROMIS defines physical function as the “ability to carry out activities that require physical actions, ranging from self-care (ADLs) to more complex activities that require a combination of skills, often within a social context”.

According to PROMIS, physical function is a domain found under the umbrella of “global health”, or overall health. Physical function is also said to refer to the full spectrum of physical ability, i.e., the domain of physical function can include those with severe impairment as well as those with exceptional physical ability. As a result, physical function is inclusive of the term “disability” as well<sup>68</sup>, and reported signs and symptoms may vary from patient to patient. Which is to say that a patient’s perception of his/her physical function may differ based on the perspective of the individual in question<sup>69</sup> or the social roles they fulfill<sup>70</sup>.

Moreover, to the patient, physiological outcomes may be secondary to being able to accomplish ADLs. Consequently, self-reported (perceived) and performance-based tests are two commonly utilized methods for evaluating the effectiveness of interventions on physical function in a variety of populations<sup>71</sup>.

Each of the methods of testing have been validated in a variety of populations<sup>26,71–74</sup>. Typically self-report methods of assessing function utilize questionnaires<sup>73,74</sup> some of which may be specific to a particular disease or pathology<sup>75–77</sup>, while others may be utilized in general populations<sup>78–80</sup>. Two of the commonly used self-report questionnaires are the generalizable 36 question Medical Outcomes Study Short Form (SF-36) and the pulmonary disease specific Functional Performance Inventory (FPI).

#### *Physical Function by Self-Report*

The SF-36 consists of two summary measures—physical health and mental health. The questions are aimed at addressing one of eight different subscales that fall under one of these two summary measures. Physical functioning, role-performance, bodily-pain and general-health constitute the physical health summary measure; whereas, vitality, social functioning, role-emotional, and mental health constitute the mental health summary measure. The questionnaire can be self-administered for individuals in a variety of age groups or by trained individuals in-person or over the phone. Higher total-scores, as well as sub-scale scores, indicate greater levels of functioning<sup>78,81</sup>. Scores are compared to

population normative values. In doing so, values that fall below the norm indicate worse outcomes; likewise, values that are above the norm are indicative of better outcomes.

Kaplan et. al. (2004) examined the relationship measures of the SF-36 and two disease specific instruments (Shortness of Breath Questionnaire and the Saint George Respiratory Questionnaire) in a 1,218 patients enrolled in the National Emphysema Treatment Trial. Scores on the physical component scale of the SF-36 were found to be significantly correlated with scores from both disease specific instruments. The physical component scale of the SF-36 was also found to be significantly correlated with performance-based measures of physical function, maximum work on a cycle ergometer ( $r = 0.18, p < 0.01$ ) and six minute walk distance ( $r = 0.19, p < 0.01$ ). Significant improvements in the physical functioning domain of the SF-36 occurred from pre to post-rehabilitation (effect size=.19,  $p < .001$ ).

The Functional Performance Inventory (FPI) is a disease specific measure of self-report physical function developed to describe a pulmonary disease patient's ability to complete ADLs as well as activities within other domains. Consisting of 65 total items, the FPI accesses function in six different domains or sub-scales: body care, household maintenance, physical exercise, recreation, spiritual activities, and social activities. Scores are reported as means with higher scores

in each of these sub-scales, as well as in the total-score, reflecting higher degrees of functioning<sup>80</sup>.

The psychometric characteristics of the FPI were examined in 1998 by Larson et. al.<sup>73</sup>. Larson surveyed 45 men and 27 women (N=72) with moderate to severe chronic obstructive pulmonary disease (defined as a forced expiratory volume in one second [FEV<sub>1</sub>] < 65% predicted). Results showed that the FPI had high internal consistency, reliability with no ceiling and floor effects. Correlations between the FPI and the Physical Functioning subscale of the SF-36 (r=.69) indicated construct validity.

One year later, Leidy and colleagues (1999) expanded these psychometric findings in a group of patients who reported their COPD to be moderate-very severe<sup>80</sup>. One-hundred fifty-four patients participated in a cross-sectional mail survey. Of those surveyed, 86 (56%) reported their breathing problems to be severe to very severe while 114 reported having fair or poor health (74%). Fifty-four patients participated in a follow-up 2-week reproducibility evaluation. Similar to the findings of Larson, the FPI showed internal consistency (Cronbach alpha = .96) and reproducibility (ICC = .85). Furthermore, the total FPI score, as well as all sub-scales of the FPI, except for the spiritual subscale, have reported construct validity (p<.01 at minimum), concurrent validity (p<.05 at minimum), as well as test-retest reliability<sup>73,80</sup>. Those with self-reported mild-moderate COPD have reported a total score of 2.03±.39, while those with self-reported severe-

very severe scored  $1.34 \pm .46$ <sup>80</sup>. Additionally, the FPI is able to differentiate between physiological measures of FEV<sub>1</sub>. Thus the FPI is able to discriminate across pulmonary disease patients with varying degrees of disease severity.

Overall, data from Larson et al., Leidy et al., and Kaplan et al. demonstrate validity and reliability in both disease-specific and generalizable measures of self-report physical function. Furthermore, in those with pulmonary disease these self-reported mechanisms of evaluating physical function have a moderate, but significant, correlation to each other, and are able to distinguish between disease severity while testing for intervention effects. Due to the similarities between ARF populations and those previously described, it seems plausible that similar physical dysfunction may be present in ARF populations as well. Lastly, these data demonstrate the potential for physical dysfunction in ARF patients to manifest itself as a lack physical function.

#### *Physical Function by Performance*

A commonly used performance-based method of assessing physical function is the Short Physical Performance Battery (SPPB). The SPPB is a performance-based assessment tool for evaluating lower extremity physical functioning in older and low functioning individuals. It was developed by the National Institute on Aging and is a collection of three different tests: 4m gait speed test, a triad of balance tests, and a timed chair sit-to-stand test<sup>82</sup>. The SPPB has been shown to

be a reliable and valid predictor of disability and morbidity, with higher scores indicating greater physical functioning<sup>82-84</sup>.

In 2000, Guralnik and colleagues evaluated the strength of the SPPB to predict disability and death in a population of Hispanic individuals after adjusting for age, sex, performance level, and years of follow-up. Data were collected from patients participating at four different sites of the Established Populations for Epidemiological Research in the Elderly study. Disability was categorized as either mobility disability (inability to walk 0.5 miles or climb stairs without help), or disability in ADLs (mobility disability plus the inability to perform one or more of the following activities without help: moving from bed to chair, using the toilet, bathing, or walking across a small room). They found that individuals with SPPB scores of 4-6 at baseline had a 3.4 - 7.4 greater risk of developing ADL disability and a 2.9 – 4.5 greater risk of developing mobility disability as compared to individuals with SPPB scores of 10 - 12.

Freire examined the psychometric properties of the SPPB in a 2012 study of elderly individuals from Brazil and Quebec<sup>85</sup>. A total of 124 adults aged 65 to 74 years old were recruited across two centers: St. Bruno Quebec (n=60), and Santa Cruz Brazil (n=64). Individuals were evaluated using the SPPB, a self-reported health status using a single question questionnaire with 5 categorical response choices, a lower extremity mobility assessment tool<sup>70</sup>, and patients provided researchers with a chronic condition status by self-report of any

pervious physician diagnoses. Patients self-reported disability status was categorized as intact mobility, limited mobility, and difficulty in any ADLs. In both the Brazil and Quebec cohorts, test retest reliability was shown for the total SPPB score (ICC=.83, 95% CI: .73,.89; ICC=.89, 95% CI: .83,.93, respectively), as well as gait (ICC=.75, 95% CI: .63,.84; ICC=.90, 95% CI: .85,.94, respectively), chair stand (ICC=.73, 95% CI: .60,.83; ICC=.78, 95% CI: .67,.87, respectively), and balance (ICC=.55, 95% CI: .38,.71; ICC=.75, 95% CI: .63,.85 respectively). Finally, when referenced against self-reported health, lower extremity mobility, and degree of disability SPPB scores were inversely related, i.e., graded decreases in SPPB scores were found with an increase in the limitation of lower limbs, disability, and self-reported poor health.

It is important to note that while both methods of testing for physical function are useful, the literature has noted that self-report and performance measures of physical function assess different constructs<sup>72</sup>. Generally it is understood that self-report measures address an individual's perception of their ability to complete an array of physical function related activities whereas performance measures reflect patient's performance in specific physical tasks<sup>86</sup>. As such, individuals may report high levels of physical function while still performing poorly on performance-based measures. Regardless, when interventions are developed with the goal of improving a patient's ability to complete instrumental ADLs, physical function is altered for the better<sup>87</sup>. Recent evidence suggests that early exercise may be able to improve many ARF related adverse outcomes<sup>21,22,44</sup>. For



that reason, exercise may be an important key to improving physical function in this same population.

### *Effects of Exercise on Physical Function in ARF Populations*

Outcomes of ARF often include reduced physical function, reduced muscle strength and mass, as well as increased ICU length of stay, hospital length of stay, and mortality<sup>7,88,89</sup>. Findings from both Herridge et. al. and Cheung et. al. indicate ICU survivors lose up to 18% of baseline body weight, and this contributes to muscle wasting and weakness, and a loss of physical function<sup>7,15</sup>. Furthermore, data from De Jonghe et. al. (2007) demonstrated that those with low maximal inspiratory and expiratory pressures, and low skeletal muscle strength were at an 8.02 (95% CI, 2.12–30.36; p = .002), 4.15 (95% CI, 1.16–14.82; p = .03), 3.03 (95% CI, 1.23–7.43; p = .02) respectively greater risk for delayed extubation from mechanical ventilation<sup>43</sup>.

Recently exercise and physical therapy have been shown to be feasible, and to provide a number of beneficial effects for ICU patients<sup>21,22,90</sup>. Evidence suggests that in ARF patients exercise training can improve physical function regardless of baseline functional status<sup>21,91</sup>. There is also evidence to support exercise as an intervention to reduce the effects of acute inflammation (a key risk factor for ICU acquired muscle weakness)<sup>92</sup>, and reduce the rates of post-discharge hospital readmission and death while increasing anti-inflammatory cytokines over time<sup>93</sup>.

Starkie and colleagues evaluated effect of exercise on the inflammatory process using healthy patients in a repeated measures design<sup>92</sup>. Patients were studied under three conditions: rest (control), exercise (biking for three hours) and use of an anti-inflammatory (infusion of recombinant human IL-6 (rhIL-6) for 3 h during a period of rest). After 2.5 hours of each condition, patients received a lipopolysaccharide endotoxin (0.06 ng/kg) in order to induce a low-grade inflammatory response. Results showed that the control group experienced a significant increase in tumor necrosis factor-alpha (a pro-inflammatory cytokine) as a response to the endotoxin. The exercise group showed elevated anti-inflammatory proteins and a significant decrease in the presence of endotoxin-induced tumor necrosis factor-alpha in comparison to the control group. These results provide experimental evidence that physical activity reduces inflammation. In doing so, it stands to reason that ARF patients receiving exercise may experience a decrease in inflammation and an improvement in physical function.

In 2008 Morris et. al. designed a standardized mobility protocol and used this protocol to assess the frequency of physical therapy, site of physical therapy initiation, and the resulting patient outcomes. Morris and colleagues compared ARF patients receiving the standardized mobility therapy (i.e., physical therapy via automatic physician order) to those receiving usual care (i.e., physical therapy via physician's patient-specific order). A total of 330 ARF patients were divided into standard of care (n = 165) or protocol groups (n = 165) based on

block ICU allocation. More patients in the protocol group received physical therapy sessions (80.0% vs. 47.4%;  $p \leq 0.001$ ). Protocol patients were also out of bed sooner (5.0 days vs. 11.3 days;  $p < 0.001$ ), and had shorter ICU (5.5 days vs. 6.9 days;  $p = 0.027$ ) and hospital (11.2 days vs. 14.5 days;  $p = 0.006$ ) length of stays. It is also notable that there were no significant differences in cost between the two groups. The early rehabilitation administered by Morris supports the use of exercise as a safe and effective therapy for promoting early activity and ICU/hospital discharge.

Schweickert et. al. further analyzed physical and occupational therapy in order to understand the potential impact on immobility due to pharmacological sedation in addition to functional and neurological ICU related outcomes<sup>21</sup>. The study randomized 49 patients into an intervention group and 55 patients into a standard of care group. The primary endpoint was defined as patient's ability to successfully perform six ADLs and to walk independently. Secondary endpoints included the number of ventilator-free days occurring during the first 28 days of the patient's hospital stay. Of the 49 patients in the intervention group, 29 (59%) returned to independent functional status at hospital discharge. In the standard of care group, 19 (35%) patients returned to independent functional status—indicating a significant between-groups difference ( $p=0.02$ ). Additionally, those in the intervention group experienced a significantly greater number of ventilator-free days. These findings provide evidence that rehabilitation—consisting of interruption of sedation and physical and occupational therapy in the earliest

days of an ICU stay results in better functional outcomes at hospital discharge and a greater number of ventilator-free days compared with standard care and provide a foundation supporting future research on exercise and ICU patients with ARF.

Morris et. al. built on the findings in their previous study and assessed a large cohort (n=280) of ARF survivors who had participated in their 2008 early ICU mobility study to determine variables that could predict cases of hospital readmission and/or death within a year of hospital discharge<sup>23</sup>. Readmission or death occurred in 47% (132) of patients within the first year. While there were a number of predictors, a lack of early ICU mobility therapy [OR, 1.77 (95%CI, 1.04–3.01)] significantly predicted readmission or death in the 12 months post hospitalization. While still unclear as the mechanisms of reduced readmission and mortality, these data support the use of early physical therapy and exercise to produce better long-term outcomes.

Castro-Avila and colleagues conducted a meta-analysis to further assess the implications of early rehabilitation on the functional status of ICU patients<sup>94</sup>. A search of MEDLINE, EMBASE, CINALH, PEDro, Cochrane Library, AMED, ISI web of science, Scielo, LILACS and different clinical trial registries was conducted in order to identify both randomized and non-randomized clinical trials of rehabilitation compared to standard care in adult ICU patients. A total of 5,733 records were screened, these were ultimately narrowed down to seven articles

included in the narrative synthesis, and six in the meta-analysis. Analysis indicated that early exercise rehabilitation led to a significant increase in the number of patients walking independently at hospital discharge (RR = 1.42; 95% CI 1.17-1.72).

Findings from these studies suggest that early initiation of exercise therapies in the ICU can be of substantial benefit for ARF patients. Furthermore, it is possible to administer ICU physical therapies with regularity to reduce both ICU and hospital length of stays and the duration of immobility time, while increasing physical function and independent functional status.

Due to the fact that ARF patients deal with negative health outcomes in the form of inflammation, muscle wasting, and muscle weakness, it is important to identify interventions that reduce these effects. These data support the idea that exercise interventions can attenuate the negative physiological and functional outcomes of ARF by reducing inflammation and mitigating long-term effects of muscle wasting and mechanical ventilation. Ultimately, identifying changes in any of these outcomes depends on the type of instrument and the condition of patients when measurements are obtained. Currently, both self-report and performance-based instruments are utilized in determining physical function of critically ill individuals<sup>24-26</sup>. However, there is no data regarding the strength of the relationship between these two methods of measurement in this population. If differences between self-report and performance-based measures do exist, than

by elucidating these differences researchers and clinicians may have a better understanding of which instrument to administer under which circumstances. Furthermore, it is unknown what effects a physical therapy and or exercise intervention may have on these relationships, nor is it known what effect time from hospital discharge may have on altering this relationship. Further research is needed to determine the effect of a rehabilitation program and time on the relationship between self-report and performance-based measures of physical function. Therefore, the purpose of this study was to examine the relationships between self-report and performance-based measures of physical function at hospital discharge and follow-up points of 2, 4 and 6 months post enrollment, in a sample of ARF patients who were exposed to either standard of care or an exercise rehabilitation program.

## **METHODS**

### *Study Design*

Data for this thesis were obtained from a phase III randomized clinical trial examining the effects of an exercise therapy program on hospital length of stay and physical function in a group of acute respiratory failure patients. Patients were randomized into one of two groups: an ExP group or a SoC group. Patients in the ExP group participated in passive range of motion exercises, progressive resistance exercises, and physical therapy. Sessions were carried out three times daily from enrollment through hospital discharge. The SoC group received physical therapy only when ordered by the attending physician. Interventions stopped once the patient was discharged from the hospital. Measures of performance-based physical function were obtained at ICU discharge, hospital discharge, as well as 2, 4, and 6 months post-discharge. See Table I for a complete timeline of when specific measures were obtained during the trial. These measures were collected by trained personnel blinded to the patient's group assignment. The trial was conducted with the approval of the institutional IRB.

Table I: Data Collection and Events Timeline

	ICU Admit	ICU D/C	Hosp D/C	2-mo	4-mo	6-mo
Consent	X					
Randomization	X					
Baseline co-morbidities	X					
Baseline Acuity	X					
Discharge Co-morbidities			X			
Dynamometer-Strength		X	X	X	X	X
SPPB		X	X	X	X	X
SF-36pfs			X	X	X	X
FPI-SF				X	X	X
<p>An outline of data collection at associated time-points. Interventions took place from ICU admission through to Hospital discharge. ICU Admit: ICU admission; ICU D/C: ICU discharge; Hospital D/C: hospital discharge; 2/4/6-mo: follow-up periods of 2, 4, and 6 months respectively; SPPB: Short Physical Performance Battery; SF-36pfs: Medical Outcomes Study Short Form 36-Item Health Survey Physical Function Subscale; FPI-SF: Functional Performance Inventory-Short Form</p>						

*Patients*

Three hundred ARF patients admitted to the Wake Forest University Baptist Medical Center ICU were randomized into one of the two groups (refer to Appendix A for consort diagram). Patients were screened by a study nurse in order to verify that they fulfilled study inclusion/exclusion criteria (see Table II). If patients were conscious at time of admittance to the ICU, informed consent was obtained from the patient by a research study nurse. If patients were unconscious at time of admittance to the ICU, informed consent was obtained from a family member by a research study nurse. Once the patient regained consciousness, re-consent was obtained from the patient.



*Table II: Patient Inclusion/Exclusion Criteria*

<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Age $\geq$ 18yrs	Cognitive impairment prior to ICU illness
Mechanical Ventilation	Inability to walk without assistance prior to ICU illness
$P_{aO_2}:F_{iO_2} < 300$	Acute stroke
	BMI $> 50\text{kg}/\text{m}^2$
	Neuromuscular disease impairing mechanical ventilation weaning
	Acute hip fracture
	Unstable cervical spine or pathologic fracture
	Ventilated $> 80$ hours OR current hospitalization $> 7$ days
	Do not intubate orders upon admission
	Considered moribund
	Enrolled in another research study
$P_{aO_2}$ : Partial Pressure of Arterial Oxygen; $F_{iO_2}$ : Fraction of Inspired Oxygen; BMI: Body Mass Index	

### *Randomization*

Patients were randomized, with equal probability, into one of the two study groups using a block randomization design to ensure that approximately equal numbers of patients were in both groups. Block sizes of varying length were determined randomly to ensure that future assignments could not be inferred from past assignments

### *Procedures and Measurements*

The ExP was administered seven days a week by a rehabilitation team consisting of a physical therapist, a nursing assistant, and an ICU nurse. The patient's level of consciousness determined whether the patient received passive range of motion, progressive resistance exercises, and/or physical therapy.

Patients were scheduled to receive three sessions per day and consciousness was assessed at the beginning of each session. Consciousness was defined based on five different commands: “Open (close) your eyes”, “Look at me”, “Open your mouth and put out your tongue”, “Nod your head”, and “Raise your eyebrows when I have counted up to 5”. If patients could not complete three of the five commands, they only received passive range of motion. Once they could complete three of the five commands, they received one session of passive range of motion, one session of physical therapy, and one session of progressive resistance exercises. Extubation was not a criteria for any form of activity.

Passive range of motion exercises included five repetitions of both upper and lower body joint extremities. Progressive resistance exercises targeted the muscles responsible for dorsiflexion, knee flexion and extension, hip flexion, elbow flexion and extension, and shoulder flexion. Progressive resistance exercises were initially conducted using no resistance. After patients were able to complete 3 sets of 8 repetitions using correct form, resistance was added using elastic resistance bands (TheraBands). Resistance started at 1.1 pounds of force

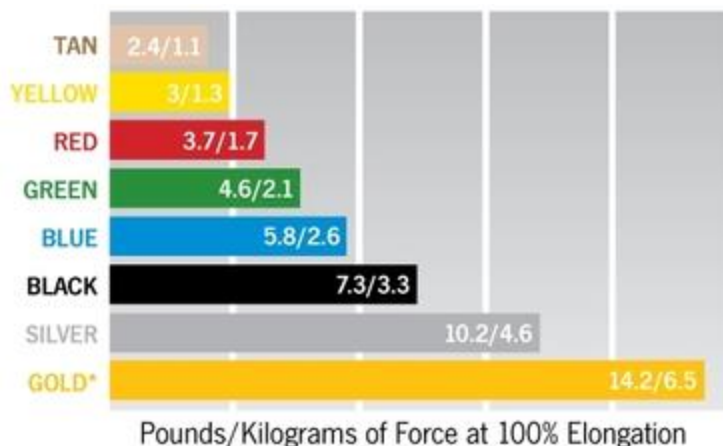


Figure 1: TheraBand Resistance Levels

when the band was stretched to 100% of its resting length. Once patients completed three sets of eight repetitions using a given color band, the resistance was increased to the next colored band. The progression of bands and force at 100 percent of elongation is shown in Figure 1.

Physical therapy included bed mobility, transfer, and balance training. Exercises required patients to transfer to the edge of their bed, and subsequently to and from their bed, a chair, or a commode. Physical therapy also included seated-balance activities, ambulation, and variations of pre-gait standing positions: forward and lateral weight shifting, and marching in place. SoC group received only received physical therapy as described above and only if ordered by the attending physician.

Physical functioning was measured using both self-report and performance-based tests. Self-report tests consisted of the functional performance inventory-short form (FPI-SF), and the physical functioning scale of the medical outcomes study short form 36-item health survey (SF-36pfs) (provided in Appendix B and C respectively). The FPI-SF consists of 32 items that are scored using 4-point scale (from activity can be performed easily to activity is no longer performed for health or other reasons). It is used to assess difficulty with physical activities across six domains which include body care (five items), maintaining the household (eight items), physical exercise (five items), recreation (five items), spiritual activities (four items), and social interaction (five items). As a disease specific measure of

physical function, the Functional Performance Inventory was developed and tested in populations of pulmonary disease patients and demonstrated construct validity and test-retest reliability in this population<sup>73,80,95</sup>. The SF-36 consists of thirty-six different questions that encompass eight different subscales: physical functioning, role-physical, bodily-pain, general health, vitality, social functioning, role-emotional, and mental health. These subscales can be combined to form two summary measures: physical health, and mental health. Total scores can fall anywhere between zero and one hundred. The SF-36 total score, as well as its two summary component scores (physical and mental health) and the physical functioning scale, have been shown to be both reliable and valid<sup>96-99</sup>. Both self-report mechanisms use higher scores to indicate greater levels of functioning.

Performance-based measures of physical function included the Short Physical Performance Battery (SPPB) (provided in Appendix D), and muscular strength as determined from a hand-held dynamometer (MicroFet 2MT Dynamometer, Hoggan Health Industries, Salt Lake City, UT). Short Physical Performance Battery scores were derived from performance on three tests: a four-meter walk, chair sit-to-stands, and a triad of balance tests. Data demonstrate that the SPPB is a reliable and valid measure of physical function and disability risk with higher scores indicating greater functioning<sup>82,83</sup>. This method of assessment has previously been used to evaluate physical function in patients with pulmonary disease<sup>100</sup>. Three trials were used to measure the muscular strength of the shoulder flexors, elbow flexors and extensors, hip flexors, knee flexors and

extensors, and ankle dorsiflexors. Patients were instructed to apply the maximum force they could for each muscle action. The tester resisted this force for 3 to 5 seconds after which time the force in pounds was read from the dynamometer. The maximum values from each muscle group were averaged to produce a single composite value of muscular strength.

### *Statistical Analysis*

Partial correlations were used to determine the level of agreement among the various measures of physical function in each group of patients at hospital discharge and 2, 4 and 6 months post discharge. Covariates included the effects of morbidity via APACHE III scores, age, and gender. Definition of correlational strength was based on that of Evans<sup>101</sup>. Very weak correlations were defined as  $r = 0.0 - 0.19$ , weak correlations were defined as  $r = 0.20 - 0.39$ , moderate correlations were defined as  $r = 0.40 - 0.59$ , strong correlations were defined as  $r = 0.60 - 0.79$ , and very strong correlations were defined as  $r = 0.80 - 1.0$ . Alpha was set at 0.05. All analyses were performed using SPSS version 22.

## **RESULTS**

Initially, 4,803 patients were screened upon entry into the ICU. Based on eligibility and willingness to participate, this narrowed the sample down to 300 patients who were randomized across the two groups.

### *Baseline Characteristics*

The characteristics of patients when randomized into the study are shown in Table III. There were no significant differences in patient characteristics between the ExP and SoC groups at baseline.

*Table III: Descriptive Statistics for Patients*

	Overall (n=300)	ExP (n=150)	SoC (n=150)
Age	56 ± 15	55 ± 17	58 ± 14
Gender *	55.3% (166)	56.0% (84)	54.7% (82)
Race ‡	77.3% (232)	76.7% (115)	78% (117)
APACHE III	76 ± 27	76 ± 26	75 ± 27
Results are presented as mean ± SD and percentages * Given in % female ‡ Given in % Caucasian			

### *Study Intervention Delivery*

Patients randomized into the ExP group were in the ICU for 1 (0-2 IQR), 3 (1-6 IQR), and 4 (2-7 IQR) days prior to the first session of passive range of motion, physical therapy, and progressive resistance exercises, respectively.

Comparatively, the SoC group was in the ICU for 7 (4-10 IRQ) days prior to the first session of physical therapy. Patients in the ExP group received passive range of motion for (mean ± SD) 87.1 ± 18.4% of the days they were

hospitalized, physical therapy for  $54.6 \pm 27.2\%$  of the days they were hospitalized, and progressive resistance exercise on  $35.7 \pm 23.0\%$  of the days they were hospitalized. The SoC group received no passive range of motion or progressive resistance exercise and only received physical therapy on  $11.7 \pm 14.5\%$  of the days they were hospitalized. In the ExP group individual patients received (mean  $\pm$  SD)  $10.6 \pm 8.3$ ,  $6.2 \pm 5.3$ , and  $4.2 \pm 4.8$  days of passive range of motion, physical therapy, and progressive resistance exercise respectively. In the SoC group, patients received  $1.6 \pm 2.3$  days of physical therapy.

#### *Variables of Primary Interest*

Mean values for self-report and performance-based measures of physical function at various time points for the two groups are shown in Table IV. Partial correlations between self-report and performance-based measures of physical function at various time points for the two groups are shown in Table V. Data for the FPI-SF was not collected at hospital discharge since these questions primarily concerned at home activities. That said, a weak, albeit significant correlation was seen between the SF-36pfs and the SPPB ( $r = 0.324$ ;  $p < 0.004$ ) at hospital discharge in the SoC group. All other correlations in the SoC and the ExP groups at hospital discharge were very weak and not significantly different from 0.0.

At 2 months, the ExP group demonstrated weak to strong correlations between all testing instruments. Specifically, significant correlations were found between

the SF-36pfs and the SPPB ( $r = 0.605$ ;  $p < 0.000$ ), the SF-36pfs and muscular strength ( $r = 0.420$ ;  $p < 0.001$ ), the FPI-SF and the SPPB ( $r = 0.537$ ;  $p < 0.001$ ), and the FPI-SF and muscular strength ( $r = 0.282$ ;  $p < 0.01$ ). The SoC group demonstrated weak to strong correlations between all testing instruments. Specifically, significant correlations were found between the SF-36pfs and SPPB ( $r = 0.468$ ;  $p < 0.001$ ), the SF-36pfs and muscular strength ( $r = 0.336$ ;  $p = 0.005$ ), the FPI-SF and SPPB ( $r = 0.641$ ;  $p < 0.001$ ), and the FPI-SF and muscular strength ( $r = 0.524$ ;  $p < 0.001$ ).

At 4 months, the ExP group demonstrated weak to moderate correlations between the majority of the testing instruments. Specifically, significant correlations between the SF-36pfs and the SPPB ( $r = 0.553$ ;  $p < 0.001$ ), the FPI-SF and the SPPB ( $r = 0.553$ ;  $p < 0.001$ ), and FPI-SF and muscular strength ( $r = 0.244$ ;  $p = 0.034$ ) were found. Non-significant correlations were found between the SF-36pfs and muscular strength ( $r = 0.207$ ;  $p = 0.072$ ). The SoC group demonstrated weak to moderate correlations between all of the testing instruments. Specifically, significant correlations between the SF-36pfs and the SPPB ( $r = 0.321$ ;  $p = 0.006$ ), the FPI-SF and the SPPB ( $r = 0.575$ ;  $p < 0.001$ ), the SF-36pfs and muscular strength ( $r = 0.346$ ;  $p = 0.003$ ) and FPI-SF and muscular strength ( $r = 0.412$ ;  $p < 0.0010$ ) were found.

At 6 months, the ExP group demonstrated weak to moderate correlations between all of the testing instruments. Specifically, significant correlations



between the SF-36pfs and the SPPB ( $r = 0.556$ ;  $p < 0.001$ ), the FPI-SF and the SPPB ( $r = 0.518$ ;  $p < 0.001$ ), the SF-36pfs and muscular strength ( $r = 0.364$ ;  $p < 0.001$ ) and FPI-SF and muscular strength ( $r = 0.351$ ;  $p = 0.002$ ) were found. The SoC group demonstrated moderate correlations between all of the testing instruments. Specifically, significant correlations between the SF-36pfs and the SPPB ( $r = 0.426$ ;  $p < 0.001$ ), the FPI-SF and the SPPB ( $r = 0.536$ ;  $p < 0.001$ ), the SF-36pfs and muscular strength ( $r = 0.532$ ;  $p < 0.001$ ) and FPI-SF and muscular strength ( $r = 0.402$ ;  $p < 0.001$ ) were found.

Table IV: Mean Values at Each Study Time Point

	Hospital Discharge			
	SPPB	MS	SF-36pfs	FPI-SF
ExP	4.9 ± 3.9	26.7 ± 13.0	41.3 ± 30.5	N/A
SoC	4.5 ± 4.1	25.5 ± 10.4	35.6 ± 29.8	N/A
	2 Months			
	SPPB	MS	SF-36pfs	FPI-SF
ExP	8.9 ± 3.3	30.8 ± 12.9	48.3 ± 31.7	2.0 ± 0.6
SoC	7.9 ± 3.7	30.7 ± 13.2	41.1 ± 30.0	2.0 ± 0.6
	4 Months			
	SPPB	MS	SF-36pfs	FPI-SF
ExP	9.0 ± 3.5	29.9 ± 14.1	53.5 ± 32.5	2.2 ± 0.6
SoC	8.1 ± 3.9	32.5 ± 13.8	45.9 ± 29.9	2.0 ± 0.6
	6 Months			
	SPPB	MS	SF-36pfs	FPI-SF
ExP	9.4 ± 3.0	33.0 ± 13.7	58.3 ± 32.4	2.3 ± 0.6
SoC	8.2 ± 3.9	34.0 ± 13.9	42.5 ± 31.0	2.0 ± 0.6
All values are presented as means ± standard deviations; SOC: Standard of Care; ExP: Exercise Program; SPPB: Short Physical Performance Battery; MS: Muscular Strength; SF-36pfs: Short Form 36 Physical Function Subscale; FPI-SF: Functional Performance Inventory Short Form				

Table V: Partial Correlations Among Outcome Measures

		Hospital Discharge		2 Months		4 Months		6 Months	
		<i>SPPB</i>	<i>MS</i>	<i>SPPB</i>	<i>MS</i>	<i>SPPB</i>	<i>MS</i>	<i>SPPB</i>	<i>MS</i>
ExP	SF-36pfs	r=0.143 p=0.188	r=0.119 p=0.276	r=0.605 p<0.001	r=0.420 p<0.001	r=0.553 p<0.001	r=0.207 p=0.072	r=0.556 p<0.001	r=0.364 p=0.001
	FPI-SF	---	---	r=0.537; p<0.001	r=0.282; p=0.010	r=0.553; p<0.001	r=0.244; p=0.034	r=0.518; p<0.001	r=0.351; p=0.002
SoC	SF-36pfs	r=0.324 p=0.004	r=-0.003 p=0.981	r=0.468 p<0.001	r=0.336 p=0.005	r=0.321 p=0.006	r=0.346 p=0.003	r=0.426 p<0.001	r=0.532 p<0.001
	FPI-SF	---	---	r=0.641 p<0.001	r=0.524 p<0.001	r=0.575 p<0.001	r=0.412 p<0.001	r=0.536 p<0.001	r=0.402 p<0.001
Partial correlations covariates include: APACHE III score, age, and gender; SOC: Standard of Care; ExP: Exercise Program; SPPB: Short Physical Performance Battery; MS: Muscular Strength; SF-36pfs: Short Form 36 Physical Function Subscale; FPI-SF: Functional Performance Inventory Short Form									

## **DISCUSSION**

Recent articles have demonstrated the importance of understanding the relationship between self-report and performance-based instruments for testing physical function<sup>102–104</sup>. In a variety of populations, these two types of instruments have been shown to represent different constructs<sup>104,105</sup>. However, this relationship has yet to be evaluated in ICU patients manifesting with ARF. It is in lieu of this literary gap that the relationships between these testing instruments in patients with ARF were examined.

Correlation coefficients between self-report and performance-based measures of physical function fell between -0.003 and 0.641. Only one of four correlations at hospital discharge was significant, indicating a weak correlation. At 2, 4, and 6 month follow-up time points, all but one correlation was significant, and the majority of these indicated a weak to moderate relationship between these self-report and performance-based measures of physical function. Additionally, the correlations at 2, 4, and 6 months of follow-up were similar between the ExP and SoC groups.

The data show that ICU patients presenting with ARF have low levels of physical function at hospital discharge and all follow-up time points, regardless of the testing instrument used. The SF-36pfs data from the current investigation demonstrates lower scores than the total SF-36 scores reported by Weberg (85.0; IQR 70.0–85.0) in a cohort of cardiac rehabilitation patients<sup>106</sup>. SPPB data

from the current investigation also indicates lower function for ARF patients than those reported by a Predicting Elderly Performance data set (mean score 8.3) in a group of older, community-dwelling adults<sup>107,108</sup>. Valpato et al. reported the mean SPPB of older adults at hospital admission for an acute medical event to be 6.0<sup>109</sup>. Interestingly, at hospital discharge, values in the present investigation were below 5.0. FPI scores in the current study were similar to those reported by Kapella (FPI total scores at baseline of 2.2) for COPD patients<sup>110</sup> and Needham for acute lung injury patients (baseline scores of 2.3)<sup>8</sup>. Overall, mean physical function scores in this study are similar to those reported for patients with similar disease etiology. They are however, lower when compared to healthy older adults and those less severely diseased. Inferentially, this means that at points of hospital discharge, or pre-rehabilitation, ARF patients have lower levels of physical function than those with different less severe pathologies.

Age may play a role in lower level of physical function reported in the current investigation. The data reported here were collected on patients with a mean age of 56 years. Using data from a cohort of ARF patients, Herridge et. al. reported that, while all patients demonstrated lower than predicted values of physical function five years post hospital discharge, younger patients, as compared to older patients, had slightly increased odds of achieving greater than 80% predicted six minute walk distance (OR = 1.46 per decade [1.04 per year]). Additionally, age significantly impacted the patient's perception of their post hospital physical function (as measured using the SF-36pfs)<sup>67</sup>.

The correlations between self-report and performance-based measures of physical function reported in the current investigation are within the range of values found in other cohorts of pulmonary disease patients<sup>112</sup>. In a cross-sectional study, Engstrom et. al. reported strong correlations ( $r = 0.61$  and  $r = 0.62$ ) between six minute walk (performance method) and St. George's Respiratory Questionnaire (disease specific self-report) and Sickness Impact Profile (generic self-report) respectively. Rueben et. al. reported a weak correlation ( $r = 0.26$ ) between the Physical Performance Test and the SF-36 in a cohort of older age participants<sup>113</sup>, while Kivinen reported a moderate correlation ( $r = 0.42$ ) between grip strength and self-reported ADL capacity in a group of patients with varying pathologies<sup>114</sup>.

Coman et. al. completed a systematic review of self-report and performance-based measures of physical function in order to describe the relationships between these measurement instruments<sup>103</sup>. Although the review includes a multitude of self-report and performance-based instruments in different populations, Coman's overall findings support the weak to moderate, yet statistically significant, correlations found at various follow-up time points throughout the current study.

The fact that only one correlation between self-report and the performance-based measures of physical function was significant at hospital discharge whereas the

majority at the subsequent follow-up periods were significant is probably due to the fact that self-report and performance-based measures represent different constructs<sup>112,113</sup>. Self-report instruments measure patient's perceptions of how well they can perform certain activities, while performance-based instruments measure what patients can do in actuality. It stands to reason that as patients are progressively removed from their ICU stay they become less sedentary and gradually increase their levels of daily physical activity. In doing so, patients not only perform and score better on performance-based measures, but also improve their level of self-efficacy towards accomplishing functional tasks. Evidence by McAuley et. al., and Mendes de Leon et. al. supports this hypothesis. In 1991, and again in 2003, data from McAuley showed that both acute and chronic bouts of exercise promote an increase in factors enhancing self-efficacy, as well as increases in patient self-efficacy in and of itself<sup>115,116</sup>. This improved self-efficacy has a marginal relationship to functional status while still being able to predict disability regardless of patient physical abilities<sup>117</sup>.

Limitations of this study can be seen in the limited follow-up time and the increased rate of dropout during this follow-up period. Future research should aim to elucidate this relationship in different populations. Further effort should also be made to identify between group differences, and potential ways in which to improve physical function in ARF patients.

The mean values reported in the current study are similar to mean self-report and performance values in those with pulmonary pathologies; however, they are lower in comparison to the elderly and patients with less debilitating pathologies. Furthermore, the weak to moderate, yet statistically significant, correlations reported in this investigation provide evidence of a relationship between these methods of testing physical function. These correlations are similar to those found throughout the literature in both clinical and nonclinical populations<sup>102,104,105</sup>. These findings suggest that self-report and performance-based measures of physical function in ARF patients surviving an ICU stay appear to assess different constructs at hospital discharge. Following recovery from an ICU stay, these measures become complementary, but do indicate different constructs continue to be assessed. As such, both methods of evaluation should be used in assessing a patient's physical function.



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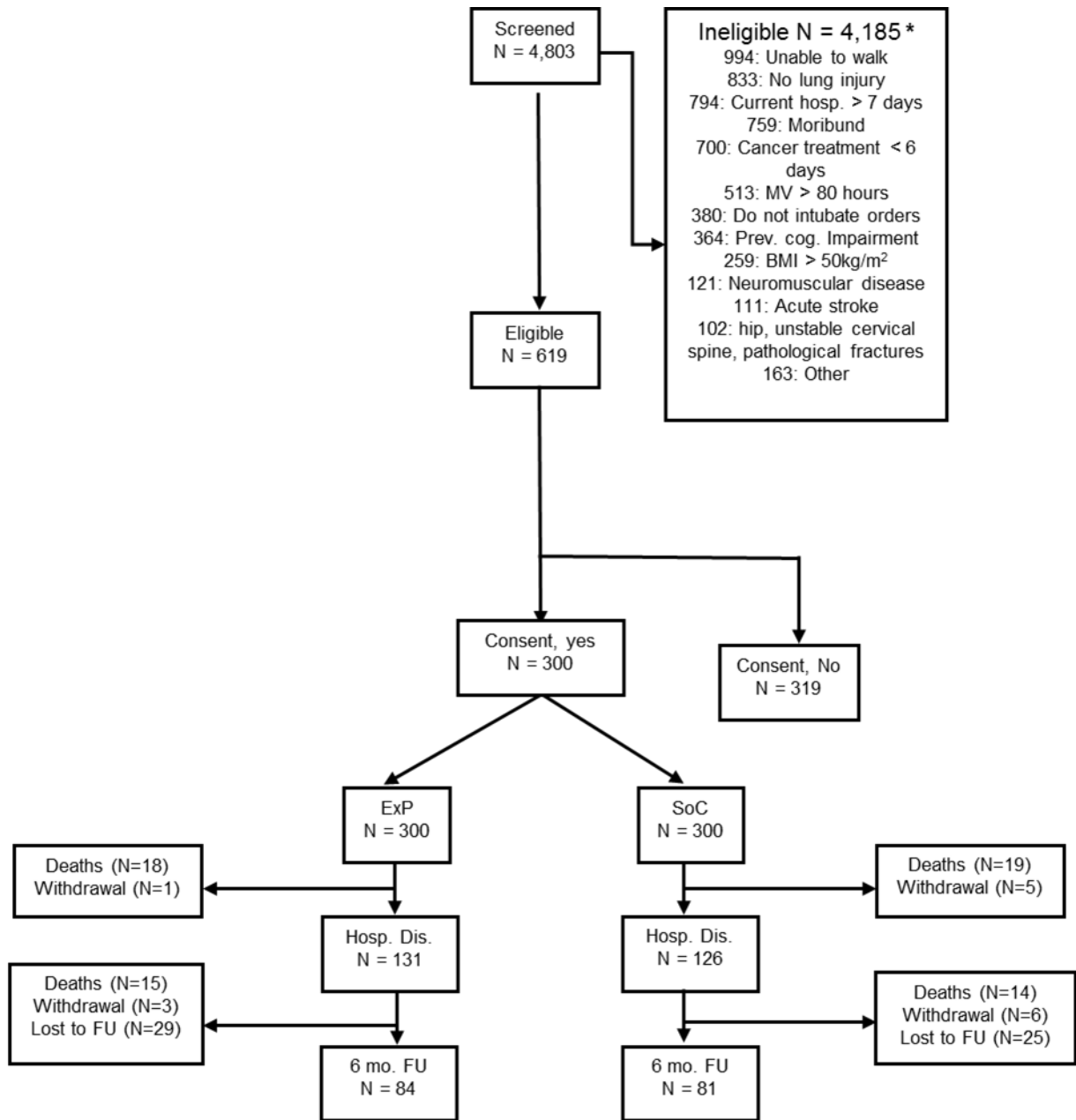
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## APPENDIX

### Appendix A: Consort Diagram



## Appendix B: Functional Performance Inventory Short Form (FPI-SF)

### TARGET FUNCTIONAL PERFORMANCE INVENTORY (FPI)

MRN

Date Completed:   /   /

Subject ID

Method of Contact:  In person  Phone

	You DO with...			You DON'T DO because..	
	No Difficulty	Some Difficulty	Much Difficulty	Health Reasons	Choose not to
<b>A. Body Care</b>					
1. Dressing and undressing	1	2	3	4	5
2. Showering or bathing	1	2	3	4	5
3. Caring for your feet	1	2	3	4	5
4. Washing your hair	1	2	3	4	5
5. Shaving or applying make-up	1	2	3	4	5
<b>B. Maintaining the Household</b>					
<i>a. Groceries and meals</i>					
1. Preparing meals/cooking	1	2	3	4	5
2. Grocery shopping	1	2	3	4	5
3. Carrying groceries	1	2	3	4	5
<i>b. Activities around the house or apartment such as:</i>					
1. Vacuuming or sweeping	1	2	3	4	5
2. Moving furniture, changing sheets, or washing windows	1	2	3	4	5
3. Cleaning bathrooms, washing floors	1	2	3	4	5
4. Mowing the lawn, shoveling the snow, raking or heavy gardening	1	2	3	4	5
5. Going to appointments (such as doctors or dentist)	1	2	3	4	5
<b>C. Physical Exercise</b>					
1. Regular stretching, moving or lifting light weights	1	2	3	4	5
2. Walking up and down a flight of stairs	1	2	3	4	5
3. Short walks around the neighborhood or mall	1	2	3	4	5
4. Long fast walk (more than 20 minutes)	1	2	3	4	5
5. Activities such as swimming or bicycling	1	2	3	4	5
<b>D. Recreation-activities for personal pleasure</b>					
<i>a. Taking vacations</i>					
1. Taking vacations	1	2	3	4	5
<i>b. Activities away from the house or apartment</i>					
1. Indoor activities such as shopping or museums	1	2	3	4	5
2. Going to the movies	1	2	3	4	5
<i>c. Activities in and around the house or apartment</i>					
1. Sitting outside	1	2	3	4	5
2. Reading	1	2	3	4	5
<b>E. Spiritual Activities</b>					
1. Attending religious services	1	2	3	4	5
2. Going to religious services	1	2	3	4	5
3. Personal reading, meditation, or prayer	1	2	3	4	5
4. Visits from spiritual friends or teachers	1	2	3	4	5
<b>F. Social Interaction-family and friends</b>					
<i>a. Dinner, cards, bingo or other activities</i>					
1. In your home	1	2	3	4	5
2. Places other than your home	1	2	3	4	5
<i>b. Helping family or friends</i>					
1. Going to the store, giving rides, doing repairs or other favors	1	2	3	4	5
2. Helping in the care of children	1	2	3	4	5
3. Distant or overnight travel to visit others	1	2	3	4	5

## Appendix C: 36-Item Medical Outcomes Survey Short Form (SF-36)

### TARGET SF-36

MRN

Date Completed:   /   /

Subject ID

1. In general, would you say your health is:

Excellent     Very good     Good     Fair     Poor

2. COMPARED TO ONE YEAR AGO, how would you rate your health in general NOW?

- MUCH BETTER than one year ago  
 Somewhat BETTER than one year ago  
 About the SAME as one year ago  
 Somewhat WORSE now than one year ago  
 MUCH WORSE now than one year ago

3. The following items are about activities you might do during a typical day. Does YOUR HEALTH NOW LIMIT YOU in these activities? If so, how much?

ACTIVITIES	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Lifting or carrying groceries?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Climbing several flights of stairs?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Climbing one flight of stairs?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Bending, kneeling or stooping?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Walking more than a mile?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Walking several blocks?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Walking one block?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. Bathing or dressing yourself?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. During the PAST 4 WEEKS, have you had any of the following problems with your work or other regular activities AS A RESULT OF YOUR PHYSICAL HEALTH?

	Yes	No
a. Cut down on the amount of time you spent on work or other activities?	<input type="checkbox"/>	<input type="checkbox"/>
b. Accomplished less than you would like?	<input type="checkbox"/>	<input type="checkbox"/>
c. Were limited in the kind of work or other activities?	<input type="checkbox"/>	<input type="checkbox"/>
d. Had difficulty performing the work or other activities (for example it took extra effort)?	<input type="checkbox"/>	<input type="checkbox"/>

5. During the PAST 4 WEEKS, have you had any of the following problems with your work or other regular daily activities AS A RESULT OF ANY EMOTIONAL PROBLEMS (such as feeling depressed or anxious)?

	Yes	No
a. Cut down on the amount of time you spent on work or other activities?	<input type="checkbox"/>	<input type="checkbox"/>
b. Accomplished less than you would like?	<input type="checkbox"/>	<input type="checkbox"/>
c. Didn't do work or other activities as carefully as usual?	<input type="checkbox"/>	<input type="checkbox"/>

MRN

6. During the PAST 4 WEEKS, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all     Slightly     Moderately     Quite a bit     Extremely

7. How much BODILY PAIN have you had during the PAST 4 WEEKS?

None     Very mild     Mild     Moderate     Severe     Very severe

8. During the PAST 4 WEEKS, how much did PAIN interfere with your normal work (including both work outside the home and housework)?

Not at all     A little bit     Moderately     Quite a bit     Extremely

9. These questions are about how you feel and how things have been with you DURING THE PAST 4 WEEKS. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the PAST 4 WEEKS.....

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of pep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Have you been a very nervous person?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Have you felt so down in the dumps that nothing could cheer you up?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Have you felt calm and peaceful?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Did you have a lot of energy?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Have you felt downhearted and blue?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Do you feel worn out?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Have you been a happy person?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Did you feel tired?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. During the PAST 4 WEEKS, how much of the time has your PHYSICAL HEALTH or EMOTIONAL PROBLEMS interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time     Most of the time     Some of the time     A little of the time     None of the time

11. How TRUE or FALSE is EACH of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. I am as healthy as anybody I know?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. I expect my health to get worse?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. My health is excellent?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Appendix D: Short Physical Performance Battery (SPPB)

TARGET SPPB

MRN

Subject ID

Date Completed:  /  /

BALANCE TEST

A. Side-by-Side Test:

Held for 10 seconds  
 Not held for 10 seconds      Number of seconds held if less than 10 sec:  .

Not attempted  
If not attempted, why?  Tried but unable  
 Could not hold position  
 Not attempted, testor felt unsafe  
 Not attempted, patient felt unsafe  
 Patient unable to understand instructions  
 Patient Refused  
 Other,

B. Semi-Tandem Stand

Held for 10 seconds  
 Not held for 10 seconds      Number of seconds held if less than 10 sec:  .

Not attempted  
If not attempted, why?  Tried but unable  
 Could not hold position  
 Not attempted, testor felt unsafe  
 Not attempted, patient felt unsafe  
 Patient unable to understand instructions  
 Patient Refused  
 Other,

C. Tandem Stand

Held for 10 seconds  
 Held for 3.00 – 9.99 seconds      Number of seconds held:  .   
 Held for < 3.00 seconds

Not attempted  
If not attempted, why?  Tried but unable  
 Could not hold position  
 Not attempted, testor felt unsafe  
 Not attempted, patient felt unsafe  
 Patient unable to understand instructions  
 Patient Refused  
 Other,

MRN

**GAIT SPEED TEST**

**A. First Gait Speed Test**

Time for 4 meters:    .

If participant did not attempt test or failed, why?

- |   |  |
|---|--|
| <input type="checkbox"/> Tried but unable                   | <input type="checkbox"/> Patient unable to understand instructions |
| <input type="checkbox"/> Could not hold position            | <input type="checkbox"/> Patient Refused                           |
| <input type="checkbox"/> Not attempted, testor felt unsafe  | <input type="checkbox"/> Other, <input type="text"/>               |
| <input type="checkbox"/> Not attempted, patient felt unsafe |  |

Aids for first walk:

- None       Cane       Other,

**B. Second Gait Speed Test**

Time for 4 meters:    .

If participant did not attempt test or failed, why?

- |   |  |
|---|--|
| <input type="checkbox"/> Tried but unable                   | <input type="checkbox"/> Patient unable to understand instructions |
| <input type="checkbox"/> Could not hold position            | <input type="checkbox"/> Patient Refused                           |
| <input type="checkbox"/> Not attempted, testor felt unsafe  | <input type="checkbox"/> Other, <input type="text"/>               |
| <input type="checkbox"/> Not attempted, patient felt unsafe |  |

Aids for second walk:

- None       Cane       Other,

**CHAIR STAND TEST**

**Single Chair Stand Test**

Safe to stand without help:       NO       YES

- Results:  Patient stood without using arms  
 Patient used arms to stand  
 Test not completed

If not attempted/completed, why?

- |   |  |
|---|--|
| <input type="checkbox"/> Tried but unable                   | <input type="checkbox"/> Patient unable to understand instructions |
| <input type="checkbox"/> Could not hold position            | <input type="checkbox"/> Patient Refused                           |
| <input type="checkbox"/> Not attempted, testor felt unsafe  | <input type="checkbox"/> Other, <input type="text"/>               |
| <input type="checkbox"/> Not attempted, patient felt unsafe |  |

**Repeated Chair Stand Test**

Safe to stand five times:       NO       YES

If five stands done successfully, record time in seconds:    .

If participant did not attempt test or failed, why?

- |   |  |
|---|--|
| <input type="checkbox"/> Tried but unable                   | <input type="checkbox"/> Patient unable to understand instructions |
| <input type="checkbox"/> Could not hold position            | <input type="checkbox"/> Patient Refused                           |
| <input type="checkbox"/> Not attempted, testor felt unsafe  | <input type="checkbox"/> Other, <input type="text"/>               |
| <input type="checkbox"/> Not attempted, patient felt unsafe |  |



## CURRICULUM VITAE

Nathan James Love B.A., ACSM-CEP  
Department of Health and Exercise Science  
Wake Forest University  
Winston-Salem, NC, 27109, PO Box 7868

### *Education*

Wake Forest University, Winston-Salem, NC  
Master of Science in Health and Exercise Science ex. 2016  
Advisor: Dr. Michael Berry

Hope College, Holland, MI  
Bachelor of Arts in Exercise Science 2012  
Advisor: Dr. Mark Northuis

### *Research Interests*

Chronic disease and disability, prevention and management of chronic disease, impact of community intervention on chronic disease prevention and management, community based participatory research, health disparities, social determinants of health, patient centered care, and impacts of chronic disease on quality of life.

### *Research Experience*

Wake Forest University  
Thesis Project: *"The Relationship Between Self-Report and Performance Based Measures of Physical Function Following an Intensive Care Unit Stay."* 2016

Wake Forest Baptist Medical Center Department of Pulmonary and Critical Care  
*"Strength Testing After Nitrate Delivery (STAND) in ICU Patients"* 2015-2016  
Role: Research Assistant

Auckland University of Technology  
*"Effects of resistance training on running economy and cross-country performance"* 2013  
Role: Research Assistant

Hope College  
*"Does Caffeine Mitigate Effects of Sleep Deprivation in Endurance Performance"* 2012  
Role: Primary Investigator

Hope College  
“Cross Sectional Analysis of Multidisciplinary Weight Loss Programs: A Search for Efficacy” 2011  
Role: Research Assistant and Data Collection

Hope College  
“Does Exercise Enhance Cognitive Function and Self Efficacy in Children” 2010  
Role: Research Assistant and Data Collection

Hope College  
“Why All the New Faces: Migrant Workers in the Holland Michigan Area” 2008  
Role: Primary Investigator

### *Presentations and Appearances*

American College of Sports Medicine National Meeting  
“The Relationship Between Self-Report and Performance Based Measures of Physical Function Following an ICU Stay.” June 2016

Wake Forest University Graduate Student Research  
“The Relationship Between Self-Report and Performance Based Measures of Physical Function Following an ICU Stay.” March 2016

Wake Forest University Aging Reimagined  
“The Relationship Between Self-Report and Performance Based Measures of Physical Function Following an ICU Stay.” March 2016

American College of Sports Medicine Southeast Regional Meeting  
“The Relationship Between Self-Report and Performance Based Measures of Physical Function Following an ICU Stay.” February 2016

Hope College Celebration of Undergraduate Research  
“Does Caffeine Mitigate Effects of Sleep Deprivation in Endurance Performance” May 2012  
“Why All the New Faces: Migrant Workers in the Holland Michigan Area” May 2008

### *Teaching Experience*

Wake Forest University  
HES101: Exercise for Health 2014-Present  
Role: Graduate Student Instructor

### *Other Related Employment*

Wake Forest University Healthy Exercise and Lifestyle ProgramS (HELPS) 2014-Present  
Role: New Patient Coordinator

Wake Forest University Student-Athlete Services Role: Student-Athlete Tutor	2014-2016
Michigan State University Spartan Nutrition and Performance Program Role: Intern	2014
Fitness Together Holland Role: Personal Trainer	2013-2014
Helen DeVos Children's Hospital Healthy Weight Center Role: Pediatric Exercise Physiology Intern	2011
Hope College Frost Research Center Role: Data Collection Employee	2010
<i>Community Activities and Service</i>	
Big Brothers Big Sisters Winston-Salem Role: Big Brother	2015-Present
Open Arms Community Church Role: Volunteer	2015-Present
Wake Forest University Alternative Spring-Break Role: Veteran's Association Hospital Volunteer	2015
Wake Forest University Graduate Student Association Role: Volunteer and Community Service Chair	2014-2015
Kissenger Farm Role: Summer Program Volunteer	2014
National Collegiate Athletic Association Role: National Student Athlete Advisory Committee Representative	2011-2013
Special Olympics Michigan Role: Promoter and Volunteer	2011-2013
Special Olympics Indiana Role: Promoter and Volunteer	2011-2013
Habitat for Humanity Role: Volunteer	2010-2012

Hope College Pew Society Role: Student Participant	2010-2012
Hope College Track and Field Role: Captain	2009-2012
Hope College Phelps Scholars Program Role: Student Participant	2008-2012
Hope College Cross Country Role: Captain	2008-2011
Urban Youth Ministries Role: Tutor and Afterschool Program Counselor	2008-2009
West Midland Family Center Role: Volunteer	2004-2014